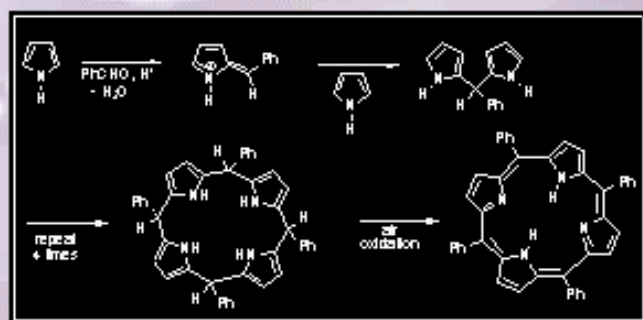


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# The comprehensive e-book of named organic reactions and their mechanisms

Elbertus Kruiswijk



2<sup>nd</sup> Edition

# Preface

The idea for this book was born in 1996 when I was doing my final undergraduate year project at the University of Utrecht. Initially, I thought that I could write this book within a year, but during my PhD I found out that there were more named organic reactions in the literature than I ever thought existed. This project was becoming more and more complicated with time.

So why a comprehensive book of named organic reactions? It is my experience that the existing books in the field only cover the 300 best-known reactions. The literature is full of named reactions. Everyone can name a reaction and of course, I did so. Please note that this book covers reaction named after a person, you will not find in this book reactions like for instance the aldol reaction. Therefore, I hope this book will cover most of the named reactions, but I know that many other named reactions are out there especially in the area of indole syntheses, see Gordon Gribble's reviews.

The emphasis of this book is to guide people in the right direction to find more information about a certain named organic reaction. The boundary between organic and inorganic is sometimes not clear. The author assumes that the reader of this book has a basic knowledge of organic chemistry at undergraduate level. An example of the reaction is given followed by a step-by-step description of how the reaction occurs and disconnection (I am aware that I use the heading mechanism even if strictly a reaction mechanism is not shown but more a reaction pathway or reaction intermediate.) The reaction is discussed briefly and references are then given. The objective of these references is where possible to first reference reactions in March's the Advanced Organic Chemistry 4<sup>th</sup> and 5<sup>th</sup> editions and then in Smith's Organic Synthesis 1<sup>st</sup> and 2<sup>nd</sup> editions. In addition, references are made to Houben – Weyl, Science of Synthesis (as far as I was able to find copies (volumes 1, 9 and 10) of this masterpiece in London, Thieme please send me a free copy of all the volumes!), Organic Reactions and Organic Syntheses (free online [www.orgsyn.org](http://www.orgsyn.org)). It must be noted that references to the standard works not always deal with the named organic reaction itself; it sometimes shows an alternative route of making similar compounds.

The literature references cover reviews, some classical and some modern articles. In addition, publications in the free online journals (Arkivoc [www.arkat-usa.org/ark/ARKIVOC/arkivoc\\_articles.asp](http://www.arkat-usa.org/ark/ARKIVOC/arkivoc_articles.asp) and Molecules [www.mdpi.org/molecules/index.htm](http://www.mdpi.org/molecules/index.htm)) are covered. I admit that some of the references are difficult to get, but I advise the readers to do a Google search and you will be surprised what you will find online and free of charge. In total there are over 7200 references and covers the literature up until first week January 2005. Finally, some space has been reserved to write down your own comments.

I have tried my best to provide as much information as possible, however the reader will discover that there are gaps in the text. This does not mean that there is no information present, it only means that I have not been able to find any information. Please contact me if you have more information about these reactions for me. I have checked over 95% of the references in this book, the reason was that I came across references in the literature that were wrong.

With the built in search or find option in Adobe Acrobat® it is easy to find an author, a particular journal or a cross reference to a named reaction. If the name of the reaction is known it is easier to use the index provided at the end of the document.

Of course, I am indebted to the following group of people who were willing to volunteer to proof read this book. In random order many thanks to Jelle Brinksma, Kiadis, Groningen, The Netherlands, Maria Hopkins, Bodmin,

United Kingdom, Derek Crockford, Imperial College London, Adam Ibrahim, University College London, Michel Meijer, Akzo Nobel, Sassenheim, The Netherlands, Howard Carless, Birkbeck College, University of London, Paul Mendonça, Imperial College London and Chris Richards and his students, Queen Mary and Westfield College, University of London. Thank you all for your time and fruitful discussions. I also thank Professor Jacob Zabicky, Ben-Gurion University, Israel for his contribution to the Dische reaction. Acros Organics for their help on the Mann dealkylation reaction and David Kelly, Cardiff University for providing me with additional information on the von Baeyer – Villiger rearrangement.

I have to thank my former employer, Birkbeck College, to give me the opportunity to write this book. Finally, I like to thank Sheryl, Samantha and Alexander without them I would have been brain dead years ago. Of course, I did spend too much time writing this book, time that could have been spent with the family.

Many thanks to Paul Heelis at Emedia publishers for his advice, patience and hard work to bring this project to a success.

Any mistakes in this book are my responsibility.

Named Organic Reactions, their Genesis will be elucidated.

This book is dedicated to past, present and future chemists.

Enjoy!

Bert Kruiswijk, Aberaman, 11-01-2005.

Contact : [namedreactions@tiscali.co.uk](mailto:namedreactions@tiscali.co.uk)

## **Forword second edition.**

I was not planning to do a second edition so soon. However, I had some time on my hands and just did it. Several new named organic reactions books have appeared on the market in the last few months. Some have much more references than this book has, but this book still covers the most named organic reactions. In this edition I have added a few more named organic reactions. I have more in the pipeline, but I am struggling to find references. I have furthermore updated some reaction schemes, added new references and made some changes in the layout and corrected typographical errors and I have added an index at the beginning of every chapter. The literature is covered until the week of 15<sup>th</sup> August 2005.

I need the support of you, the reader, to make this book, THE BOOK on named organic reactions. Any comments or additions, and queries about mechanisms are welcome, please send me an email, and I mean send me an email. References to science of synthesis are very welcome. The best method to search this book is by using the search option in Adobe Acrobat 7.

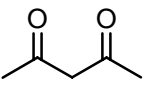
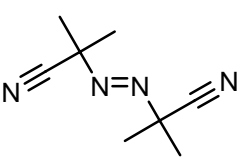
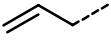
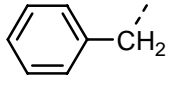
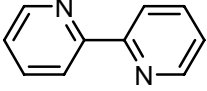
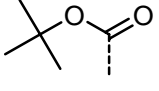
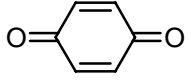
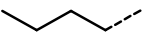
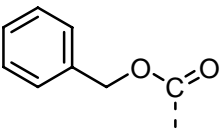
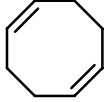

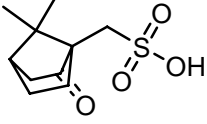
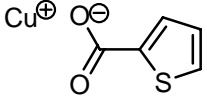
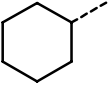
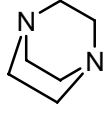
I like to thank the handful of people who bought the first edition of this book. Thank you for your support. Spread the word, but do not make any illegal copies please. This is an extremely time consuming project, that is running now for 9 years. You would be surprised what it costs to run this project. I will carry on with the work in the hope that one day every chemist has it own copy.

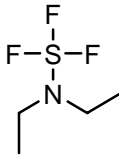
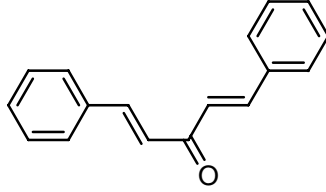
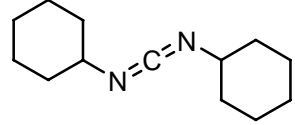
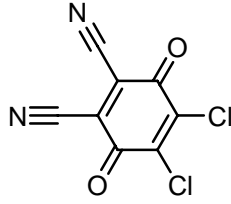
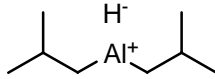
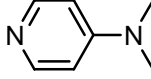
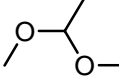
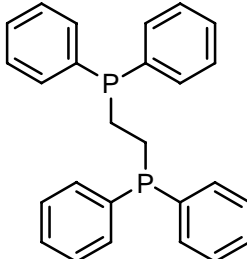
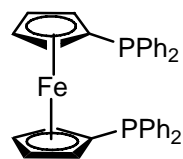
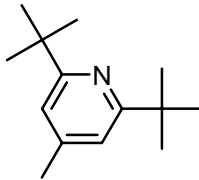
What are the future plans? First of all to expand, and I hope to incorporate a list of chemical transformations cross-referenced to the named reaction and make an index of reagents.

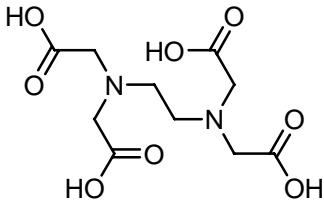
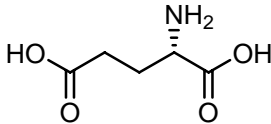
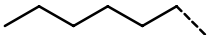
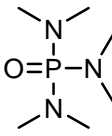
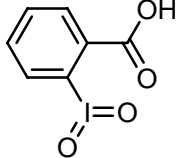
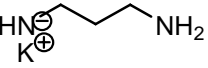
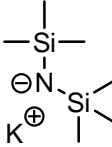
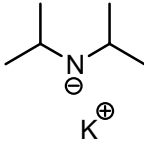
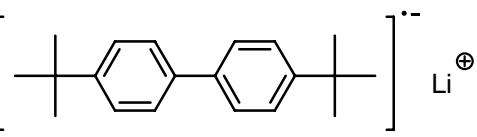
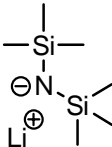
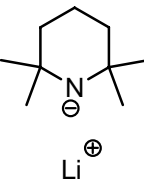
Bert Kruiswijk, Aberaman, 01-09-2005.

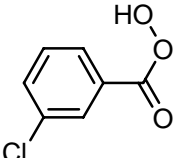
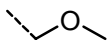
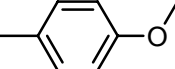
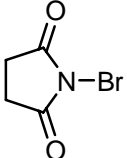
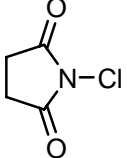
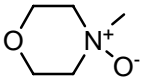
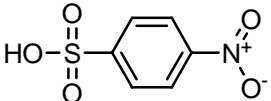
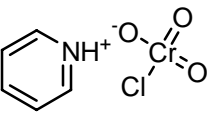
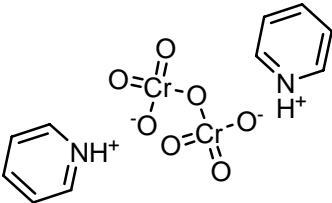
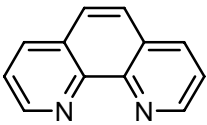
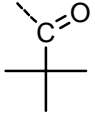
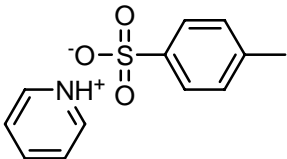



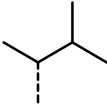
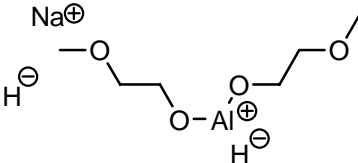
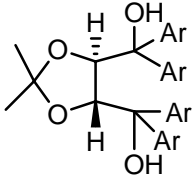
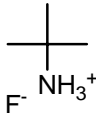
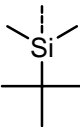
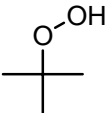
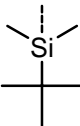
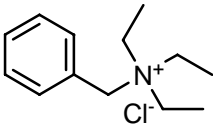
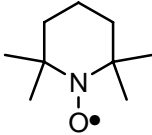
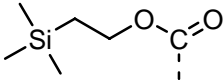
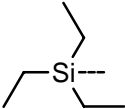
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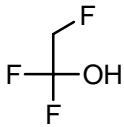
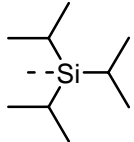

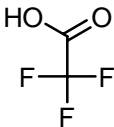
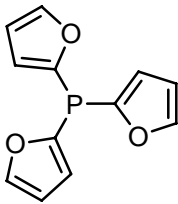
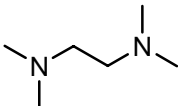
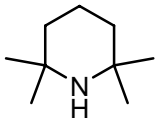

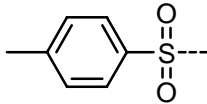
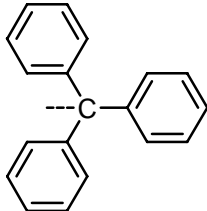
Abbreviations	Chemical name	Chemical structure
*	Chiral centre	
acac	Acetylacetonate	
AIBN	2,2'-Azobisisobutyronitrile	
Alk	Alkyl	
All	Allyl	
aq.	Aqueous	
Ar	Aryl	
Bn	Benzyl	
Bipy	Bipyridine	
Boc	<i>tert</i> -Butoxycarbonyl	
BQ	Benzoquinone	
Bu	Butyl	
Cbz	Benzyloxycarbonyl	
COD	1,5-Cyclooctadiene	
Cp	Cyclopentadienyl	
CSA	Camphorsulfonic acid	
CuTC	Copper(I) thiophene-2-carboxylate	
Cy	Cyclohexyl	
DABCO	1,4-Diazabicyclo[2.2.2]octane	

DAST	Diethylaminosulfur trifluoride	
dba	Dibenzylideneacetone	
DCC	Dicyclohexylcarbodiimide	
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone	
DIBAL	Diisobutylaluminium hydride	
DMAP	4-Dimethylaminopyridine	
DME	Dimethoxyethane	
dpe	1,2-bis(Diphenylphosphino)ethane	
DPPF	Diphenylphosphino ferrocene	
DTBMP	2,6-di-tert-butyl-4-methylpyridine	
E	Electrophile	
e <sup>-</sup>	Electron	
EDG	Electron donating group	

EDTA	Ethylenediaminetetraacetic acid	
EWG	Electron withdrawing group	
FVP	Flash vacuum pyrolysis	
L-Glu	L-Glutamic acid	
Hal	Halogen	
Hex	Hexyl	
HMPA	Hexamethylphosphoramide	
IBX	<i>o</i> -Iodoxybenzoic acid	
KAPA	Potassium 3-aminopropylamide	
KHMDS	Potassium hexamethyldisilazane	
L	Ligand	
LDA	Lithium diisopropylamine	
LG	Leaving group	
LiDBB	Lithium 4,4'-di- <i>tert</i> -butyl-biphenylide	
LiHMDS	Lithium hexamethyldisilazane	
LiTMP	Lithium 2,2,6,6-tetramethylpiperidine	

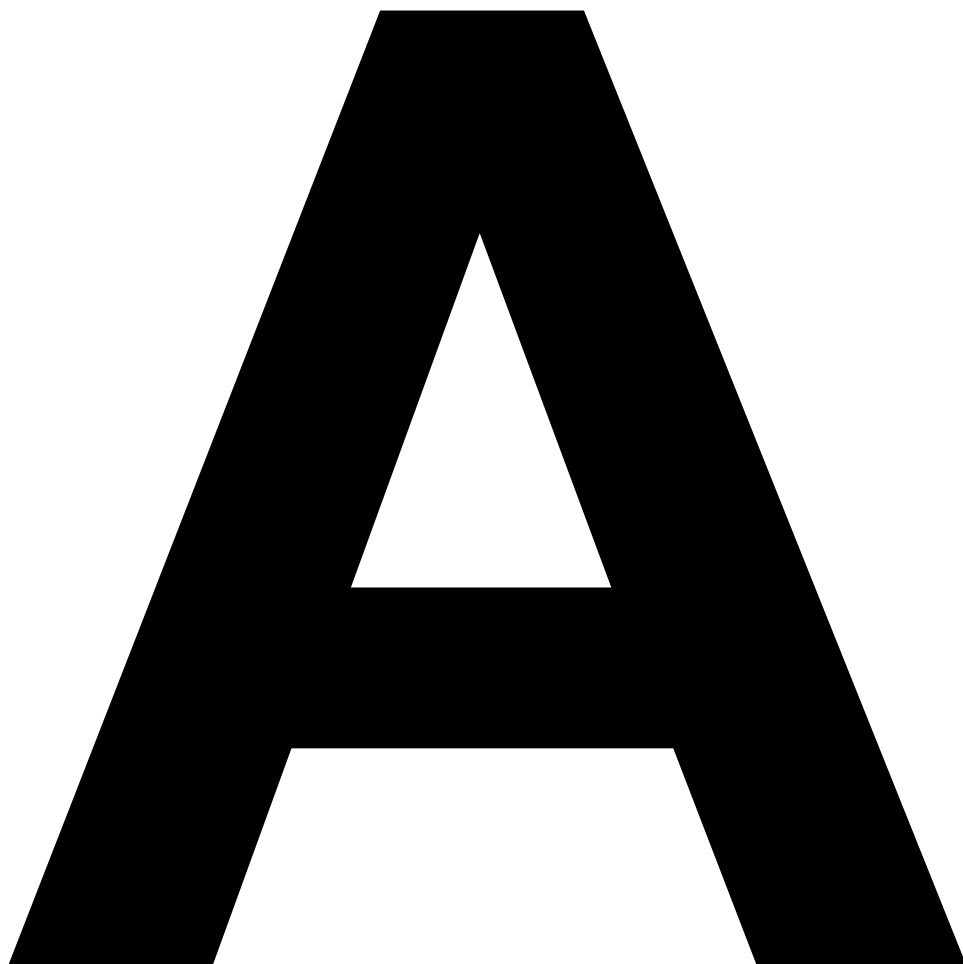
mCPBA	<i>meta</i> -Chloroperoxybenzoic acid	
MOM	Methoxymethyl	
MPM	( <i>p</i> -methoxyphenyl)methyl	
MS	Molecular Sieves	
Ms	Mesyl	
NBS	<i>N</i> -Bromosuccinimide	
NCS	<i>N</i> -Chlorosuccinimide	
NMO	<i>N</i> -Methylmorpholine oxide	
PBNSA	<i>p</i> -Nitrobenzene sulfonic acid	
PCC	Pyridinium chlorochromate	
PDC	Pyridinium dichromate	
Phen	1,10-Phenanthroline	
Piv	Pivaloyl	
PPFA	<i>N,N</i> -Dimethyl-1-[2-(diphenylphosphino)ferrocenylethylamine]	
PPTS	Pyridinium <i>p</i> -toluenesulfonate	
PMHS	Polymethylhydrosiloxane	

Pyr	Pyridine	
R <sub>f</sub>	Perfluoroalkyl chain	
R <sub>l</sub>	Large R-group	
R <sub>s</sub>	Small R-group	
RT	Room temperature	
S	Solvent	
Sia	Siameyl	
SMEAH	Sodium bis(2-methoxyethoxy)aluminium hydride	
TADDOL	α,α,α',α',-Tetraaryl-1,3-dioxolane-4,5-dimethanol	
TBAF	<i>tert</i> -Butyl ammonium fluoride	
TBDMS	<i>tert</i> -Butyldimethylsilyl	
TBHP	<i>tert</i> -Butyl hydroperoxide	
TBS	<i>tert</i> -Butyldimethylsilyl	
TEBA	Benzyltriethylammonium chloride	
TEMPO	2,2,6,6-Tetramethylpiperidinoxy, free radical	
TeoC	2-Trimethylsilylethoxycarbonyl	
TES	Triethylsilyl	

TFE	Trifluoroethanol	
TIPS	Triisopropylsilyl	
THF	Tetrahydrofuran	
TFA	Trifluoroacetic acid	
TFP	Tris(2-furyl)phosphine	
TMBG	<i>N',N'</i> -Tetramethyl- <i>N</i> -2- <i>tert</i> -butylguanidine	
TMEDA	<i>l</i> , <i>N,N',N'</i> -Tetramethylethylenediamine	
TMP	2,2,6,6-Tetramethylpiperidine	
TMS	Trimethylsilyl	
Tos/Ts	Tosyl	
Tr	Trityl	
X	Halogen	
xs	Excess	







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**A**

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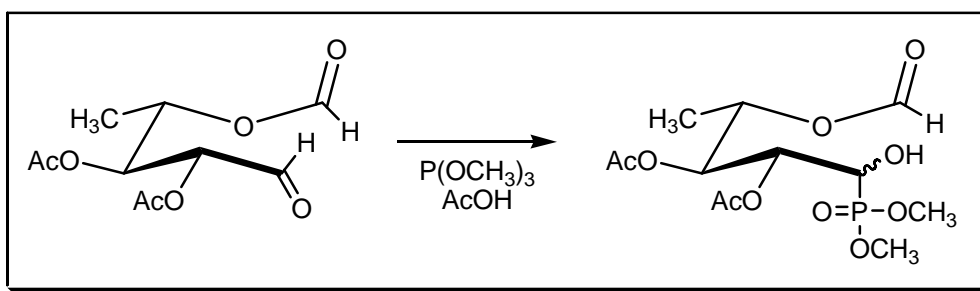
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**W**

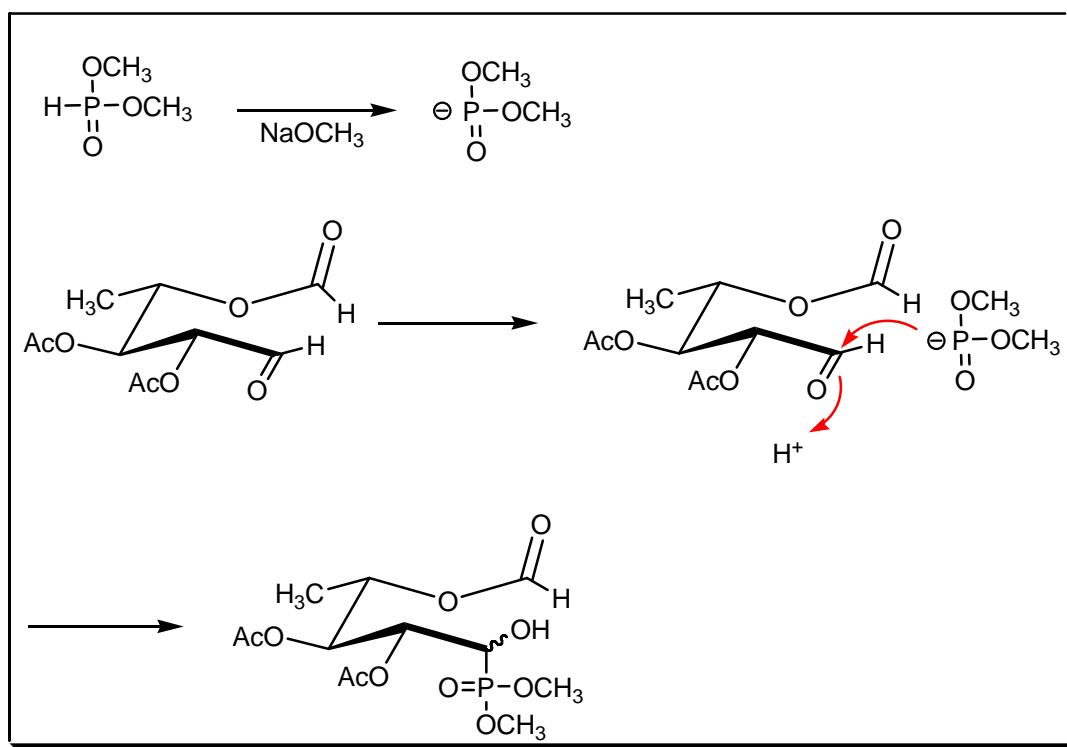
WILDS – MEADER MODIFICATION · 60

## ABRAMOV PHOSPHONYLATION REACTION

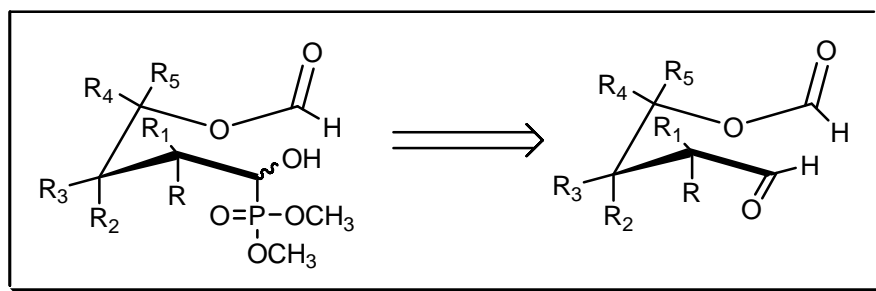
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The O-benzylated glycal is oxidatively cleaved to the aldehyde sugar bearing a formate ester at C-5. This carbon atom is originally the anomeric carbon atom. The condensation with trimethyl phosphite in glacial acetic acid or with

dimethyl phosphonate under basic conditions introduces the dimethylphosphonyl moiety. See also **Arbuzov** (**Michaelis – Arbuzov**), **Michaelis – Becker – Nylén** and **Perkow** reactions.

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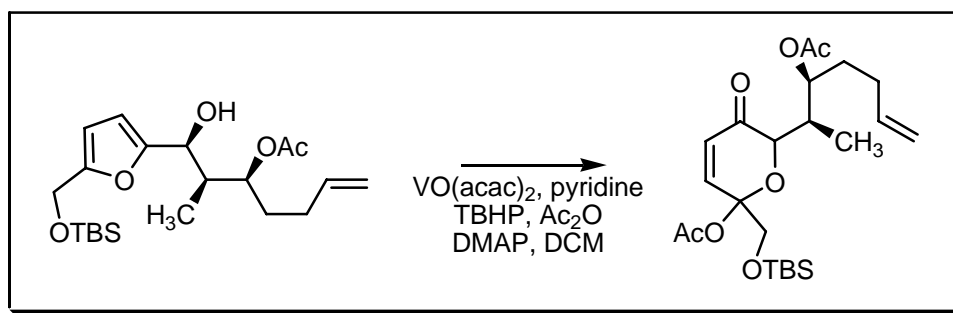
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#### COMMENTS :

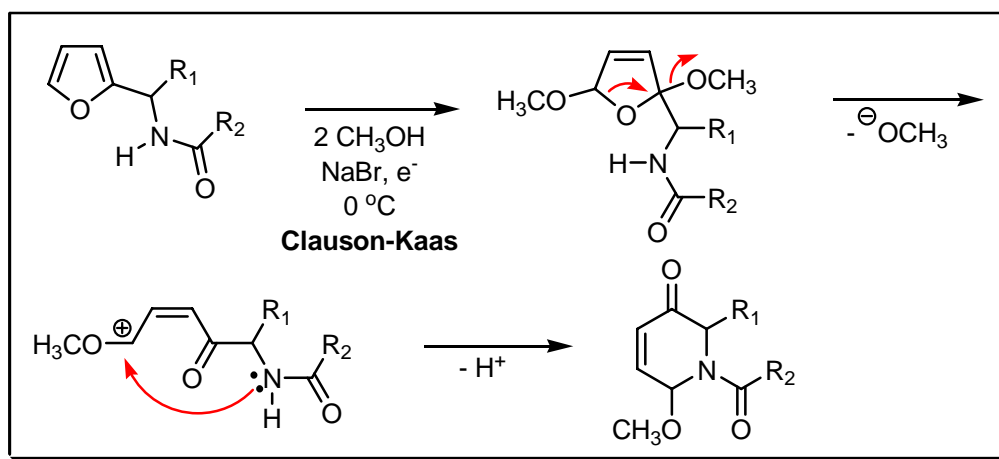
### ACHMATOWICZ PYRANONE REACTION

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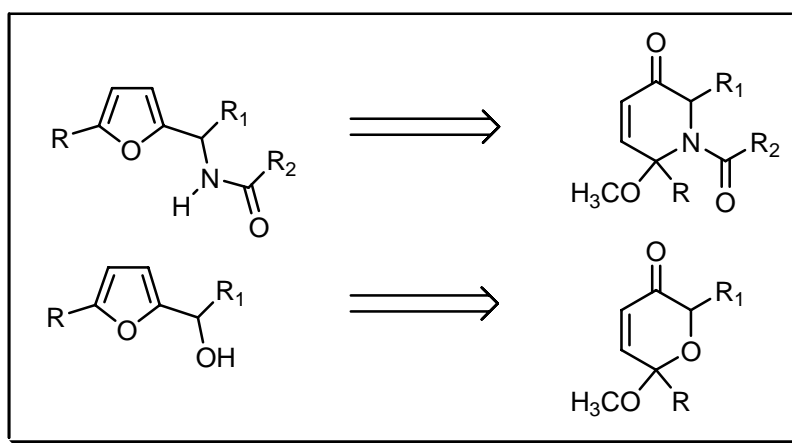
#### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of pyran-3-ones starting with furfuryl alcohols, which are first converted to dialkoxydihydrofurans by e.g. **Clauson-Kaas** electrochemical oxidation, followed by acid hydrolysis. There is also an aza-analogue known based on furylacetamides. See also **Clauson-Kaas** reaction.

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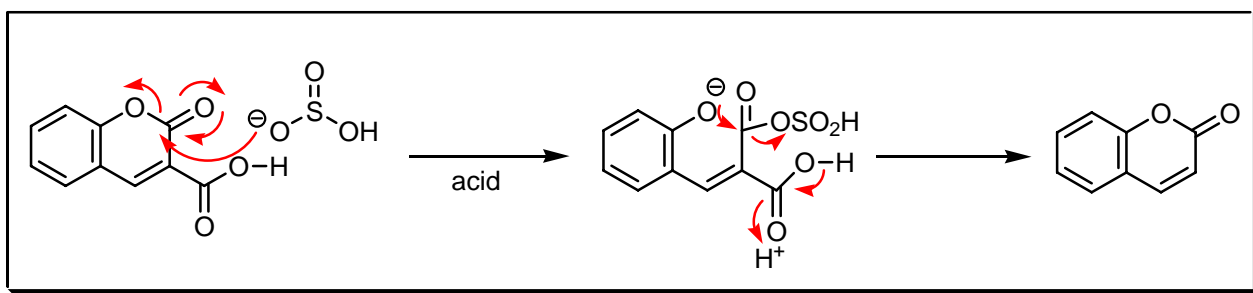
COMMENTS :

## ADAMS DECARBOXYLATION

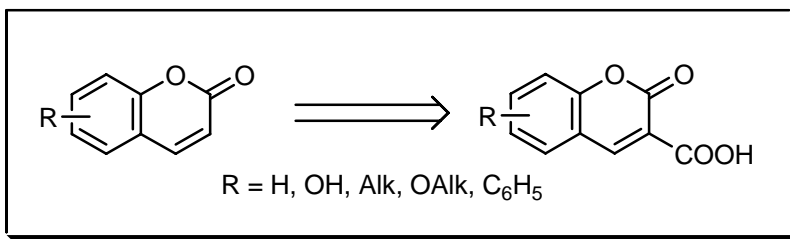
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

Coumarin acids (2-oxo-2H-chromene-3-carboxylic acid) are decarboxylated by heating with aqueous sodium hydrogensulfite followed by treatment with concentrated alkali or acid.

REFERENCES :

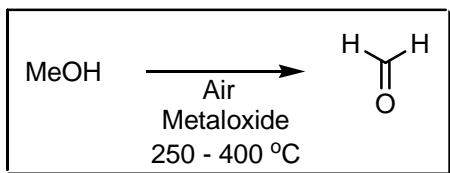
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**COMMENTS :**

## ADKINS – PETERSON FORMALDEHYDE REACTION

---

**EXAMPLE :**



**NOTES :**

An air methanol mixture, containing 5 – 8 % methanol vapour is passed over a metal oxide (Iron oxide, molybdenum oxide or iron molybdenum oxide) catalyst to afford 40% aqueous formaldehyde free of methanol.

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**REFERENCES :**

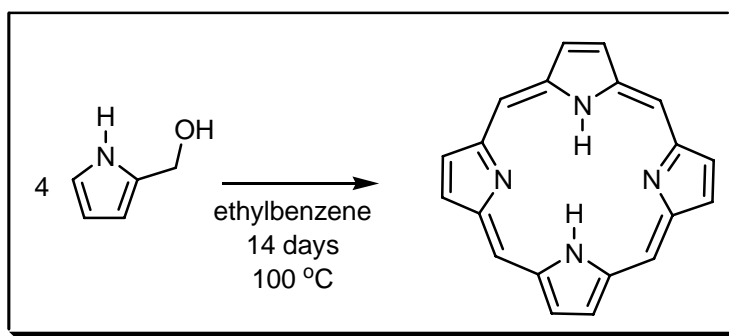
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**COMMENTS :**

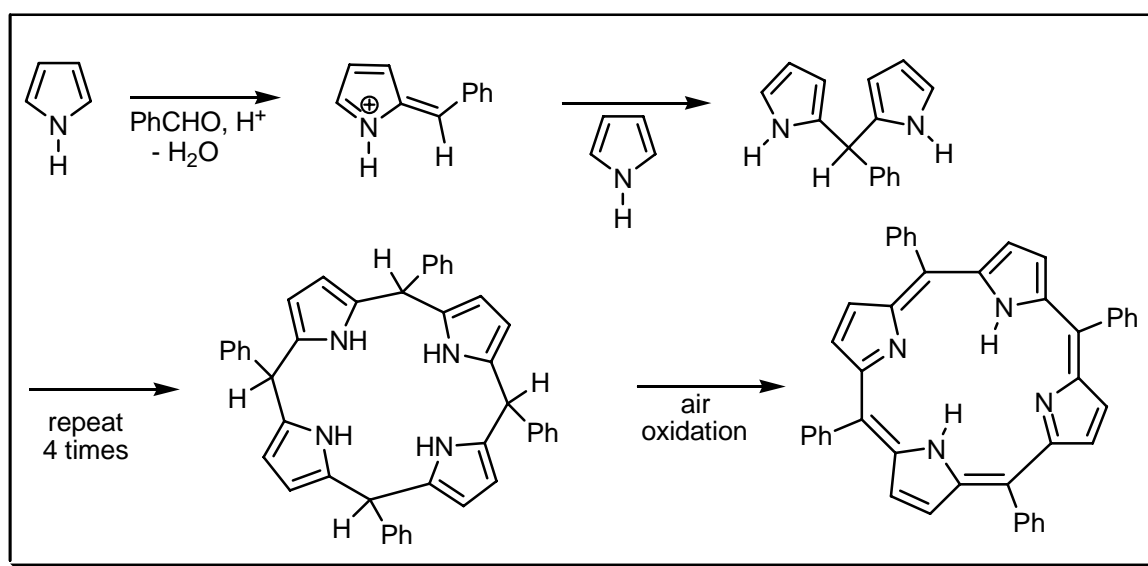


## ADLER – LONGO PORPHYRIN REACTION

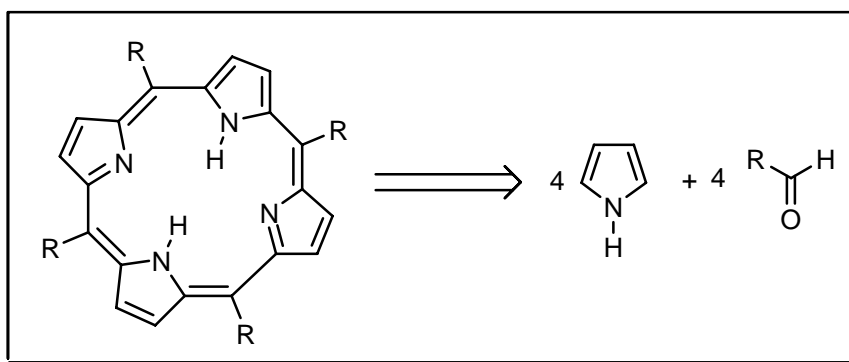
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This is a very low yielding and slow reaction for the formation of porphyrins. Several improved syntheses have been published over the years. See also **Lindsey**, **MacDonald**, **Rothmund** and **Taniguchi** reactions.

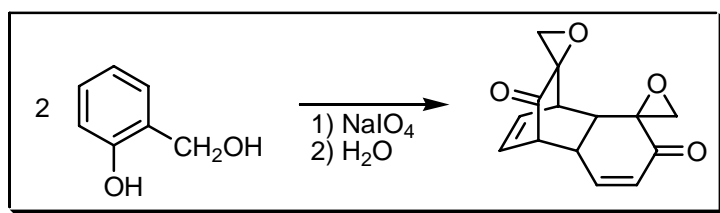
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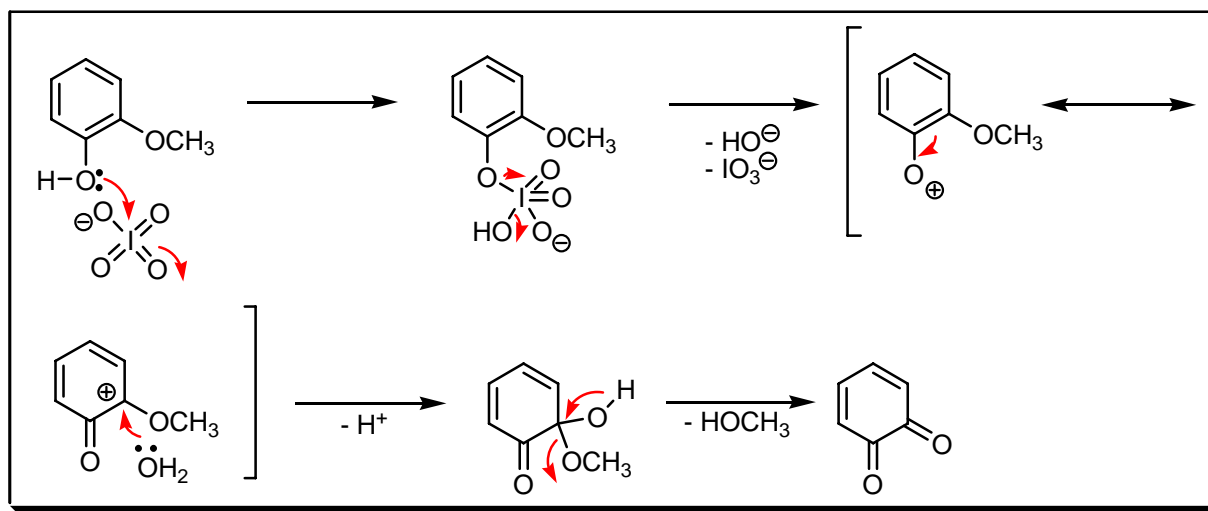
## COMMENTS :

## ADLER PHENOL OXIDATION

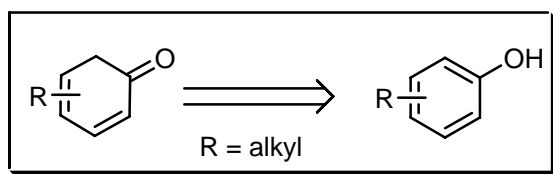
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

Sodium periodate reacts very slowly with unsubstituted phenols, however when alkyl substituents are present on the phenol the periodate is rapidly consumed and the phenolic hydroxyl is oxidised. See also **Teuber** reaction.

## REFERENCES :

**March** : 1171

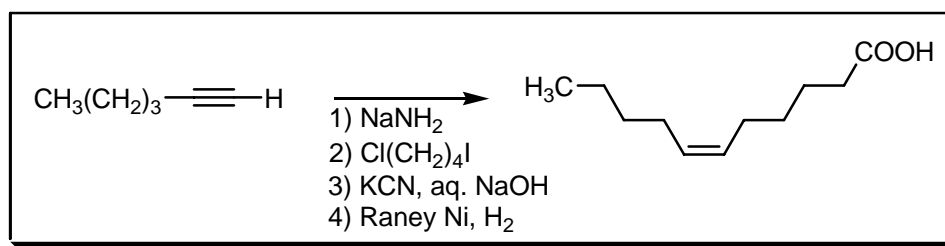
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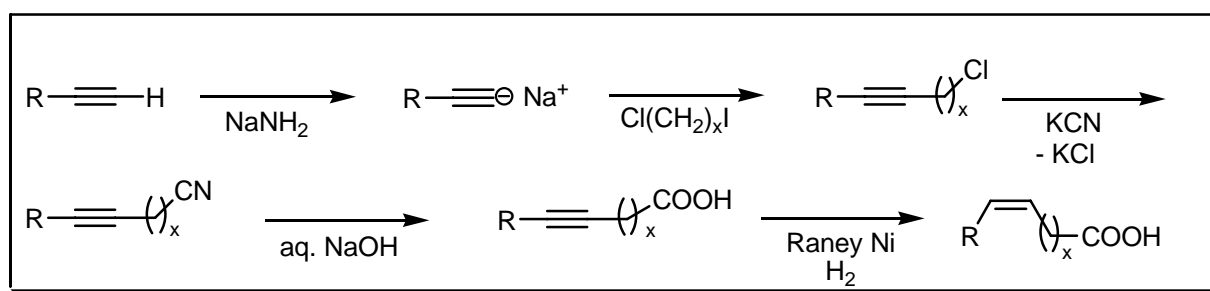
## COMMENTS :

## AHMED – STRONG SYNTHESIS

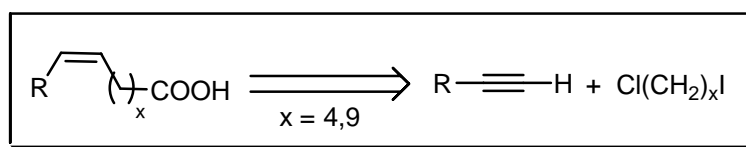
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Alkyl acetylenes react in the presence of sodamide with chloro iodo alkanes to form acetylenic chlorides. These in turn, *via* the nitrile or **Grignard** reagent, and with subsequent selective hydrogenation of the triple bond in the presence of Raney nickel are converted into mono-unsaturated fatty acids. (*cis*-form). See also **Raphael** synthesis.

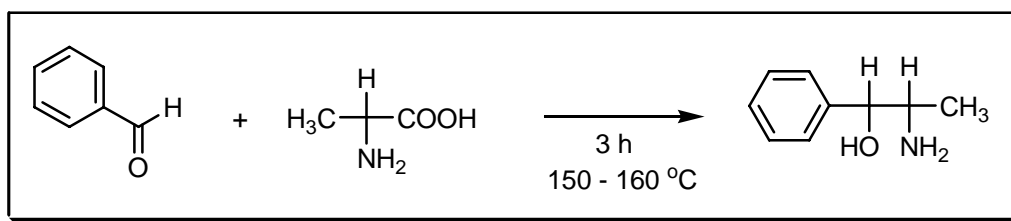
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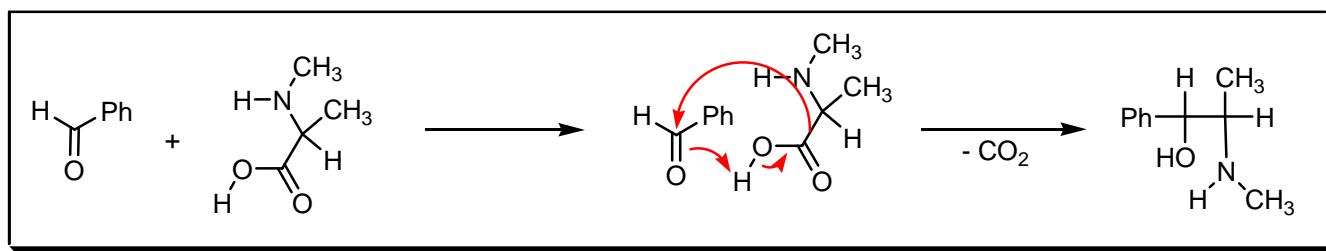
### COMMENTS :

## AKABORI – MOMOTANI AMINO ALCOHOL SYNTHESIS

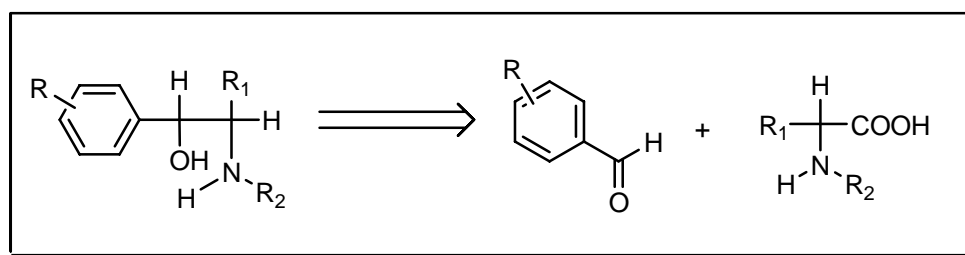
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The formation of an amino alcohol formed by an aldol-addition between an amino acid and an aromatic aldehyde. With tertiary amino groups no reaction takes place. See also **Akabori – Neuberg – Fischer** and **Erlenmeyer – Früstück** reactions.

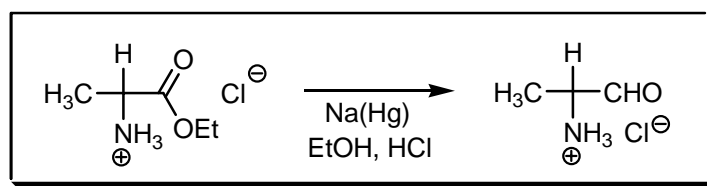
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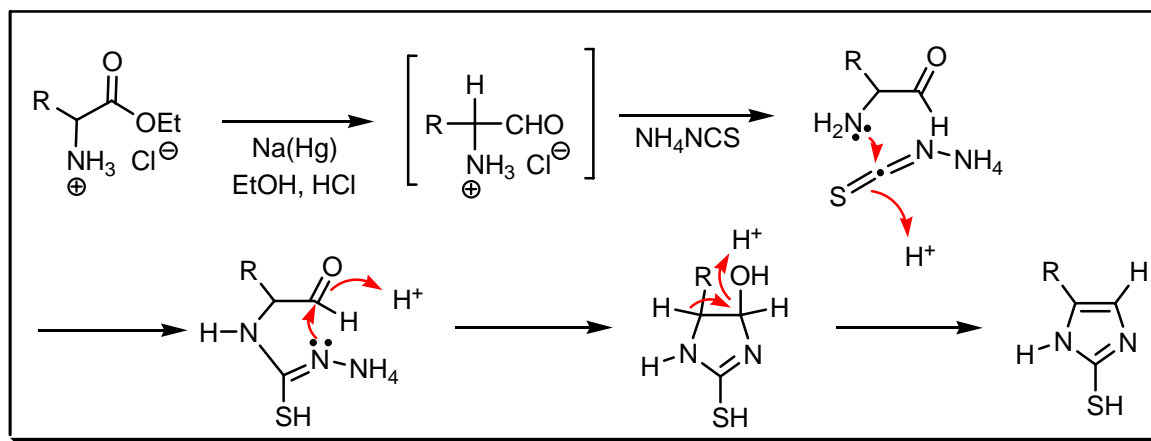
### COMMENTS :

## AKABORI – NEUBERG – FISCHER AMINO ACID REACTION

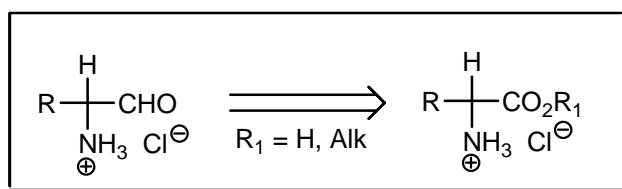
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

$\alpha$ -Amino acids and their esters are reduced by sodium amalgam and ethanolic hydrogen chloride to the corresponding  $\alpha$ -amino aldehydes. It was **Fischer**, who first discovered the reaction on carbohydrates. **Akabori** used **Neuberg's** approach to reduce the ethyl ester group to the aldehyde, followed by cyclisation to the imidazole. See also **Brackeen**, **Bredereck**, **Debus – Radziszewski**, **Maquenne**, **Wallach** and **Weidenhagen** reactions.

### REFERENCES :

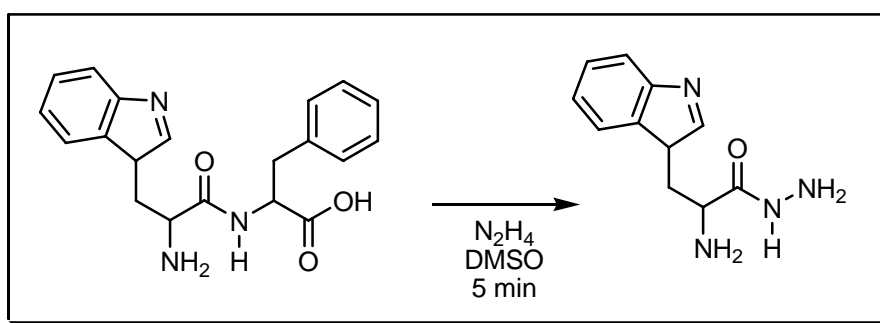
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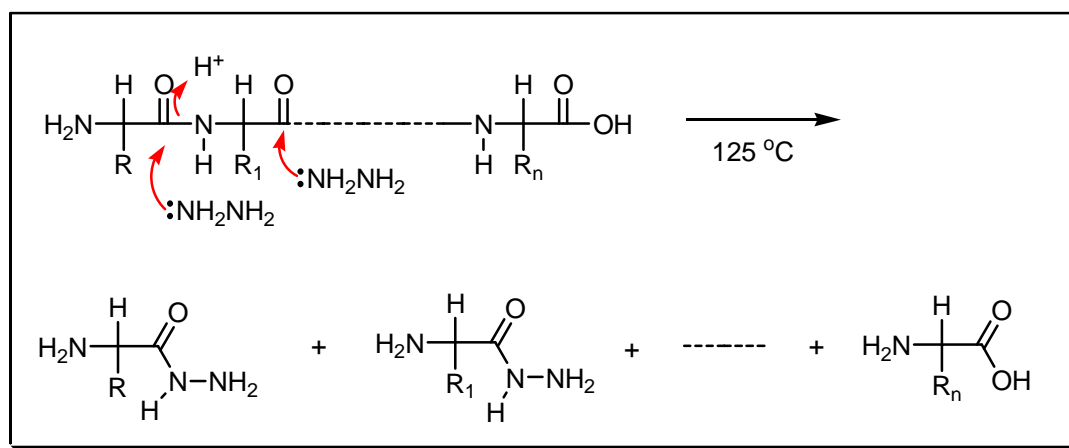
**COMMENTS :**

**AKABORI HYDRAZINOLYSIS**

**EXAMPLE :**



**MECHANISM :**



**NOTES :**

A linear peptide is heated in the presence of anhydrous hydrazine to identify the C-terminus amino acid in the polypeptide.

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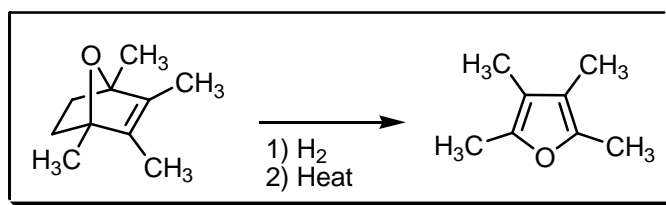


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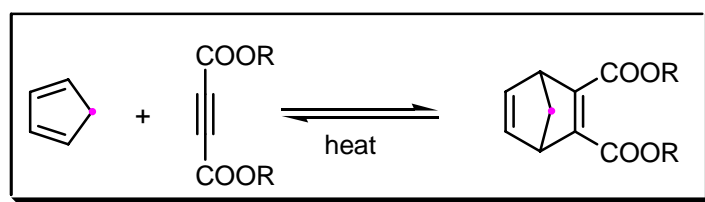
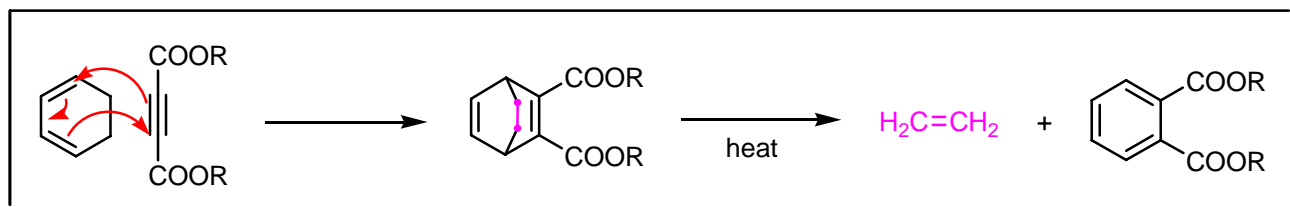
**COMMENTS :**

**ALDER – RICKERT REACTION**

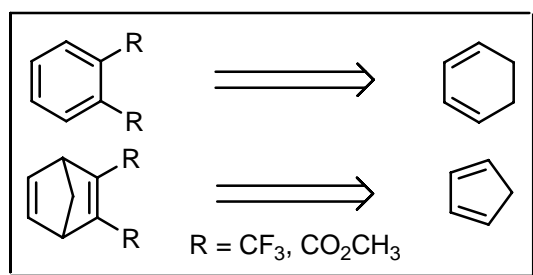
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

The cycloaddition of electron-deficient alkynes to furan or cyclopentadienes is followed by cycloreversion after selective hydrogenation at the less-hindered double bond. This is a classical method to discriminate between cyclic penta- and hexadienes. Nowadays, the reaction is widely used in the construction of polysubstituted benzenes. See also **Carboni – Lindsey** and **Diels – Alder** reactions.

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**Science of Synthesis** : 9, 222

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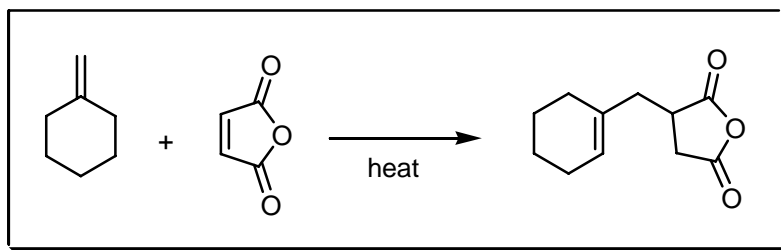
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## COMMENTS :

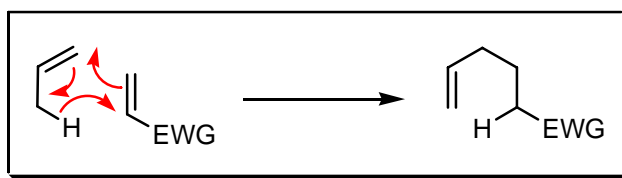
## ALDER ENE REACTION

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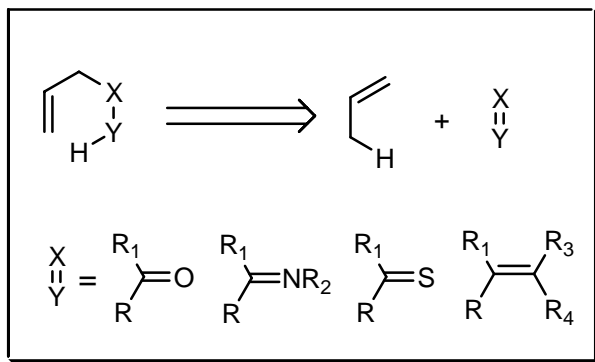
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

This is an orbital-symmetry allowed reaction, using 4-electrons from the  $\pi$ -bonds and 2-electrons from the  $\sigma$ -bond (6-electron system). It is a concerted sigmatropic reaction and can take place either *intra*- or *intermolecularly*. The thermal intermolecular ene reactions have a higher negative entropy of activation than the Diels-Alder reaction, so they require a higher temperature. Lewis acid catalysis, most through a probably step-wise mechanism, can be used for less-reactive enophiles. Several metallo-ene-type reactions have been published in the literature. The nitroso-ene reaction has been reviewed by **Adam** *et al.* If the ene reaction occurs with  $^1\text{O}_2$  than it is called the **Schenck** reaction. See also **Conia**, **Diels – Alder**, **Felkin** cyclisation and **Riley – Sharpless** reactions.

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**Smith – March** : 1021

**Smith** : 1249

**Smith 2<sup>nd</sup>** : 1030

**Org. React.** : **20**, 133

**Org. Synth.** : **31**, 85; **43**, 27; **65**, 159

**Org. Synth. Coll. Vol.** : **4**, 766; **5**, 459; **8**, 427

**Science of Synthesis** : **1**, 463

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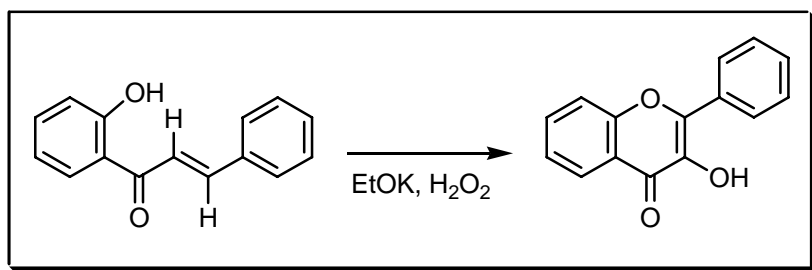
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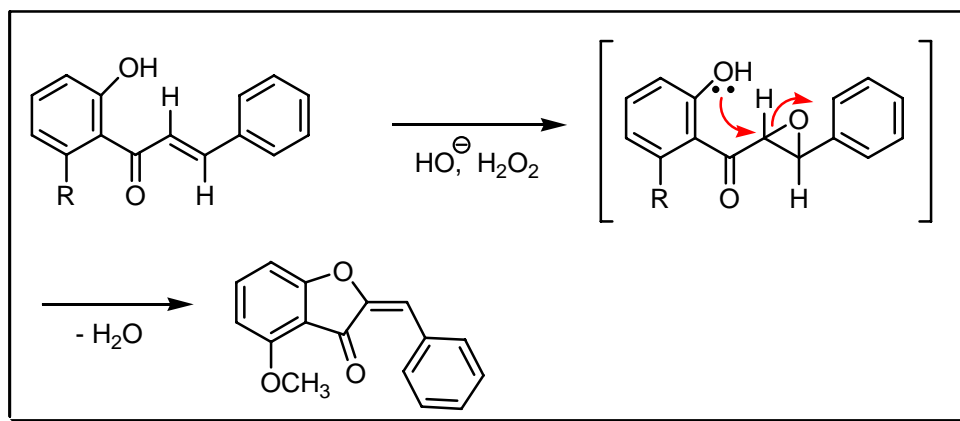
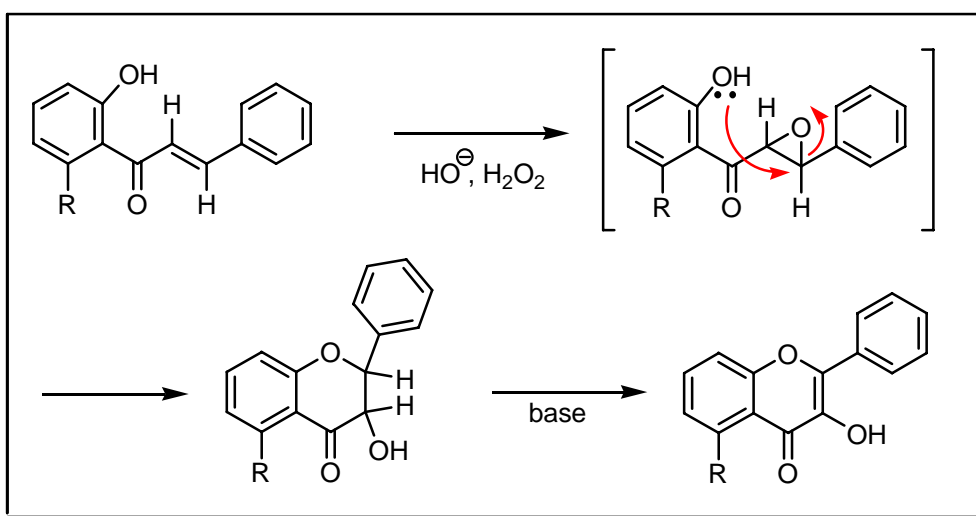
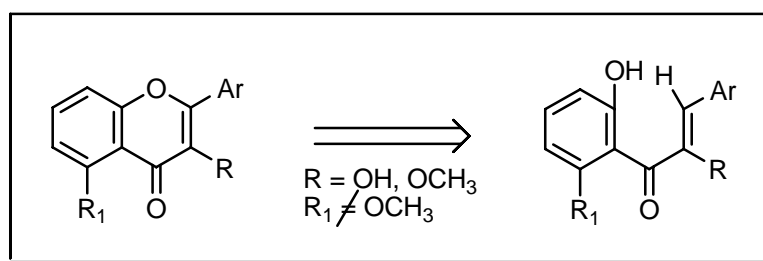
COMMENTS :

## ALGAR – FLYNN – OYAMADA FLAVANONE REACTION

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EXAMPLE :



**MECHANISM :****R = OCH<sub>3</sub>, OH :****R = anything else :****DISCONNECTION :****NOTES :**

Flavanones or *ortho*-hydroxyphenyl styryl ketones yield flavonols when treated with ethanolic alkali and hydrogen peroxide. In some cases 1-benzofuran-3-ones are formed. Dihydroflavonols and other products have also been isolated. **Burke** *et al.* has published some interesting details about the possible mechanism. The **Seshadri** modification uses methoxychalcones to afford flavonol methyl ethers. See also **Auwers** flavonol, **Baker – Ollis**, **von Kostanecki** (**Allan – Robinson**), **Ranjorwa** and **Rasoda** reactions.

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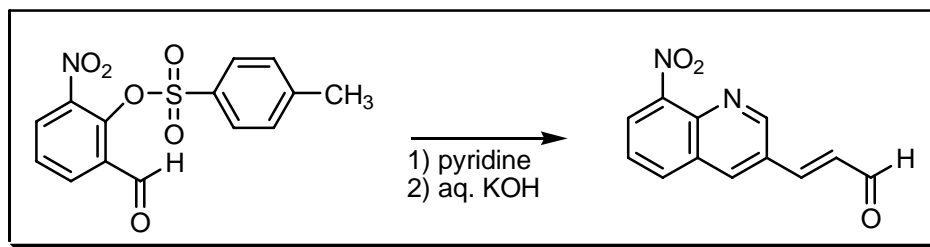
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## COMMENTS :

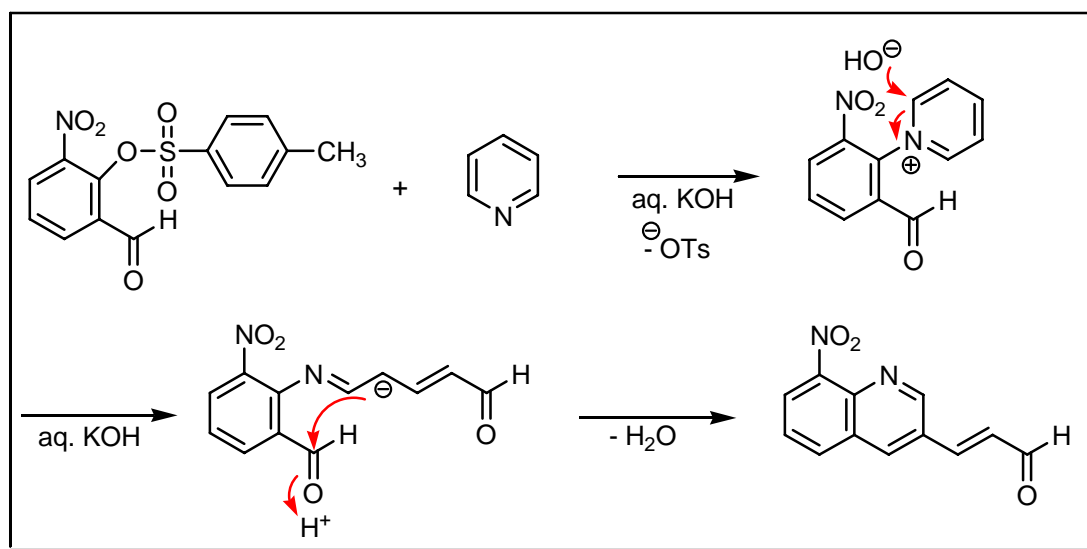
## ALLAN – LOUDON QUINOLINE SYNTHESIS

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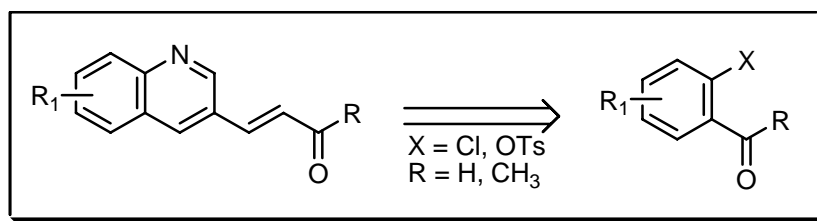
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Derivatives of benzaldehyde or benzophenone with a sufficiently mobile chloro- or toluene-*p*-sulfonyloxy- substituent in the *ortho* position react with pyridine to form pyridinium salts. The addition of alkali to aqueous solutions of these salts results in the ring-opening of the pyridinium ring, ring-closure affords 3-quinoliny-2-propenal derivatives. See also **von Baeyer – Drewson** quinoline, **Camps, Combes** quinoline, **Conrad – Limpach**, **Doebner** quinoline, **Doebner – von Miller**, **Foulds – Robinson**, **Friedländer**, **Knorr** quinoline, **Meth-Cohn**, **von Niementowski** quinoline, **Pfitzinger – Borsche**, **Riehm** quinoline and **Skraup** quinoline reactions.

### REFERENCES :

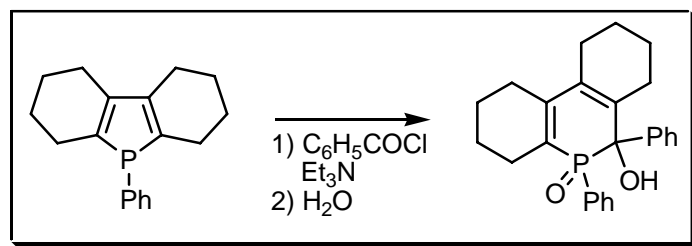
D. Allan; J.D. Loudon, *J. Chem. Soc.*, 1949, 821.

### COMMENTS :

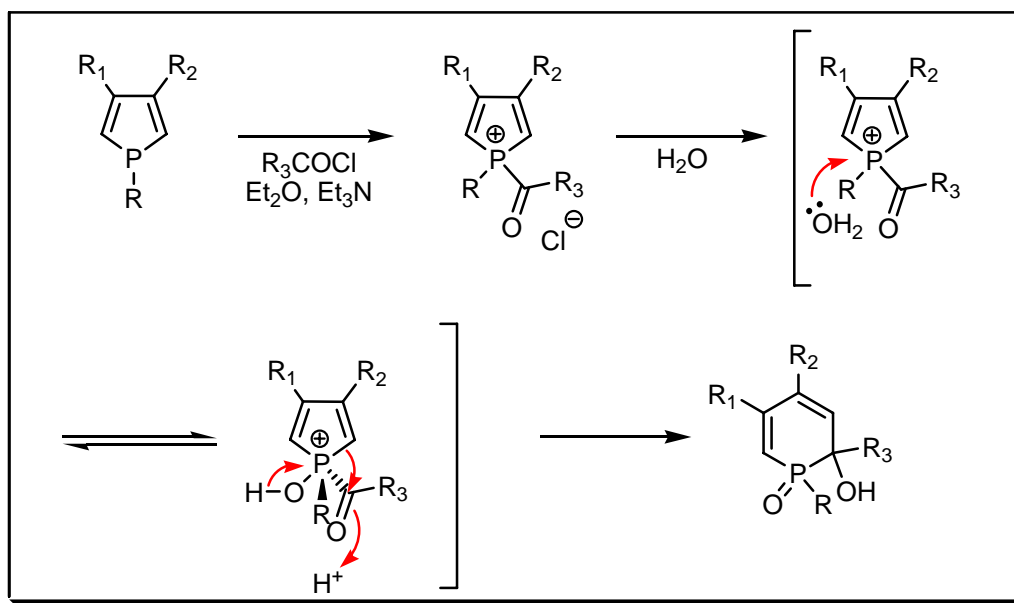
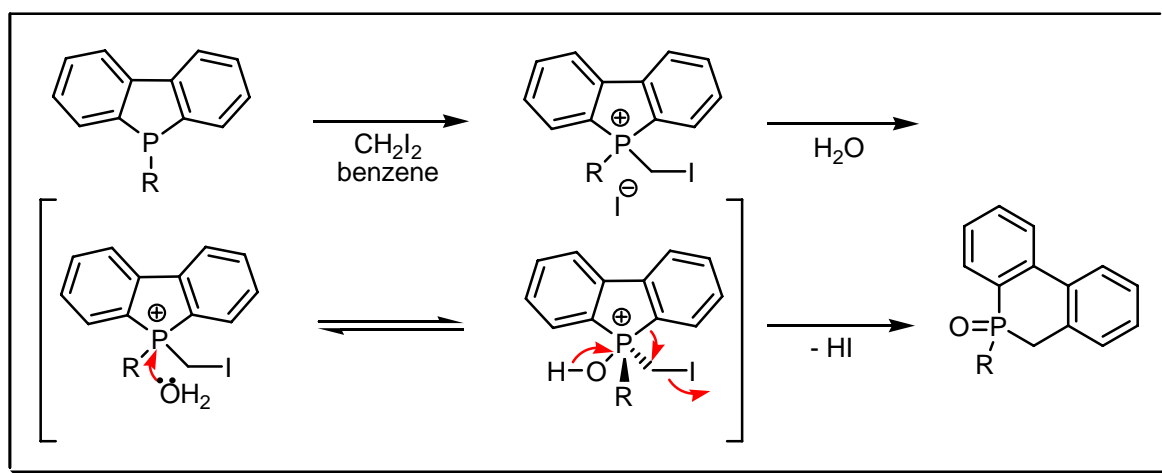


## ALLEN – MILLAR – MATHEY REARRANGEMENT

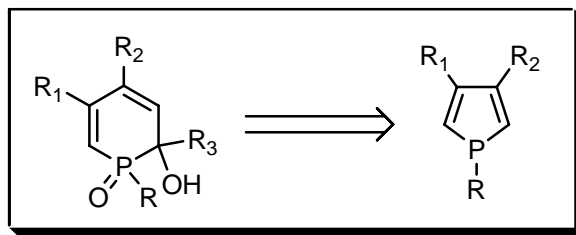
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The initial discovery was that certain cyclic phosphonium salts of e.g. 9-phosphafluorene with diiodomethane gave on hydrolysis dihydrophosphaphenanthrenes. Later, it was discovered that phosphole rings could be enlarged through their acylphosphonium salt. See also **McCormack – Kukhtin – Ramirez** phosphole synthesis.

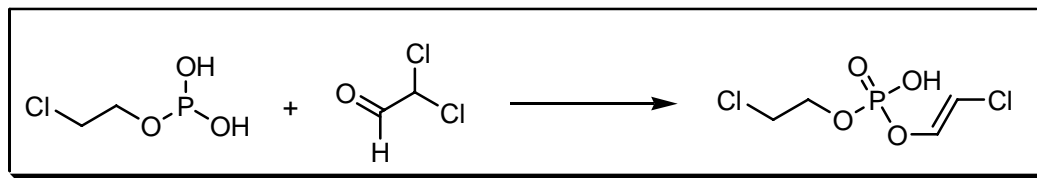
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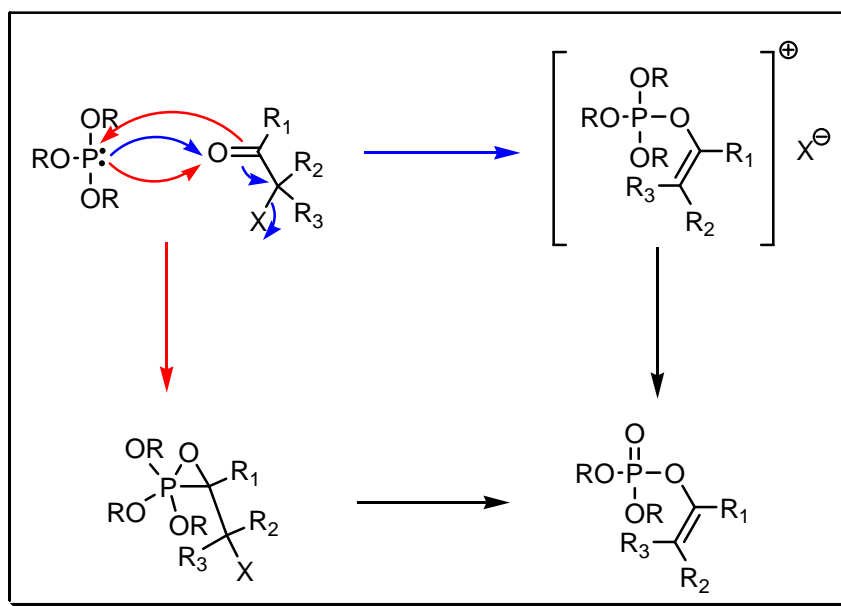
## COMMENTS :

## ALLEN REACTION

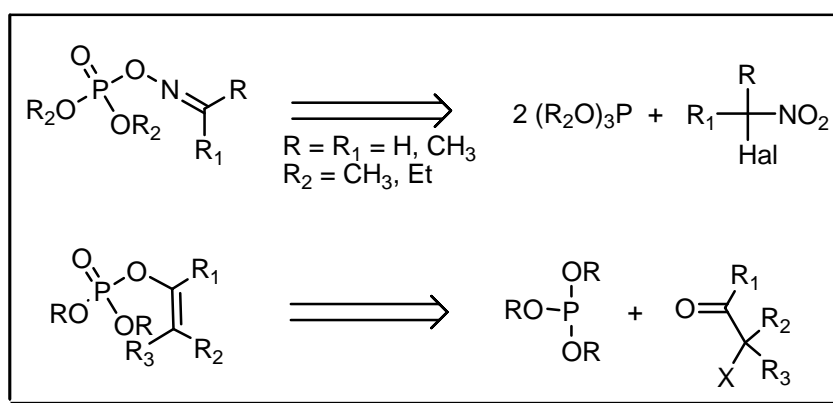
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This reaction is the synthesis of monovinyl esters of phosphorous acids. The reaction has been extended to the synthesis of oxime esters of dialkylphosphoric acid from trialkyl phosphites and α-halonitro compounds. See also **Arbuzov (Michaelis – Arbuzov)** reaction.

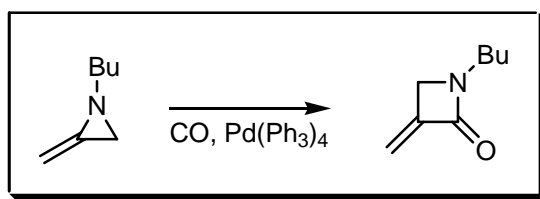
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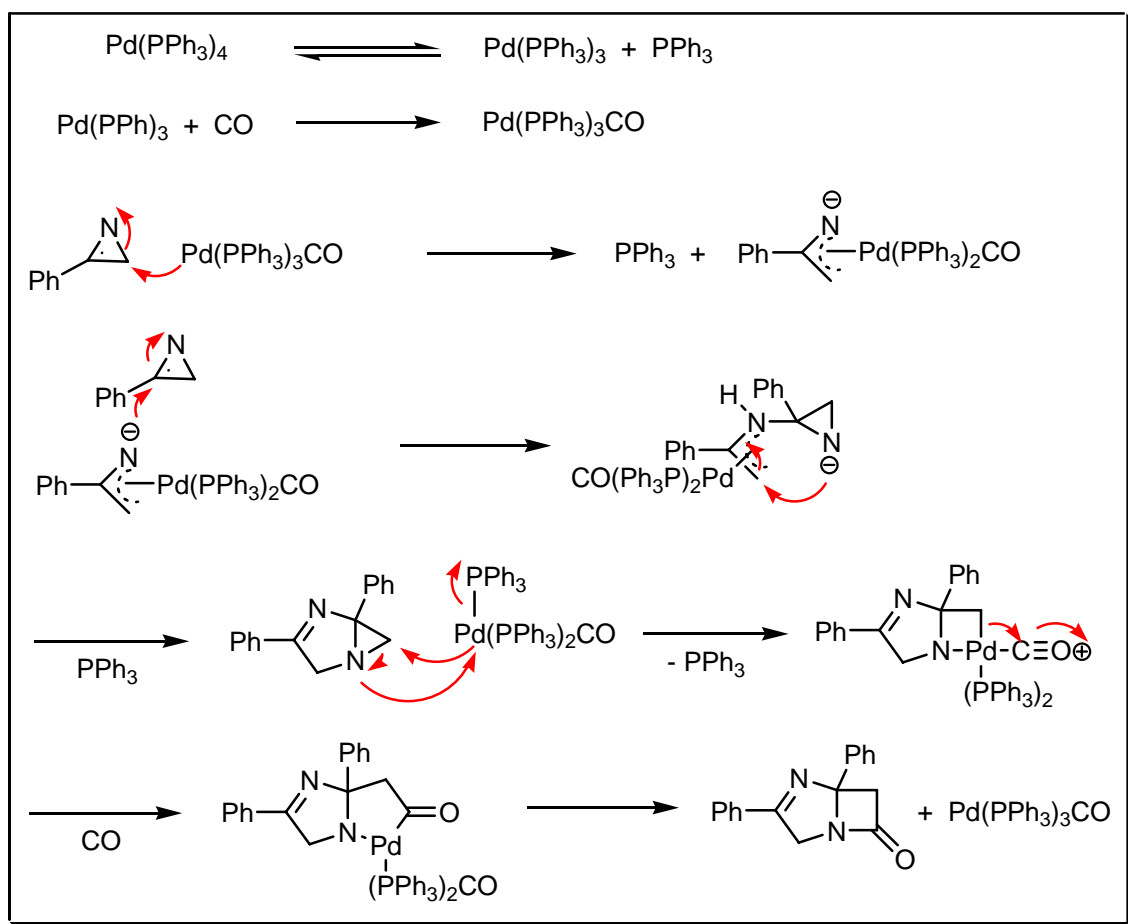
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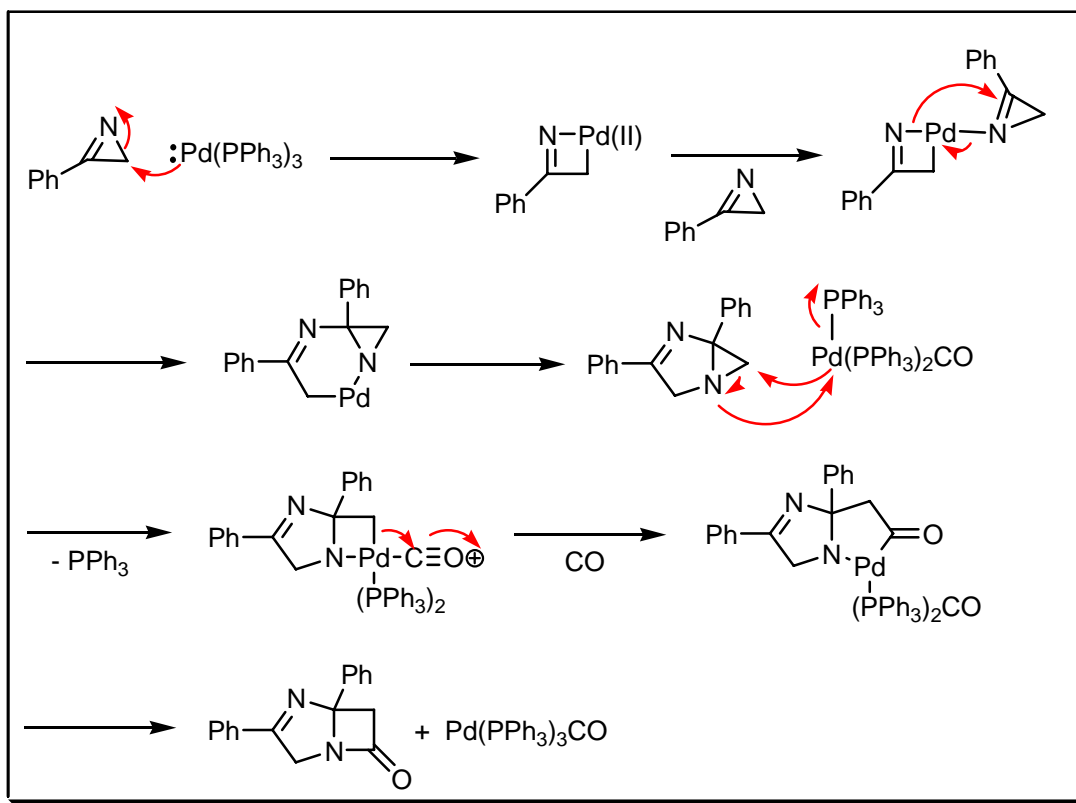
## ALPER CARBONYLATION

EXAMPLE :

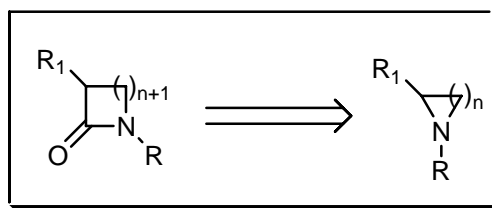


MECHANISM :





#### DISCONNECTION :



#### NOTES :

This named reaction is a collection of hydroxycarboxylation, carbonylation and hydroformylation of olefins catalysed by metal complexes (Pd, Rh or Co). There are two possible reaction mechanisms.

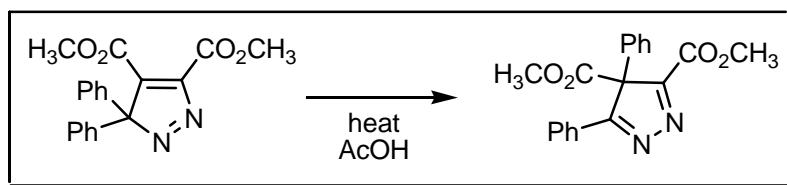
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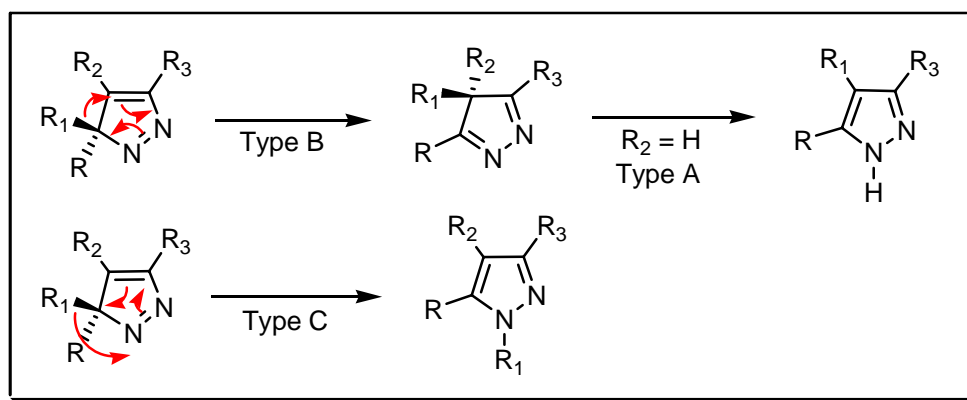
COMMENTS :

## van ALPHEN – HÜTTEL PYRAZOLE REARRANGEMENT

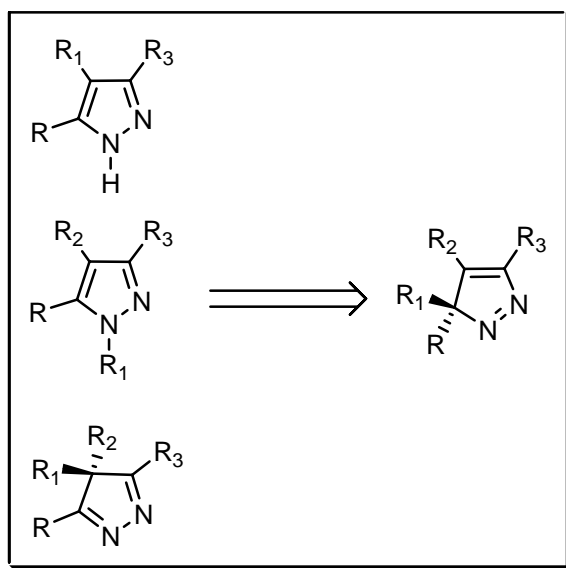
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

The formation of the three types (A, B, C) of 3*H*-pyrazoles has been accommodated in terms of competitive suprafacial [1,5]-shift by a substituent at the quaternary carbon (3-position) to carbon-4 or to the nitrogen atom. A radical pathway is most likely.

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## REFERENCES :

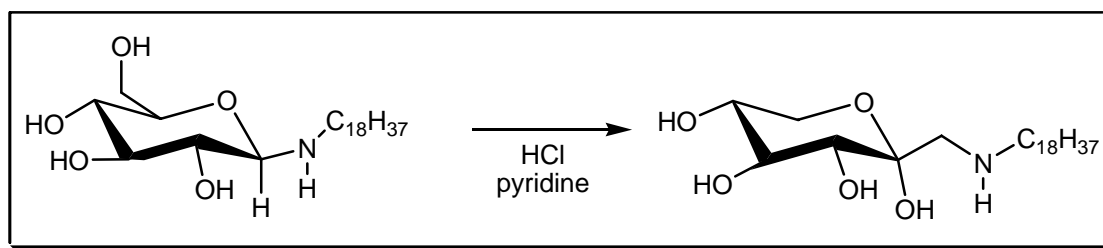
Houben – Weyl : E8b, 549, 810

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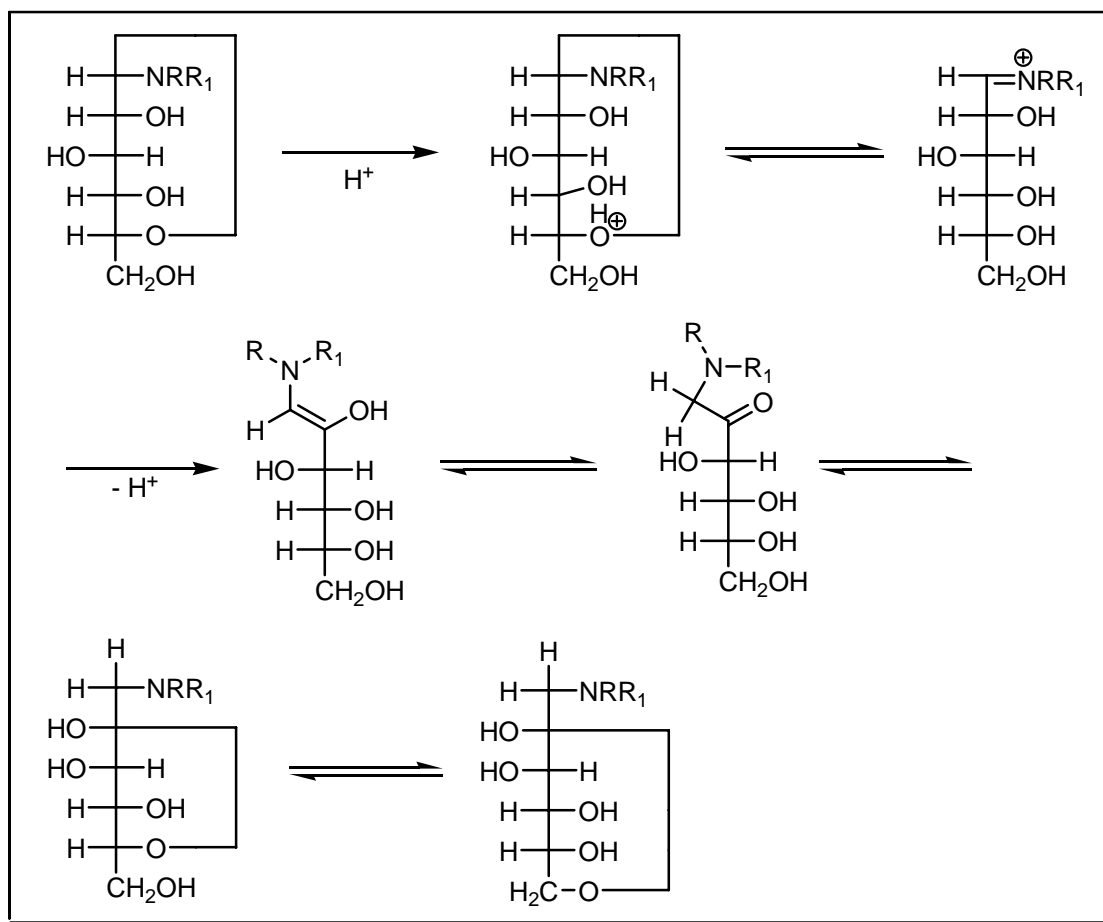
## COMMENTS :

## AMADORI REARRANGEMENT

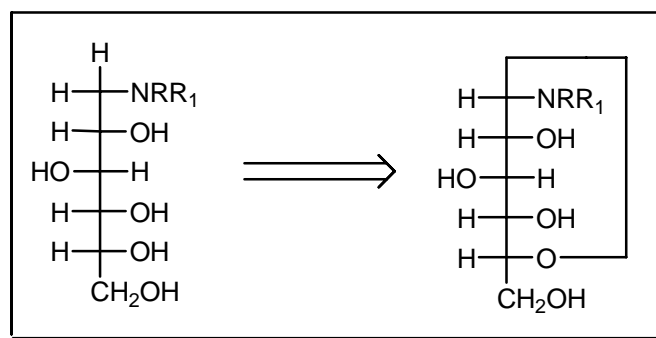
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

N-Substituted glycosylamines derived from primary aromatic amines and certain other bases give 1-deoxy-1-amino-2-ketoses slowly at room temperature or rapidly in hot ethanolic solutions in the presence of compounds containing active methylenic hydrogen atoms or in the presence of catalytic amounts of acids. A variety of Lewis acids have been employed as catalysts (CuCl<sub>2</sub>, MgCl<sub>2</sub>, SnCl<sub>4</sub>). There are two mechanisms proposed one by **Kuhn** *et al.* and one by **Michael** *et al.* The mechanism of **Kuhn** is shown here. The first few steps upto the aminoketose (**Amadori** product) are the early stages of the **Maillard** reaction. This reaction is not discussed in this book.

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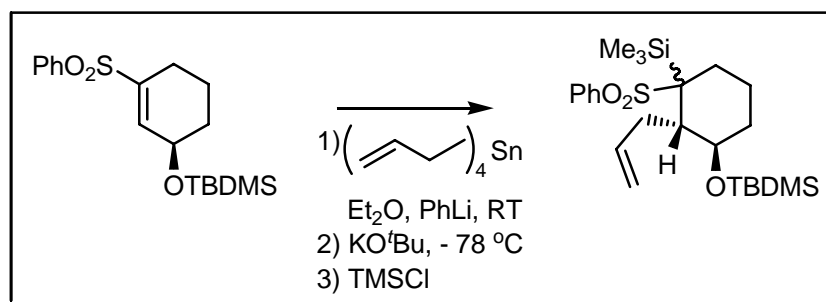
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**COMMENTS :**

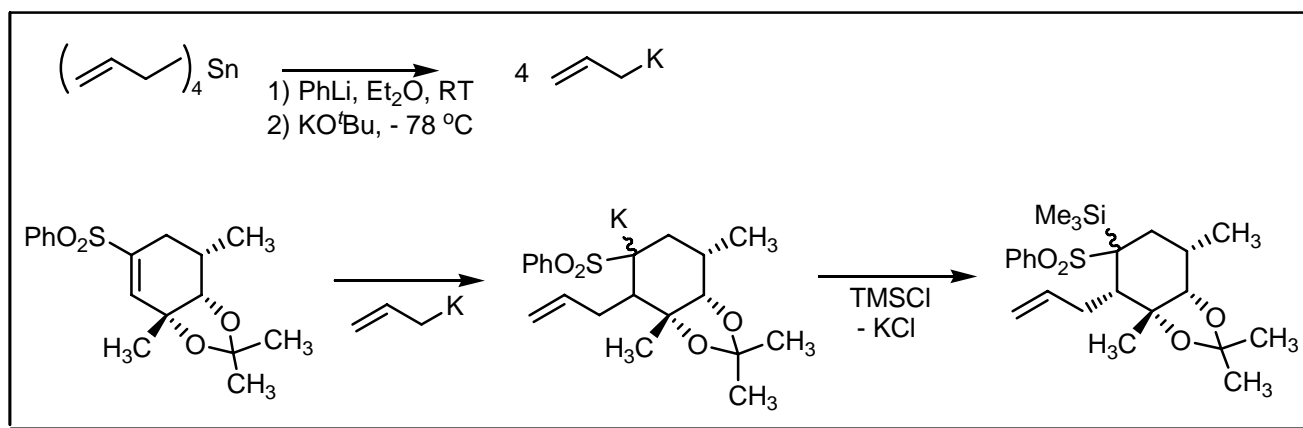
**ANDERSON – FUCHS REACTION**

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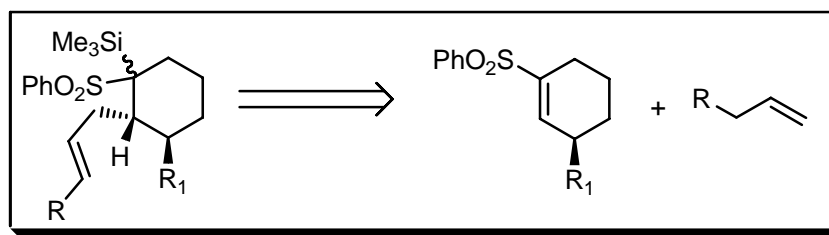
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

This reaction uses  $\alpha$ -silyl or  $\alpha$ -stannyl sulfones as latent  $\alpha$ -sulfonyl anions. After the conjugate addition of allyl potassium to vinyl sulfones followed by carbon silylation  $\alpha$ -silyl sulfones are obtained.

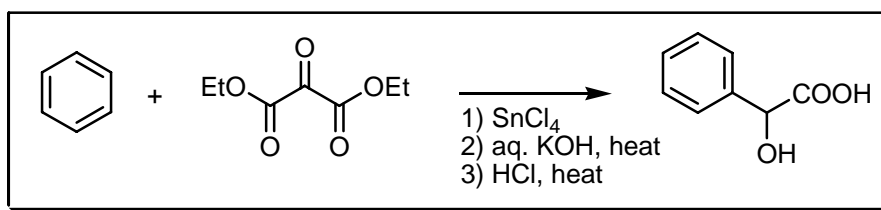
## REFERENCES :

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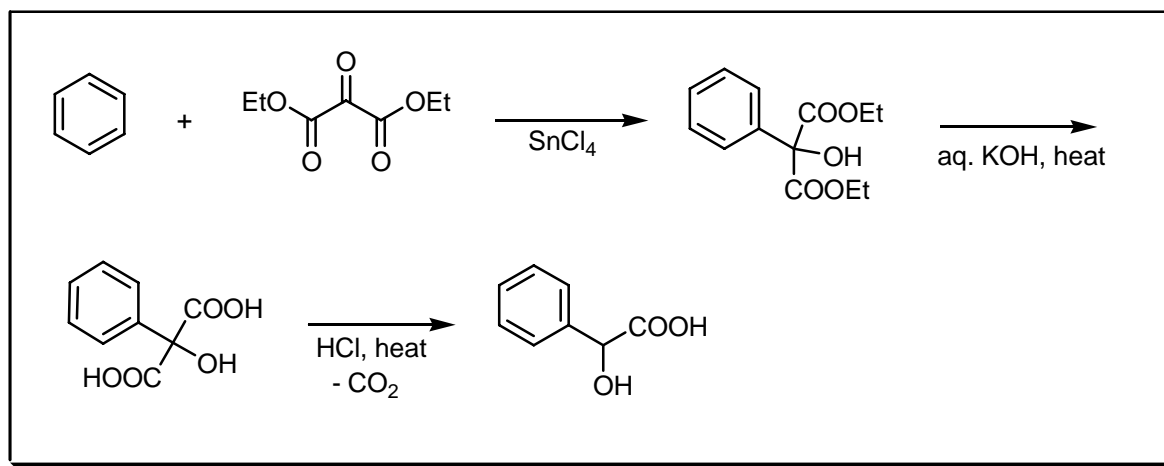
## COMMENTS :

## ANDO MANDELIC ACID SYNTHESIS

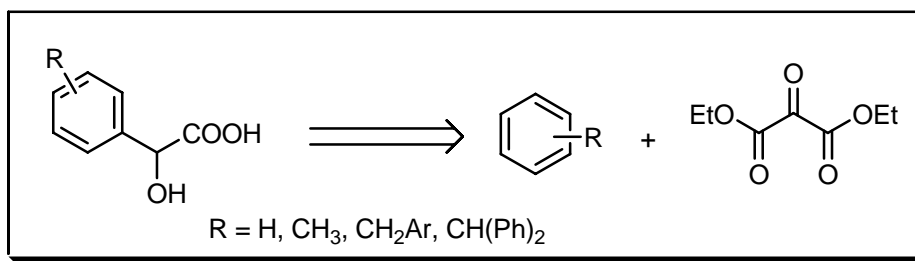
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Mandelic acids are prepared from ethyl oxomalonate and aromatic hydrocarbons or their derivatives by treatment with suitable condensing agents.

## REFERENCES :

March : 549

Smith – March : 720

Org. Synth. : 25, 33

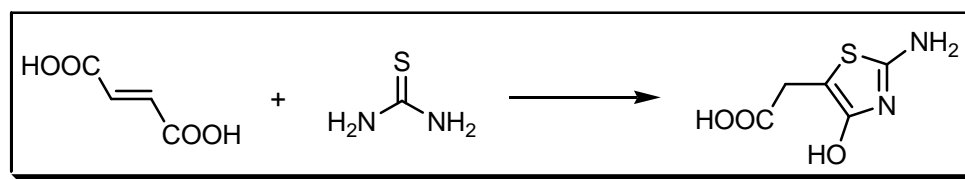
Org. Synth. Coll. Vol. : 3, 326

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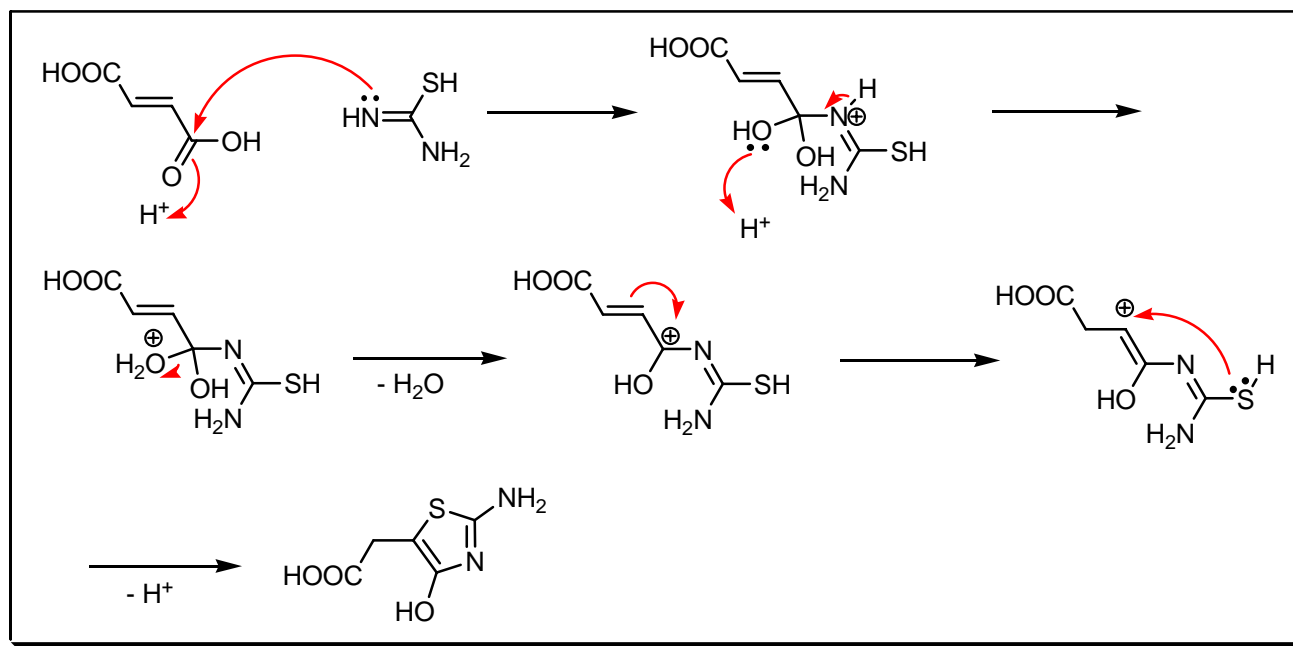
## COMMENTS :

# ANDREASCH THIAZOLE SYNTHESIS

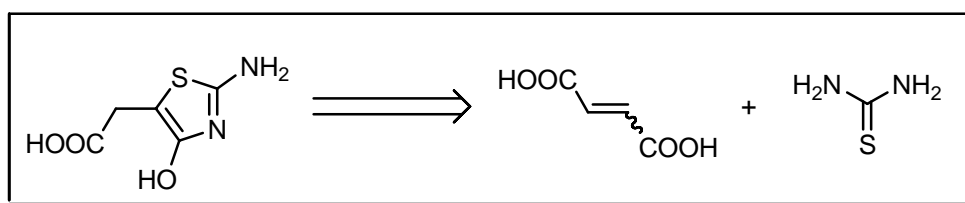
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The action of thiourea on unsaturated dibasic acids such as maleic or fumaric acids yields derivatives of thiazole. The use of cinnamic acid affords a pyrimidine. See also **Asinger**, **Hantzsch** thiazole and **Wohl – Marckwald** reactions.

## REFERENCES :

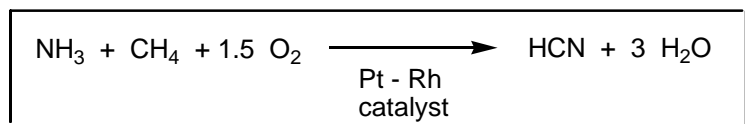
- 1) R. Andreasch, *Monatsh. Chem.*, 1895, **16**, 789.
- 2) H. Erlenmeyer; F. Heitz, *Helv. Chim. Acta*, 1942, **25**, 832.

**COMMENTS :**

## ANDRUSOV AMMOXIDATION

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**EXAMPLE :**



**NOTES :**

This is the hydrogen cyanide production by the ammoxidation of methane over Pt - Rh gauze catalyst. The process has been elaborated wherever natural gas is abundant.

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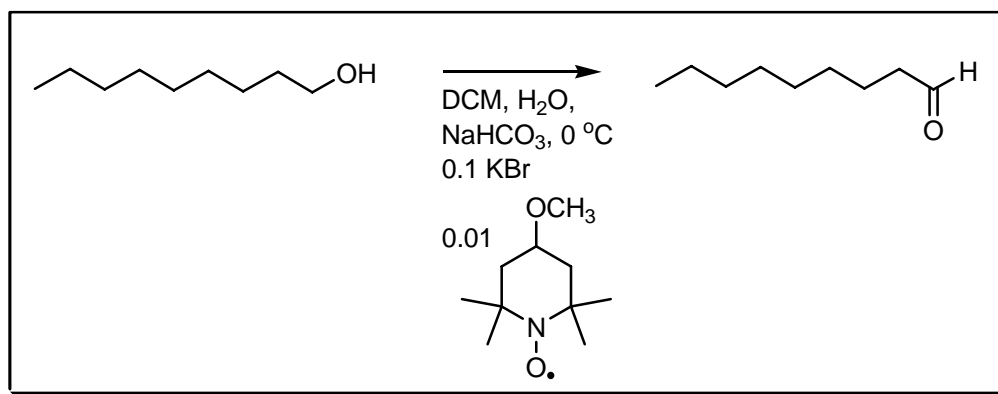
**REFERENCES :**

- 1) L. Andrussov, *Ber. Dtsch. Chem. Ges.*, 1927, **60**, 2005.
  - 2) L. Andrussov, *Angew. Chem.*, 1935, **48**, 593.
  - 3) D.A. Hickman; M. Huff; L.D. Schmidt, *Ind. Eng. Chem. Res.*, 1993, **32**, 809.
  - 4) A.S. Bodke; D.A. Olschki; L.D. Schmidt, *Appl. Catal. A: General*, 2000, **201**, 13.
- 

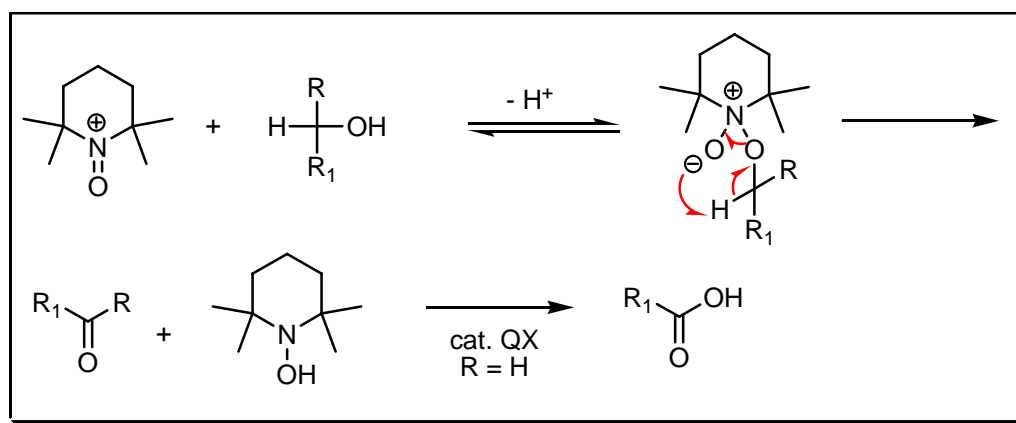
**COMMENTS :**

## ANELLI OXIDATION

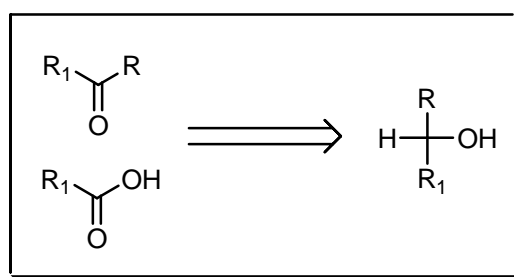
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Primary alcohols are oxidised to aldehydes, secondary alcohols to ketones, in a few minutes at  $0^\circ\text{C}$  in DCM – 0.35 M NaOCl in the presence of a catalytic amount of TEMPO. Co-catalysis by bromide ions and buffer at pH 8.6 with sodium bicarbonate is also required. Further oxidation of the aldehyde to the carboxylic acid is very slow but can be speeded up by the addition of catalytic amounts of phase-transfer catalyst (QX). The TEMPO catalyst can be supported on silica. See also **Ball – Goodwin – Morton, Collins, Corey – Kim, Corey – Schmidt, Corey – Suggs, David – Thieffry, Delépine, Dess – Martin, Einhorn** oxidation, **Fétizon, Jones** oxidation, **Ley, Maurer – Drefahl,**

Mukaiyama oxidation, Nicolaou, Oppenauer, Parikh – von Doering, Pfitzner – Moffatt, Pinnick, Sarett, Swern and Uemura reactions.

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**REFERENCES :**

**Org. Synth. :** **69**, 212

**Org. Synth. Coll. Vol. :** **8**, 367

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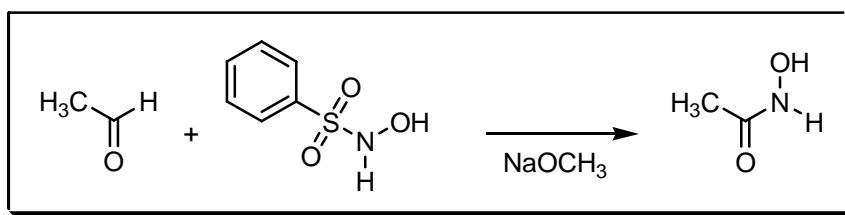
- 1) P.L. Anelli; C. Biffi; F. Montanari; S. Quici, *J. Org. Chem.*, 1987, **52**, 2559.
  - 2) P.L. Anelli; S. Banfi; F. Montanari; S. Quici, *J. Org. Chem.*, 1989, **54**, 2970.
  - 3) A.E.J. de Nooy; A.C. Besemer; H. van Bekkum, *Synthesis*, 1996, 1153.
  - 4) A. Heeres; H.A. van Doren; K. Gottlieb; I.P. Bleeker, *Carbohydr. Res.*, 1997, **299**, 221.
  - 5) T. Fey; H. Fischer; S. Bachmann; K. Albert; C. Bolm, *J. Org. Chem.*, 2001, **66**, 8154.
  - 6) A. Dijksman; I.W.C.E. Arends; R.A. Sheldon, *Synlett*, 2001, 102.
- 

**COMMENTS :**

## ANGELI – RIMINI SYNTHESIS

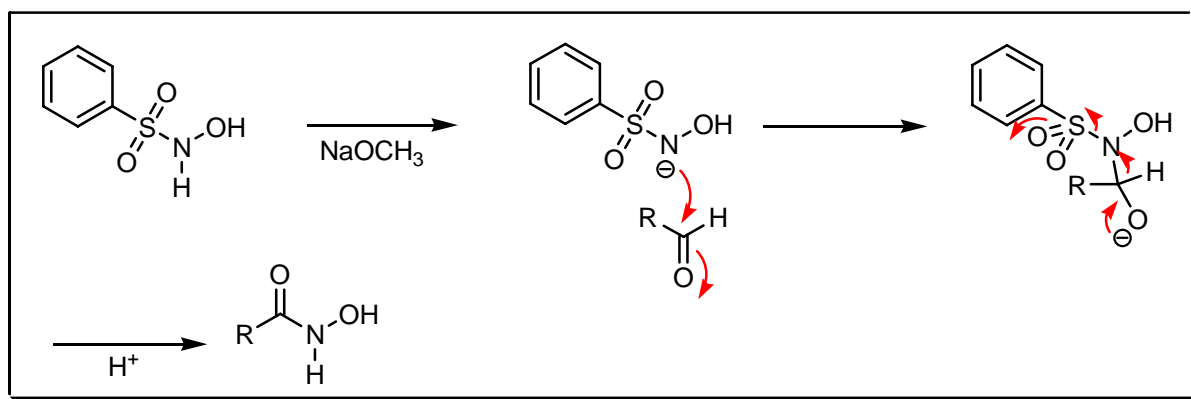
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**EXAMPLE :**

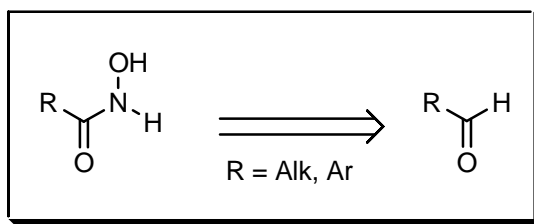


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**MECHANISM :**



## DISCONNECTION :



## NOTES :

Aldehydes form hydroxamic acids when treated with salts of nitrohydroxamic acid or of benzenesulfohydroxamic acid. With  $\text{FeCl}_3$  an intensely coloured iron-complex is formed. This can be used as a test for aliphatic and aromatic aldehydes.

## REFERENCES :

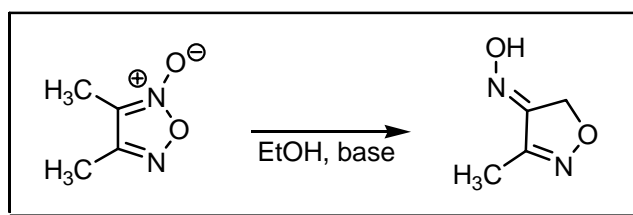
Houben – Weyl : **2**, 437

- 1) A. Angeli, *Gazz. Chim. Ital.*, 1896, **26/2**, 17.
- 2) A. Angeli, *Gazz. Chim. Ital.*, 1897, **27/2**, 357.
- 3) E. Rimini, *Gazz. Chim. Ital.*, 1901, **31/1**, 84.
- 4) H.L. Yale, *Chem. Rev.*, 1943, **33**, 228.
- 5) W. Lwowski, *Angew. Chem., Int. Ed. Engl.*, 1967, **6**, 897.
- 6) A. Hassner; E. Wiederkehr; A.J. Kascheres, *J. Org. Chem.*, 1970, **35**, 1952.
- 7) B.M. Vlasov; O.V. Zaharova, *J. Org. Him.*, 1974, **10**, 66.
- 8) S. Zhou; F. Xie; Z. Xu; S. Ni, *Huaxue Shiji*, 2001, **23**, 154.

## COMMENTS :

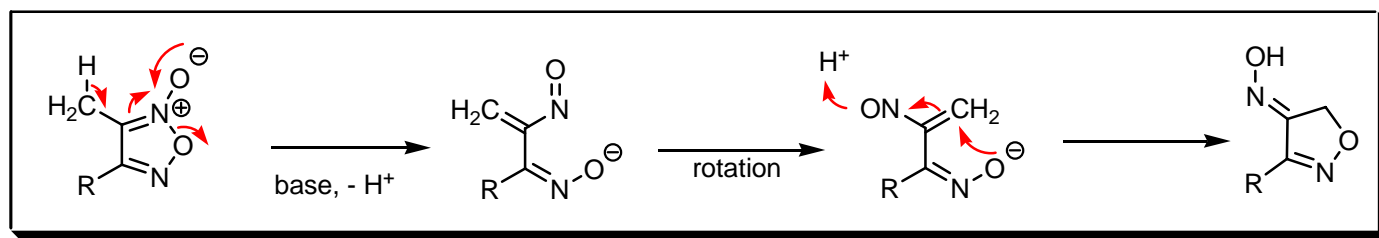
## ANGELI FURAZAN OXIDE REARRANGEMENT

### EXAMPLE :

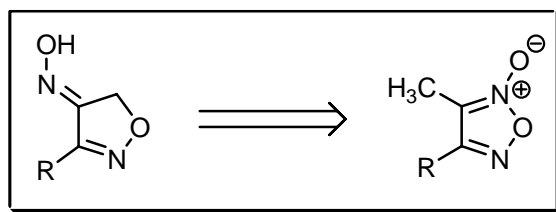




## MECHANISM :



## DISCONNECTION :



## NOTES :

The ring-opening of furazan-2-oxides (1,2,5-oxadiazol-2-ium-2-olate) and recyclisation with ethanolic base to afford hydroximino-1,2-oxazoles (4-(5H)-isoxazolone oxime).

## REFERENCES :

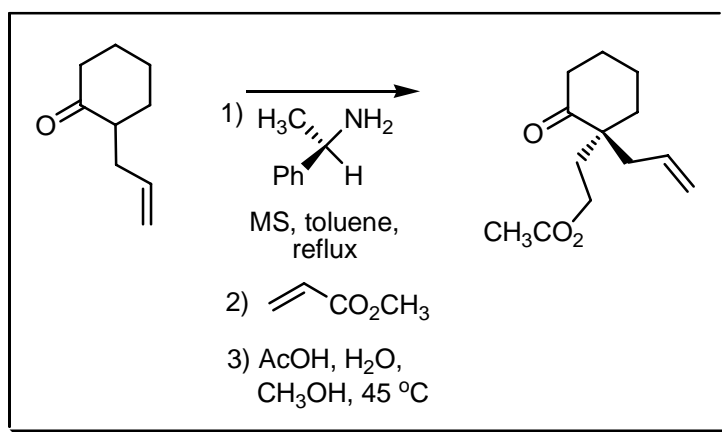
Houben – Weyl : E8c, 751

- 1) P. Tönnies, *Ber. Dtsch. Chem. Ges.*, 1880, **13**, 1845.
- 2) A. Angeli, *Ber. Dtsch. Chem. Ges.*, 1891, **24**, 3994.
- 3) H. Wieland; L. Semper, *Liebigs Ann. Chem.*, 1907, **358**, 36.
- 4) A.J. Boulton; D.E. Coe; P.G. Tsoungas, *Gazz. Chim. Ital.*, 1981, **112**, 167.
- 5) W. Naixing; C. Boren; O. Yuxiang, *Propellants, Explosives, Pyrotechnics*, 1994, **19**, 145.

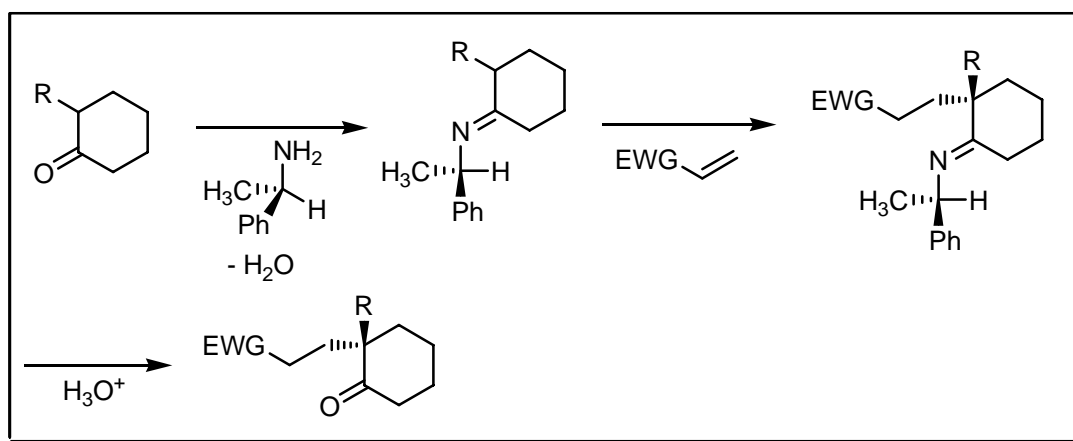
## COMMENTS :

## d'ANGELO'S ASYMMETRIC MICHAEL ADDITION

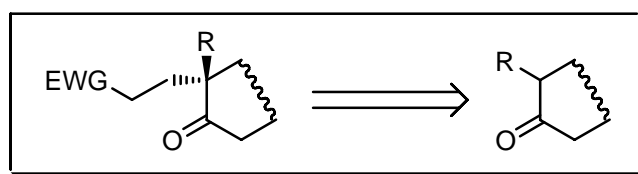
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This is an asymmetric version of the **Michael** reaction (deracemising alkylation) for the enantioselective construction of quaternary stereogenic centres using (S)-1-phenylethylamine. See also **Hajos – Parrish – Eder – Sauer – Wiechert** and **Michael** reactions.

### REFERENCES :

- 1) M. Pfau; G. Revial; A. Guignant; J.D. d'Angelo, *J. Am. Chem. Soc.*, 1985, **107**, 273.
- 2) J.D. d'Angelo; G. Revial; T. Volpe; M. Pfau, *Tetrahedron Lett.*, 1988, **29**, 4427.
- 3) J.D. d'Angelo; D. Desmaele; F. Dumas; A. Guigant, *Tetrahedron: Asymmetry*, 1992, **3**, 459.

4) J.C.F. Alves; A.B.C. Simas; P.R.R. Costa, *Tetrahedron: Asymmetry*, 1999, **10**, 297.

5) M. Toyota; T. Wada; M. Ihara, *J. Org. Chem.*, 2000, **65**, 4565.

6) C. Camara; L. Keller; F. Dumas, *Tetrahedron: Asymmetry*, 2003, **14**, 3263.

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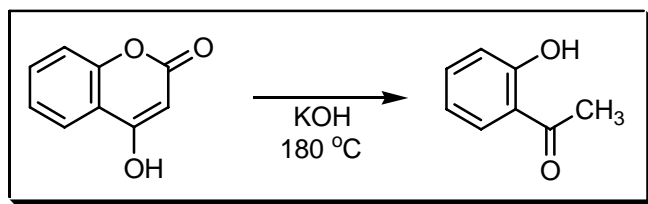
**COMMENTS :**

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## ANSCHÜTZ – SCHOLL HYDROXYACETOPHENONE SYNTHESIS

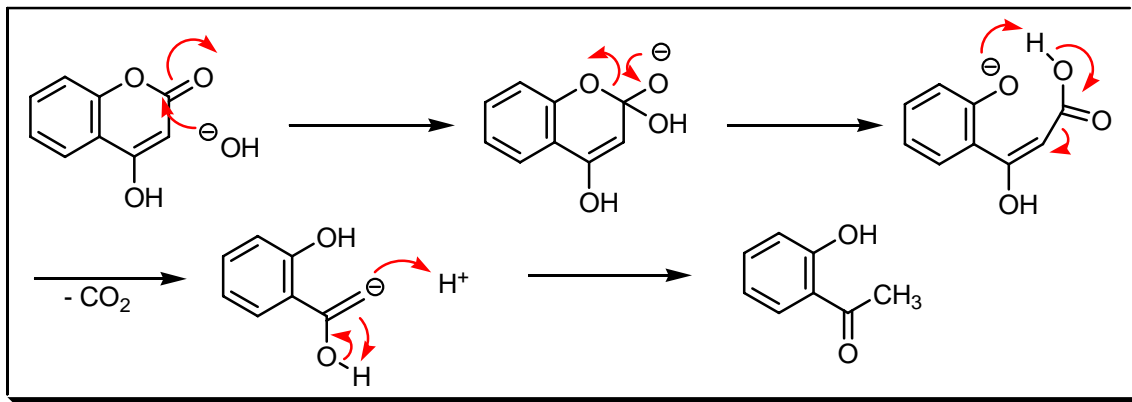
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**EXAMPLE :**

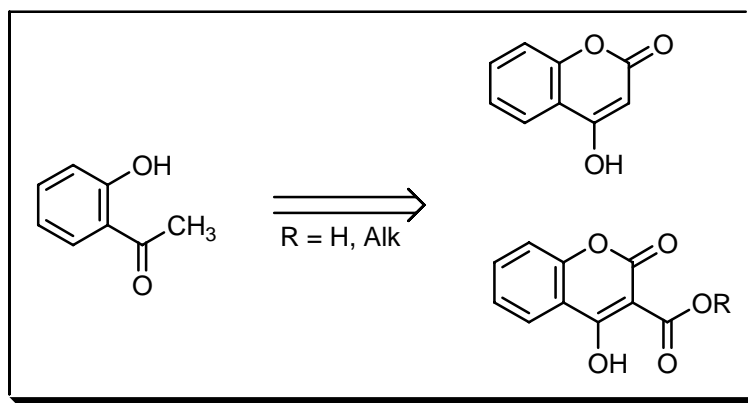


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**MECHANISM :**



## DISCONNECTION :



## NOTES :

4-Hydroxycoumarin, 4-hydroxycoumarin-3-carboxylic acid or its esters yield on treatment with alkali at 180 °C o-hydroxyacetophenones. In some cases the molecule will not decarboxylate and the corresponding salts can be obtained. See also **Anschütz** hydroxy coumarin, **Bargellini**, **Boyd – Robinson**, **Knoevenagel** coumarin, **Pauly – Lockemann**, **von Pechmann – Duisberg** and **Perkin** coumarin reactions.

## REFERENCES :

- 1) R.A. Anschütz; N.E. Scholl, *Liebigs Ann. Chem.*, 1909, **367**, 169.
- 2) R.A. Anschütz; N.E. Scholl, *Liebigs Ann. Chem.*, 1911, **379**, 333.
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- 4) I.C. Ivanov; S.K. Karagiosov; K. Stoyan; I. Manolov, *Arch. Pharm. (Weinheim, Ger.)*, 1991, **324**, 61.
- 5) O. Bozdağ; G. Ayhan-Kilcigil; M. Tunçbilek; R. Ertan, *Turk. J. Chem.*, 1999, **23**, 163.

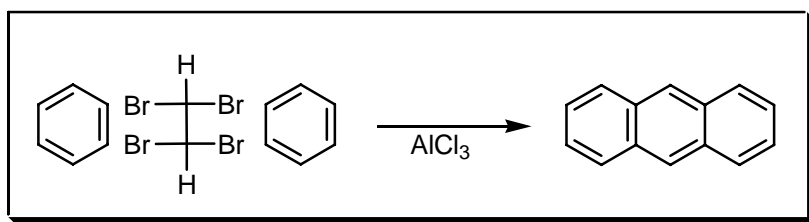
## COMMENTS :

## ANSCHÜTZ ANTHRACENE SYNTHESIS

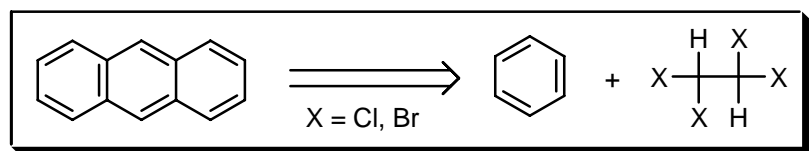
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The synthesis of anthracenes from benzene, 1,1,2,2-tetrachloroethane or 1,1,2,2-tetrabromoethane and aluminium trichloride. See also **Friedel – Crafts** and **Nenitzescu** acylation reactions.

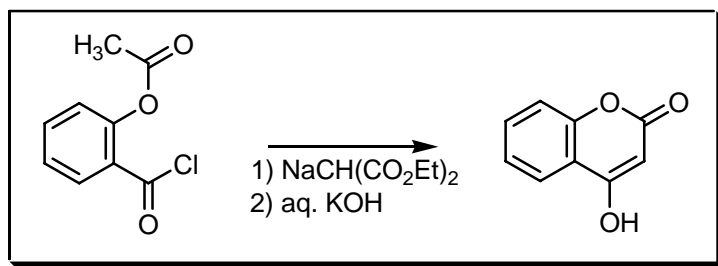
### REFERENCES :

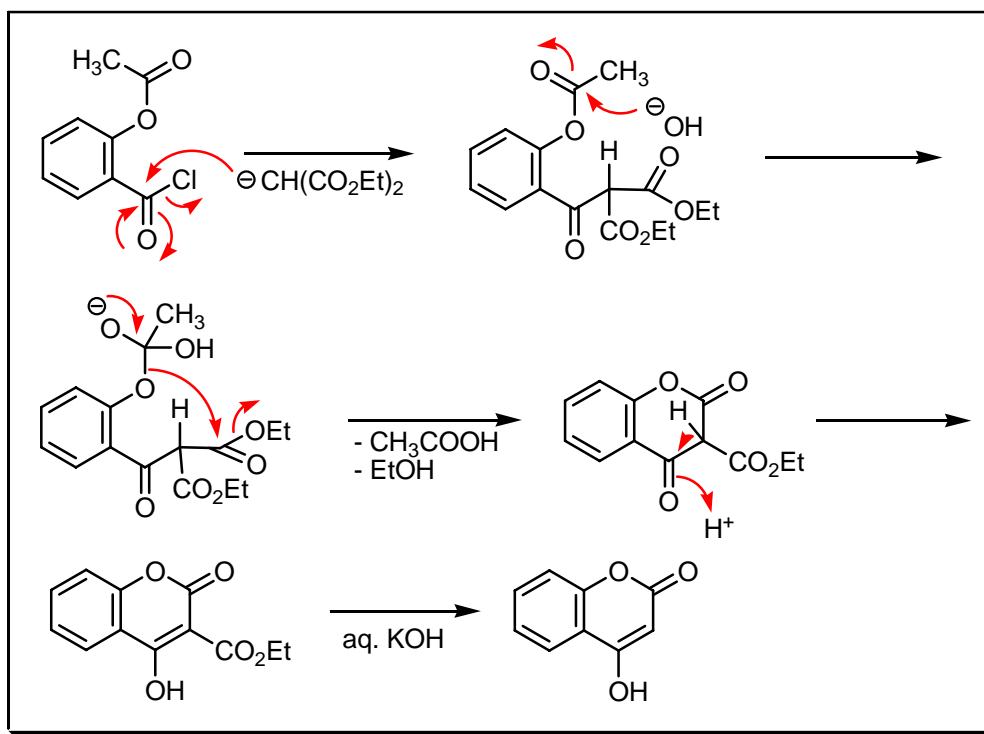
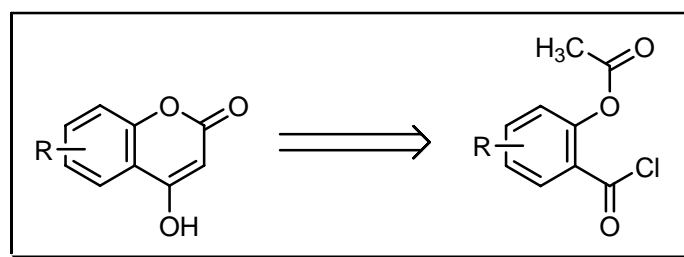
- 1) R.A. Anschütz; A. Angelbis, *Ber. Dtsch. Chem. Ges.*, 1884, **17**, 165.
- 2) R.A. Anschütz, *Liebigs Ann. Chem.*, 1886, **235**, 150.

### COMMENTS :

## ANSCHÜTZ HYDROXYCOUMARIN SYNTHESIS

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

*Ortho*-acetoxybenzoyl chlorides are condensed with sodium diethylmalonate to yield 3-ethoxycarbonyl-4-hydroxycoumarins, which are saponified and decarboxylated. See also **Anschütz – Scholl**, **Bargellini**, **Boyd – Robinson**, **Knoevenagel** coumarin, **Pauly – Lockemann**, **von Pechmann – Duisberg** and **Perkin** coumarin reactions.

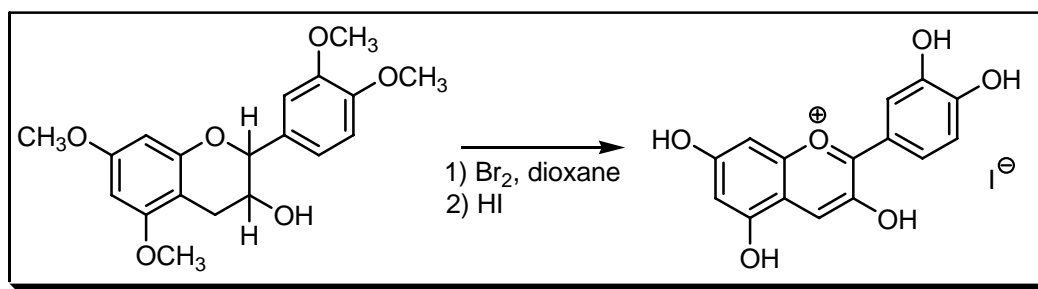
**REFERENCES :**

- 1) R.A. Anschütz, *Ber. Dtsch. Chem. Ges.*, 1903, **36**, 463.
- 2) R.A. Anschütz, *Liebigs Ann. Chem.*, 1909, **367**, 169.

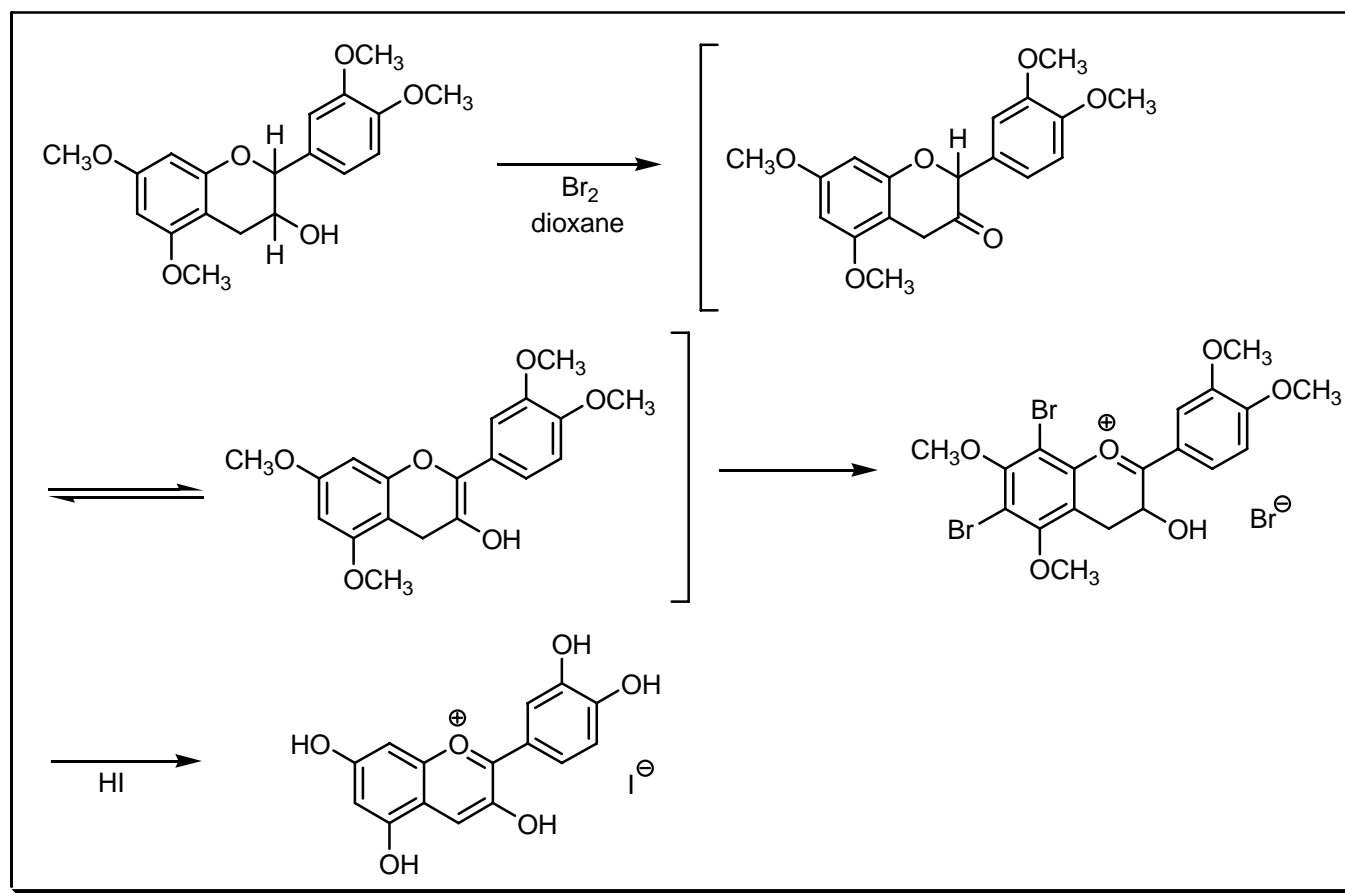
**COMMENTS :**

## APPEL – ROBINSON OXIDATION

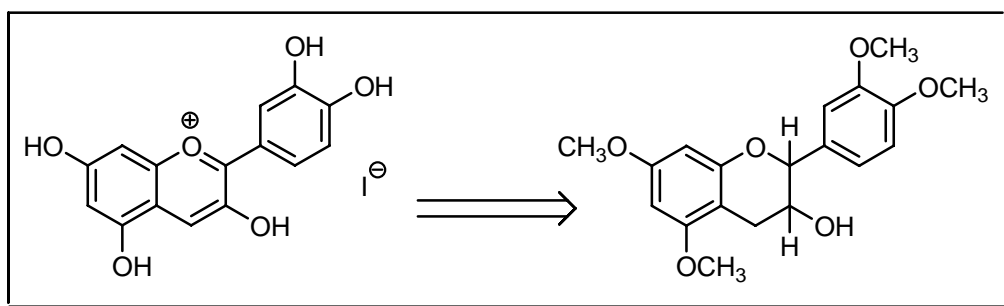
**EXAMPLE :**



**MECHANISM :**



### DISCONNECTION :

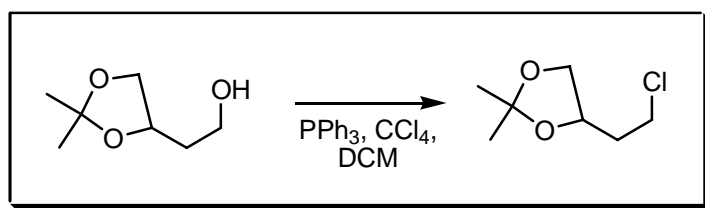
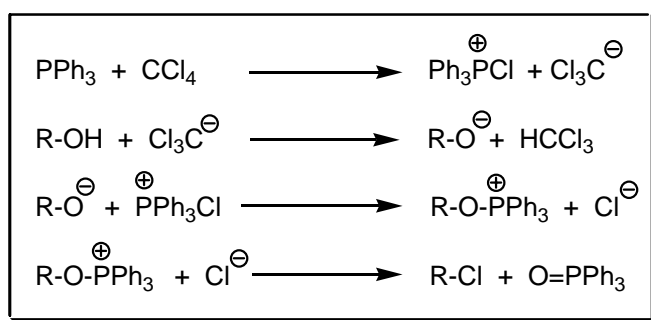
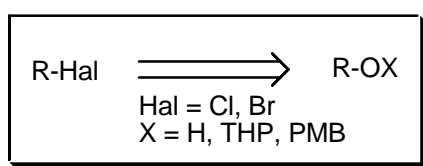


**NOTES :**

The oxidation of the tetramethyl ether of D-catechin. Technical dioxane has to be used as solvent. This has most probably to do with the presence peroxide, which is needed for the attack on the pyran ring. Benzoyl peroxide can also be used.

**REFERENCES :**

- 1) H. Appel; R. Robinson, *J. Chem. Soc.*, 1935, 426.
- 2) A.K. Ganguli; T.R. Seshadri; P. Subramanian, *Proc. Indian Acad. Sci.*, 1957, **46**, 25.

**COMMENTS :****APPEL REACTION****EXAMPLE :****MECHANISM :****DISCONNECTION :**



## NOTES :

The transformation of mainly primary and secondary alcohols and their THP and PMB ethers into chlorides or bromides with triphenylphosphine and carbon tetrachloride or carbon tetrabromide. The driving force for this reaction is the formation of the triphenylphosphine oxide and the oxidation of the phosphor atom. **Vorbrüggen** *et al.* adapted this reaction to prepare oxazolines. See also **Blum**, **Darzens** method, **Landauer – Rydon**, **Miller** synthesis and **Vorbrüggen – Krolikiewicz** reactions.

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## REFERENCES :

**Smith – March** : 519

**Smith** : 154

**Smith 2<sup>nd</sup>** : 123

**Org. React.** : 29,1

**Org. Synth.** : 54, 63

**Org. Synth. Coll. Vol.** : 6, 634

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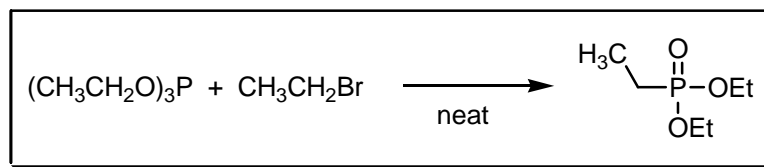
- 1) R. Appel, *Angew. Chem., Int. Ed. Engl.*, 1975, **14**, 801.
  - 2) H. Vorbrüggen; K. Krolikiewicz, *Tetrahedron Lett.*, 1981, **22**, 4471.
  - 3) H. Vorbrüggen; K. Krolikiewicz, *Tetrahedron*, 1993, **49**, 9353.
  - 4) A. Scheurer; P. Mosset; W. Bauer; R.W. Saalfrank, *Eur. J. Org. Chem.*, 2001, 3067.
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  - 6) L. Desmaris; N. Percina; L. Cottier; D. Sinou, *Tetrahedron Lett.*, 2003, **44**, 7589.
  - 7) T.W. Baughman; J.C. Sworen; K.B. Wagener, *Tetrahedron*, 2004, **60**, 10943.
- 

## COMMENTS :

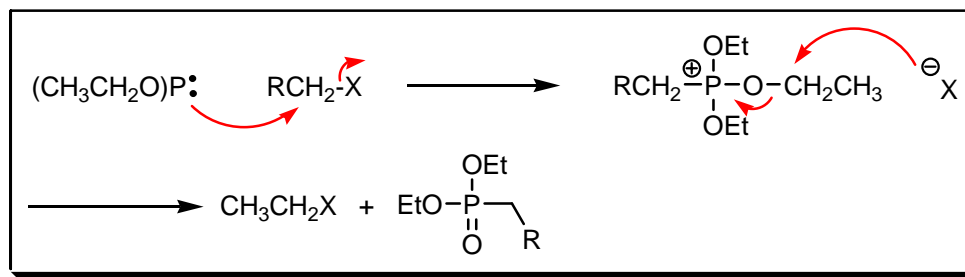
## ARBUZOV REACTION (MICHAELIS – ARBUZOV)

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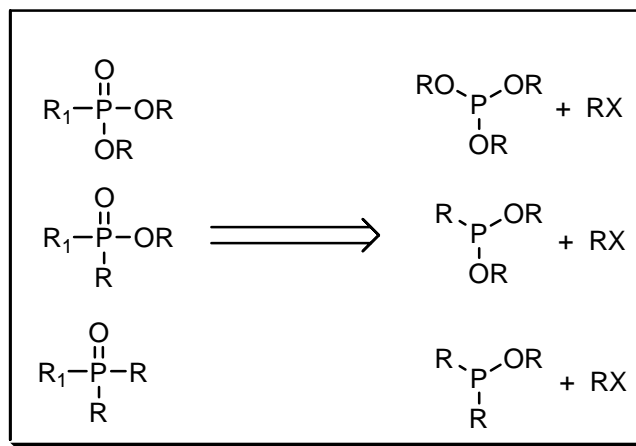
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

This reaction in its simplest form consists in the transformation of a trialkyl phosphite into a dialkylalkane phosphonate by warming with concentrated alkyl halide. When the reaction is carried out with an  $\alpha$ -bromo ketone it is called the **Perkow** reaction. Photo-**Arbuzov** reactions are also known. Furthermore, this reaction can be Lewis acid-catalysed or protic acid catalysed. See also **Abramov**, **Allen**, **Landauer – Rydon**, **Michaelis – Becker – Nylén** and **Perkow** reactions.

## REFERENCES :

**March** : 959

**Smith – March** : 1234

**Smith** : 136

**Smith 2<sup>nd</sup>** : 109

**Houben – Weyl** : **12/1**, 150, 171, 251, 433; **12/2**, 80, 284, 463; **E7a**, 628; **E7b**, 732; **E15**, 1679

**Org. React.** : **6**, 273; **29**, 1

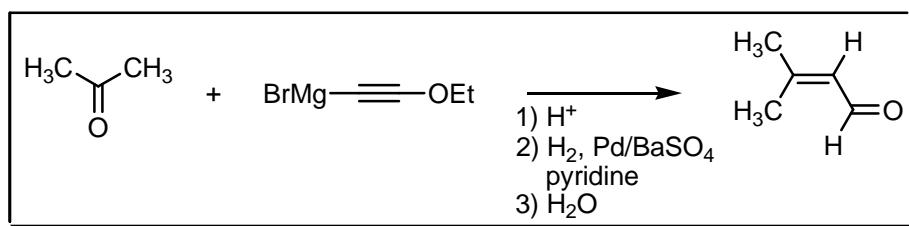
- 1) A. Michaelis; R. Kaehne, *Ber. Dtsch. Chem. Ges.*, 1898, **31**, 1048.
- 2) A.E. Arbuzov, *J. Russ. Phys. Chem.*, 1906, **38**, 687.
- 3) L.D. Freeman; G.O. Doak, *Chem. Rev.*, 1957, **57**, 479.
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- 6) T.B. Brill; S.J. Landon, *Chem. Rev.*, 1984, **84**, 577.
- 7) G. Baccolini; R. Dalpozzo; V. Mele; E. Mezzina, *Phosphorus Sulfur*, 1988, **39**, 179.
- 8) R. Boetzel; G. Hagele, *J. Fluorine Chem.*, 1994, **68**, 11.
- 9) W. Bhanthumnavin; A. Arif; W.G. Bentrude, *J. Org. Chem.*, 1998, **63**, 7753.
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- 11) W. Bhanthumnavin; W.G. Bentrude, *J. Org. Chem.*, 2001, **66**, 980.
- 12) P.-Y. Renard; P. Vayron; E. Leclerc; A. Valleix; C. Mioskowski, *Angew. Chem., Int. Ed.*, 2003, **42**, 3981.
- 13) A.A. Kadyrov; D.V. Silaev; K.N. Makarov; L.L. Gervits; G.-V. Röscenthaler, *J. Fluorine Chem.*, 2004, **125**, 1407.
- 14) W. Bhanthumnavin; W.G. Bentrude, *J. Org. Chem.*, 2005, **70**, 4643.

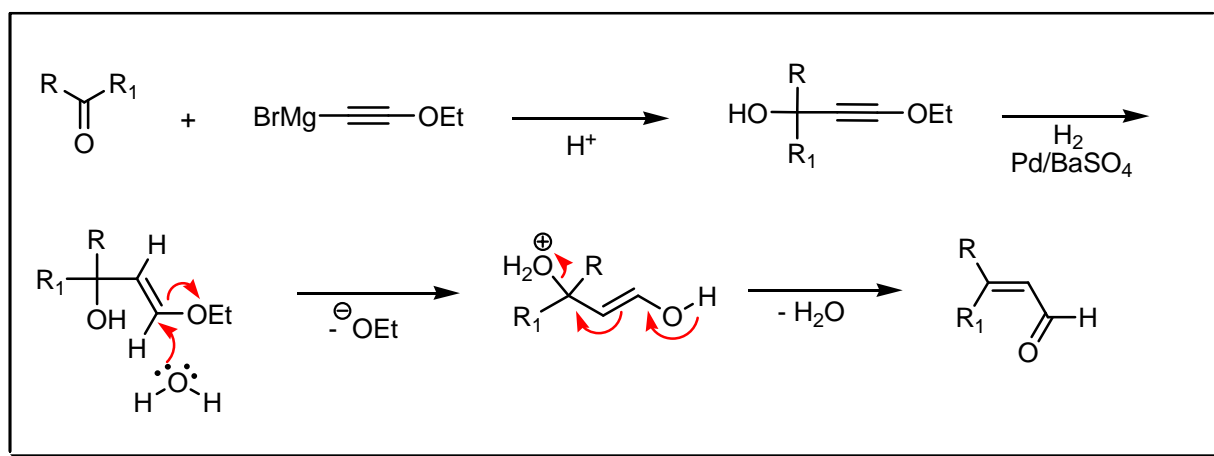
## COMMENTS :

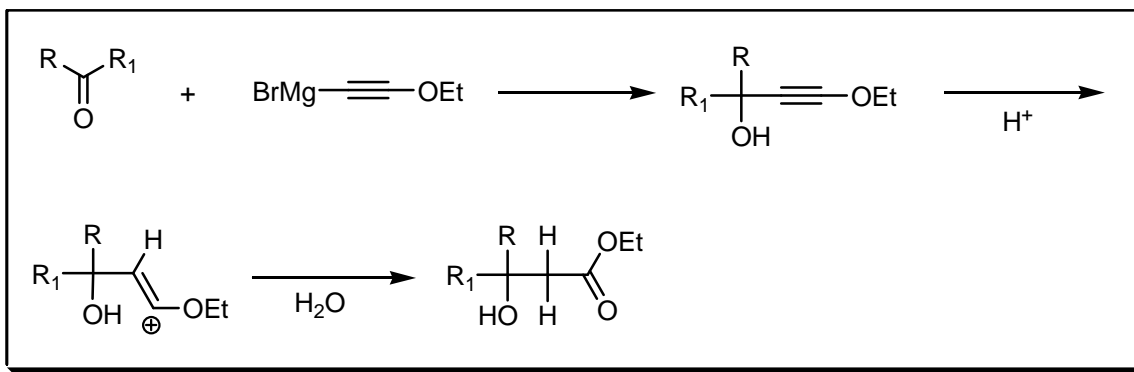
## ARENS – van DORP SYNTHESIS

### EXAMPLE :

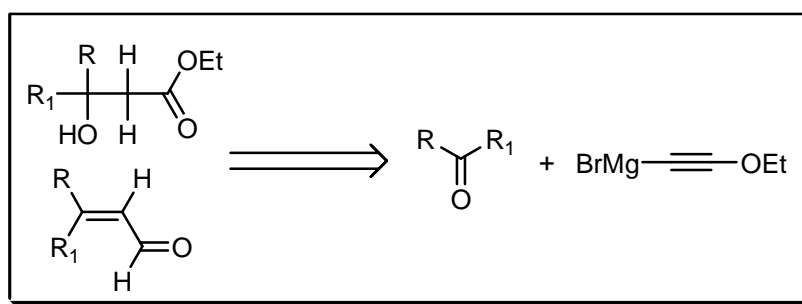


### MECHANISM :





#### DISCONNECTION :



#### NOTES :

A ketone is treated with the organometallic derivative of ethoxyacetylene. If the hydroxy acetylene is hydrogenated  $\alpha,\beta$ -unsaturated aldehydes are obtained. If however the hydroxyl acetylene is treated with acid hydroxyl esters are obtained. This reaction was one of the key steps in the synthesis of vitamin A. For the synthesis of a secondary carbinol, see **Isler** reaction. See also **Favorskii – Babayan**, **Inhoffen**, **Isler**, **Jones – Weedon**, **Nef** synthesis and **Reppe** acetylene reactions.

#### REFERENCES :

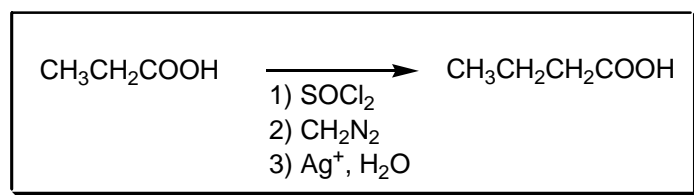
**Houben – Weyl** : 6/3, 189

- 1) N.A. Preobrazhenskii; V.V. Shokina, *J. Allg. Chem.*, 1945, **15**, 65.
- 2) D.A. van Dorp; J.F. Arens, *Nature*, 1947, **160**, 189.
- 3) J.F. Arens; D.A. van Dorp, *Recl. Trav. Chim. Pays-Bas*, 1948, **67**, 973.
- 4) J.F. Arens, *Adv. Org. Chem.*, 1960, **2**, 117.
- 5) P.P. Monti; E. Harryvan; L. Brandsma, *Recl. Trav. Chim. Pays-Bas*, 1964, **83**, 1211.

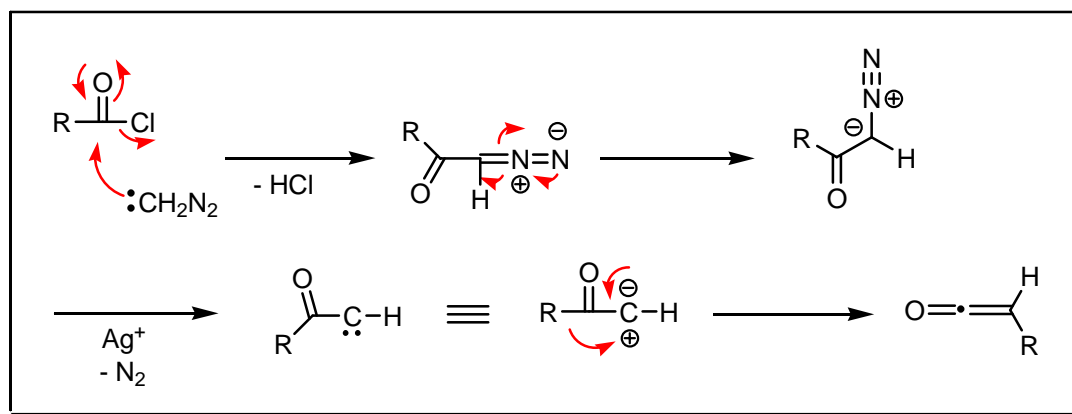
#### COMMENTS :

## ARNDT – EISTERT SYNTHESIS

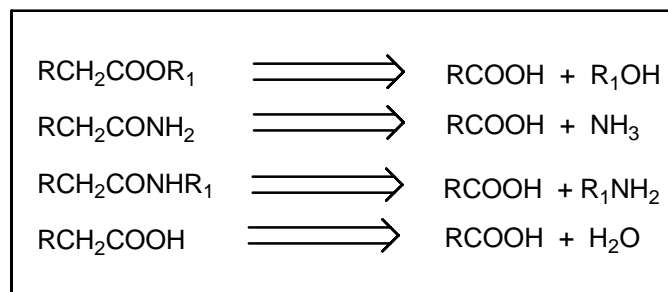
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This is the chain elongation of carboxylic acids by one methylene group. A base or 2 equivalents of diazomethane can remove the formed hydrogen chloride. The rearrangement of the ketene with water is called the **Wolff** rearrangement. When an alkenyl acid chloride or an aromatic acid chloride is used, the reaction is called the **Nierenstein** reaction. The **Newman – Beal** modification uses triethylamine (to bind the  $\text{HCl}$ ) and silver benzenecarboxylate, while the **Wilds – Meader** modification works with higher alcohols and does not use catalysts. Photochemical **Arndt – Eistert** reactions are also known. See also **Büchner – Curtius – Schlotterbeck**, **Clibbens – Nierenstein**, **Kowalski** and **Wolff** reactions.

### REFERENCES :

March : 1083

Smith – March : 573, 1405

Smith 2<sup>nd</sup> : 1199

Houben – Weyl : **8**, 556; **E5**, 283, 287; **E6b**, 1212; **E14b**, 1371

Org. React. : **1**, 38

Org. Synth. : **26**, 13; **50**, 77; **53**, 35; **69**, 180

Org. Synth. Coll. Vol. : **3**, 119; **6**, 386, 613; **8**, 196

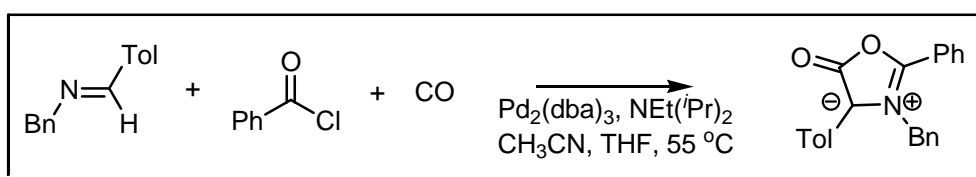
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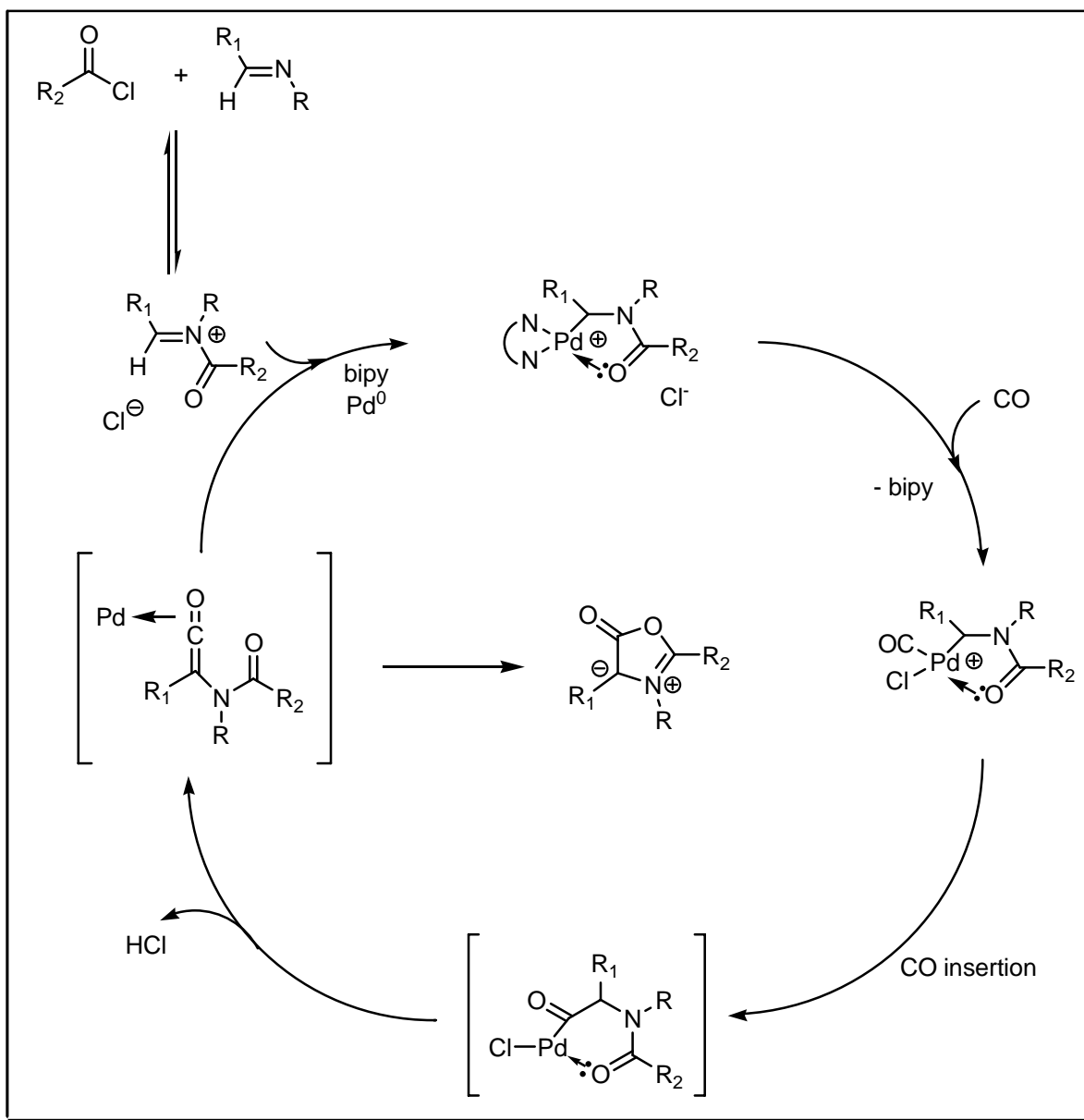
## ARNDTSEN MÜNCHNONE REACTION

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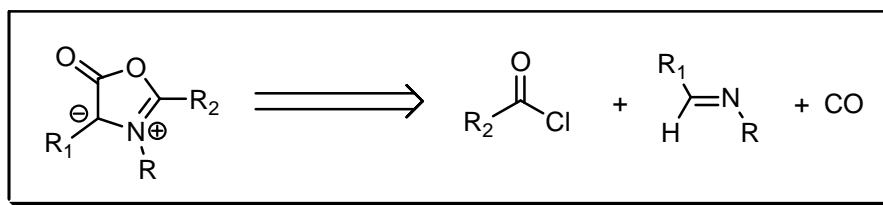
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The palladium-catalysed synthesis of münchnones starting with imines, carbon monoxide and acid chlorides. The mechanism is based on **Arndtsen's** palladium-catalysed imidazoline synthesis and resembles the mechanism for amidocarbonylation. See also **Wakamatsu** synthesis.

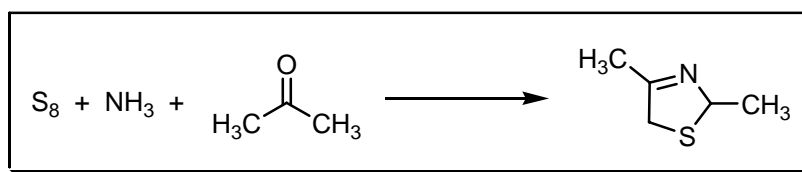
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## COMMENTS :

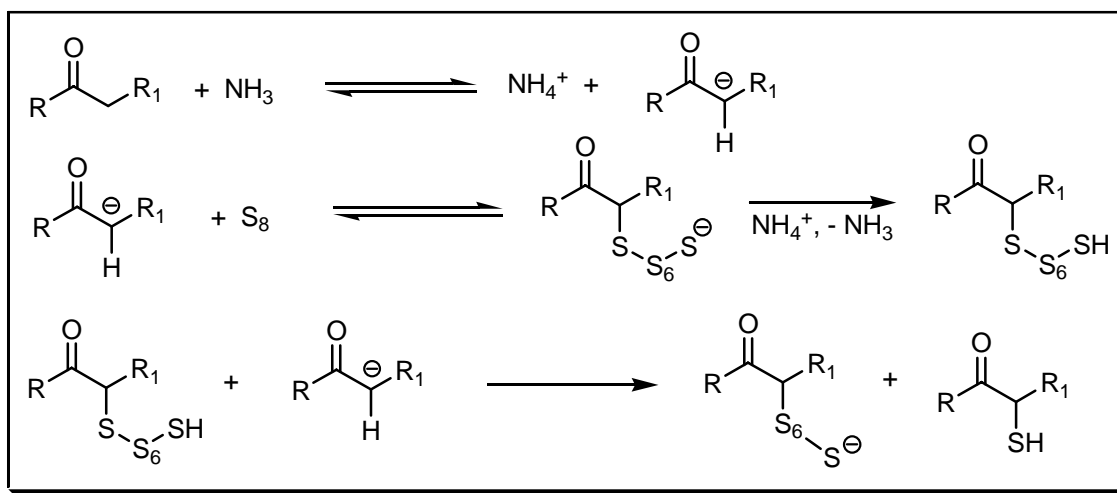
## ASINGER REACTION

### EXAMPLE :

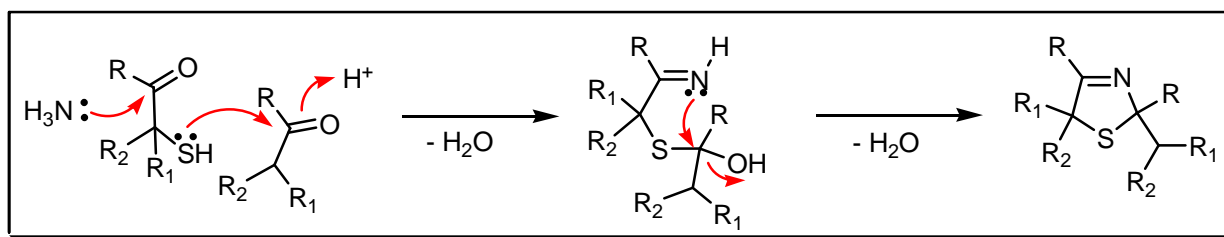


### MECHANISM :

#### First step :

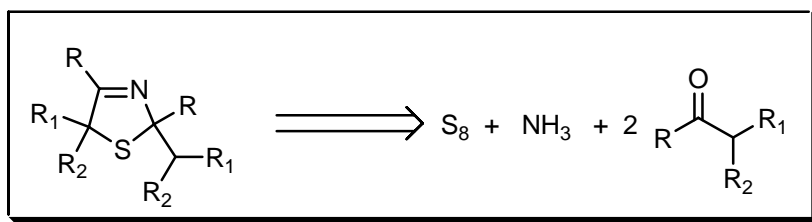


#### Ring formation :





## DISCONNECTION :



## NOTES :

The reaction between sulfur, ammonia or amines on ketones to afford thiazolines (imidazolin-5-thiones). The first step is the base-catalysed replacement of an H-atom  $\alpha$  to the carbonyl group by a mercapto group. The ring formation can be regarded as an  $\alpha$ -aminoalkylation of a thio-acid and subsequent stabilisation by ring-closure with elimination of water. See also **Andreasch**, **Hantzsch** thiazole, **Mannich** and **Wohl – Marckwald** reactions.

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## REFERENCES :

Houben – Weyl : E5, 1469

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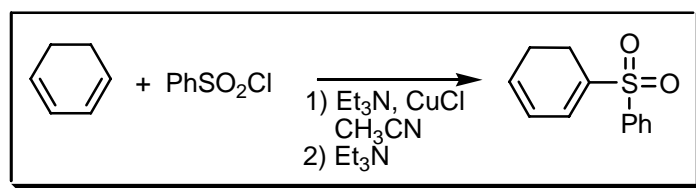
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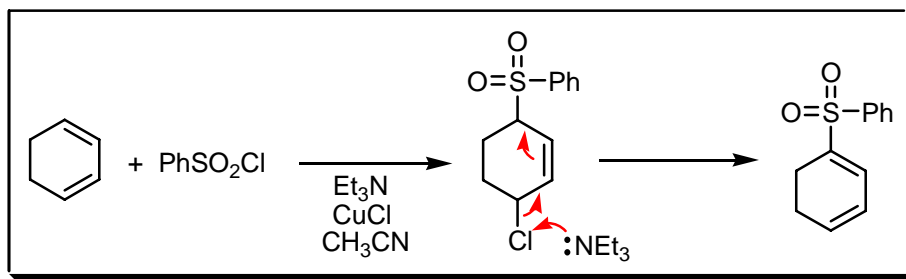
## ASSCHER – VOFSI REACTION

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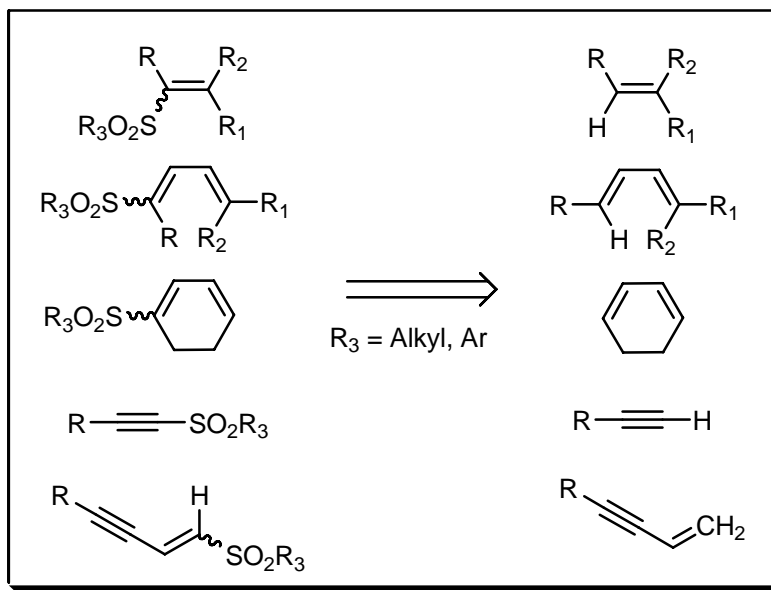
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The addition of aliphatic and aromatic sulfonyl chlorides to multiple C=C bonds under copper catalysis in acetonitrile.

## REFERENCES :

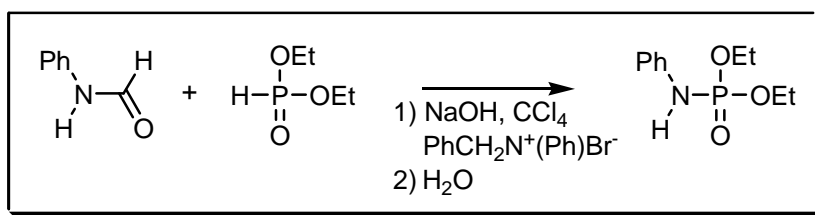
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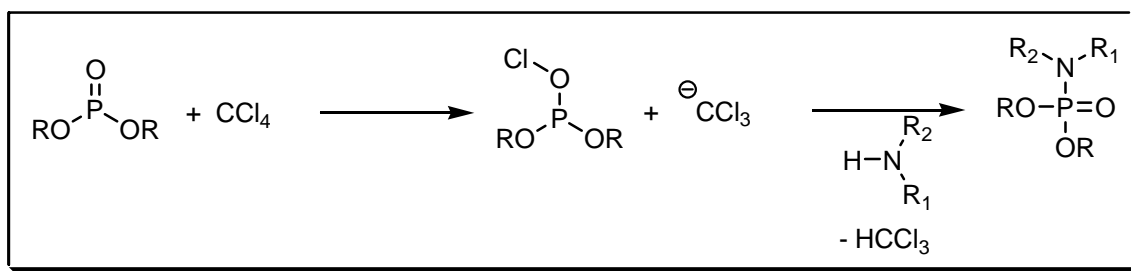
## COMMENTS :

# ATHERTON – OPENSHAW – TODD SYNTHESIS

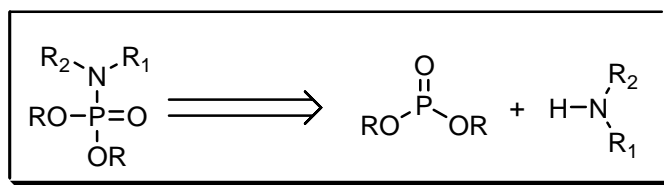
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of phosphoramidates from formamides and dialkyl phosphite. Carbon tetrachloride is the source of positive charged chlorine. Similar results can be obtained with carbon tetrabromide and a large variety of chloro compounds. The procedure has been modified by **Lukanov et al.** and **Zwierzak et al.** See also **Michaelis – Becker – Nylén** reaction.

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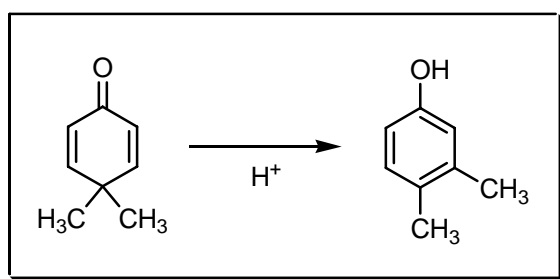
**COMMENTS :**

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**von AUWERS – INHOFFEN REARRANGEMENT**

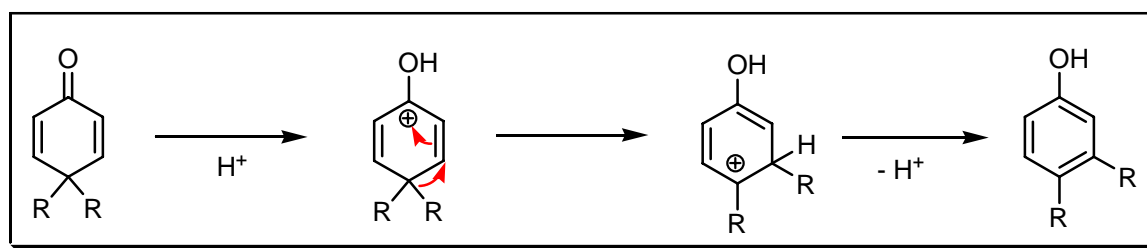
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**EXAMPLE :**



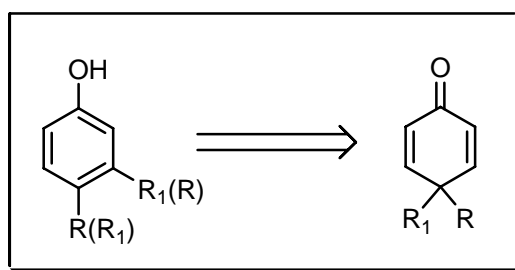
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**MECHANISM :**



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**DISCONNECTION :**



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**NOTES :**

The acid or Lewis acid-catalysed rearrangement of dienones to phenols. This reaction is also known under the name of dienone-phenol rearrangement.

## REFERENCES :

March : 1079

Smith – March : 1402

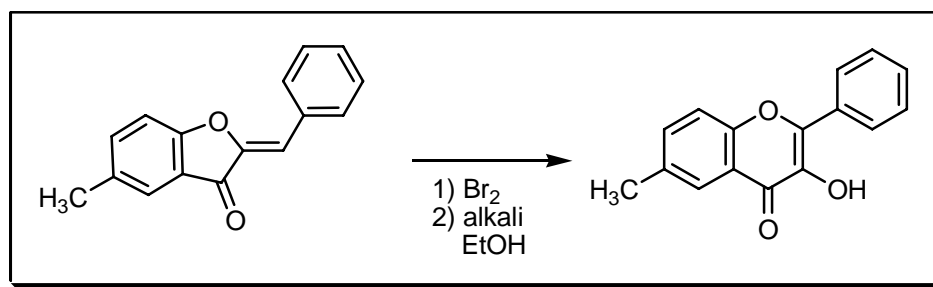
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## COMMENTS :

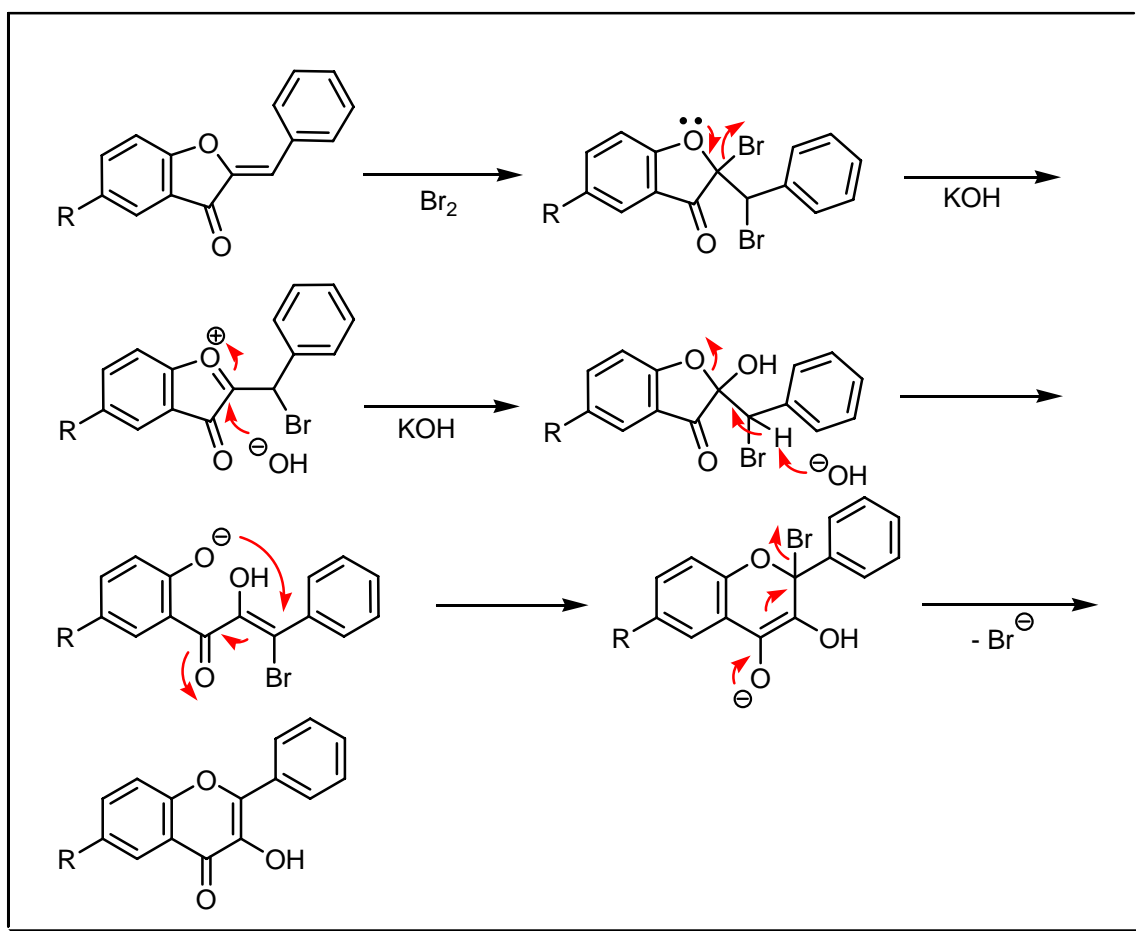
## von AUWERS FLAVONOL SYNTHESIS

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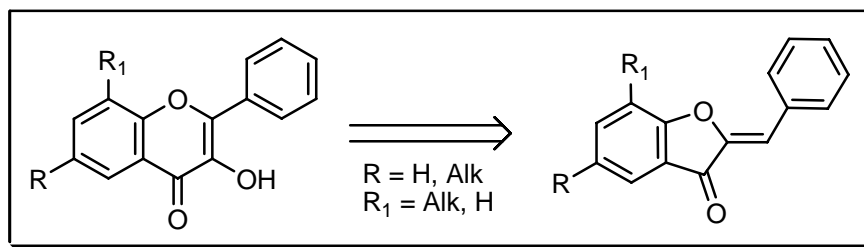
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The formation of flavonol (3-hydroxy-2-phenyl-4H-chromen-4-one) from 2-bromo-2-[bromo(phenyl)methyl]-1-benzofuran-3(2H)-one (2-benzylidenecoumaranone dibromide) by warming with aqueous ethanolic alkali hydroxides. Substituents in the *ortho* or *para* position to the heterocyclic oxygen atom promote flavonol formation. See also **Algar – Flynn – Oyamada**, **Baker – Ollis**, **von Kostanecki (Allan – Robinson)**, **Ranjorwa** and **Rasoda** reactions.

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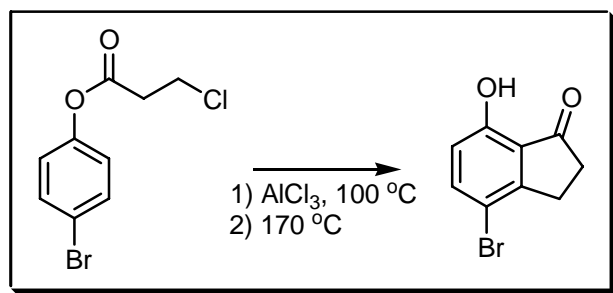
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**COMMENTS :**

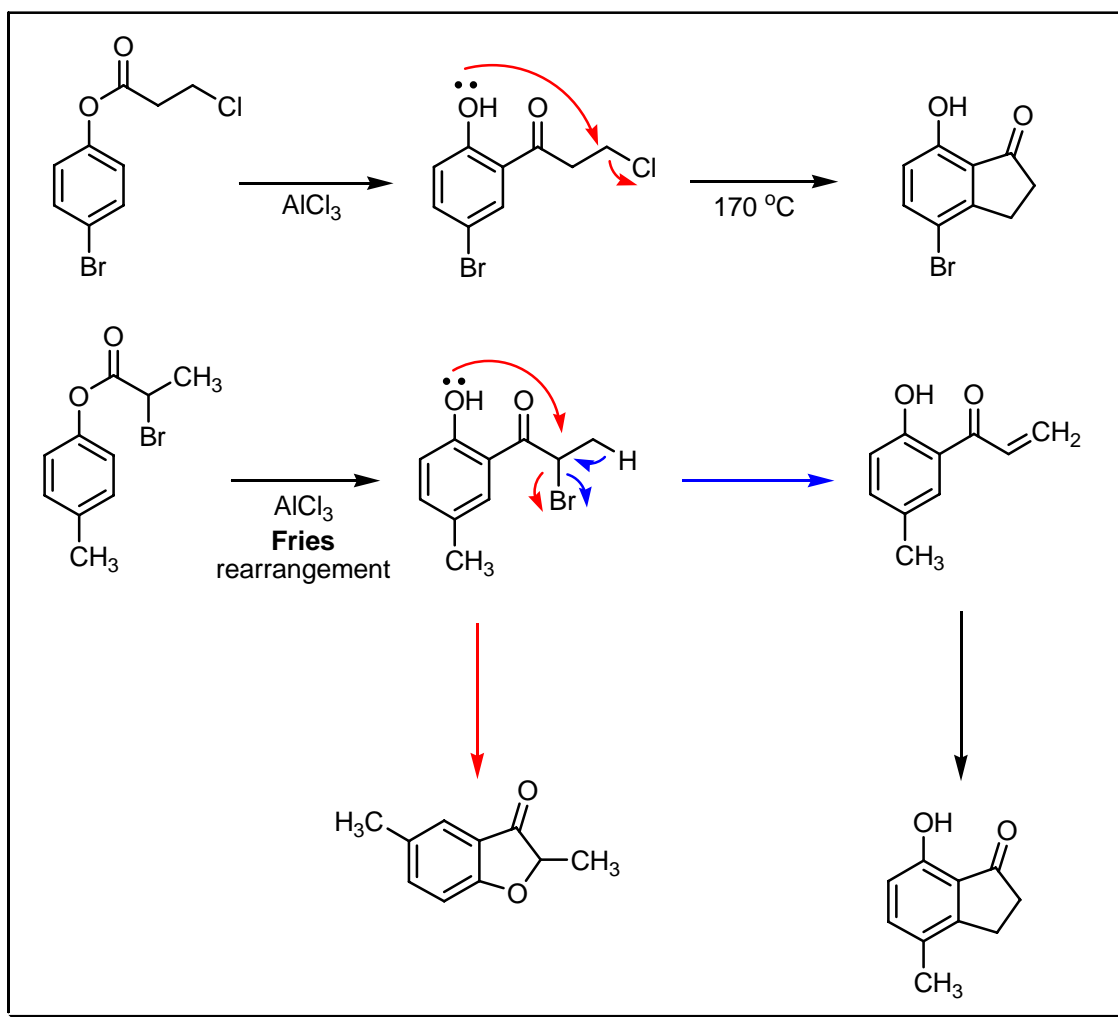
### von AUWERS INDANE-1-ONE SYNTHESIS

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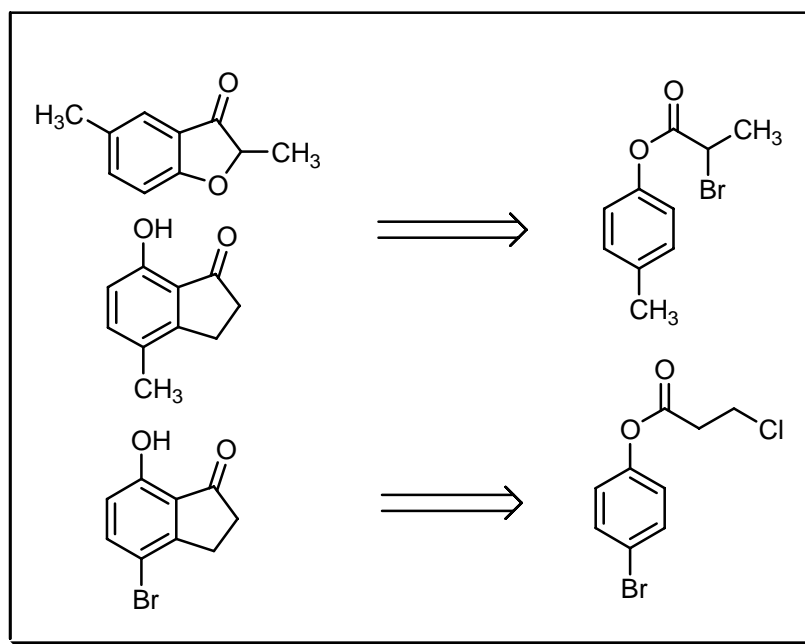
**EXAMPLE :**



# MECHANISM :



# DISCONNECTION :





## NOTES :

There are two steps in this synthesis, the first step is a **Fries** rearrangement of the phenolic ester of an  $\alpha$ - or a  $\beta$ -halogenopropionic acid, followed by the cyclisation of the intermediate halogeno-ketone. Coumarones are also produced. See also **Fries** rearrangement.

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## REFERENCES :

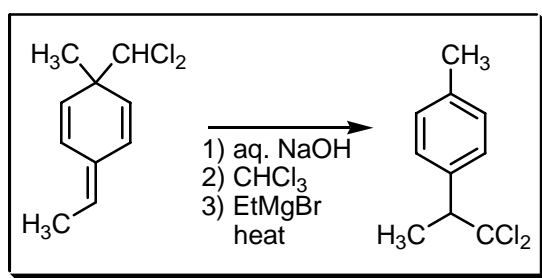
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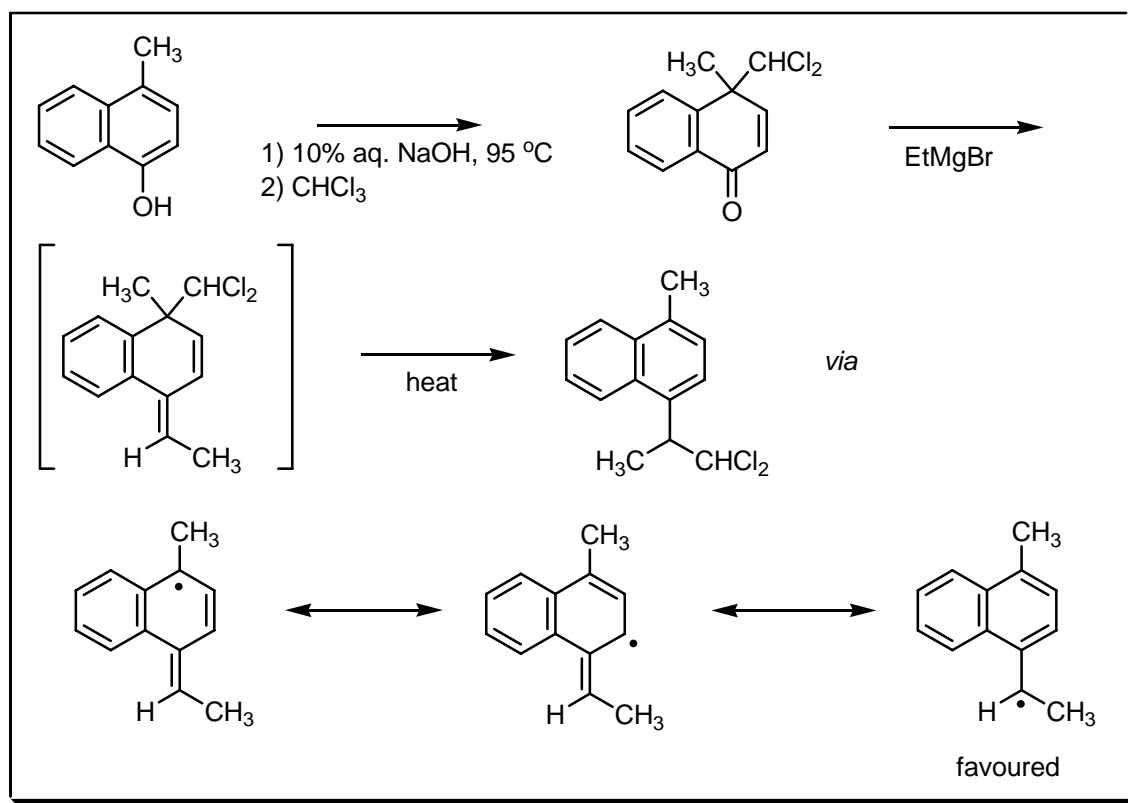
## von AUWERS REARRANGEMENT

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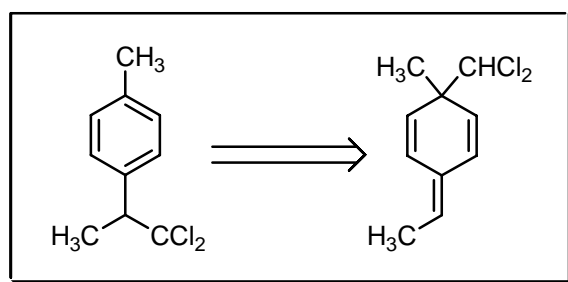
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Certain 3-(dichloromethyl)-6-alkylidene-3-methyl-1,4-cyclohexadienes undergo thermal non-catalytic rearrangement involving aromatisation of the ring and transfer of the dichloromethyl group to the  $\alpha$ -carbon of the alkylidene side chain. This reaction is also possible on naphthalene compounds.

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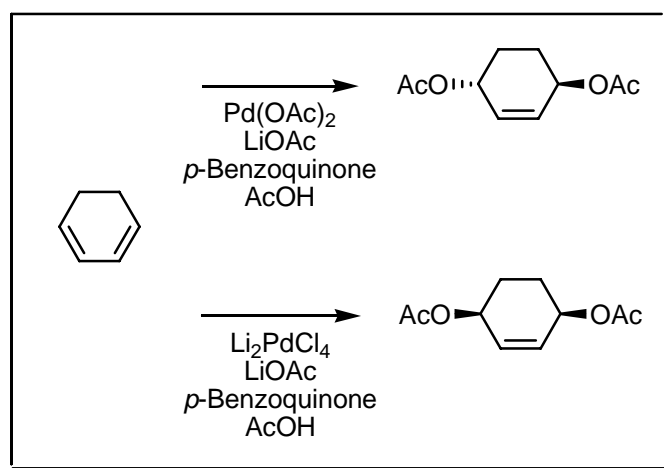
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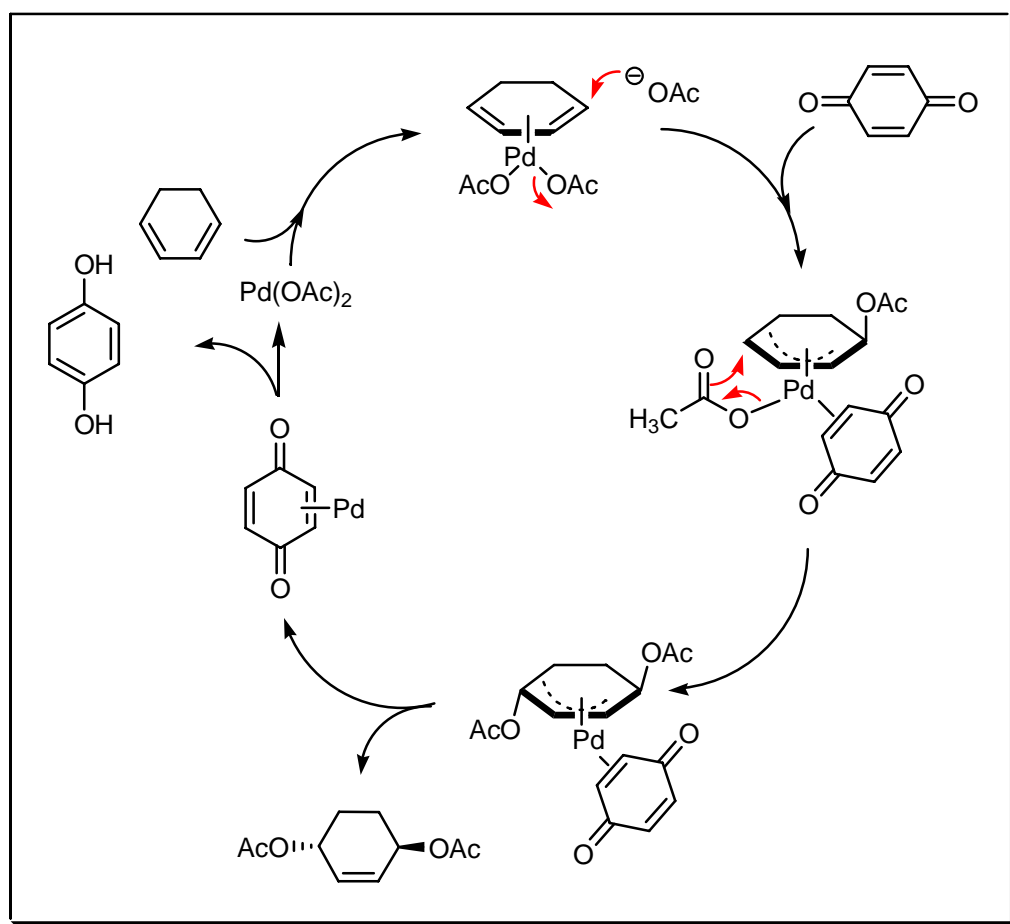
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## BÄCKVALL ACETOXYLATION REACTION

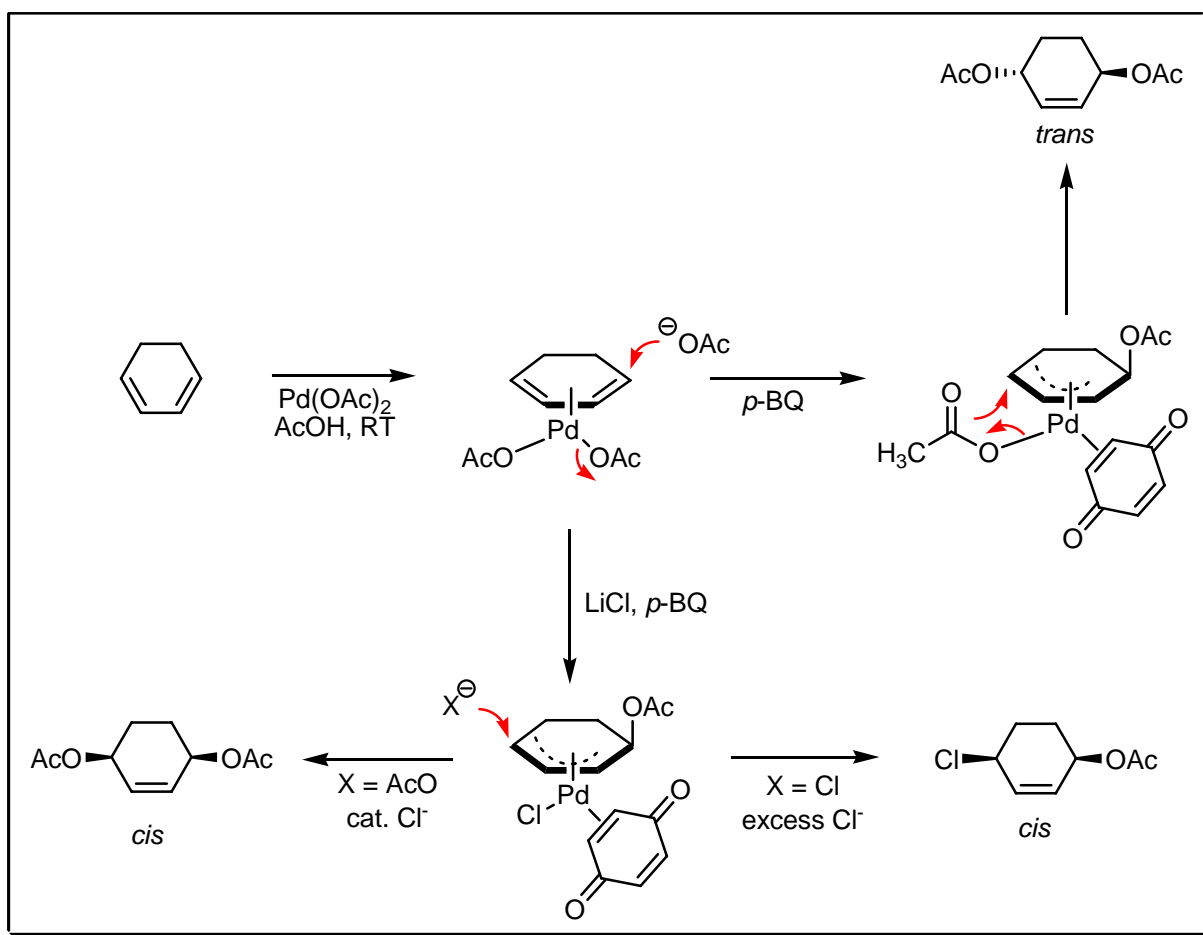
**EXAMPLE :**



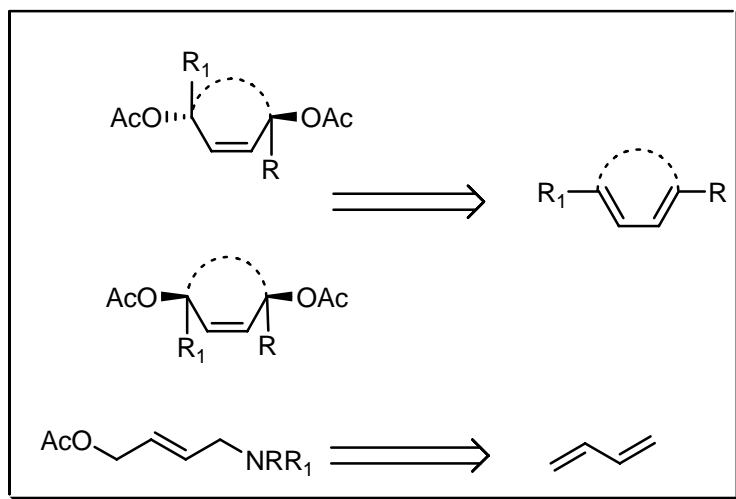
**MECHANISM :**



## Chloride effect :



## DISCONNECTION :



## NOTES :

An efficient method based on the palladium-catalysed 1,4-acetoxy-chlorination of 1,3-dienes and palladium-catalysed amination of allylic substrates. Compared to other methods, this method is more convenient and more general. It allows complete control of the 1,4-relative configuration when the carbons bearing nitrogen and oxygen are stereogenic. The formation of *E/Z* stereoisomers can be fully controlled (chloride effect). For review on halide effects, see Lautens *et al.*

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Org. Synth. : 67, 105

Org. Synth. Coll. Vol. : 8, 9

Science of Synthesis : 1, 70

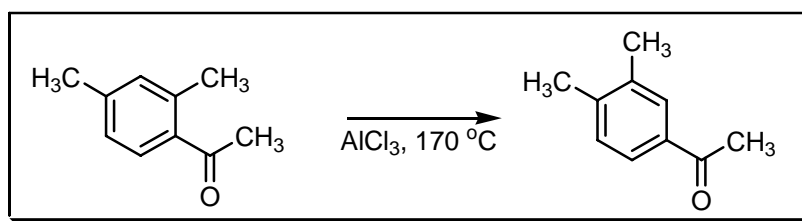
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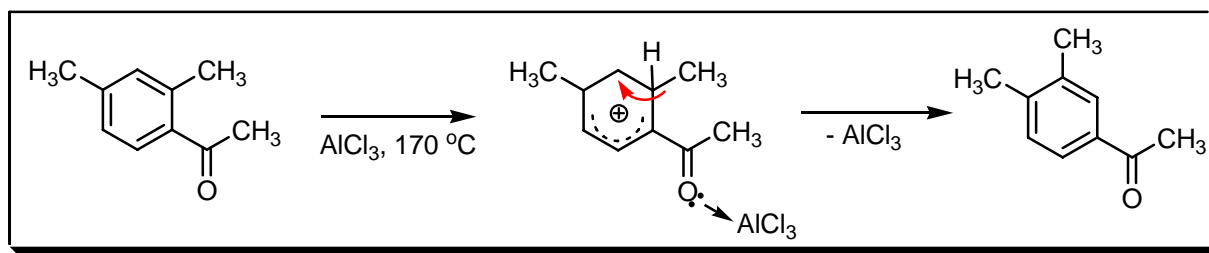
## BADDELEY REARRANGEMENT

### EXAMPLE :

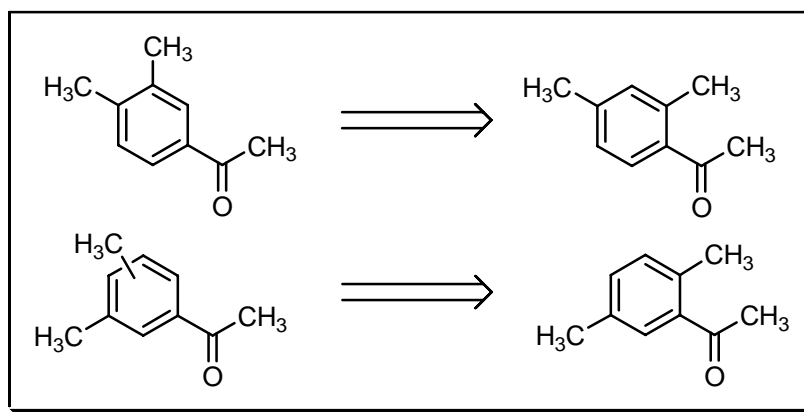




### MECHANISM :



### DISCONNECTION :



### NOTES :

An excess of aluminium chloride or bromide is used in the isomerisation of alkyl homologues of acetophenone. The aluminium chloride or bromide fixes the carbonyl group and thus prevents condensation, hydrolytic cleavage and it promotes rearrangement. See also **Jacobsen** rearrangement.

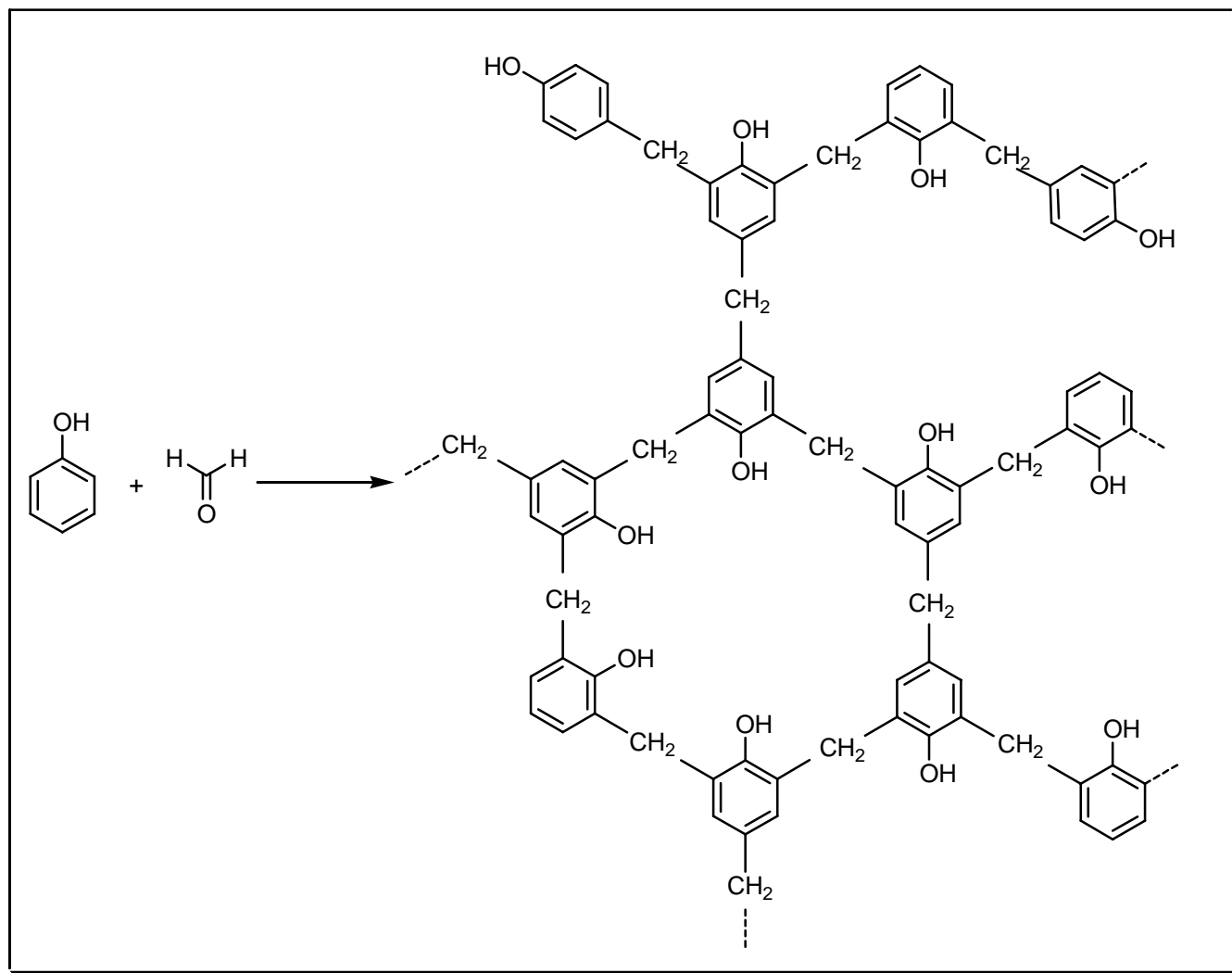
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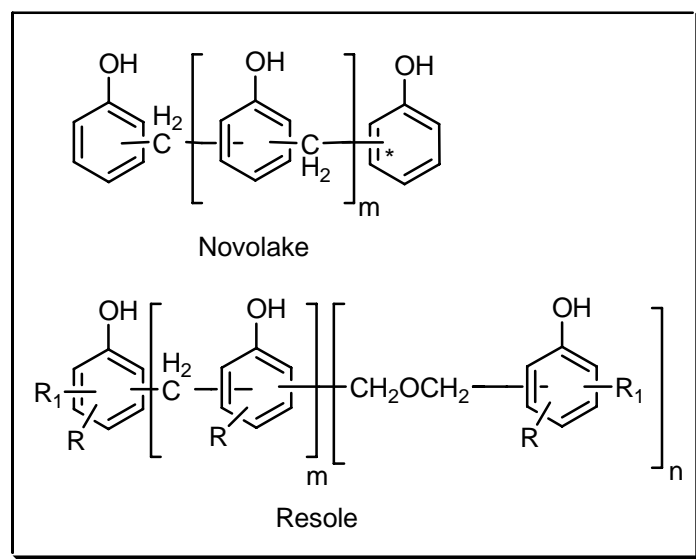
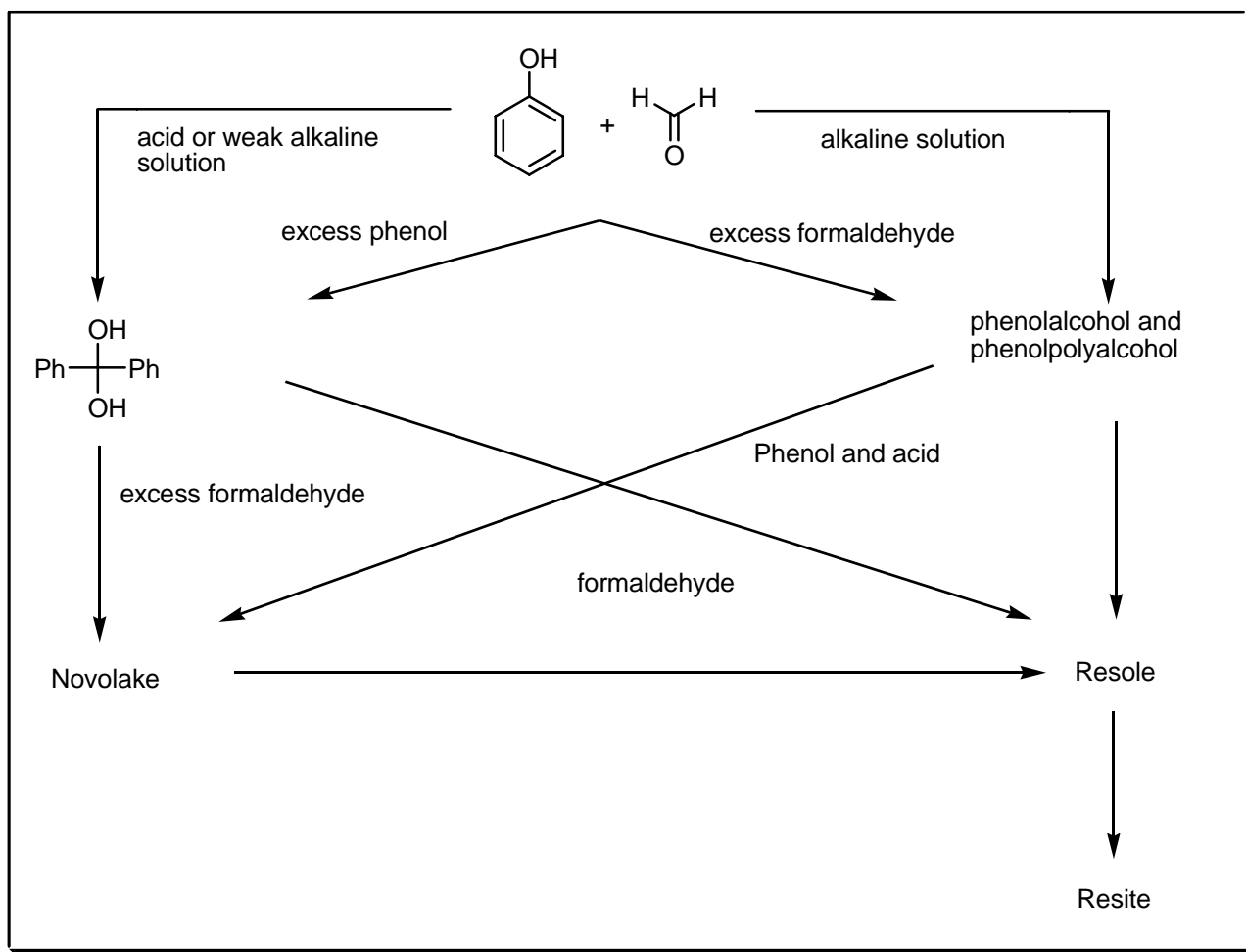
### COMMENTS :

## BAEKELAND POLYCONDENSATION

EXAMPLE :



## MECHANISM :



## NOTES :

The production of resins by the interaction of phenols and formaldehyde. See also **von Baeyer** aldehyde and **Lederer – Manasse** reactions.

## REFERENCES :

Houben – Weyl : **14/2**, 193

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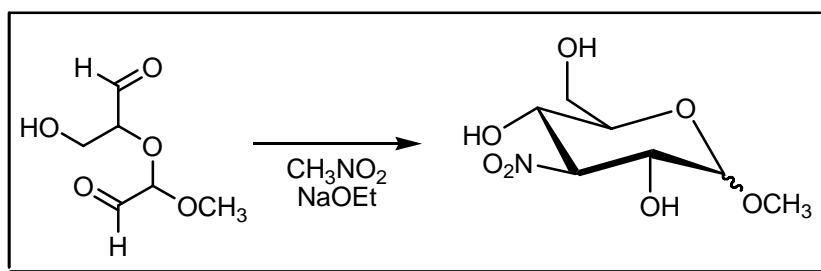
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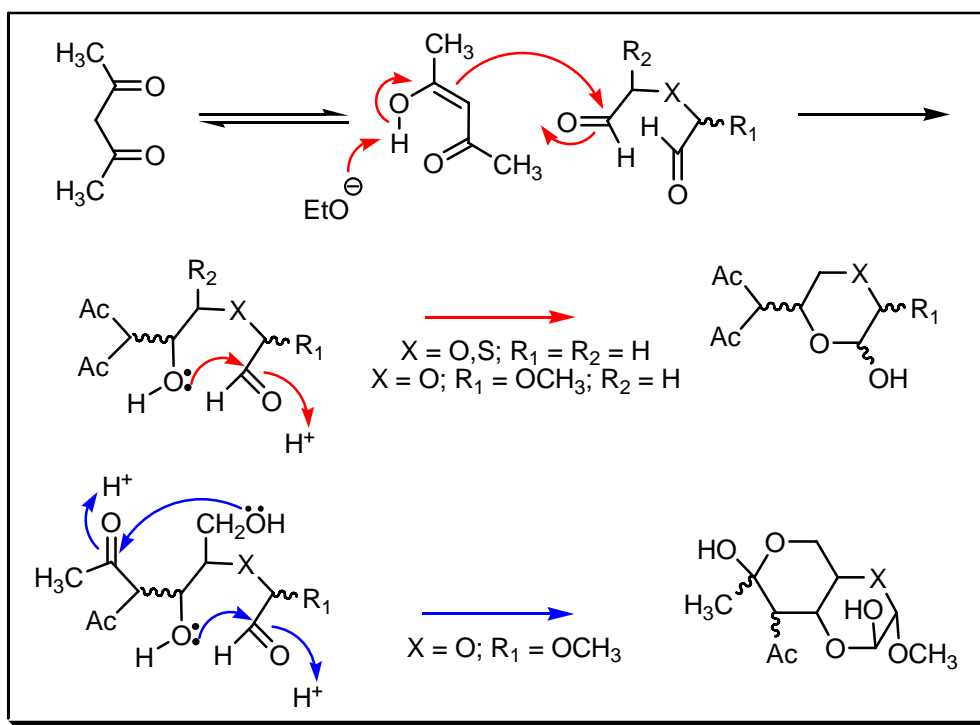
## BAER – FISCHER SYNTHESIS

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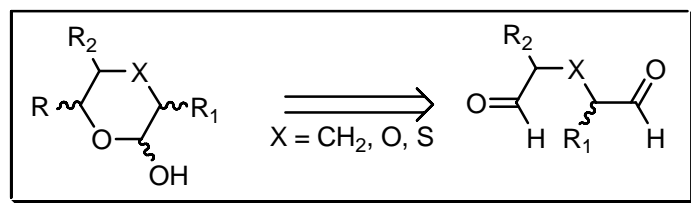
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of 3-nitro and 3-amino sugars by aldol condensation of sugar-derived dialdehydes. This synthesis allows for the introduction of acetyl, alkoxy carbonyl, carbamoyl and cyano groups into the sugar ring.

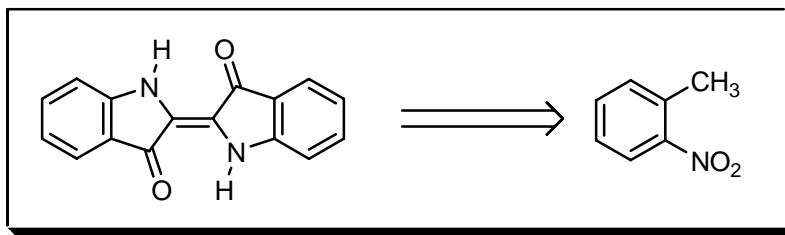
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## COMMENTS :



## DISCONNECTION :



## NOTES :

The aldol condensation of *o*-nitrobenzaldehydes with acetone, pyruvic acid or acetaldehyde to give indigo derivatives. The final coupling of the indoxyl can take place under radical coupling. The **Harley–Mason** modification gives higher yields. See also **von Baeyer – Drewson** quinoline and **Heumann** reactions.

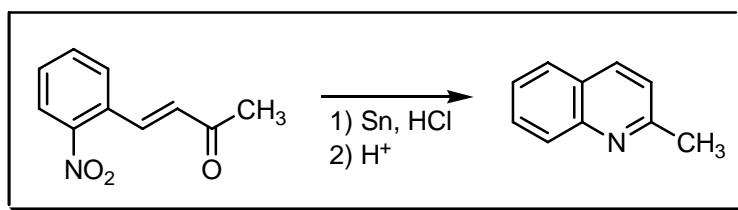
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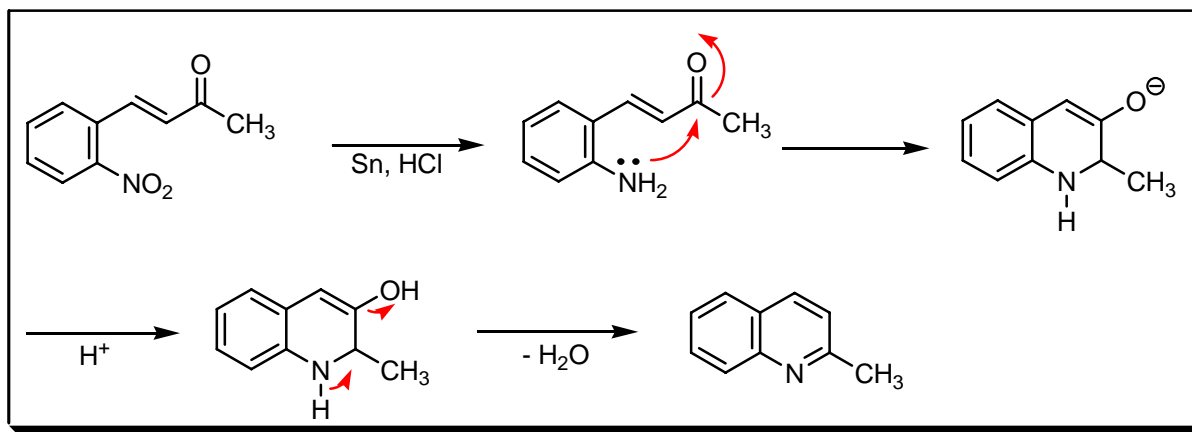
## COMMENTS :

## von BAEYER – DREWSEN QUINOLINE SYNTHESIS

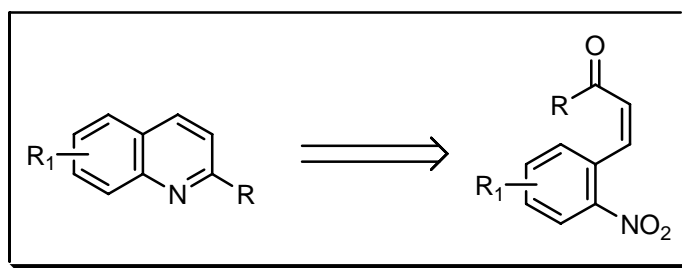
## EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

o-Nitrocinnamic aldehydes or o-nitrostyryl ketones derivatives are reduced and cyclised by dehydration to give quinolines. See also **Allan – Loudon**, **Camps**, **Combes** quinoline, **Conrad – Limpach**, **Doebner** quinoline, **Doebner – von Miller**, **Foulds – Robinson**, **Friedländer**, **Knorr** quinoline, **Meth-Cohn**, **von Niementowski** quinoline, **Pfitzinger – Borsche**, **Riehm** quinoline and **Skraup** quinoline reactions.

### REFERENCES :

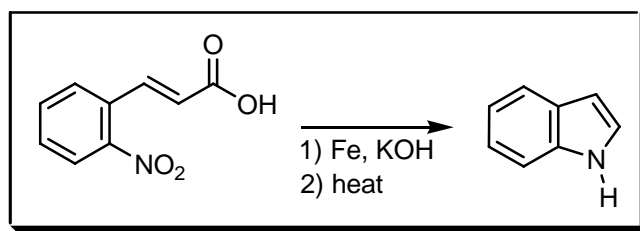
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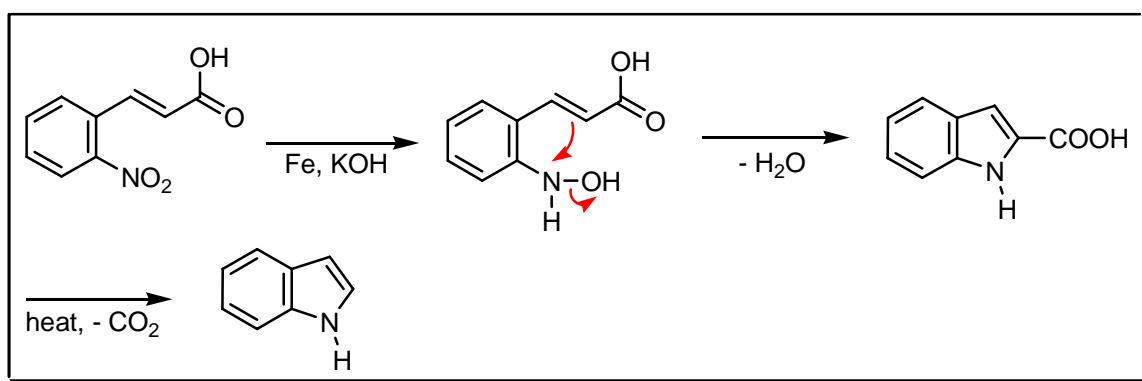


## von BAEYER – EMMERLING INDOLE SYNTHESIS

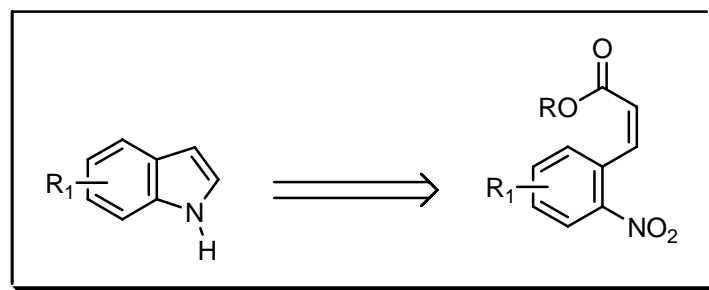
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

o-Nitrocinnamic acid undergoes reductive cyclisation when heated with iron fillings and potassium hydroxide to afford an indole. Several other compounds can induce the cyclisation step. See also **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Neenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

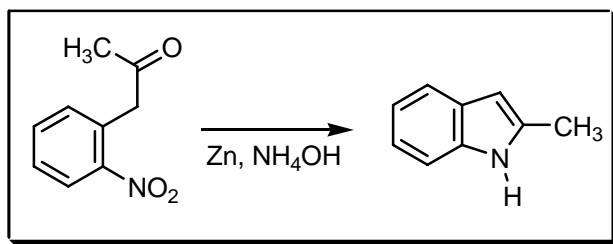
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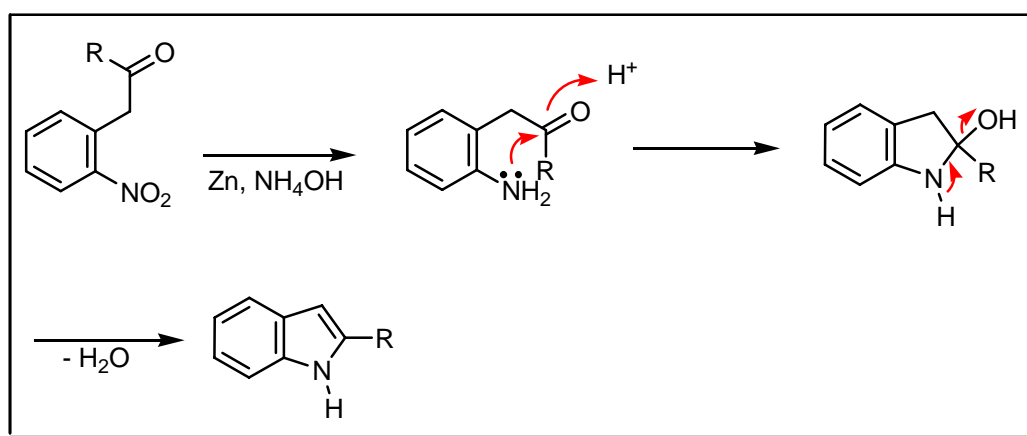
## COMMENTS :

## von BAEYER – JACKSON INDOLE SYNTHESIS

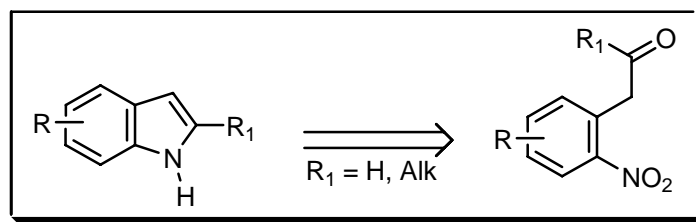
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

*o*-Nitrophenylacetaldehyde and *o*-nitrobenzyl ketones undergo reductive cyclisation to form indoles. Several reagents can be used for the cyclisation step. The reaction can easily be mistaken for the **Reissert** indole synthesis. See also **von Baeyer – Emmerling**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

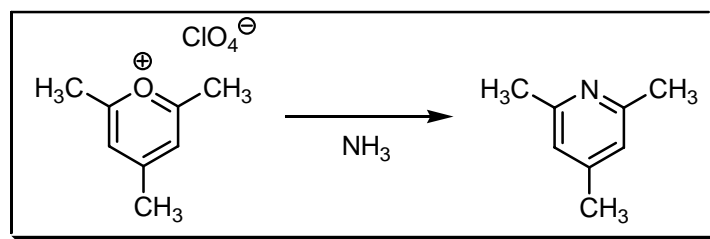
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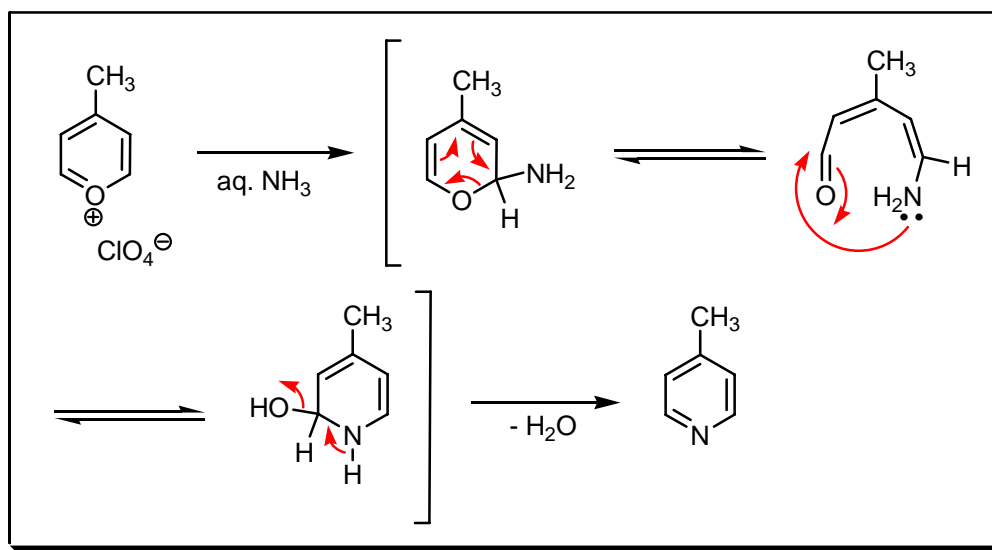
## COMMENTS :

## VON BAEYER – PICTET CONVERSION OF PYRYLIUM SALTS (KATRITZKY PYRYLIUM – PYRIDINIUM METHOD)

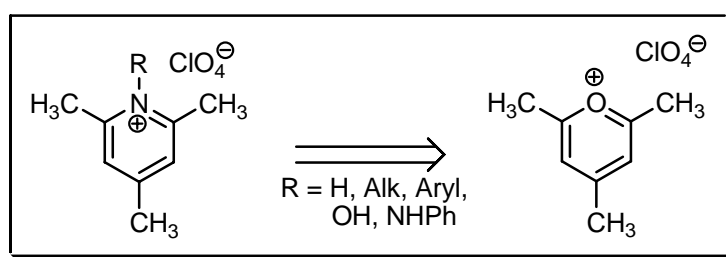
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The treatment of pyrylium salts with ammonia, primary amines, hydroxylamine or phenylhydrazine gives derivatives of pyridine. The reaction is very common and very frequently used. The oxygen can also be substituted by a sulfur using sodium sulfide. The reaction is also known as **von Baeyer – Piccard** reaction or **Katritzky** pyrylium – pyridinium method. See also **von Baeyer** pyrone and **Balaban – Nenitzescu – Prail** reactions.

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Smith – March : 447, 489, 499

Org. Synth. : 60, 34

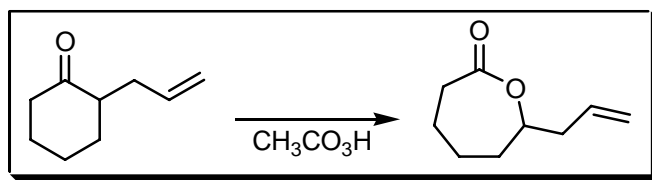
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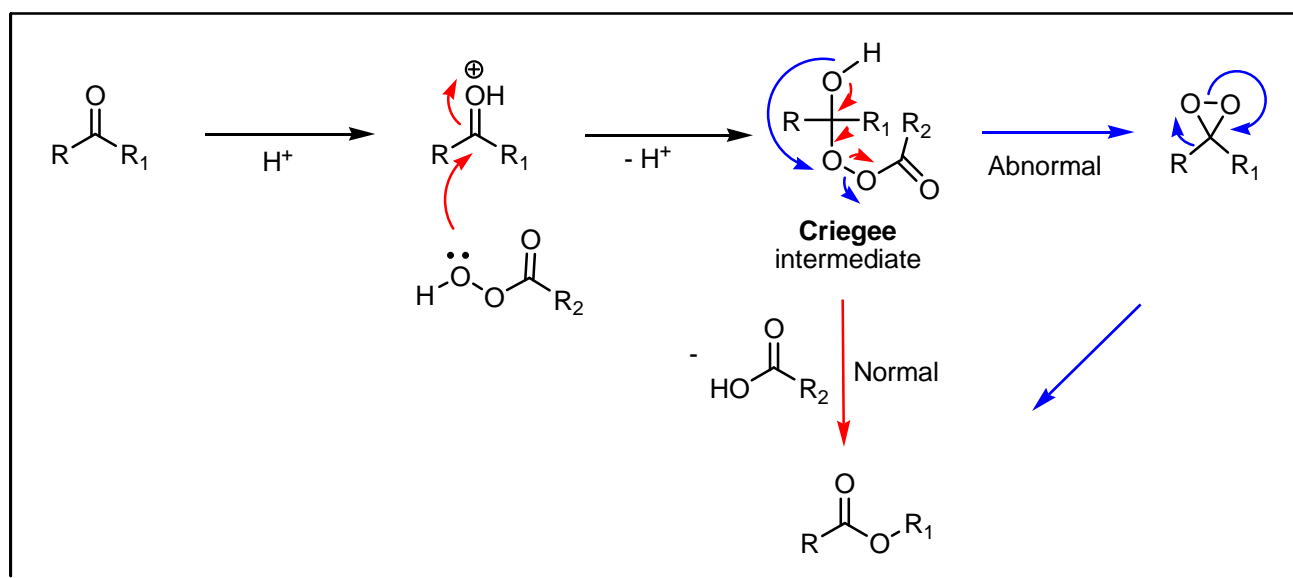
## COMMENTS :

## von BAEYER – VILLIGER REARRANGEMENT

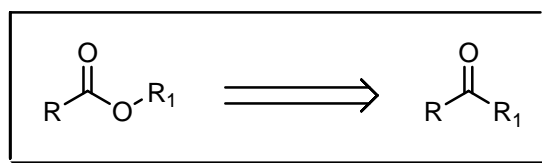
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The oxidative rearrangement of ketones using peracids, but also e.g. hydrogen peroxides with acids and bis(trimethylsilyl)monoperoxysulfate, to yield esters or lactones. Note that other functional groups can compete for the peroxyacid. The normal **von Baeyer – Villiger** reaction proceeds *via* nucleophilic addition to the ketone to afford the **Criegee** intermediate. This intermediate undergoes an *intramolecular* migration while at the same time the peroxide bond is cleaved. In the abnormal **von Baeyer – Villiger** reaction the hydroperoxide bears an extremely good leaving group. The **Criegee** intermediate gives the dioxirane *via* an *intramolecular* nucleophilic displacement. The dioxirane slowly rearranges to the lactone. Enzyme-catalysed and metal-catalysed **von Baeyer – Villiger** reactions are also known. See also **Böeseken – Ballio**, **Criegee** rearrangement and **Wagner – Meerwein** reactions.

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Smith 2<sup>nd</sup> : 258

Houben – Weyl : 6/2, 707; E3, 639; E5, 651, 712; E6a, 854; E6b, 1162; E7a, 151; E16b, 798; E19c, 408

Org. React. : 9, 73; 43, 251

Org. Synth. : 8, 30

Org. Synth. Coll. Vol. : 1, 131

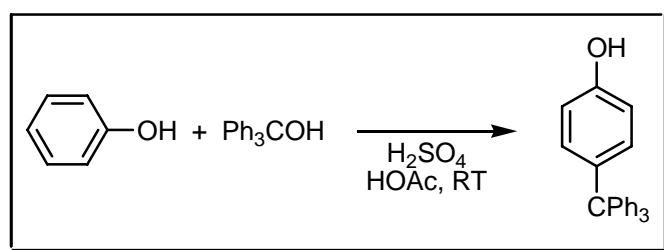
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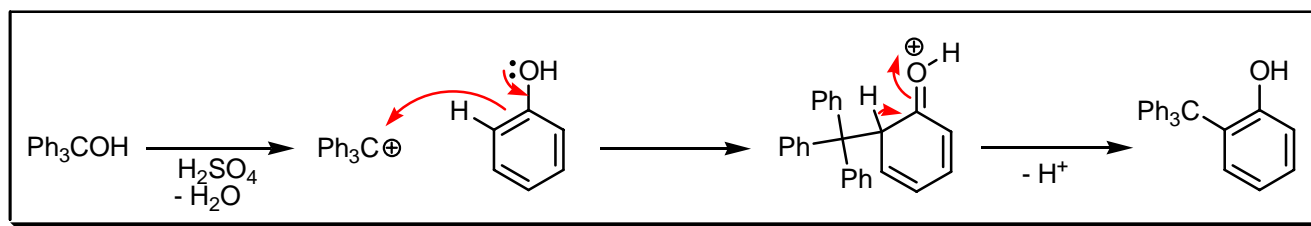
**COMMENTS :**

**von BAEYER – VILLIGER TRITYLATION**

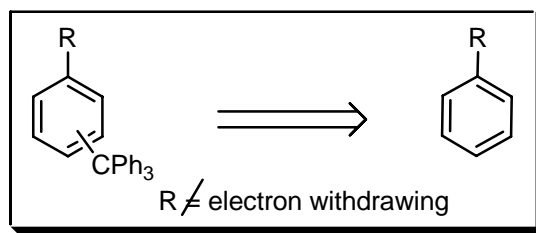
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

The introduction of a triphenylmethyl group into an aromatic ring at the *ortho* or *para* position. Electron-withdrawing groups will inhibit this reaction.

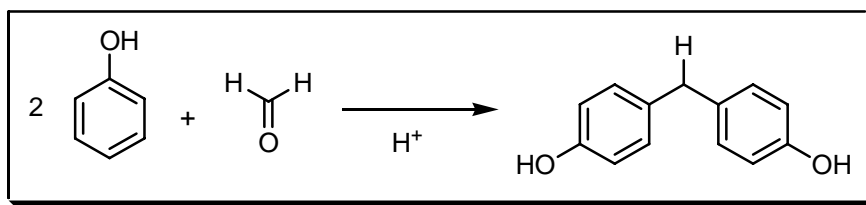
## REFERENCES :

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- 2) D.R. Boyd; G. Chignell, *J. Chem. Soc.*, 1923, 813.
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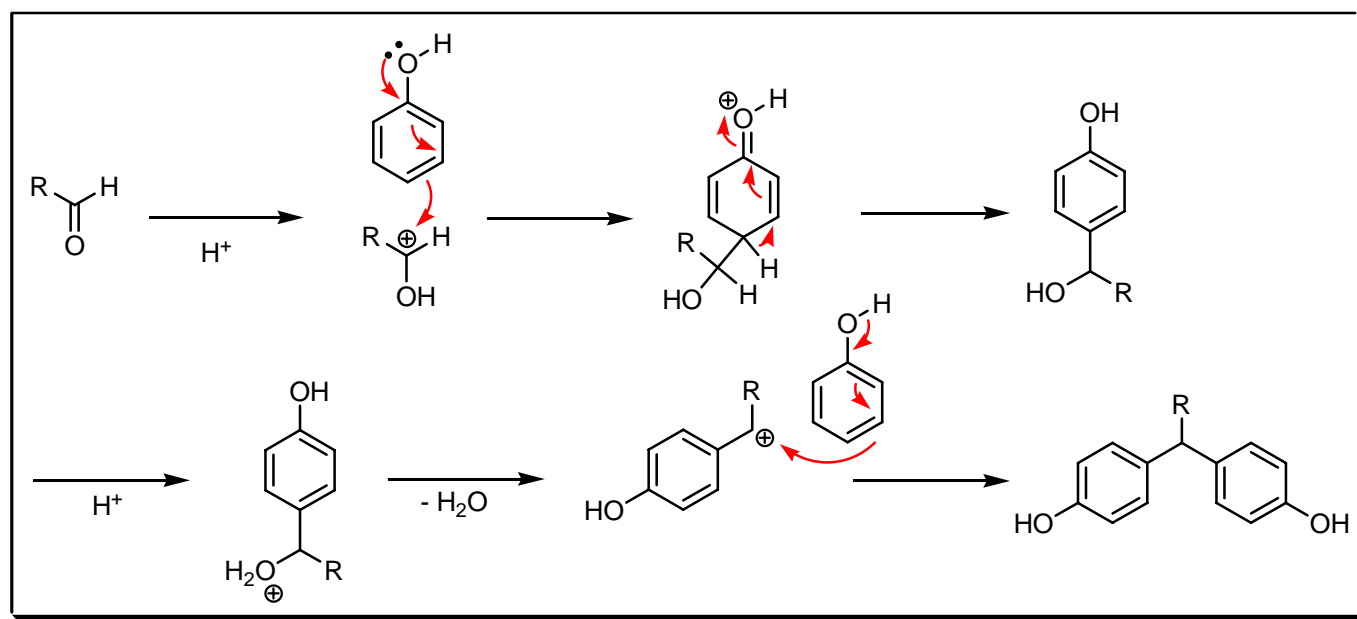
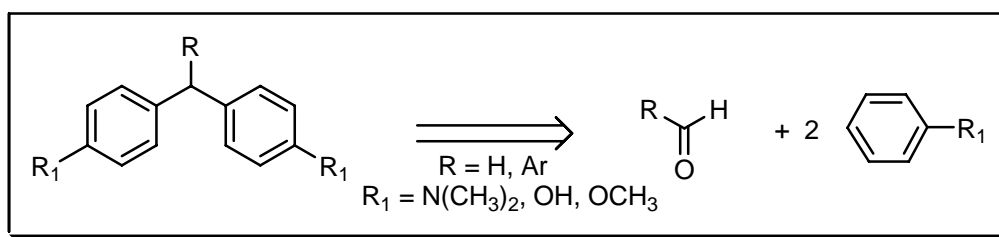
## COMMENTS :

## von BAEYER ALDEHYDE CONDENSATION

### EXAMPLE :





**MECHANISM :****DISCONNECTION :****NOTES :**

Activated aromatic compounds such as *N,N*-dimethylaniline, phenol or anisole, condense in the presence of acids, with aldehydes, e.g. formaldehyde or benzaldehyde, to form triphenylmethanes. In some cases with formaldehyde and phenol in alkaline solution resins are obtained. See also **Baekeland**, **Lederer – Manasse** and **Zinke – Ziegler** reactions.

**REFERENCES :**

**March** : 548

**Smith – March** : 719

**Org. Synth.** : 2, 17; 42, 57; 55, 45; 68, 234

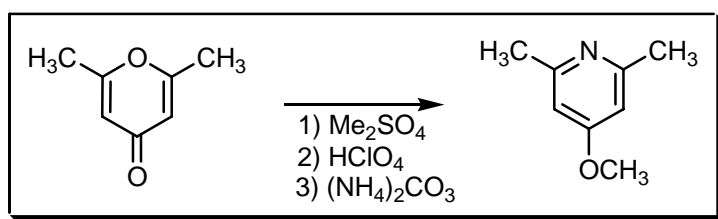
**Org. Synth. Coll. Vol.** : 1, 214; 5, 422; 6, 471; 8, 75

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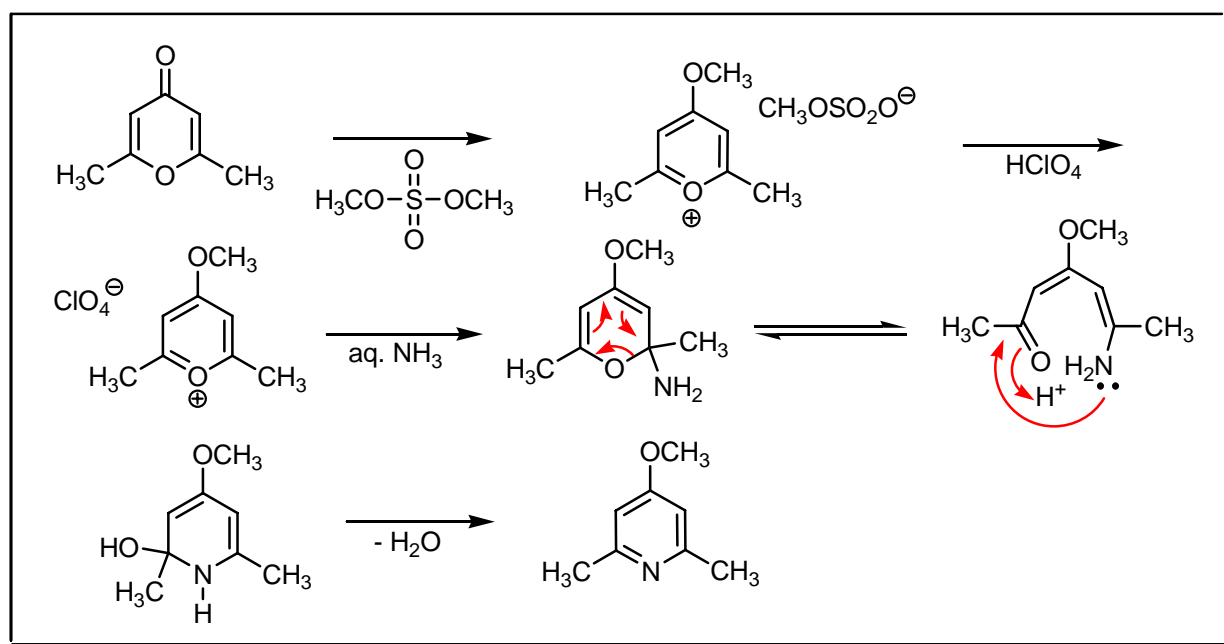
## COMMENTS :

## von BAEYER CONVERSION OF PYRONE

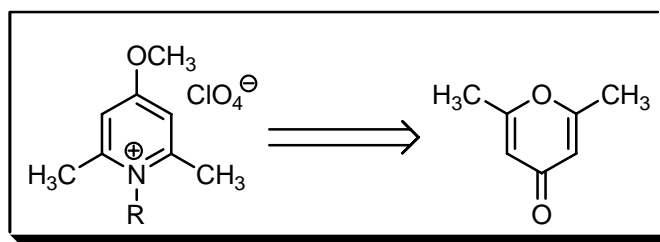
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

A pyrone when treated with dimethyl sulfate and perchloric acid and then with ammonium carbonate yields the corresponding 4-methoxypyridine. Many alkyl and aryl pyrylium salts can be converted this way into the corresponding pyridine derivatives. This reaction is a special case of the **von Baeyer – Pictet** reaction. See also **von Baeyer – Pictet (Katritzky pyrylium – pyridinium)** reaction.

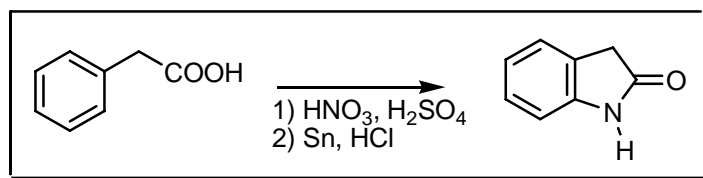
## REFERENCES :

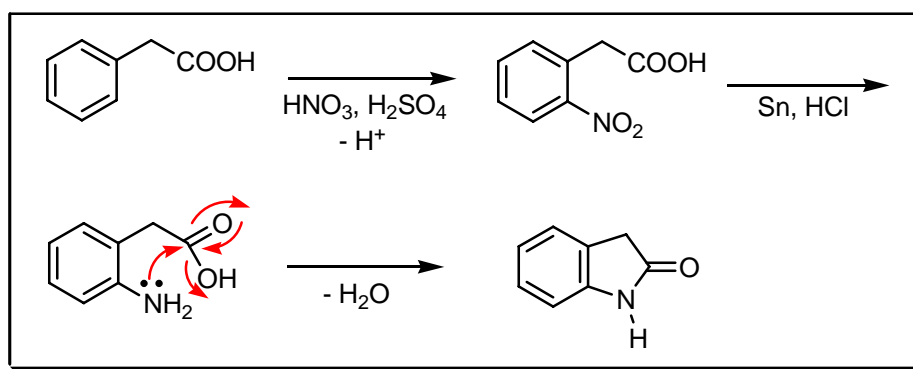
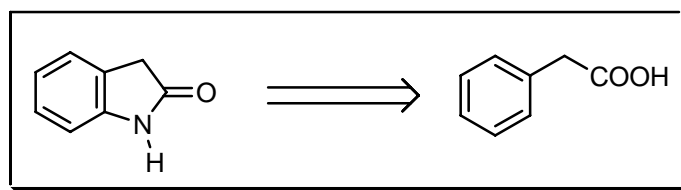
- 1) A. von Baeyer, *Ber. Dtsch. Chem. Ges.*, 1910, **43**, 2337.
- 2) W. Dilthey, *J. Prakt. Chem.*, 1916, **94**, 53.
- 3) L.F. Cavalieri, *Chem. Rev.*, 1947, **41**, 525.
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- 6) T.S. Balaban; I. Tămășan; C. Deleanu, *Liebigs Ann. Chem.*, 1992, 173.

## COMMENTS :

## von BAEYER OXINDOLE SYNTHESIS

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

The formation of an oxindole from o-aminophenylacetic acid. See also **Brunner**, **Gassman** oxindole, **Hinsberg** oxindole, **Martinet**, **Neber – Bosset** and **Stollé** reactions.

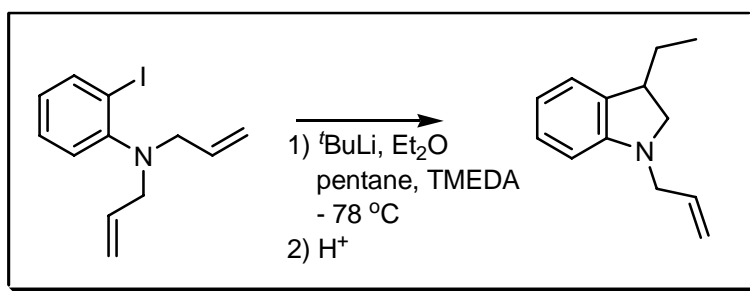
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- 2) P. Wispek, *Ber. Dtsch. Chem. Ges.*, 1883, **16**, 1577.

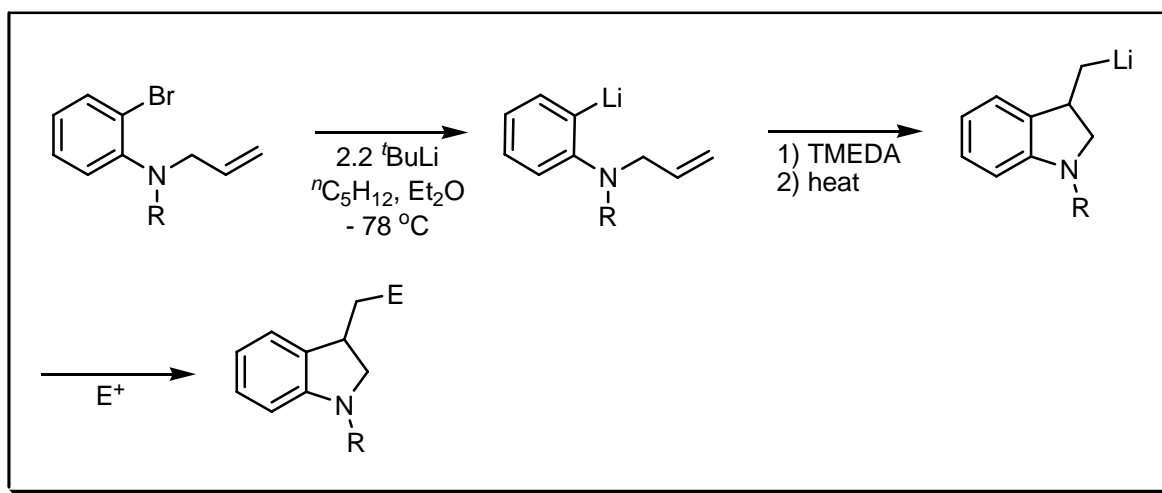
**COMMENTS :**

## BAILEY – LIEBESKIND INDOLINES SYNTHESIS

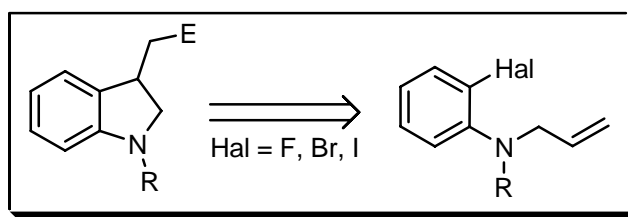
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The synthesis of 3-substituted indolines derived from [2-[N-allylamino]phenyl] lithium derivatives. Instead of bromine or iodine, the use of 2-fluoro or 3-fluoro derivatives will afford 3,4-substituted indolines.

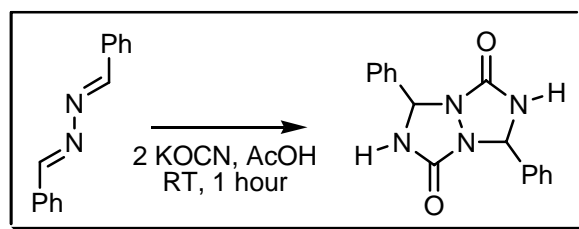
### REFERENCES :

- 1) D. Zhang; L.S. Liebeskind, *J. Org. Chem.*, 1996, **61**, 2594.
- 2) W.F. Bailey; X.-L. Jiang, *J. Org. Chem.*, 1996, **61**, 2596.
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- 4) T.S. Yokum; P.K. Tungaturthi; M.L. McLaughlin, *Tetrahedron Lett.*, 1997, **38**, 5111.

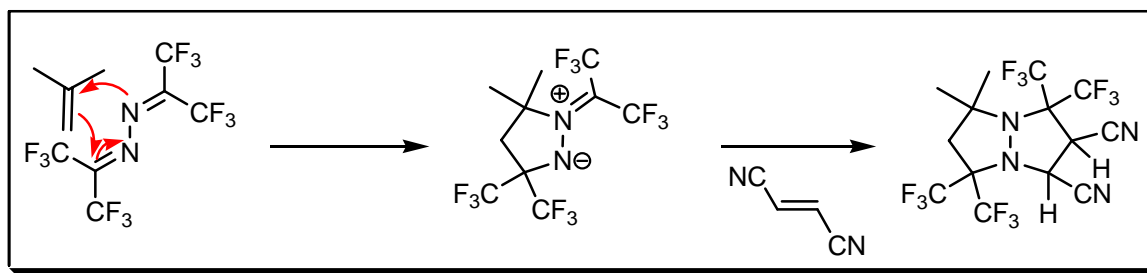
## COMMENTS :

## BAILEY CYCLOADDITION

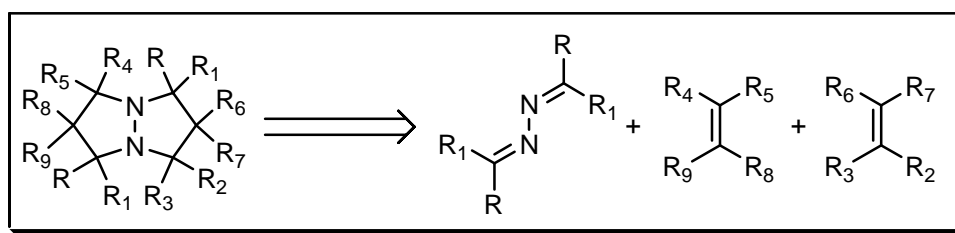
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The reaction between hydrazones and cyanic acid, thiocyanic acid, isocyanates and electron-rich olefins and acetylenes afford 1,2,4-triazolo[1,2-a][1,2,4]triazoles.

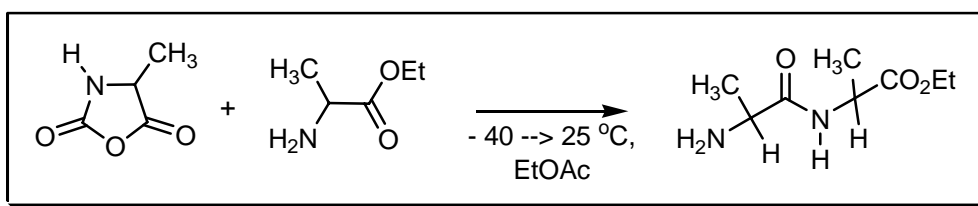
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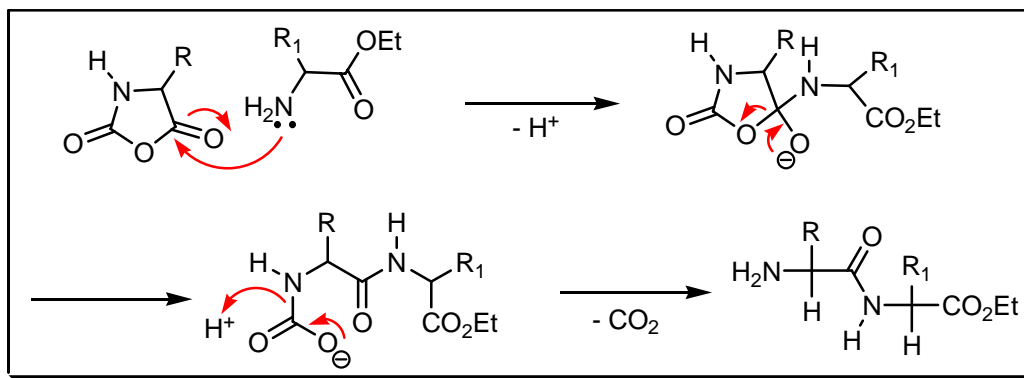
COMMENTS :

BAILEY PEPTIDE SYNTHESIS

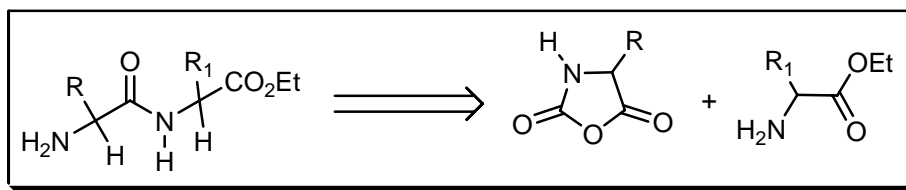
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

Peptides are prepared by the base-catalysed reaction of the corresponding anhydro-*N*-carboxy amino acids with amino acids or peptide esters in anhydrous solvents at low temperatures. See also **Cook – Levy** reaction.

## REFERENCES :

- 1) J.L. Bailey, *J. Chem. Soc.*, 1950, 3461.
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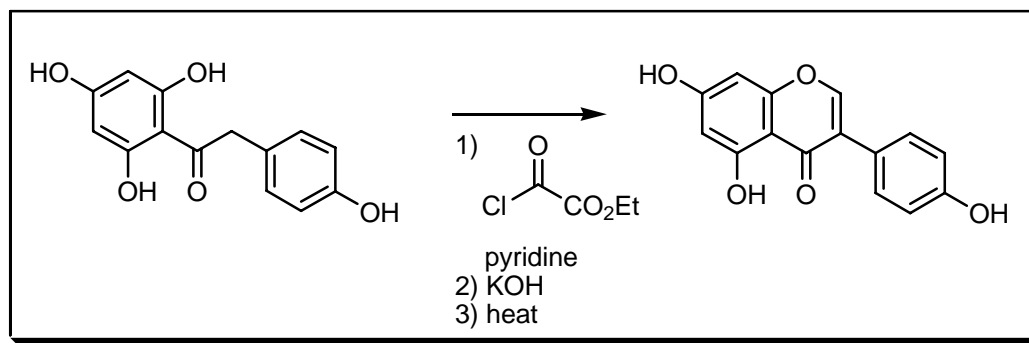
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## COMMENTS :

## BAKER – OLLIS SYNTHESIS

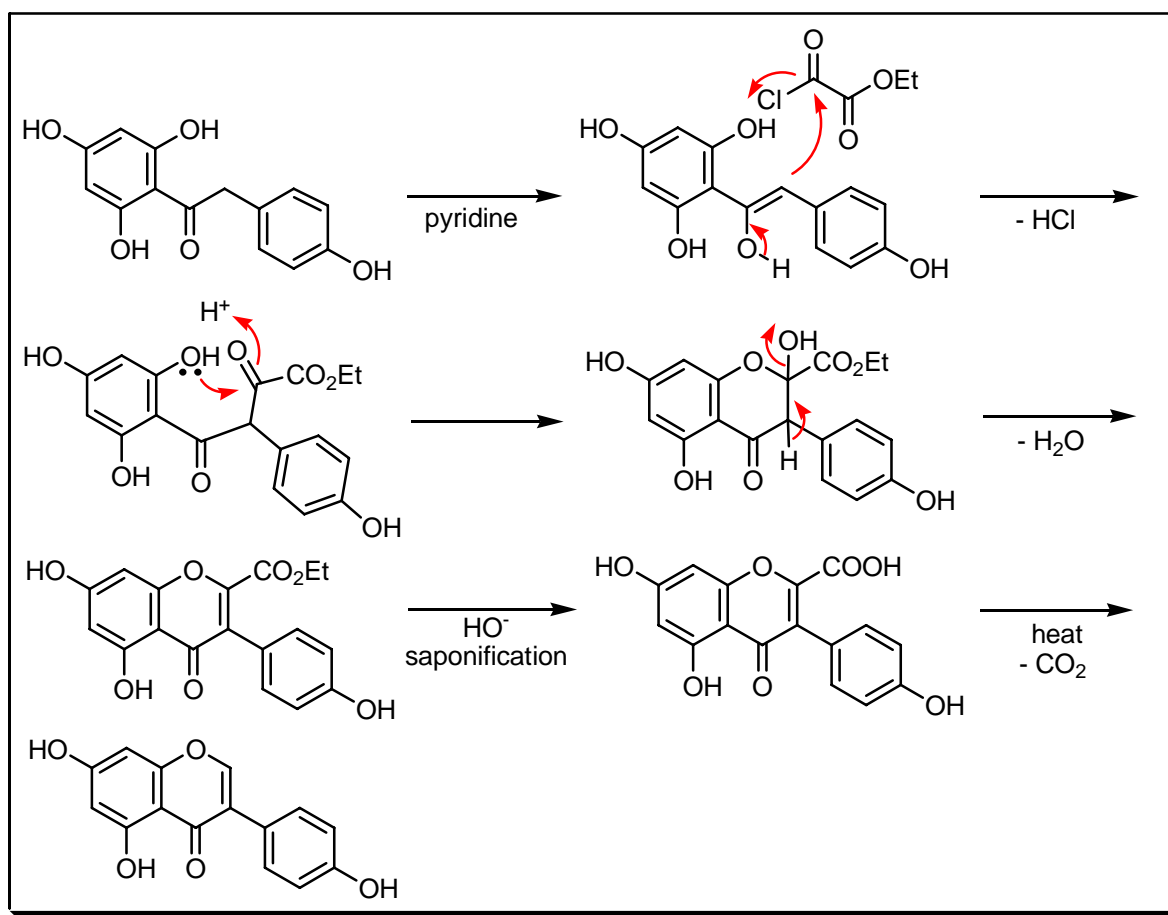
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### EXAMPLE :

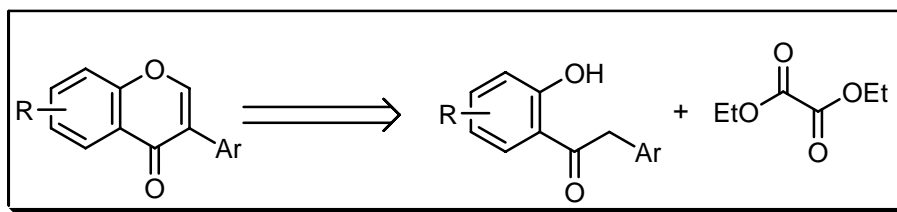




## MECHANISM :



## DISCONNECTION :



## NOTES :

Benzyl *o*-hydroxyphenyl ketones react at room temperature with 2-ethoxy-2-oxoacetyl chloride in pyridine to give 2-ethoxycarbonylisoflavones, which are hydrolysed, and decarboxylated. See also **Algar – Flynn – Oyamada**, **von Auwers** flavonol, **von Kostanecki (Allan – Robinson)** acylation, **Ranjorwa** and **Rasoda** reactions.

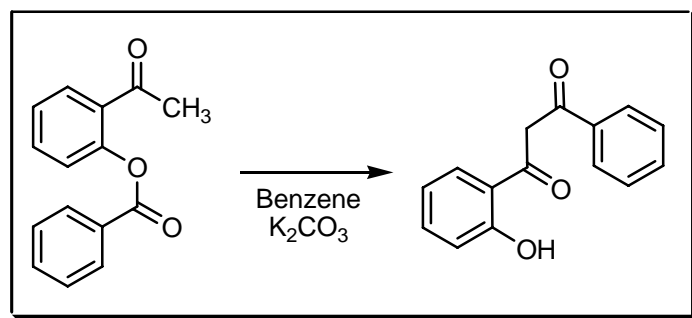
## REFERENCES :

- 1) W. Baker; J. Chadderton; J.B. Harbonne; W.D. Ollis, *J. Chem. Soc.*, 1953, 1852.
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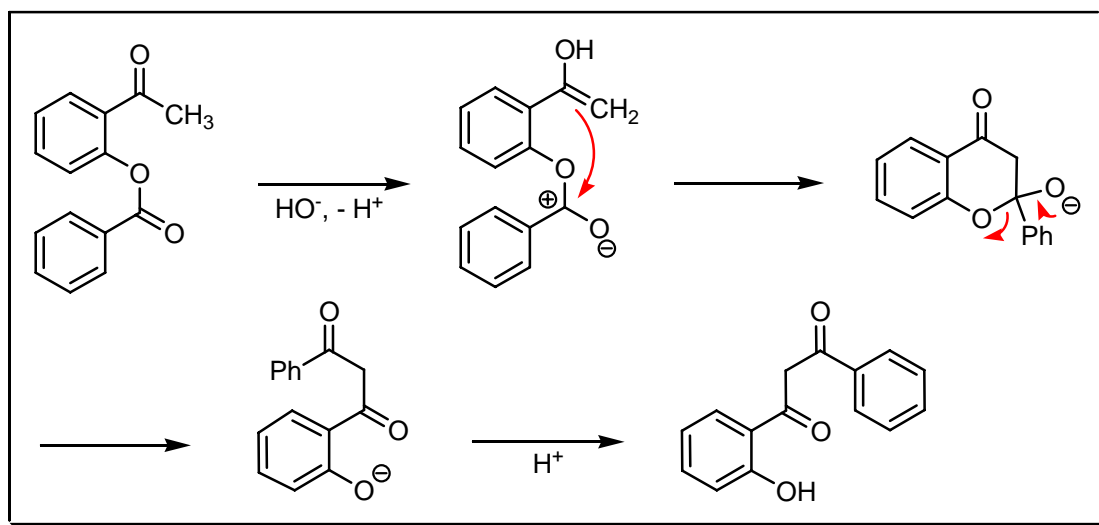
COMMENTS :

## BAKER – VENKATARAMAN REARRANGEMENT

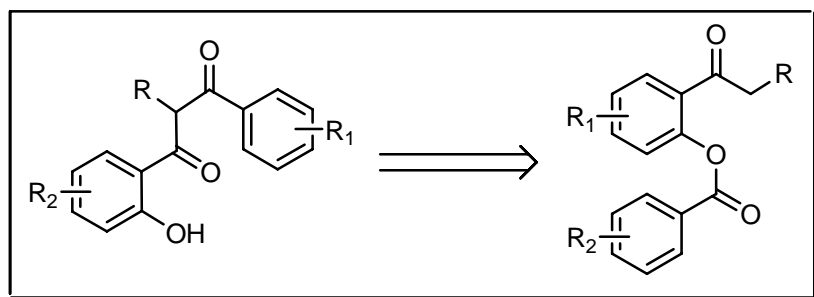
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

Originally, the base-catalysed  $\beta$ -diketone transformation of *o*-aryloxyaryl alkyl ketones into *o*-hydroxydiaroylmethanes. This reaction is widely used in the synthesis of flavones and other chromone derivatives. See also **Algar – Flynn – Oyamada**, **von Auwers** flavonol, **Baker – Ollis**, **von Kostanecki – Robinson (Allan – Robinson)**, **Ranjorwa**, **Rasoda** and **Simonis** reactions.

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## REFERENCES :

**Houben – Weyl** : 8, 580; **E8a**, 318

**Org. React.** : 8, 59.

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- 1) W. Baker, *J. Chem. Soc.*, 1933, 1381.
  - 2) H.S. Mahal; K. Venkataraman, *J. Chem. Soc.*, 1934, 1767.
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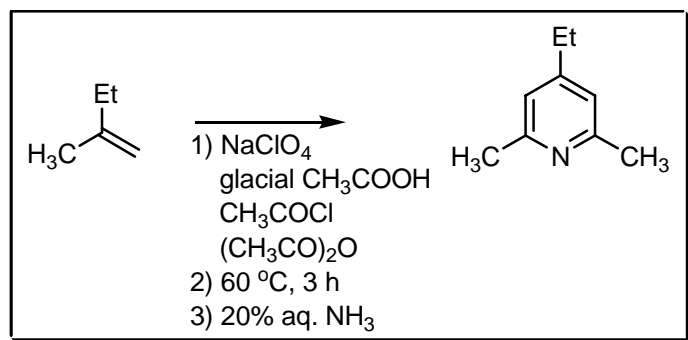
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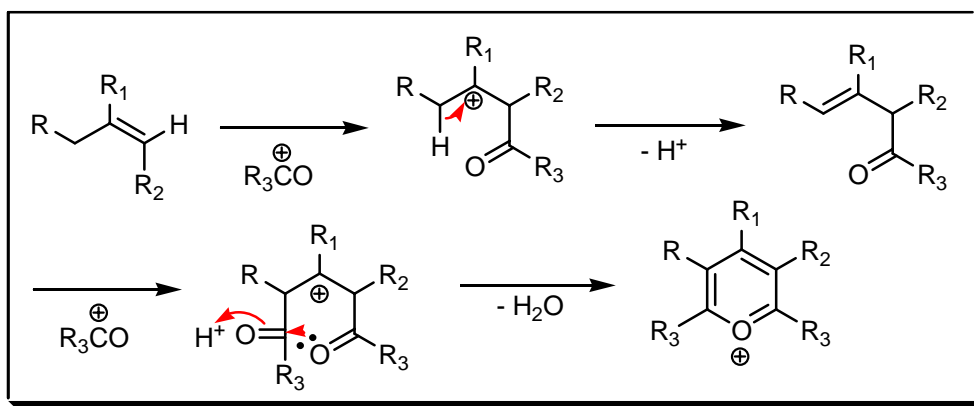
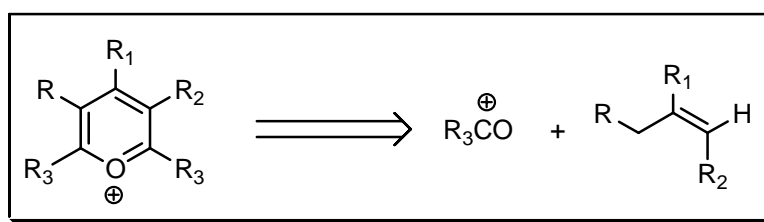
## COMMENTS :

## BALABAN – NENITZESCU – PRAILL SYNTHESIS

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### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

Pyrylium salts are obtained from olefins by **Friedel – Crafts** diacetylation. These pyrylium salts can be converted easily to pyridines. See also **von Baeyer – Pictet** conversion of pyrylium salts (**Katritzky** pyrylium – pyridinium method).

**REFERENCES :**

**March** : 354, 399, 411, 436, 445, 467

**Smith – March** : 447, 489, 499

**Org. Synth.** : **44**, 98, **49**, 121

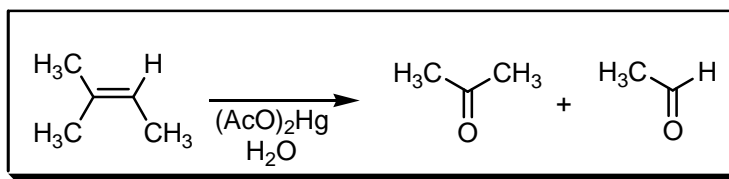
**Org. Synth. Coll. Vol.** : **5**, 1106, 1112, 1114

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- 2) A.T. Balaban; C.D. Nenitzescu, *J. Chem. Soc.*, 1961, 3553.
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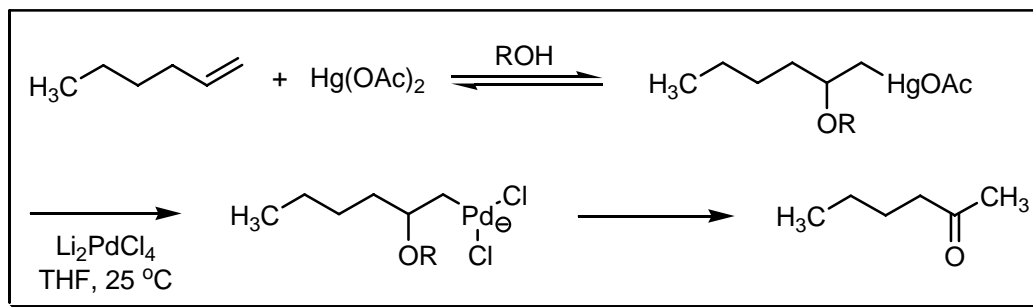
**COMMENTS :**

## BALBIANO OLEFIN OXIDATION

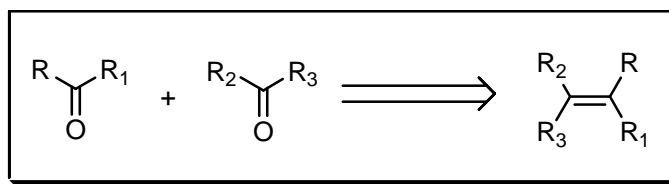
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Mercuric acetate oxidises olefins in aqueous solution. Mercuric acetate followed by palladium dichloride is also used to oxidise olefins. See also **Hofmann – Sand**, **Kutscheroff – Denigès** and **Tsuji – Wacker** reactions.

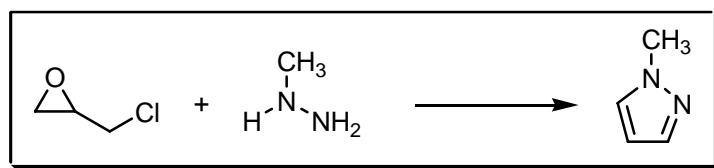
### REFERENCES :

- 1) L. Balbiano; V. Paolini, *Ber. Dtsch. Chem. Ges.*, 1902, **35**, 2994.
- 2) L. Balbiano, *Gazz. Chim. Ital.*, 1906, **36/1**, 238.
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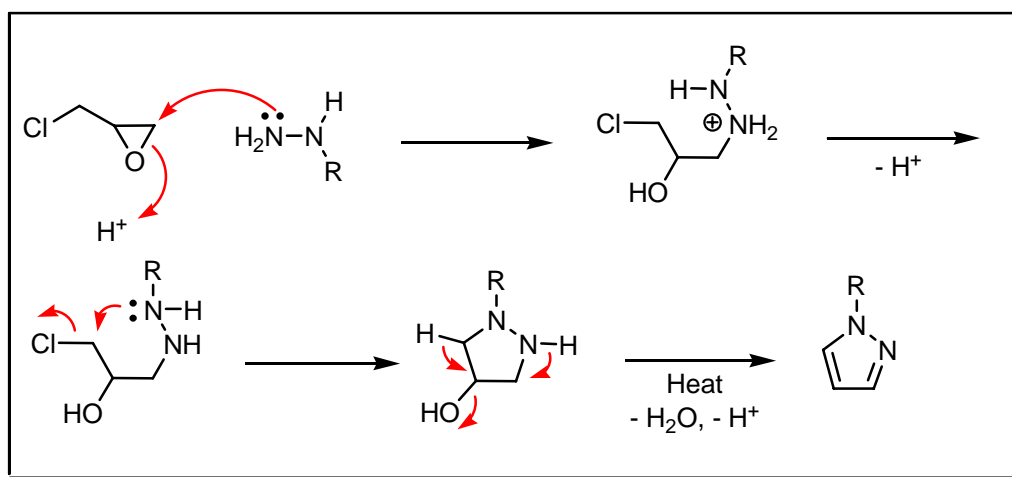
COMMENTS :

## BALBIANO PYRAZOLE SYNTHESIS

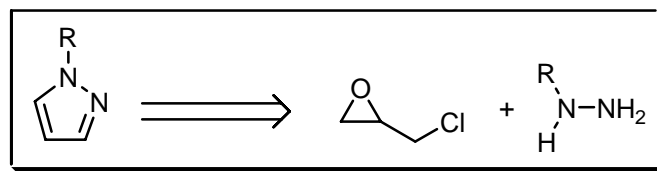
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

Epichlorohydrin and hydrazines react to form pyrazolidines, which on heating dehydrate to give pyrazoles. The reaction can also be done in the presence of zinc chloride. See also **Knorr** pyrazole and **von Pechmann** reactions.

REFERENCES :

- 1) L. Balbiano, *Gazz. Chim. Ital.*, 1887, **17**, 177.
- 2) L. Balbiano, *Ber. Dtsch. Chem. Ges.*, 1890, **23**, 1452.

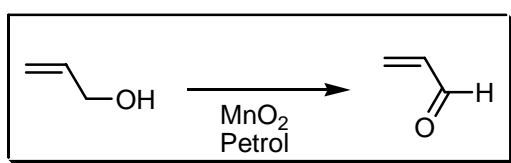
3) R. Stoermer; O. Martinsen, *Liebigs Ann. Chem.*, 1907, **352**, 322.

4) I.L. Finar; K.E. Godfrey, *J. Chem. Soc.*, 1954, 2293.

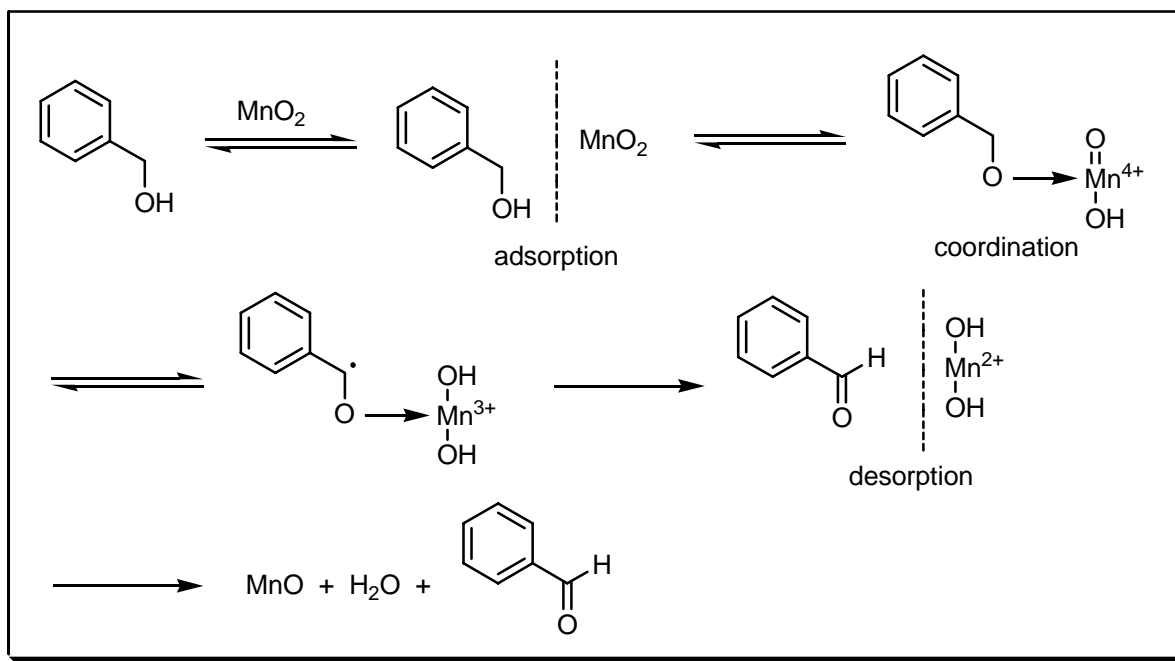
COMMENTS :

## BALL – GOODWIN – MORTON OXIDATION

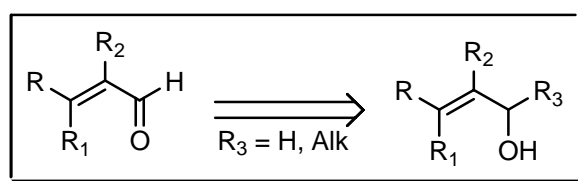
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

The oxidation of primary or secondary allylic alcohols in an inert solvent (light petroleum) by manganese dioxide, yields the corresponding aldehyde or ketone. The method has been extended to acetylenic alcohols, heterocyclic alcohols, steroidal allylic alcohols and to aromatic alcohols. The mechanism is most probably radical in nature, but an ionic mechanism has been proposed. See also **Anelli, Collins, Corey – Kim, Corey – Schmidt, Corey – Suggs, David – Thieffry, Delépine, Dess – Martin, Einhorn** oxidation, **Fétizon, Jones** oxidation, **Ley, Maurer – Drefahl, Mukaiyama** oxidation, **Nicolaou, Oppenauer, Parikh – von Doering, Pfitzner – Moffatt, Pinnick, Sarett, Swern** and **Uemura** reactions.

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## REFERENCES :

**March** : 1167

**Smith** : 245

**Smith 2<sup>nd</sup>** : 213

**Houben – Weyl** : 7/1, 178

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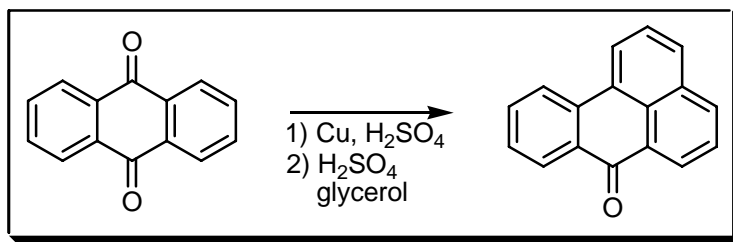
- 1) S. Ball; T.W. Goodwin; R.A. Morton, *Biochem. J.*, 1948, **42**, 516.
  - 2) N.L. Wendler; H.L. Slates; M. Tischler, *J. Am. Chem. Soc.*, 1949, **71**, 3267.
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  - 4) E.J. Corey; N.W. Gilman; B.E. Ganem, *J. Am. Chem. Soc.*, 1968, **90**, 5616.
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  - 6) G. Struve; S. Seltzer, *J. Org. Chem.*, 1982, **47**, 2109.
  - 7) B.M. König; W. Friedrichsen, *Tetrahedron Lett.*, 1987, **28**, 4279.
  - 8) X.Y. Xiao; G.D. Prestwich, *Synth. Commun.*, 1990, **20**, 3125.
  - 9) J.A. Haugan, *Tetrahedron Lett.*, 1996, **37**, 3887.
  - 10) I. Hemeon; N.W. Barnett; N. Gathergood; P.J. Scammells; R.D. Singer, *Aust. J. Chem.*, 2004, **57**, 125.
- 

## COMMENTS :

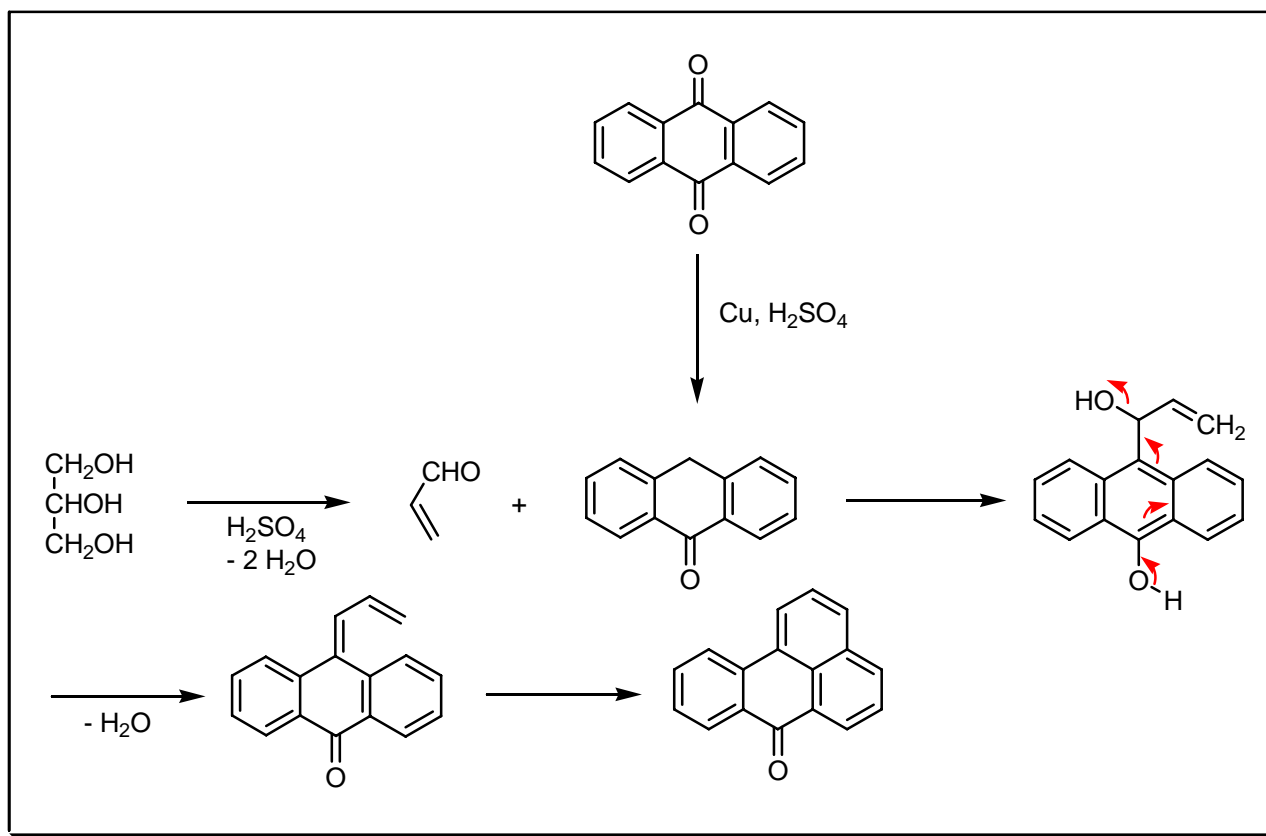


## BALLY – SCHOLL SYNTHESIS

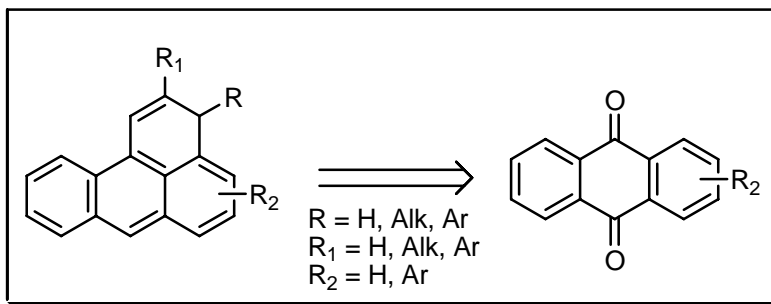
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The synthesis of mesobenzanthrones from glycerol or its derivatives and sulfuric acid on anthraquinones or anthranols. The yields are normally low due to the strong acidic conditions used. See also **Haworth** and **Skraup** reactions.

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## REFERENCES :

Smith : 1330

Smith 2<sup>nd</sup> : 1094, 1101

Org. Synth. : 14, 4

Org. Synth. Coll. Vol. : 2, 62

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- 1) O. Bally, *Ber. Dtsch. Chem. Ges.*, 1905, **38**, 194.
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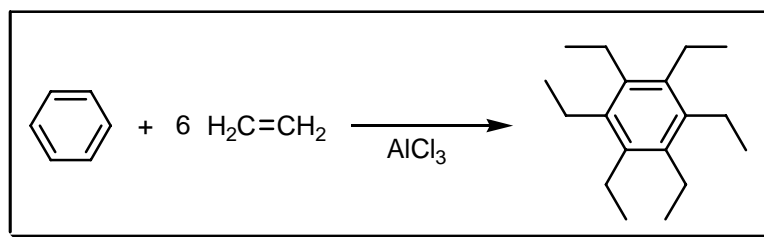
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## COMMENTS :

## BALSOHN ADDITION

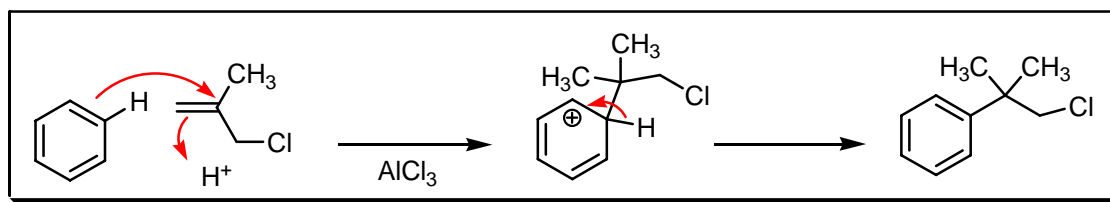
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### EXAMPLE :

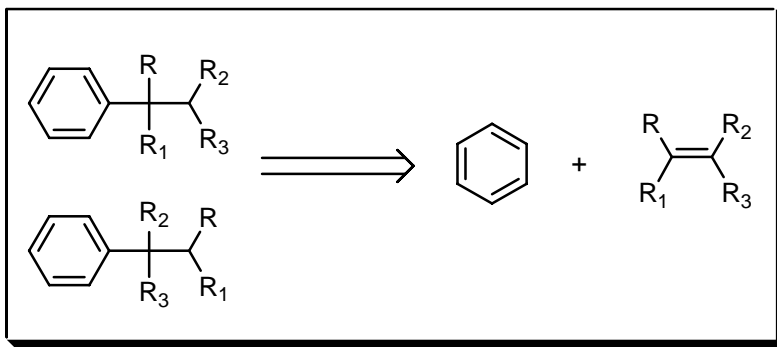


---

### MECHANISM :



## DISCONNECTION :



## NOTES :

The reaction between an olefin or compounds which under the reaction conditions would be expected to react like olefins and benzene (or another isocyclic compound) to give a hexaalkylbenzene. Many groups are tolerated on the aromatic ring. Acids or Lewis acids are normally used as catalysts. The mechanism is similar to the **Friedel – Crafts** mechanism. See also **Friedel – Crafts** reaction.

## REFERENCES :

**Org. Synth.** : **32**, 90

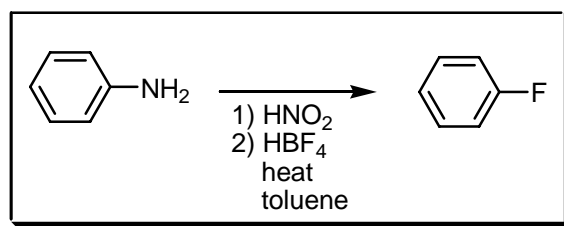
**Org. Synth. Coll. Vol.** : **4**, 702

- 1) M. Balsohn, *Bull. Soc. Chim. Fr.*, 1879, **31**, 539.
- 2) W.M. Potts; L.L. Carpenter, *J. Am. Chem. Soc.*, 1939, **61**, 663.
- 3) W.S. Calcot; J.M. Tinker; V. Weinmayr, *J. Am. Chem. Soc.*, 1939, **61**, 1010.
- 4) I. Schmerling; V.N. Ipatieff, *J. Am. Chem. Soc.*, 1945, **67**, 1862.

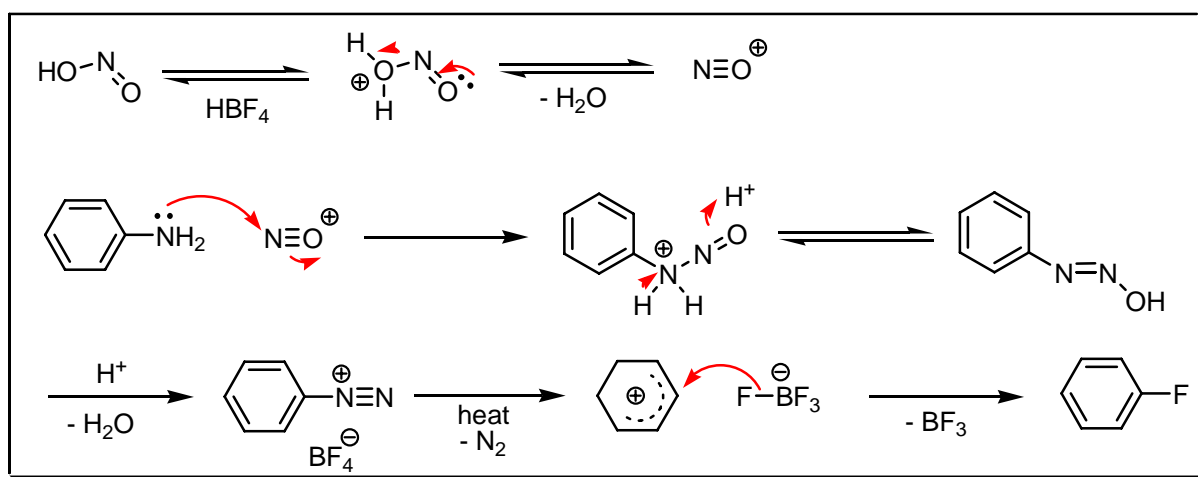
## COMMENTS :

## BALZ – SCHIEMANN REACTION

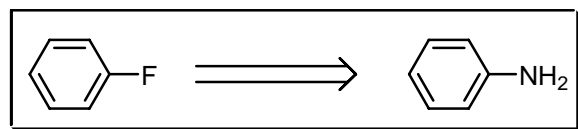
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

A two-stage preparation of aryl fluorides involving the preparation of a dry diazonium borofluoride by the interaction of an amine, nitrous acid and fluoroboric acid followed by the thermal decomposition of the diazonium borofluoride. See also **Cadogan** arylation, **Craig** exchange, **Demjanov** rearrangement, **Gattermann** diazo, **Gattermann** sulfinic acid, **Griess** deamination, **Knoevenagel** diazotation, **Körner – Contardi**, **Meerwein** arylation, **Sandmeyer** diazonium, **Schwechten** and **Witt** diazotation reactions.

## REFERENCES :

March : 671

Smith – March : 875

Houben – Weyl : 5/3, 214; E6b, 1162; E10a, 705; E10/b1, 249; E16a, 1091; E18, 264

Org. React. : 5, 193

Org. Synth. : 43, 12

Org. Synth. Coll. Vol. : 2, 299

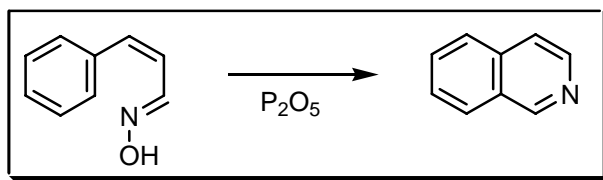
- 
- 1) G. Balz; G. Schiemann, *Ber. Dtsch. Chem. Ges.*, 1927, **60**, 1186.
  - 2) R. Stephens; J.C. Tatlow, *J. Chem. Soc., Quat. Rev.*, 1961, **15**, 54.
  - 3) K.G. Rutherford; W. Redmond; J. Rigamonti, *J. Org. Chem.*, 1961, **26**, 5149.
  - 4) D.E. Horning; D.A. Ross; J.M. Muchowski, *Can. J. Chem.*, 1973, **51**, 2347.
  - 5) M. Matsumoto; Y. Ishida; N. Hatanaka, *Heterocycles*, 1986, **24**, 1667.
  - 6) N. Yoneda; T. Fukuhara; T. Kikuchi; A. Suzuki, *Synth. Commun.*, 1989, **19**, 865.
  - 7) D.J. Milner, *Synth. Commun.*, 1992, **22**, 73.
  - 8) K.K. Laali; V.J. Gettewert, *J. Fluorine Chem.*, 2001, **107**, 31.
  - 9) Y. Nishiyama; S. Ishizuka; K. Kurita, *Tetrahedron Lett.*, 2001, **42**, 8797.
  - 10) R. Gronheid; G. Lodder; T. Okuyama, *J. Org. Chem.*, 2002, **67**, 693.
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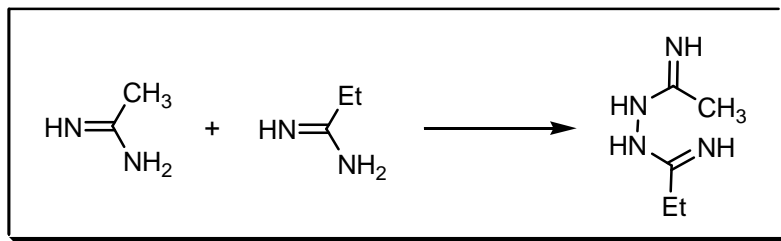
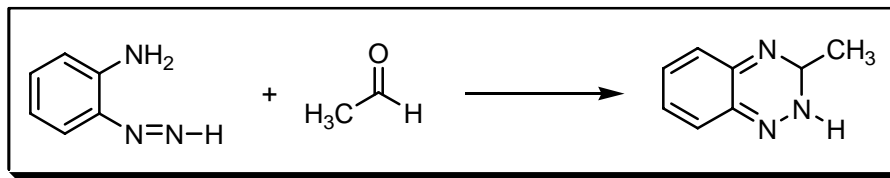
## COMMENTS :

## BAMBERGER – GOLDSCHMIDT SYNTHESIS

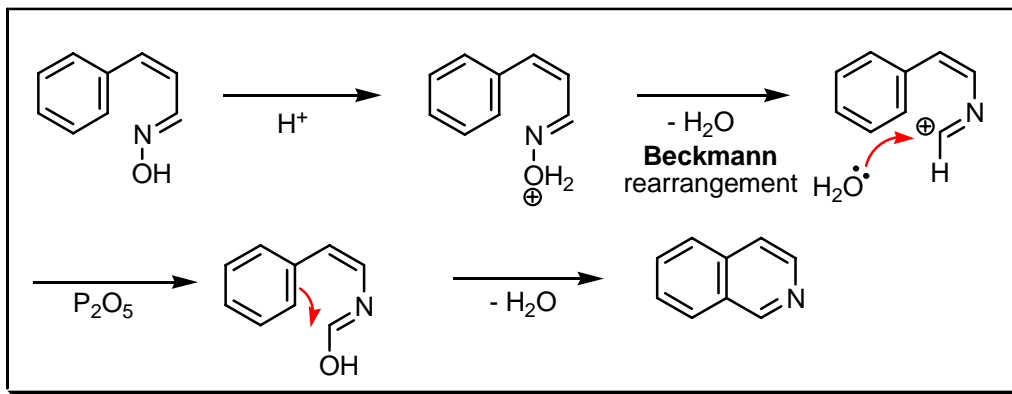
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### EXAMPLE :

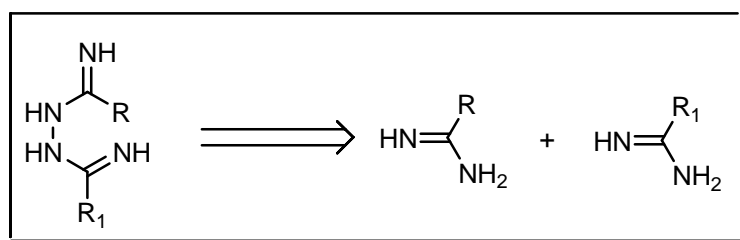
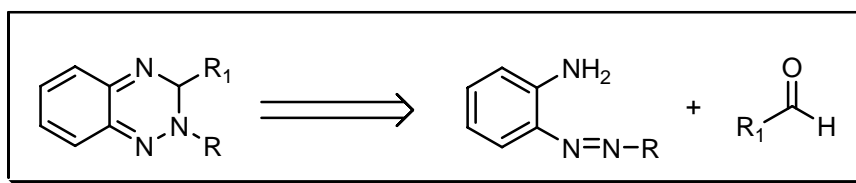
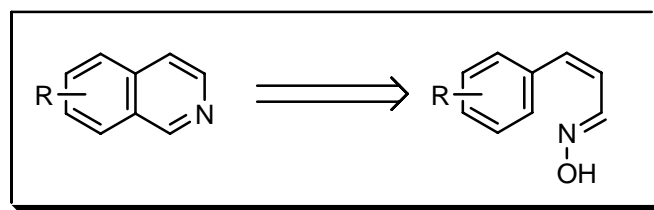




### MECHANISM :



### DISCONNECTION :



## NOTES :

Styryl oximes on treatment with phosphorous pentoxide undergo a **Beckmann** rearrangement followed by internal condensation to yield isoquinolines. Dihydroisoquinolines may be obtained from phenylethyl oximes. Besides the mentioned reaction other sources name the synthesis of 1,2,4-triazines and 1,3,5-triazines the **Bamberger – Goldschmidt** reaction (H. Goldschmidt), I have included two examples. See also **Beckmann** rearrangement, **Bischler – Napieralski**, **Bobbit**, **Bruckner**, **Larock** indole, **Pictet – Gams**, **Pictet – Sprengler**, **Pomeranz – Fritsch**, **Simchen** and **Schlitter – Müller** ring-closure reactions.

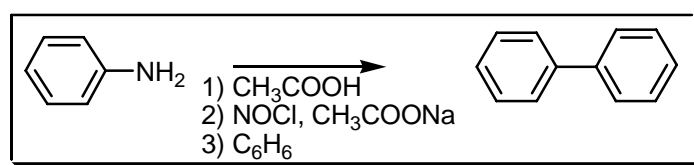
## REFERENCES :

- 1) H. Goldschmidt; Y. Rosell, *Ber. Dtsch. Chem. Ges.*, 1890, **23**, 487.
- 2) E. Bamberger; W. Dieckmann, *Ber. Dtsch. Chem. Ges.*, 1892, **25**, 534.
- 3) E. Bamberger; C. Goldschmidt, *Ber. Dtsch. Chem. Ges.*, 1894, **27**, 1954.
- 4) C. Goldschmidt, *Ber. Dtsch. Chem. Ges.*, 1894, **27**, 2795.
- 5) C. Goldschmidt, *Ber. Dtsch. Chem. Ges.*, 1895, **28**, 1532.
- 6) R.H. Manske, *Chem. Rev.*, 1942, **30**, 145.

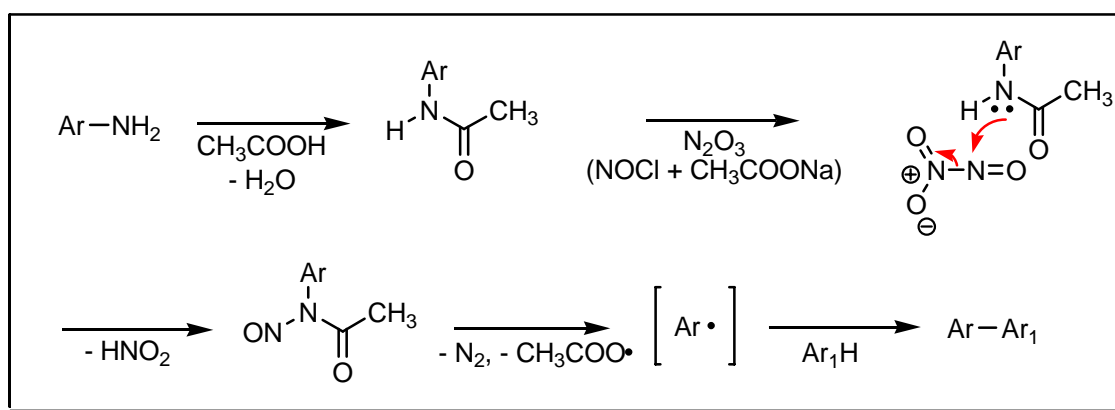
## COMMENTS :

## BAMBERGER – HEY DIARYL SYNTHESIS

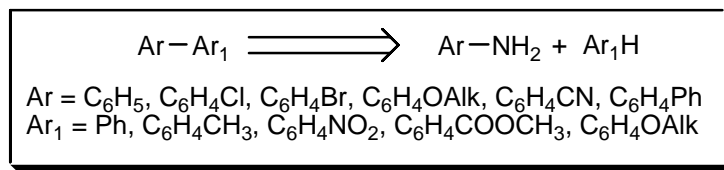
### EXAMPLE :



### MECHANISM :



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**DISCONNECTION :**

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**NOTES :**

Acylarylnitrosamines react with liquid aromatic hydrocarbons to yield diaryls. The mechanism is radical in nature. See also **Gomberg – Bachman – Hey** reaction.

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**REFERENCES :**

**Org. React. : 2, 224**

- 
- 1) E. Bamberger, *Ber. Dtsch. Chem. Ges.*, 1897, **30**, 366.
  - 2) W.S.M. Grieve; D.H. Hey, *J. Chem. Soc.*, 1934, 1797.
  - 3) D.R. Angood; G.H. Williams, *Chem. Rev.*, 1957, **57**, 123.

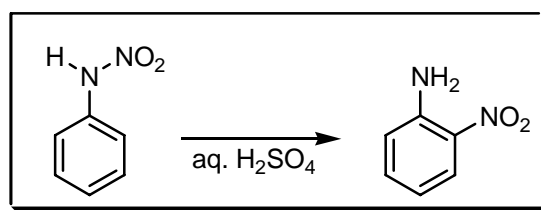
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**COMMENTS :**

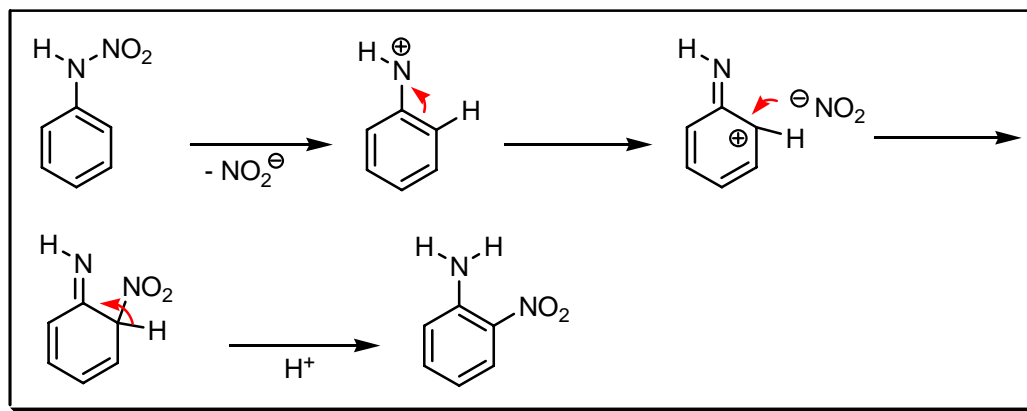
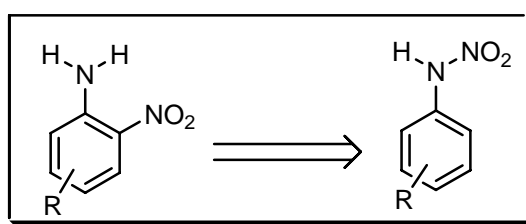
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**BAMBERGER ARYLNITRAMINES REARRANGEMENT**

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**EXAMPLE :**



**MECHANISM :****DISCONNECTION :****NOTES :**

Arylnitramines undergo rearrangement on treatment with aqueous strong acids or with hydrogen chloride in organic solvents or with a mixture of glacial acetic acid and sulfuric acid to give mainly *o*-nitranilines and a small amount of *p*-nitranilines.

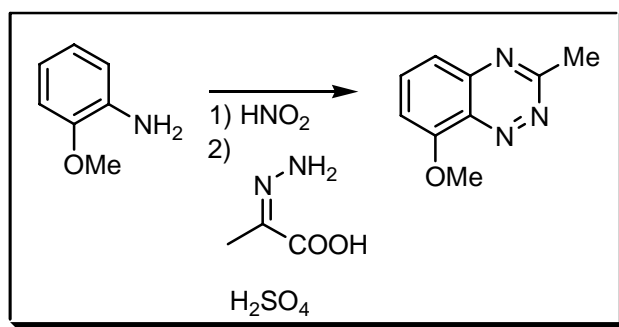
**REFERENCES :**

- 1) E. Bamberger; K. Landsteiner, *Ber. Dtsch. Chem. Ges.*, 1893, **26**, 482.
- 2) E. Bamberger, *Ber. Dtsch. Chem. Ges.*, 1899, **32**, 1809.
- 3) P.H. Gore, *J. Chem. Soc.*, 1957, 1437.

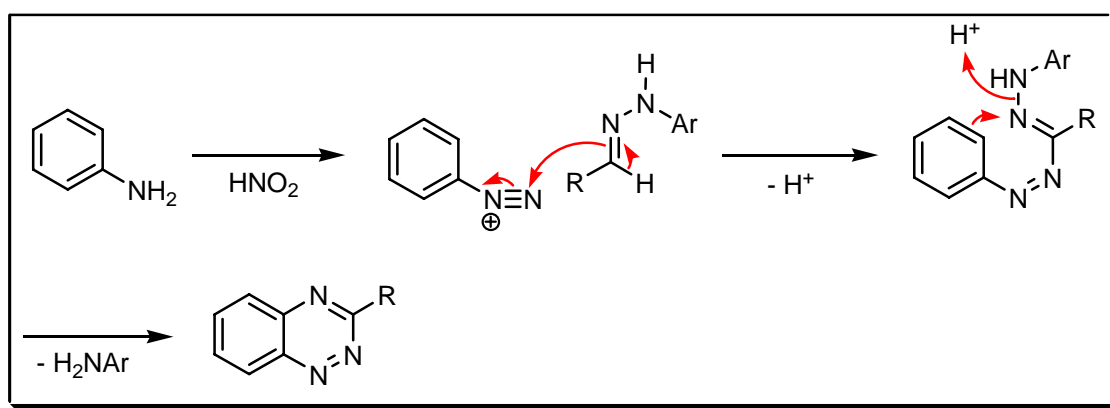
**COMMENTS :**

# BAMBERGER BENZOTRIAZINE SYNTHESIS

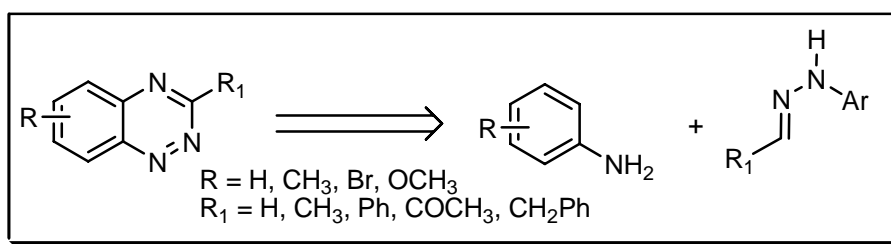
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Benzotriazine is synthesised from a hydrazone and aryldiazoamine salts.

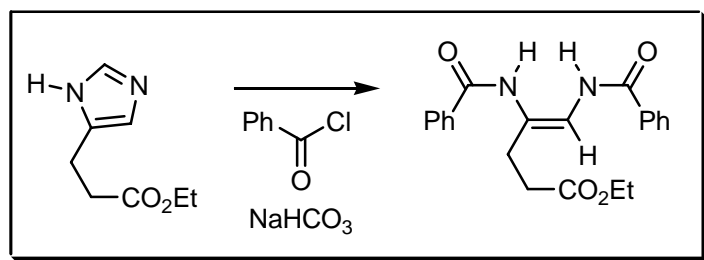
## REFERENCES :

- 1) E. Bamberger; E. Wheelwright, *Ber. Dtsch. Chem. Ges.*, 1892, **25**, 3201.
- 2) E. Bamberger; J. Lorenzen, *Ber. Dtsch. Chem. Ges.*, 1892, **25**, 3539.
- 3) E. Bamberger; H. Witter, *Ber. Dtsch. Chem. Ges.*, 1893, **26**, 2786.
- 4) E. Bamberger; R. Padova; E. Ormered, *Liebigs Ann. Chem.*, 1925, **446**, 260.

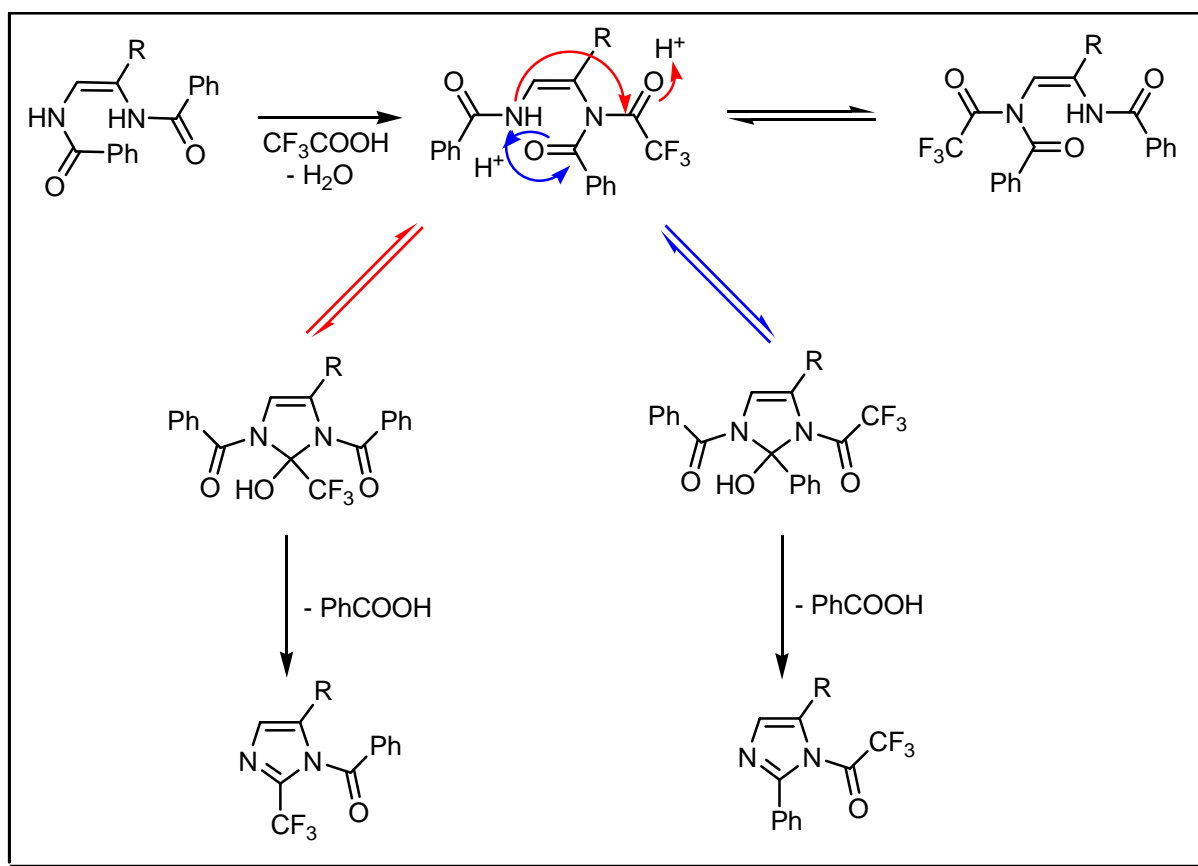
COMMENTS :

## BAMBERGER IMIDAZOLE REARRANGEMENT

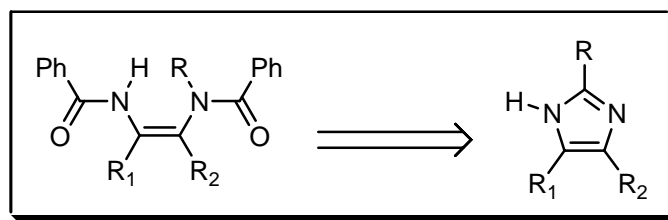
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The cleavage of imidazoles with acid chlorides or similar compounds to enediamides, 2-substituted imidazoles are formed if the enediamides are cyclised again.

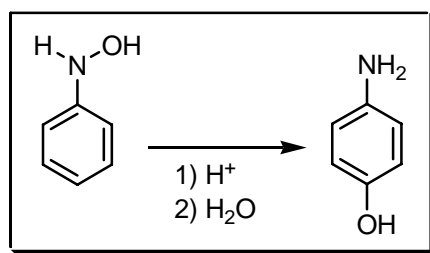
## REFERENCES :

- 1) E. Bamberger; B. Berl , *Liebigs Ann. Chem.*, 1893, **273**, 342.
- 2) H. Kimoto; K.L. Kirk; L.A. Cohen, *J. Org. Chem.*, 1978, **43**, 3403.
- 3) M.E. Grace; M.J. Loosemoore; M.L. Semmel; R.F. Pratt, *J. Am. Chem. Soc.*, 1980, **102**, 6784.
- 4) J. Altman; N. Shoef; M. Wilchek; A. Warshawsky, *J. Chem. Soc., Perkin Trans. 1*, 1984, 59.

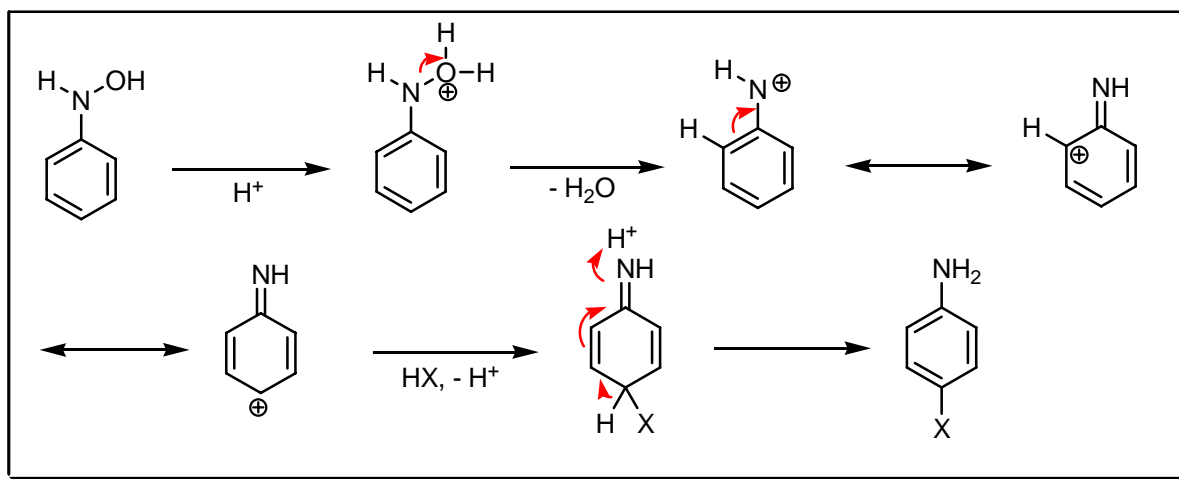
## COMMENTS :

## BAMBERGER REARRANGEMENT

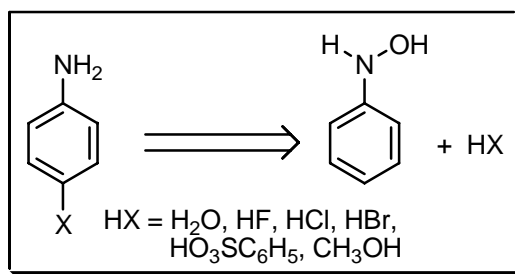
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Arylnitramines undergo rearrangement on treatment with aqueous strong acids or with hydrogen chloride in organic solvents or with a mixture of glacial acetic acid and sulfuric acid to give mainly o-nitranilines. The reaction seems to resemble the **Hoffman – Martius (Reilly – Hickingbottom)** reaction. However, while the **Hoffman – Martius** reaction follows an electrophilic mechanism, the **Bamberger** reaction seems to follow a nucleophilic mechanism. See also **Hoffman – Martius (Reilly – Hickingbottom)** and **Orton** reactions.

## REFERENCES :

March : 674

Smith – March : 878

Houben – Weyl : 10/1, 1249; E8a, 144; E19c, 382

Org. Synth. : 67, 187

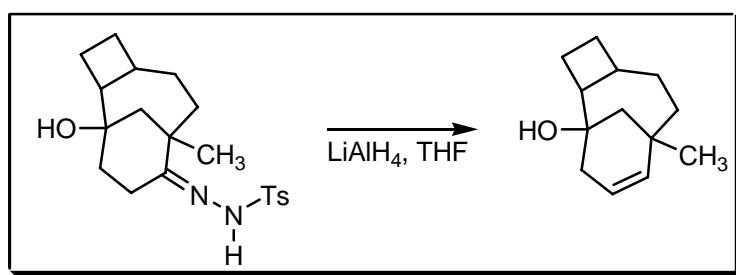
Org. Synth. Coll. Vol. : 8, 16

- 1) E. Bamberger, *Ber. Dtsch. Chem. Ges.*, 1894, **27**, 1347.
- 2) E.D. Hughes; C.K. Ingold, *J. Chem. Soc., Quat. Rev.*, 1952, **6**, 45.
- 3) J.C. Hardy; M. Venet, *Tetrahedron Lett.*, 1982, **21**, 1255.
- 4) J.C. Fishbein; R.A. McClelland, *J. Am. Chem. Soc.*, 1987, **109**, 2824.
- 5) A. Zoran; O. Khodzhaev; Y. Sasson, *Chem. Commun.*, 1994, 2239.
- 6) M. Novak; J. Lin, *J. Org. Chem.*, 1999, **64**, 6032.

**COMMENTS :**

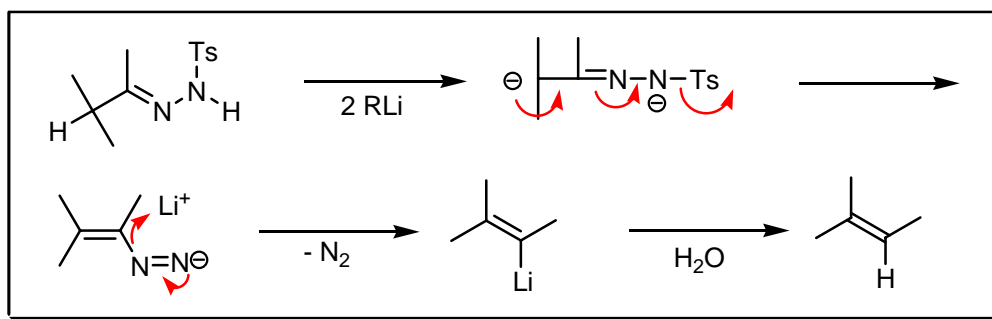
**BAMFORD – STEVENS REACTION (CAGLIOTI – SHAPIRO REACTION)**

**EXAMPLE :**

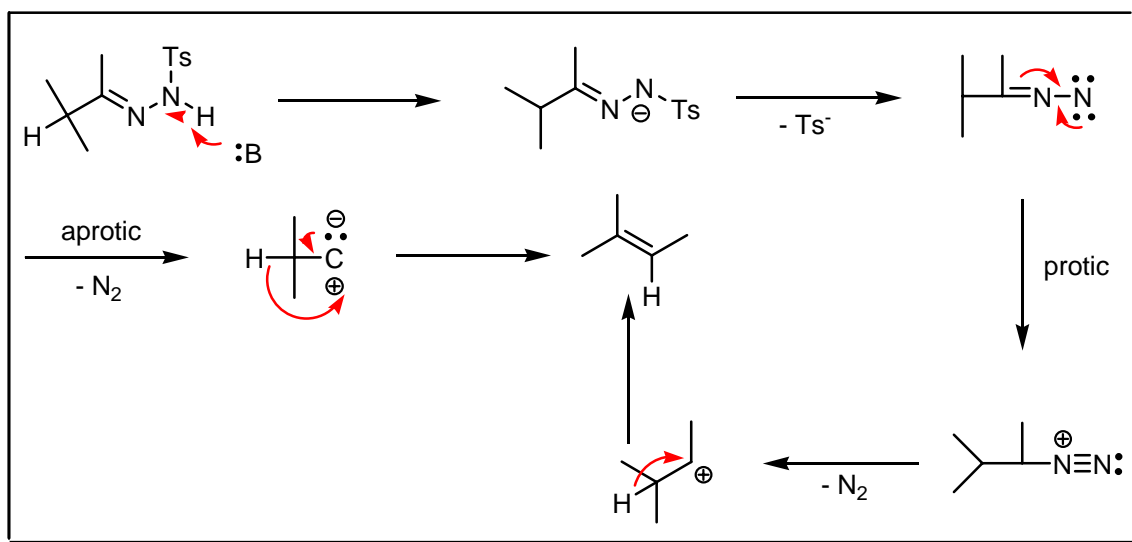


**MECHANISM :**

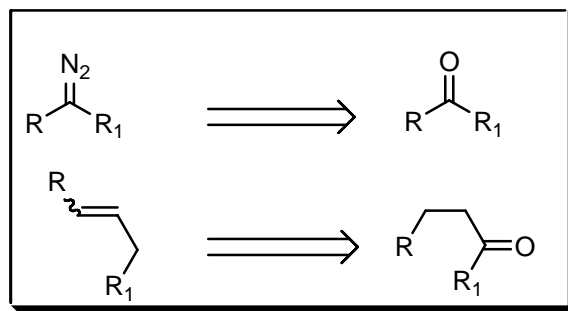
**Dianion mechanism (Shapiro) :**



## Carbene mechanism :



## DISCONNECTION :



## NOTES :

The major difference between the **Caglioti – Shapiro** and the **Bamford – Stevens** reaction is the use of the base. In the **Caglioti – Shapiro** reaction two equivalents of base (RLi) are used, and the alkene formed is generally the less-substituted one. With other bases, the alkene is often the more-substituted one. When sodium and ethylene glycol are used as base, a carbene mechanism is probable; whereas with other bases, the anion or carbene mechanisms may be involved. See also **Cava** rearrangement.

## REFERENCES :

March : 1020

Smith – March : 1335

Smith : 1454

Smith 2<sup>nd</sup> : 1200

Houben – Weyl : 5/1b, 698; E5, 148; E8b, 492; E8d, 83; E8d, 83; E11, 622; E14b, 606, 626, 1009, 1140, 1330; E19b, 225, 610, 675

Org. React. : 23, 405; 39, 1

Org. Synth. : 51, 66

Org. Synth. Coll. Vol. : 6, 172

- 1) W.R. Bamford; T.S. Stevens, *J. Chem. Soc.*, 1952, 4735.
- 2) R. Caglioti, *Tetrahedron Lett.*, 1962, **3**, 1261.
- 3) R.H. Shapiro, *Tetrahedron Lett.*, 1968, **9**, 345.
- 4) A. Nikon; P.S. Zurer, *J. Org. Chem.*, 1981, **46**, 4685.
- 5) R.M. Adlington; A.G.M. Barrett, *Acc. Chem. Res.*, 1983, **16**, 55.
- 6) A. Nickon; A.G. Stern; M.C. Ilao, *Tetrahedron Lett.*, 1993, **34**, 1391.
- 7) K. Maruoka; M. Oishi; H. Yamamoto, *J. Am. Chem. Soc.*, 1996, **118**, 2289.
- 8) K.K. Olmstead; A. Nickon, *Tetrahedron*, 1999, **55**, 7389.
- 9) M.S. Addie; R.J.K. Taylor, *Arkivoc*, 2000, **1**, 660.
- 10) S. Chandrasekhar; G. Rajaiah; L. Chandraiah; D.N. Swamy, *Synlett*, 2001, 1779.
- 11) J.A. May; B.M. Stolz, *J. Am. Chem. Soc.*, 2002, **124**, 12426.

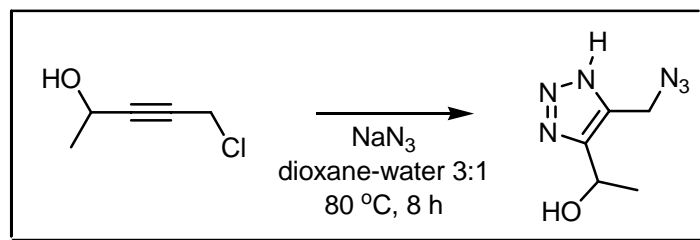
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**COMMENTS :**

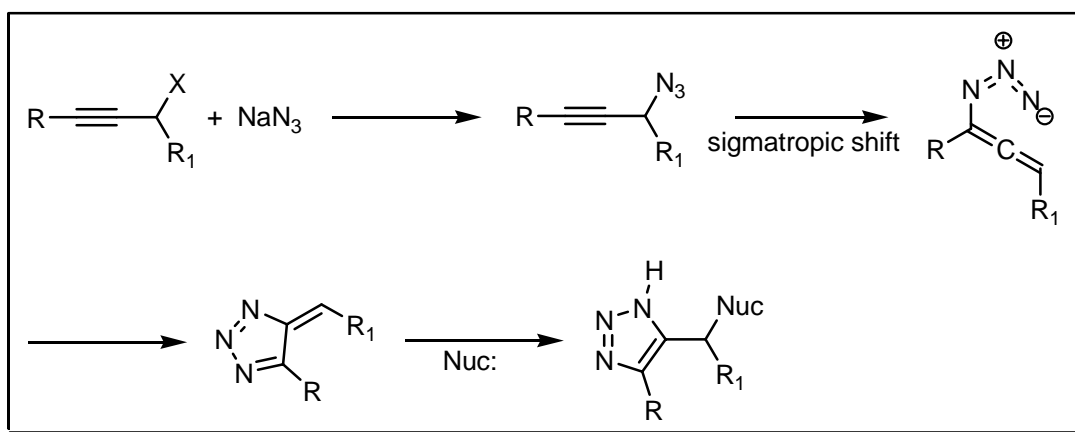
**BANERT CASCADE REACTION**

---

**EXAMPLE :**



**MECHANISM :**





## DISCONNECTION :



## NOTES :

The **Banert** cascade is an organic reaction in which a NH-1,2,3-triazole is prepared from a propargyl halide or sulphate and sodium azide in a dioxane-water mixture at elevated temperatures. This cascade reaction is unusual because it consists of two consecutive rearrangement reactions. The starting material is prepared from propargyl chloride and an aldehyde or ketone such as acetaldehyde. In the first step an azido compound is formed *in situ* in a nucleophilic displacement of chloride by the azide ion. A 3,3-sigmatropic reaction takes place between the azide and the alkyne to the allenyl azide. This allene rearranges to the triazafulvene in a 1,3-dipolar cycloaddition. The exocyclic alkene in this intermediate is very electrophilic because the triazole group has a dipole moment of 5 Debye. The reaction sequence concludes with nucleophilic attack of a nucleophile or second azide ion on this alkene with more double bond rearrangements and proton abstraction from a proton source. See also **Huisgen** reaction.

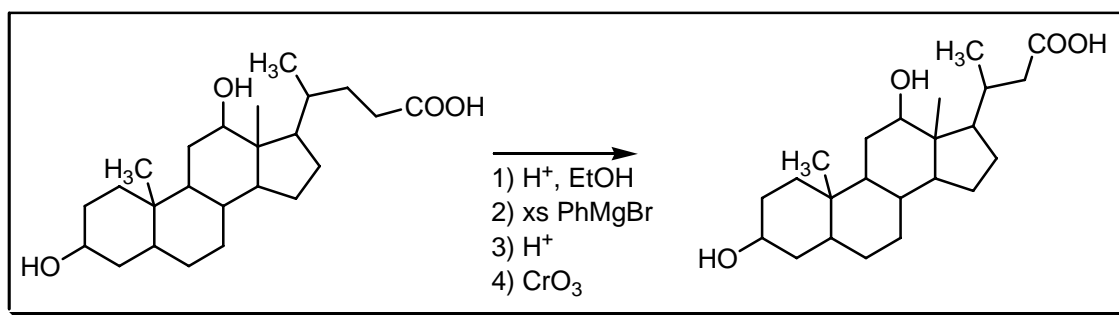
## REFERENCES :

- 1) K. Banert, *Chem. Ber.*, 1989, **122**, 911.
- 2) K. Banert, *Chem. Ber.*, 1989, **122**, 1175.
- 3) K. Banert, *Chem. Ber.*, 1989, **122**, 1963.
- 4) T. Harrison; A.P. Owens; B.J. Williams; C.J. Swain; A. Williams; E.J. Carlson; W. Rycroft; F.D. Tattersall; M.A. Cascieri; G.G. Chicchi; S. Sadowski; N.M.J. Rupniak; R.J. Hargreaves, *J. Med. Chem.*, 2001, **44**, 4296.
- 5) J.C. Loren; K.B. Sharpless, *Synthesis*, 2005, 1514.

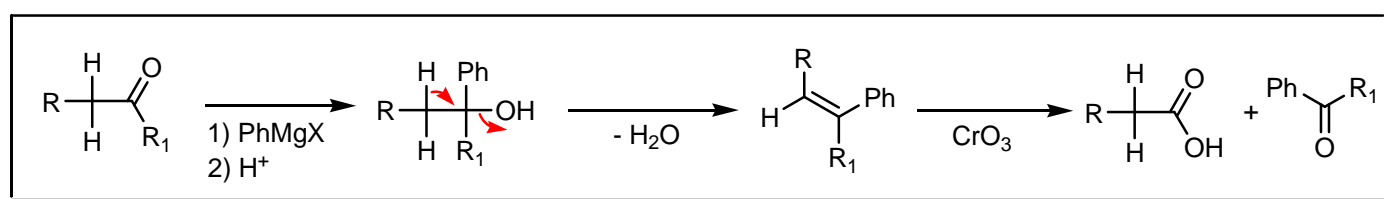
## COMMENTS :

## BARBIER – LOCQUIN – WIELAND DEGRADATION

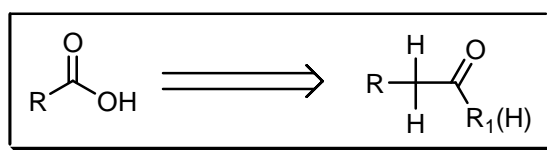
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The step-wise degradation of a carboxylic acid in which one carbon atom is removed at the time, by use of alternate **Grignard** reactions and oxidation of the resulting carbinols. The presence of a branch in the side chain is demonstrated by the formation of a ketone. The reaction is the oxidative cleavage of a 1,1-diphenyl alkene. See also **Gallagher – Hollander**, **Hoehn – Mason**, **Krafft**, **Miescher**, **Trost** oxidative decarboxylation and **Wieland – Dane** reactions.

### REFERENCES :

**March** : 1182

**Smith – March** : 1526

**Smith** : 303

**Smith 2<sup>nd</sup>** : 266, 589

**Houben – Weyl** : E3, 528

**Org. Synth.** : 24, 38

**Org. Synth. Coll. Vol.** : 3, 234

- 1) H. Wieland, *Ber. Dtsch. Chem. Ges.*, 1912, **45**, 484.
- 2) P. Barbier; R. Locquin, *C.R. Séances Acad. Sci.*, 1913, **156**, 1443.
- 3) H.K. Black; B.C.L. Weedon, *J. Chem. Soc.*, 1953, 1785.
- 4) J.R. Dias; R. Ramachandra, *Tetrahedron Lett.*, 1976, **17**, 3685.
- 5) C.S. Subramaniam; P.J. Thomas; V.R. Mamdapur; M.S. Chadha, *Synthesis*, 1978, 468.

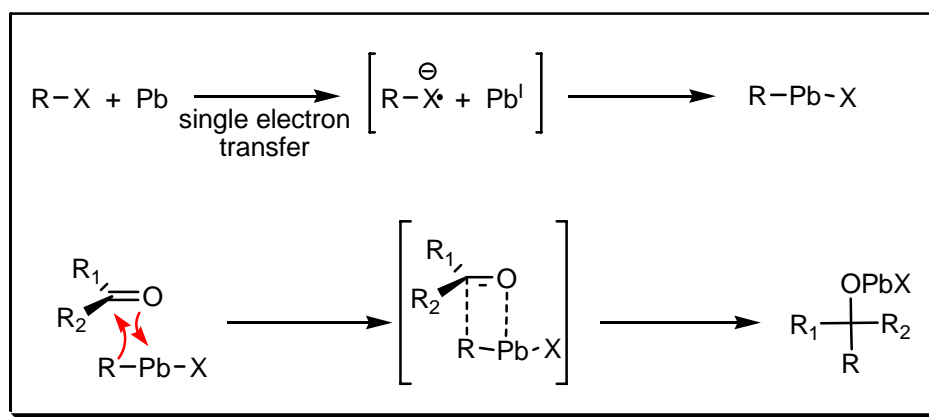
**COMMENTS :**

## BARBIER REACTION

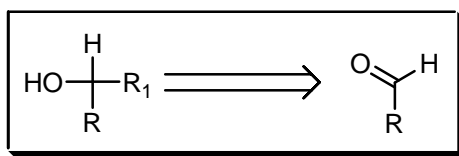
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

This reaction is similar to the **Grignard** reaction but is carried out by adding the halogen compound to a mixture of the second reactant in diethyl ether solution with magnesium or in modern variants zinc, lead, indium or samarium diiodide. Secondary reactions are avoided with this procedure when applied to an unsaturated alkyl halide. The mechanism of the organometallic reagent is identical to the formation of a **Grignard** reagent. The pathway can be either concerted (as shown) or radical stepwise. **Luche** introduced a similar reaction between allylic halides and ketones or aldehydes in the presence of zinc in aqueous media sometimes known as the **Luche** allylation. See also **Grignard – Cologne**, **Imamoto** alkylation and **Kagan – Molander** reactions.

## REFERENCES :

**Smith – March** : 1205

**Smith** : 685

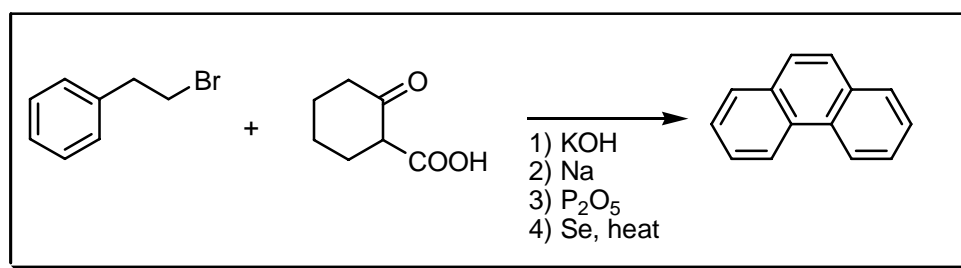
**Smith 2<sup>nd</sup>** : 580

- 1) P. Barbier, *C.R. Séances Acad. Sci.*, 1899, **128**, 110.
- 2) C. Blomberg; F.A. Hartog, *Synthesis*, 1977, 18.
- 3) P. Bauer; G. Molle, *Tetrahedron Lett.*, 1978, **19**, 4853.
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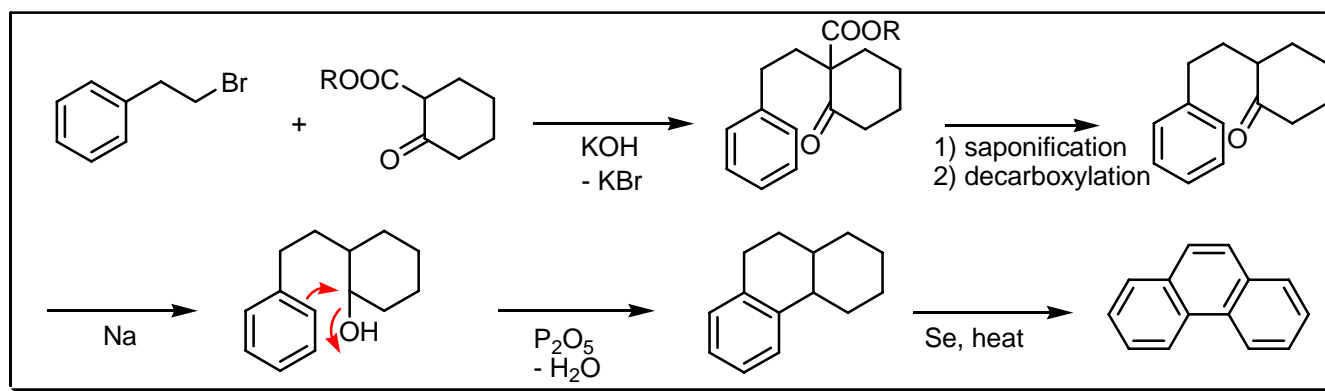
## COMMENTS :

## BARDHAN – SENGUPTA PHENANTHRENE SYNTHESIS

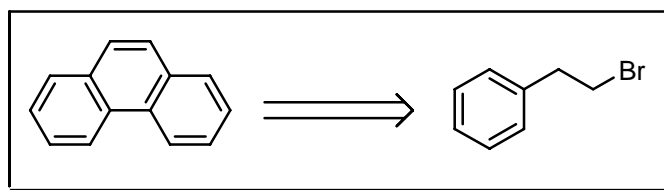
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The cyclodehydration of 2-β-phenylethylcyclohexanols gives octahydrophenanthrenes. The method can also be applied to cyclopentanols. See also **Bogert – Cook** and **Darzens** synthesis of tetralin reactions.

### REFERENCES :

Smith : 1330

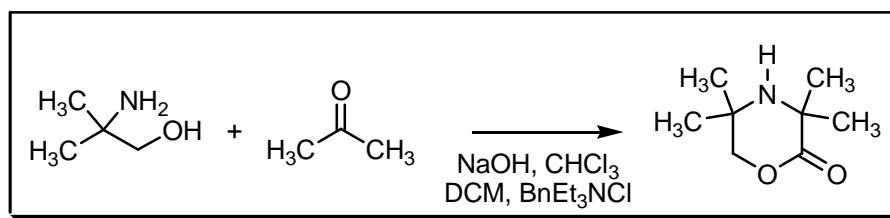
Smith 2<sup>nd</sup> : 1095

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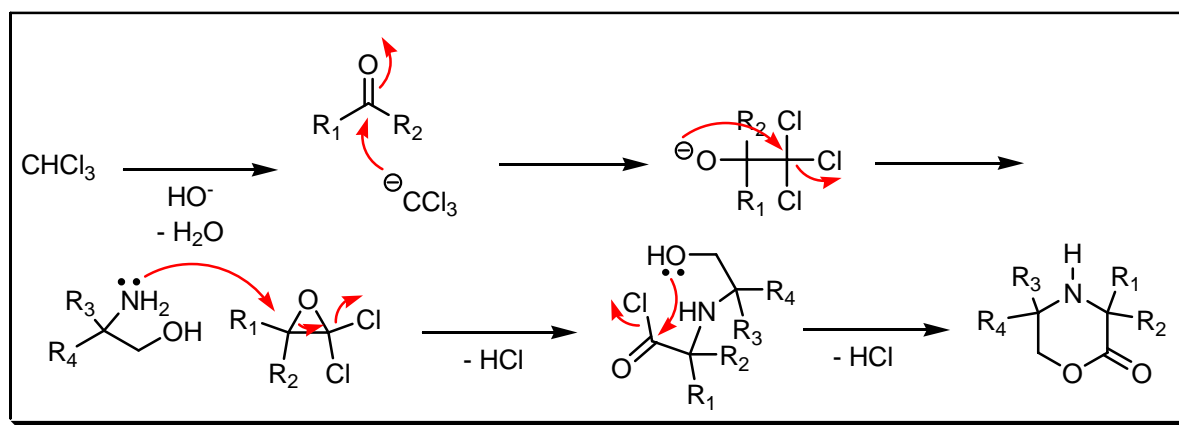
**COMMENTS :**

## BARGELLINI REACTION

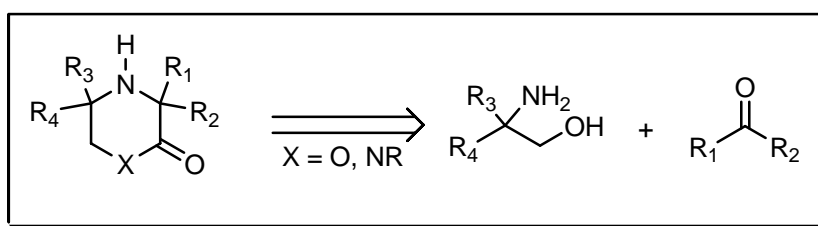
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**

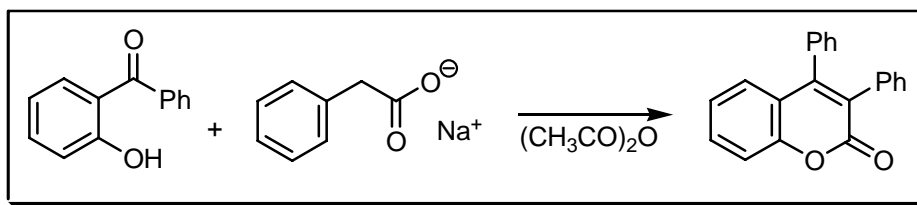
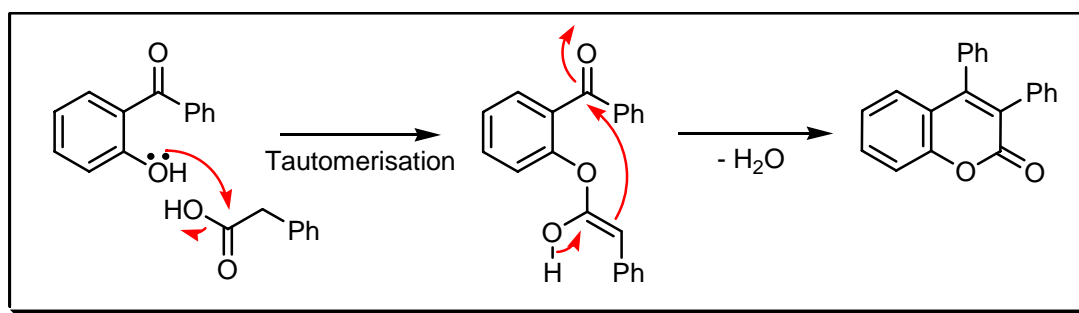


**NOTES :**

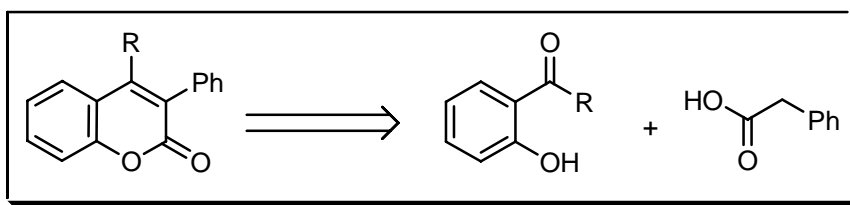
Hindered piperazinones and morpholinones are synthesised from ketones and substituted 2-amino-1-propanols.

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**COMMENTS :****BARGELLINI RING-CLOSURE****EXAMPLE :****MECHANISM :**

## DISCONNECTION :



## NOTES :

The production of 3-phenylcoumarins from *o*-hydroxyacetophenones, an acid anhydride and sodium phenyl acetate. This reaction is a variation of the **von Kostanecki (Allan – Robinson)** chromone reaction. See also **von Kostanecki (Allan – Robinson)** and **Perkin** reactions.

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## REFERENCES :

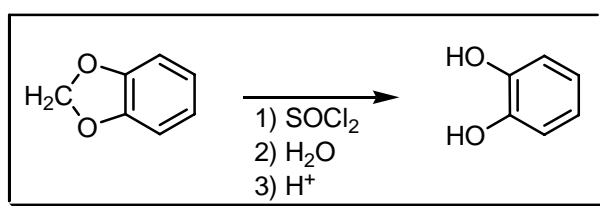
G. Bargellini, *Atti Reale Accad. Naz. Lincei, Rend.*, 1925, **2**, 178.

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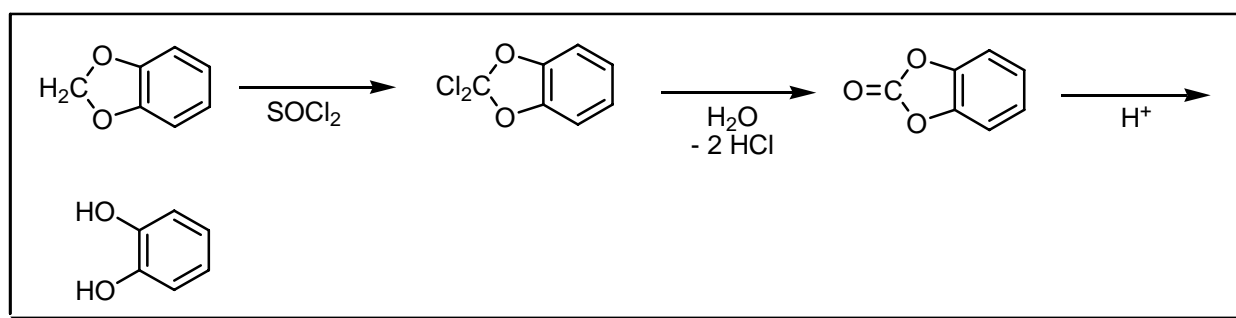
## COMMENTS :

## BARGER DEMETHYLATION

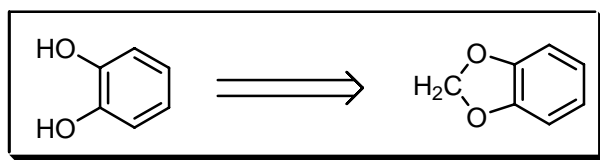
### EXAMPLE :



### MECHANISM :



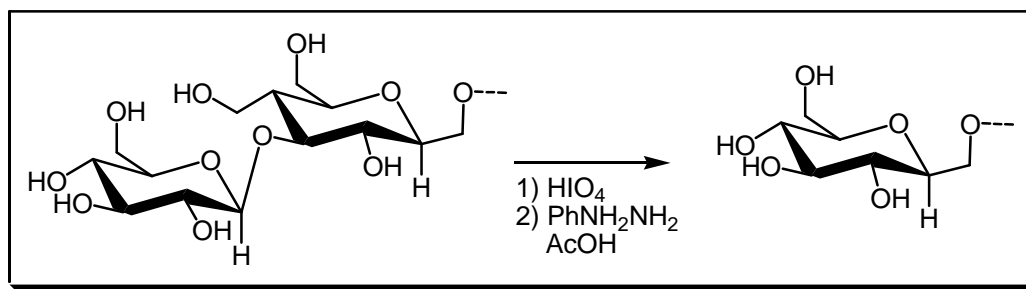


**DISCONNECTION :****NOTES :**

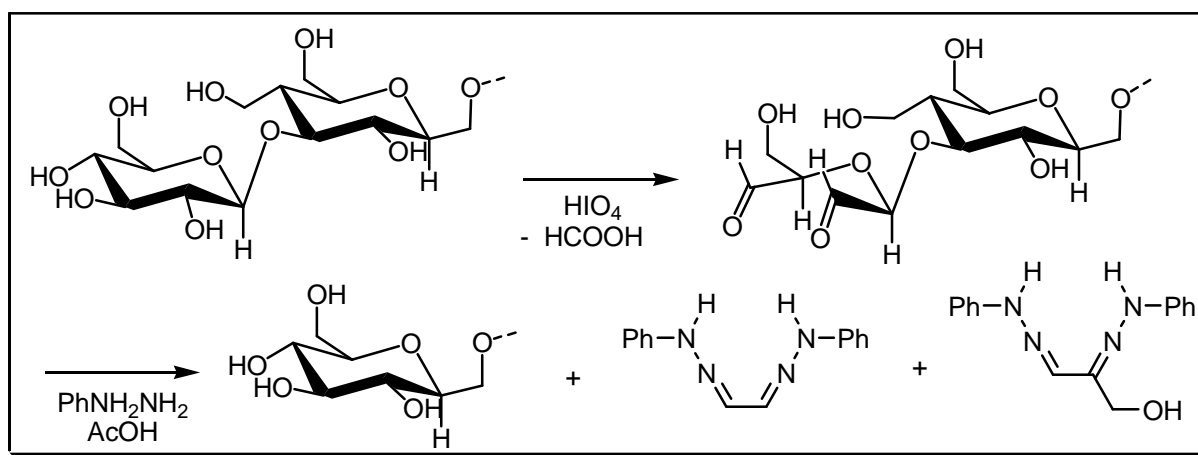
Compounds containing the methylenedioxy-group are transformed by treatment with thionyl chloride or phosphorous pentachloride and water into the cyclic carbonate, which is readily hydrolysed to the corresponding diol derivative.

**REFERENCES :**

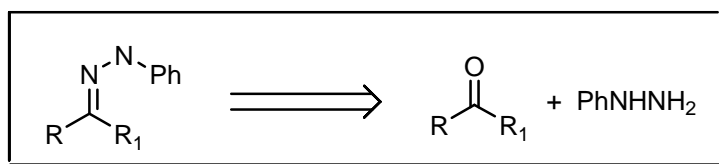
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**COMMENTS :****BARRY REACTION****EXAMPLE :**

## MECHANISM :



## DISCONNECTION :



## NOTES :

The main reaction is between a carbonyl compound and phenylhydrazine. With 1,3-linked polysaccharides: This reaction is based on the fact that an acetal of glyoxal can be converted by phenylhydrazine into glyoxalosazone with the liberation of the alcohol. The oxypolysaccharide is warmed with phenylhydrazine in acetic acid solution. This produces a rapid separation of glyoxalosazone and the polysaccharide – the chain length of which is now shorter by one hexose unit – may be readily recovered. The periodic acid-phenylhydrazine treatment may be repeated on the new terminal non-reducing unit, so that the sugar units may be eliminated one by one from the non-reducing end of a polysaccharide chain. With polysaccharide composed of sugar residues some of which contain  $\alpha$ -glycol groupings: Periodate oxidation followed by treatment with the phenylhydrazine reagent causes fragmentation of the macromolecule and provides polysaccharide residues, which may be examined by conventional methods. See also **Djerassi – Rylander, Fischer, Hudson – Hirst, Malaprade and Ohle** reactions.

## REFERENCES :

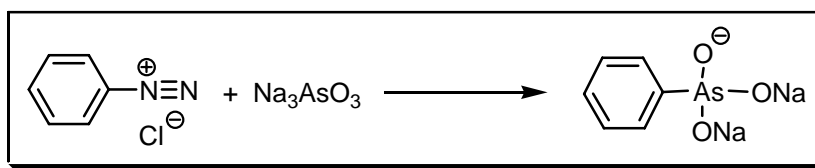
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## COMMENTS :

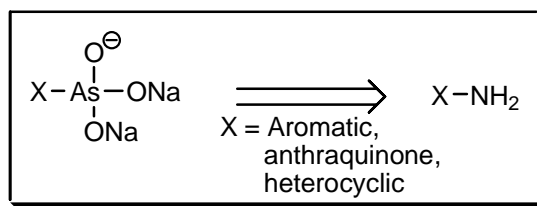
## BART (BART – SCHMIDT) REACTION

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### EXAMPLE :



### DISCONNECTION :



### NOTES :

The formation of an arylarsonic acid from a diazonium salt and an arsenic compound (alkali arsenite, antimony chloride in the **Bart – Schmidt** reaction), preferably in the presence of a copper salt or another metal. There is a modification introduced by **Scheller** (primary aromatic amines are diazotised in the presence of arsenious chloride and a trace of cuprous chloride) and the **Starkey** modification (The use of the more stable diazonium borofluoride). The **Schmidt** modification uses a neutral medium and no catalysts. See also **Béchamp**, **Gattermann** diazo, **Rosenmund**, **Sandmeyer** diazonium and **Scheller** reactions.

### REFERENCES :

Org. React. : **2**, 415

Org. Synth. : **15**, 59; **26**, 60

Org. Synth. Coll. Vol. : **2**, 494; **3**, 665

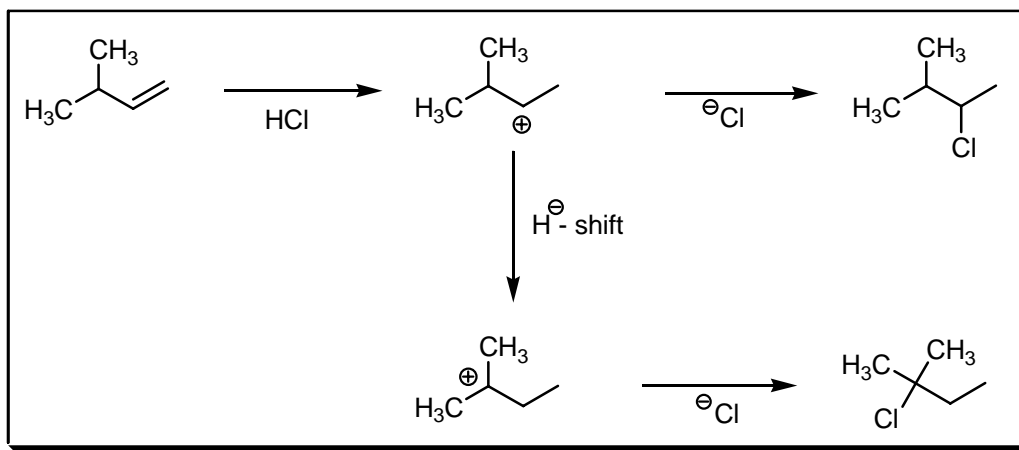
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## BARTLETT – CONDON – SCHNEIDER REACTION

$$\text{H}_3\text{C}-\text{CH}(\text{CH}_3)-\text{CH}=\text{CH}_2 \xrightarrow{\text{HCl}} \text{H}_3\text{C}-\text{CH}(\text{CH}_3)-\text{CH}(\text{Cl})-\text{CH}_3 + \text{H}_3\text{C}-\text{C}(\text{Cl})(\text{CH}_3)-\text{CH}_2\text{CH}_3$$

The process will repeat itself until a fully deuterated *tert*-butyl cation is formed

The *intermolecular* hydride transfer takes place between the cation and the proton of the tertiary position of the isobutane.



#### NOTES :

The *intra*- and *intermolecular* exchange of halogen and hydrogen atoms between organic halides and alkanes.

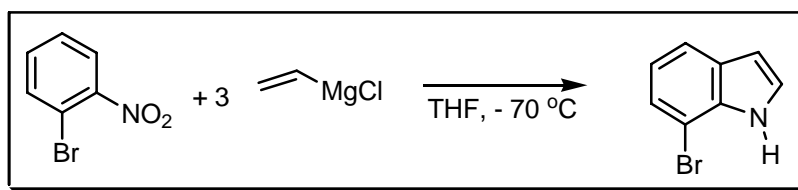
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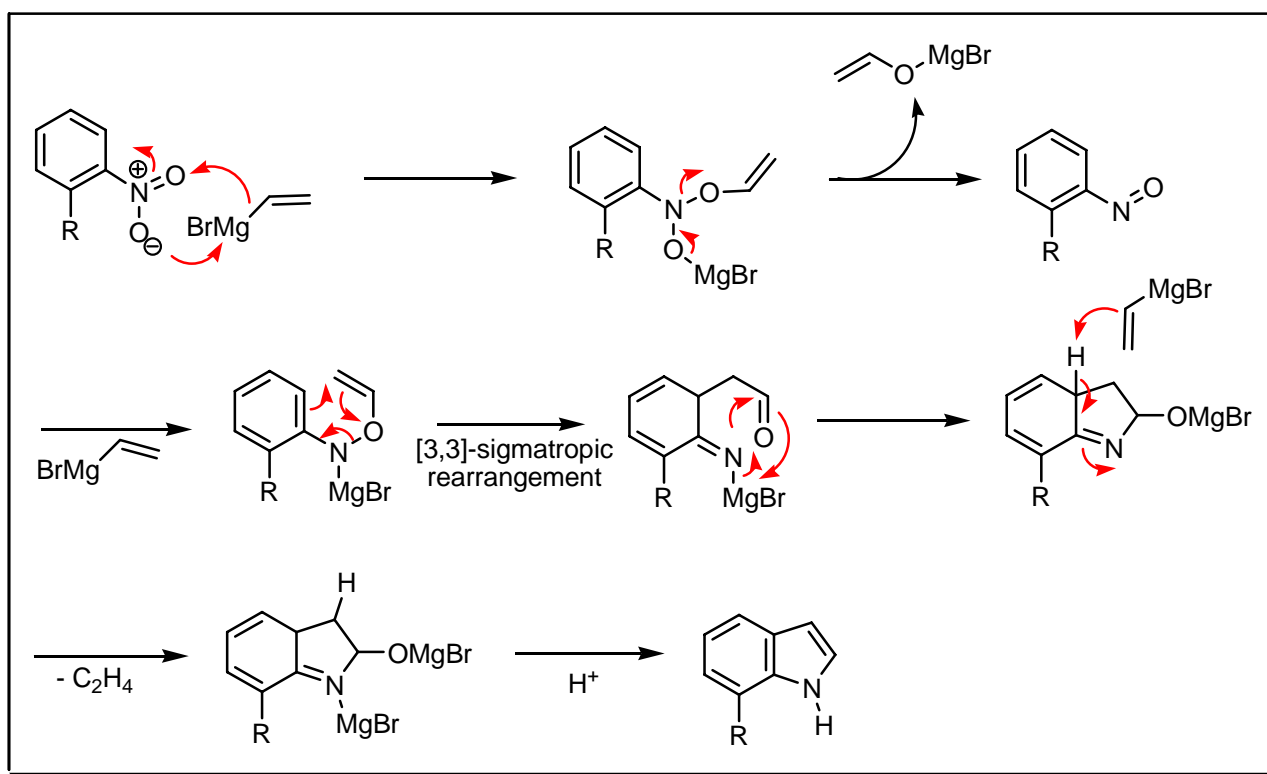
#### COMMENTS :

### BARTOLI INDOLE SYNTHESIS

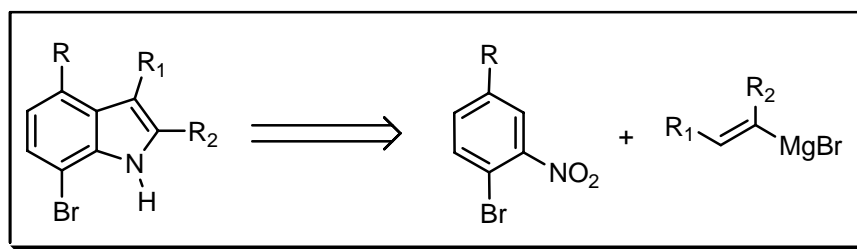
#### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

This indole synthesis is the treatment of an *ortho*-substituted nitro-aromatic compound with 3 equivalents of vinylmagnesium bromide or chloride. **Bartoli** and **Rosini** showed that nitroarenes under similar conditions gave after reductive C-alkylation *ortho* alkyl anilines. The mechanism of the reaction is not clear in every detail. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

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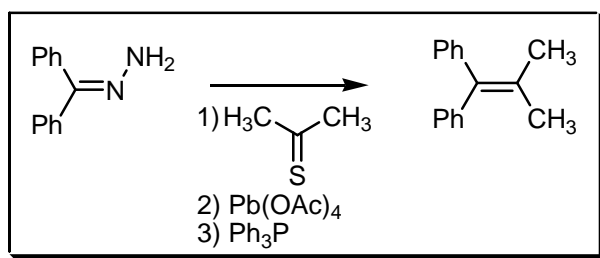
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**COMMENTS :**

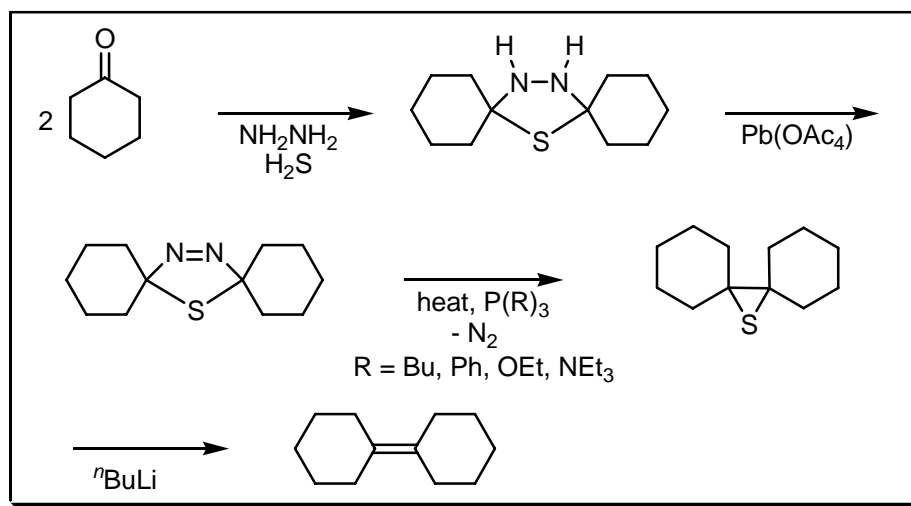
## BARTON – KELLOGG OLEFINATION

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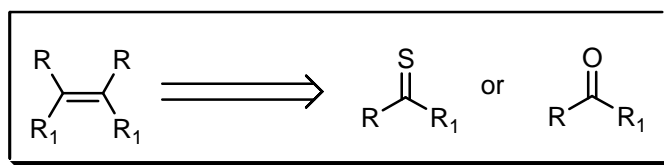
**EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

The olefin synthesis by two-fold extrusion of nitrogen and sulfur from a  $\Delta^3$ -1,3,4-thiadiazoline intermediate. Particularly applicable to the synthesis of moderately hindered *tetra*-substituted ethylenes. See also **Corey – Kwiatkowski**, **Horner – Wadsworth – Emmons**, **Julia – Paris – Kocienski – Lythgoe**, **Krief – Reich – Chow**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Paquette**, **Petasis** reaction, **Peterson**, **Ramberg – Bäcklund**, **Smiles** rearrangement, **Still – Gennari**, **Takeda**, **Tebbe** and **Wittig** olefination reactions.

## REFERENCES :

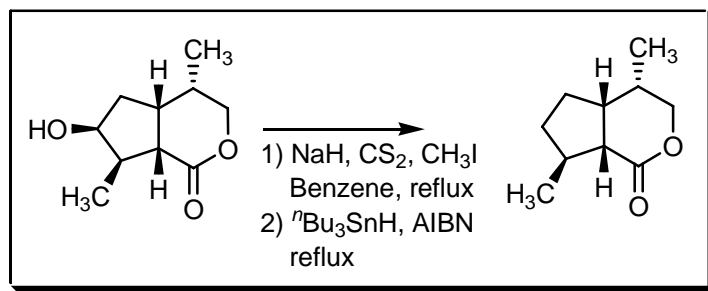
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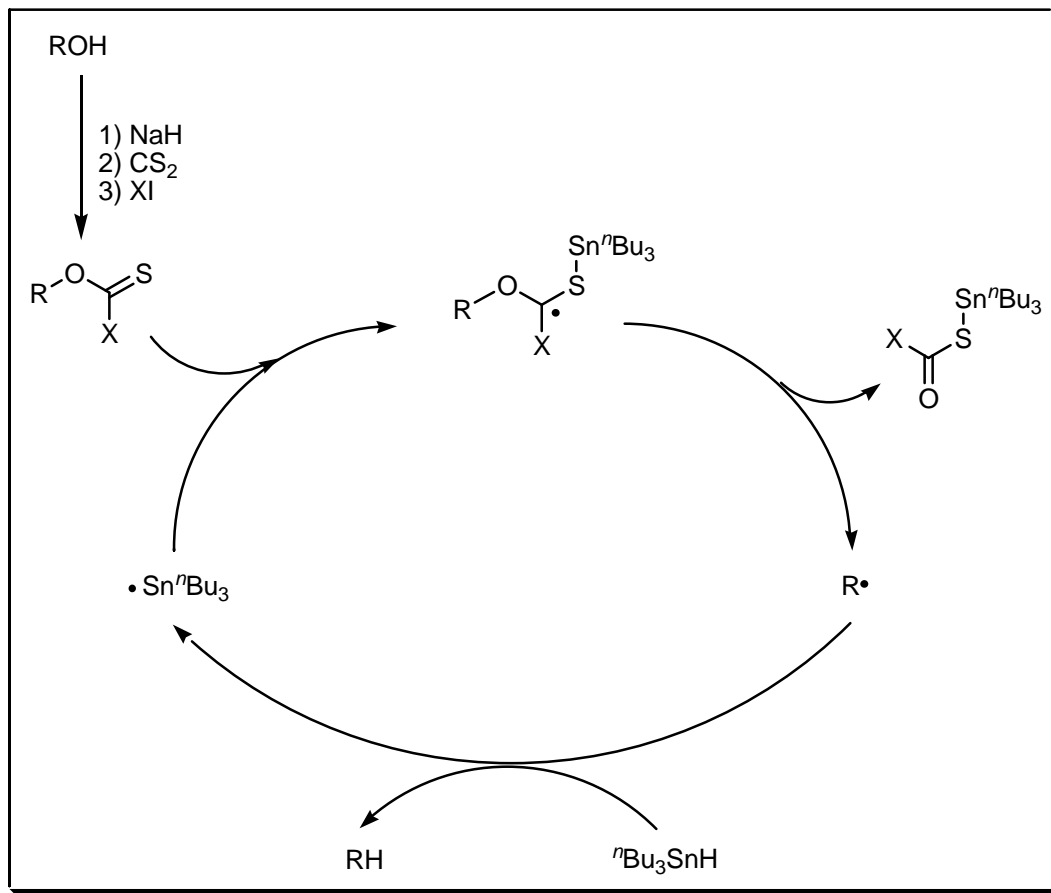
**COMMENTS :**

## BARTON – McCOMBIE DEOXYGENATION

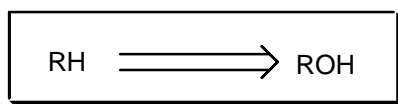
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



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## NOTES :

The alcohol is converted to a xanthate and then reduced with tributyltin hydride and a catalytic amount of AIBN. The tributyltin hydride can be replaced by silicon hydrides. In this reaction there is no need to convert the alcohol first to a halide. There is a thionocarbonate modification published by Robins.

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## REFERENCES :

**Smith – March** : 527

**Smith 2<sup>nd</sup>** : 140, 407, 1164

**Houben – Weyl** : **E19a**, 105, 174, 431

**Org. Synth.** : **64**, 57; **77**, 153

**Org. Synth. Coll. Vol.** : **7**, 139; **10**, 2378

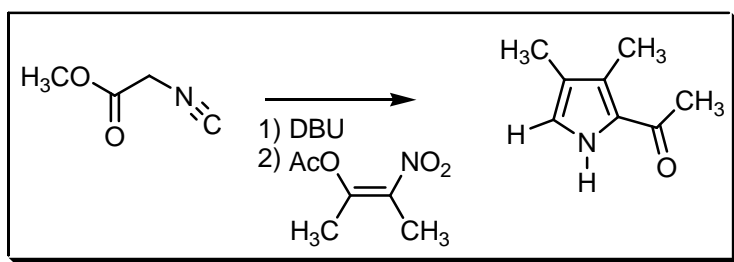
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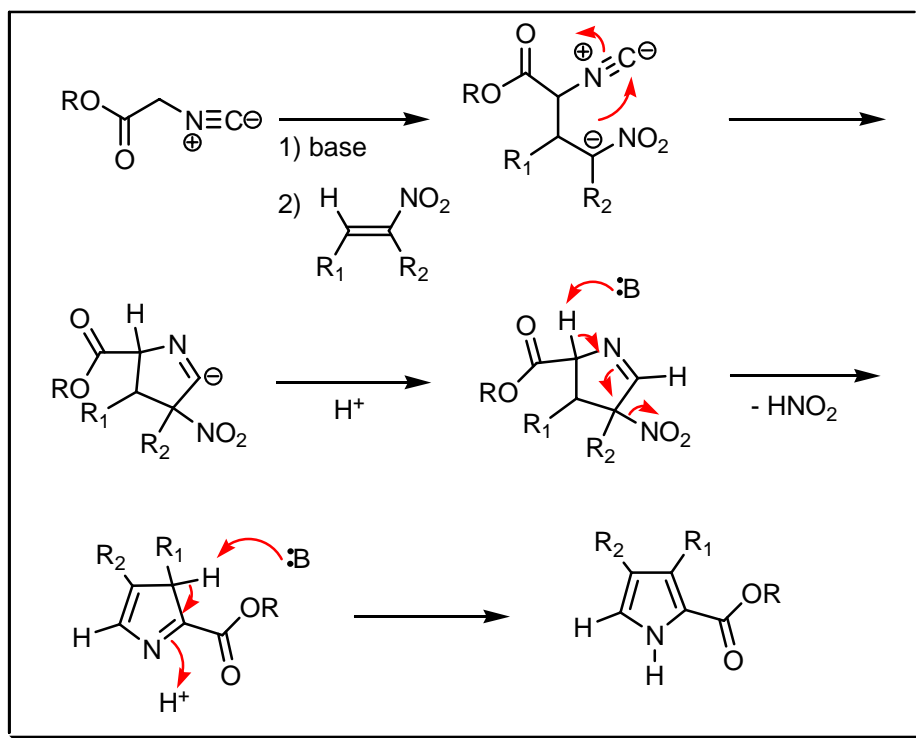
## COMMENTS :

## BARTON – ZARD PYRROLE SYNTHESIS

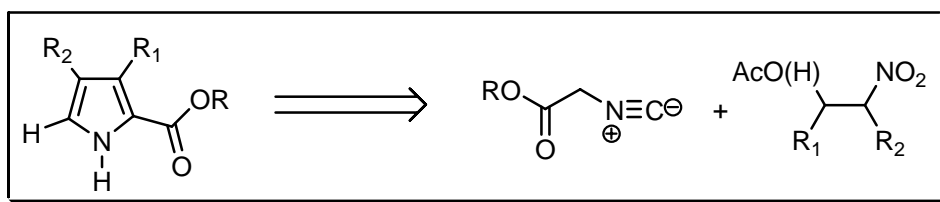
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The base-catalysed **Michael** addition of an  $\alpha$ -isocyanoacetate to a nitroalkane. The cyclisation of the nitronate anion onto the isocyano group leads to the pyrroline, base-catalysed expulsion of nitrite from the pyrroline and double bond rearrangement would finally give the pyrrole, unsubstituted in the 5-position. See also **Clauson-Kaas**, **Fischer – Fink**, **Grob – Camenisch**, **Hantzsch** pyrrole, **Harries** pyrrole, **Kenner**, **Knorr** pyrrole, **Miller – Plöchl**, **Paal – Knorr**, **Padwa**, **Piloty – Robinson**, **Schwanert**, **Trofimov** and **Zav'yalov** reactions.

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Org. Synth. : 70, 68

Org. Synth. Coll. Vol. : 9, 242

Science of Synthesis : 9, 489

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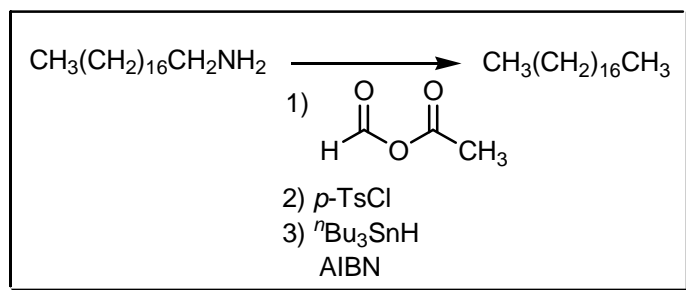
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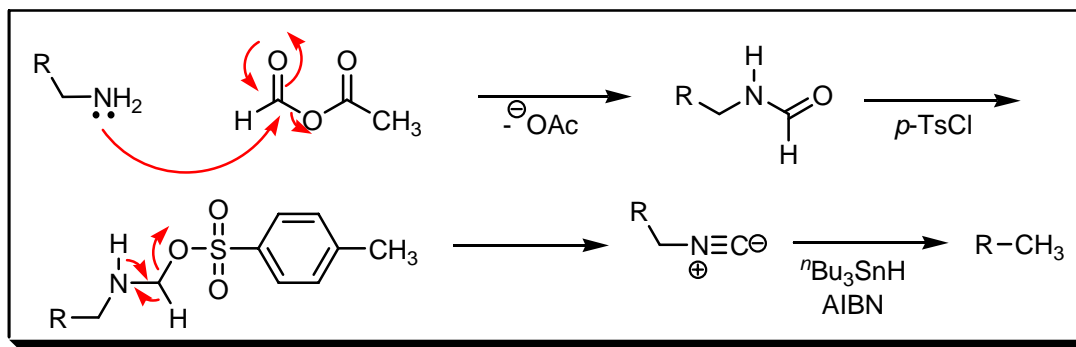
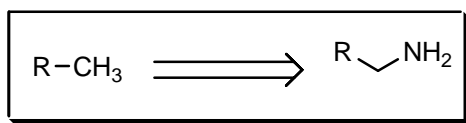
## COMMENTS :

## BARTON DEAMINATION

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### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

The free radical deamination of primary amines *via* isocyanides.

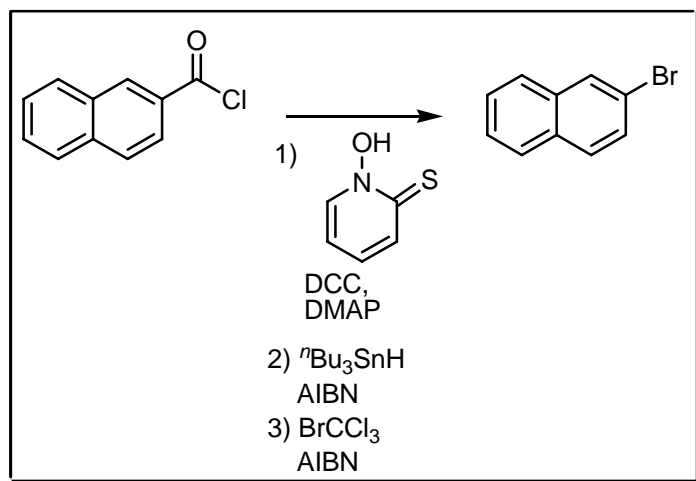
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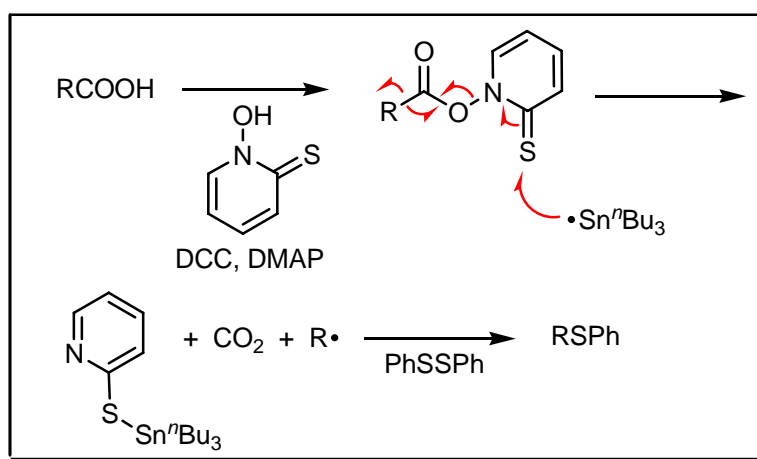
**COMMENTS :**

## BARTON DECARBOXYLATION

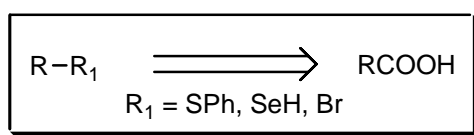
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The radical decarboxylation of a mixed anhydride (thiohydroxamic-carboxylic) using  $n\text{Bu}_3\text{SnH}$  or  $n\text{Bu}_3\text{SH}$  and interception of radicals as a sulfide (PhSSPh), selenide or bromo (BrCCl3) derivative. **Biehl et al.** used these esters for the syntheses of thieno[2,3-*b*]pyridines.

## REFERENCES :

Org. React. : **48**, 301

Org. Synth. : **75**, 124

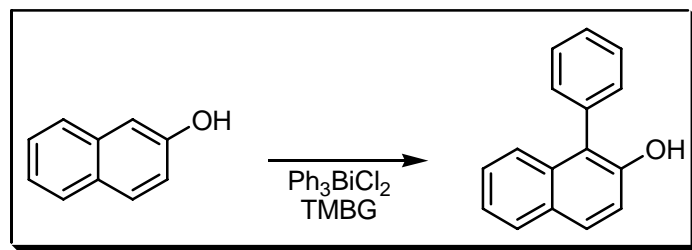
Org. Synth. Coll. Vol. : **10**, 2318

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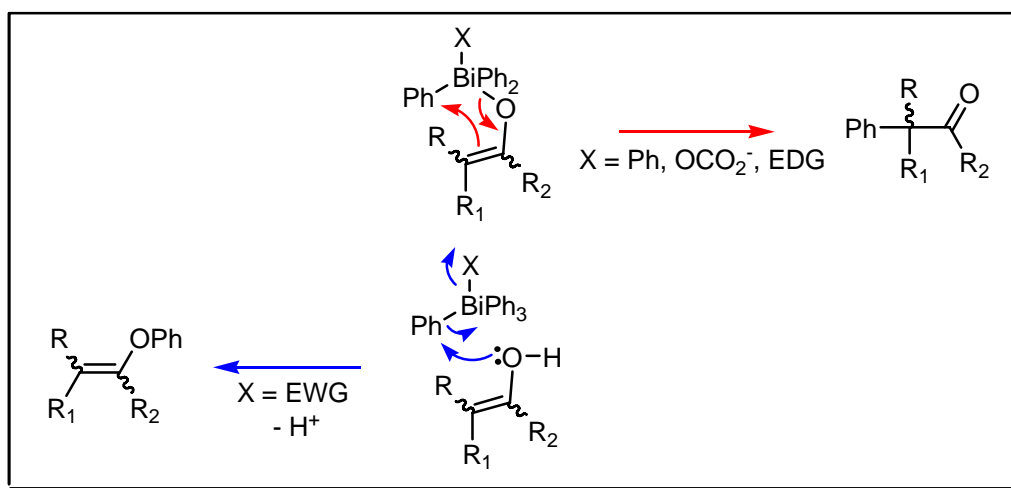
## COMMENTS :

## BARTON PHENYLATION

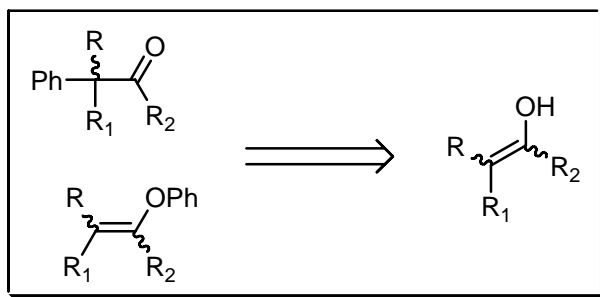
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The regiospecific arylation of phenols and enols under acidic, basic or neutral conditions by covalent organobismuth(5+) reagents.

## REFERENCES :

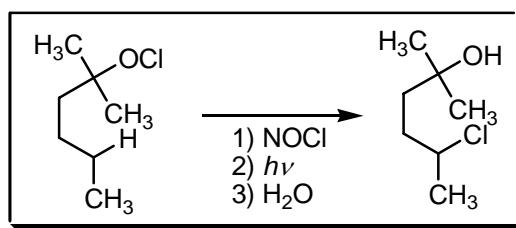
- 1) D.H.R. Barton; D.J. Lester; W.B. Motherwell; M.T.B. Papoula, *J. Chem. Soc., Chem. Commun.*, 1980, 246.
- 2) D.H.R. Barton; J.-C. Blazejewski; B. Charpiot; D.J. Lester; W.B. Motherwell; M.T.B. Papoula, *J. Chem. Soc., Chem. Commun.*, 1980, 827.
- 3) D.H.R. Barton; B. Charpiot; W.B. Motherwell, *Tetrahedron Lett.*, 1982, **23**, 3365.
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## COMMENTS :

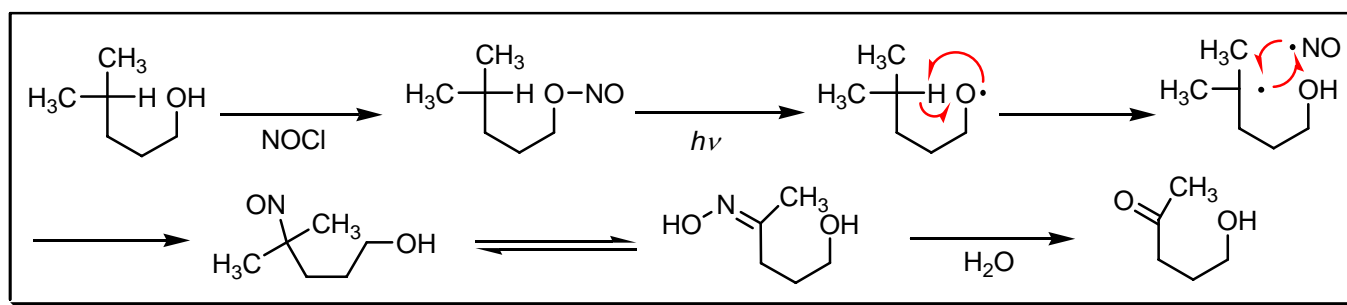


## BARTON REACTION

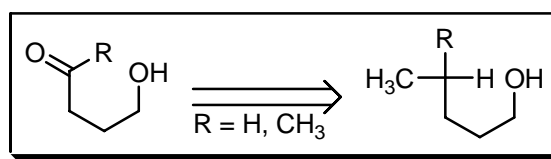
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This method provides a way to oxidise a carbon atom separated from an hydroxyl group by three other carbon atoms via a nitrite ester. The mechanism is similar to the **Hoffmann – Löffler – Freytag** reaction. See also **Hoffmann – Löffler – Freytag** reaction.

### REFERENCES :

March : 1153

Smith – March : 1463

Smith : 1415

Smith 2<sup>nd</sup> : 1166

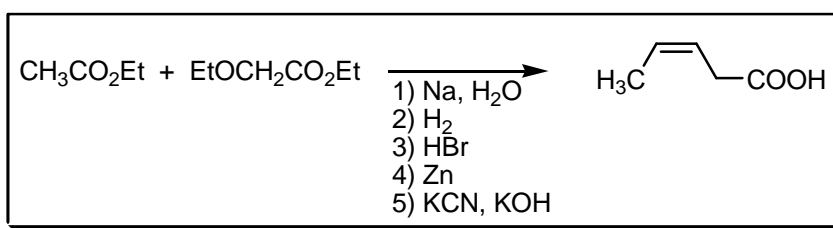
- 1) D.H.R. Barton; I.M. Beaton; L.E. Geller; M.M. Pechet, *J. Am. Chem. Soc.*, 1960, **82**, 2640.
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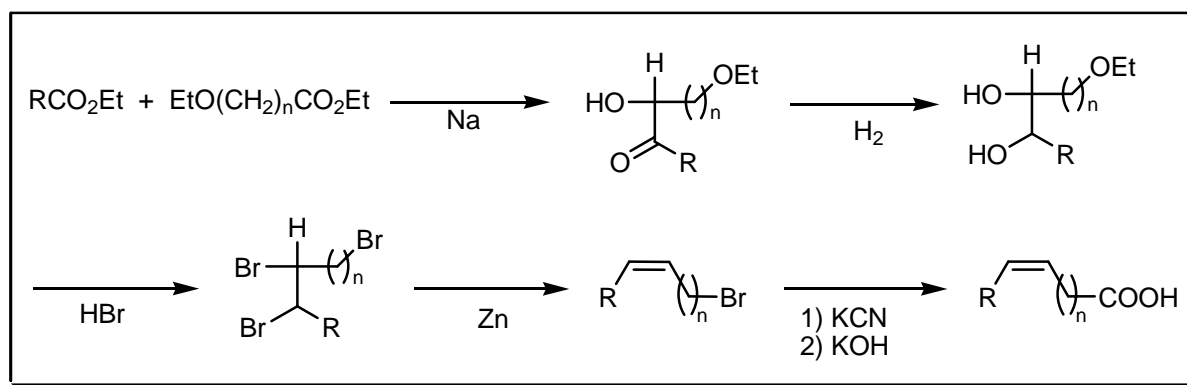
**COMMENTS :**

**BAUDART ACYLOIN SYNTHESIS**

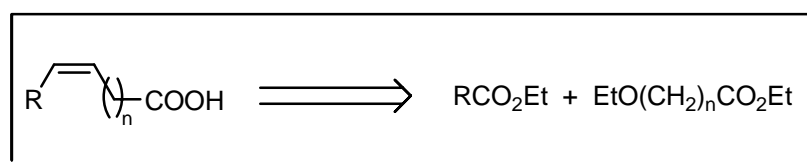
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**

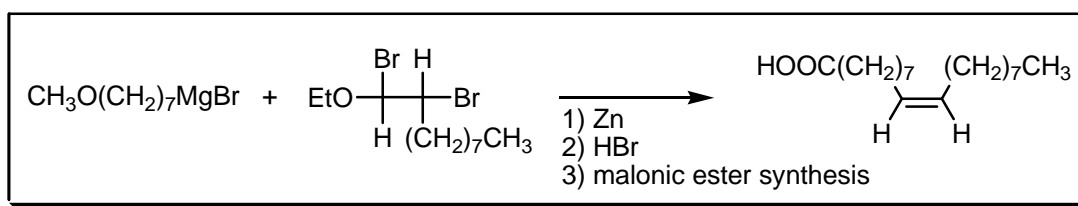
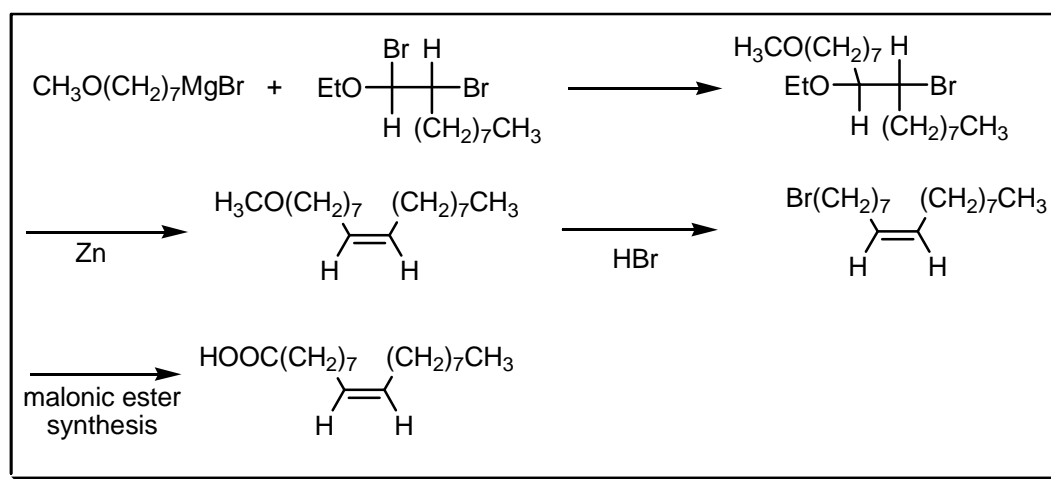


**NOTES :**

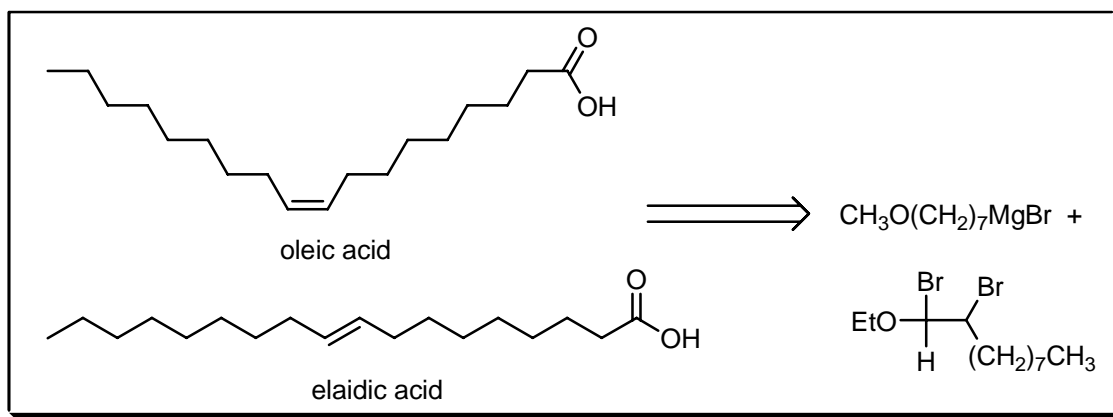
The necessary double bond is obtained by reducing an acyloin of suitable structure to a glycol and converting the glycol into the corresponding dibromide. The latter product is treated with zinc.

**REFERENCES :**

P. Baudart, *C.R. Séances Acad. Sci.*, 1945, **220**, 404.

**COMMENTS :****BAUDART SYNTHESIS****EXAMPLE :****MECHANISM :**

## DISCONNECTION :



## NOTES :

The application of this method to the synthesis of a mixture of oleic acid and elaidic acids ( $\text{C}_{18}$  chain *E/Z* at C9). See also **Boord**, **Bowman**, **Kapp – Knoll**, **Noller** and **Robinson – Robinson** reactions.

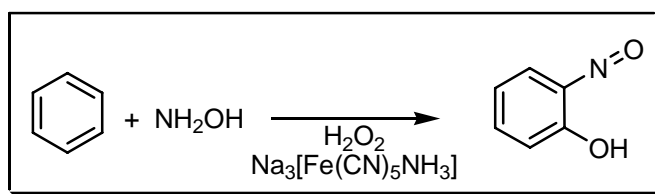
## REFERENCES :

P. Baudart, *C.R. Séances Acad. Sci.*, 1943, **217**, 399.

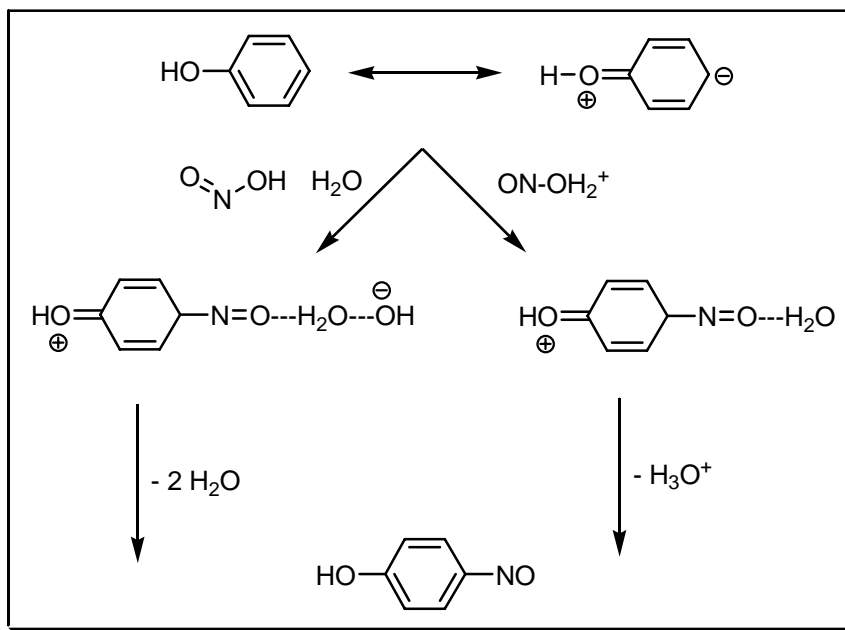
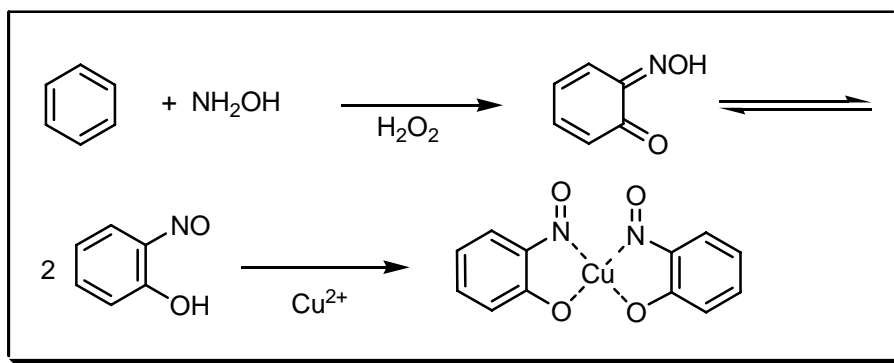
## COMMENTS :

## BAUDISCH REACTION

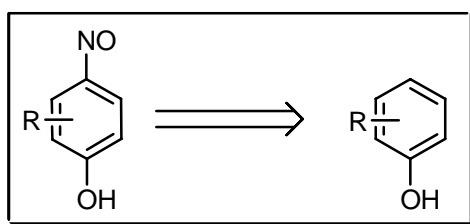
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The formation of o-nitrosophenols by oxidation of aromatic compounds sometimes in the presence of a metal salt to stabilise the nitrosyl radical. The nitrosyl radical is prepared by reduction of nitrous acid or by the oxidation of hydroxylamine.

## REFERENCES :

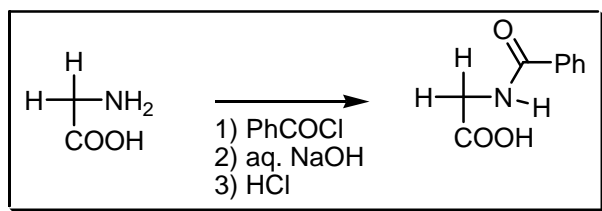
Houben – Weyl : 10/1, 1025

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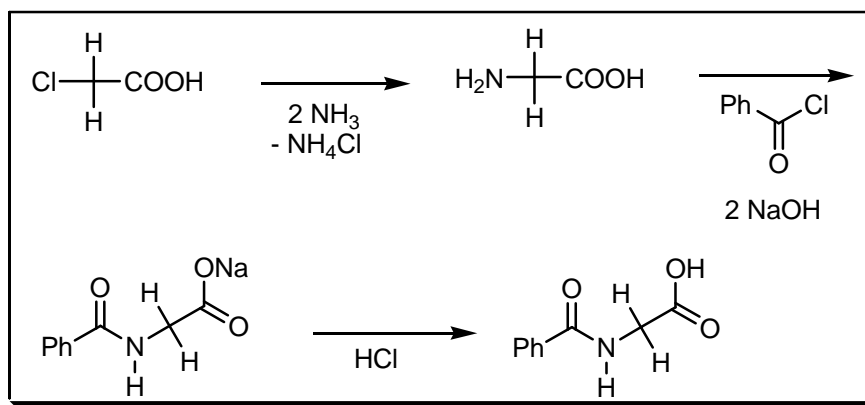
**COMMENTS :**

**BAUM BENZOYLATION**

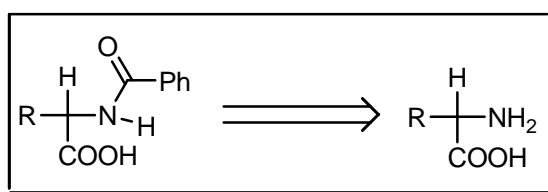
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

The amino acid reacts with benzoyl chloride in the presence aqueous sodium hydroxide. The reaction is worked up with hydrochloric acid to afford the benzylated amino acid. See also **Schotten – Baumann** reaction.

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## REFERENCES :

Smith : 662

Smith 2<sup>nd</sup> : 561

Org. Synth. : 12, 40

Org. Synth. Coll. Vol. : 2, 328

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1) J. Baum, *Ber. Dtsch. Chem. Ges.*, 1886, **19**, 500.

2) H.E. Carter; C.M. Stevens, *J. Biol. Chem.*, 1941, **138**, 627.

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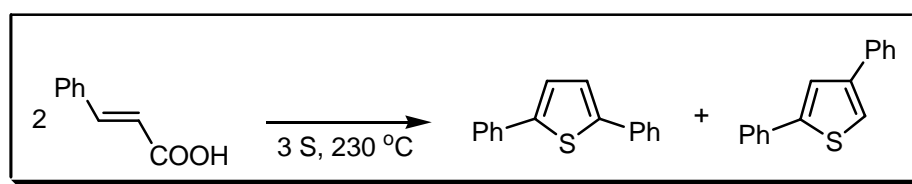
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## COMMENTS :

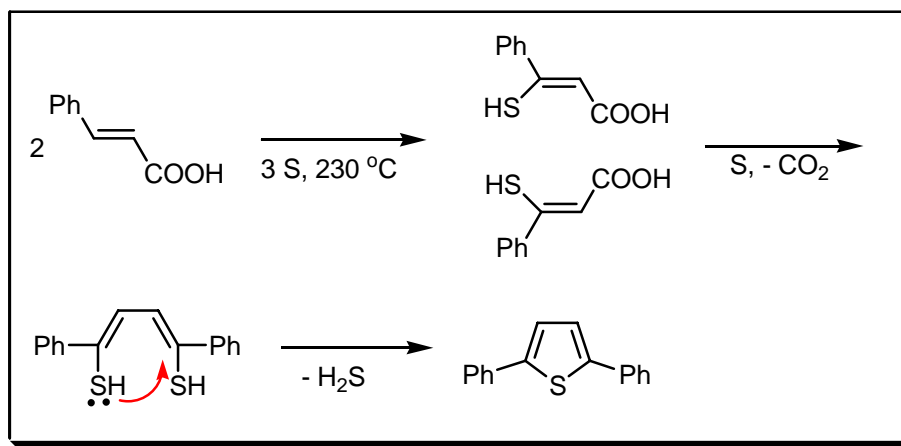
## BAUMANN – FROMM SYNTHESIS

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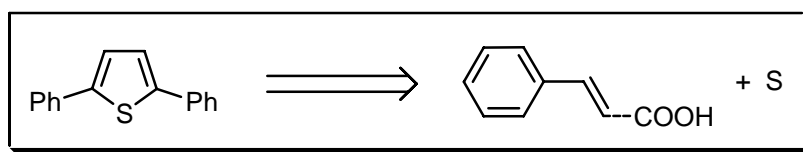
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Sulfur and cinnamic acid or styrene react on heating to form 2,4- and 2,5-diphenylthiophene. The mechanism is assumed to be similar to the **Bogert – Herrera** reaction. See also **Bogert – Herrera**, **Fiesselmann**, **Harries** pyrrole, **Hinsberg** thiophene, **Volhard – Erdmann** and **Willgerodt – Kindler** reactions.

## REFERENCES :

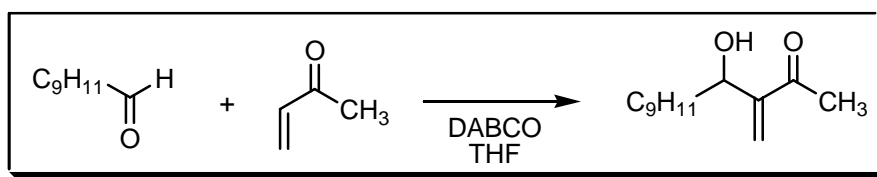
- 1) E. Baumann; E. Fromm, *Ber. Dtsch. Chem. Ges.*, 1891, **24**, 1446.
- 2) E. Baumann; E. Fromm, *Ber. Dtsch. Chem. Ges.*, 1895, **28**, 890.
- 3) P. Demerseman; Ng.Ph. Buu-Hoï; R. Royer; A. Cheutin, *J. Chem. Soc.*, 1954, 2720.

## COMMENTS :



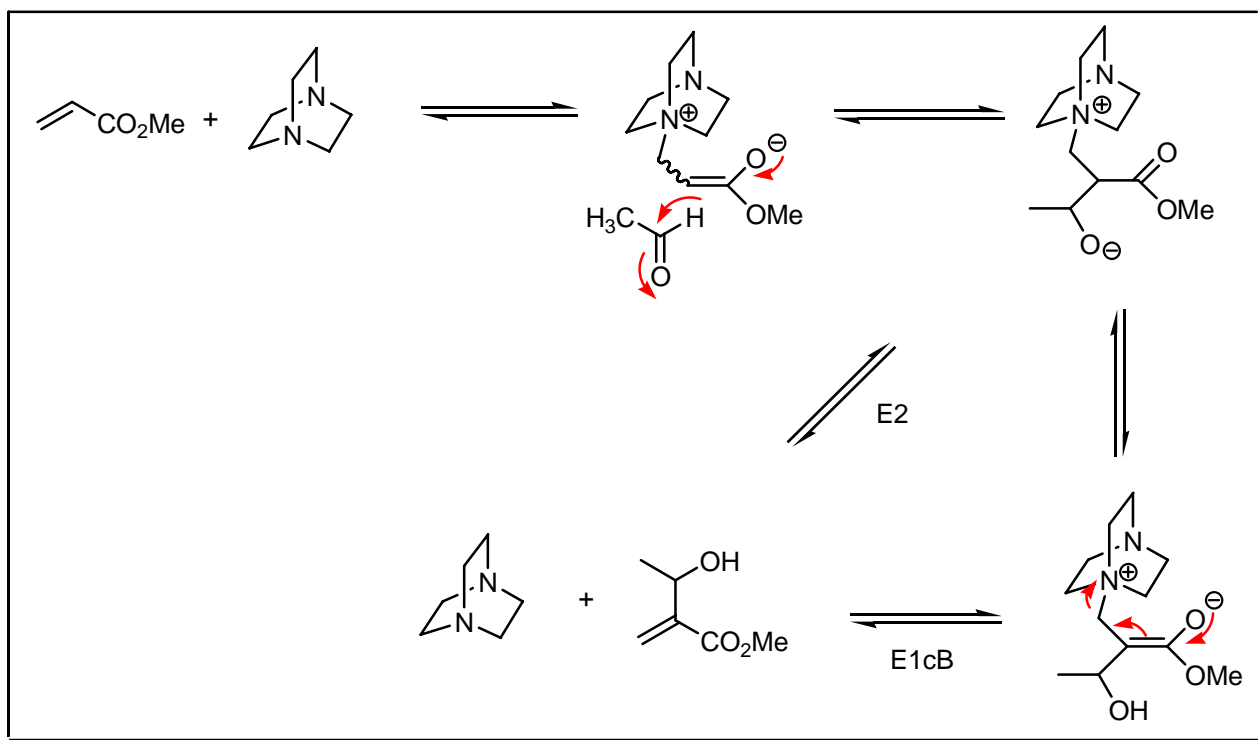
## BAYLIS – HILLMAN – MORITA REACTION

### EXAMPLE :

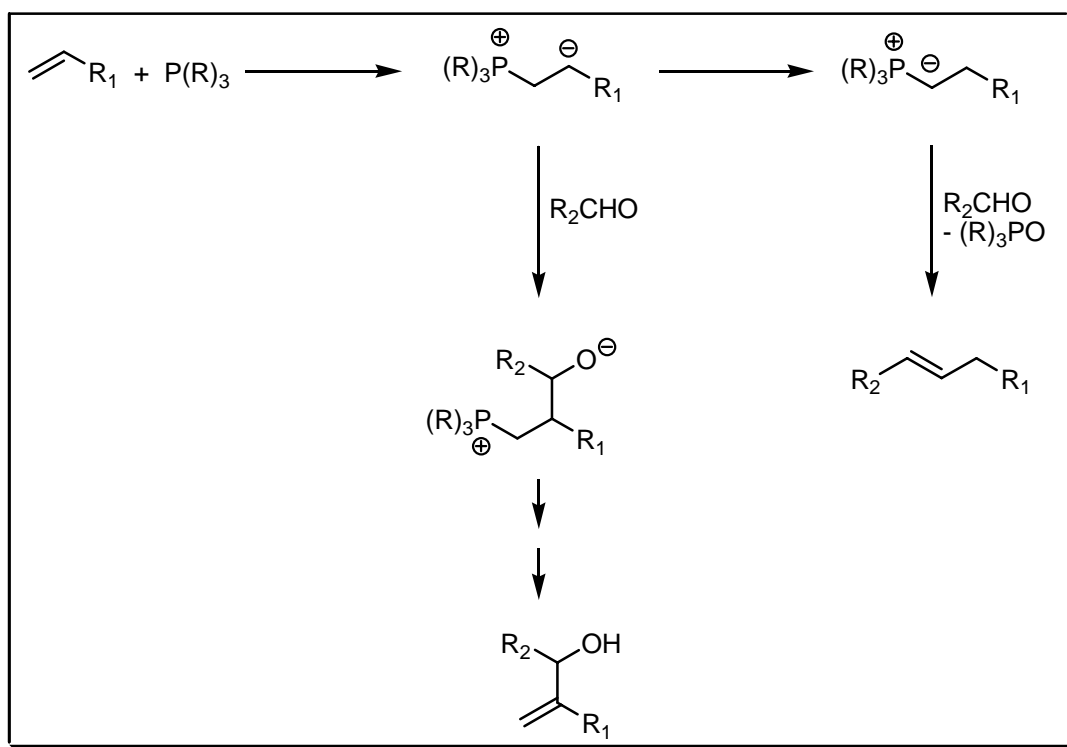


### MECHANISM :

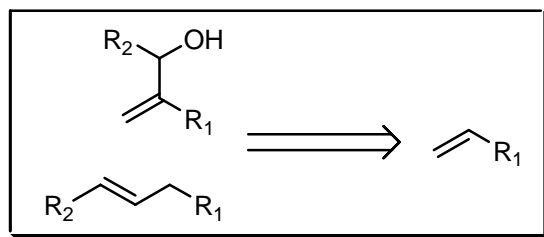
#### DABCO :



## Phosphines :



## DISCONNECTION :



## NOTES :

The amine catalyses the conversion of acrylates to  $\alpha$ -(hydroxyalkyl) acrylates or of vinyl ketones to  $\alpha$ -(hydroxyalkyl) vinyl ketones. The reaction can be catalysed by DABCO, phosphines or transition metal complexes, although DMAP is becoming more popular than DABCO because of its better selectivity and higher yields. Aza and asymmetric **Baylis – Hillman – Morita** reactions have also been published. A new interpretation of the reaction mechanism is published by *Price et. al.* See also **Rauhut – Currier** reaction.

## REFERENCES :

Smith – March : 1212

Smith 2<sup>nd</sup> : 795

Org. React. : 51, 201

Org. Synth. : 68, 64; 75, 106

Org. Synth. Coll. Vol. : 8, 420; 10, 2316

Science of Synthesis : 10, 761

- 1) R. Oda; S. Tanimoto, *Tetrahedron Lett.*, 1964, **25**, 1653.
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- 14) R. Murugan; E.F.V. Scriven, *Aldrichimica Acta*, 2003, **36**, 21.
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- 17) P.R. Krishna; V. Kannan; P.V.N. Reddy, *Adv. Synth. Catal.*, 2004, **346**, 603.
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- 20) K.E. Price; S.J. Broadwater; H.M. Jung; D.T. McQuade, *Org. Lett.*, 2005, **7**, 147.

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**COMMENTS :**

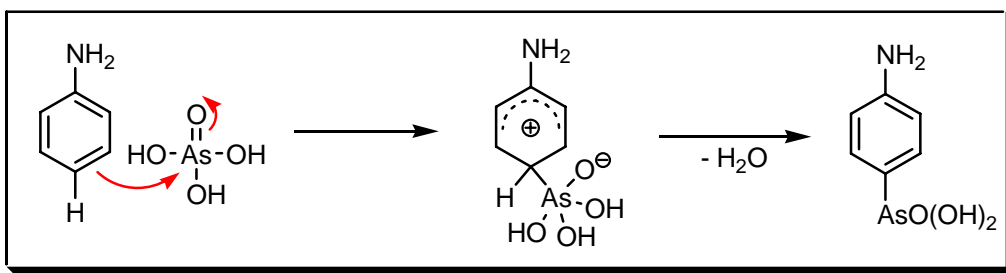
## BÉCHAMP ARSONYLATION

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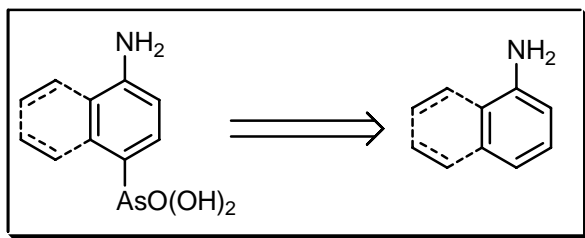
**EXAMPLE :**



### MECHANISM:



### DISCONNECTION :



### NOTES :

The direct *para*-arsenylation of aromatic amines, phenols, and certain derivatives with arsenic acid. *Ortho*-arsenylation does not occur even when the *para*-position is blocked. This arsylation is mechanistically similar to sulfonation. See also **Bart** (**Bart – Schmidt**) and **Rosenmund** reactions.

### REFERENCES :

Org. React. : 2, 415

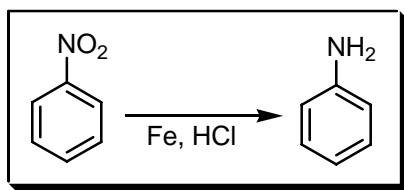
- 1) A.J. Béchamp, *C.R. Séances Acad. Sci.*, 1863, **56**, 1172.
- 2) P. Ehrlich; A. Bertheim, *Ber. Dtsch. Chem. Ges.*, 1907, **40**, 3292.
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### COMMENTS :

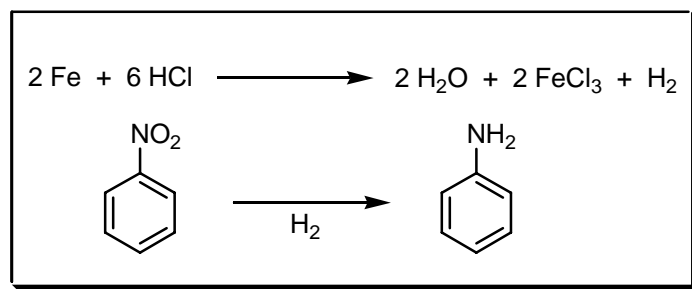
## BÉCHAMP REDUCTION

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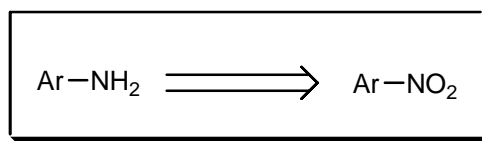
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The use of ferrous salts or iron in dilute acid in the reduction of aliphatic and aromatic nitro groups to amino groups. See also **Zinin** reduction.

### REFERENCES :

**March** : 1216

**Smith – March** : 1552

**Houben – Weyl** : 11/1, 394

**Org. Synth.** : 11, 32; 15, 55

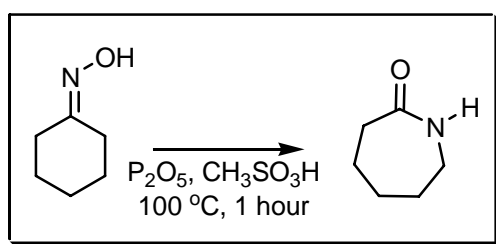
**Org. Synth. Coll. Vol.** : 2, 160, 471

- 1) A.J. Béchamp, *Ann. Chim. (Paris)*, 1854, **42**, 186.
- 2) S.E. Hazlet; C.A. Dornfeld, *J. Am. Chem. Soc.*, 1944, **66**, 1781.
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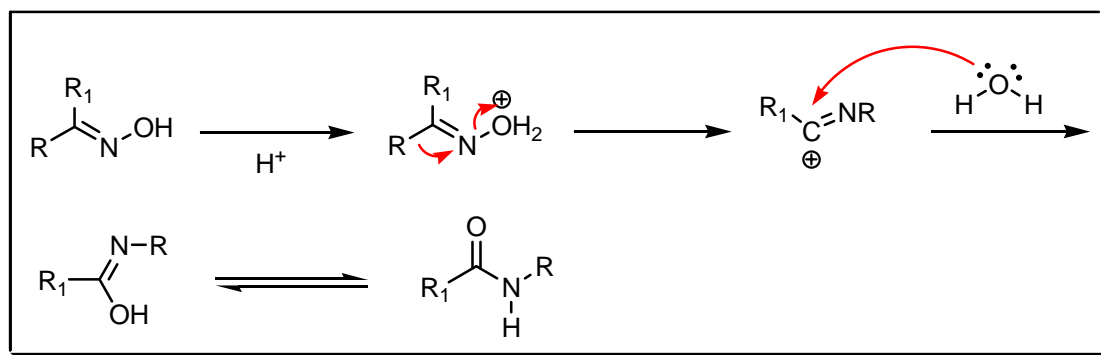
**COMMENTS :**

**BECKMANN REARRANGEMENT**

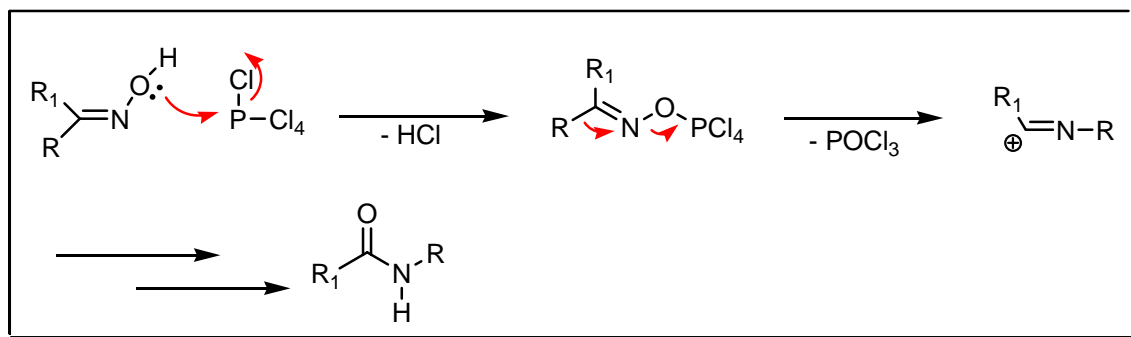
**EXAMPLE :**



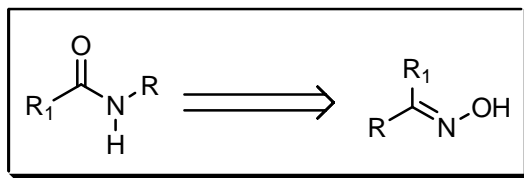
**MECHANISM :**



**If a Lewis acid is used as catalyst :**



## DISCONNECTION :



## NOTES :

The rearrangement of ketoximes to substituted acid amides on treatment with phosphorous pentachloride, polyphosphoric acid, sulfuric acid, acetyl chloride, benzenesulfonyl chloride, boron trifluoride, metallic chlorides or other reagents. Aldoximes normally require the use of polyphosphoric acid. The general observation is that the group in the position *anti* to the leaving group will migrate preferentially to the nitrogen atom. There are also rearrangements known in the solid state. See also **Bamberger – Goldschmidt** rearrangement.

## REFERENCES :

**March** : 1095

**Smith – March** : 1415

**Houben – Weyl** : **10/4**, 228; **E3**, 568; **E6b**, 141; **E7a**, 460, 615; **E7b**, 161, 178, 183; **E8a**, 254, 736, 759, 1024; **E8b**, 303; **E8c**, 682; **E8d**, 185; **E14b**, 391; **E15**, 678; **E16c**, 909; **E16d**, 627, 1141; **E19c**, 408

**Org. React.** : **11**, 1; **35**, 1

**Org. Synth.** : **63**, 188; **66**, 185

**Org. Synth. Coll. Vol.** : **7**, 254; **8**, 568

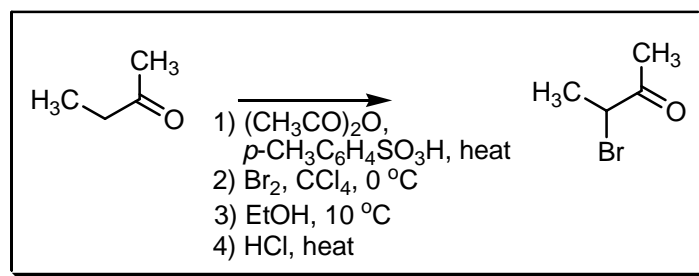
**Science of Synthesis** : **10**, 75, 258, 582, 740

- 1) E. Beckmann, *Ber. Dtsch. Chem. Ges.*, 1886, **19**, 988.
- 2) E. Beckmann, *Ber. Dtsch. Chem. Ges.*, 1887, **20**, 1507.
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- 12) M. Boero; T. Ikeshoji; C.C. Liew; K. Terakura; M. Parrinello, *J. Am. Chem. Soc.*, 2004, **126**, 6280.
- 13) M.K. Dongare; V.V. Bhagwat; C.V. Ramana; M.K. Gurhar, *Tetrahedron Lett.*, 2004, **45**, 4759.
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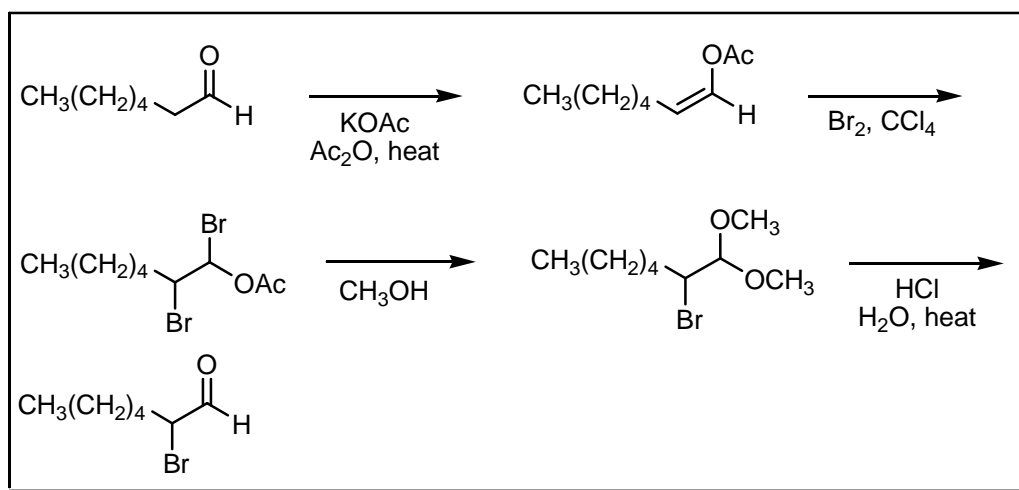
COMMENTS :

## BEDOUKIAN REACTION

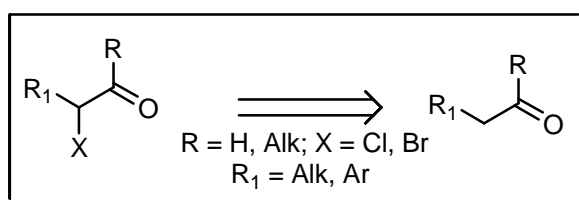
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The synthesis of  $\alpha$ -halogen ketones and  $\alpha$ -halogen aldehydes from enol acetones. Tosic acid is used for ketones, while potassium acetate is used for aldehydes. See also **Fritsch – Kling** and **Hell – Volhard – Zelinsky** reactions.



## REFERENCES :

Org. Synth. : 29, 14

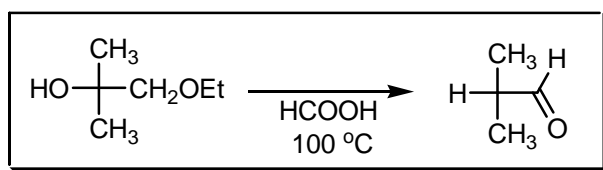
Org. Synth. Coll. Vol. : 3, 127

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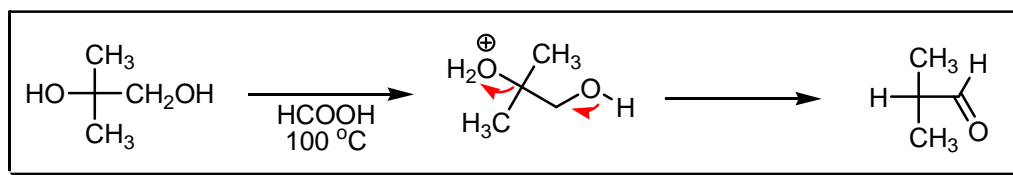
## COMMENTS :

## BÉHAL – SOMMELET SYNTHESIS

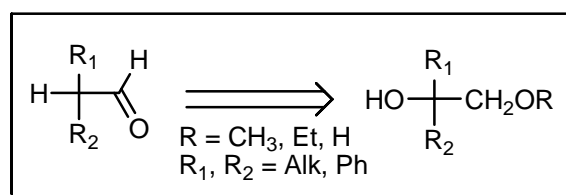
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Primary-secondary and primary-tertiary ethylene glycols yield aldehydes when heated with acids (anhydrous formic or oxalic acids). Ethers of the type R<sub>2</sub>C(OH)CH<sub>2</sub>OR react particularly easily.

## REFERENCES :

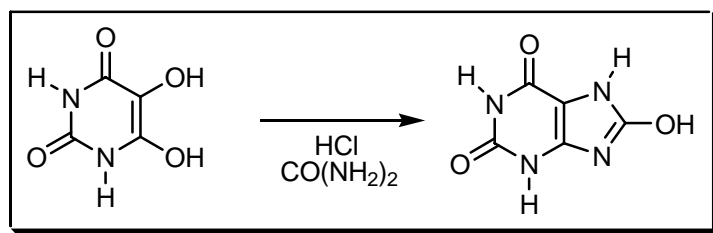
Houben – Weyl : 7/1, 104, 233

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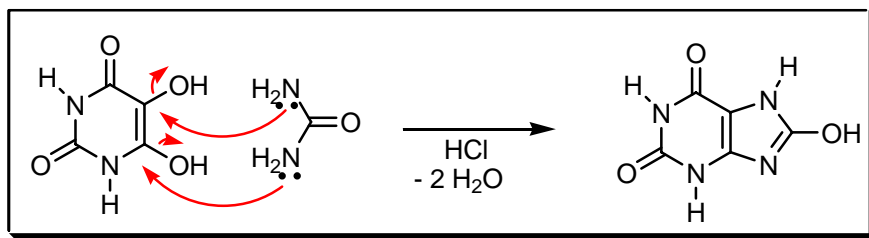
## COMMENTS :

## BEHREND – ROOSEN SYNTHESIS

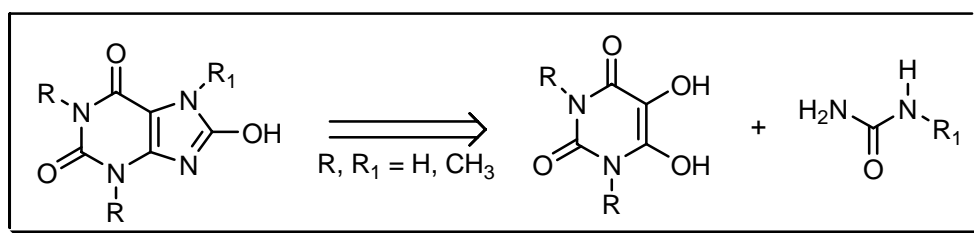
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



The condensation of isodialuric acids with derivatives of urea. The mechanism can be step-wise. See also **Fischer – Ach, Horbaczewski** and **Traube** reactions.

- 1) R. Behrend; O. Roosen, *Ber. Dtsch. Chem. Ges.*, 1888, **21**, 999.
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## BEHREND REARRANGEMENT

Chemical reaction scheme showing the equilibrium between two resonance structures of a 4-nitrophenyl-substituted iminium salt, catalyzed by  $\text{Et}_3\text{N}$  in dioxane.

**Left Structure (Reactant):** A 4-nitrophenyl ring is attached to a carbon atom. This carbon atom is double-bonded to a nitrogen atom. The nitrogen atom is also bonded to a hydrogen atom and an oxygen atom with a negative charge ( $\text{O}^-$ ). The carbon atom is also bonded to a hydrogen atom and a quaternary carbon atom. This quaternary carbon atom is bonded to a methyl group ( $\text{CH}_3$ ), an isopropyl group ( $\text{CH}_2\text{CH}(\text{CH}_3)_2$ ), and a cyano group ( $\text{CN}$ ).

**Right Structure (Product):** A 4-nitrophenyl ring is attached to a carbon atom. This carbon atom is double-bonded to a nitrogen atom. The nitrogen atom is also bonded to a hydrogen atom and an oxygen atom with a negative charge ( $\text{O}^-$ ). The carbon atom is also bonded to a hydrogen atom and a quaternary carbon atom. This quaternary carbon atom is bonded to a methyl group ( $\text{CH}_3$ ), an isopropyl group ( $\text{CH}_2\text{CH}(\text{CH}_3)_2$ ), and a cyano group ( $\text{CN}$ ).

The reaction is reversible, as indicated by the equilibrium arrows.

$$\begin{array}{ccccc} \begin{array}{c} \text{R} \\ | \\ \text{H}-\text{C}^+-\text{N}=\text{C}(\text{R}_2)-\text{H} \\ | \quad \quad | \\ \text{R}_1 \quad \quad \ominus\text{O} \end{array} & \rightleftharpoons & \begin{array}{c} \text{R} \\ | \\ \text{R}_1-\text{C}=\text{N}^--\text{C}(\text{R}_2)=\text{H} \\ \quad \quad | \\ \quad \quad \text{O} \end{array} & \rightleftharpoons & \begin{array}{c} \text{R} \\ | \\ \text{R}_1-\text{C}=\text{N}^+-\text{C}(\text{R}_2)-\text{H} \\ | \quad \quad | \\ \ominus\text{O} \end{array} \end{array}$$
$$\begin{array}{ccc} \begin{array}{c} \text{R} \\ | \\ \text{R}_1\text{C}=\text{N}^+\text{O}^- \\ | \\ \text{R}_2\text{CH}_2\text{H} \end{array} & \rightleftharpoons & \begin{array}{c} \text{R} \\ | \\ \text{H}-\text{C}-\text{N}^+\text{O}^- \\ | \\ \text{R}_1\text{CH}_2\text{H} \end{array} \\ \text{R, R}_1, \text{R}_2 = \text{Alk, Ar} & & \end{array}$$

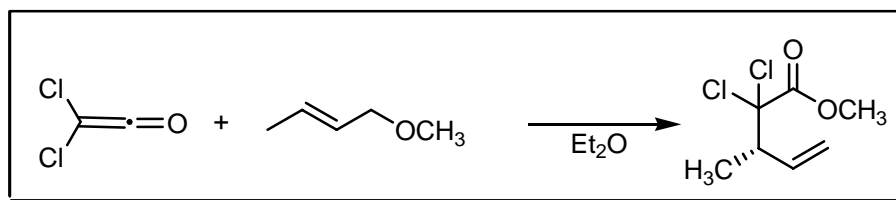
**NOTES :**

This is the 1,3-prototropic isomerisation of nitrones. This isomerisation is closely related to the isomerisation of imines.

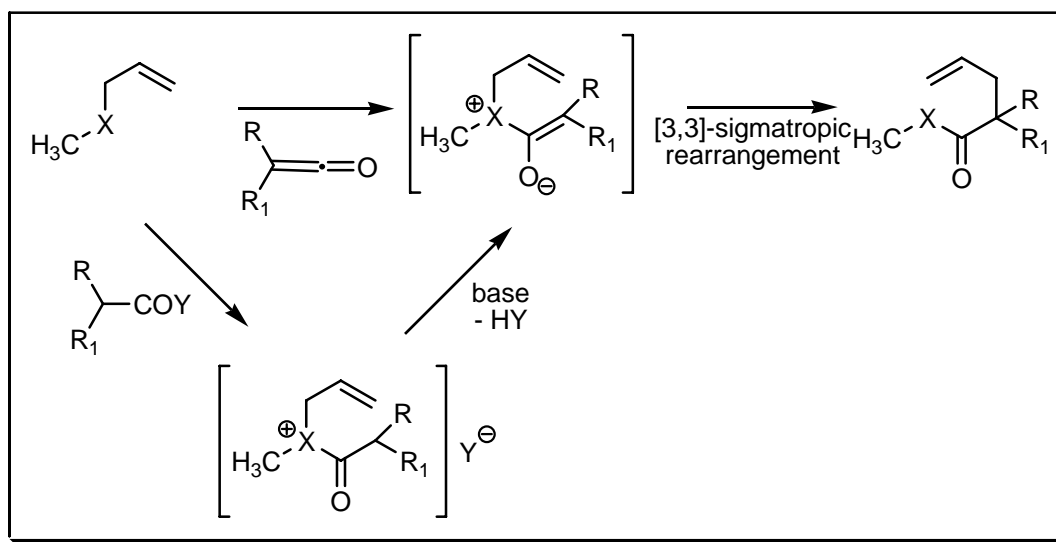
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**REFERENCES :**

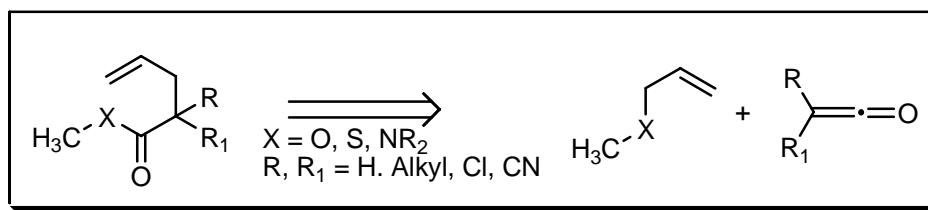
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- 

**COMMENTS :****BELLUŠ – CLAISEN REARRANGEMENT****EXAMPLE :**

## MECHANISM :



## DISCONNECTION :



## NOTES :

This is the reaction of an allylic ether, thioether or amine with a ketene. [3,3]-Sigmatropic rearrangement of the zwitterionic intermediate leads to an (*E*) unsaturated ester, thioester or amide. When applied to cyclic allylic compounds, a ring-enlargement by four carbons in one step takes place to provide medium-ring unsaturated (*E*)-lactones, thiolactones and lactams. See also **Carroll (Kimel – Cope)**, **Claisen (Claisen – Ireland)** rearrangement, **Cope**, **Eschenmoser – Meerwein – Claisen** rearrangement, **Ficini – Claisen**, **Johnson – Claisen**, **Marbet – Saucy** and **Overman** rearrangement reactions.

## REFERENCES :

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## COMMENTS :

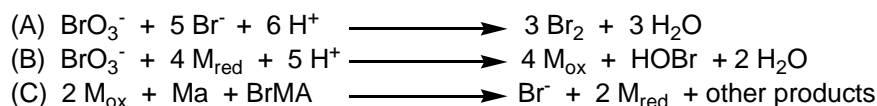
## BELOUSOV – ZHABOTINSKY REACTION

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### EXAMPLE :

- 1)  $\text{KBrO}_3$   
2)  $\text{CH}_2(\text{COOH})_2 + \text{aq. H}_2\text{SO}_4 + \text{KBr} \longrightarrow \text{oscillations}$   
3)  $[\text{Fe}(\text{phen})]^{2+}$
- 

### MECHANISM :



### NOTES :

This reaction involves the oxidation of an organic species (malonic acid) from an acidified bromate solution, in the presence of a metal ion catalyst. Different metal ions have been used, with  $\text{Ce}^{3+}/\text{Ce}^{4+}$  and  $[\text{Fe}(\text{phen})]^{2+}/[\text{Fe}(\text{phen})]^{3+}$  being more common. The reaction mechanism is still being studied and is extremely complicated but can be divided in 3 main reactions as shown.

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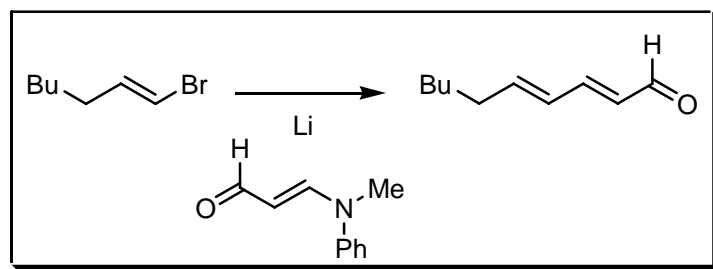
### REFERENCES :

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  - 2) R.J. Fields; E. Körös; R.M. Noyes, *J. Am. Chem. Soc.*, 1972, **94**, 8649.
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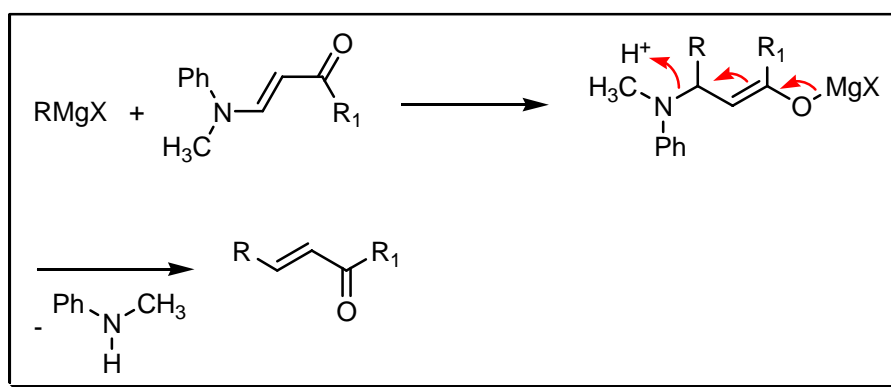
## COMMENTS :

## BENARY REACTION

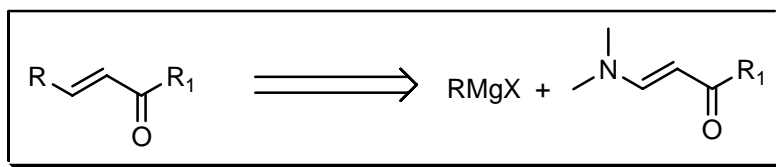
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The formation of polyunsaturated aldehydes from vinyl halides and enaminoaldehydes. Lithium metal or a **Grignard** reagent can be used.

### REFERENCES :

- 1) E. Benary, *Chem. Ber.*, 1930, **63**, 1573.
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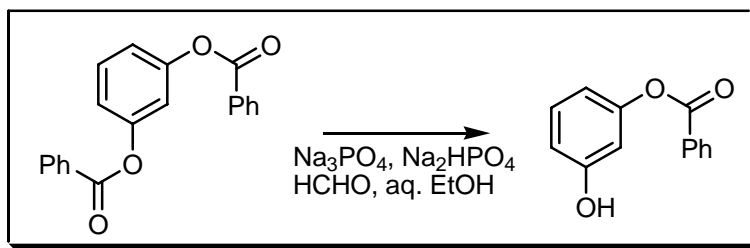
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- 

**COMMENTS :**

## BENET SYNTHESIS

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**EXAMPLE :**



**NOTES :**

Resorcinol dibenzoate in aqueous ethanol is refluxed with a mixture of sodium hydrogenphosphate and sodium phosphate to hydrolyse one of the benzoate groups. The addition of formaldehyde increases the yield.

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**REFERENCES :**

J. Benet, *Bull. Soc. Chim. Fr.*, 1932, **51**, 963.

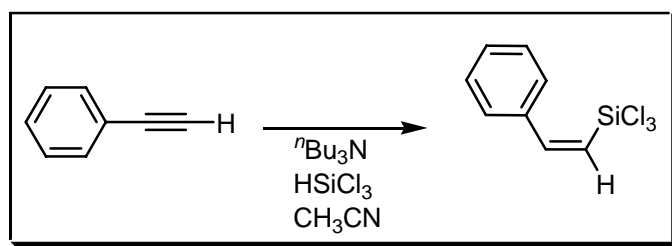
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**COMMENTS :**

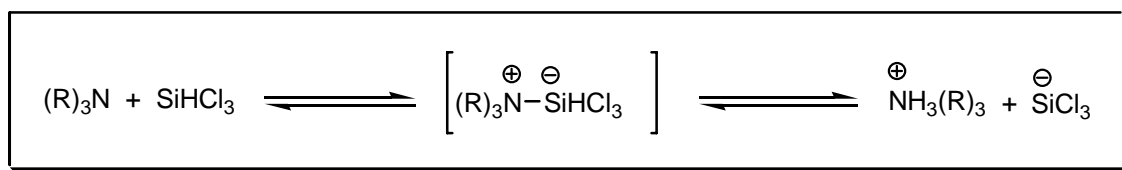


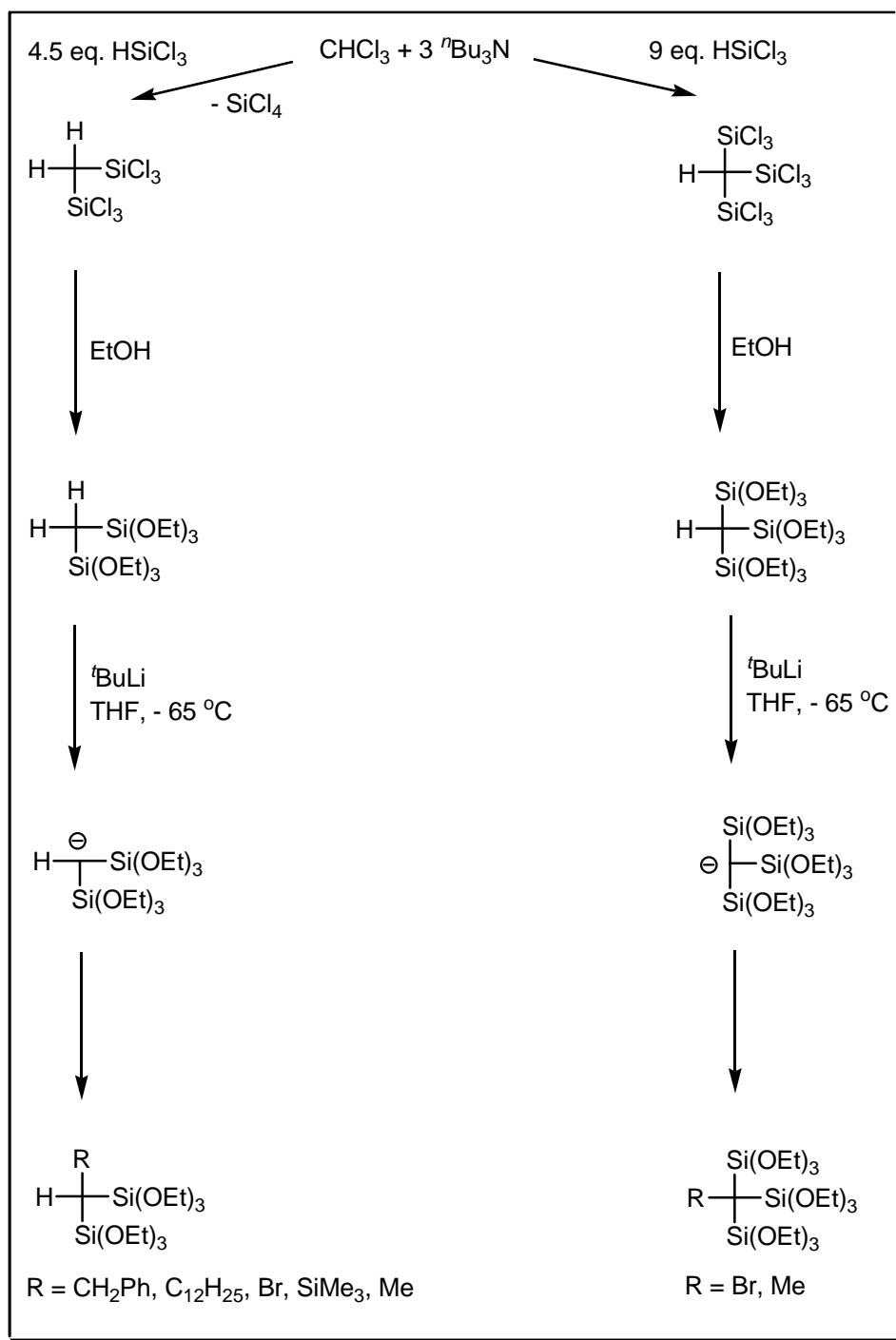
## BENKESER REACTION

EXAMPLE :

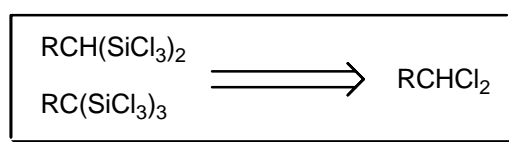


MECHANISM :





DISCONNECTION :



## NOTES :

In the initial experiments by **Benkeser** the silicon – carbon bond was formed mainly by the selective reduction of poly-halo compounds with  $\text{HSiCl}_3$  /  $^n\text{Bu}_3\text{N}$ . However, the method was only highly efficient for synthesising benzylic silanes and analogues. The extension to alkyl halides failed due to the reaction of trichlorosilane with  $\text{R}_3\text{NHCl}$ . Later, **Corriu** *et al.* optimised the reaction conditions.

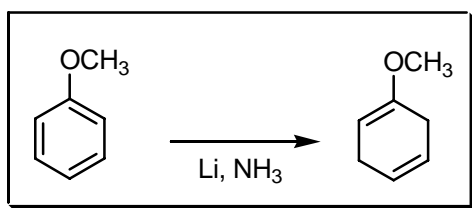
## REFERENCES :

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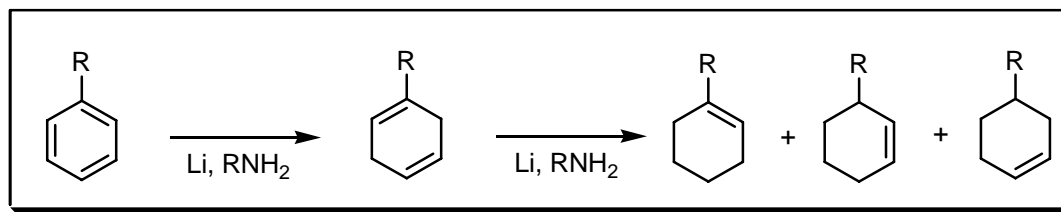
## COMMENTS :

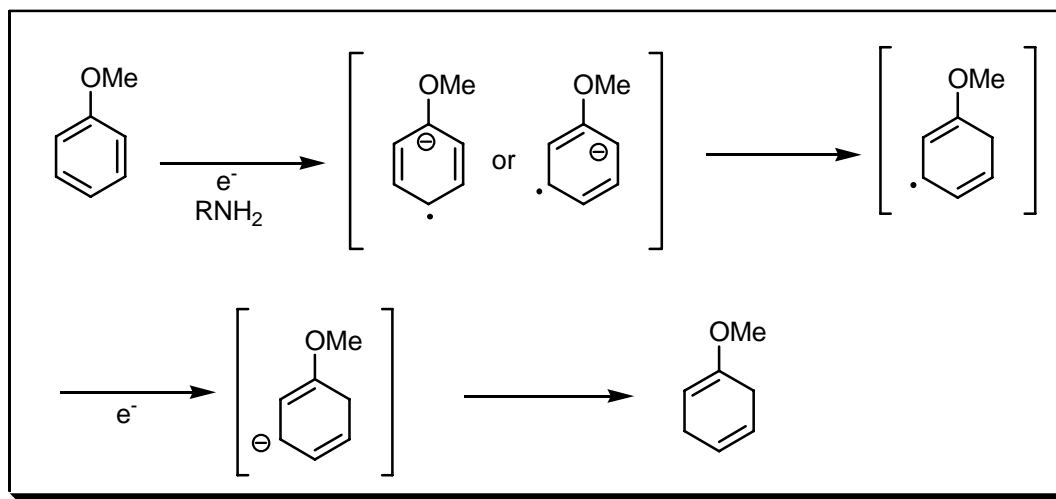
## BENKESER REDUCTION

### EXAMPLE :

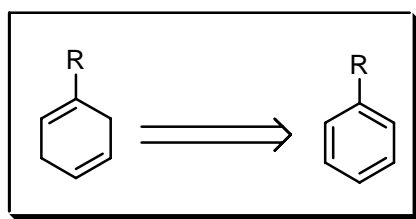


### MECHANISM :





#### DISCONNECTION :



#### NOTES :

The hydrogenation of aryls to non-conjugated dienes or mono-olefins with lithium or calcium in low molecular weight amines on a large scale (this is where the **Birch** reduction usually fails). The same reagents are also effective in the reduction of epoxides. The reaction can also be performed electro-chemical. See also **Birch** reduction.

#### REFERENCES :

**March** : 782

**Smith – March** : 1012

**Smith** : 466

**Smith 2<sup>nd</sup>** : 402

**Org. Synth.** : **50**, 88

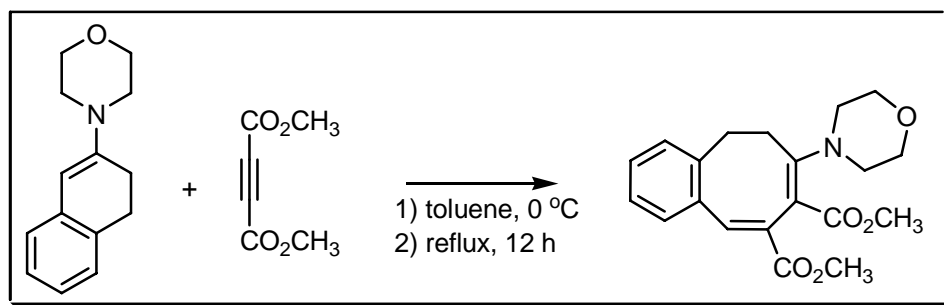
**Org. Synth. Coll. Vol.** : **6**, 852

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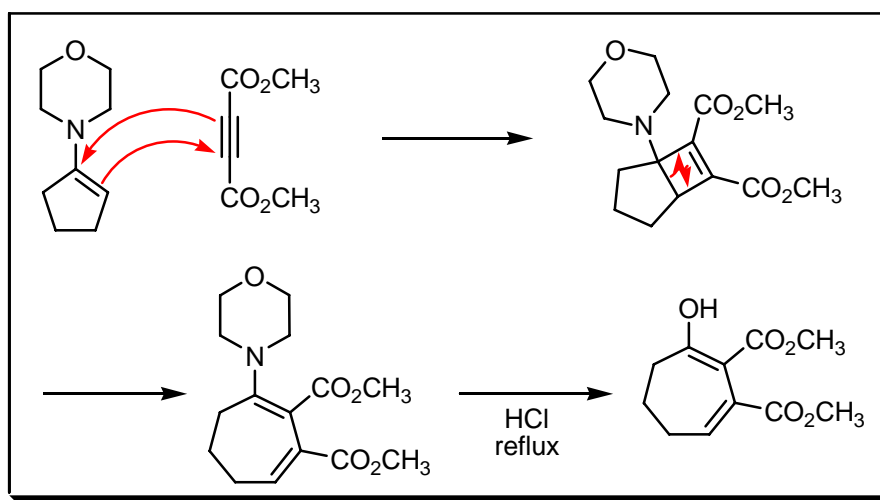
COMMENTS :

## BERCHTOLD REACTION

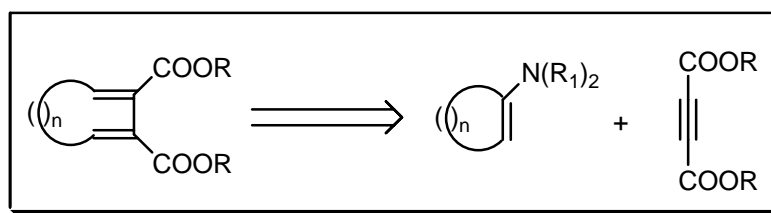
EXAMPLE :



MECHANISM :



DISCONNECTION :



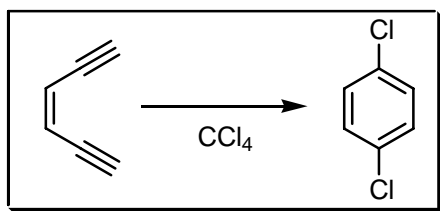
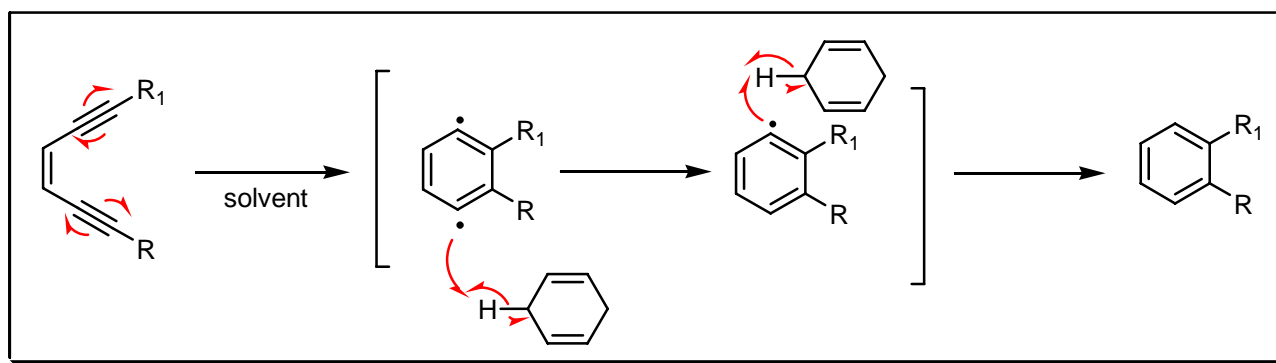
**NOTES :**

Dimethyl acetylenedicarboxylate reacts with enamines of cyclic ketones. The formed cyclobutene intermediate rearranges leading to a cyclic ketone with 2 more carbon atoms.

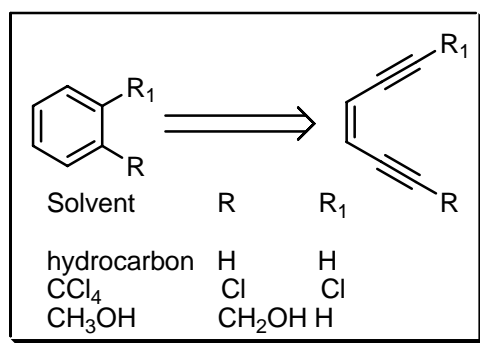
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- 

**COMMENTS :****BERGMAN – MASAMUNE CYCLISATION****EXAMPLE :****MECHANISM :**

## DISCONNECTION :



## NOTES :

The **Cope** rearrangement of hex-3-ene-1,5-diyne, which results in concerted cyclisation to *p*-benzyne, was first reported by **Bergman**. Ene-diyne undergo cycloaromatisation, which is a thermally allowed electrocyclic reaction. There are a few examples of aza-**Bergman**, photo-**Bergman** and metal-accelerated cyclisations. In the last one the cyclisation can take place at more ambient temperature. See also **Cope** rearrangement and **Myers – Moore – Saito – Schmittel** reactions.

## REFERENCES :

**Smith – March** : 1432, 1447

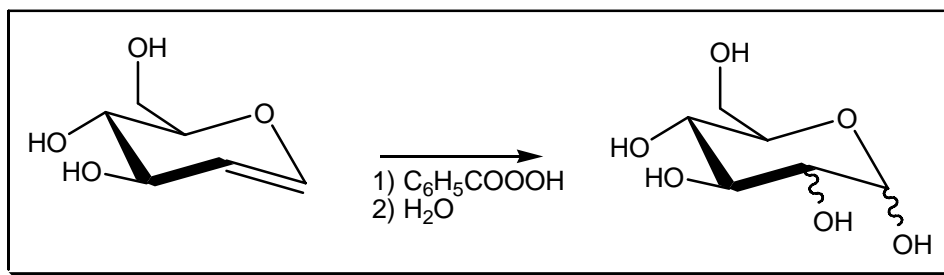
**Smith 2<sup>nd</sup>** : 1181

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- 19) K.D. Lewis; A.J. Matzger, *J. Am. Chem. Soc.*, 2005, **127**, 9968.

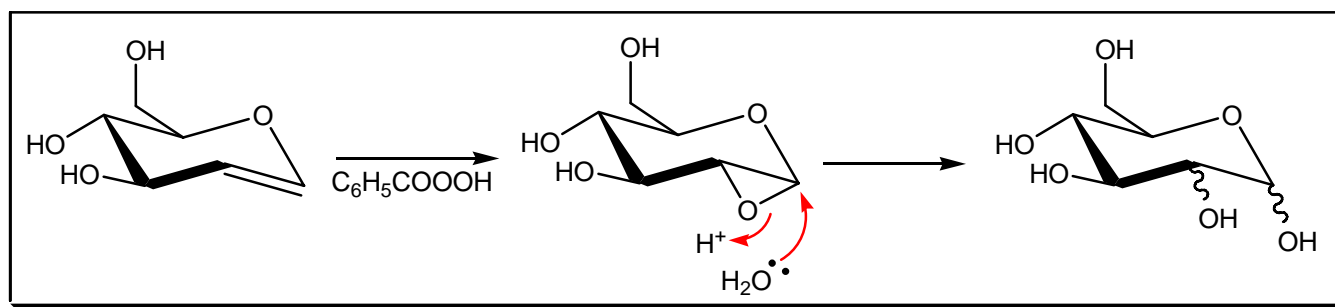
COMMENTS :

## BERGMANN – SCHOTTE REACTION

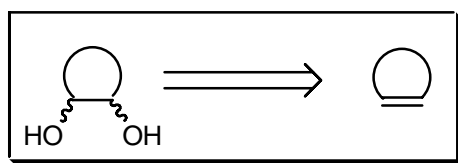
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The oxidation of unsaturated sugars with peroxybenzoic acid to produce epimeric carbohydrates. See also **Criegee** osmium tetroxide, **Fenton**, **Milas**, **Prévost**, **Sharpless** dihydroxylation and **Woodward** dihydroxylation reactions.

REFERENCES :

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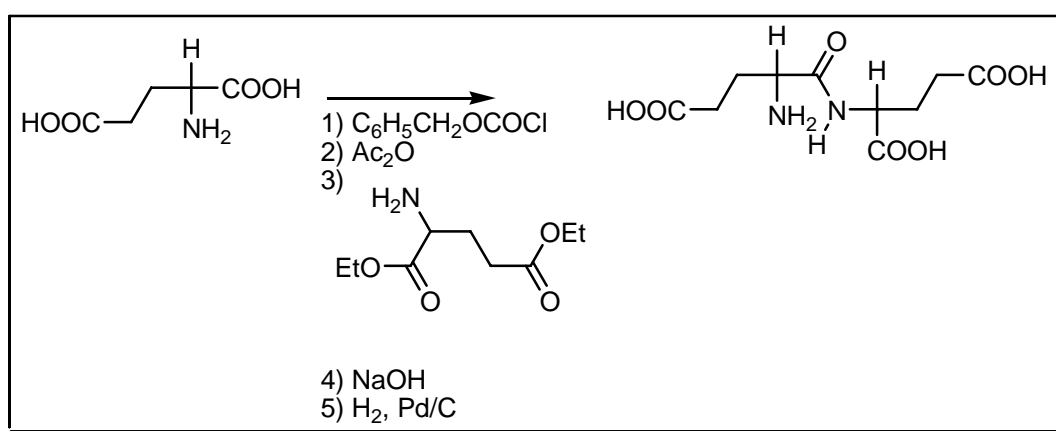


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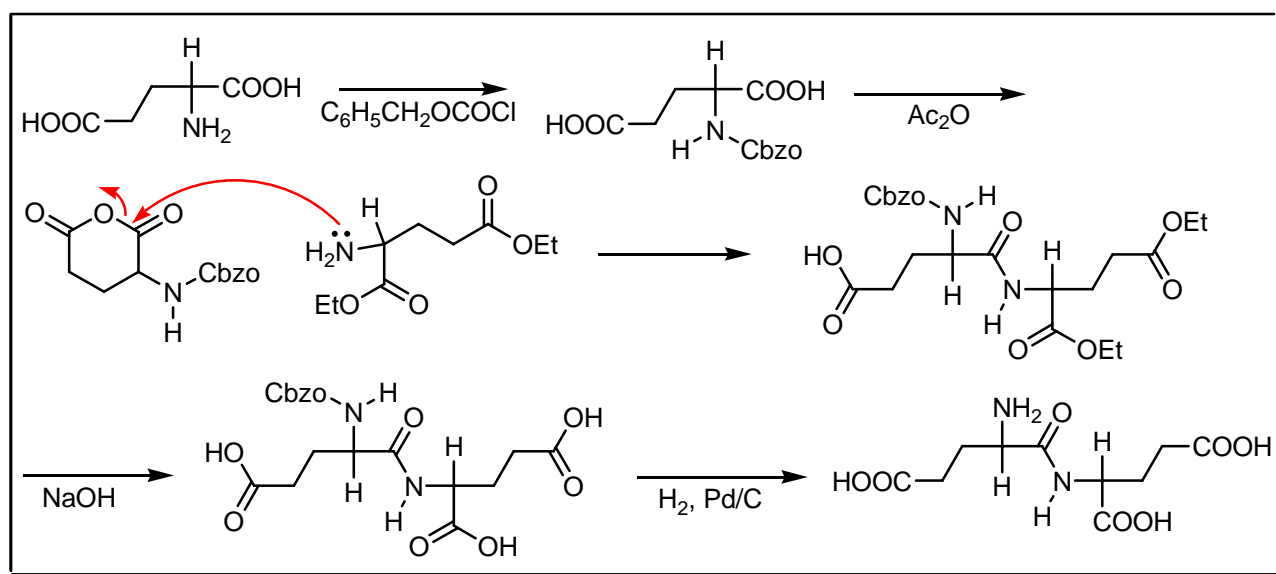
COMMENTS :

## BERGMANN – ZERVARS CARBOBENZOXY METHOD

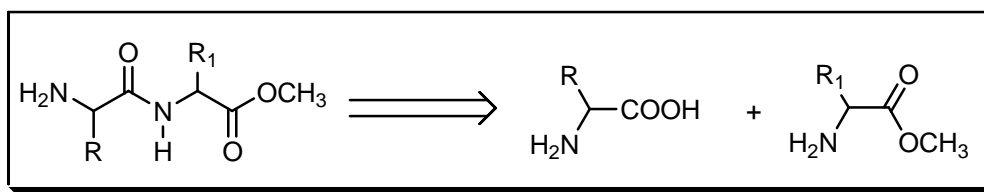
EXAMPLE :



MECHANISM :



## DISCONNECTION :



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## NOTES :

A development of the **Fischer** peptide synthesis in which an amino acid is transformed by benzyl chloroformate into the *N*-carbobenzoxy derivative. The protected amino acid is converted into the acid chloride, azide or anhydride, which is condensed with a second amino acid or suitable derivative. The carbobenzoxy group (Cbzo) is removed by catalytic hydrogenation of the resulting peptide. The method permits amino dicarboxylic acids to be used in the preparation of polypeptides. See also **Fischer** peptide, **Leuchs – Bergmann** and **Sheehan – Frank** reactions.

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## REFERENCES :

**Org. Synth.** : **23**, 13

**Org. Synth. Coll. Vol.** : **3**, 167

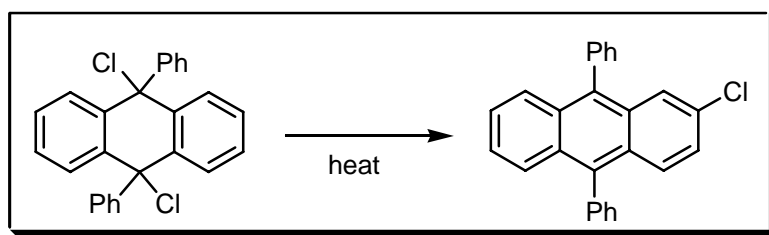
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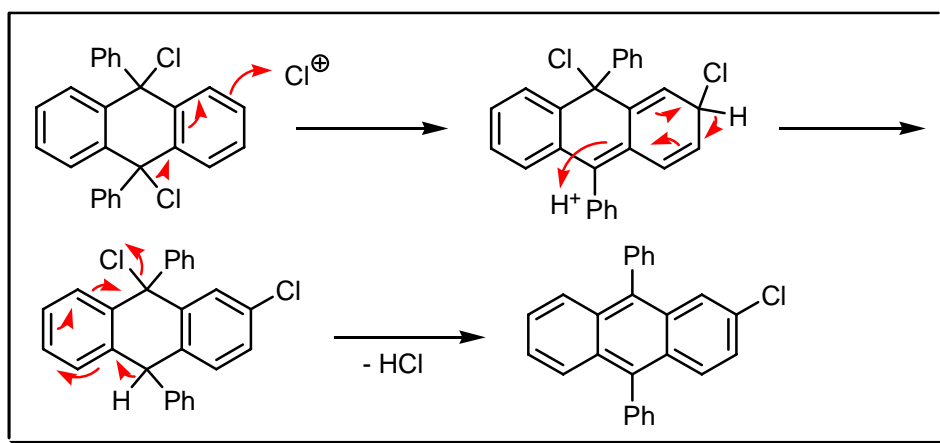
## COMMENTS :

## BERGMANN ANTHRACENE REACTION

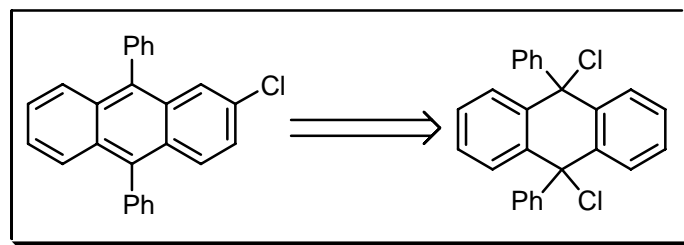
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This reaction is exemplified by the fact that 9,10-dichloro-9,10-diphenyl-9,10-dihydroanthracene forms 2-chloro-9,10-diphenylanthracene on heating. See also **Robert** reaction.

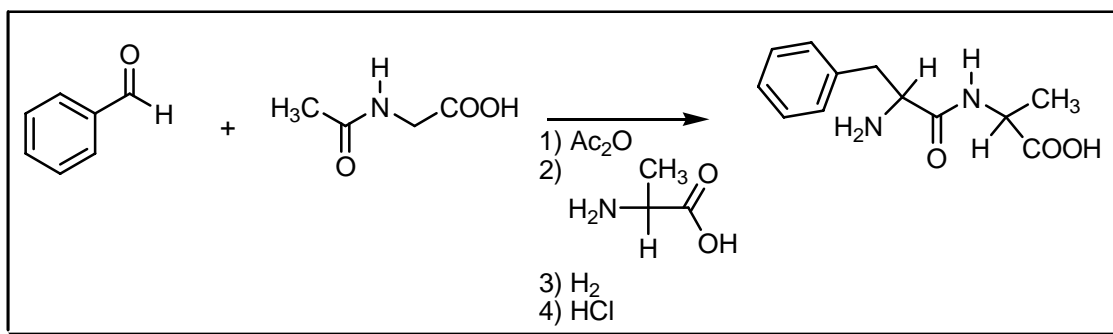
### REFERENCES :

E. Bergmann; O. Blum–Bergmann, *J. Am. Chem. Soc.*, 1937, **59**, 1439.

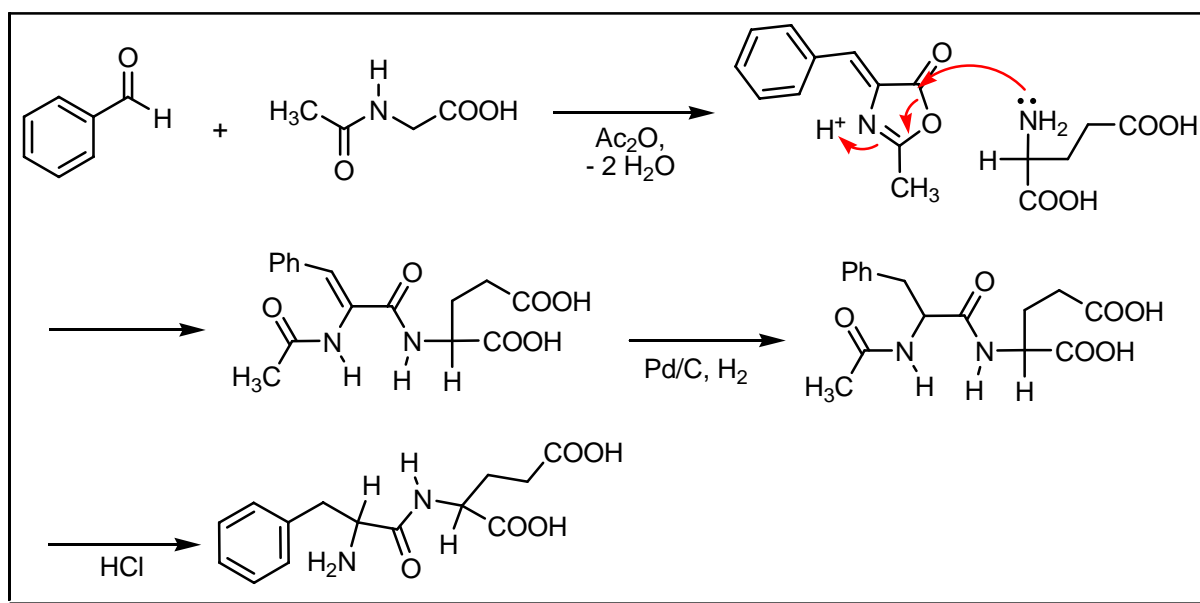
COMMENTS :

## BERGMANN AZLACTONE PEPTIDE SYNTHESIS

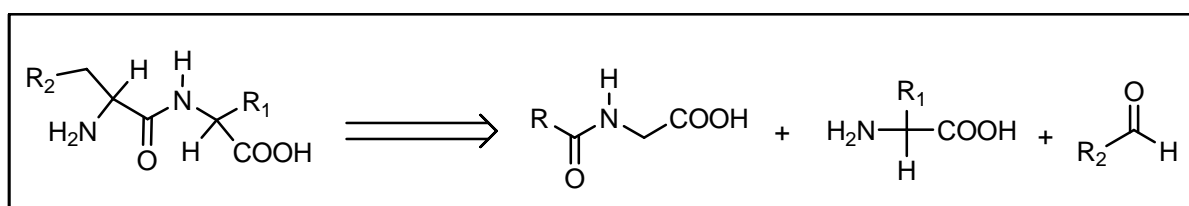
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

The formation of peptides from amino acids and azlactones of acylated amino acids. The formation of the azlactone is the **Erlenmeyer – Früstück** reaction. See also **Dakin** azlactone, **Erlenmeyer – Früstück** and **Erlenmeyer – Plöchl** reactions.

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## REFERENCES :

Houben – Weyl : 11/2, 374

Org. React. : 3, 216

Org. Synth. : 19, 1

Org. Synth. Coll. Vol. : 2, 1

- 
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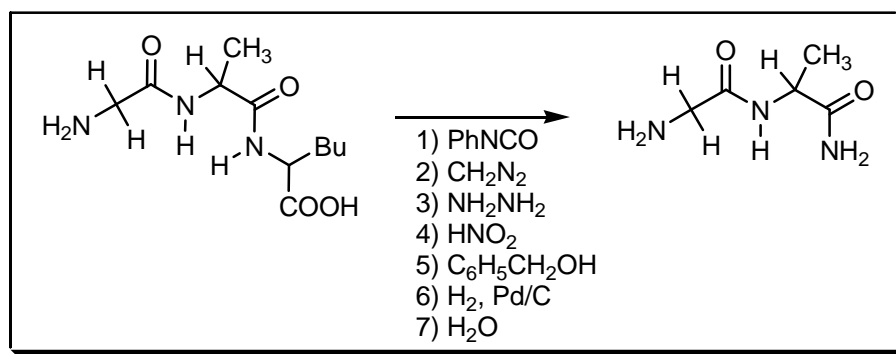
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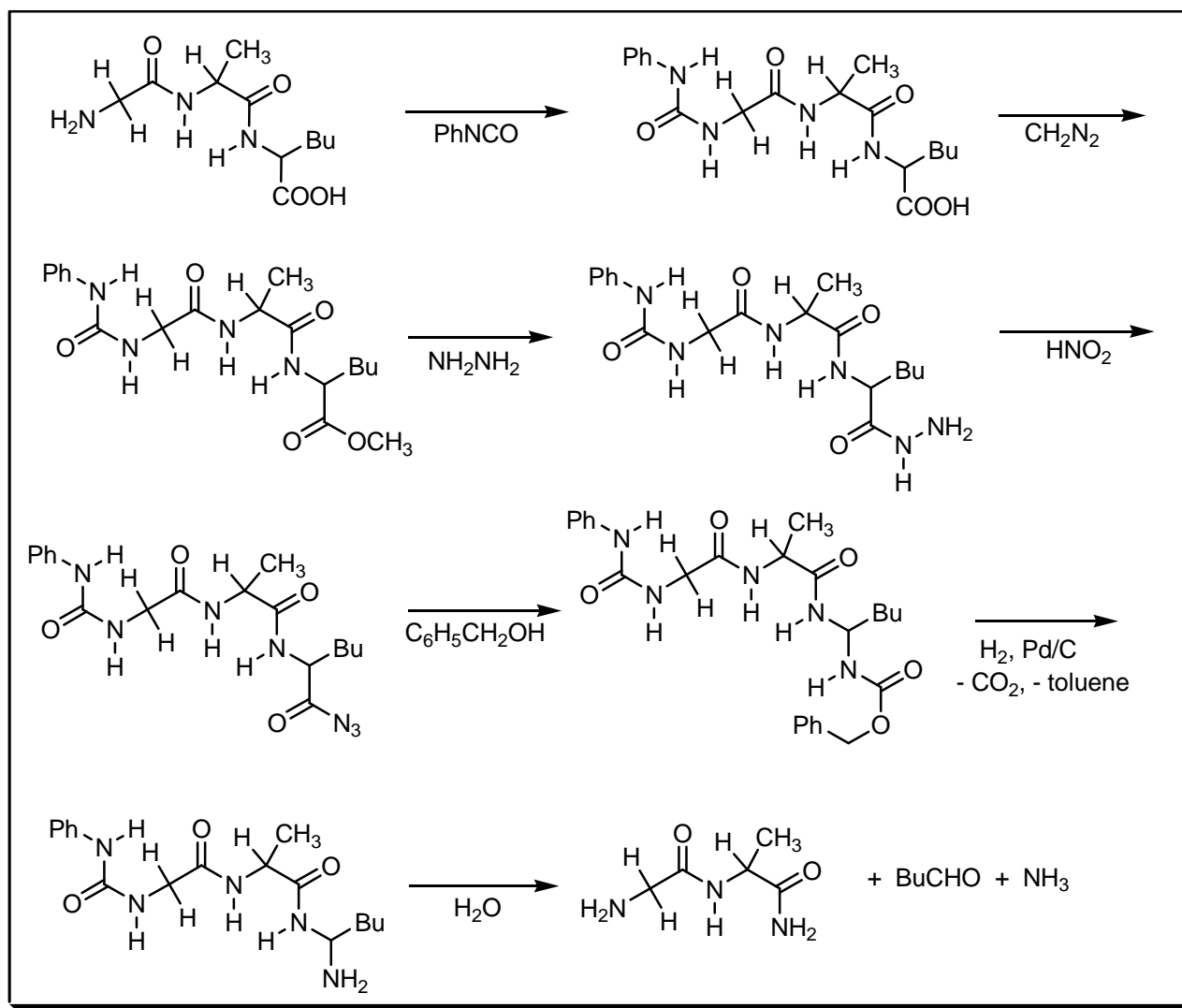
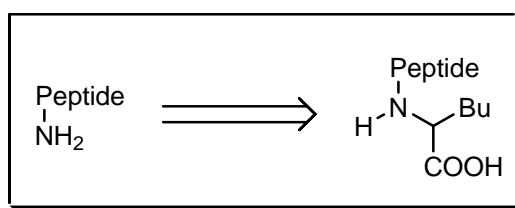
## COMMENTS :

## BERGMANN DEGRADATION OF PEPTIDES

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### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

The free amino group of the polypeptide is protected by treatment with phenyl isocyanate and the free carboxyl group is methylated with diazomethane. The ester is converted by hydrazine into the hydrazide, which yields the azide with nitrous acid. Treatment of the azide with benzyl alcohol forms the benzylurethane. This urethane is catalytically hydrogenated ( $\text{H}_2, \text{Pd/C}$ ) to yield the phenylurethane of a polypeptide amide with one less amino acid than the starting material, an identifiable aldehyde and toluene. The peptide amide can be further treated with an equivalent amount of hydrazine and again converted into the hydrazide and through the azide into the benzylurethane and so on. See also **Bergmann – Zervas**, **Curtius**, **Edman** degradation and **Schlack – Kumpf** reactions.

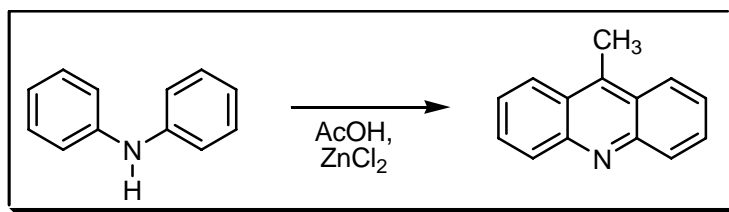
## REFERENCES :

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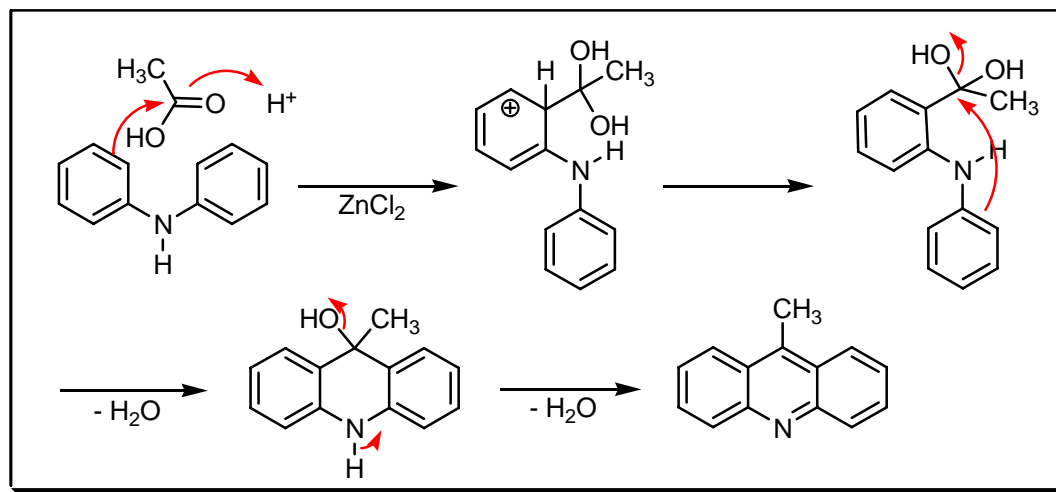
## COMMENTS :

## BERNTHSEN ACRIDINE SYNTHESIS

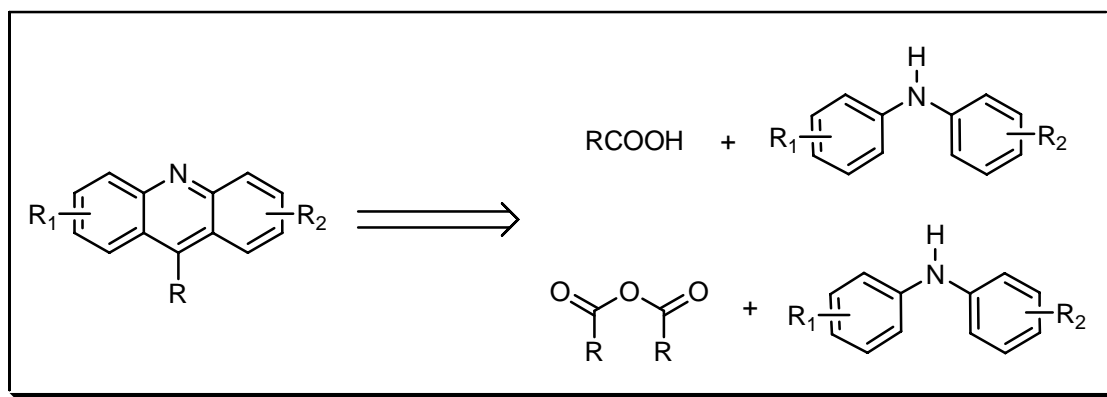
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of 5-substituted acridines by heating a diarylamine with an organic acid or anhydride in the presence of a Lewis acid, usually zinc chloride. See also **Pfitzinger – Borsche**, **Ullmann – Fetvadjan** and **Ullmann – La Torre** reactions.

## REFERENCES :

**Smith** : 1346

**Smith 2<sup>nd</sup>** : 1107

**Houben – Weyl** : **E7b**, 133

- 1) A. Bernthsen, *Liebigs Ann. Chem.*, 1878, **192**, 1.
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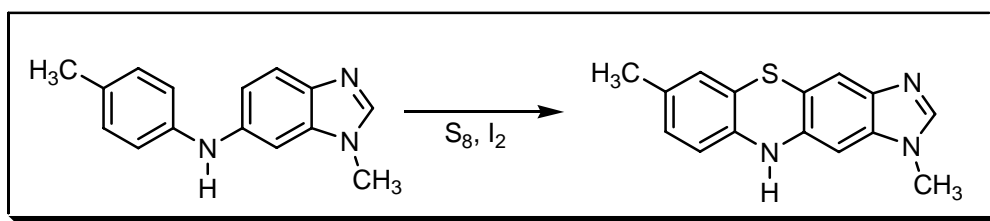
## COMMENTS :



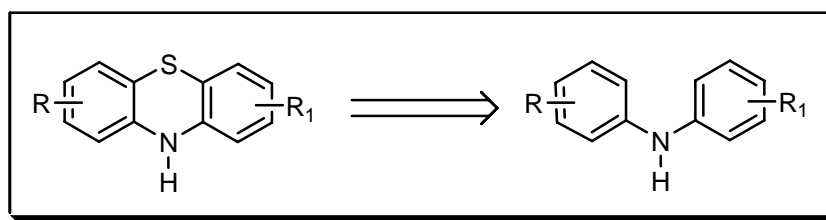
## BERNTHSEN PHENOTHIAZINE SYNTHESIS

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### EXAMPLE :



### DISCONNECTION :



### NOTES :

The synthesis of phenothiazine from diphenyl amine. Iodine or aluminium chloride are used as catalyst. See also **Ferrario – Ackerman** reaction.

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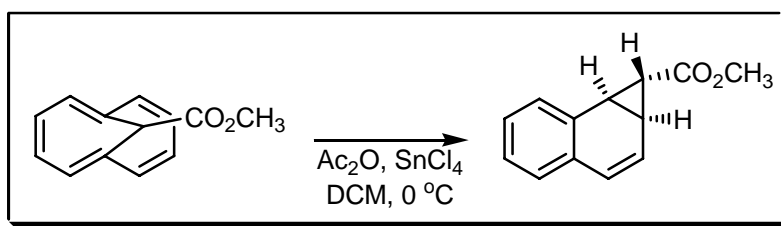
### REFERENCES :

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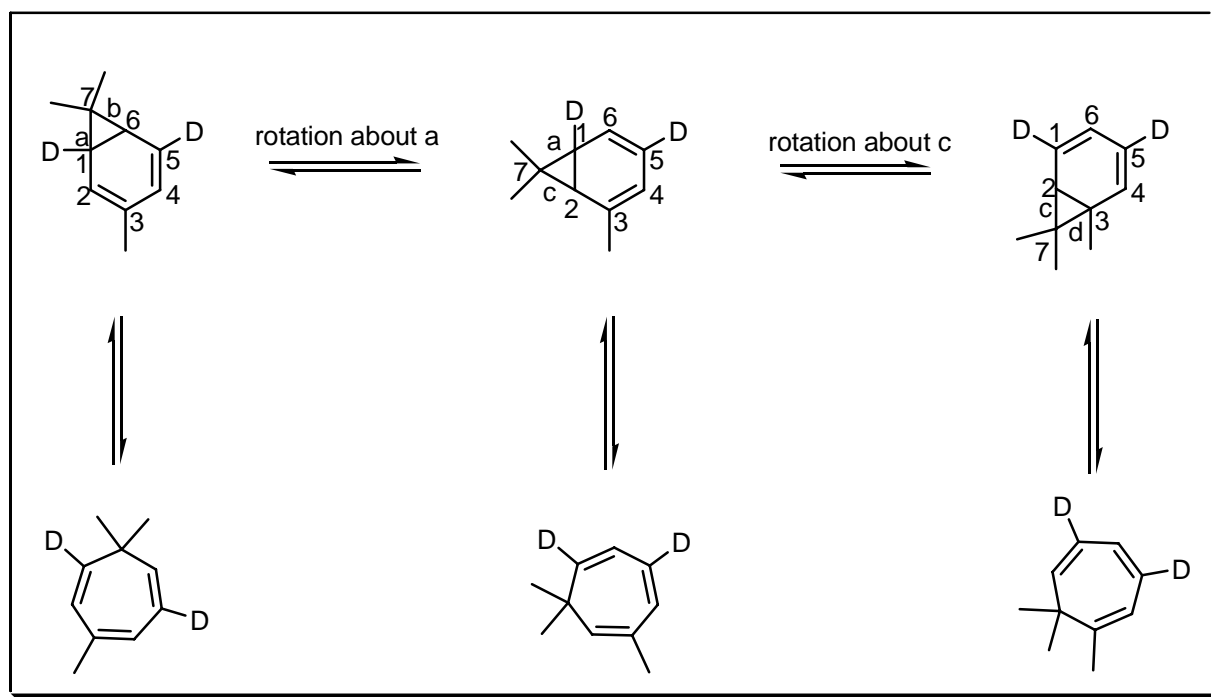
### COMMENTS :

## BERSON – WILLCOTT REARRANGEMENT

### EXAMPLE :



### MECHANISM :



### NOTES :

Originally, this rearrangement involves the *intramolecular* skeletal reorganisation of tropilidene. This rearrangement can be expanded to many other systems.

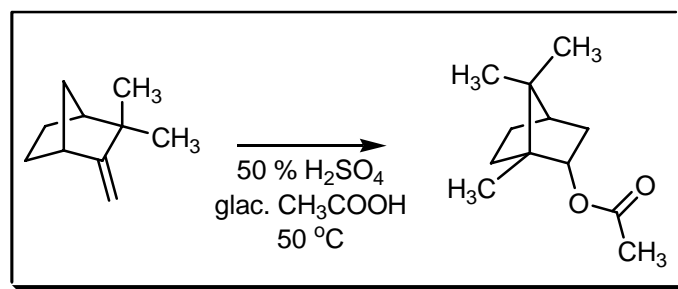
### REFERENCES :

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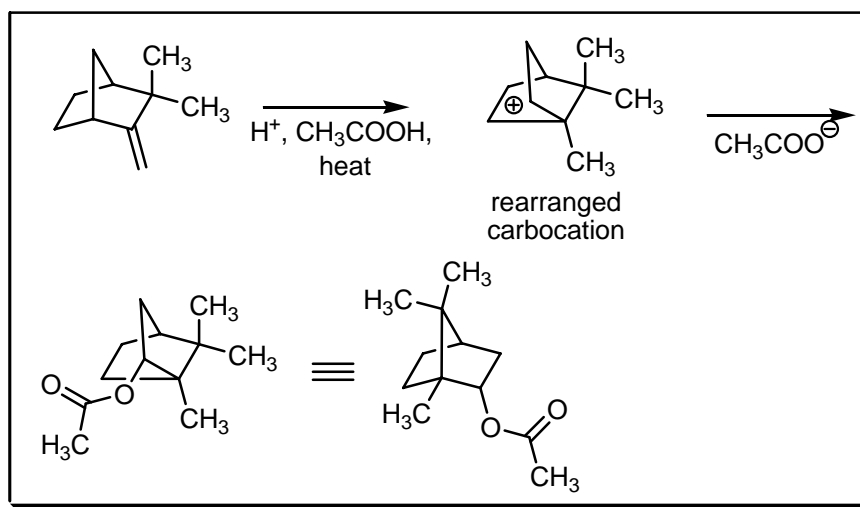
COMMENTS :

## BERTRAM – WALBAUM SYNTHESIS

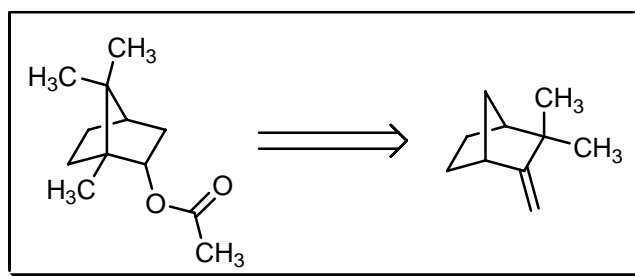
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

The formation of isobornyl esters from camphene by the action of organic acids in the presence of sulfuric acid. See also **Wagner – Meerwein** rearrangement.

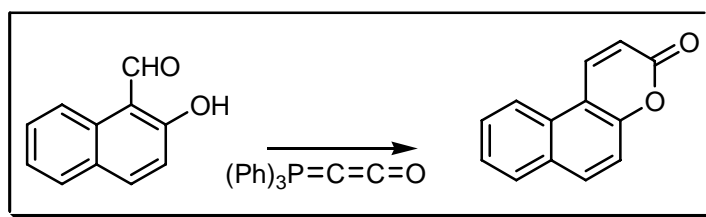
## REFERENCES :

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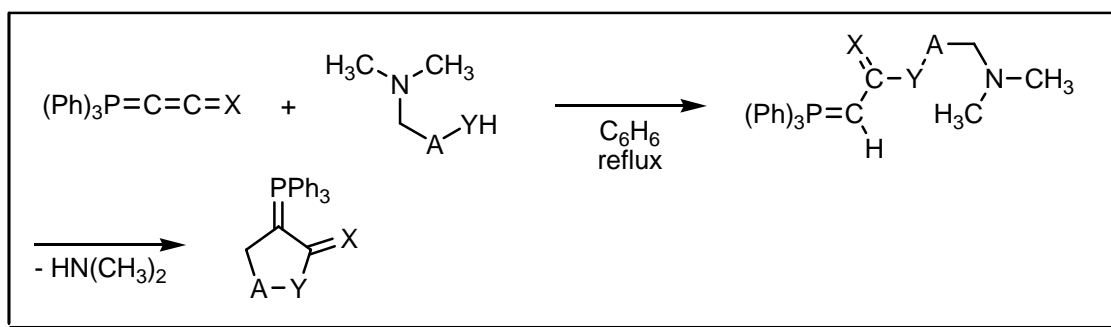
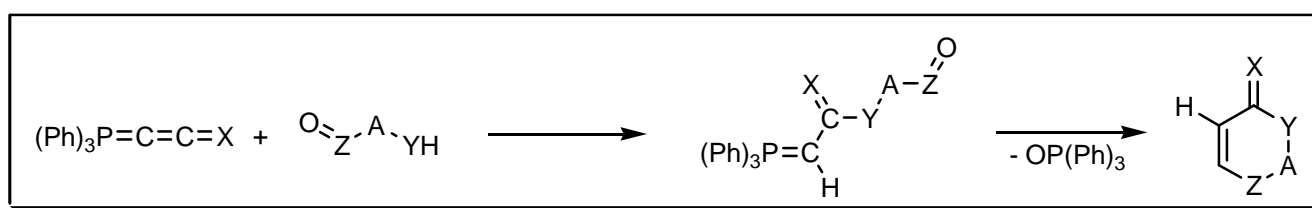
## COMMENTS :

## BESTMANN REACTION

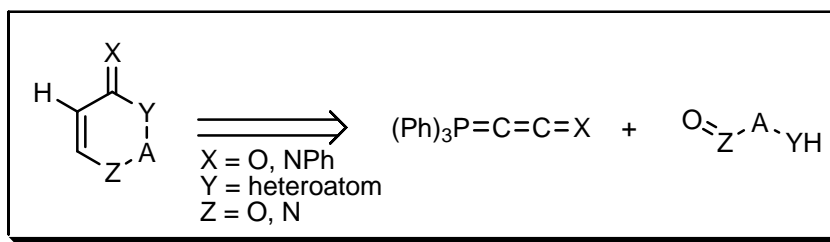
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

Cumulated ylides react with compounds containing an acidic Y-H bond and a carbonyl group or a nitroso group in the same molecule to give heterocyclic compounds.

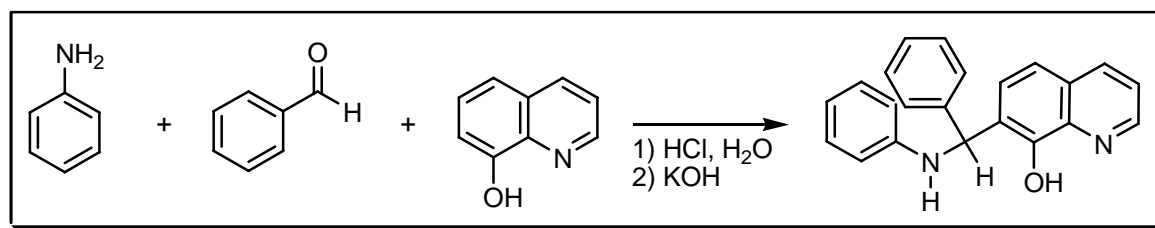
## REFERENCES :

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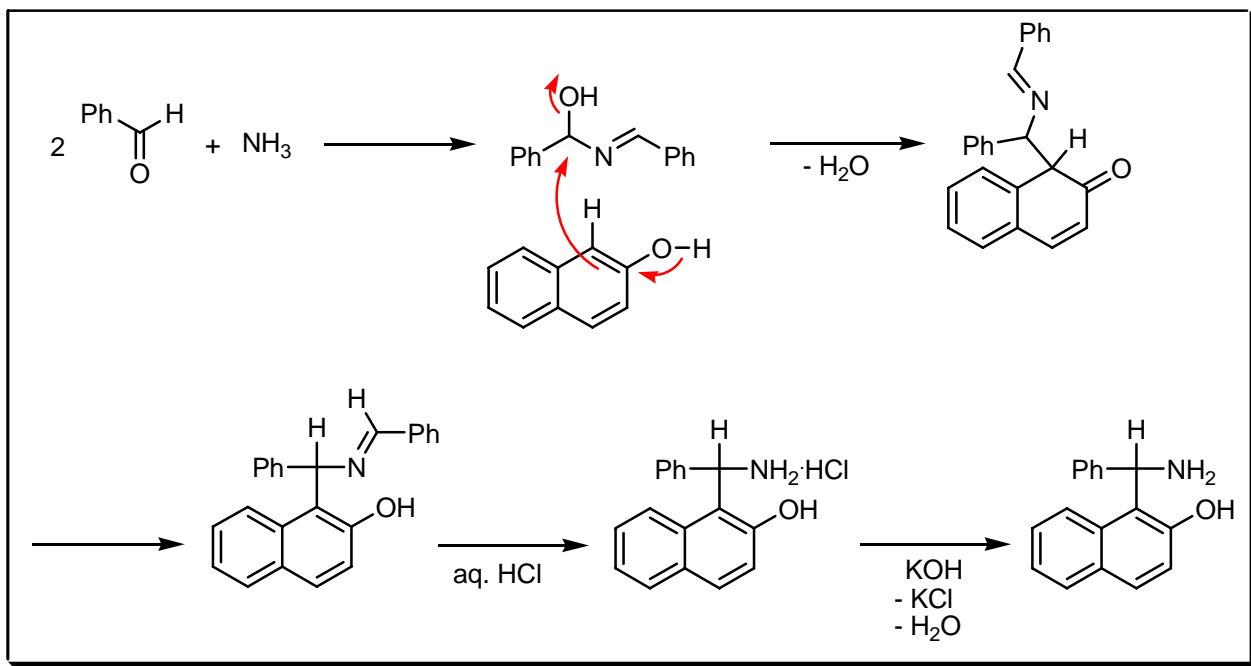
## COMMENTS :

## BETTI REACTION

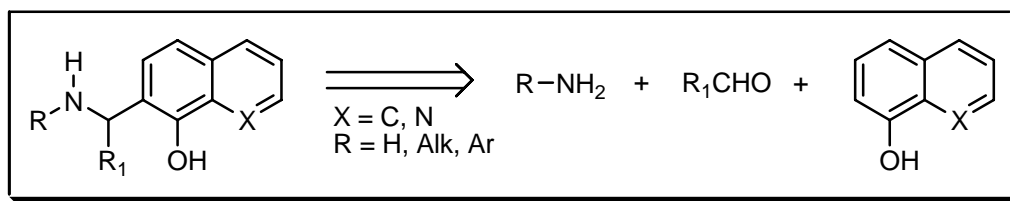
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Naphthols, quinolinols condense with aromatic aldehydes and primary aromatic or heterocyclic amines to yield aminomethyl derivatives. In some cases cyclic compounds are obtained. Ammonia and amides have also been employed. The formed amino phenol compounds have been reported as ligands in metal ion-catalysed asymmetric reactions. See also **Mannich** and **Pictet – Spengler** reactions.

## REFERENCES :

Houben – Weyl : 11/1, 759

Org. Synth. : 9, 60

Org. Synth. Coll. Vol. : 1, 381

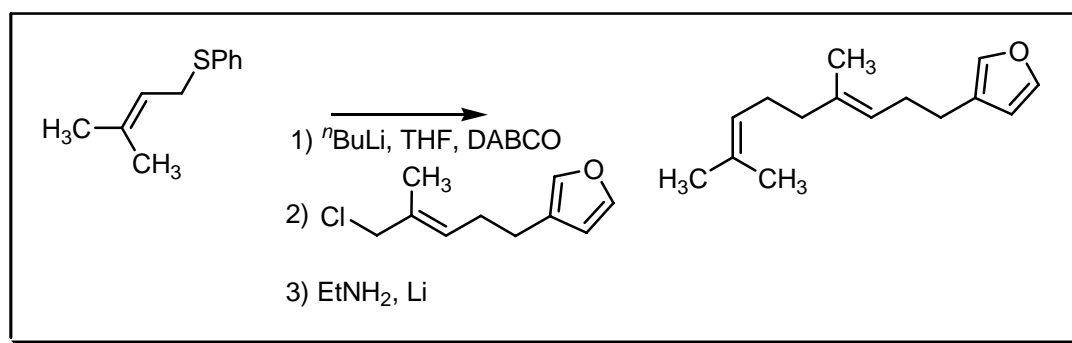
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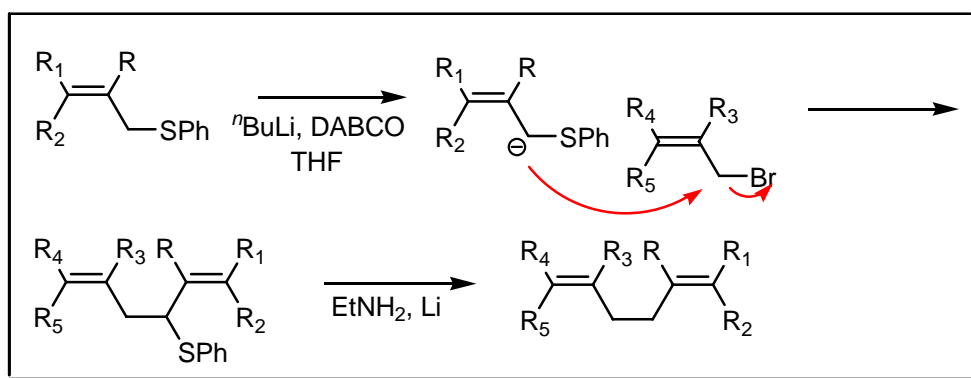
COMMENTS :

## BIELLMANN ALKYLATION

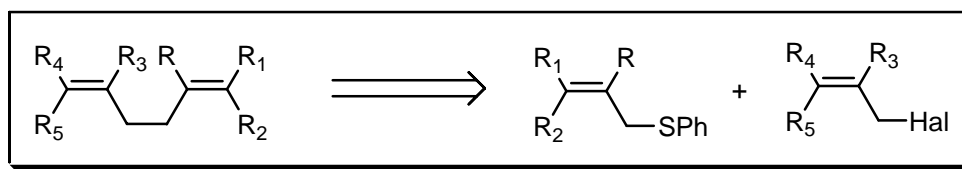
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The coupling of allylic halides and allylic thiocarbanions. The thiophenyl group is removed after activation of the adjacent carbon for nucleophilic attack.

## REFERENCES :

March : 457

Smith – March : 542

Smith : 744

Smith 2<sup>nd</sup> : 630

Org. React. : 27,1

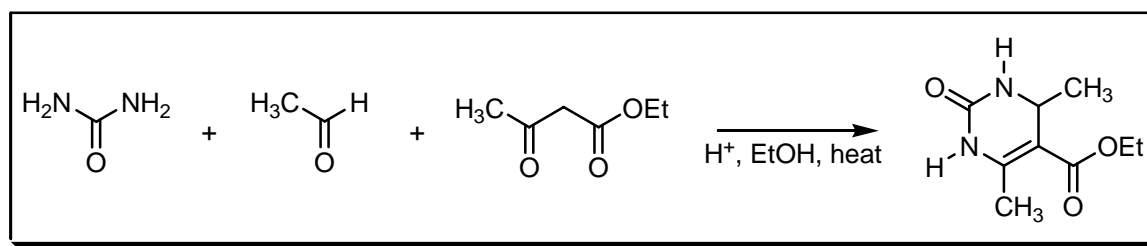
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## COMMENTS :

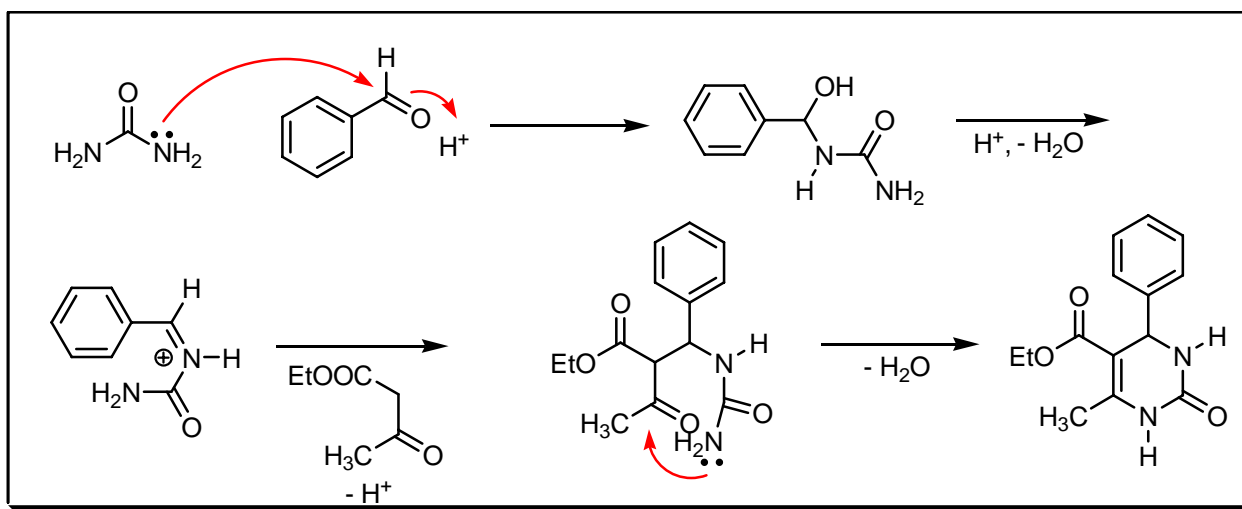


## BIGINELLI PYRIMIDONE SYNTHESIS

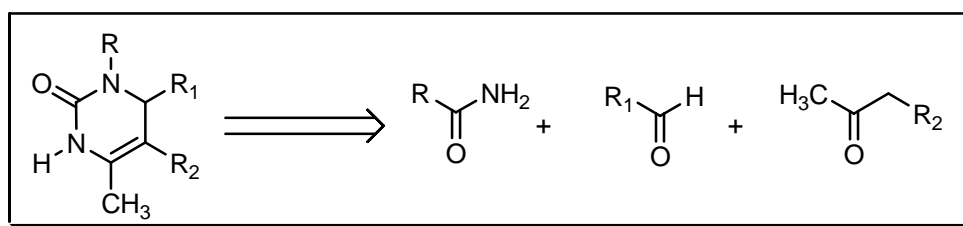
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The formation of pyrimidines from aldehydes,  $\beta$ -ketocarboxylic esters and urea. There are four ways to assemble the pyrimidine ring. Over the last 100 years several mechanistic proposals appeared in the literature. The best known modification brought about by the need for better yields is done by **Atwal *et al.*** An enone is reacted with a protected urea or thiourea derivative under neutral conditions. Several other improved syntheses have been reported, e.g. bismuth triflate catalysed by **Adapa *et al.*** and lithium bromide catalysed by **Maiti *et al.***

### REFERENCES :

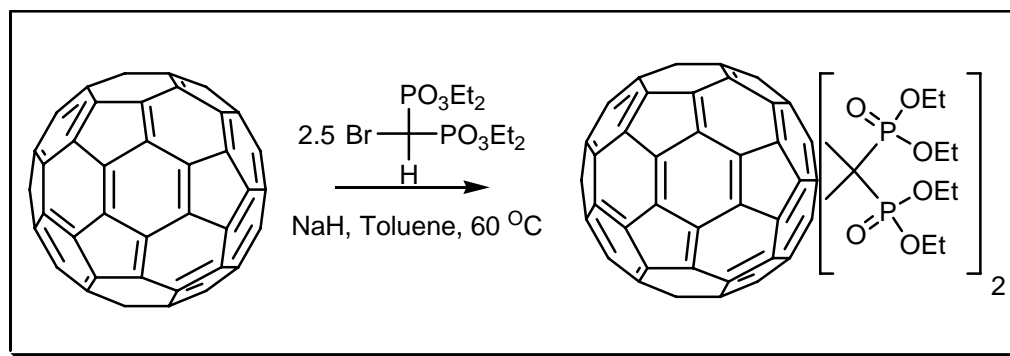
**Org. React.** : 14, 88; 63, 1

- 1) P. Biginelli, *Ber. Dtsch. Chem. Ges.*, 1891, **24**, 1317.
- 2) L.E. Hinkel; D.H. Hey, *Recl. Trav. Chim. Pays-Bas*, 1929, **48**, 1280.
- 3) K. Folkers; T.B. Johnson, *J. Am. Chem. Soc.*, 1933, **55**, 3784.
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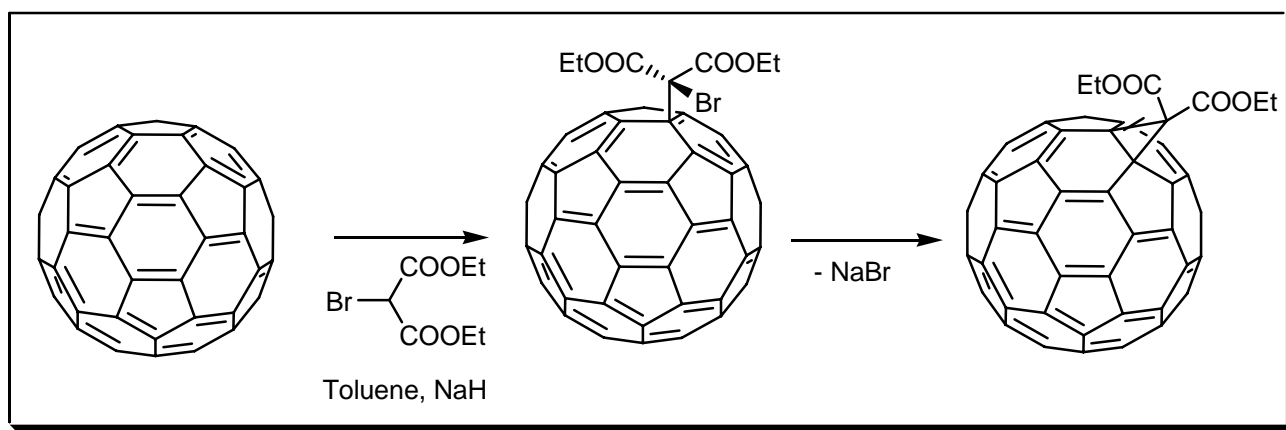
## COMMENTS :

## BINGEL REACTION

### EXAMPLE :



## MECHANISM :



## NOTES :

This is one of the most common fullerene functionalisation methods. It is the nucleophilic cyclopropanation with 2-halomalonates. Retro-Bingel reaction have also been investigated.

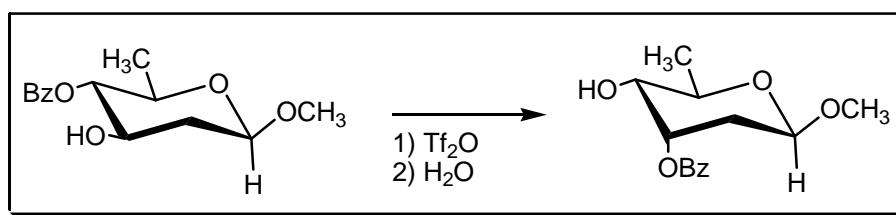
## REFERENCES :

- 1) C. Bingel, *Chem. Ber.*, 1993, **126**, 1957.
- 2) A. Hirsch; I. Lamparth; H.R. Karfunkel, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 437.
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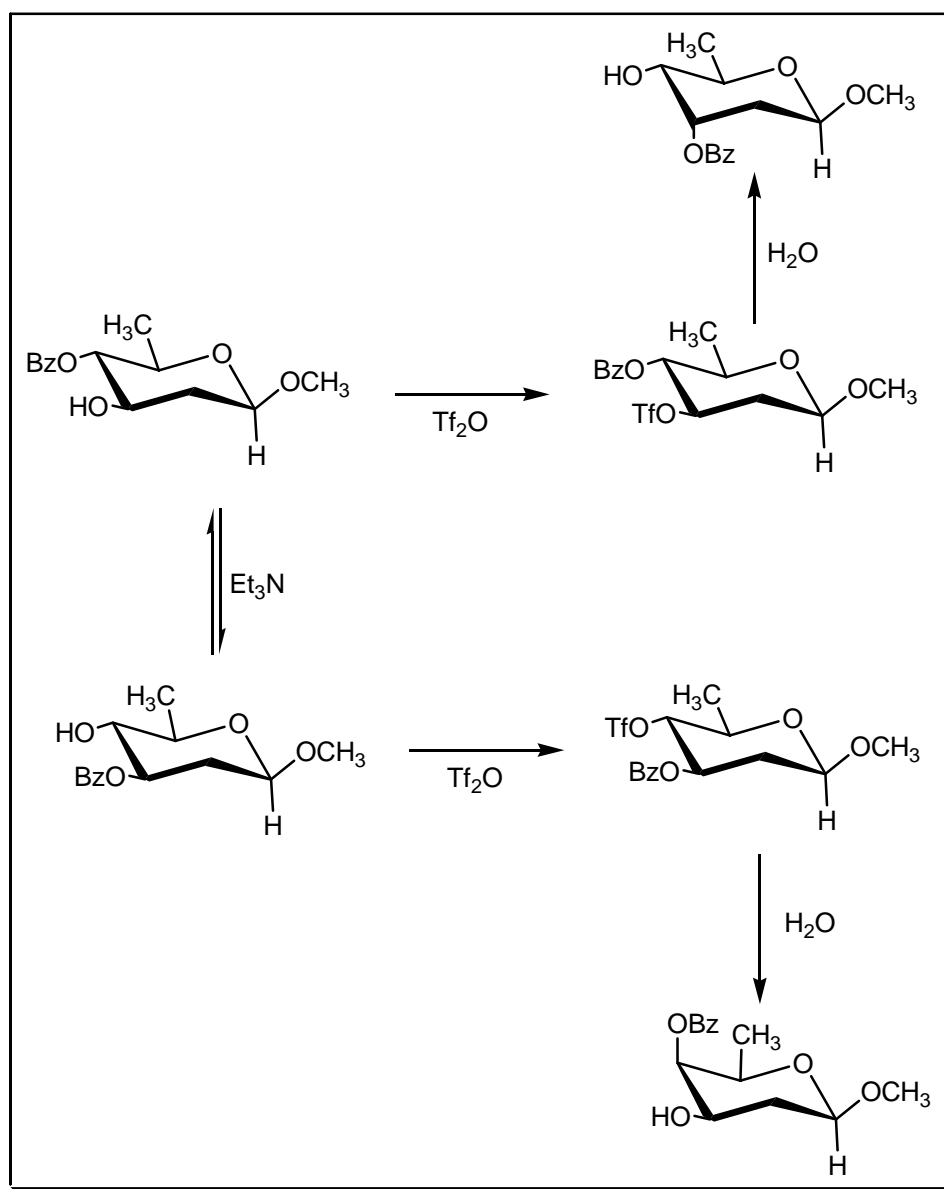
## COMMENTS :

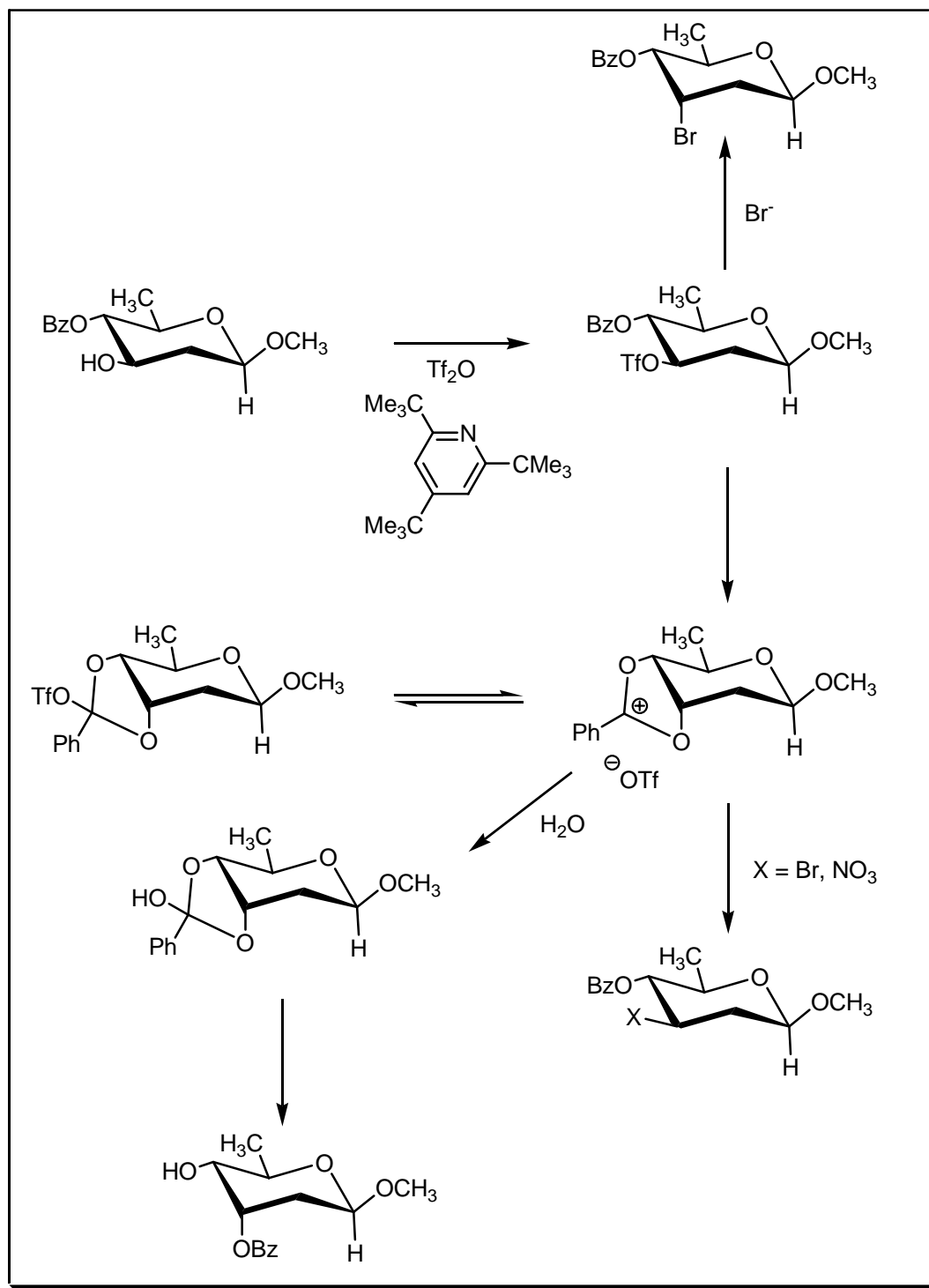
## BINKLEY TRIFLATE DISPLACEMENT

### EXAMPLE :



**MECHANISM :**





#### NOTES :

The interconversion of 2,6-dideoxysugars at room temperature by internal triflate displacement by a neighbouring benzoyl group. The reaction is well-suited for the inversion of configuration. The reaction is similar to the **Hanessian – Hullar** reaction except that in the **Hanessian – Hullar** reaction the intermediate cation can only be captured by the bromide ion and not by other nucleophiles. In this reaction the cation is formed but without an effective nucleophile present. See also **Hanessian – Hullar** reaction.

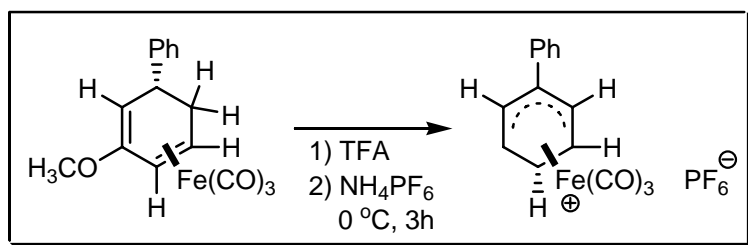
## REFERENCES :

- 1) R.W. Binkley; M.R. Sivik, *J. Carbohydr. Chem.*, 1986, **5**, 647.
- 2) R.W. Binkley; M.R. Sivik, *J. Org. Chem.*, 1986, **51**, 2619.
- 3) R.W. Binkley, *J. Org. Chem.*, 1991, **56**, 3892.

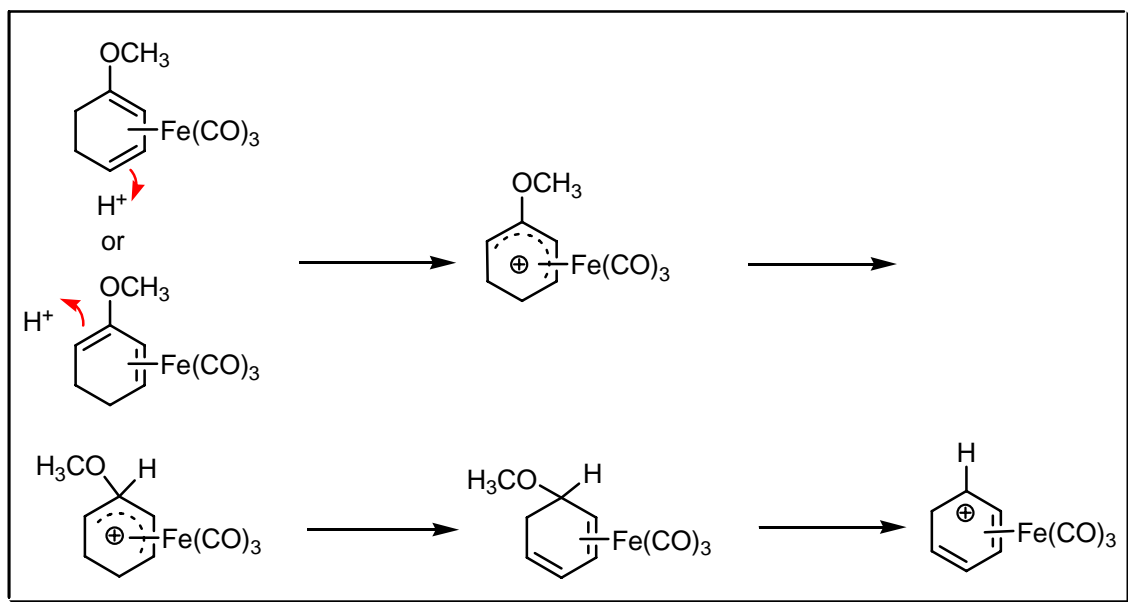
## COMMENTS :

## BIRCH – HAAS REACTION

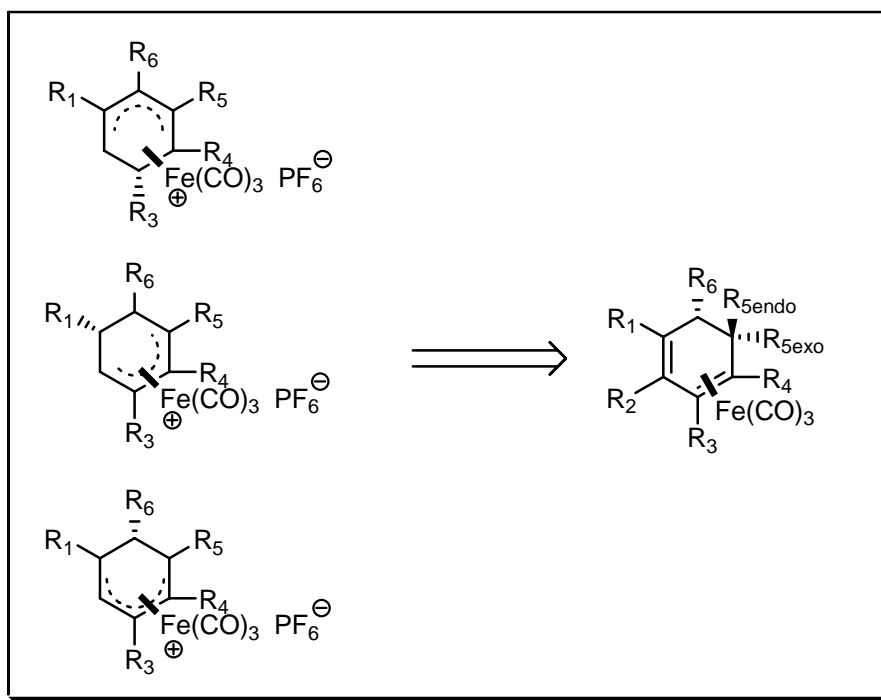
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The removal of methoxy groups of tricarbonyliron complexes of 1- or 2-methoxycyclohexadienes using concentrated sulfuric acid or trifluoroacetic acid and ammonium hexafluorophosphate to give tricarbonyl- $\pi$ -cyclohexadienyl iron salts. The reaction proceeds by rearrangement of the diene complex until an allylic leaving group is encountered.

## REFERENCES :

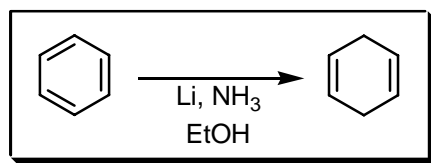
**Science of Synthesis** : 1, 765

- 1) A.J. Birch; M.A. Haas, *J. Chem. Soc. (C)*, 1971, 2465.
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- 3) A.J. Birch; B. Chauncy; L.F. Kelly; D.J. Thompson, *J. Organomet. Chem.*, 1985, **286**, 37.
- 4) A. McKillop; G.R. Stephenson; H. Finch; S. Swanson, *Tetrahedron Lett.*, 1989, **30**, 2607.
- 5) R.D.A. Hudson; S.A. Osborne; G.R. Stephenson, *Tetrahedron*, 1997, **53**, 4095.

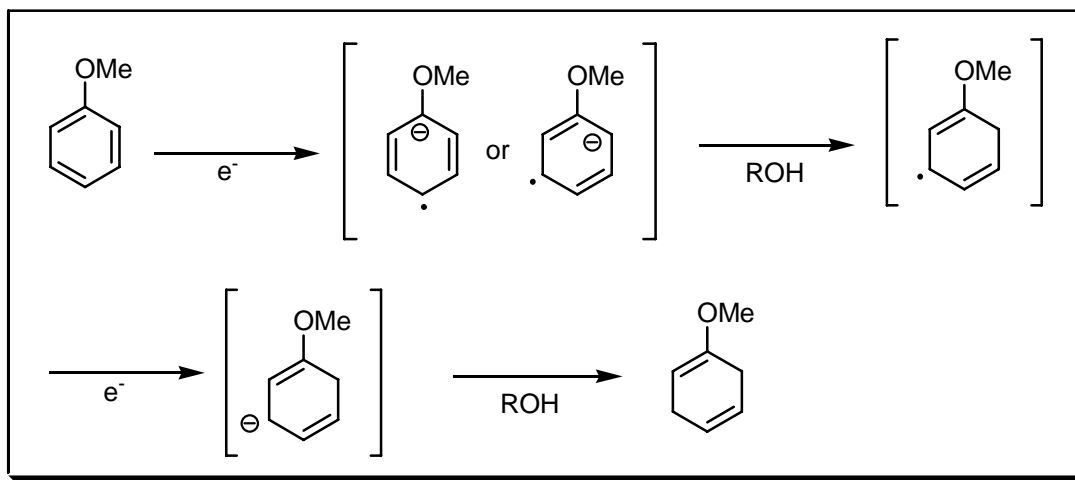
## COMMENTS :

## BIRCH REDUCTION

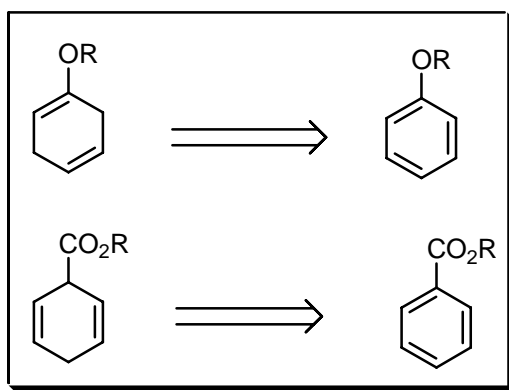
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The reduction of aromatics using metals and ammonia on a small scale. Other functional groups may react under **Birch** conditions. Note the difference in orientation between the donor and acceptor groups. See also **Benkeser** reduction.



## REFERENCES :

**March** : 781

**Smith – March** : 1010

**Smith** : 463

**Smith 2<sup>nd</sup>** : 400

**Houben – Weyl** : **E3**, 475; **E6a**, 496, 857; **E6b**, 145, 1021, 1224; **E7b**, 673; **E15**, 111; **E16d**, 457, 814

**Org. React.** : **42**, 1

**Org. Synth.** : **37**, 80; **43**, 22, **49**, 62; **54**, 11; **61**, 59

**Org. Synth. Coll. Vol.** : **4**, 887; **5**, 400, 467; **6**, 731; **7**, 249

**Science of Synthesis** : **10**, 212

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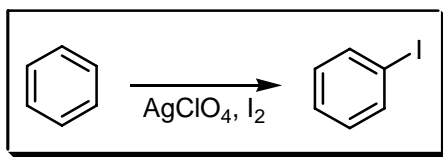
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  - 15) M.C. Elliott; M.J. Gist; F. Binns; R.G. Jones, *Tetrahedron Lett.*, 2004, **45**, 2899.
- 

## COMMENTS :

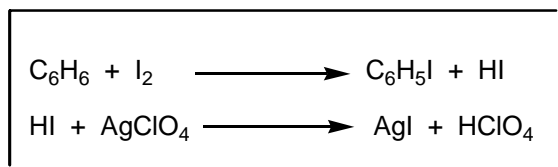
## BIRCKENBACH – GOUBEAU – WATERS REACTION

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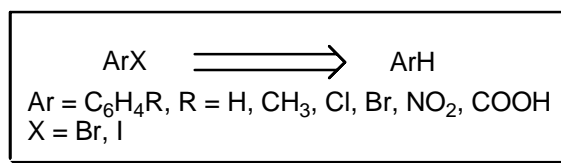
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The halogenation (bromine and iodine) of aromatic compounds (substituted benzene and naphthalenes) with halide cations in the presence of silver perchlorate with or without magnesium oxide.

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### REFERENCES :

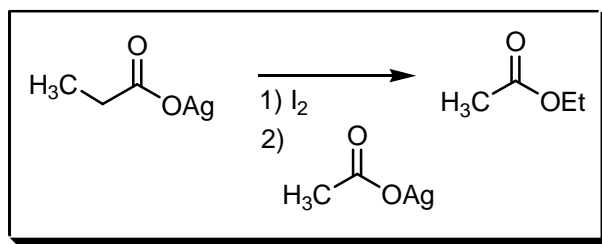
- 1) L. Birckenbach; J. Goubeau, *Ber. Dtsch. Chem. Ges.*, 1932, **65**, 395.
  - 2) L. Birckenbach; J. Goubeau, *Ber. Dtsch. Chem. Ges.*, 1933, **66**, 1280.
- 

### COMMENTS :

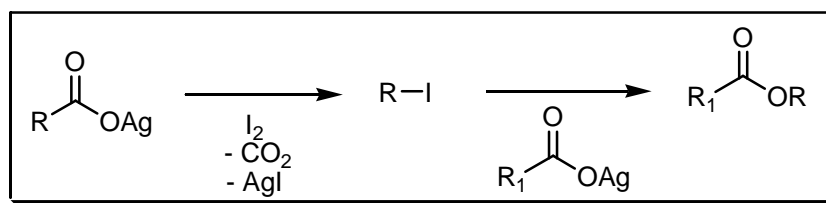
## BIRNBAUM – SIMONINI SYNTHESIS

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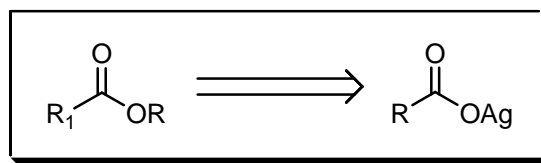
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The decarboxylation of carboxylic acids with iodine to afford esters (2:1 ratio salt ester, a 1:1 ratio will give the alkyl iodide). Lead salts can be used instead of silver salts. See also **Hunsdiecker – Borodin**, **Prévost** and **Woodward** *cis*-hydroxylation reactions.

### REFERENCES :

**March** : 731

**Smith – March** : 942

**Houben – Weyl** : 5/4, 659

**Org. React.** : 9, 332

1) A. Simonini, *Monatsh. Chem.*, 1892, **13**, 320.

2) J. Kleinberg, *Chem. Rev.*, 1947, **40**, 381.

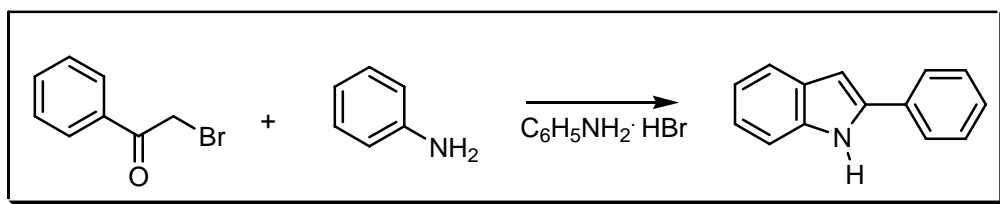
3) R.G. Johnson; R.K. Ingham, *Chem. Rev.*, 1956, **56**, 219.

4) N.J. Bunce; N.G. Murray, *Tetrahedron*, 1971, **27**, 5323.

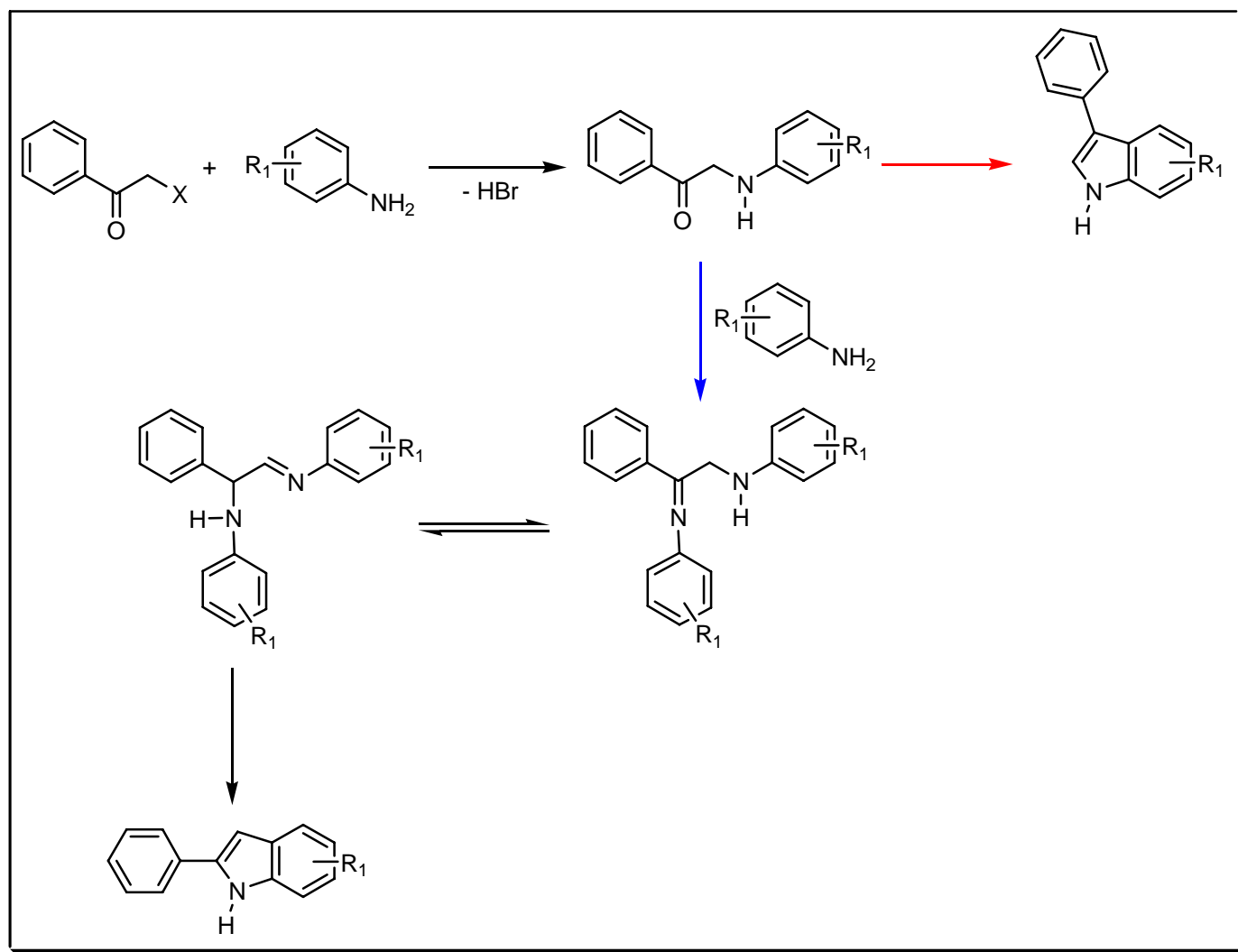
COMMENTS :

BISCHLER – MÖHLAU INDOLE SYNTHESIS

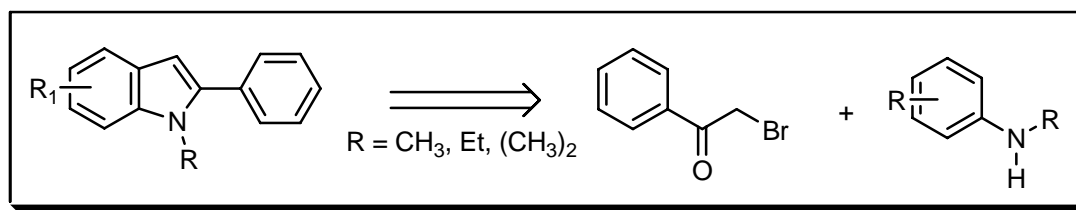
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

An  $\alpha$ -alkylaminoaryl ketone reacts with an aromatic amine to give an indole.  $\alpha$ -Halogeno- and  $\alpha$ -hydroxy-ketones can also be employed with intermediate formation of the  $\alpha$ -amino compound. It is noteworthy that 2-arylindoles and not the expected 3-aryl compounds are obtained. The **Nordlander** modification involves a combination of trifluoroacetic acid and trifluoroacetic anhydride to affect the cyclisation. **Sundberg** later used titanium(IV)chloride in the cyclisation step. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

## REFERENCES :

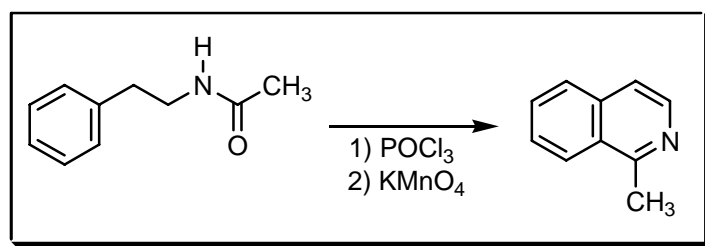
**Science of Synthesis : 10**, 390

- 1) R. Möhlau, *Ber. Dtsch. Chem. Ges.*, 1881, **14**, 171.
- 2) A. Bischler; H. Brion, *Ber. Dtsch. Chem. Ges.*, 1892, **25**, 2860.
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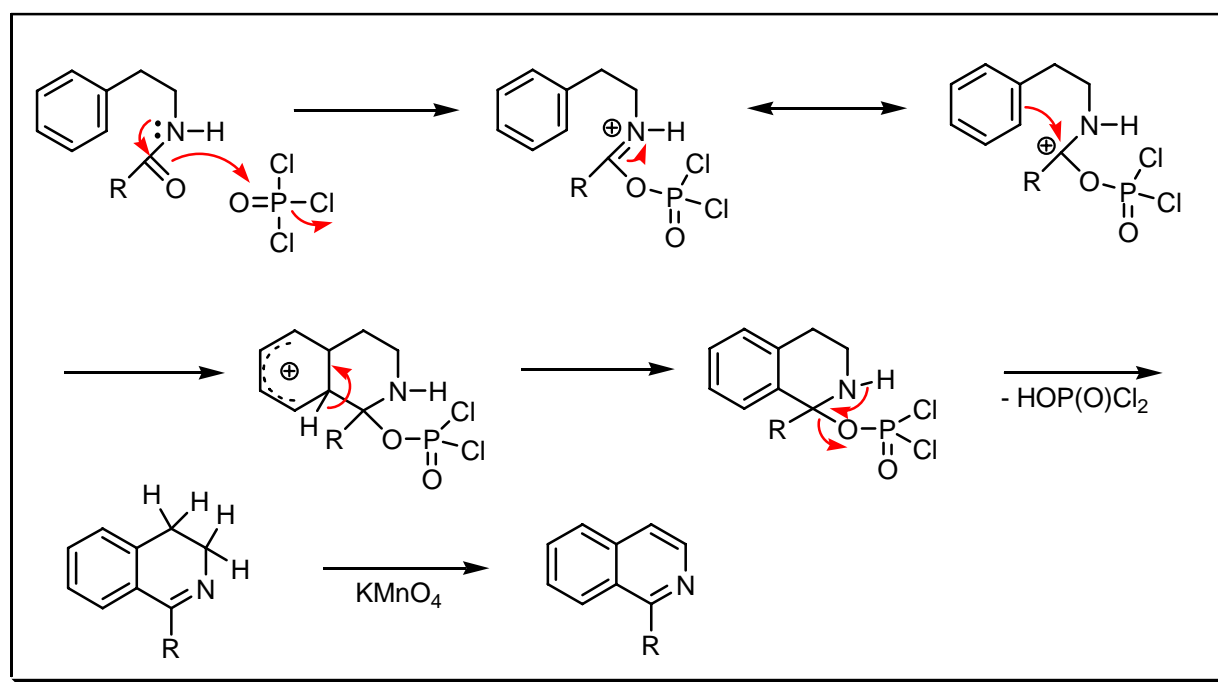
## COMMENTS :

## BISCHLER – NAPIERALSKI REACTION

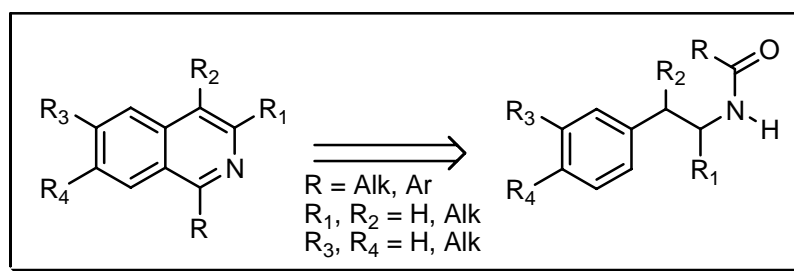
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The cyclodehydration of β-phenylethylamides to 3,4-dihydroisoquinolines by treatment with phosphorous oxychloride, phosphorous pentoxide, phosphorous pentachloride, polyphosphoric acid, anhydrous zinc chloride or other dehydrating agents. See also **Bamberger – Goldschmidt**, **Bobbit**, **Bruckner**, **Larock** indole, **Pictet – Gams**, **Pictet – Sprengler**, **Pomeranz – Fritsch**, **Simchen** and **Schlitter – Müller** ring-closure reactions.

## REFERENCES :

March : 549

Smith – March : 721

Smith : 1339

Smith 2<sup>nd</sup> : 1101

Houben – Weyl : **E7a**, 612, 622, 648, 672; **E7b**, 351; **E8a**, 364

Org. React. : **6**, 74

Org. Synth : **56**, 3

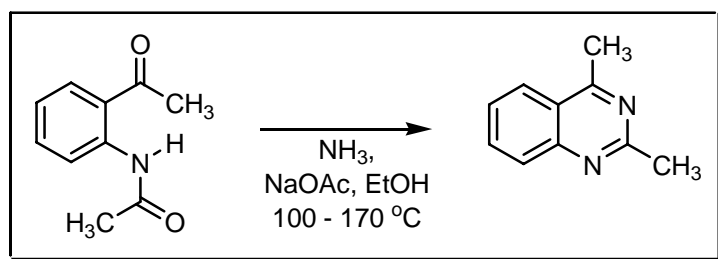
Org. Synth. Coll. Vol. : **6**, 1

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  - 8) P.A. Wender; T.E. Smith, *J. Org. Chem.*, 1996, **61**, 824.
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  - 10) M. Nicoletti; D.J. O'Hagan; A.M.Z. Slawin, *J. Chem. Soc., Perkin Trans. 1*, 2002, 116.
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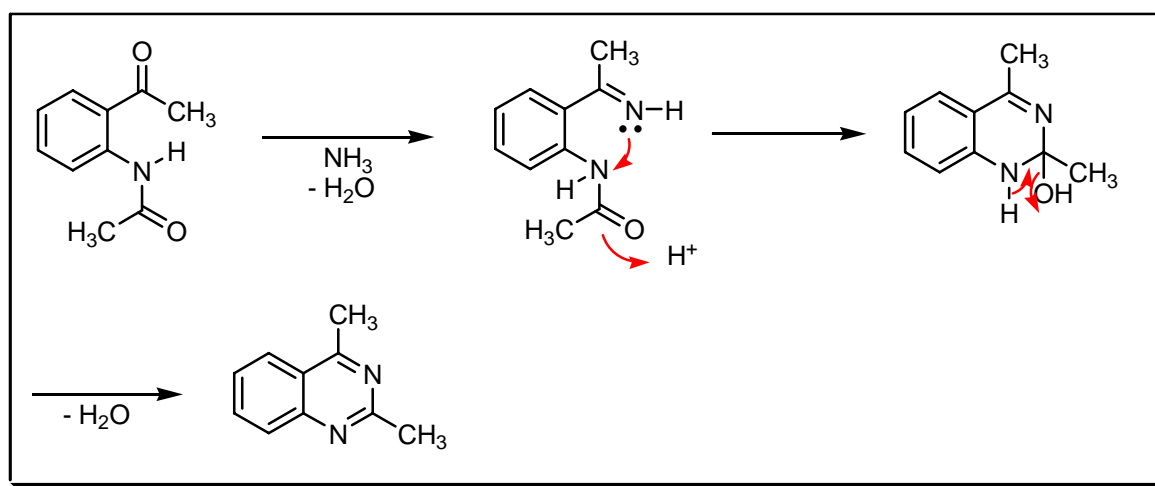
## COMMENTS :

## BISCHLER CYCLISATION

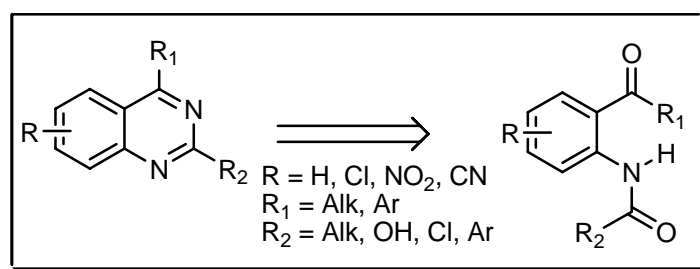
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

*o*-Acylamino-aldehydes and -ketones cyclise to yield a quinazoline derivatives by heating with aqueous alcoholic ammonia or with ammonia in the presence of molten ammonium acetate.

### REFERENCES :

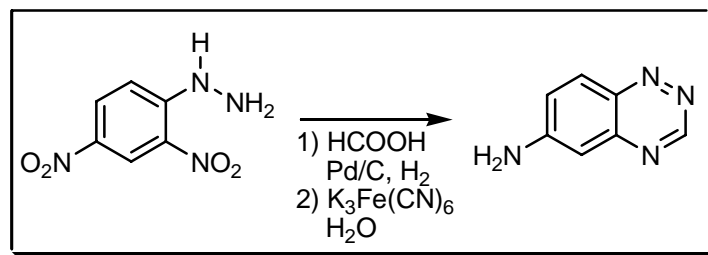
- 1) A. Bischler, *Ber. Dtsch. Chem. Ges.*, 1891, **24**, 506.
- 2) A. Bischler; D. Barad, *Ber. Dtsch. Chem. Ges.*, 1892, **25**, 3080.
- 3) K. Schofield; T. Swain; R.S. Theobald, *J. Chem. Soc.*, 1952, 1924.



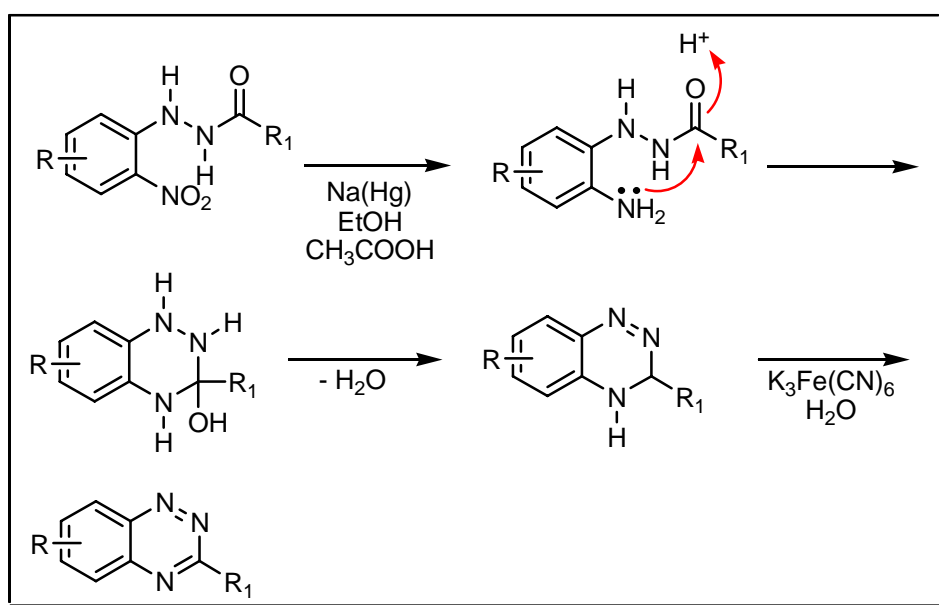
COMMENTS :

## BISCHLER TRIAZINE SYNTHESIS

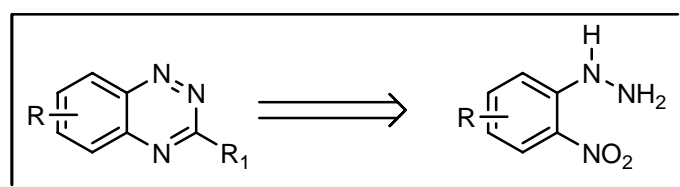
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

The benzotriazine synthesis from *o*-nitrophenylhydrazines. See also **Bamberger** triazine reaction.

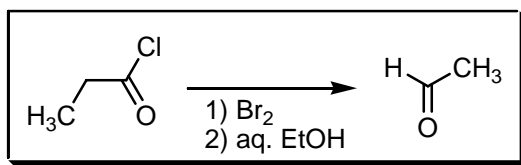
## REFERENCES :

- 1) A. Bischler, *Ber. Dtsch. Chem. Ges.*, 1899, **22**, 2801.
- 2) A. Bischler; S. Brodsky, *Ber. Dtsch. Chem. Ges.*, 1889, **22**, 2809.
- 3) A. Hempel, *J. Prakt. Chem.*, 1890, **41**, 161.
- 4) R.R. Abramovitch; K. Schofield, *J. Chem. Soc.*, 1955, 2326.

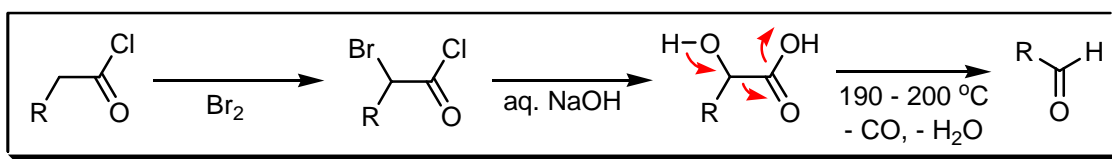
## COMMENTS :

## BLAISE – GUERIN (BLAISE – LeSUEUR) DEGRADATION

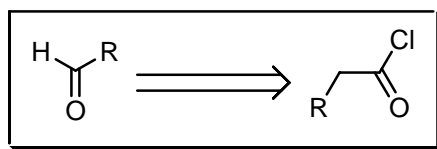
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The acid chloride is  $\alpha$ -brominated followed by hydrolysis with aqueous or alcoholic sodium hydroxide. Thermal degradation at 190 – 200 °C affords the aldehyde.

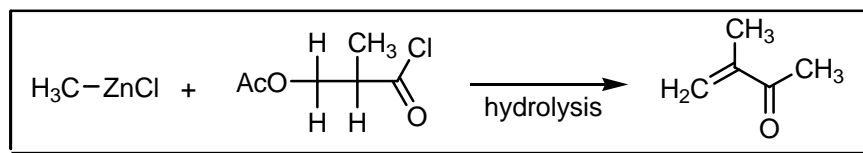
## REFERENCES :

- 1) H.R. LeSueur, *J. Chem. Soc.*, 1904, **85**, 827.
- 2) E.E. Blaise, *C.R. Séances Acad. Sci.*, 1904, **138**, 697.
- 3) E.E. Blaise; E. Guerin, *Ber. Schimmel and Co. A.G., Miltitz, Bez. Leipzig*, 1929, **11**, 17.
- 4) R.R. Davies; H.H. Hodgson, *J. Soc. Chem. Ind.*, 1943, **62**, 128.

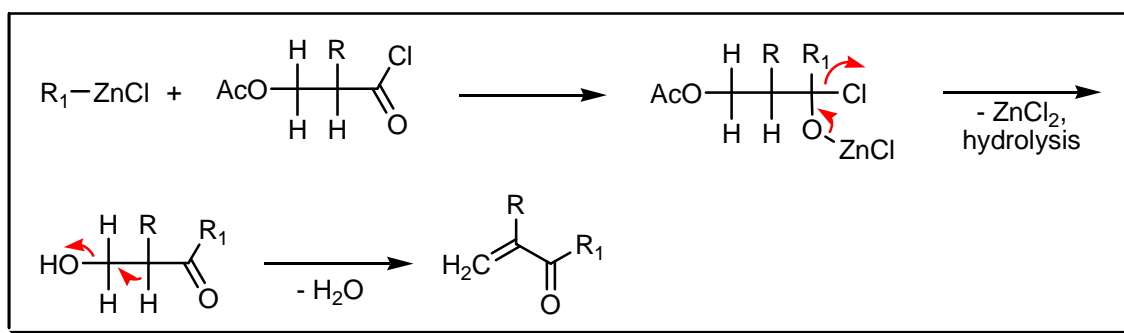
## COMMENTS :

## BLAISE – MAIRE KETONE SYNTHESIS

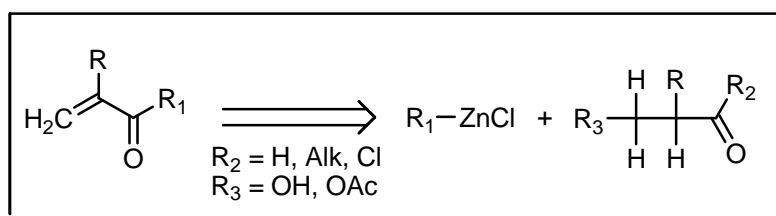
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The use of organometallic derivatives of zinc in the synthesis of  $\beta$ -hydroxy ketones and  $\alpha,\beta$ -unsaturated ketones from  $\beta$ -acetoxy-acid chlorides. See also **Cason** and **Grignard** reactions.

## REFERENCES :

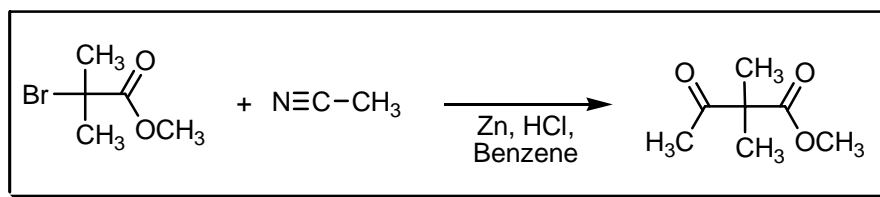
Org. React. : 8, 29

- 1) E.E. Blaise; M. Maire, *C.R. Séances Acad. Sci.*, 1907, **145**, 73.
- 2) E.E. Blaise; A. Koehler, *Bull. Soc. Chim. Fr.*, 1910, **7**, 215.
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- 6) J. Cason, *Chem. Rev.*, 1947, **40**, 15.

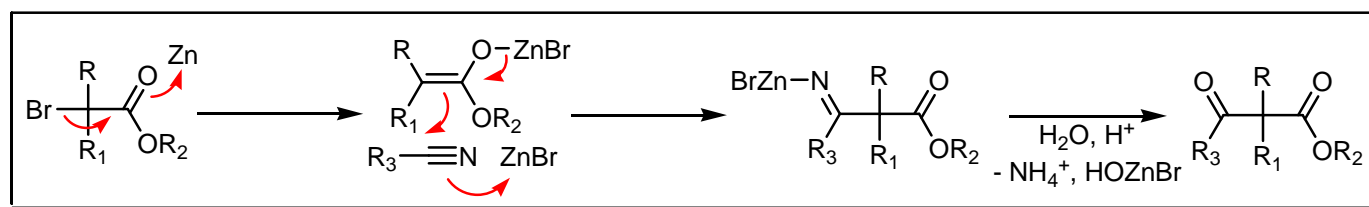
## COMMENTS :

## BLAISE KETOESTER REACTION

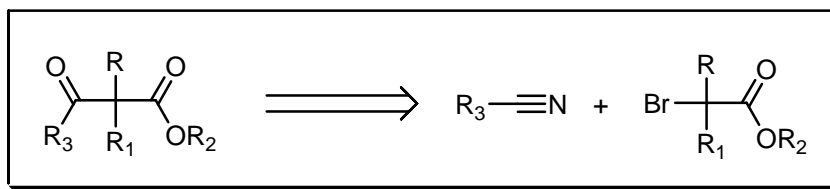
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of  $\beta$ -ketoesters from  $\alpha$ -bromoesters and nitriles in the presence of zinc. See also **Grignard**, **Horeau – Ormancey** and **Reformatsky** reactions.

## REFERENCES :

**March** : 930

**Smith – March** : 1213

**Houben – Weyl** : 7/2a, 518

**Org. Synth.** : 35, 15; 37, 37; 74, 158

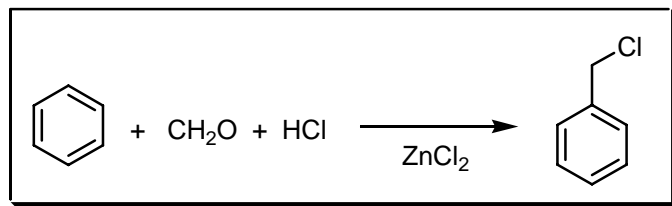
**Org. Synth. Coll. Vol.** : 4, 120, 444; 9, 275

- 1) E.E. Blaise, *C.R. Séances Acad. Sci.*, 1901, **132**, 38.
- 2) E.E. Blaise, *C.R. Séances Acad. Sci.*, 1901, **132**, 478.
- 3) J. Cason; K.L. Rinehart, jr.; S.D. Thornton, jr., *J. Org. Chem.*, 1953, **18**, 1594.
- 4) H.B. Kagan; Y. Heng–Suen, *Bull. Soc. Chim. Fr.*, 1960, 1823.
- 5) S.M. Hammick; Y. Kishi, *J. Org. Chem.*, 1983, **48**, 3833.
- 6) J.J. Duffield; A.C. Regan, *Tetrahedron: Asymmetry*, 1996, **7**, 663.
- 7) K. Narkunan; B.-L. Uang, *Synthesis*, 1998, 1713.
- 8) A.W. Enian, *J. Prakt. Chem.*, 1999, **341**, 147.
- 9) H.M. Deutsch; X.C. Ye; Q. Shi; Z.Z. Liu; M.M. Schweri, *Eur. J. Med. Chem.*, 2001, **36**, 303.
- 10) A.F.L. Creemers; J. Lugtenburg, *J. Am. Chem. Soc.*, 2002, **124**, 6324.

## COMMENTS :

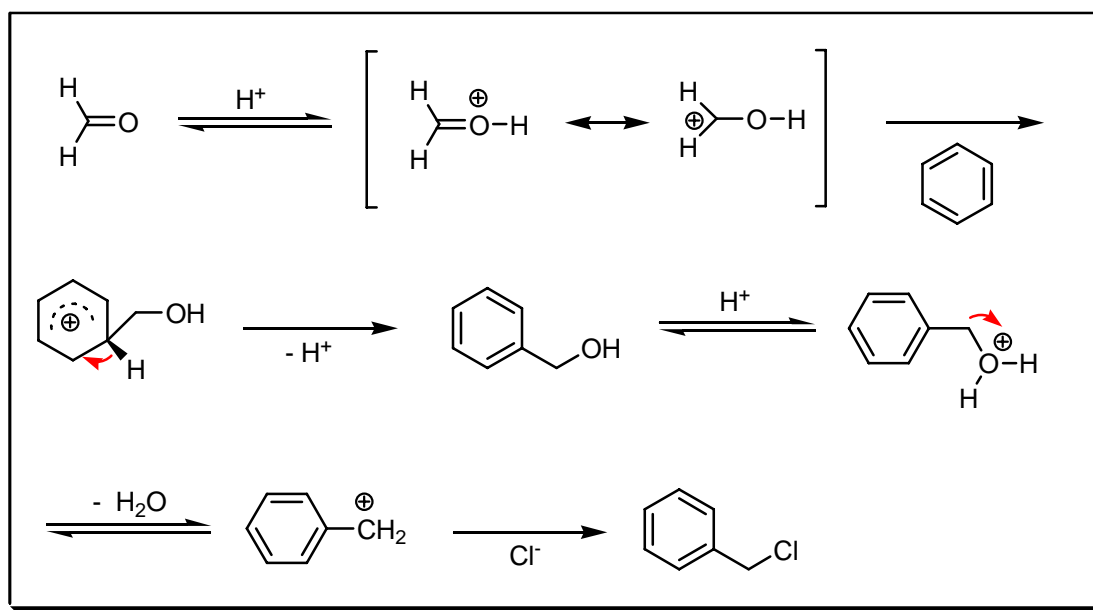
## BLANC – QUELLET CHLOROMETHYLATION / CHLOROALKYLATION REACTION

EXAMPLE :

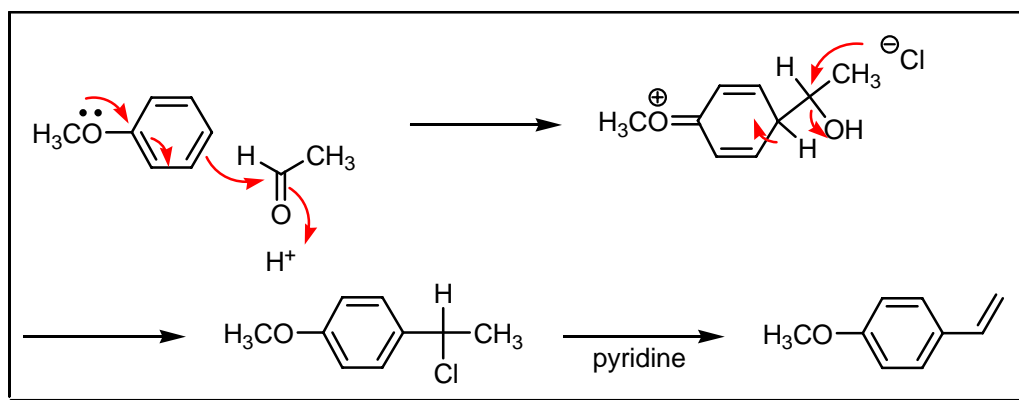


MECHANISM :

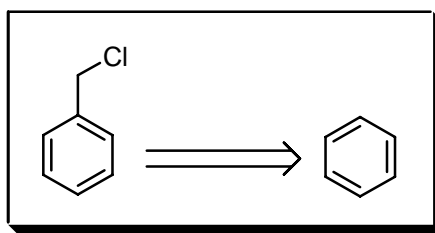
Blanc variation :



Quellet variation :



## DISCONNECTION :



## NOTES :

The replacement of a hydrogen atom in an aromatic hydrocarbon by a chloromethyl group, also bromomethyl and some cases iodomethyl groups using formaldehyde or a derivative and hydrogen chloride usually in the presence of a catalyst such as zinc chloride, aluminium chloride, stannic chloride or sulfuric acid. Alkyl and alkoxy substituents increase the reaction rate, while halide, carboxyl and especially nitro groups slow down the reaction. The **Quelet** variant starts with the phenolether.

## REFERENCES :

**March** : 550

**Smith – March** : 721

**Houben – Weyl** : 5/3, 1001

**Org. React.** : 1, 63

**Org. Synth.** : 20, 59; 24, 30; 25, 69; 29, 35

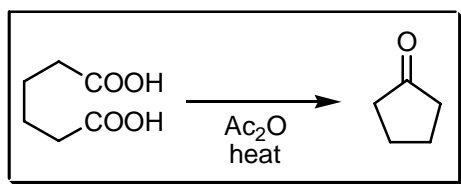
**Org. Synth. Coll. Vol.** : 3, 195, 197, 468, 557

- 1) G. Grassi; C. Maselli, *Gazz. Chim. Ital.*, 1898, **28**, 477.
- 2) M.G. Blanc, *Bull. Soc. Chim. Fr.*, 1923, **33**, 313.
- 3) R. Quelet, *C.R. Séances Acad. Sci.*, 1932, **199**, 150.
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- 5) N. Rabjohn, *J. Am. Chem. Soc.*, 1954, **76**, 5479.
- 6) G.A. Olah; D.A. Deal; J.A. Olah, *J. Org. Chem.*, 1976, **41**, 1627.
- 7) A. McKillop; F.A. Madjidabadi; D.A. Long, *Tetrahedron Lett.*, 1983, **24**, 1933.
- 8) R.H. Mitchell; V.S. Iyer, *Synlett*, 1989, 55.
- 9) J. De Mendoza; P.M. Nieto; P. Prados; C. Sanchez, *Tetrahedron*, 1990, **46**, 671.
- 10) K. Ito; Y. Ohba; E. Shinagawa; S. Nakayama; S. Takahashi; K. Honda; H. Nagafuji; A. Suzuki; T. Sone, *J. Heterocycl. Chem.*, 2000, **37**, 1479.

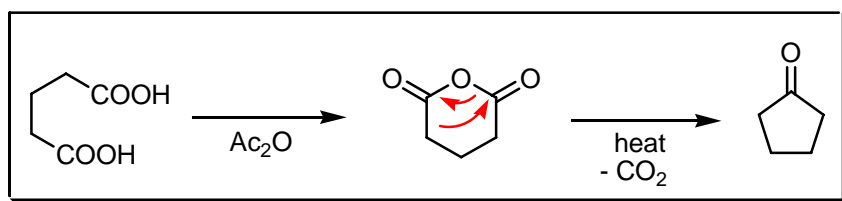
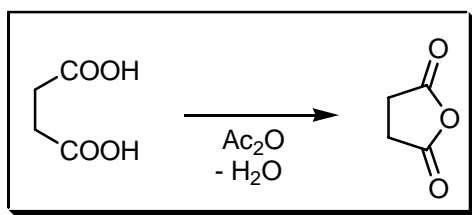
COMMENTS :

## BLANC REACTION

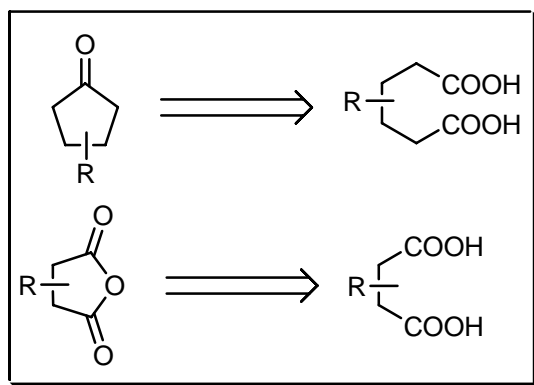
EXAMPLE :



MECHANISM :



DISCONNECTION :





## NOTES :

Adipic and pimelic acids, when heated with acetic anhydride and then distilled give cyclic ketones, whereas succinic and glutaric acids yield cyclic anhydrides. This rule is not always valid. Branching of the carbon chain promotes cyclisation. See **Ružička** large ring synthesis.

## REFERENCES :

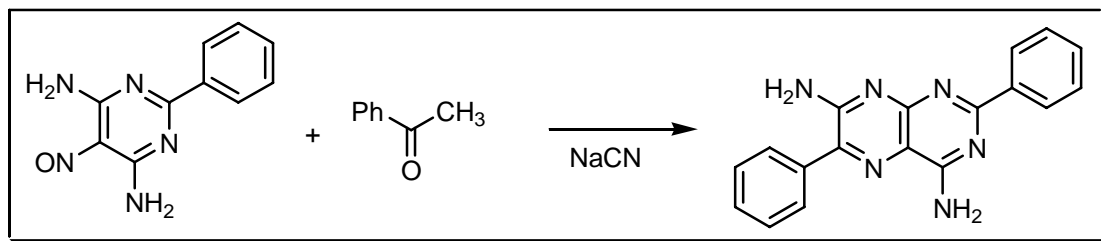
Houben – Weyl : 7/2, 640

- 1) H.G. Blanc, *C.R. Séances Acad. Sci.*, 1907, **144**, 1356.
- 2) F. Vocke, *Liebigs Ann. Chem.*, 1934, **508**, 1.
- 3) W.E. Bachman; N.C. Deno, *J. Am. Chem. Soc.*, 1949, **71**, 3540.

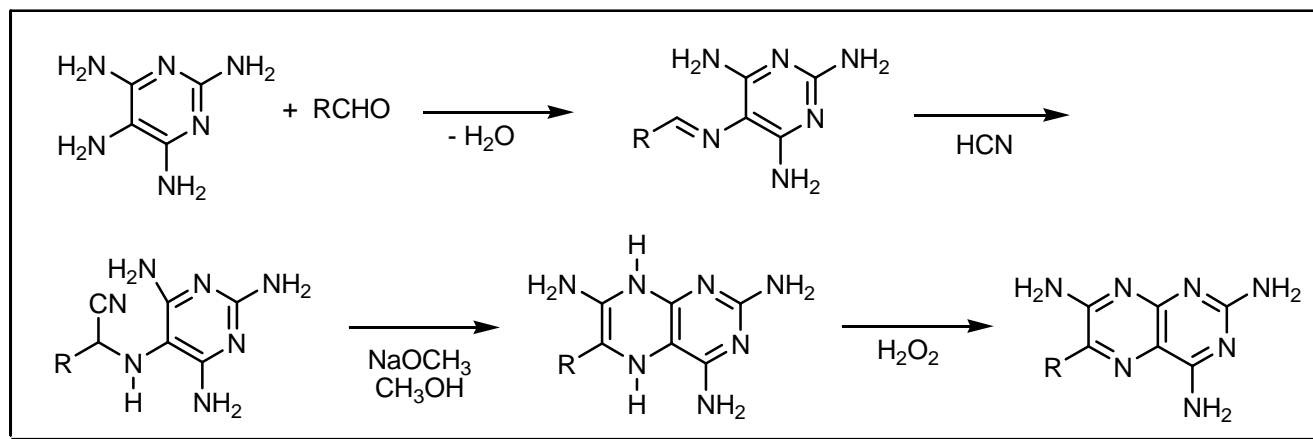
## COMMENTS :

## BLICKE – PACHTER SYNTHESIS

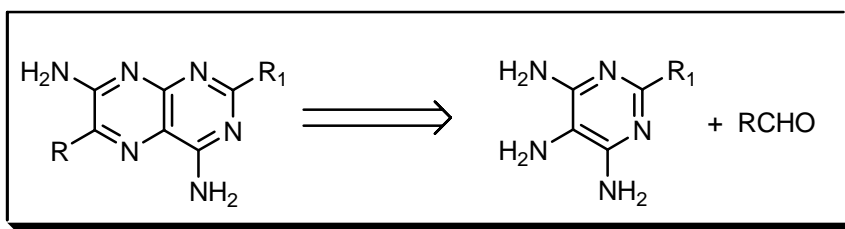
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

Pteridines are synthesised from aminopyrimidines with aldehydes and cyanide. The cyclisation step is done with sodium methoxide. See also **Boon – Polonovski**, **Isay**, **Taylor** and **Timmis** reactions.

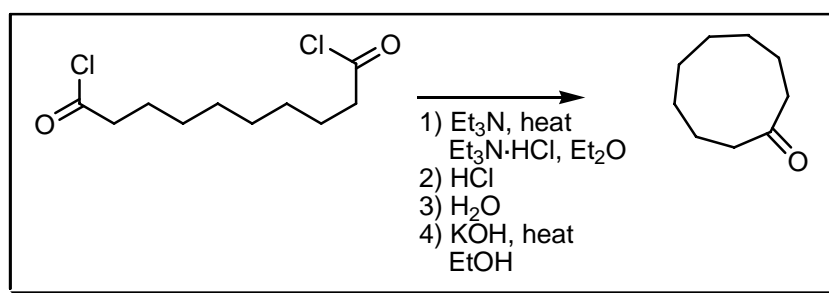
## REFERENCES :

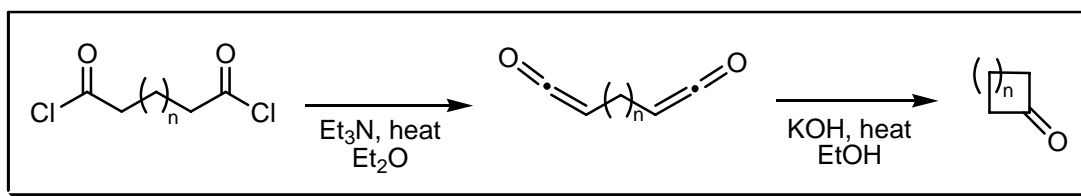
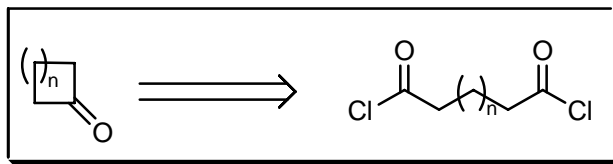
- 1) F.F. Blicke; H.C. Godt, *J. Am. Chem. Soc.*, 1954, **76**, 2798.
- 2) I.J. Pachter; P.E. Nemeth, *J. Org. Chem.*, 1963, **28**, 1187.
- 3) I.J. Pachter, *J. Org. Chem.*, 1963, **28**, 1191.
- 4) I.J. Pachter; P.E. Nemeth; A.J. Villani, *J. Org. Chem.*, 1963, **28**, 1197.
- 5) I.J. Pachter; P.E. Nemeth, *J. Org. Chem.*, 1963, **28**, 1203.

## COMMENTS :

## BLOMQUIST REACTION

### EXAMPLE :

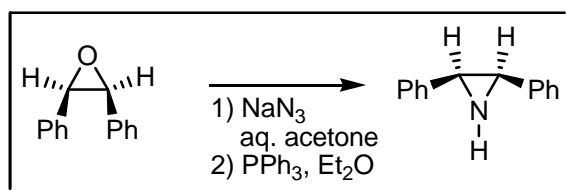


**MECHANISM :****DISCONNECTION :****NOTES :**

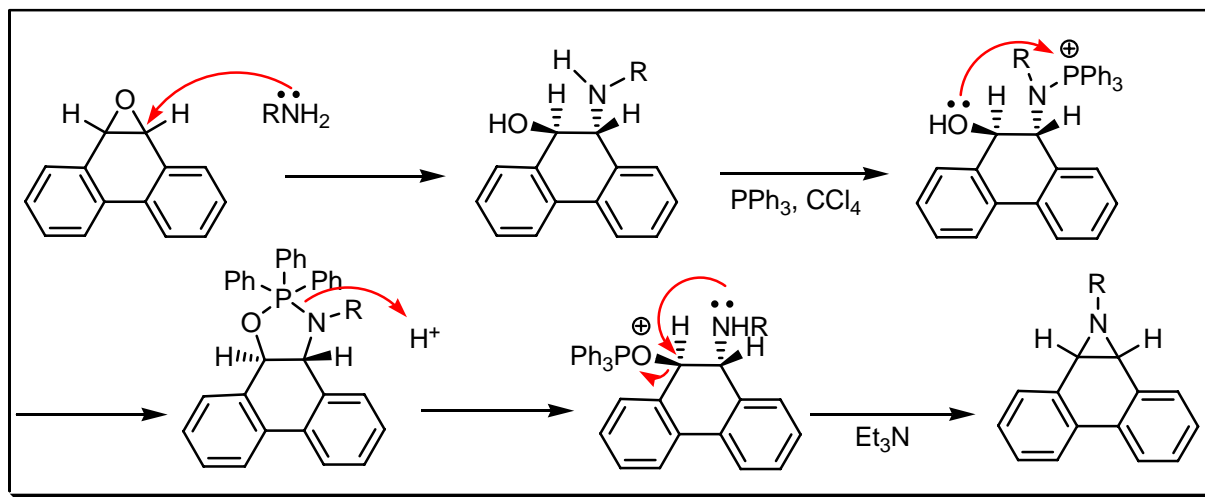
Synthesis of macrocyclic ketones by *intramolecular* condensation of aliphatic diketenes obtained from acyl chlorides of dicarboxylic acids or acyl chlorides of unsaturated acids.

**REFERENCES :**

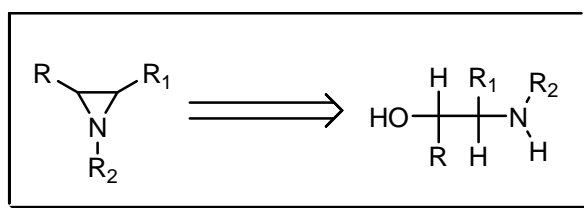
- 1) A.T. Blomquist; R.D. Spencer, *J. Am. Chem. Soc.*, 1947, **69**, 472.
- 2) A.T. Blomquist; R.D. Spencer, *J. Am. Chem. Soc.*, 1948, **70**, 30.

**COMMENTS :****BLUM AZIRIDINE SYNTHESIS****EXAMPLE :**

## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of aziridines from epoxides *via* amino alcohols or azido alcohols and reaction with phosphines or phosphites. See also **Appel**, **Hassner** azide aziridine, **Gabriel – Marckwald – Cromwell** ethylenimine method, **Hoch – Campbell**, **Mansuy – Evans**, **Scheiner** and **Wenker** ring-closure reactions.

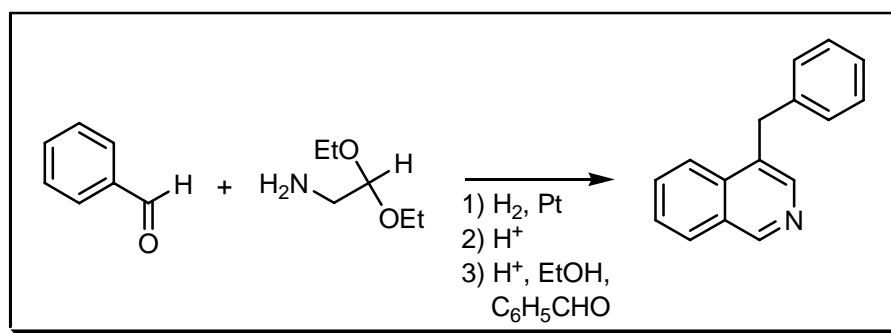
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- 5) R. Appel; M. Halstenberg, *Chem. Ber.*, 1978, **111**, 814.
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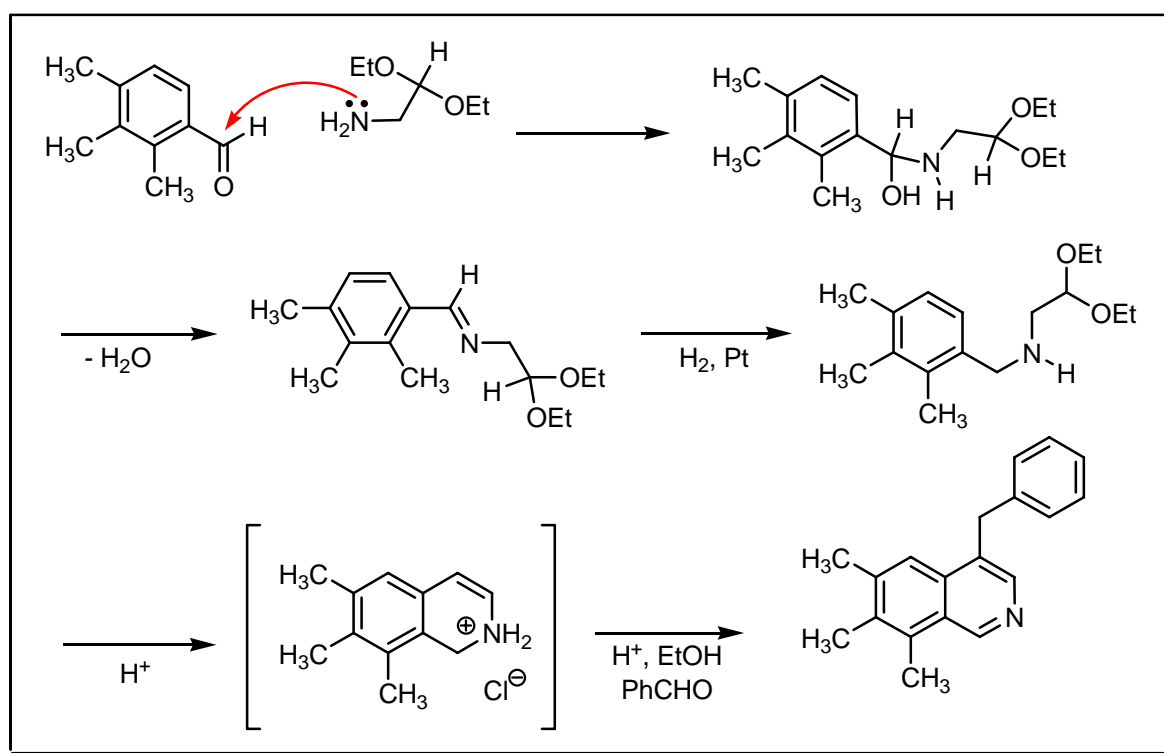
## COMMENTS :

## BOBBIT REACTION

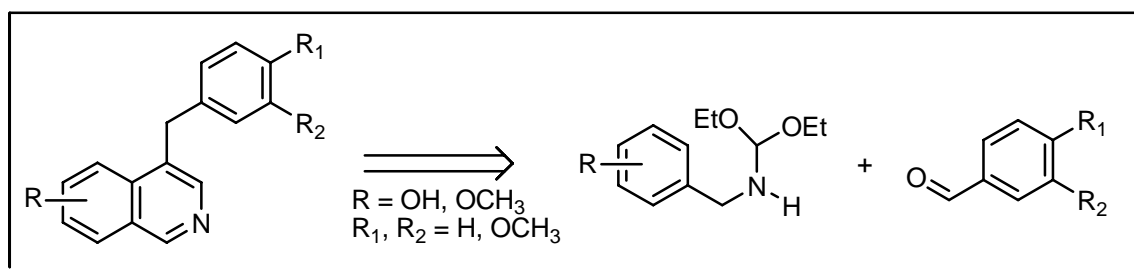
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The synthesis of 4-substituted isoquinolines by cyclocondensation of substituted benzylaminoacetals with aromatic aldehydes in the presence of ethanolic hydrogen chloride. This reaction is based on the **Fischer** modification of the

**Pomeranz – Fritsch** reaction. See also **Bamberger – Goldschmidt**, **Bischler – Napieralski**, **Bruckner, Larock** indole, **Pictet – Gams**, **Pictet – Sprengler**, **Pomeranz – Fritsch**, **Schlitter – Müller** ring-closure and **Simchen** reactions.

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#### REFERENCES :

**Org. React. : 6, 19**

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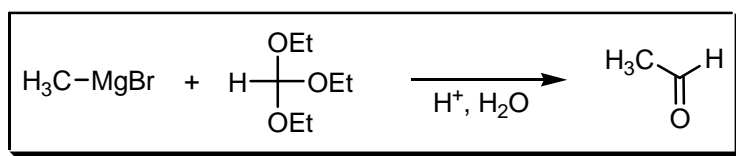
- 1) W.D. Burrows; E.P. Burrows, *J. Org. Chem.*, 1963, **28**, 1180.
  - 2) J.M. Bobbit; K.L. Khanna; J.M. Kiely, *Chem. Ind. (London)*, 1964, 1950.
  - 3) R. Grewe; W. Krüger; E. Vangermain, *Chem. Ber.*, 1964, **97**, 119.
  - 4) J.M. Bobbit; J.M. Kiely; K.L. Khanna; R. Eberman, *J. Org. Chem.*, 1965, **30**, 2247.
  - 5) J.M. Bobbit; D.P. Winter; J.M. Kiely, *J. Org. Chem.*, 1965, **30**, 2459.
  - 6) W.J. Genster; K.T. Shamasundar; S. Marbury, *J. Org. Chem.*, 1968, **33**, 2861.
  - 7) J.M. Bobbit; T.E. Moore, *J. Org. Chem.*, 1968, **33**, 2958.
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#### COMMENTS :

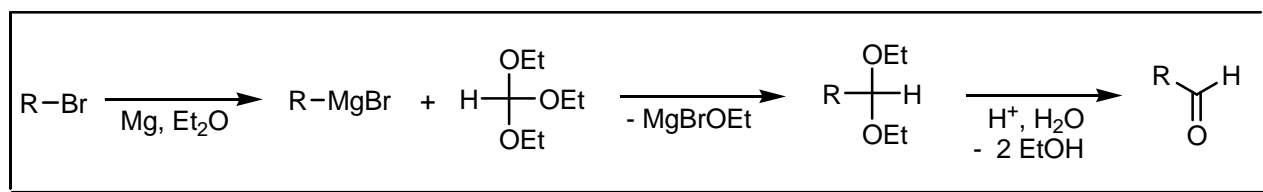
### BODROUX – CHICHIBABIN ALDEHYDE SYNTHESIS

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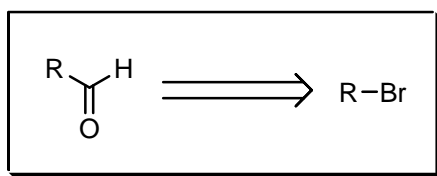
#### EXAMPLE :



#### MECHANISM :



## DISCONNECTION :



## NOTES :

The products obtained by the action of **Grignard** reagents on ethyl orthoformate give aldehydes by acid hydrolysis. See also **Bouveault** aldehyde, **Gattermann – Maffezzoli** and **Zelinsky** reactions.

## REFERENCES :

Houben – Weyl : 6/3, 243; 7/1, 65

Org. Synth. : 16, 41

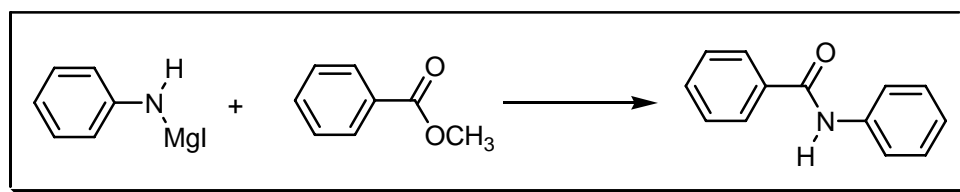
Org. Synth. Coll. Vol. : 2, 323

- 1) A.E. Chichibabin, *J. Russ. Phys. Chem. Ges.*, 1903, **35**, 1284.
- 2) F. Bodroux, *C.R. Séances Acad. Sci.*, 1904, **138**, 92.
- 3) L.I. Smith; M. Bayliss, *J. Org. Chem.*, 1941, **6**, 437.
- 4) N.A. LeBel; M.E. Post; J.J. Whang, *J. Am. Chem. Soc.*, 1964, **86**, 3759.
- 5) W.H. Urry; D.J. Trecker; H.D. Hartzler, *J. Org. Chem.*, 1964, **29**, 1663.
- 6) D.K. Hutchinson; P.L. Fuchs, *J. Am. Chem. Soc.*, 1987, **109**, 4755.

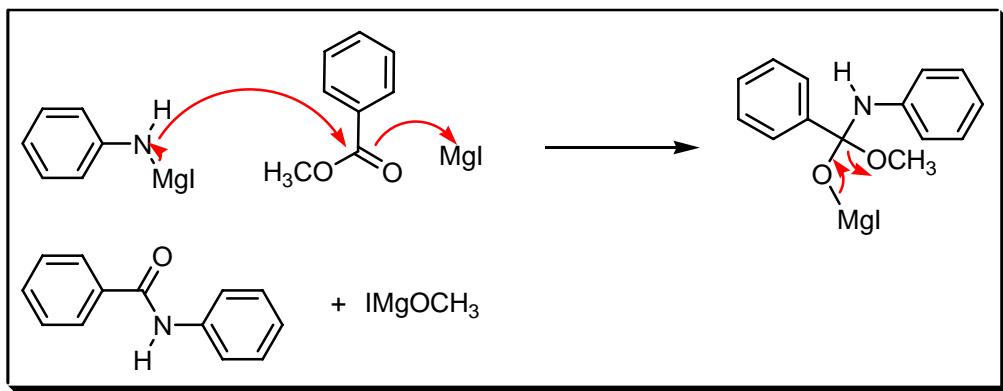
## COMMENTS :

## BODROUX REACTION

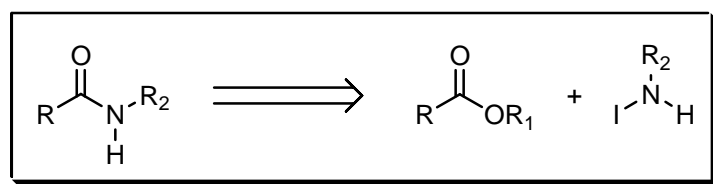
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

An aminomagnesium halide, formed when a primary or secondary amine combines with a **Grignard** reagent at room temperature, reacts with a simple aliphatic or aromatic ester to yield a substituted amide.

### REFERENCES :

Houben – Weyl : 13/2a, 278

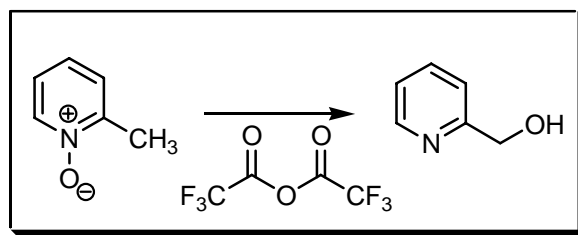
- 1) F. Bodroux, *C.R. Séances Acad. Sci.*, 1904, **138**, 1427.
- 2) F. Bodroux, *Bull. Soc. Chim. Fr.*, 1906, **35**, 519.
- 3) H.L. Bassett; C.R. Thomas, *J. Chem. Soc.*, 1954, 1188.

### COMMENTS :

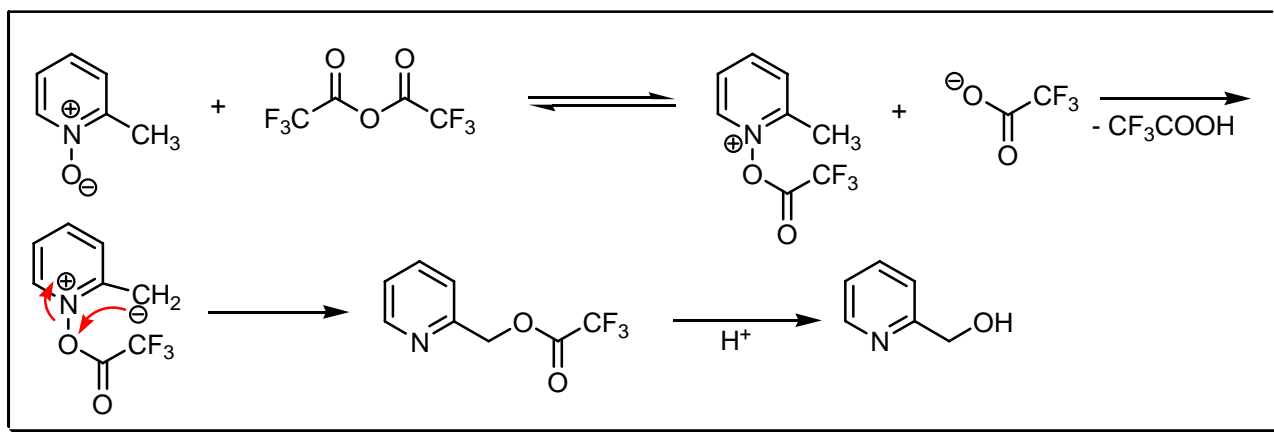


## BOEKELHEIDE REACTION

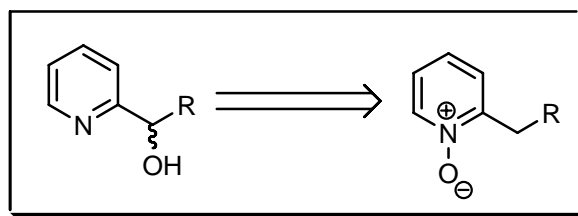
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Aromatic pyridine *N*-oxides react with acylating agents to form 2-substituted pyridines. The negative charge can be delocalised through out the benzene ring giving rise to isomers.

### REFERENCES :

Smith – March : 1421

- 1) V. Boekelheide; W.J. Linn, *J. Am. Chem. Soc.*, 1954, **76**, 1286.
- 2) T. Koenig, *J. Am. Chem. Soc.*, 1966, **88**, 4045.
- 3) S. Oae; S. Tamagaki; T. Negero; K. Ogino; S. Kozuka, *Tetrahedron Lett.*, 1968, **9**, 917.
- 4) S. Oae; S. Tamagaki; T. Negero; S. Kozuka, *Tetrahedron*, 1970, **26**, 4051.

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8) J.A. Zoltewicz; M.P. Cruskie, jr.; C.D. Dill, *Tetrahedron*, 1996, **52**, 4239.  
9) K. Goerlitzer; U. Bartke, *Pharmazie*, 2002, **57**, 804.

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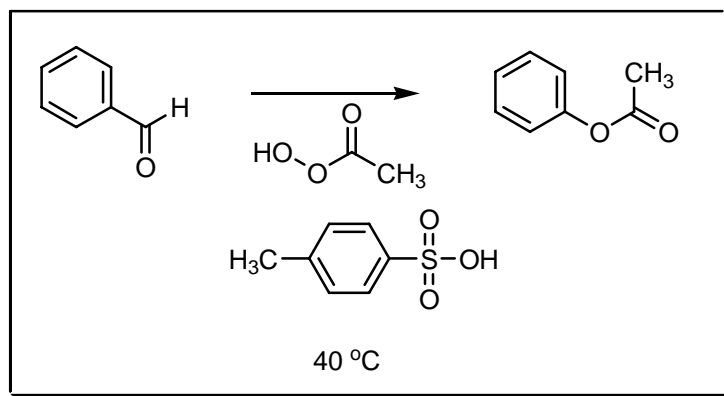
**COMMENTS :**

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**BÖESEKEN – BALLIO SYNTHESIS**

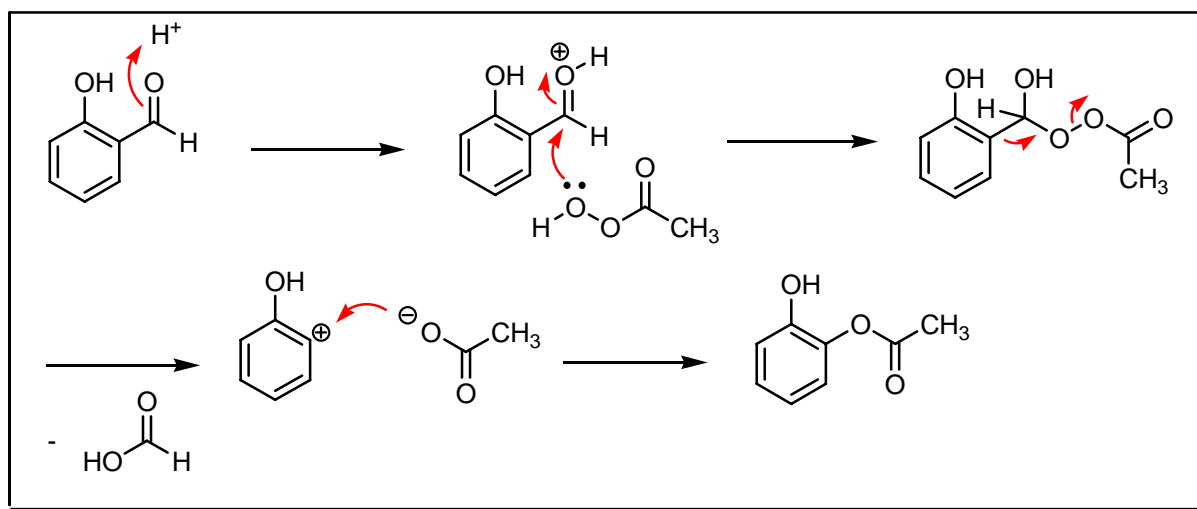
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**EXAMPLE :**

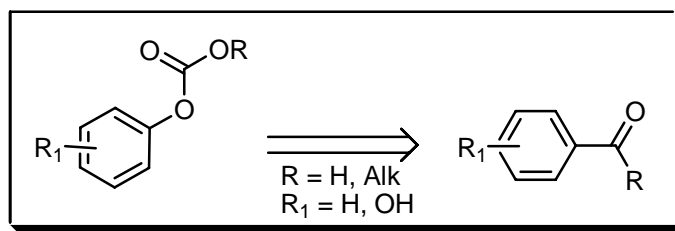


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**MECHANISM :**



## DISCONNECTION :



## NOTES :

The oxidation by peracetic acid of aryl aldehydes, ketones, or of compounds containing the group  $\text{C}=\text{CCOR}$  yields esters. Peroxytrifluoroacetic acid is also an effective reagent. See also **von Baeyer – Villiger** rearrangement and **Dakin** phenol aldehyde oxidation.

## REFERENCES :

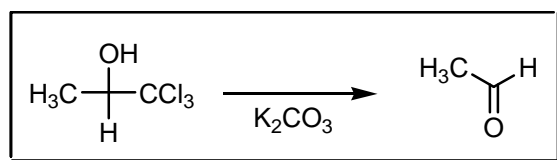
Houben – Weyl : 7/1, 489

- 1) J. Böeseken; A. Kremer, *Recl. Trav. Chim. Pays-Bas*, 1931, **50**, 827.
- 2) J. Böeseken; A.L. Soesman, *Recl. Trav. Chim. Pays-Bas*, 1933, **52**, 874.
- 3) J. Böeseken; J. Greup, *Recl. Trav. Chim. Pays-Bas*, 1939, **56**, 528.
- 4) W.D. Emmons; G.B. Lucas, *J. Am. Chem. Soc.*, 1955, **77**, 2287.
- 5) D.G. Crosby, *J. Org. Chem.*, 1961, **26**, 1215.

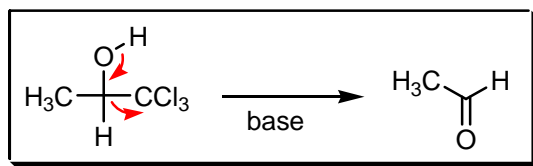
## COMMENTS :

## BÖESSNECK – HÉBERT REACTION

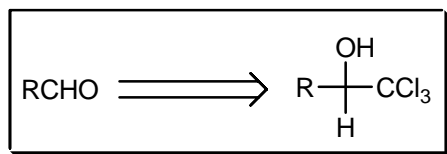
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of aldehydes by breaking down alcohols that contain  $\alpha$ -trichloromethyl groups.

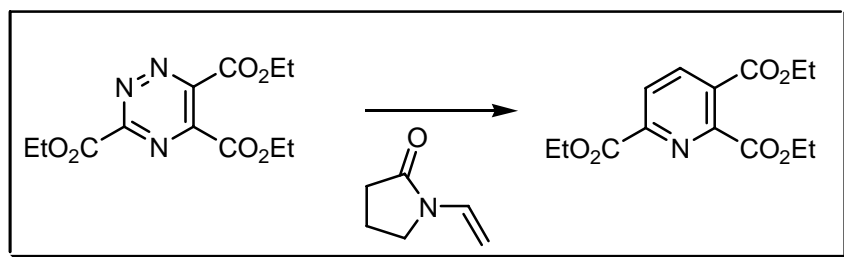
## REFERENCES :

- 1) P. Böessneck, *Ber. Dtsch. Chem. Ges.*, 1885, **18**, 1516.
- 2) P. Hébert, *Bull. Soc. Chim. Fr.*, 1920, **27**, 45.
- 3) K. Bodendorf; J. Mildner; T. Lehmann, *Liebigs Ann. Chem.*, 1949, **563**, 1.
- 4) J. Colonge; A. Perrot, *Bull. Soc. Chim. Fr.*, 1957, 658.

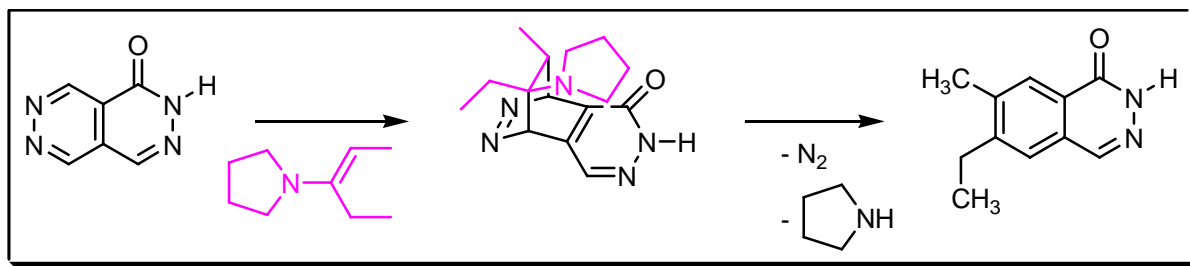
## COMMENTS :

## BOGER – PANEK PYRIDINE SYNTHESIS

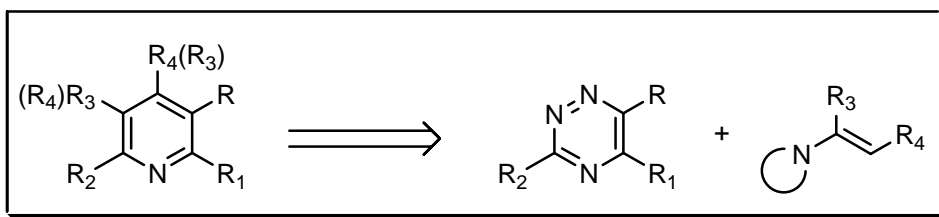
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

An electron-deficient heterocyclic aza-diene reacts with an electron-rich dienophile under inverse-electron-demand **Diels – Alder** reaction to afford a pyridine. See also **Carboni – Lindsey** and **Diels – Alder** reactions.

## REFERENCES :

**Org. Synth.** : **66**, 142

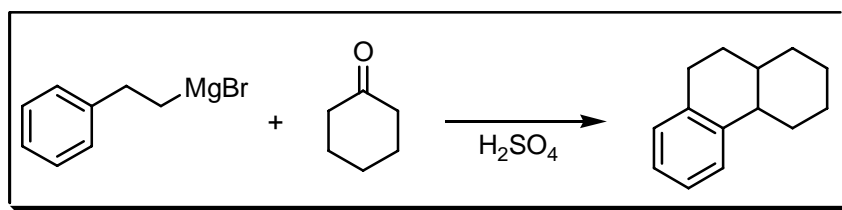
**Org. Synth. Coll. Vol.** : **8**, 597

- 1) D.L. Boger; J.S. Panek, *J. Org. Chem.*, 1981, **46**, 2179.
- 2) D.L. Boger; J.S. Panek, M.M. Meier, *J. Org. Chem.*, 1982, **47**, 895.
- 3) D.L. Boger; J.S. Panek, *J. Org. Chem.*, 1982, **47**, 3763.
- 4) D.L. Boger; J.S. Panek, *J. Org. Chem.*, 1983, **48**, 621.
- 5) D.L. Boger, *Tetrahedron*, 1983, **39**, 2869.
- 6) D.L. Boger; J.S. Panek, *J. Am. Chem. Soc.*, 1985, **107**, 5745.
- 7) A. Rykowski; E. Olender; D. Branowska; H.C. van der Plas, *Org. Prep. Proced. Int.*, 2001, **33**, 501.
- 8) S.P. Stanforth; B. Tarbit; M.D. Wilson, *Tetrahedron Lett.*, 2003, **44**, 693.

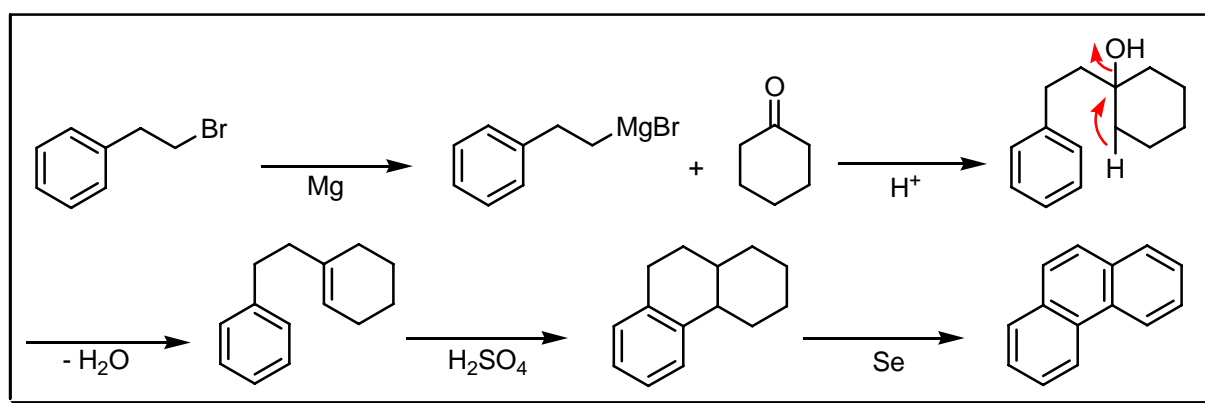
## COMMENTS :

## BOGERT – COOK REACTION

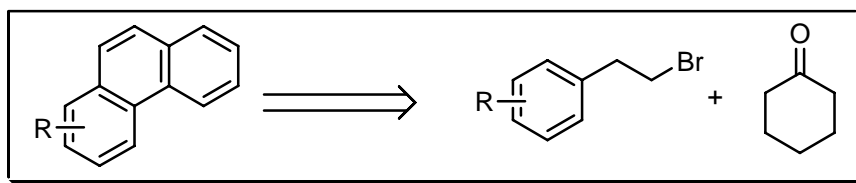
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The synthesis of octahydrophenanthrenes by the cyclodehydration by acid catalysts of a 1- $\beta$ -arylethylcyclohexanol. Derivatives of 1- $\beta$ -arylethylcyclohexene are intermediates in the reaction and cyclisation of these intermediate olefins is known as the **Bogert** reaction. This method can also be applied to cyclopentanol derivatives. See also **Bardhan – Sengupta** and **Darzens** synthesis of tetralin reactions.

### REFERENCES :

Smith : 1331

Smith 2<sup>nd</sup> : 1095

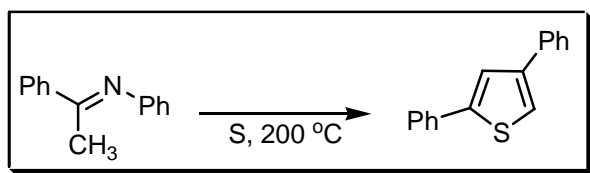
- 1) M.T. Bogert, *Science*, 1933, **77**, 289.
- 2) J.W. Cook; C.L. Hewitt, *J. Chem. Soc.*, 1933, 1098.
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- 6) D.A. Evans; P.A. Cain; R.Y. Wong, *J. Am. Chem. Soc.*, 1977, **99**, 7083.

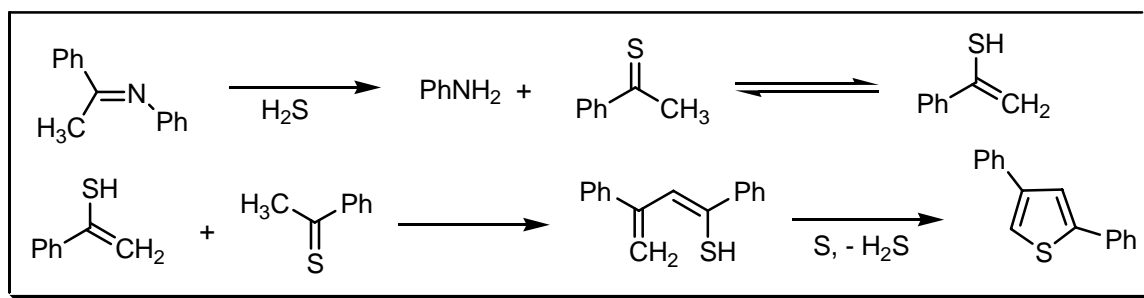
**COMMENTS :**

## BOGERT – HERRERA SYNTHESIS

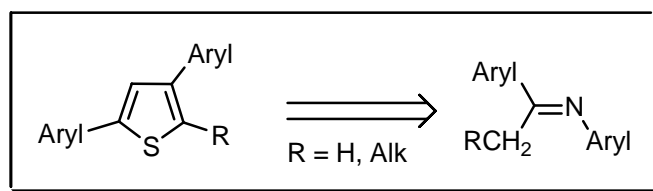
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

The anils of alkyl aryl ketones react with sulfur or selenium to form 2,4-diaryl-thiophenes and –selenophenes. The anil is decomposed by hydrogen disulfide (initially formed as a side reaction from sulfur). See also **Baumann – Fromm**, **Fiesselmann**, **Hinsberg** thiophene, **Volhard – Erdmann** and **Willgerodt – Kindler** reactions.

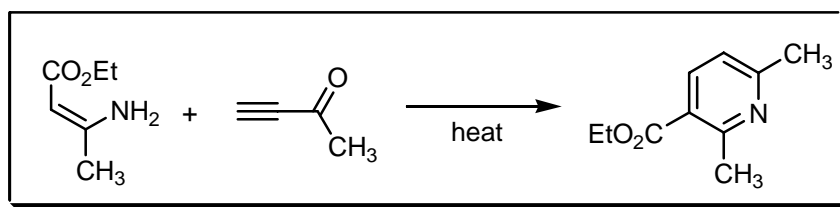
## REFERENCES :

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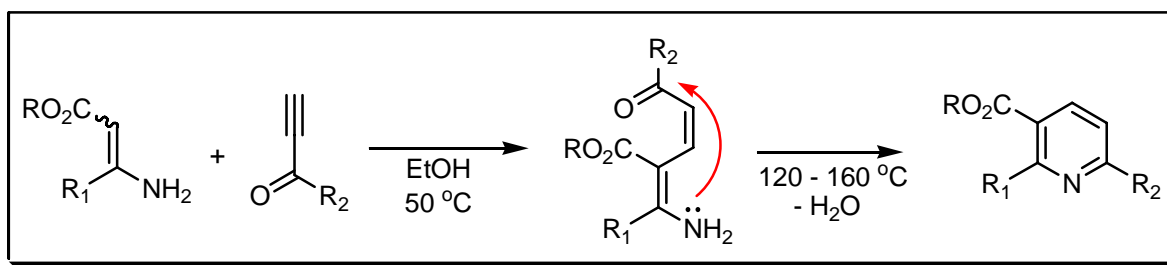
## COMMENTS :

## BOHLMANN – RAHTZ REACTION

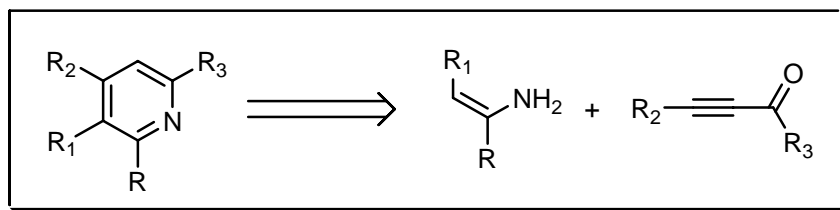
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :





## NOTES :

The formation of pyridines from enamines and ynones in a two-step **Michael** addition. The reaction can be Lewis acid-catalysed and affords the pyridine ring in a single step. See also **Chichibabin** pyridine, **Gattermann – Skita**, **Guareschi – Thorpe**, **Hantzsch – Beyer**, **von Meyer – Mohr**, **Petrenko–Kritschenko**, **Riehm** pyridine and **Wakatsuki – Yamazaki – Bönnemann** reactions.

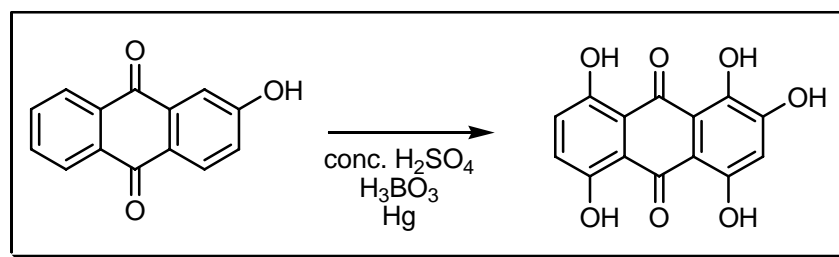
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- 5) M.C. Bagley; C. Brace; J.W. Dale; M. Ohnesorge; N.G. Phillips; X. Xiong; J. Bower, *J. Chem. Soc., Perkin Trans. 1*, 2002, 1663.
- 6) D.D. Hughes; M.C. Bagley, *Synlett*, 2002, 1332.
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- 8) M.C. Bagley; J.W. Dale; X. Xiong; J. Bower, *Org. Lett.*, 2003, **5**, 4421.
- 9) M.C. Bagley; J.W. Dale; R.L. Jenkins; J. Bower, *Chem. Commun.*, 2004, 102.
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- 12) M.C. Bagley; C. Glover; D. Chevis, *Synlett*, 2005, 649.

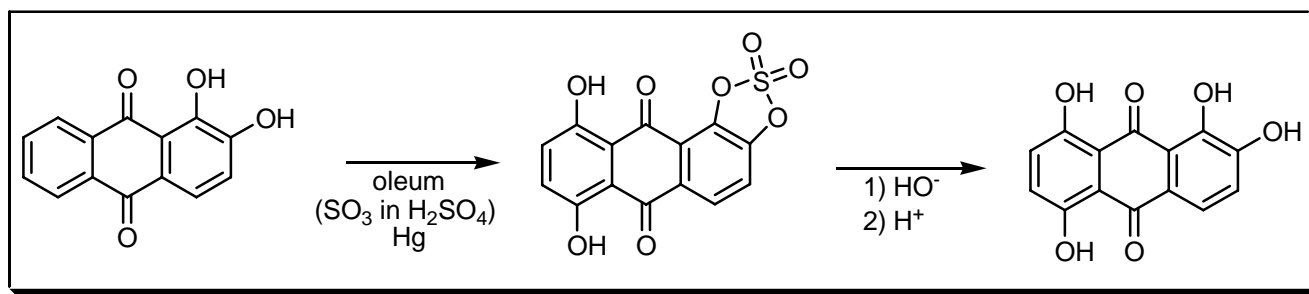
## COMMENTS :

## BOHN – SCHMIDT REACTION

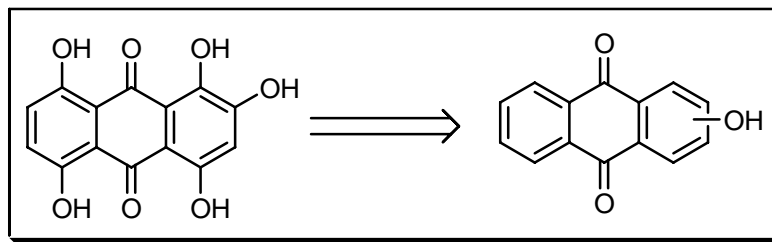
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This reaction involves the hydroxylation of anthraquinones or hydroxyanthraquinones by the action of oleum (10 – 30% SO<sub>3</sub> in H<sub>2</sub>SO<sub>4</sub>) in the presence of a catalyst such as selenium or mercury. The sulfuric esters are hydrolysed to the hydroxyanthraquinones. If boric acid is added to the reaction mixture concentrated sulfuric acid may be used instead of oleum. See also **Dakin** phenol aldehyde oxidation.

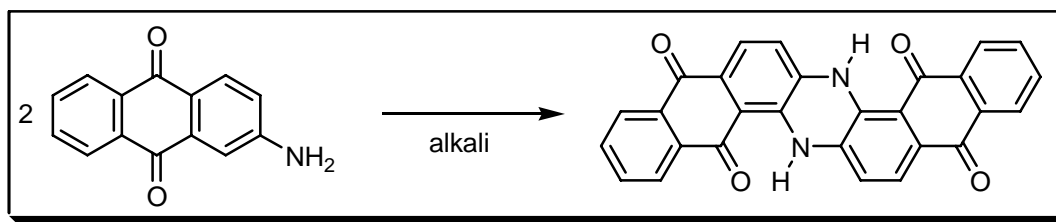
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- 2) R.E. Schmidt, *German Patent*, 1891, 60855.
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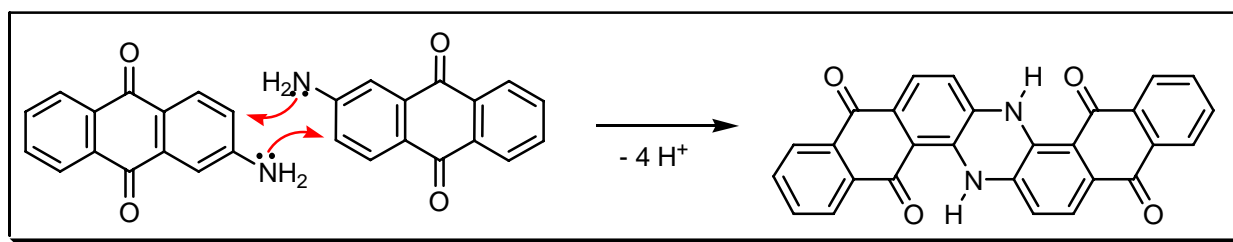
### COMMENTS :

## BOHN SYNTHESIS

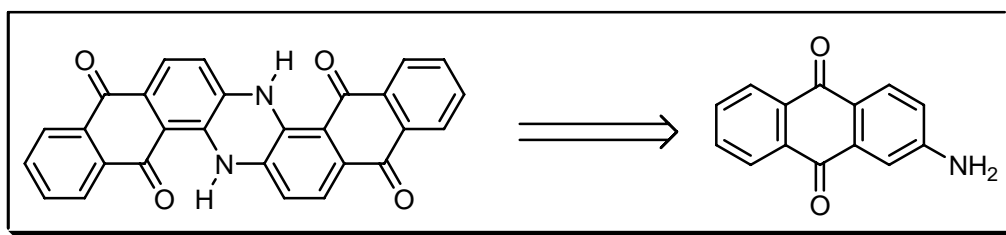
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The fusion of  $\beta$ -aminoanthraquinone with alkali at 200 – 250 °C yields indanthrone or Indanthrone Blue R. The reaction can be step-wise.

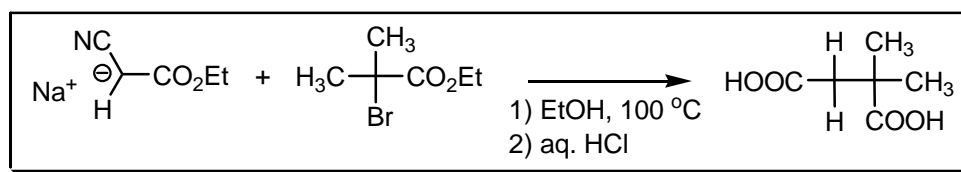
### REFERENCES :

- 1) R. Scholl, *Ber. Dtsch. Chem. Ges.*, 1905, **36**, 3410.
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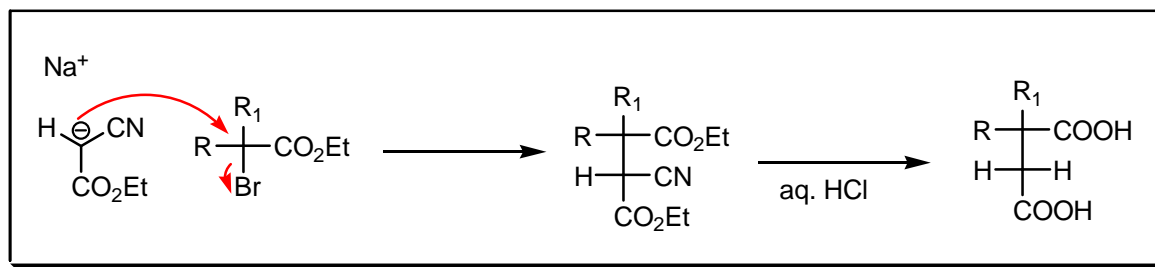
### COMMENTS :

## BONE – SPRANKLING SYNTHESIS

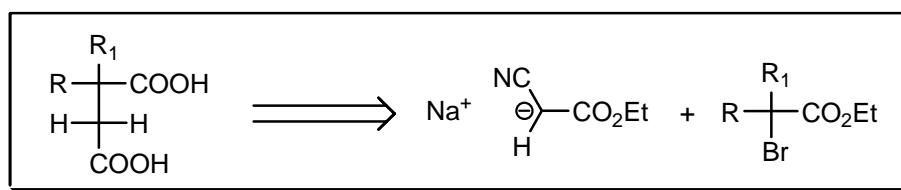
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The condensation of sodium ethyl 2-cyanoacetate with  $\alpha$ -bromoaliphatic esters gives alkyl cyanosuccinic diesters; which are hydrolysed and decarboxylated to the corresponding alkylsuccinic acids.

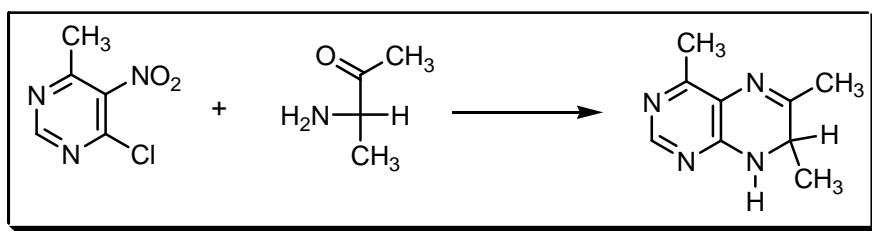
### REFERENCES :

- 1) W.A. Bone; C.H.G. Sprankling, *J. Chem. Soc.*, 1899, **75**, 839.
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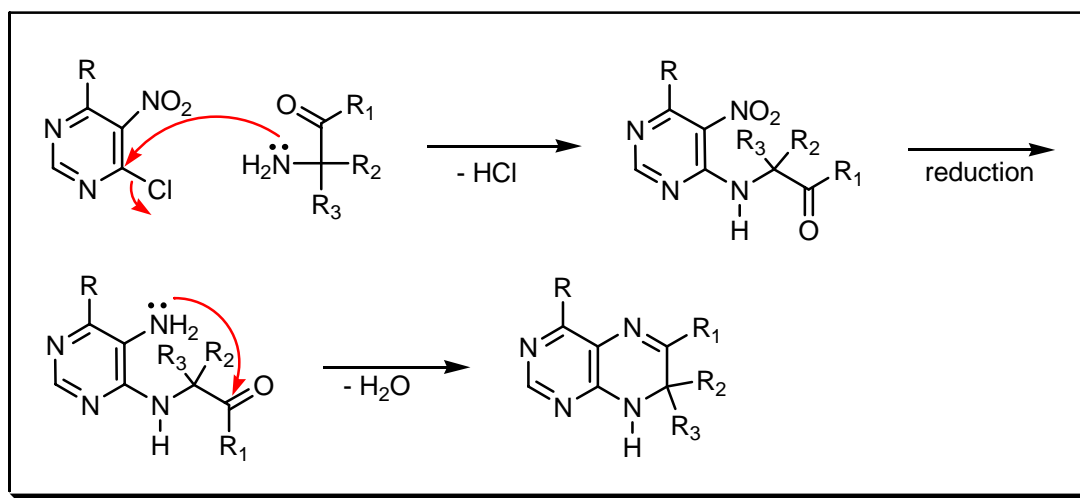
### COMMENTS :

## BOON – POLONOVSKI PTERIDINE REACTION

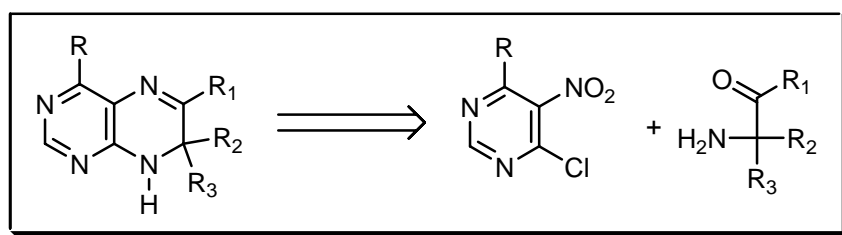
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

6-Chloro-5-nitro pyrimidines react with  $\alpha$ -aminocarbonyl compounds to afford 7,8-dihydropteridines. See also **Blicke – Pachter**, **Isay**, **Taylor** and **Timmis** reactions.

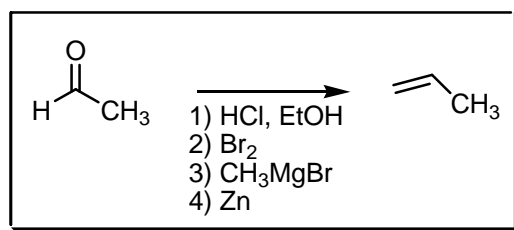
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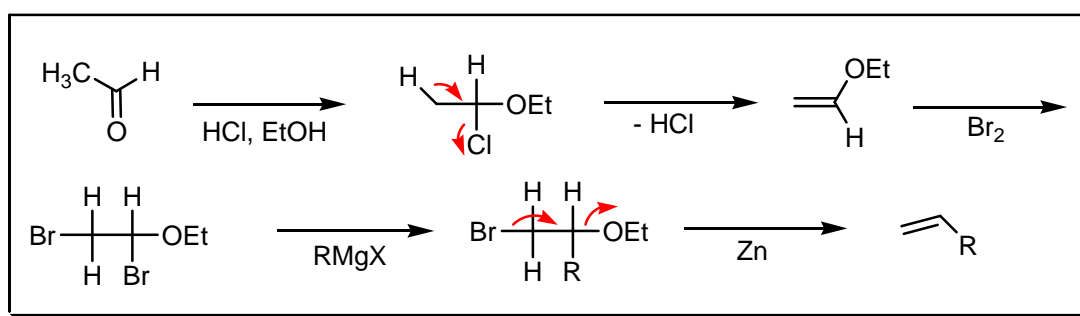
COMMENTS :

## BOORD OLEFIN SYNTHESIS

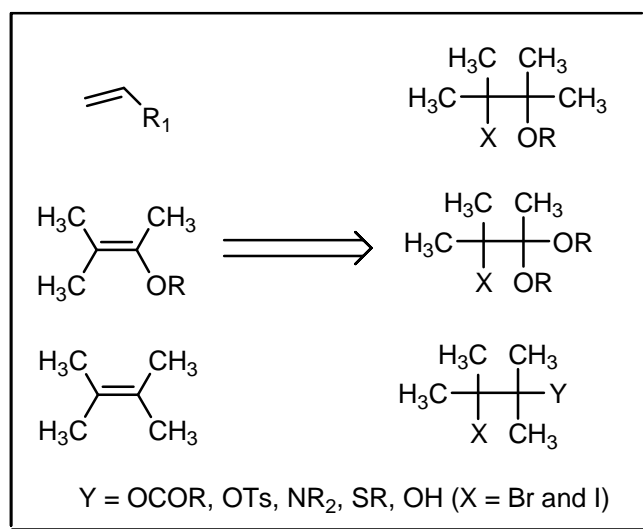
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

The synthesis involves four steps. The first three lead to the preparation of a  $\beta$ -ethoxyalkyl bromide and in the fourth step zinc is used for the simultaneous removal of the ethoxy group and bromine.  $\beta$ -Haloacetals yield vinylic ethers. The reaction can be further expanded to esters, tosylates, amines, sulfur and hydroxyl groups. Only in the last case the halogen atom must be bromine or iodine. See also **Baudart** reaction.

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## REFERENCES :

**March** : 1034

**Smith – March** : 1344

**Houben – Weyl** : 5/1b, 213

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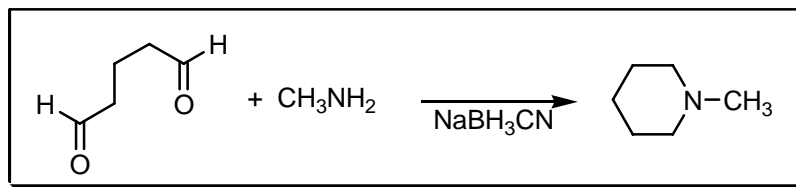
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## COMMENTS :

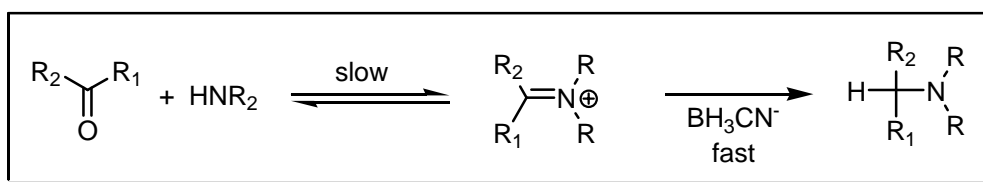
## BORCH REDUCTION

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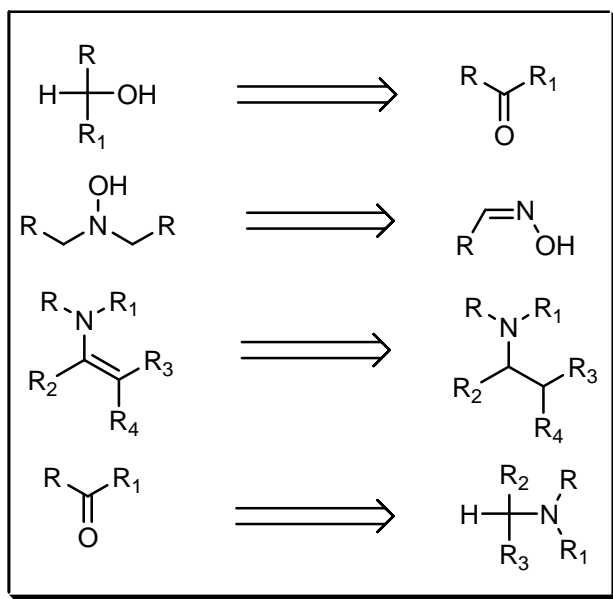
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The reductive amination of aldehydes or ketones by cyanoborohydride (or triacetoxyborohydride) anion (pH 6-7).  
Selective reduction of carbonyls to alcohol, oximes to *N*-alkylhydroxylamines, enamines to amines.

## REFERENCES :

Smith – March : 526

Smith : 384

Smith 2<sup>nd</sup> : 336

Org. React. : 4, 174; 59, 1

Org. Synth. : 52, 124

Org. Synth. Coll. Vol. : 6, 499

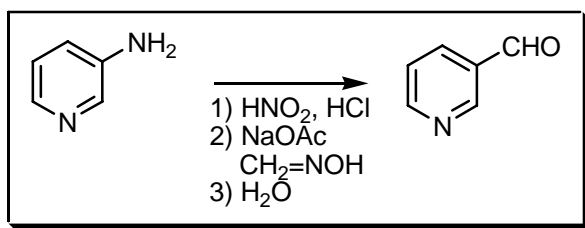
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## COMMENTS :

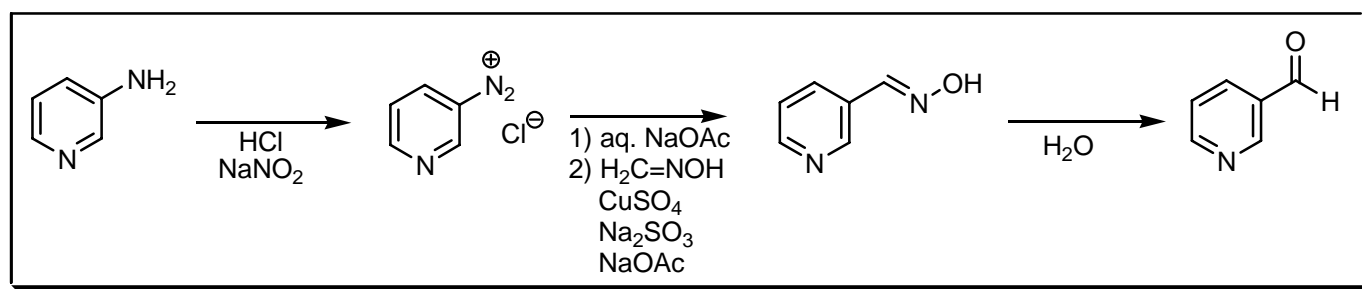


## BORSCHÉ – BEECH AROMATIC ALDEHYDE SYNTHESIS

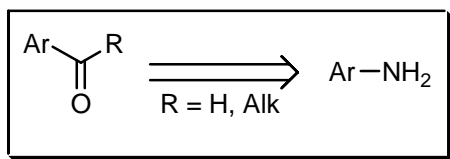
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The synthesis of aromatic aldehydes and of alkyl aryl ketones from aldoximes or semicarbazones and aromatic diazonium salts. See also **Bouveault – Wahl** reaction.

### REFERENCES :

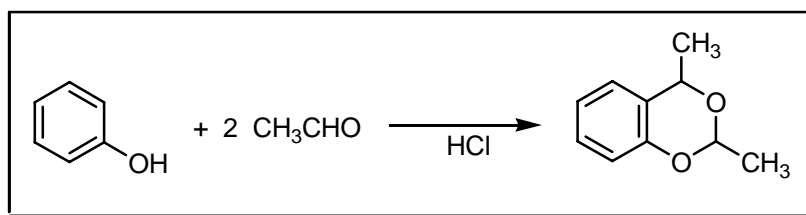
Houben – Weyl : 10/3,185; E3, 145

- 1) C. Borsche, *Chem. Ber.*, 1907, **40**, 737.
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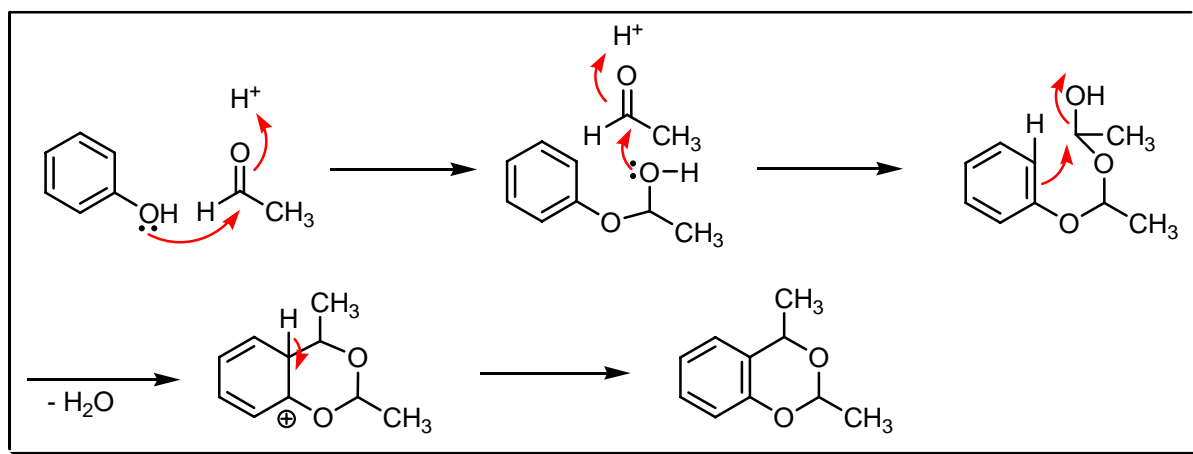
COMMENTS :

## BORSCHKE – BERKHOUT SYNTHESIS

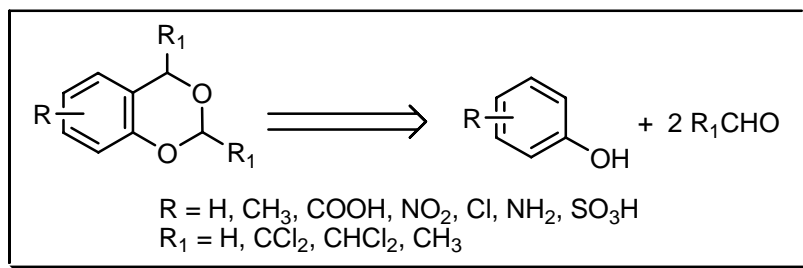
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The *intermolecular* condensation of phenols and aldehydes in the presence of acids to afford 1,3-benzodioxanes.

## REFERENCES :

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- 5) F. Bigi; G. Casiraghi; G. Casnati; G. Sartori, *Synthesis*, 1980, 724.

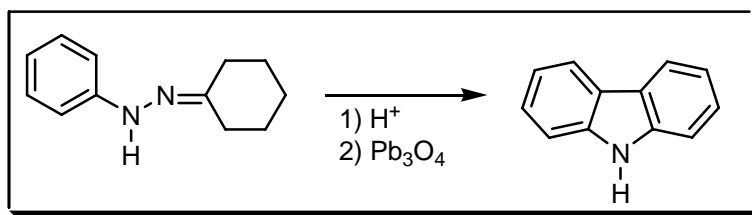
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## COMMENTS :

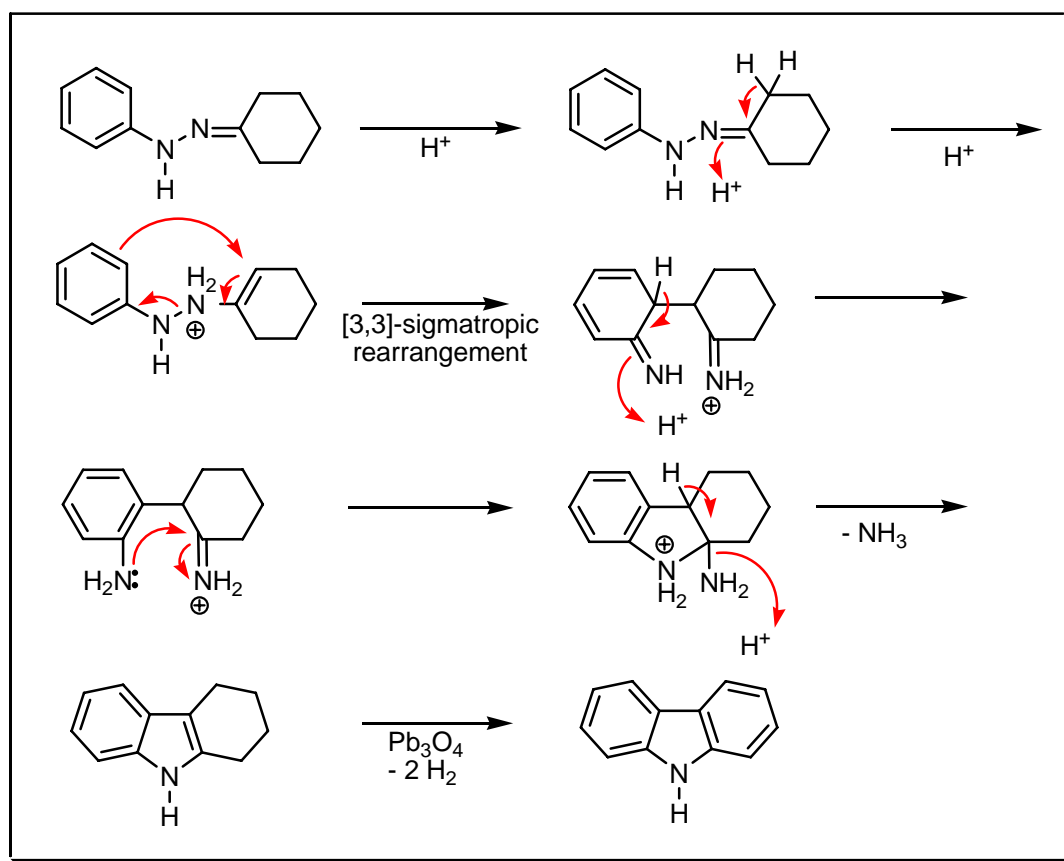
## BORSCHÉ – DRECHSEL CYCLISATION

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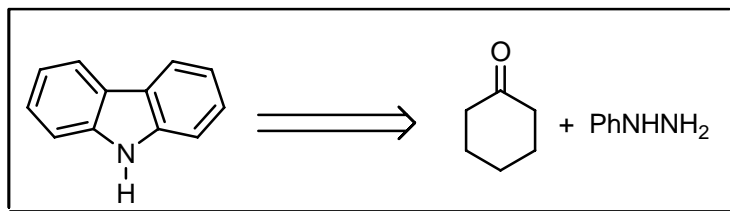
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The phenylhydrazones of cyclohexanone derivatives give tetrahydrocarbazoles in the presence of acids. The main transformation is a [3,3]-sigmatropic rearrangement. The product is oxidised by lead(III,IV) oxide to a carbazole. See also **Bucherer** carbazole, **Fischer** indole, **Friedel – Crafts** and **Piloty – Robinson** reactions.

## REFERENCES :

Smith : 1346

Smith 2<sup>nd</sup> : 1107

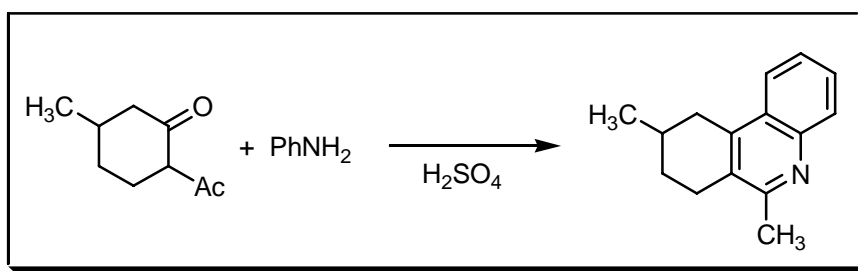
- 1) E. Drechsel, *J. Prakt. Chem.*, 1888, **38**, 69.
- 2) W. Borsche; M. Feise, *Ber. Dtsch. Chem. Ges.*, 1904, **40**, 378.
- 3) N. Campbell; B.M. Barclay, *Chem. Rev.*, 1947, **40**, 359.
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 7) G. Lin; A. Zhang, *Tetrahedron*, 2000, **56**, 7163.  
 8) G.L. Rebeiro; B.M. Khadilkar, *Synthesis*, 2001, 370.

**COMMENTS :**

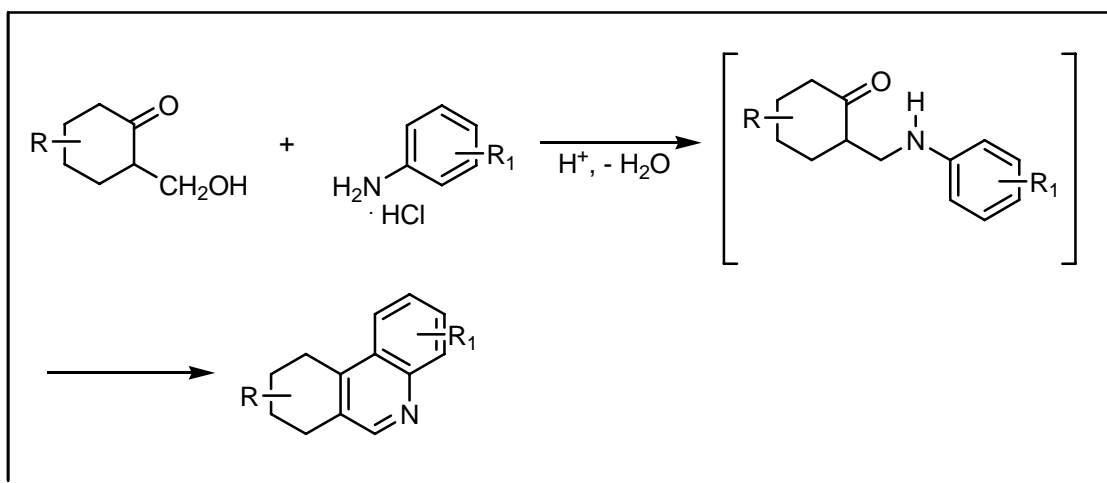
## BORSCHKE – KENNER SYNTHESIS

**EXAMPLE :**

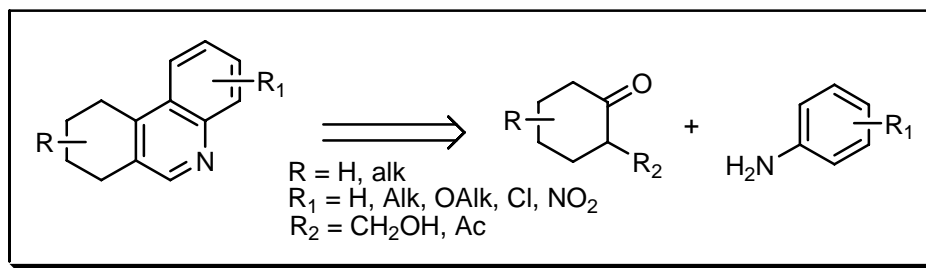


**MECHANISM :**

**Kenner variation :**



## DISCONNECTION :



## NOTES :

The cyclic condensation of a 2-acylcyclohexanone and a primary aromatic amine by hot concentrated sulfuric acid gives a tetrahydrophenanthridine. Alternatively (**Kenner** modification), the 2-acylcyclohexanone is replaced by a 2-( $\omega$ -hydroxymethyl)cyclohexanone, which is treated with an arylamine or its hydrochloride with or without the addition of stannic chloride. See also **Combes** quinoline, **Doebner – Miller** and **Pictet – Hubert** reactions.

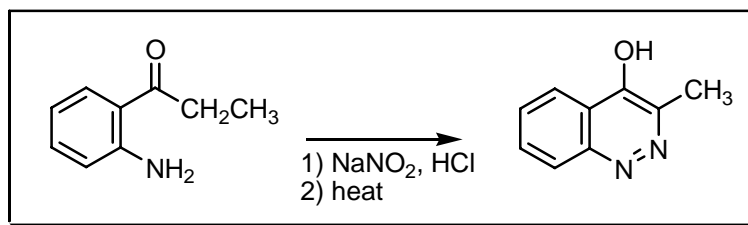
## REFERENCES :

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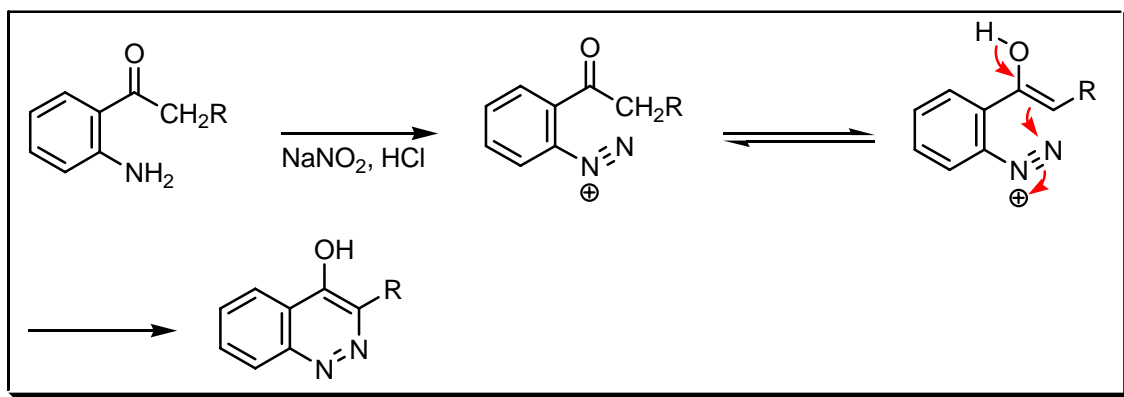
## COMMENTS :

## BORSCHKE – KOELSCH CINNOLINE SYNTHESIS

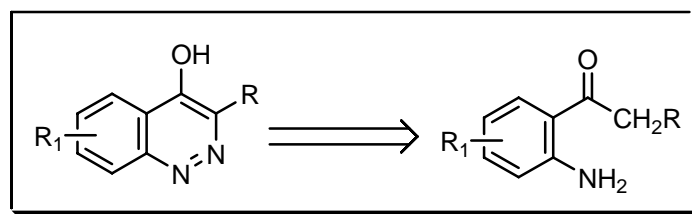
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

A method for the preparation of 4-hydroxycinnolines, which consists of the diazotisation of the appropriate 2-aminoaryl ketones. The diazonium salt readily cyclises. See also **Pschorr, von Richter** and **Widman – Stoermer** reactions.

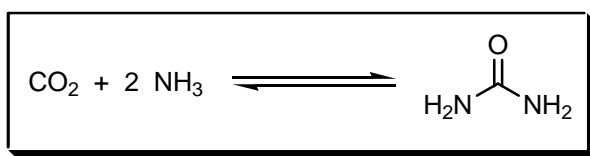
### REFERENCES :

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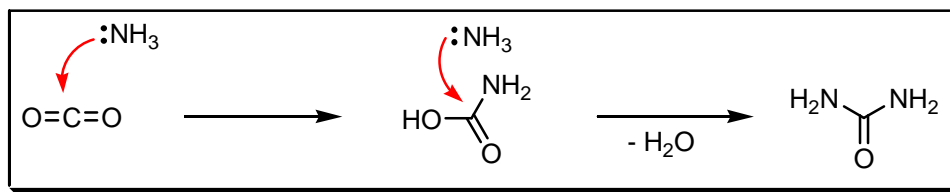
### COMMENTS :

## BOSCH – MEISER UREA PROCESS

### EXAMPLE :



### MECHANISM :



### NOTES :

The synthesis of urea from carbon dioxide and ammonia. See also **Wöhler** urea synthesis.

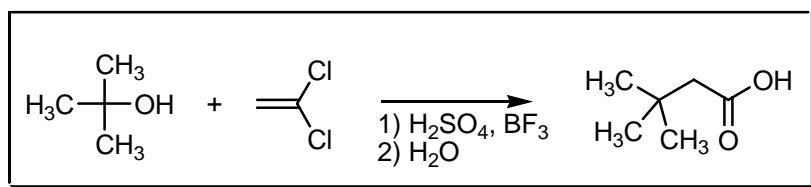
### REFERENCES :

C. Bosch; W. Meiser, *U.S. Patent*, 1922, 1429483.

### COMMENTS :

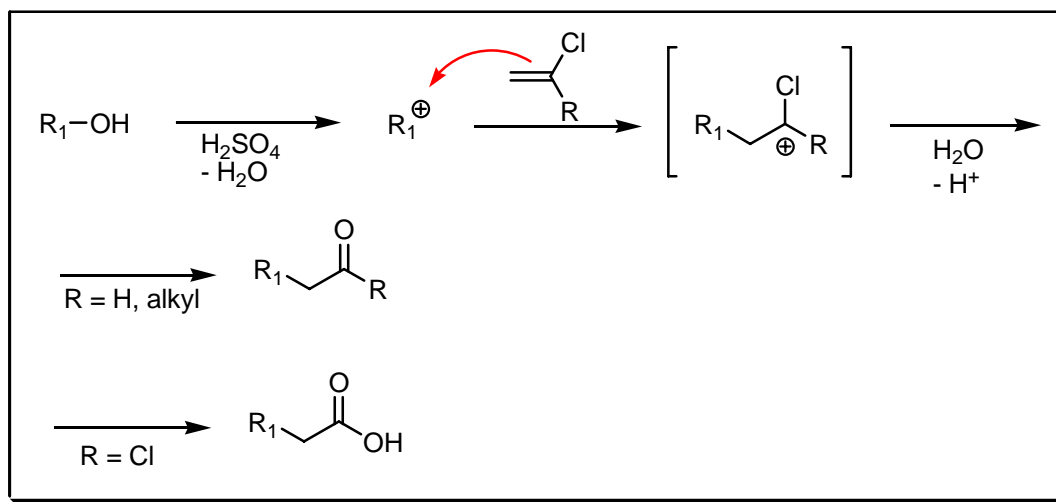
## BOTT – HELLMANN REACTION

### EXAMPLE :

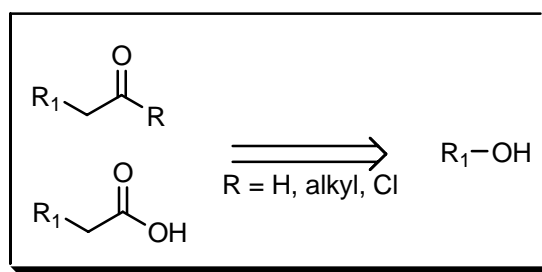




## MECHANISM :



## DISCONNECTION :



## NOTES :

The addition of carbenium ions in acidic solution to 1,1-dichloro-1-alkenes or 1-chloro-1-alkenes. Hydrolysis results in a carboxylic acid or ketone, 2 carbon atoms longer. See also **Ritter** reaction.

## REFERENCES :

Houben – Weyl : E5, 435; E19c, 324

- 1) K. Bott, *Angew. Chem.*, 1965, **77**, 967.
- 2) K. Bott; H. Hellmann, *Angew. Chem., Int. Ed. Engl.*, 1966, **5**, 870.
- 3) D.J. Raber; R.C. Fort; E. Wiskott; C.W. Woodworth; P. von Ragué Schleyer; J. Weber; H. Stetter, *Tetrahedron*, 1971, **27**, 3.
- 4) K. Bott, *Angew. Chem., Int. Ed. Engl.*, 1980, **19**, 171.

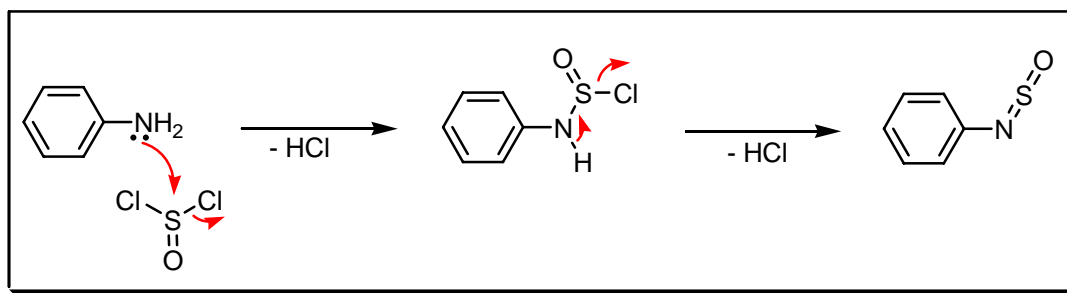
## COMMENTS :

# BÖTTINGER – MICHAELIS REACTION

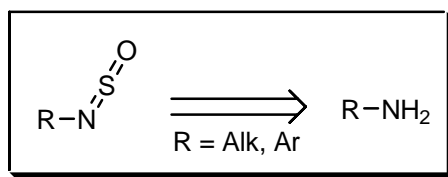
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Thionylamines are obtained by the action of thionyl chloride on alkyl or aryl primary amines. See also **Kaluza** reaction.

## REFERENCES :

**Org. Synth.** : **49**, 70

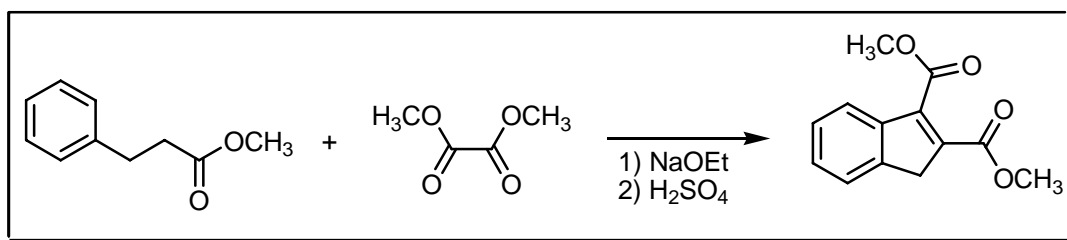
**Org. Synth. Coll. Vol.** : **5**, 504

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- 2) A. Michaelis, *Liebigs Ann. Chem.*, 1893, **274**, 173.
- 3) H.M. Kissman; D.S. Tarbell; J. Williams, *J. Am. Chem. Soc.*, 1953, **75**, 2959.
- 4) J.R. Grunwell; A. Kochan, *J. Org. Chem.*, 1973, **38**, 1610.
- 5) S. Sakai; T. Fujinami; K. Komizo, *J. Org. Chem.*, 1975, **40**, 3291.
- 6) H.-J. Niclas; D. Habisch; D. Martin, *Tetrahedron*, 1979, **35**, 2353.
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- 8) H. Shimizu; N. Okada; M. Yoshimatsu, *Tetrahedron Lett.*, 2001, **42**, 4183.

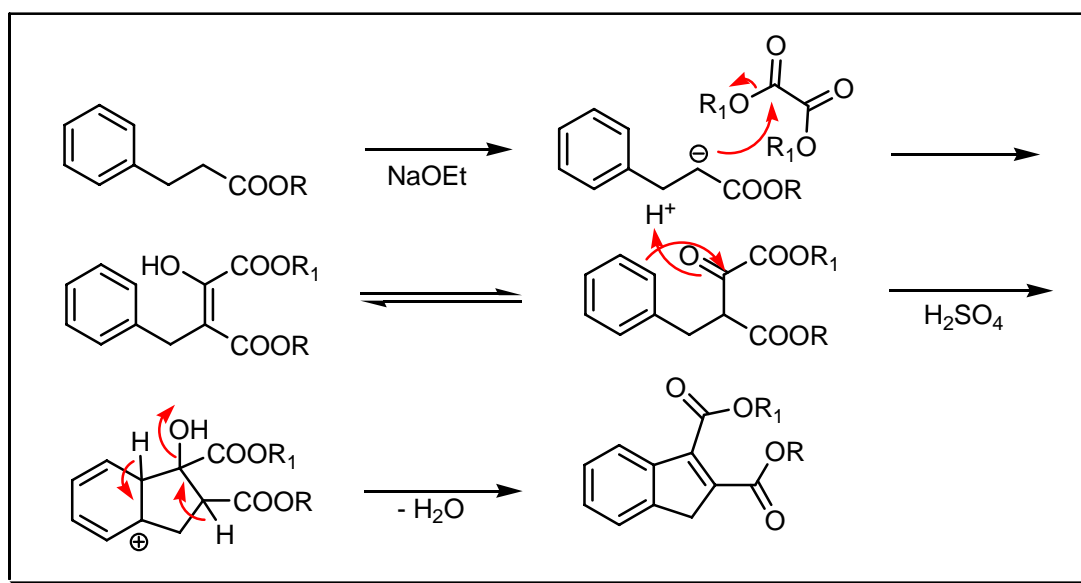
COMMENTS :

## BOUGAULT SYNTHESIS

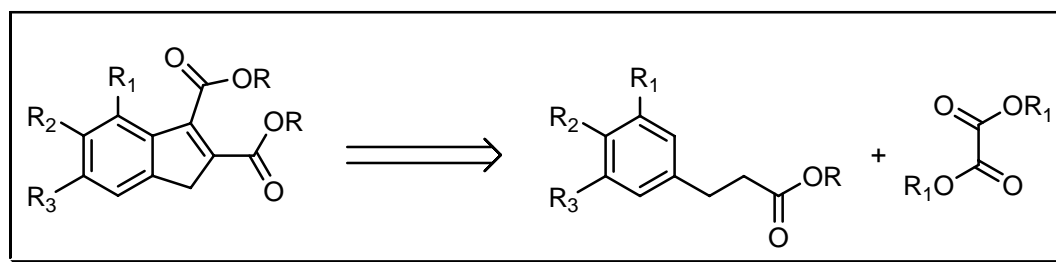
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

This method for the preparation of indene 2,3-dicarboxylic esters involves the cyclisation with sulfuric or polyphosphoric acid of an ester derived from an ethyl  $\beta$ -phenylpropionate and ethyl oxalate. The reaction has been extended to the synthesis of six- and seven-membered rings.

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## REFERENCES :

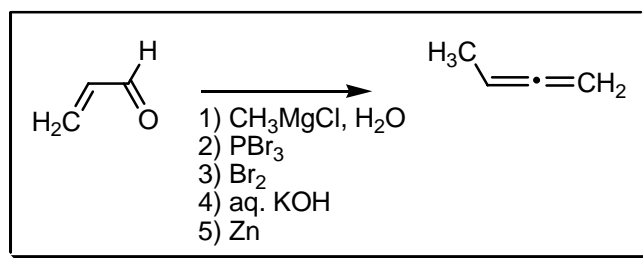
- 1) W. Roser, *Liebigs Ann. Chem.*, 1888, **247**, 152.
  - 2) J. Bougeault, *C.R. Séances Acad. Sci.*, 1915, **159**, 745.
  - 3) K. Auwers; K. Möller, *J. Prakt. Chem.*, 1925, **109**, 124.
  - 4) L.F. Fiesel; E.B. Hershberg, *J. Am. Chem. Soc.*, 1935, **57**, 1508.
  - 5) L.F. Fiesel; E.B. Hershberg, *J. Am. Chem. Soc.*, 1935, **57**, 1851.
  - 6) E.C. Horning; J. Koo, *J. Am. Chem. Soc.*, 1951, **73**, 5826.
  - 7) A. Guy; J.-P. Guette; G. Lang, *Synthesis*, 1980, 222.
  - 8) C.S. Rao; R. Ramachandra; S. Kshirsagar; D.M. Vashi; V.S.N. Murty, *Indian J. Chem.*, 1983, **22B**, 230.
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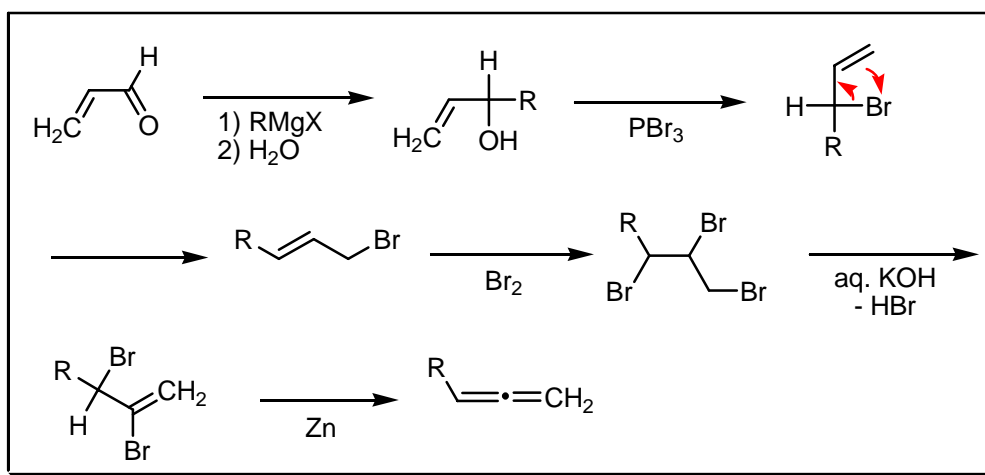
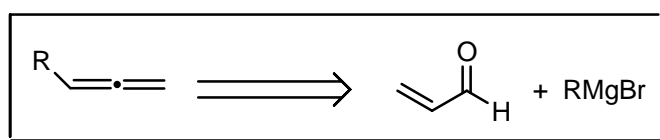
## COMMENTS :

## BOUIS SYNTHESIS

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### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

Acrolein reacts with a **Grignard** reagent to give a substituted allyl alcohol after hydrolysis, which with phosphorous tribromide yields by allylic rearrangement a 1-bromo-2-olefin. This olefin adds bromine and hydrogen bromide is then eliminated by treatment with alkali hydroxide. Finally the two bromine atoms are removed by zinc to give the allene derivative.

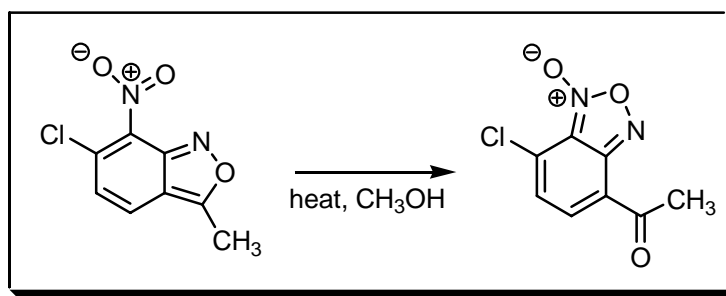
**REFERENCES :**

M. Bouis, *Ann. Chim. (Paris)*, 1928, **9**, 402.

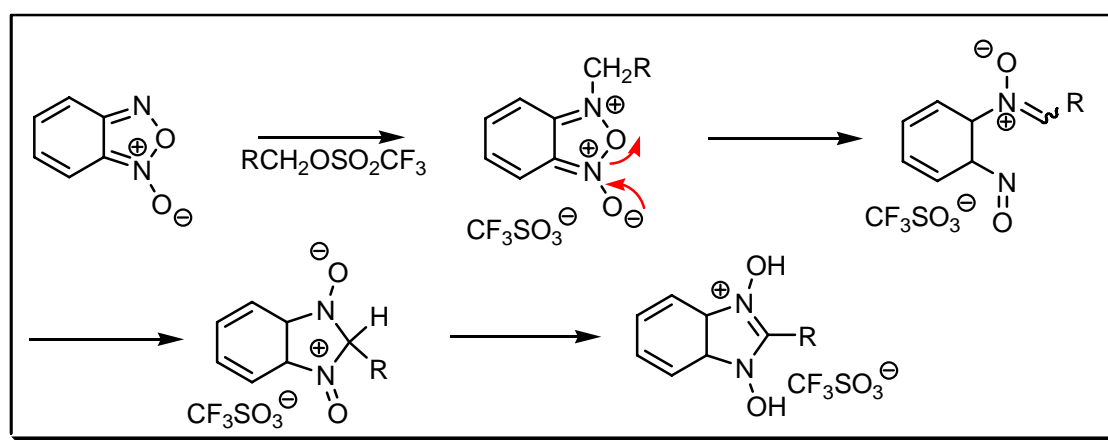
**COMMENTS :**

## BOULTON – KATRITZKY REARRANGEMENT

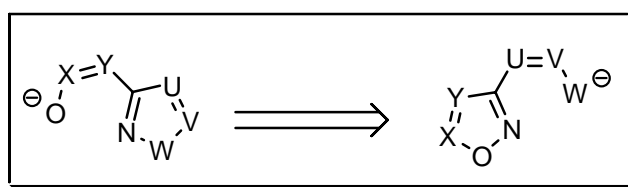
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Isoxazoles and other five-membered heteroaromatics containing an N-O bond undergo a thermal or base-catalysed rearrangement. The reaction is in some cases reversible.

### REFERENCES :

Houben – Weyl : **E8a**, 401, 433; **E8b**, 527; **E8c**, 516, 686, 799

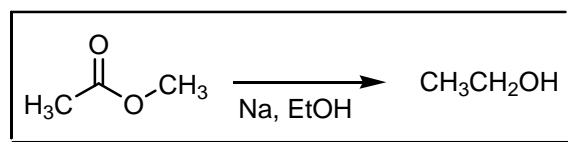
- 1) A.J. Boulton; A.R. Katritzky, *Rev. Chim. (Romania)*, 1962, **7**, 691.
- 2) A.J. Boulton; A.R. Katritzky; A.M. Hamid, *J. Chem. Soc. (C)*, 1967, 2005.
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- 5) S. Ostrowski; K. Wojciechowski, *Can. J. Chem.*, 1990, **68**, 2239.
- 6) V.G. Andrianov; S.V. Makushenkov; A.V. Ereemeev, *Mendeleev Commun.*, 1992, 129.
- 7) A.R. Katritzky; M.F. Gordeev, *Heterocycles*, 1993, **35**, 483.
- 8) F. Eckert; G. Rauhut, *J. Am. Chem. Soc.*, 1998, **120**, 13478.
- 9) G. Rauhut, *J. Org. Chem.*, 2001, **66**, 5444.
- 10) A. Peña-Gallego; J. Rodríguez-Otero; E.M. Cabaleiro-Lago, *J. Org. Chem.*, 2004, **69**, 7013.

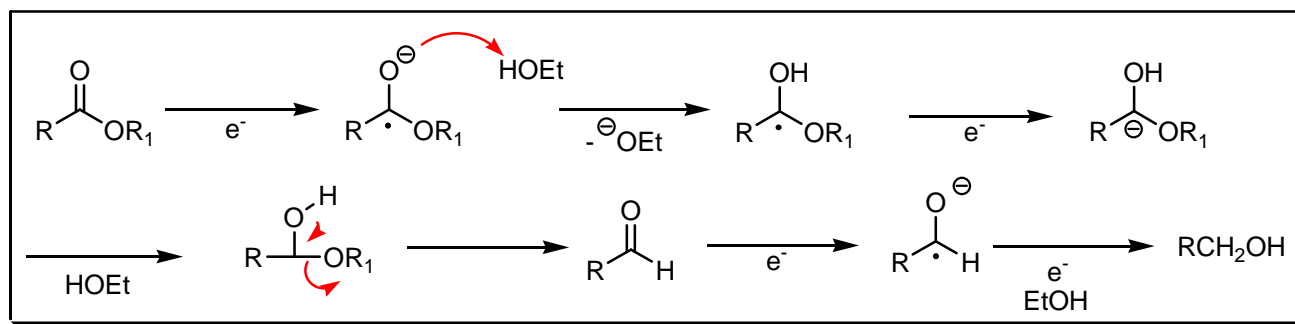
**COMMENTS :**

## BOUVEAULT – BLANC REDUCTION

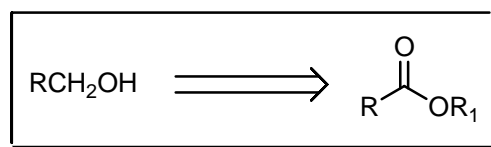
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

Although a once popular reduction, it has largely been replaced by modern hydride reducing agents. Sometimes the reduction of an aldehyde, carboxylic acid or ketone under these conditions is called a **Bouveault – Blanc** reduction. Here, the thermodynamically more stable alcohol will result from the reduction. There is also a **Hansley – Prelog** –

**Stoll** modification, which uses sodium and a reducing alcohol in an inert solvent such as xylene. (*Ind. Eng. Chem.*, 1947, **39**, 55) Another modification is the one by **Prins**. This reaction, the **Prins** reduction, relates to the reduction of esters by sodium in diethyl ether – acetic acid mixture in the presence sodium acetate. See also **Bouveault – Locquin** acyloin and **Hansley – Prelog – Stoll** reactions.

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#### REFERENCES :

**March** : 913, 916

**Smith – March** : 1199, 1551

**Houben – Weyl** : **8**, 643

**Org. Synth.** : **10**, 62; **14**, 20; **15**, 51; **29**, 80; **33**, 76

**Org. Synth. Coll. Vol.** : **2**, 154, 372, 468; **3**, 671; **4**, 798

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1) L. Bouveault; G. Blanc, *C.R. Séances Acad. Sci.*, 1903, **136**, 1676.

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3) H.J. Prins, *Recl. Trav. Chim. Pays-Bas*, 1923, **42**, 1050.

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5) E. Albano–Garcia; R.G. Lorica; De leon, *Philippine J. of Coconut Studies*, 1980, **5**, 13.

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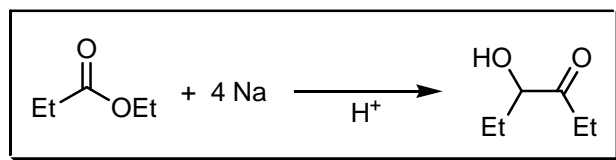
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#### COMMENTS :

### BOUVEAULT – LOCQUIN ACYLOIN SYNTHESIS

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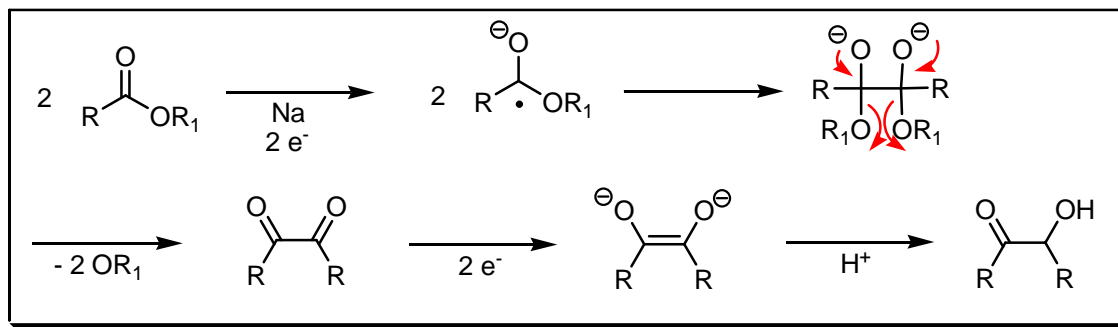
#### EXAMPLE :



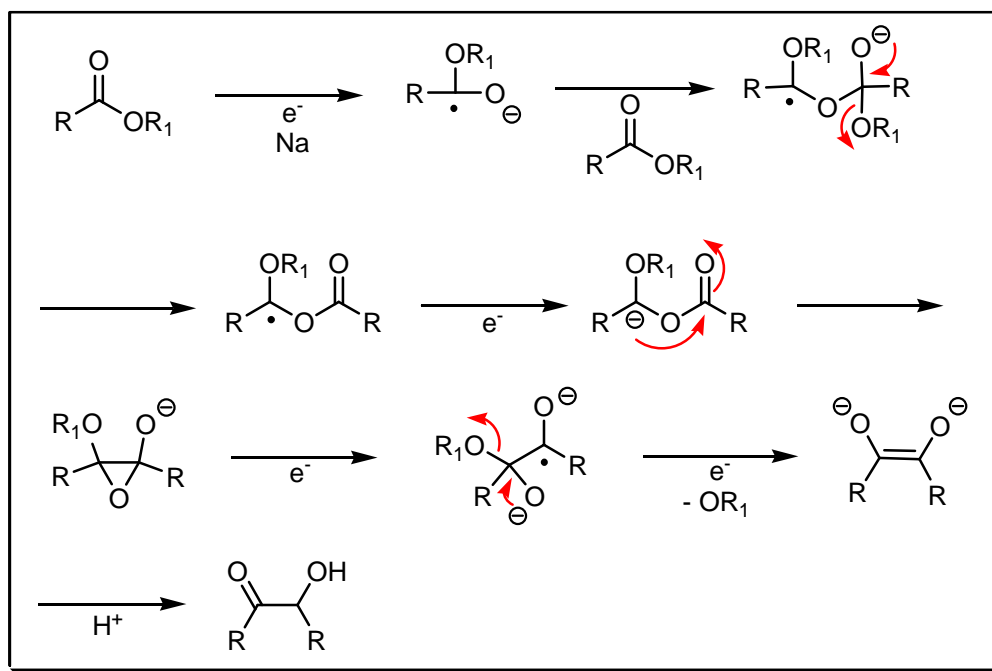


## MECHANISM :

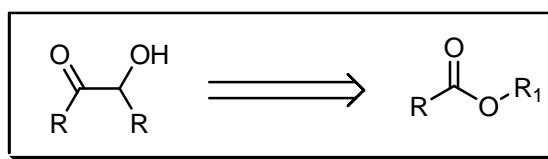
### Mechanism 1 :



### Mechanism 2 :



## DISCONNECTION :



## NOTES :

Acyloins are formed by the action of sodium (sometimes potassium or better sodium-potassium alloy) on esters in an inert solvent. Mixed acyloins are similarly obtained. There has been a great deal of controversy over the mechanism of the acyloin reaction. Two possible reaction mechanism are shown here. See also **Baudart** acyloin synthesis, **Bouveault – Blanc**, **Claisen** and **Hansley – Stoll – Prelog** reactions.

## REFERENCES :

March : 1228

Smith – March : 1562

Smith : 1442

Smith 2<sup>nd</sup> : 1189

Org. React. : 4, 256; 23, 259

Org. Synth. : 13, 24; 57, 1

Org. Synth. Coll. Vol. : 2, 114; 6, 167

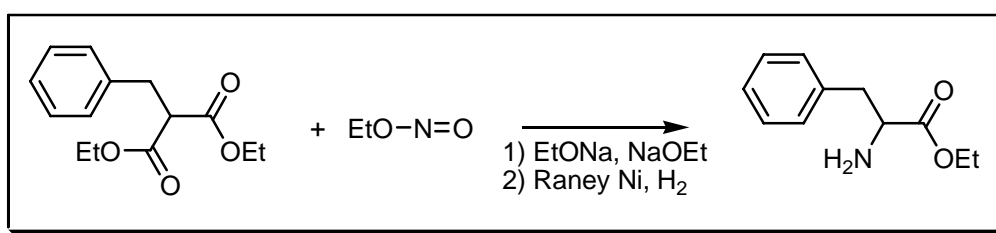
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- 1) L. Bouveault; R. Locquin, *C.R. Séances Acad. Sci.*, 1903, **136**, 1676.
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  - 6) T.S. Daynard; P.S. Eby; J.H. Hutchinson, *Can. J. Chem.*, 1993, **71**, 1022.
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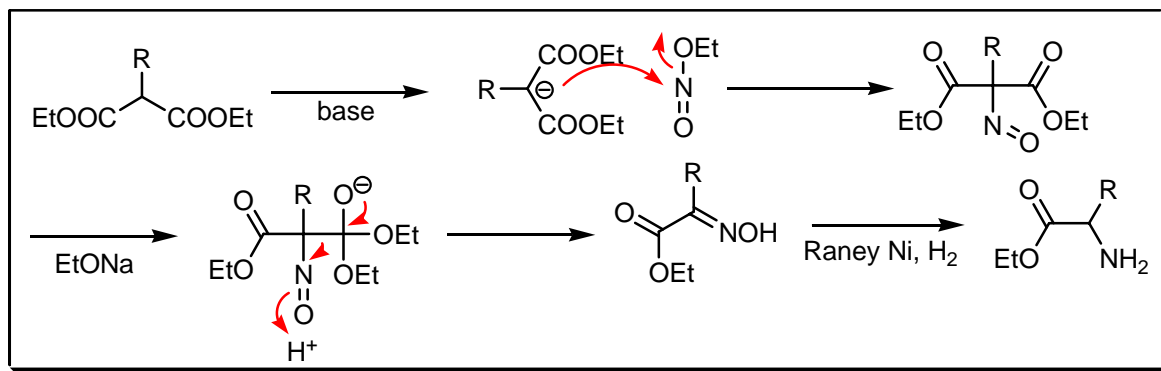
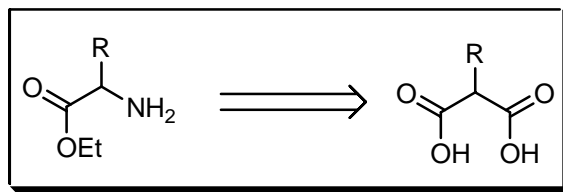
## COMMENTS :

## BOUVEAULT – LOCQUIN AMINO ACID SYNTHESIS

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### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

The synthesis of  $\alpha$ -amino acids from malonate esters by nitrosation.

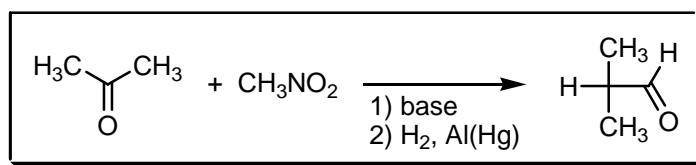
**REFERENCES :**

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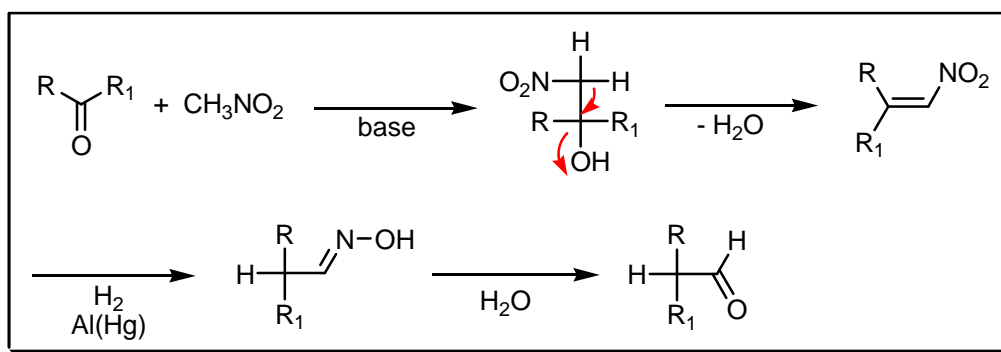
**COMMENTS :**

## BOUVEAULT – WAHL SYNTHESIS

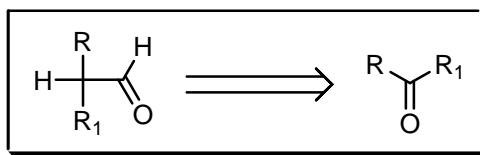
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Nitro-olefins (obtained by condensing carbonyl compounds with nitro-methane) on reduction with aluminium amalgam yield oximes from which aldehydes may be obtained. See also **Borsche – Beech**, **Henry** and **Nef** reactions.

### REFERENCES :

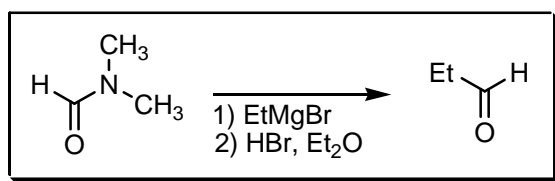
Houben – Weyl : 7/1, 272

- 1) L. Bouveault; A. Wahl, *C.R. Séances Acad. Sci.*, 1902, **134**, 1226.
- 2) L. Bouveault; A. Wahl, *Bull. Soc. Chim. Fr.*, 1903, **29**, 643.
- 3) K. Johnson; E.F. Degering, *J. Org. Chem.*, 1943, **8**, 7.
- 4) K. Johnson; E.F. Degering, *J. Org. Chem.*, 1943, **8**, 10.

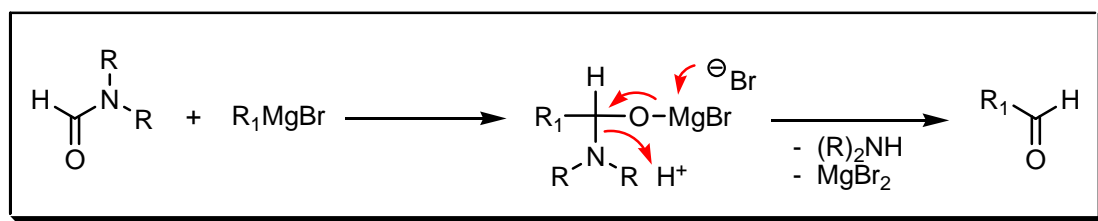
COMMENTS :

## BOUVEAULT ALDEHYDE SYNTHESIS

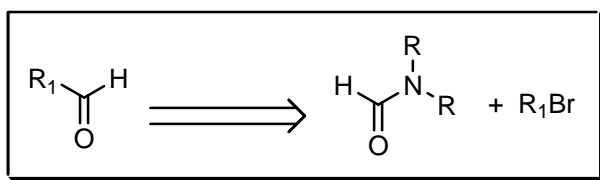
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

Dialkylformamides are treated with a **Grignard** reagent and the product hydrolysed by acid to yield aldehydes. Lithium compounds can be used instead of **Grignard** reagents. See also **Bodroux – Chichibabin** and **Claisen – Mauthner – Bouveault** reactions.

REFERENCES :

March : 932

Smith – March : 1214

Houben – Weyl : 7/1, 66

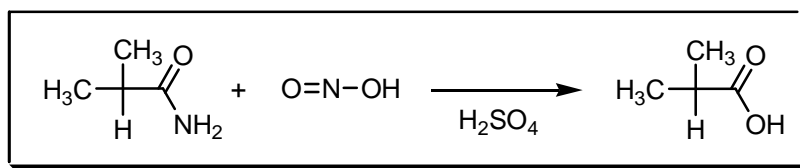
1) L. Bouveault, *C.R. Séances Acad. Sci.*, 1903, **137**, 987.

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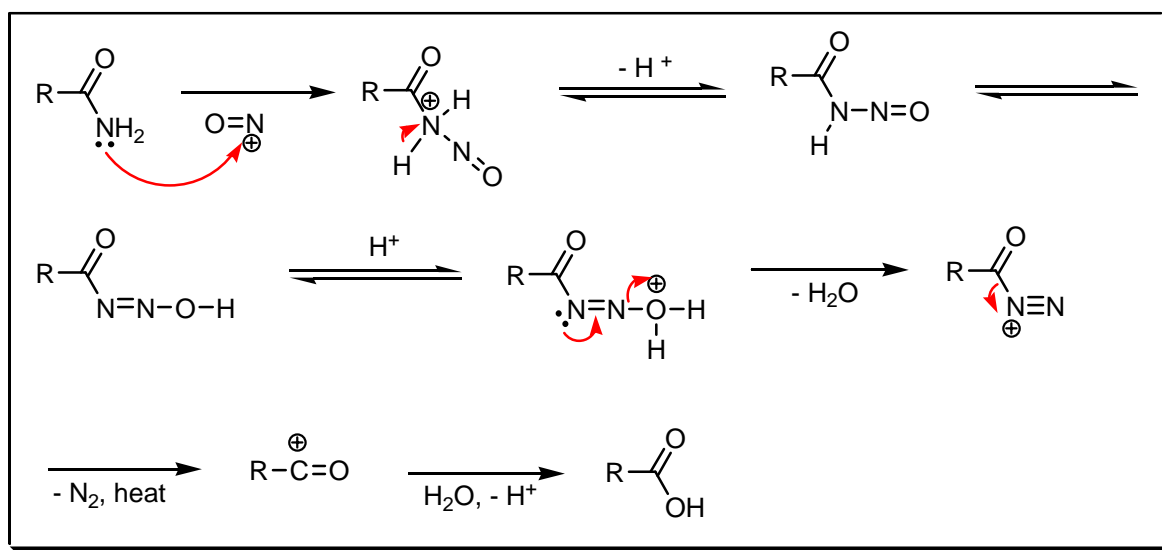
COMMENTS :

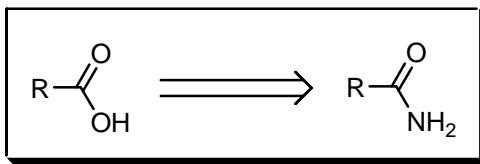
## BOUVEAULT HYDROLYSIS OF AMIDES

EXAMPLE :



MECHANISM :



**DISCONNECTION :**

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**NOTES :**

The nitrile is converted into the amide by concentrated sulfuric acid and the acid solution is treated with aqueous sodium nitrite to afford the carboxylic acid.

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**REFERENCES :**

Houben – Weyl : 8, 432

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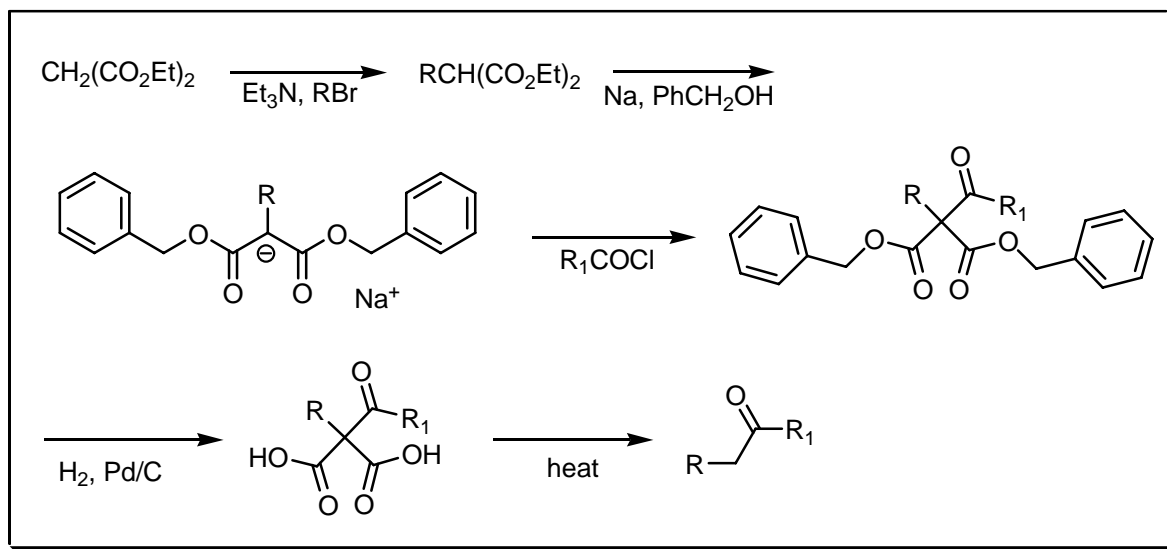
- 1) L. Bouveault, *Bull. Soc. Chim. Fr.*, 1893, **9**, 368.
  - 2) J.J. Sudborough, *J. Chem. Soc.*, 1895, **67**, 602.
  - 3) F.G. Mann; J.W.G. Porter, *J. Chem. Soc.*, 1945, 752.
  - 4) F.J. Kezdy; I. Jaz; A. Bruylants, *Bull. Soc. Chim. Belg.*, 1958, **67**, 68.
- 

**COMMENTS :**

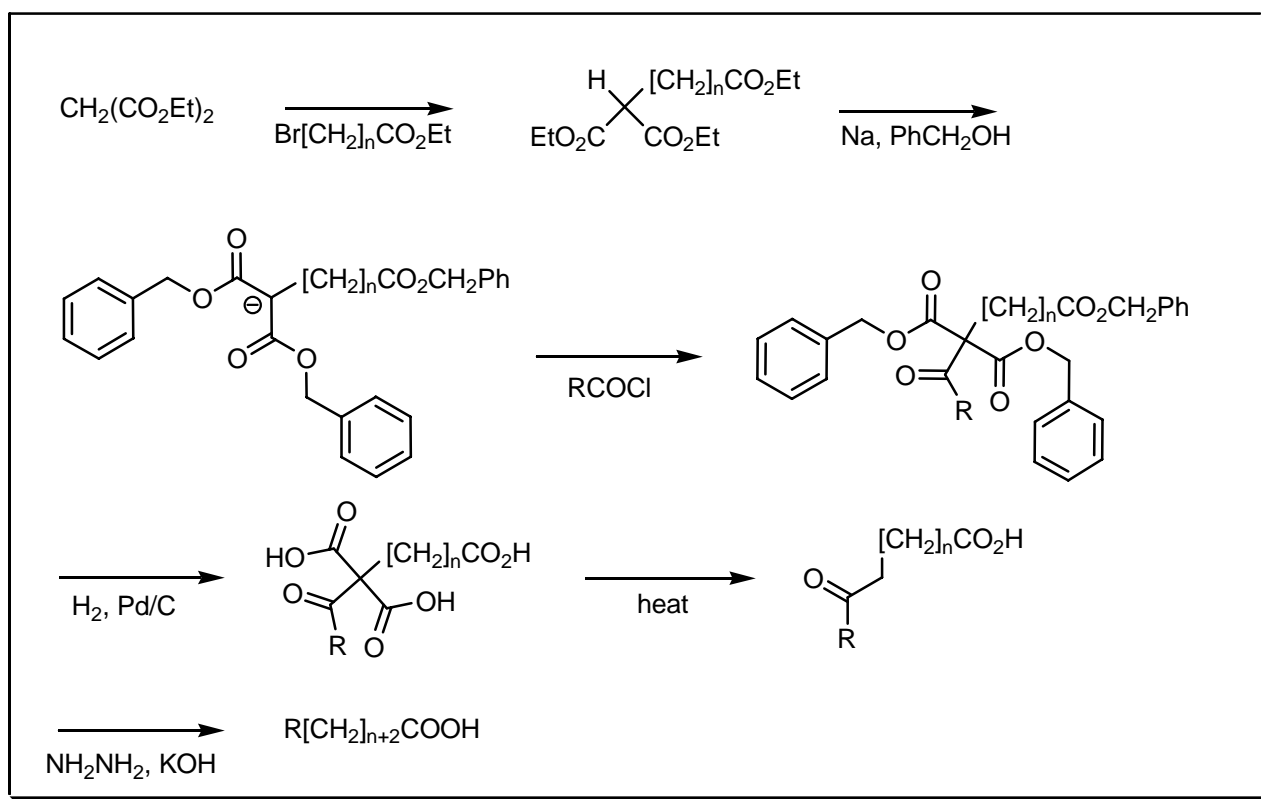
## BOWMAN DEBENZYLATION

### MECHANISM :

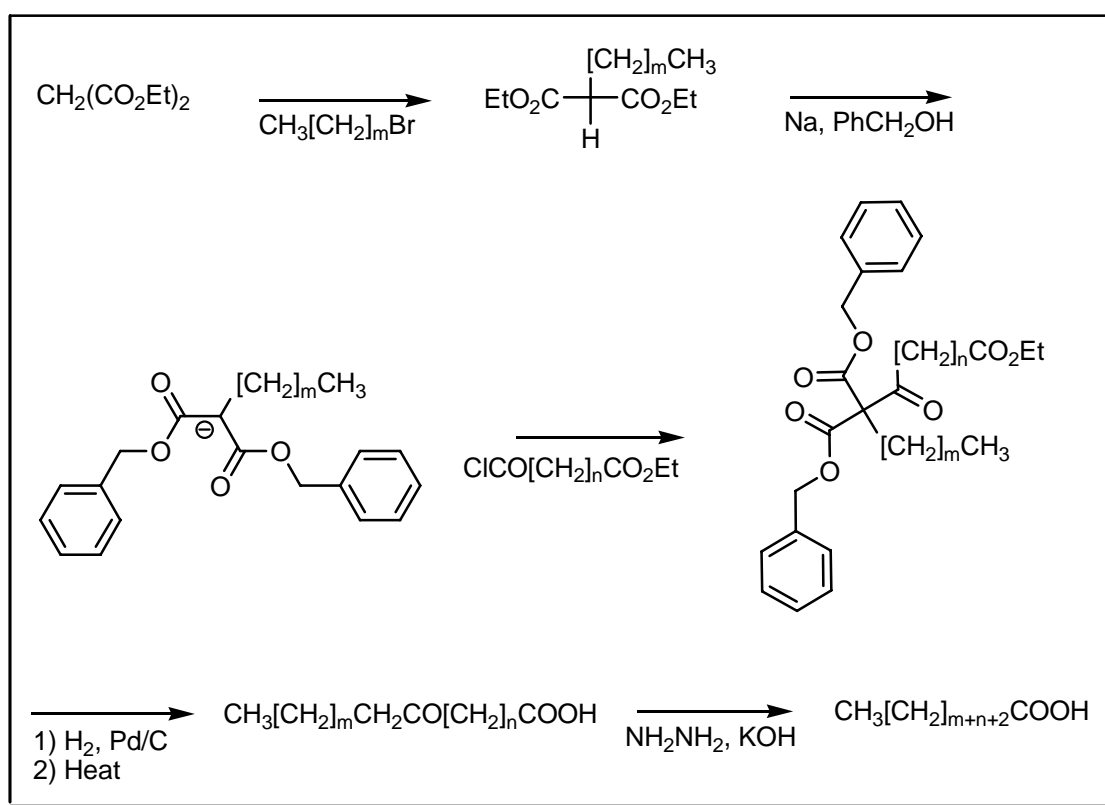
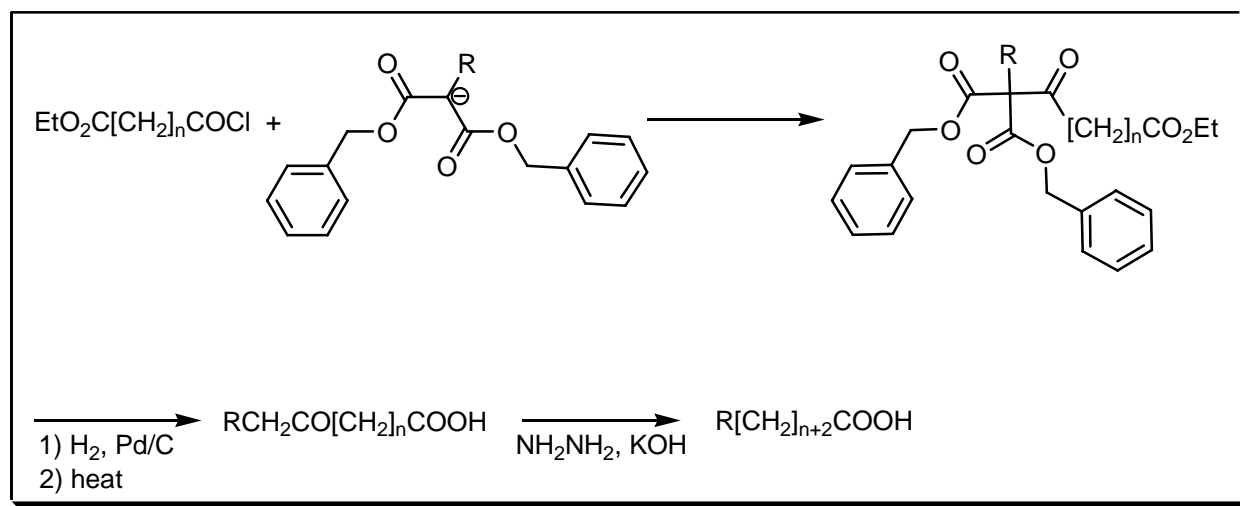
#### Ketones :



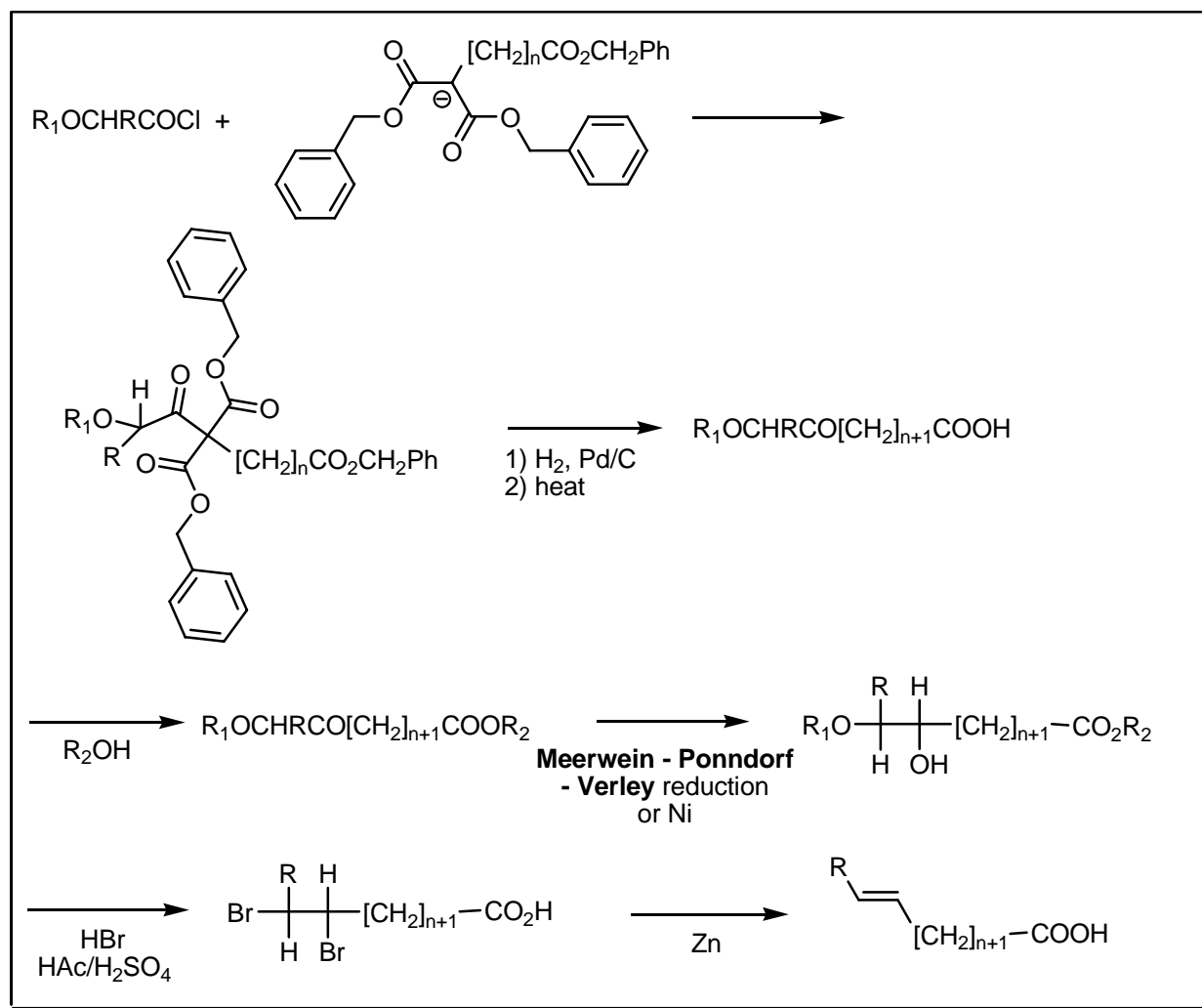
#### Fatty acids :



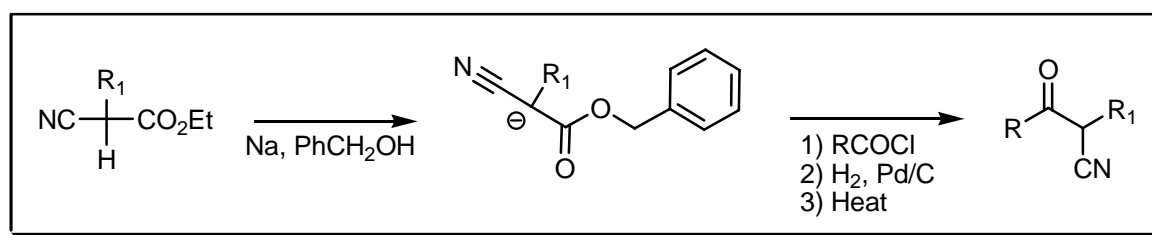
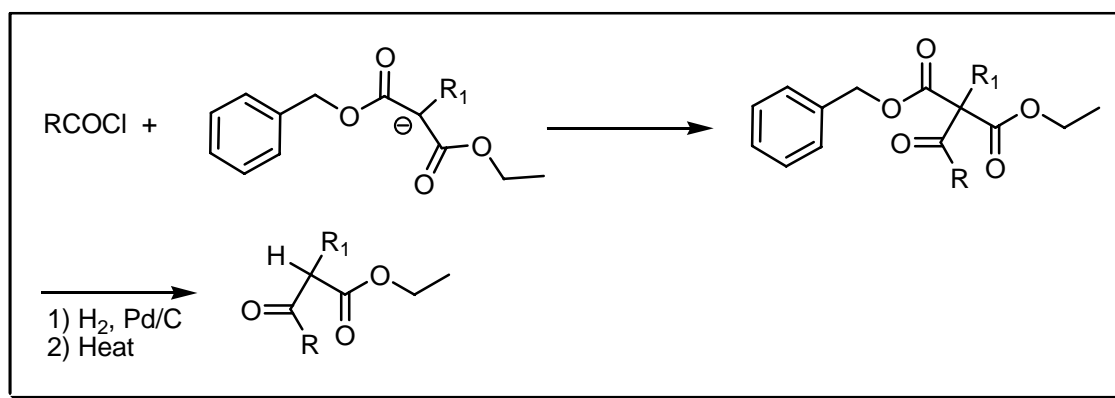




## Olefinic acids :



## $\beta$ -Keto esters and nitriles :



## NOTES :

The benzyl esters of acylmalonic acids undergo hydrogenolysis with the formation of the parent keto-acids, which readily lose two molecules of carbon dioxide to give the corresponding ketone. The reaction can be applied in numerous ways. See also **Baudart**, **Bowman**, **Fonken – Johnson**, **Kapp – Knoll** and **Robinson – Robinson** reactions.

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## REFERENCES :

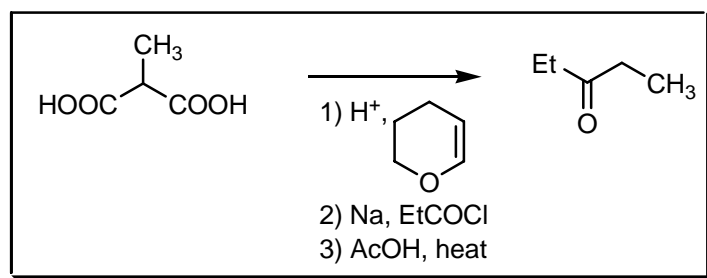
- 1) D.E. Ames; R.E. Bowman; R.G. Mason, *J. Chem. Soc.*, 1950, 174.
  - 2) R.E. Bowman, *J. Chem. Soc.*, 1950, 177.
  - 3) R.E. Bowman, *J. Chem. Soc.*, 1950, 322.
  - 4) R.E. Bowman, *J. Chem. Soc.*, 1950, 325.
  - 5) D.E. Ames; R.E. Bowman, *J. Chem. Soc.*, 1951, 1079.
  - 6) R.E. Bowman; W.D. Fordham, *J. Chem. Soc.*, 1951, 2758.
- 

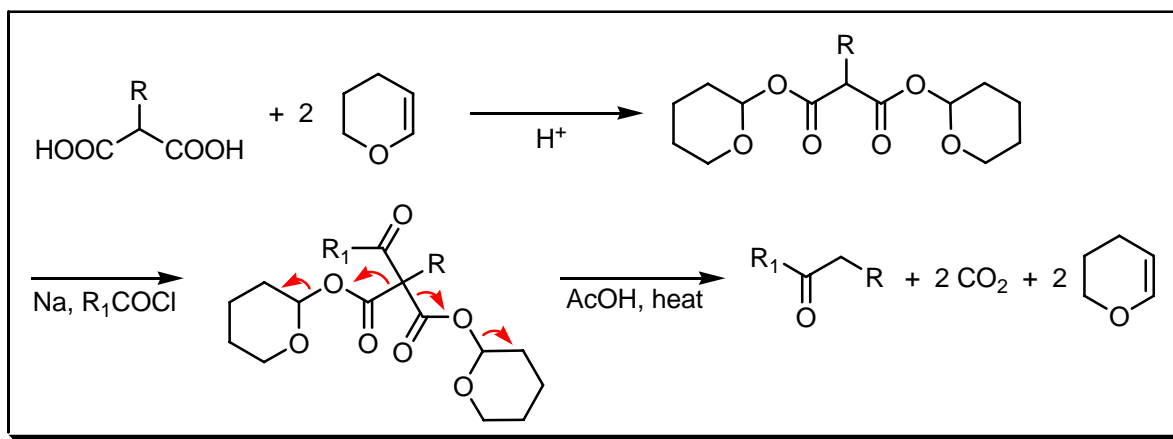
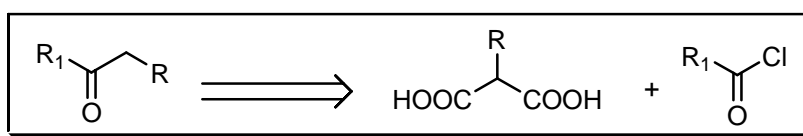
## COMMENTS :

## BOWMAN REACTION

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### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

This synthesis involves the reaction of dihydropyran with a substituted malonic acid in the presence of an acid catalyst to give a malonic diester, which is converted into the sodium-derivative, and treated with an acid chloride to yield a tetrahydropyran diester; all operations are conducted below  $40^\circ\text{C}$  in benzene. To produce the ketone, the reaction mixture is heated under reflux in the presence of a small amount of acetic acid, until no further evolution of carbon dioxide takes place. See also **Bowman** debenzylation reaction.

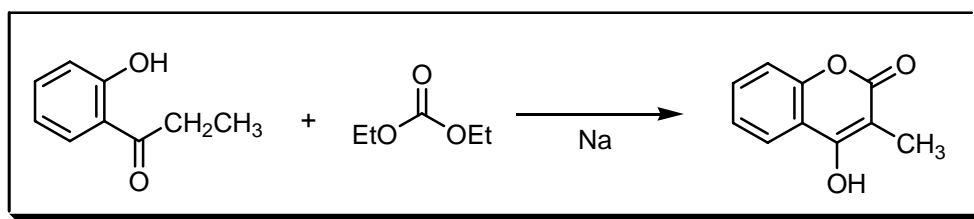
**REFERENCES :**

- 1) R.E. Bowman, *Nature*, 1948, **162**, 111.
- 2) R.E. Bowman; W.D. Fordham, *J. Chem. Soc.*, 1951, 2753.
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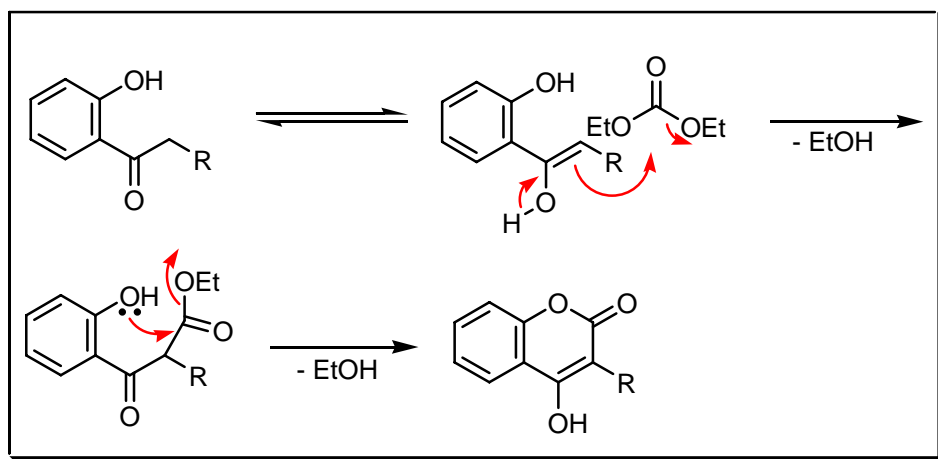
**COMMENTS :**

## BOYD – ROBINSON 4-HYDROXYCOUMARINS SYNTHESIS

### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This reaction involves the condensation of *o*-hydroxyacetophenones and their  $\omega$ -substituted derivatives with ethyl carbonate using sodium. See also **Anschütz** hydroxycoumarin, **Bargellini**, **Knoevenagel** coumarin, **Pauly – Lockemann, von Pechmann – Duisberg** and **Perkin** coumarin reactions.

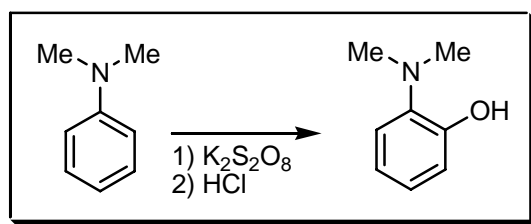
### REFERENCES :

J. Boyd; A. Robertson, *J. Chem. Soc.*, 1948, 174.

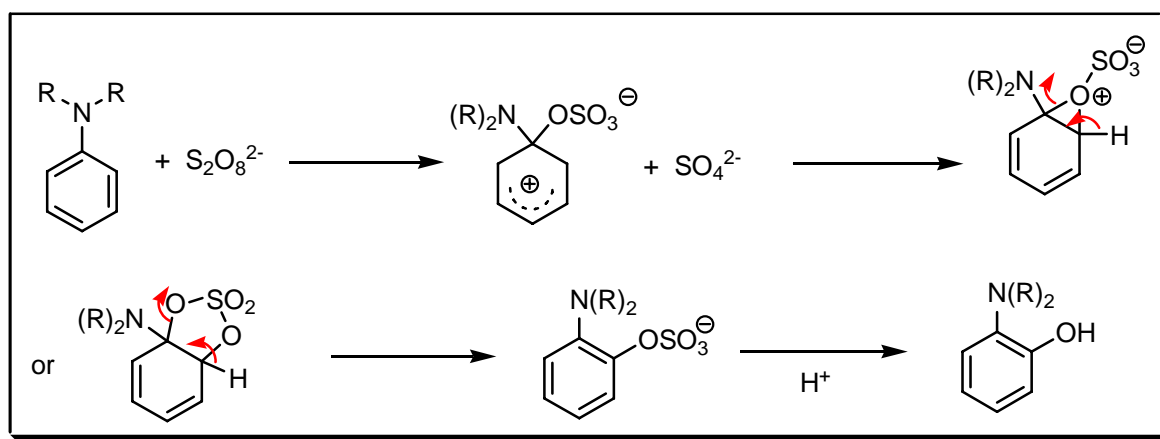
### COMMENTS :

## BOYLAND – SIMS *ORTHO*-HYDROXYANILINE SYNTHESIS

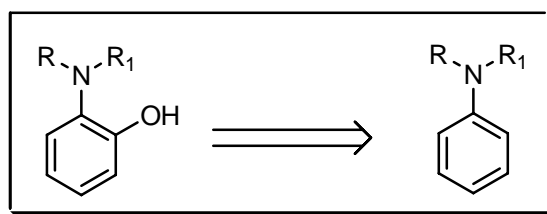
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The oxidation of anilines with persulfates *via* arylhydroxylamine-O-sulfonate to *ortho*-aminophenols and a substantial quantity of *para*-isomer by attack at the nitrogen atom followed by rearrangement to the product. The *ortho* product is favoured compared to the **Elbs** reaction where the *para* product is preferred. See also **Dakin** phenol aldehyde oxidation and **Elbs** reaction.

### REFERENCES :

March : 554

Smith – March : 724

Org. React. : 35, 421

- 1) E. Boyland; D. Manson; P. Sims, *J. Chem. Soc.*, 1953, 3623.
- 2) E. Boyland; P. Sims, *J. Chem. Soc.*, 1954, 980.
- 3) C. Walling; D.M. Camaioni; S.S. Kim, *J. Am. Chem. Soc.*, 1978, **100**, 4814.
- 4) C. Srinivasan; S. Perumal; N. Arumugami, *J. Chem. Soc., Perkin Trans. 2*, 1985, 1855.
- 5) J.E. Toth; J. Ray; W.J. Ehlhardt, *Bioorg. Med. Chem. Lett.*, 1992, **2**, 1013.
- 6) E.J. Behrman, *J. Org. Chem.*, 1992, **57**, 2266.

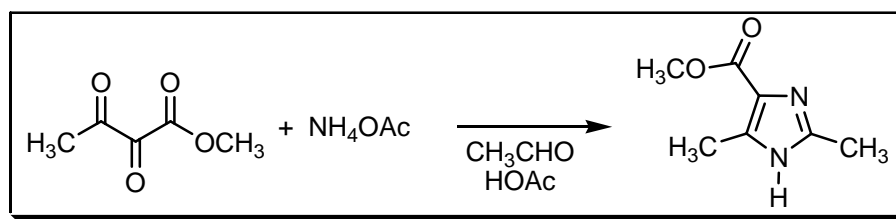
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**COMMENTS :**

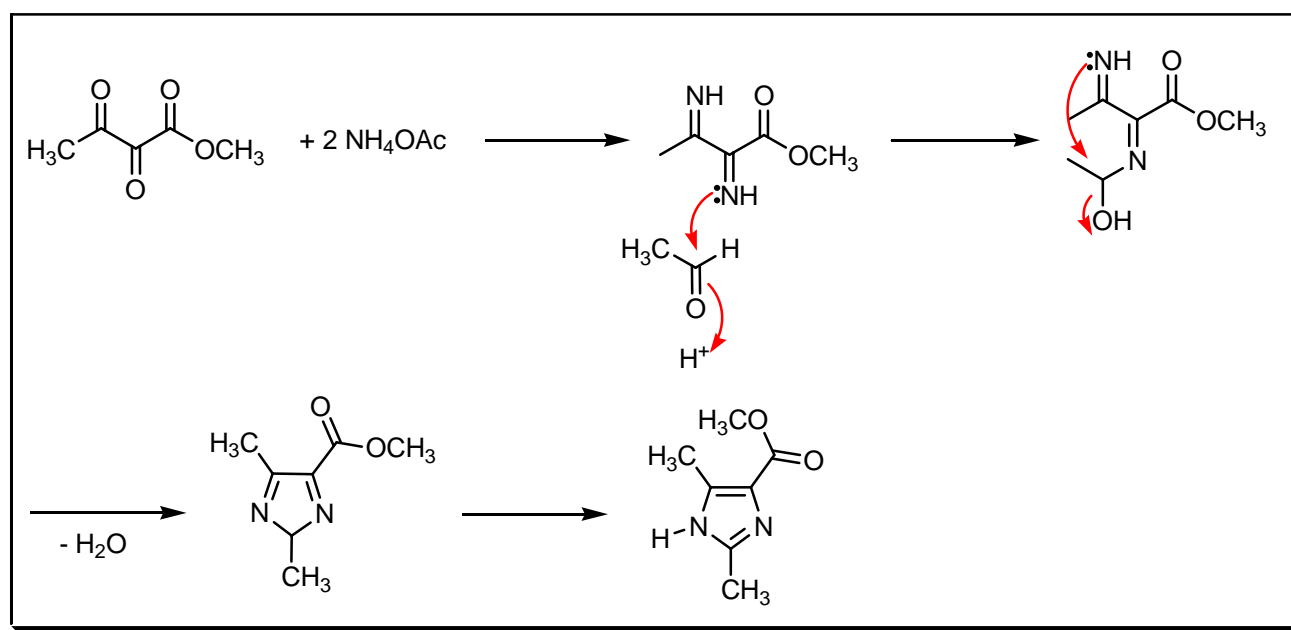
**BRACKEEN SYNTHESIS**

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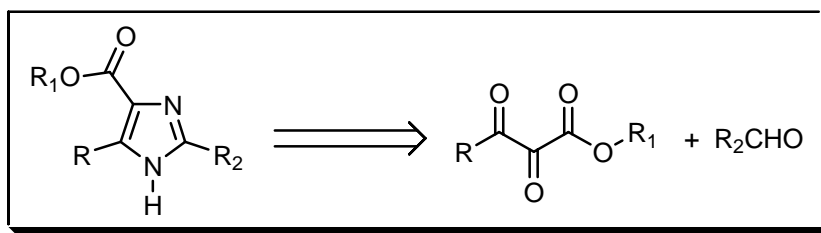
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

A versatile one-step imidazole synthesis employing *vicinal* tricarbonyl compounds. See also **Akabori – Neuberg – Fischer**, **Bredereck**, **Debus – Radziszewski**, **Maquenne**, **Wallach** imidazole and **Weidenhagen** reactions.

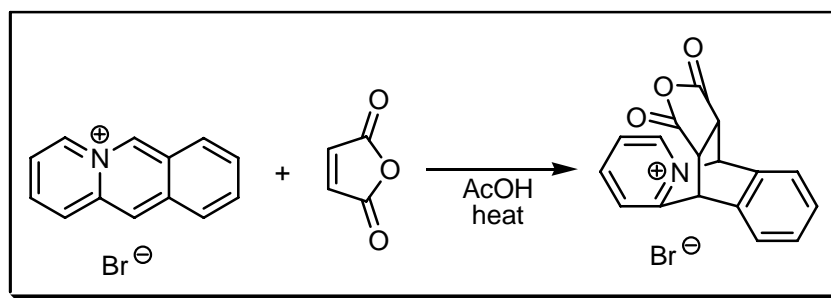
## REFERENCES :

M.F. Brackeen; J.A. Stafford; P.L. Feldman; D.S. Karanewsky, *Tetrahedron Lett.*, 1994, **35**, 1635.

## COMMENTS :

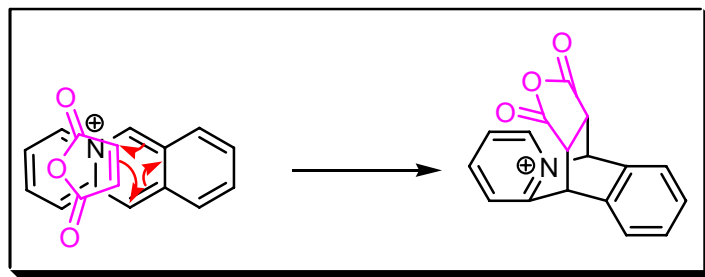
## BRADSHER CYCLOADDITION REACTION

### EXAMPLE :

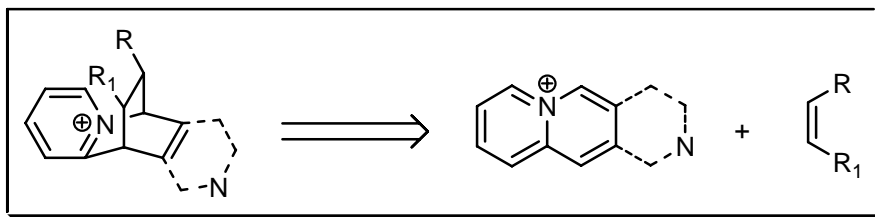




### MECHANISM :



### DISCONNECTION :



### NOTES :

The [4+2]-addition of a common dienophile with cationic aromatic aza-dienes such as acridizinium or isoquinolinium. See also **Diels – Alder** reaction.

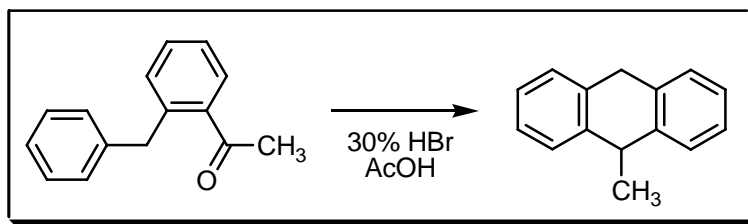
### REFERENCES :

- 1) C.K. Bradsher; T.W.G. Solomons, *J. Am. Chem. Soc.*, 1958, **80**, 933.
- 2) C.K. Bradsher; J.A. Stone, *J. Org. Chem.*, 1968, **33**, 519.
- 3) C.K. Bradsher; F.H. Day, *Tetrahedron Lett.*, 1971, **12**, 409.
- 4) T.-K. Chen; C.K. Bradsher, *J. Org. Chem.*, 1979, **44**, 4680.
- 5) S. Manna; J.R. Falk; C. Mioskowski, *J. Org. Chem.*, 1982, **47**, 5021.
- 6) R.B. Gupta; R.W. Franck; K.D. Onan; C.E. Soll, *J. Org. Chem.*, 1989, **54**, 1097.
- 7) T.E. Nicolas; R.W. Franck, *J. Org. Chem.*, 1995, **60**, 6904.
- 8) D. Urban; E. Duval; Y. Langlois, *Tetrahedron Lett.*, 2000, **41**, 9251.

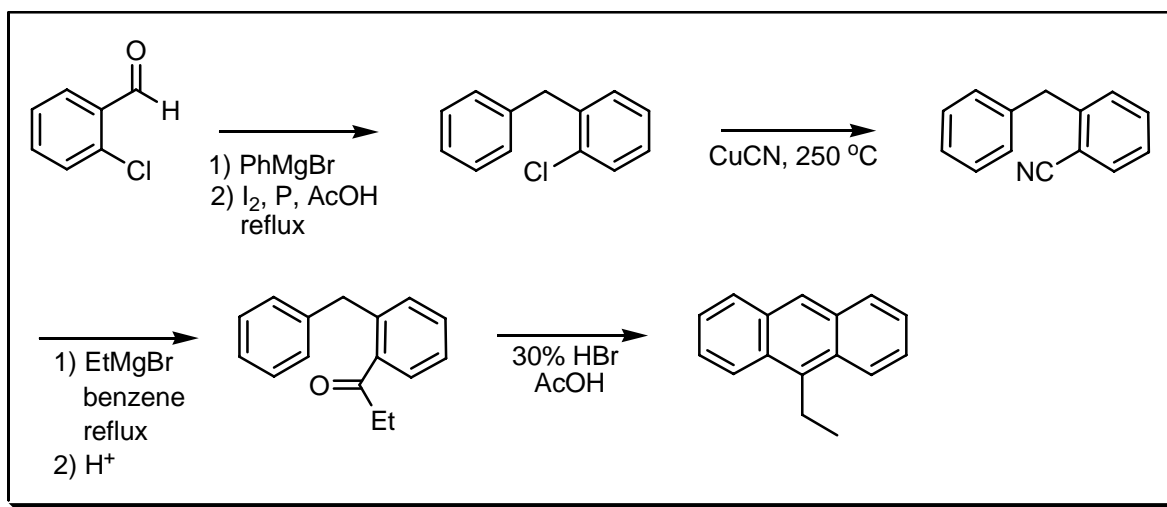
### COMMENTS :

## BRADSHER REACTION

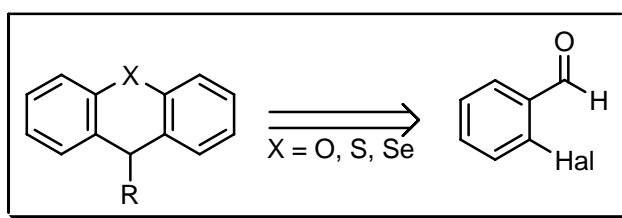
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The cyclo-condensation of diaryl ketones, which contain an arylmethylene group in the *ortho*-position, in the presence of acidic catalysts, afford condensed aromatic systems. See also **Bischler – Napieralski** reaction.

### REFERENCES :

Smith – March : 720

Smith : 1332

Smith 2<sup>nd</sup> : 1096, 1108

Houben – Weyl : E6a, 888

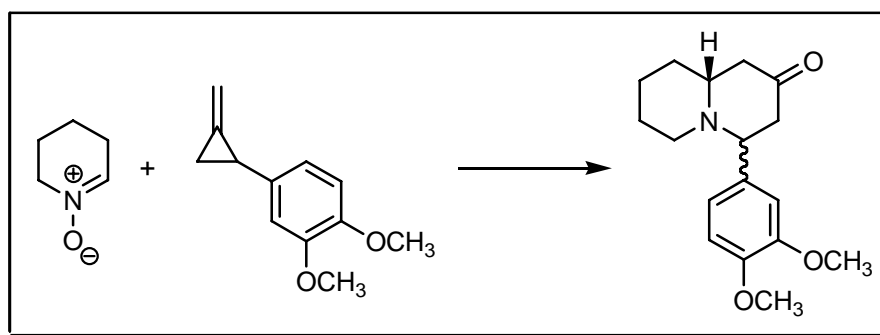
Science of Synthesis : 10, 239

- 1) C.K. Bradsher, *J. Am. Chem. Soc.*, 1940, **62**, 486.
- 2) C.K. Bradsher, *Chem. Rev.*, 1946, **38**, 447.
- 3) C.D. Saraf; F.A. Vingiello, *Synthesis*, 1970, 655.
- 4) J. Ashby; M. Ayad; O. Meth-Cohn, *J. Chem. Soc., Perkin Trans. 1*, 1973, 1104.
- 5) C.K. Bradsher, *Chem. Rev.*, 1987, **87**, 1277.
- 6) H. Sard, *J. Heterocycl. Chem.*, 1994, **31**, 1085.
- 7) E. Magnier; Y. Langlois, *Tetrahedron Lett.*, 1998, **39**, 837.

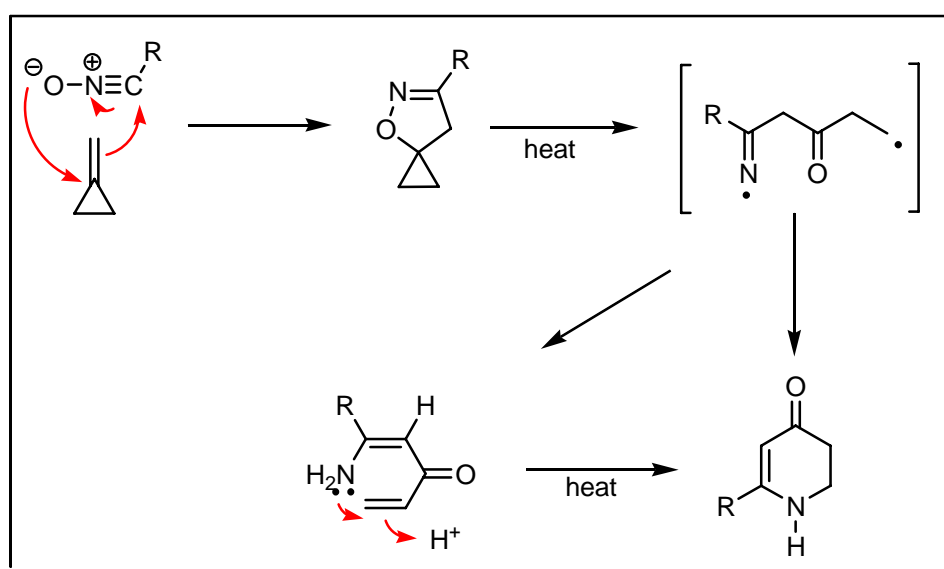
**COMMENTS :**

## BRANDI – GUARNA REARRANGEMENT

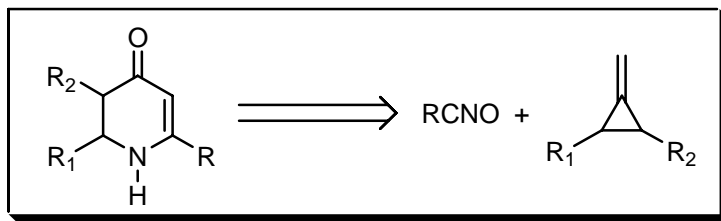
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

Isoxazoline-5-spiro cyclopropanes are prepared by cycloaddition of nitrile oxides with methylenecyclopropane. The rearrangement of these compounds affords 5,6-dihydro-4-pyridones.

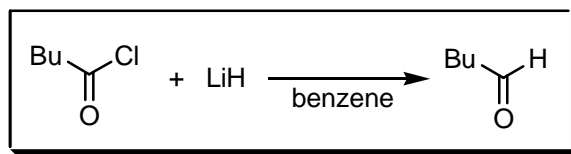
## REFERENCES :

- 1) A. Guarna; A. Brandi; A. Goti; F. De Sarlo, *J. Chem. Soc., Chem. Commun.*, 1985, 1518.
- 2) A. Guarna; A. Brandi; F. De Sarlo; A. Goti; F. Periccioli, *J. Org. Chem.*, 1988, **53**, 2426.
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- 4) A. Goti; B. Arichini; A. Brandi; S. Kozhushkov; C. Gratkowski; A. de Meijere, *J. Org. Chem.*, 1996, **61**, 1665.
- 5) C. Zorn; A. Goti; A. Brandi; K. Johnsen; S.I. Kozhushkov; A. de Meijere, *Chem. Commun.*, 1998, 903.
- 6) A. Goti; S. Cicchi; F.M. Cordero; V. Fedi; A. Brandi, *Molecules*, 1999, **4**, 1.

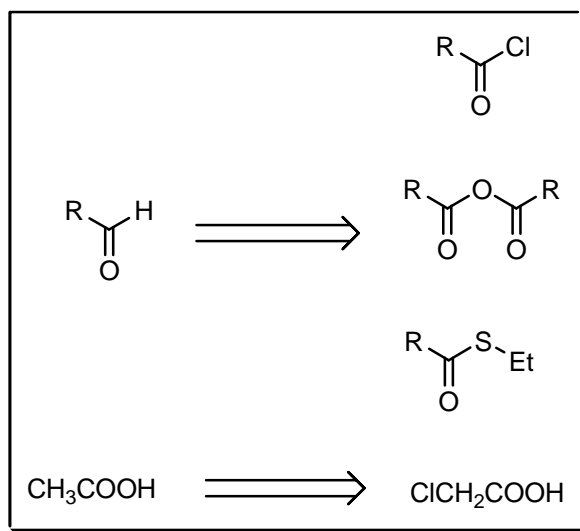
## COMMENTS :

## BRANDT ALDEHYDE SYNTHESIS

### EXAMPLE :



## DISCONNECTION :



## NOTES :

Lithium hydride heterogeneously reduces acyl halides to aldehydes. With aliphatic acid chlorides improved yields are obtained by forming the thiol ester which is then treated with lithium hydride. See also **Grundmann** and **Rosenmund** – **Saytzeff** reactions.

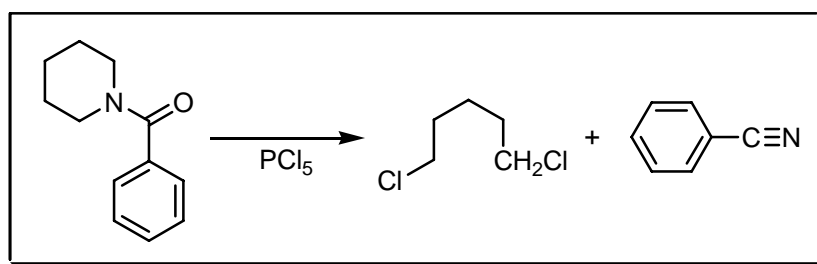
## REFERENCES :

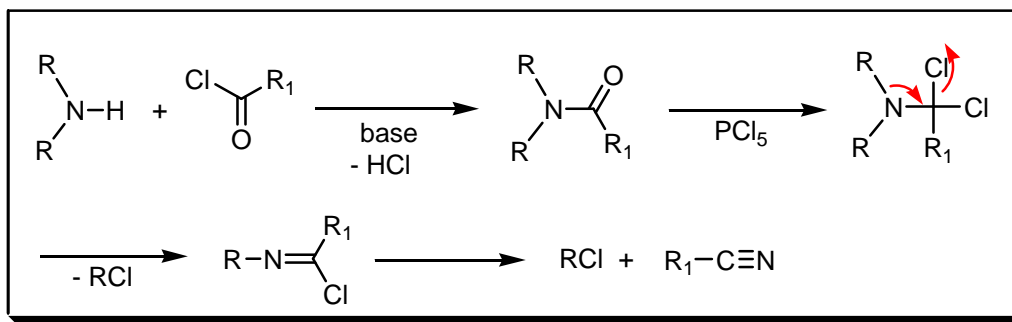
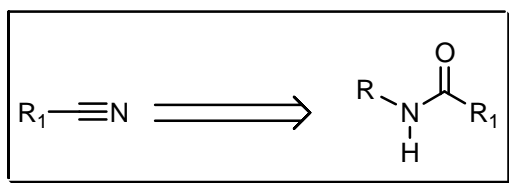
P. Brandt, *Acta Chem. Scand.*, 1949, **3**, 1050.

## COMMENTS :

## von BRAUN AMIDE DEGRADATION

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

A reaction in which phosphorous pentahalide converts primary and secondary non aromatic amines to their corresponding chloride or bromide. This method is also valuable for opening nitrogen containing rings. See also **Emde** and **Hofmann** degradation reactions.

**REFERENCES :**

**March** : 1042

**Smith – March** : 1350

**Houben – Weyl** : 5/3, 921; 5/4, 451

**Org. Synth.** : 9, 70; 10, 66; 25, 65; 29, 75; 37, 12

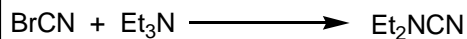
**Org. Synth. Coll. Vol.** : 1, 428; 2, 379; 3, 535, 646; 4, 166

- 1) H. von Pechmann, *Ber. Dtsch. Chem. Ges.*, 1900, **33**, 611.
- 2) J. von Braun, *Ber. Dtsch. Chem. Ges.*, 1904, **37**, 2678.
- 3) D.T. Mowry, *Chem. Rev.*, 1948, **42**, 189.
- 4) B.A. Philips; G. Fodor; J. Gal; F. Letourneau; J.J. Ryan, *Tetrahedron*, 1973, **29**, 3309.
- 5) R.B. Perni; G.W. Gribble, *Org. Prep. Proced. Int.*, 1983, **15**, 297.

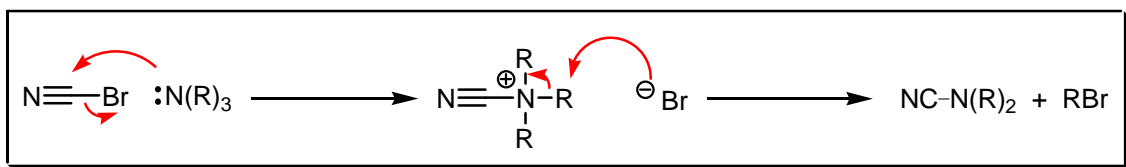
**COMMENTS :**

## VON BRAUN CYANOGEN BROMIDE REACTION

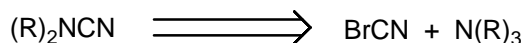
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Cyanogen bromide reacts with tertiary nitrogen compounds to break one carbon to nitrogen linkage. The cyano group becomes attached to the nitrogen to form a disubstituted cyanamide and the bromine atom to the carbon. Reactions with secondary amines afford lower yields.

### REFERENCES :

March : 436

Smith – March : 522

Houben – Weyl : 5/4, 151

Org. React : 7, 198

Org. Synth. : 27, 56

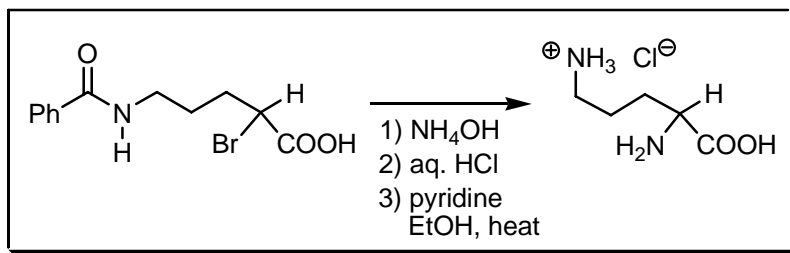
Org. Synth. Coll. Vol. : 3, 608

- 1) J. von Braun, *Ber. Dtsch. Chem. Ges.*, 1900, **33**, 1438.
- 2) H. Rapoport; C.H. Lovell; H.R. Reist; M.E. Warren, jr., *J. Am. Chem. Soc.*, 1967, **89**, 1942.
- 3) G. Fodor; S. Nagubandi, *Tetrahedron*, 1980, **36**, 1279.
- 4) J.H. Cooley; E.J. Evain, *Synthesis*, 1989, 1.
- 5) S. Laabs; A. Scherrmann; A. Sudau; M. Diederich; C. Kierig; U. Nubbemeyer, *Synlett*, 1999, 25.
- 6) S. Chambert; F. Thomasson; J.-L. Décout, *J. Org. Chem.*, 2002, **67**, 1898.

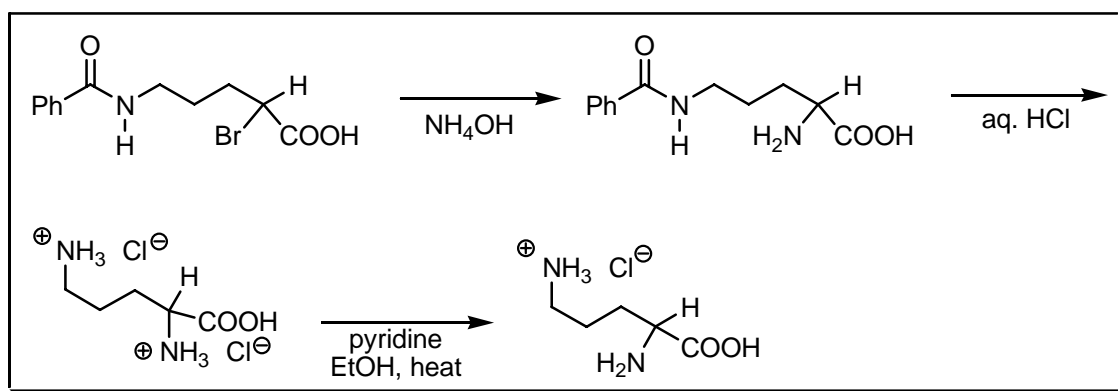
COMMENTS :

## von BRAUN AMINO ACID SYNTHESIS

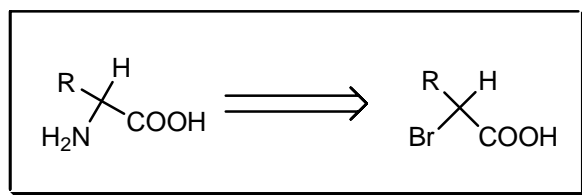
EXAMPLE :



MECHANISM :



DISCONNECTION :





## NOTES :

In the classic example 6-benzoylaminocaproic acid is converted by phosphorous and bromine through the  $\alpha$ -bromo acid (**Hell – Vollhard – Zelinsky reaction**). This acid is ammonolysed and hydrolysed to *d*-serine. The benzoylaminocaproic acid, which can be also be chlorinated with sulfuryl chloride in the presence of iodine, is obtained using a **von Braun amide degradation** reaction on benzoylpiperidine. The resulting *N*-(5-chloroamyl)benzamide is converted into the acid through the nitrile. See also **Erlenmeyer – Früstück** and **du Vigneaud** reactions.

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## REFERENCES :

**Org. Synth.** : **19**, 18, 61; **21**, 60

**Org. Synth. Coll. Vol.** : **2**, 74, 374; **3**, 495

- 
- 1) J. von Braun, *Ber. Dtsch. Chem. Ges.*, 1909, **42**, 839.
  - 2) J.C. Eck; C.S. Marvel, *J. Biol. Chem.*, 1934, **106**, 387.
  - 3) A. Galat, *J. Am. Chem. Soc.*, 1947, **69**, 86.
  - 4) H.E. Carter; C.L. Zirkle, *J. Biol. Chem.*, 1949, **178**, 709.
  - 5) H.W. Buston; J. Churchman; J. Bishop, *J. Biol. Chem.*, 1953, **204**, 665.
  - 6) R.K. Khare; J.M. Becker; F.R. Naider, *J. Med. Chem.*, 1988, **31**, 650.
  - 7) J. Xia; Y. Xia; I.A. Nnanna, *J. Agric. Food Chem.*, 1995, **43**, 867.

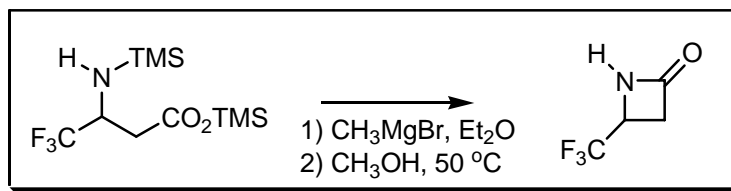
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## COMMENTS :

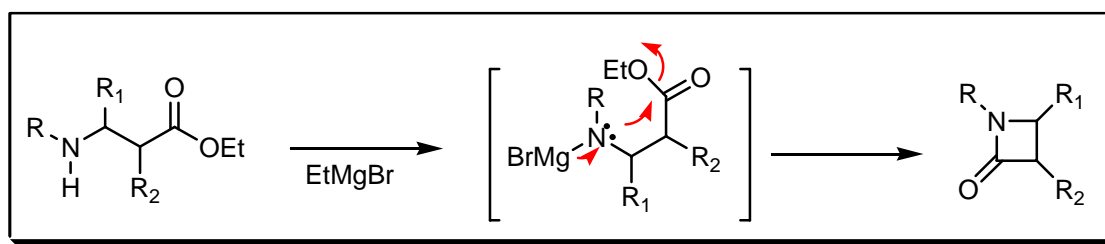
## BRECKPOT REACTION

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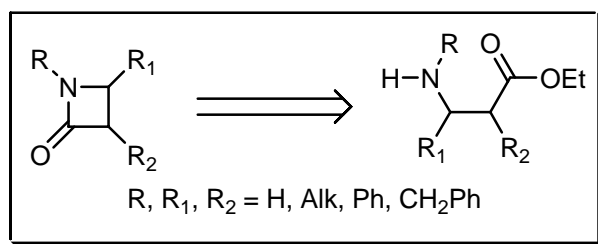
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The cyclisation of  $\beta$ -amino alcohols esters to substituted  $\beta$ -lactams with **Grignard** reagents as base.

### REFERENCES :

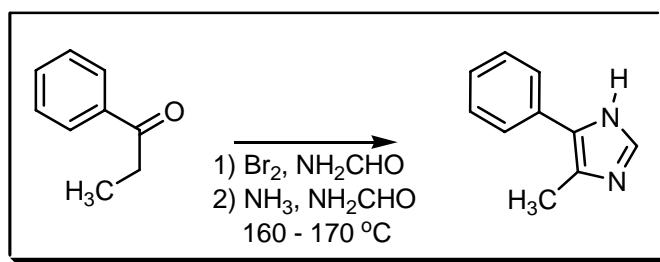
**Org. React.** : **9**, 388

- 1) R. Breckpot, *Bull. Soc. Chim. Belg.*, 1923, **32**, 412.
- 2) T. Shono; K. Tsubata; N. Okinaga, *J. Org. Chem.*, 1984, **49**, 1056.
- 3) P.T. Bevilacqua; D.D. Keith; J.L. Roberts, *J. Org. Chem.*, 1984, **49**, 1430.
- 4) O. Miyata; M. Namba; M. Ueda; T. Naito, *Org. Biomol. Chem.*, 2004, **2**, 1274.

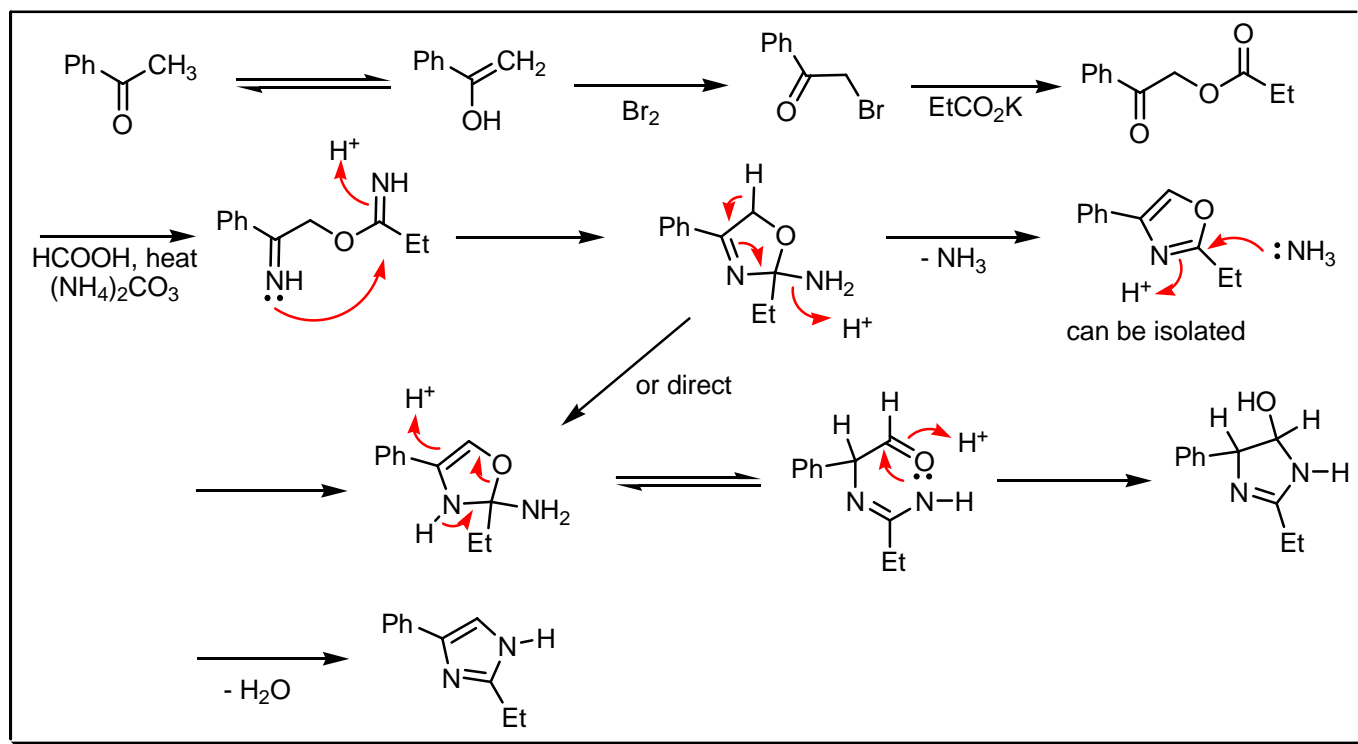
### COMMENTS :

## BREDERECK IMIDAZOLE SYNTHESIS

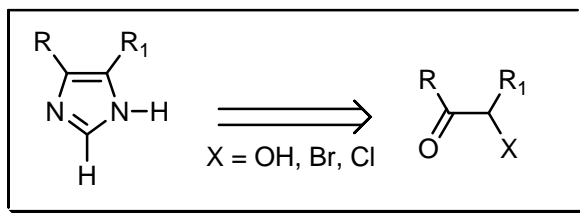
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The synthesis of imidazoles from formamide (acetamide) and  $\alpha$ -diketones,  $\alpha$ -ketols,  $\alpha$ -aminoketones,  $\alpha$ -oximinoketones. See also **Akabori – Neuberg – Fischer**, **Brackeen**, **Debus – Radziszewski**, **Maquenne**, **Wallach** imidazole and **Weidenhagen** reactions.

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## REFERENCES :

**Houben – Weyl** : 7/2c, 2239; 11/1, 659; **E8c**, 15, 48

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1) H. Bredereck; G. Theiling, *Chem. Ber.*, 1953, **86**, 88.

2) A. Novelli; A. de Santis, *Tetrahedron Lett.*, 1967, **8**, 265.

3) R. Paul; J.A. Brockman; W.A. Hallet; M.E. Tarrant; L.W. Torley; F.M. Callahan, *J. Med. Chem.*, 1985, **28**, 1704.

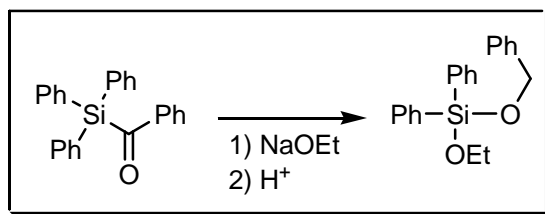
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## COMMENTS :

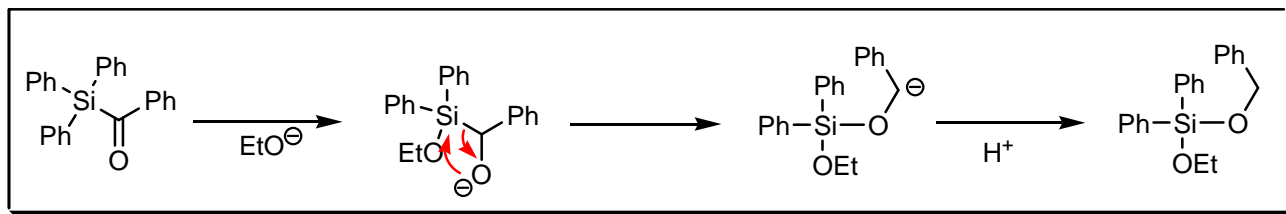
## BROOK SILAKETONE REARRANGEMENT

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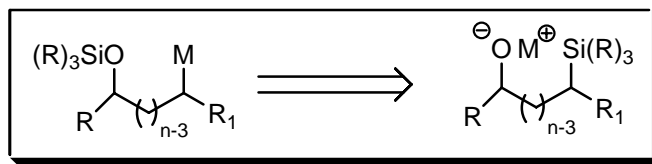
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The rearrangement of silaketones to silyl ethers with chirality transfer, comprising a family of [1,n]-carbon to oxygen silyl migrations. Aza-**Brook**, stanna-**Brook** and radical rearrangements are also known.

## REFERENCES :

Org. Synth. : **76**, 199

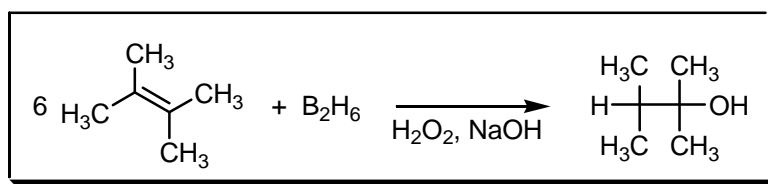
Org. Synth. Coll. Vol. : **10**, 2352

- 1) J.L. Speier, *J. Am. Chem. Soc.*, 1952, **74**, 1003.
- 2) A.G. Brook, *J. Am. Chem. Soc.*, 1958, **80**, 1886.
- 3) A.G. Brook; N.V. Schwartz, *J. Org. Chem.*, 1962, **27**, 2311.
- 4) A.G. Brook, *Acc. Chem. Res.*, 1974, **7**, 77.
- 5) T. Matsuda; S. Sato; M. Hattori; Y. Izumi, *Tetrahedron Lett.*, 1985, **26**, 3215.
- 6) P.C.B. Page; S.S. Klair; S. Rosenthal, *Chem. Soc. Rev.*, 1990, **19**, 147.
- 7) P. Janowski; P. Raubo; J. Wicha, *Synlett*, 1994, 985.
- 8) M.E. Jung; C.J. Nichols, *J. Org. Chem.*, 1996, **61**, 9065.
- 9) Y. Wang; M. Dolg, *Tetrahedron*, 1999, **55**, 12751.
- 10) M.D. Paredes; R. Alonso, *J. Org. Chem.*, 2000, **65**, 2292.
- 11) W.H. Moser, *Tetrahedron*, 2001, **57**, 2065.
- 12) K. Takeda; Y. Sawada; K. Sumi, *Org. Lett.*, 2002, **4**, 1031.
- 13) G. Liu; S.McN. Sieburth, *Org. Lett.*, 2003, **5**, 4677.
- 14) M.R. Paleo; M.I. Calaza; P. Graña; F.J. Sardina, *Org. Lett.*, 2004, **6**, 1061.

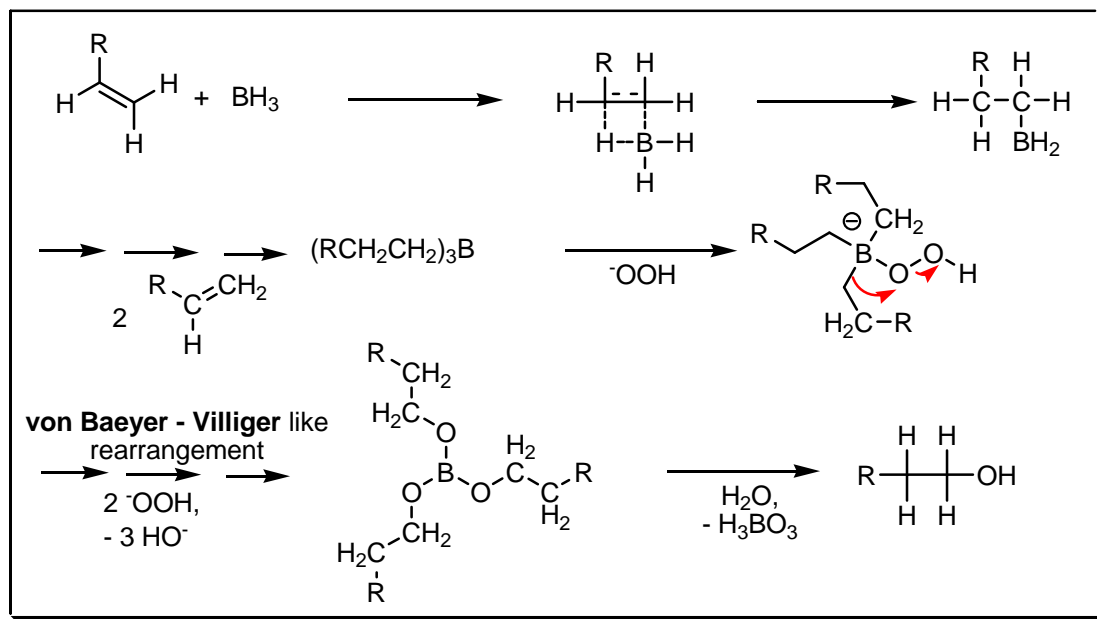
## COMMENTS :

## BROWN HYDROBORATION

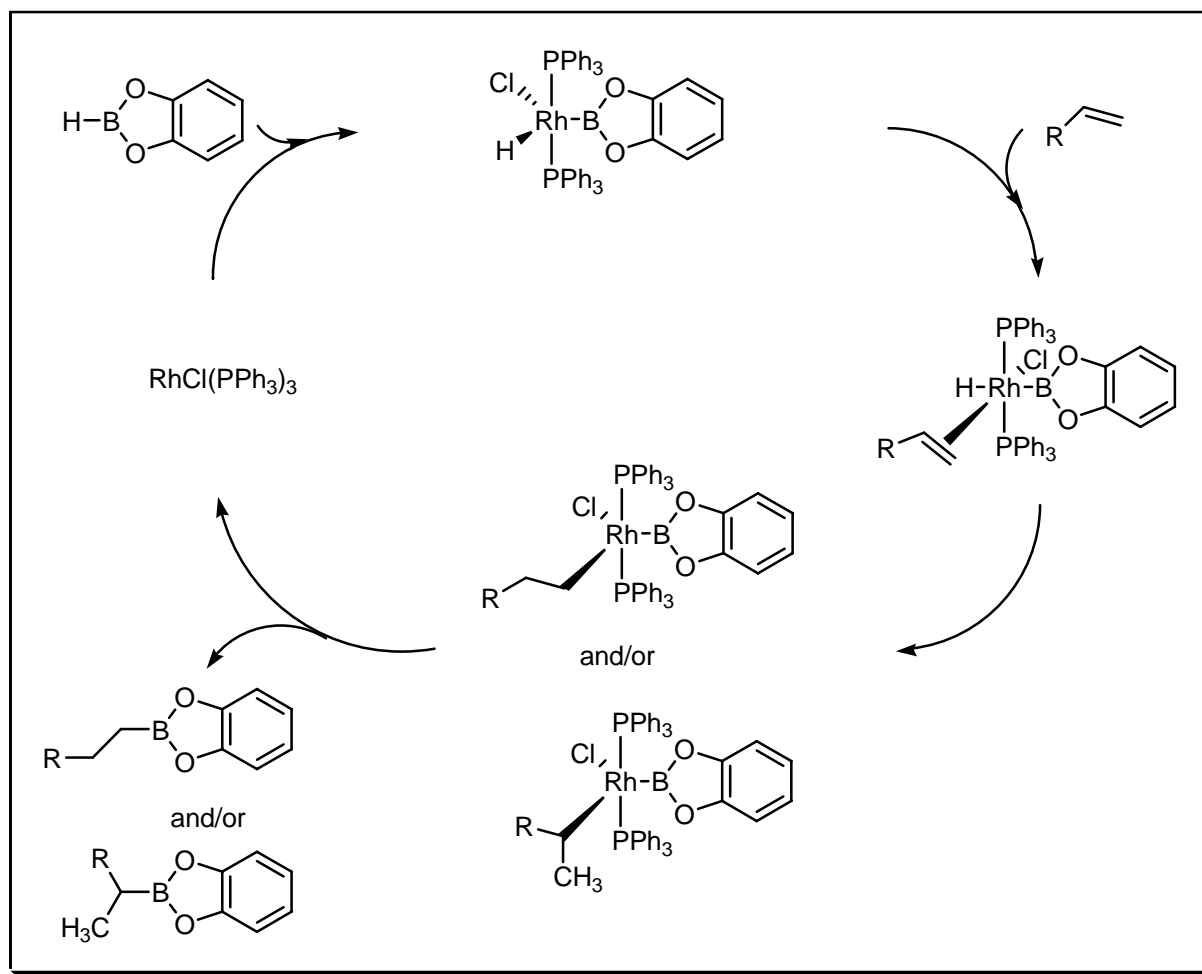
EXAMPLE :



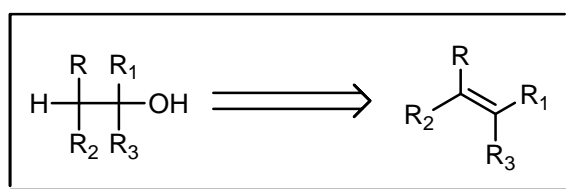
MECHANISM :



## Rhodium-catalysed hydroboration :



## DISCONNECTION :



## NOTES :

Hydroboration – regioselective and stereoselective (*syn*) addition of  $\text{BH}_3$  ( $\text{RBH}_2$ ,  $\text{R}_2\text{BH}$ ) complexes to olefins with one to four substituents. Synthesis of alcohols including optically active alcohols from olefins. See also **Bäckvall**, **Birnbaum – Simonini**, **Milas**, **Prévost** and **Woodward** *cis*-hydroxylation reactions.

## REFERENCES :

March : 783

Smith – March : 1012

Smith : 506

Smith 2<sup>nd</sup> : 442

Houben – Weyl : 13/3a; 13/3b; 13/3c

Org. React. : 13, 1

Org. Synth. : **50**, 88; **52**, 59; **53**, 77; **58**, 24; **61**, 103; **63**, 44, 57; **70**, 169; **73**, 116; **77**, 29, 176

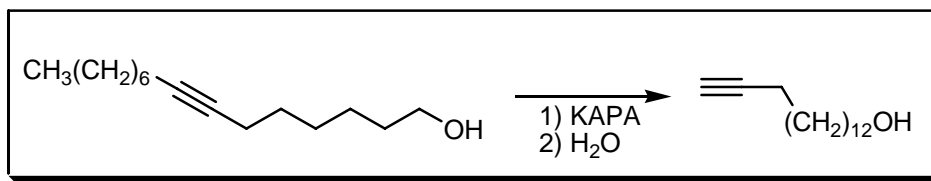
Org. Synth. Coll. Vol. : **6**, 137, 719, 852, 919; **7**, 339, 402, 427; **9**, 95, 522; **10**, 2366, 2380

- 1) H.C. Brown; B.C.S. Rao, *J. Am. Chem. Soc.*, 1956, **78**, 2582.
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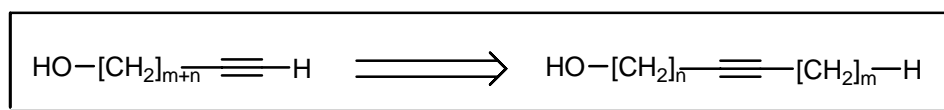
#### COMMENTS :

## BROWN REACTION

#### EXAMPLE :



#### DISCONNECTION :



#### NOTES :

The rapid isomerisation of internal acetylenes by potassium 3-aminopropylamide. The mechanism is not understood.



## REFERENCES :

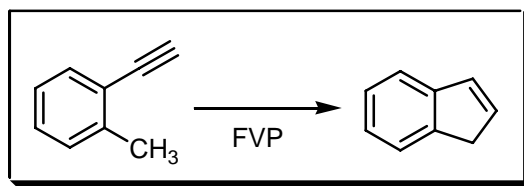
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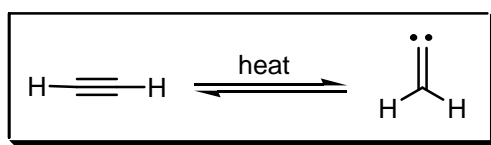
## COMMENTS :

## BROWN REARRANGEMENT

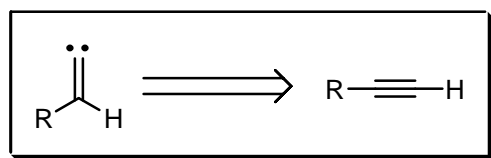
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This reaction interconverts alkynes and vinylidenes (1,2-shift) and plays an important role in diverse high-temperature chemistry.

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## REFERENCES :

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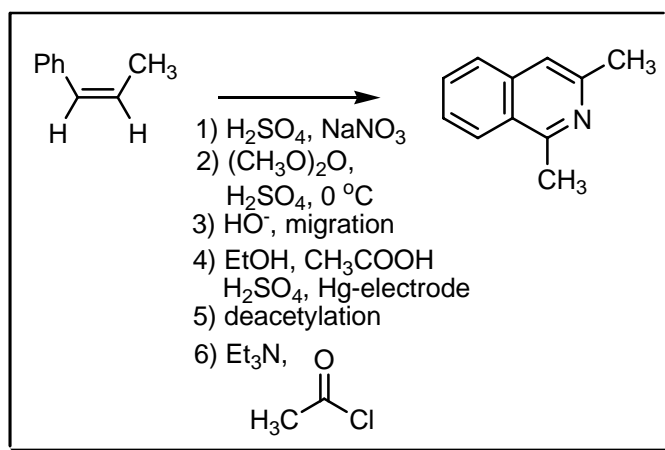
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**COMMENTS :**

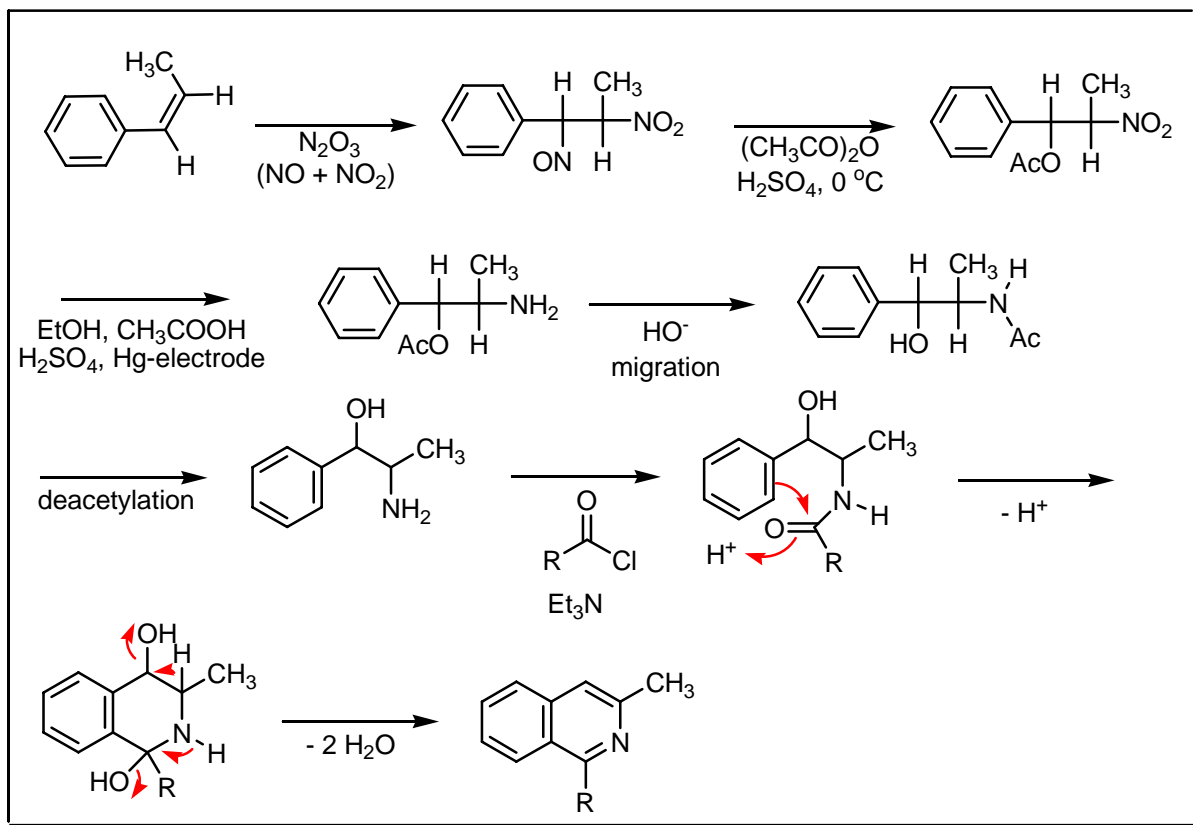
## BRUCKNER SYNTHESIS

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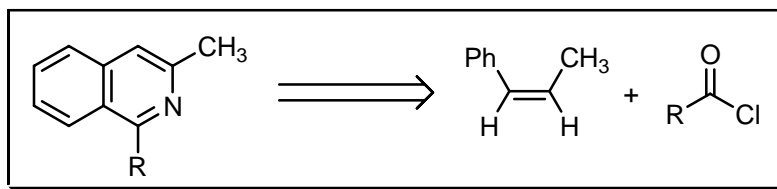
**EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

A 1-arylpropene is converted by dinitrogen trioxide into a  $\psi$ -nitrosite, which by acetylation yields a 1-aryl-2-nitropropyl acetate. This is reduced to the 2-amino compound. The addition of alkali causes an O to N migration of the acetyl group to give a 2-acetamido-1-aryl-propanol which is deacetylated, suitably acylated and cyclised by the **Pictet – Gams** method. The method has been extended to phenanthridines. See also **Bamberger – Goldschmidt**, **Bischler – Napieralski**, **Bobbit**, **Larock** indole, **Pictet – Gams**, **Pictet – Sprengler**, **Pomeranz – Fritsch**, **Simchen** and **Schlitter – Müller** ring-closure reactions.

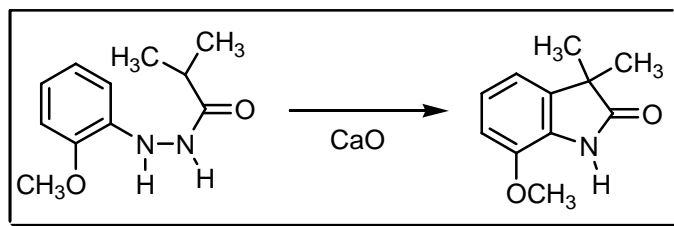
## REFERENCES :

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- 2) V. Bruckner; G. Fodor; J. Kiss; J. Kovács, *J. Chem. Soc.*, 1948, 885.
- 3) T.R. Givindachari; K. Nagarajan; B.R. Pai; N. Arumugan, *J. Chem. Soc.*, 1956, 4280.

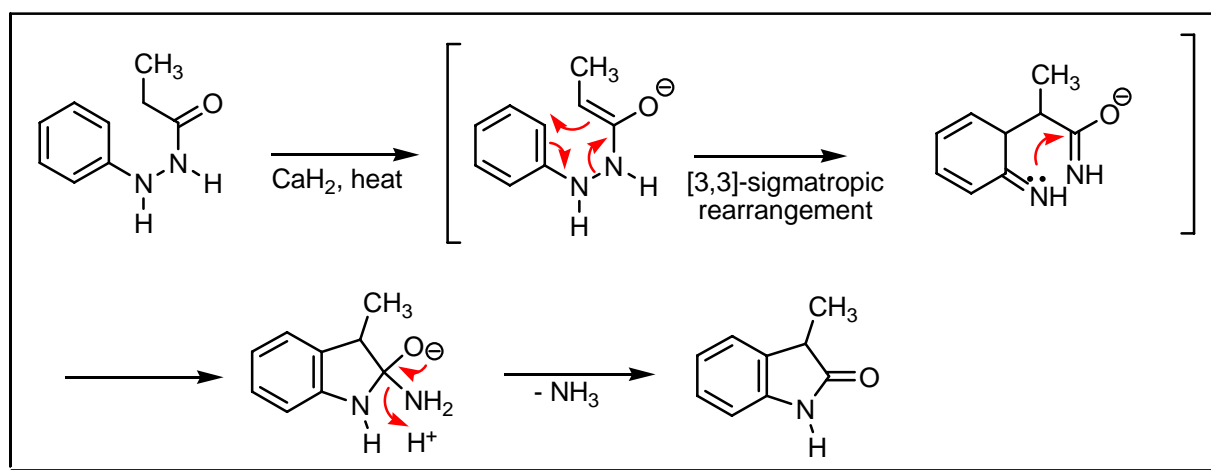
COMMENTS :

## BRUNNER OXINDOLE RING-CLOSURE

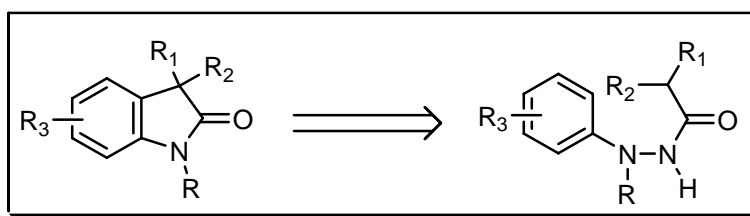
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

Acylphenylhydrazines when heated with alkaline reagents undergo a [3,3]-sigmatropic rearrangement followed by elimination of ammonia to give oxindoles. See also **von Baeyer** oxindole, **Brunner**, **Gassman** oxindole, **Hinsberg** oxindole, **Martinet**, **Neber – Bosset** and **Stollé** reactions.

## REFERENCES :

Org. Synth. : **37**, 60

Org. Synth. Coll. Vol. : **4**, 657

Science of Synthesis : **10**, 604

1) K. Brunner, *Monatsh. Chem.*, 1896, **17**, 267.

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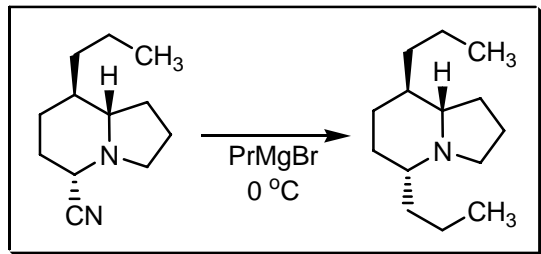
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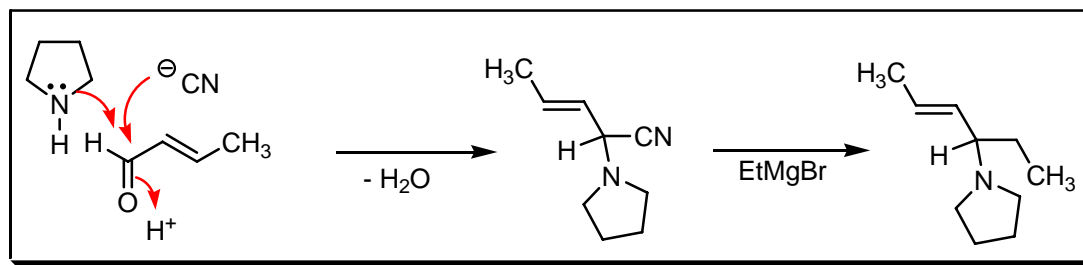
## COMMENTS :

## BRUYLANTS AMINATION

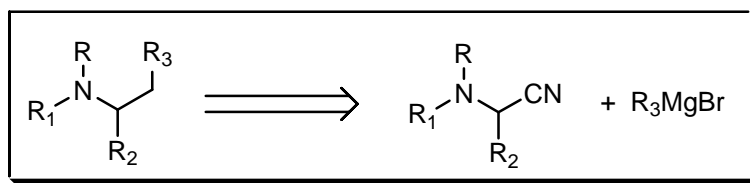
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The reaction of  $\alpha$ -amino nitriles with a **Grignard** reagent to prepare  $\alpha$ -substituted amines.

## REFERENCES :

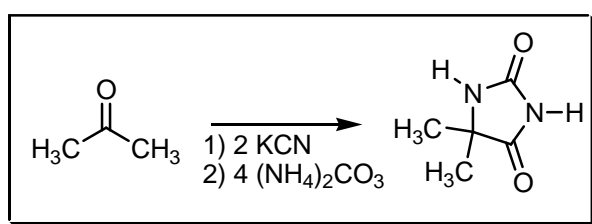
Houben – Weyl : E16d, 1112

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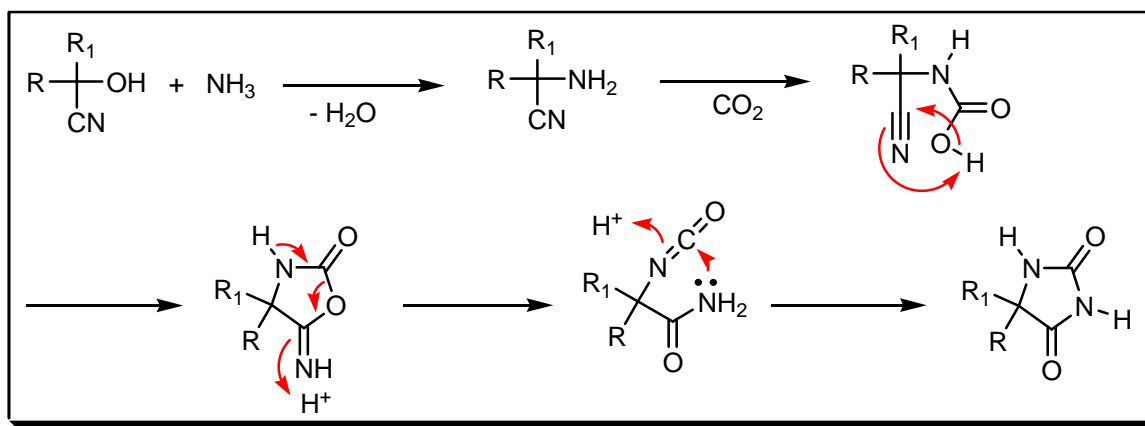
## COMMENTS :

## BUCHERER – BERGS REACTION

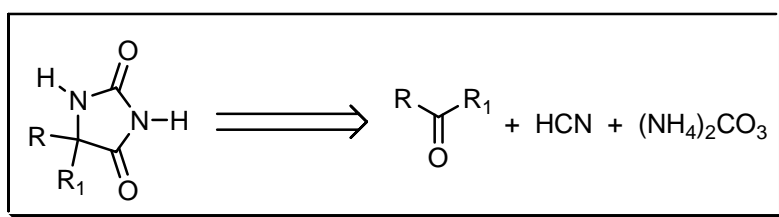
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of 5-substituted hydantoins by the interaction of an aldehyde or ketone, hydrogen cyanide and ammonium carbonate, or of the cyanohydrin and ammonium carbonate, or of the  $\alpha$ -aminonitrile and ammonium carbonate or carbon dioxide. The ketone, potassium cyanide and ammonium carbonate in alcoholic solution may also be used. See also **Corey – Link**, **Strecker** amino acid, **Tiemann**, **Ultee**, **Urech** and **Zelinsky – Stadnikoff** reactions.

## REFERENCES :

Houben – Weyl : 11/2, 305, 371

Org. Synth. : 20, 42

Org. Synth. Coll. Vol. : 3, 323

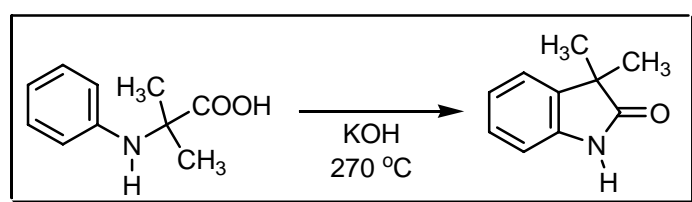
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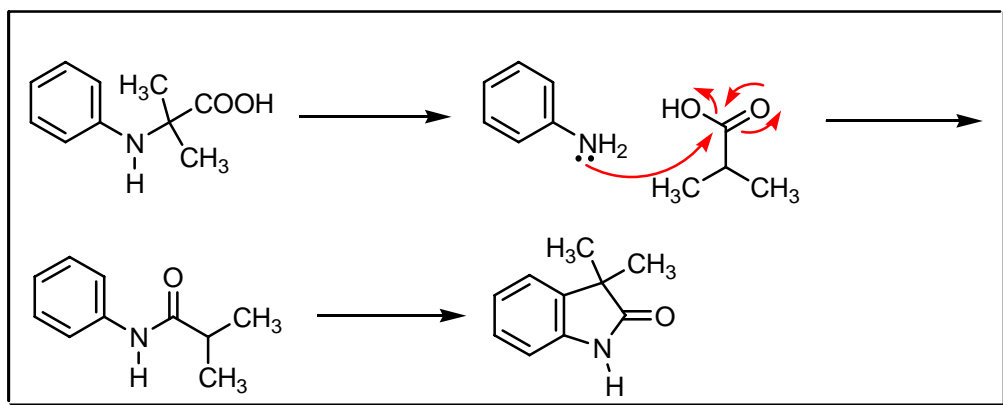
COMMENTS :

## BUCHERER – GROLÉE SYNTHESIS

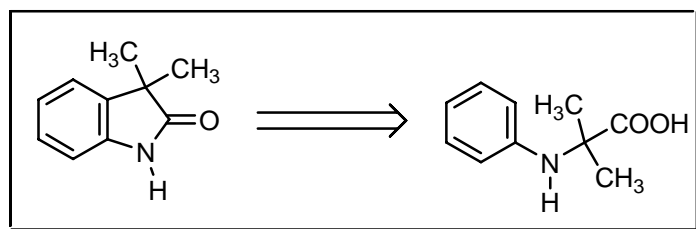
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

This synthesis is typified by the treatment of anilino-isobutyric acid (formed by hydrolysis of the product obtained by the action of aniline on acetone cyanohydrin) with sodium ethoxide or potassium hydroxide at 270 – 320 °C. The



product is 3,3-dimethyloxindole, formed by fission of the nitrogen carbon bond. See also **von Baeyer** oxindole, **Brunner**, **Gassman** oxindole, **Hinsberg** oxindole, **Martinet**, **Neber – Bosset** and **Stollé** reactions.

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#### REFERENCES :

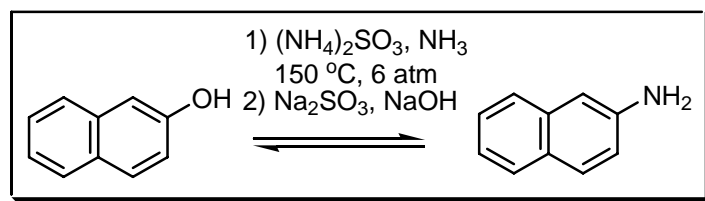
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#### COMMENTS :

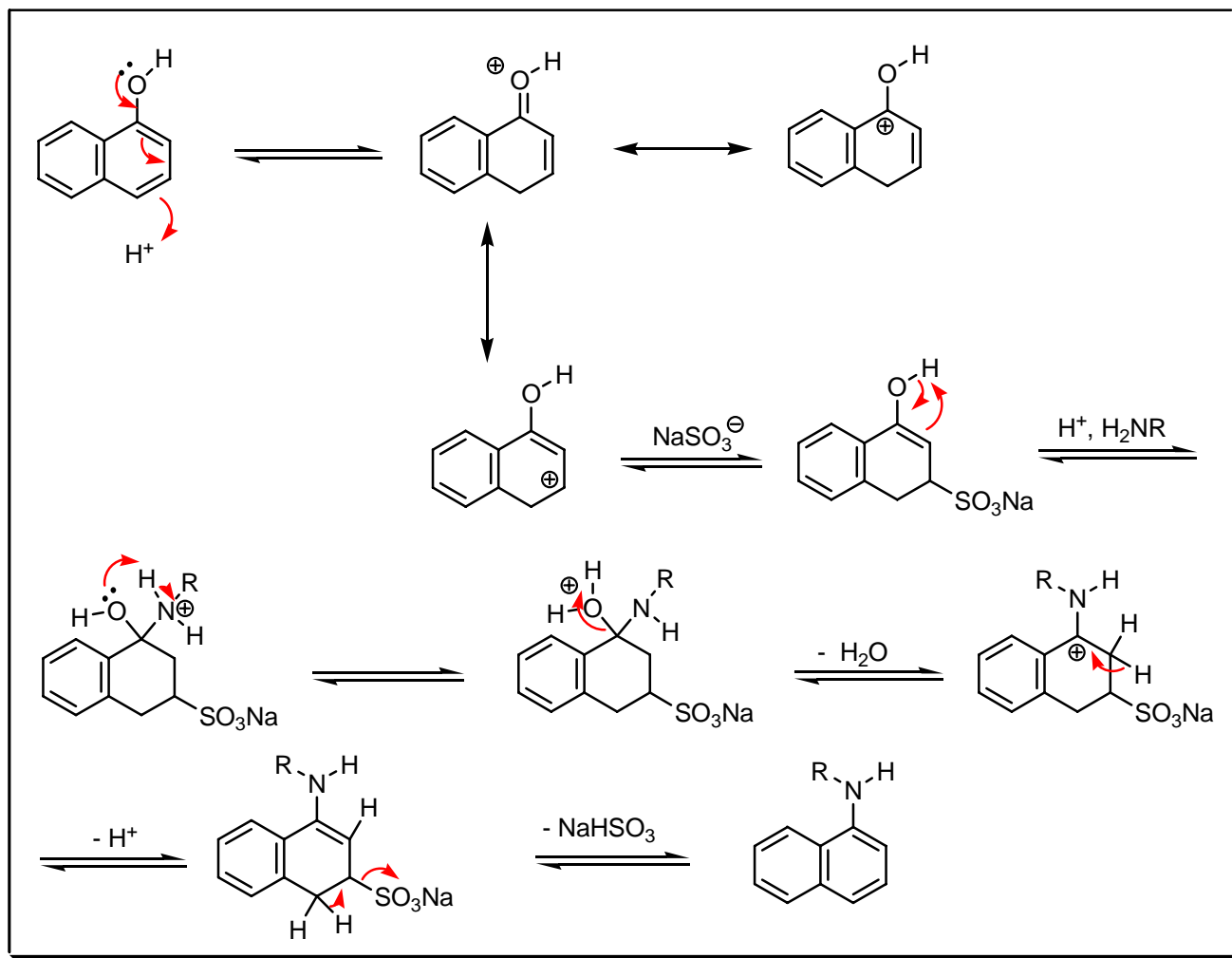
### BUCHERER – LE PETIT REACTION

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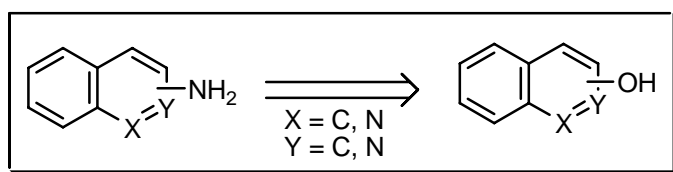
#### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The reversible conversion of a naphthylamine (also quinoline and isoquinoline) into a naphthol by an aqueous solution of a sulfite or a hydrogen sulfite. See also **Bucherer** carbazole synthesis.

## REFERENCES :

Houben – Weyl : 11/1, 143

Org. React. : 1, 105

Org. Synth. : 22, 19

Org. Synth. Coll. Vol. : 3, 78

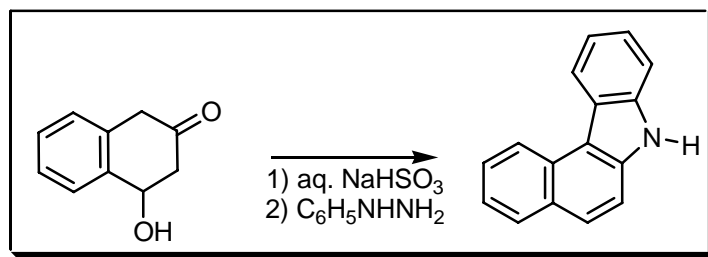
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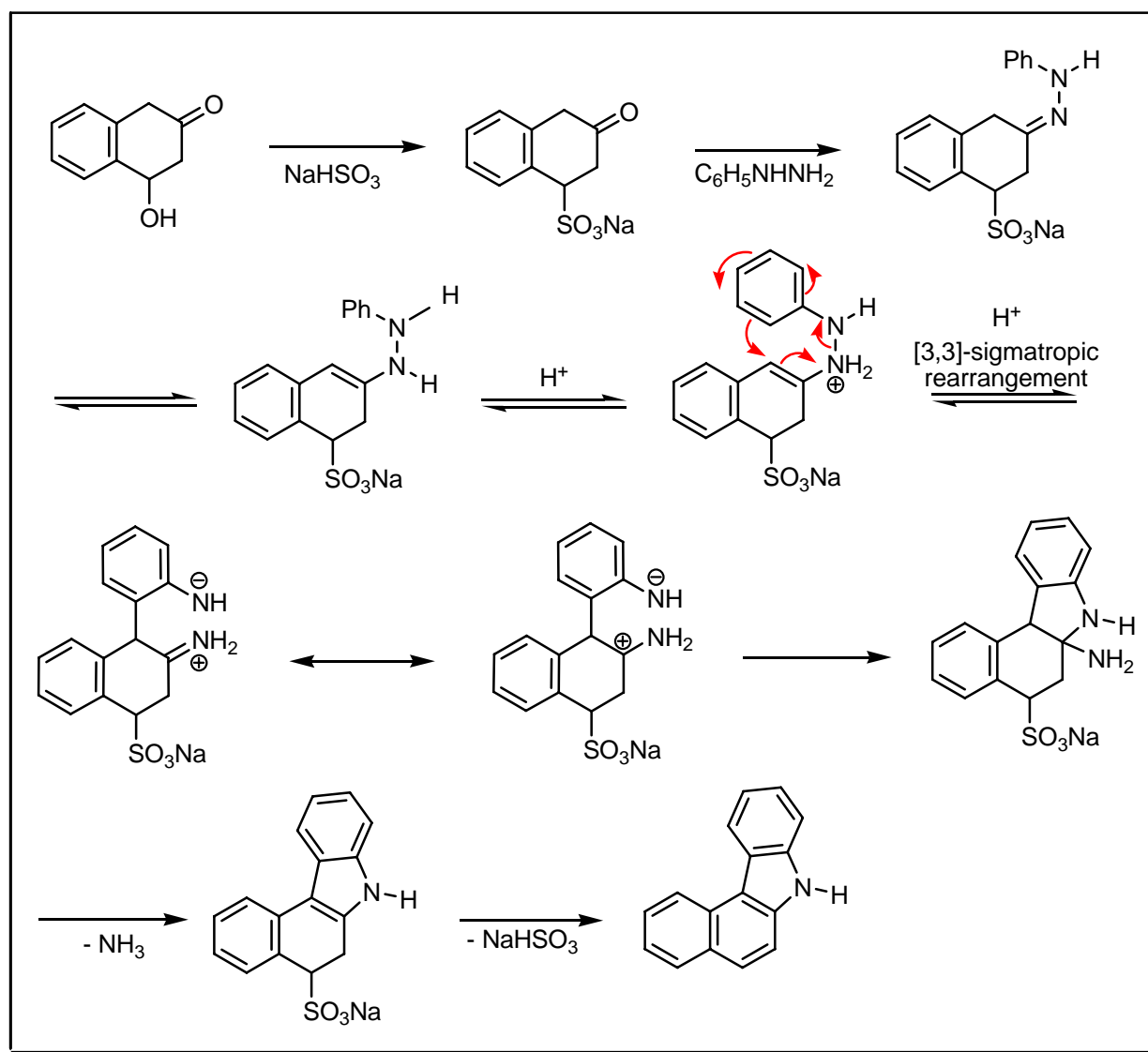
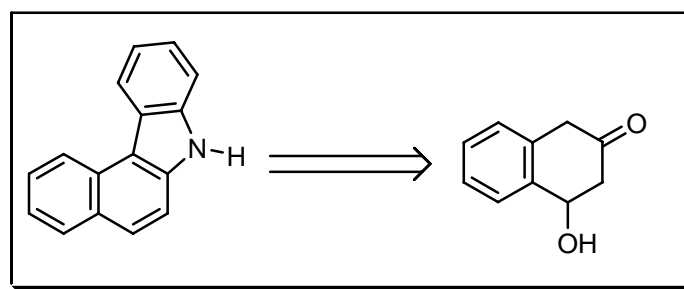
**COMMENTS :**

## BUCHERER CARBAZOLE SYNTHESIS

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**EXAMPLE :**



**MECHANISM :****DISCONNECTION :****NOTES :**

$\alpha$ -Naphthols yield 1,2-benzocarbazole derivatives when treated with phenylhydrazine and aqueous sodium bisulfite. With  $\beta$ -naphthols and naphthylamines dihydrocarbazole sulfonates will be formed from which 3,4-benzocarbazoles are obtained. See also **Borsche – Drechsel** and **Bucherer – Le Petit** reactions.

## REFERENCES :

Houben – Weyl : **10/2**, 250; **E6a**, 944

Org. React. : **1**, 105

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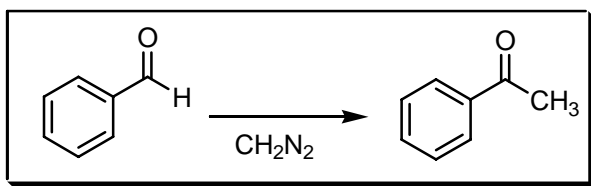
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## COMMENTS :

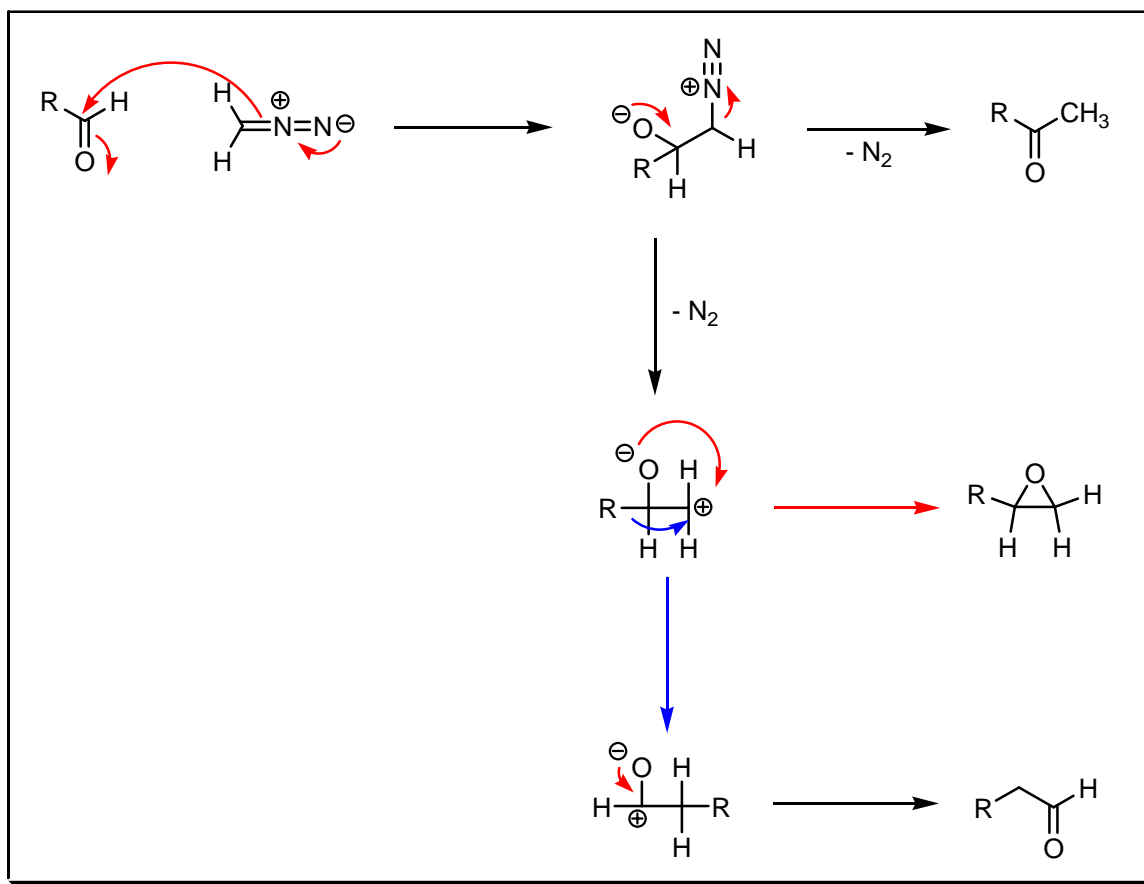
## BÜCHNER – CURTIUS – SCHLOTTERBECK REACTION

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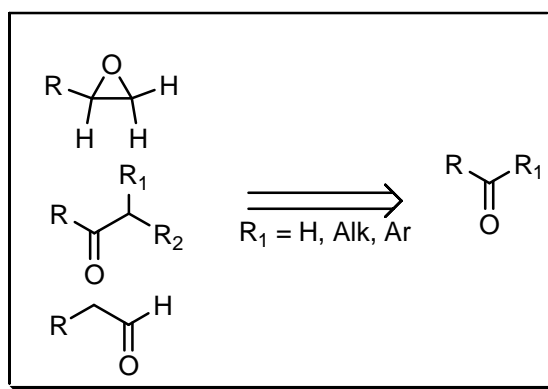
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The interaction of an aldehyde with diazo-compounds yields products which lose nitrogen to give ketonic derivatives. An epoxide (if  $R$  has a strong positive character) or a homologue of the initial aldehyde can also be formed. Ketones react in a similar fashion. See also **Arndt – Eistert**, **Clibbens – Nierenstein**, **Corey – Chaykovsky**, **Jacobsen – Katsuki**, **Juliá – Colonna**, **Katsuki – Sharpless**, **Mukaiyama – Yamada**, **Prileschajew**, **Shi**, **Weitz – Scheffer** and **Wolff** reactions.

## REFERENCES :

Houben – Weyl : E6b, 1163

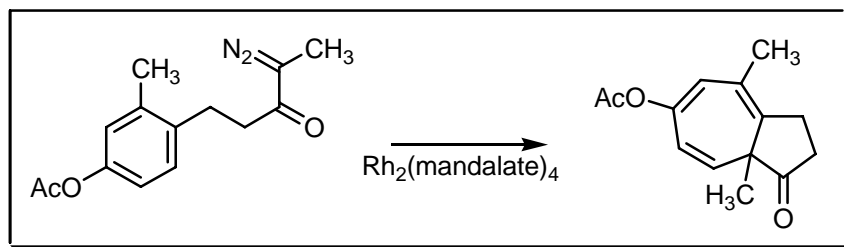
Org. React. : 8, 364

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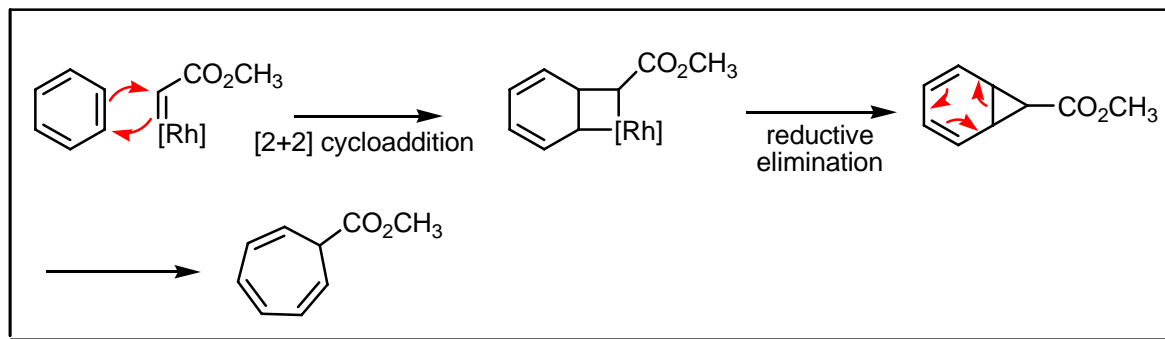
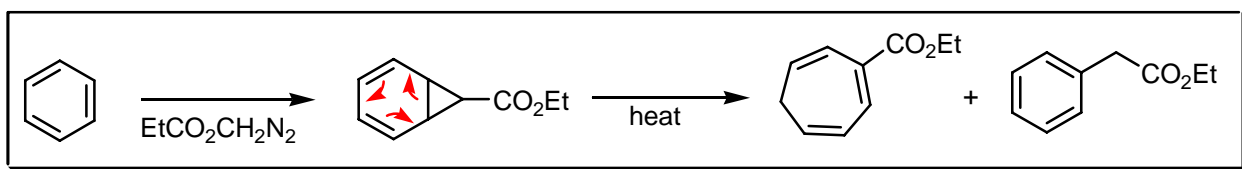
## COMMENTS :

## BÜCHNER METHOD OF RING ENLARGEMENT

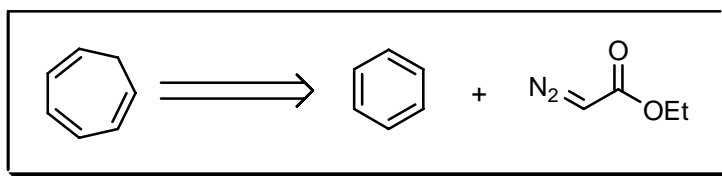
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Aromatic hydrocarbons react with ethyl diazoacetate to yield, among other products, derivatives of cycloheptatriene. This method has been applied to the synthesis of the tropolone and azulene ring systems. Other olefinic bonds also react. The use of rhodium carboxylates is to increase the selectivity of the *intramolecular* C-H insertion. There are two possible ways for the first step. The one involving the metallocyclobutane is shown here. The other way involves a metal-stabilised carbocation where the  $\alpha$ -carbon is the electrophilic centre. See also **St. Pfau – Plattner** reaction.

## REFERENCES :

**Org. React. : 18, 217**

- 1) E. Büchner, *Ber. Dtsch. Chem. Ges.*, 1888, **21**, 2637.
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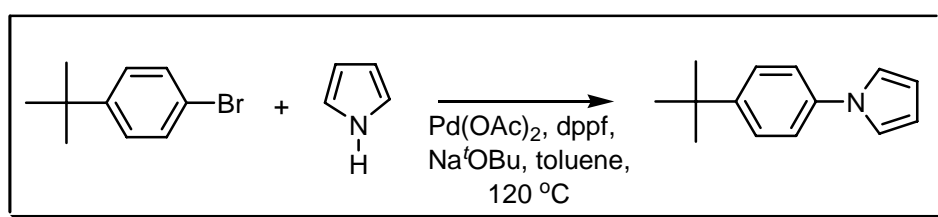
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**COMMENTS :**

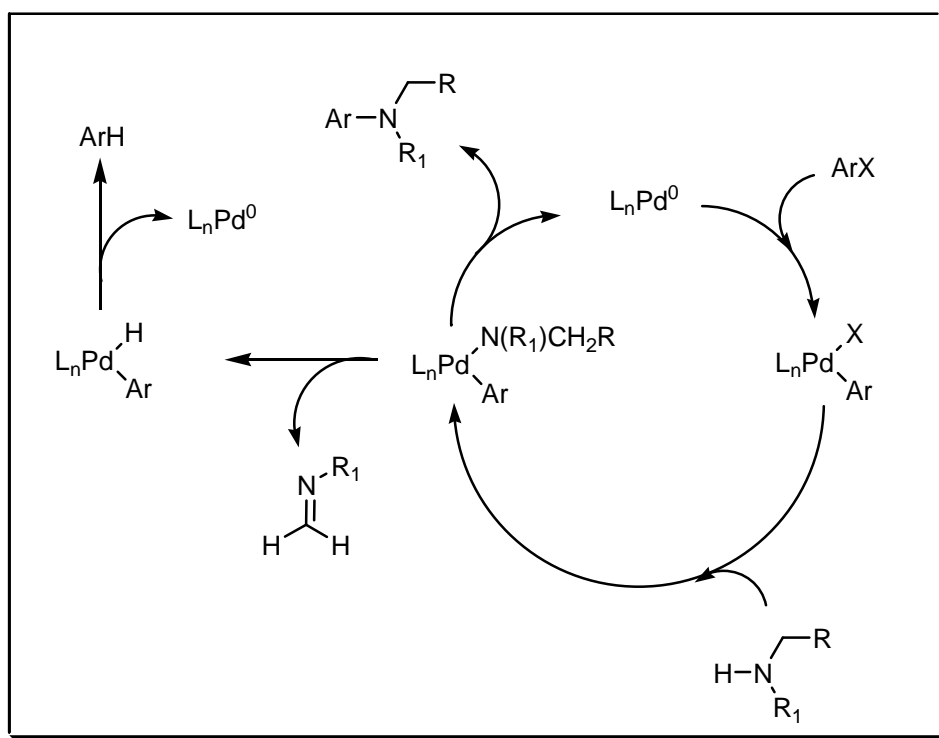
## BUCHWALD – HARTWIG REACTION

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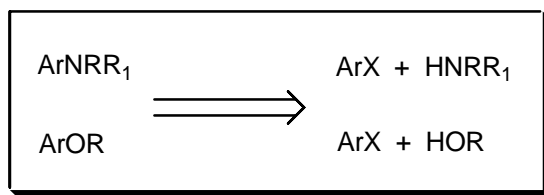
**EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

This is the direct palladium-catalysed C-N or C-O bond formation of aryl halides with amines in the presence of stoichiometric amount of base. The base should not bear any  $\beta$ -hydrogens. The palladium catalyst is usually complexed with chelating phosphine type ligands.

## REFERENCES :

Org. Synth. : 78, 23

Org. Synth. Coll. Vol. : 10, 2606

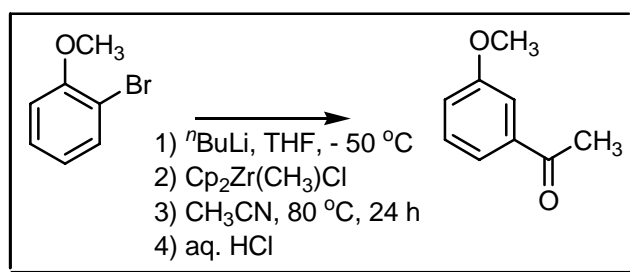
- 1) M. Kosugi; M. Kameyama; T. Migata, *Chem. Lett.*, 1983, 927.
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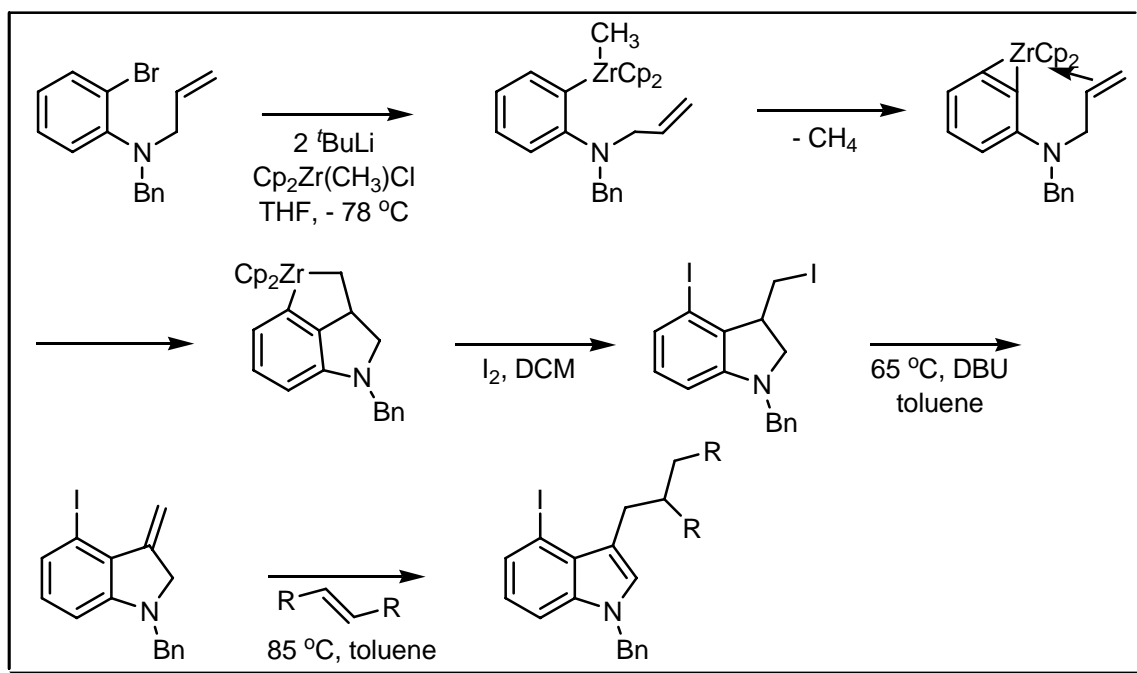
**COMMENTS :**

**BUCHWALD ZIRCONOCENE REACTION**

**EXAMPLE :**



**MECHANISM :**



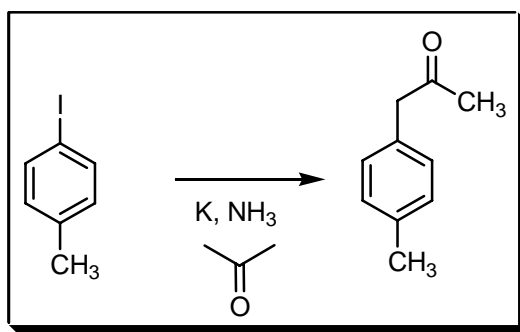
**NOTES :**

In this reaction zirconocene complexes of mainly substituted benzyne are used for the preparation of a variety of polysubstituted aromatic molecules including indoles. Besides polysubstituted aromatic molecules substituted pyrroles and butenolides are accessible *via* zirconocene complexes.

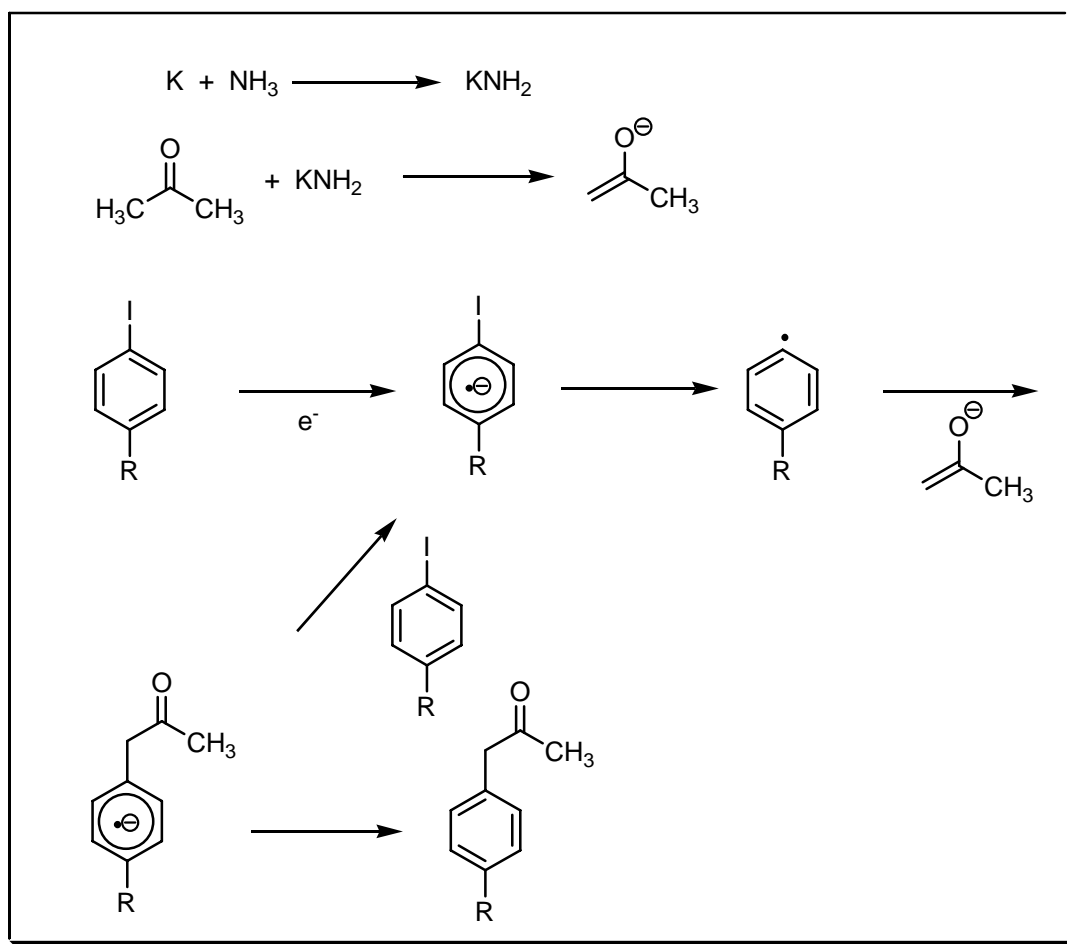
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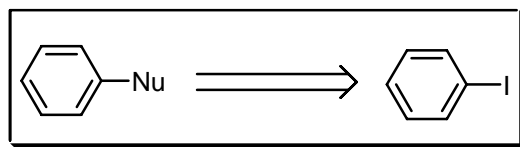
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**COMMENTS :****BUNNETT REACTION****EXAMPLE :**

## MECHANISM :



## DISCONNECTION :



## NOTES :

The nucleophilic aromatic substitution *via* a radical chain mechanism of substituted aryl iodides. Potassium or light can be used as a catalyst.

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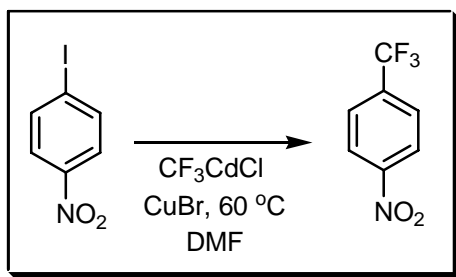
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COMMENTS :

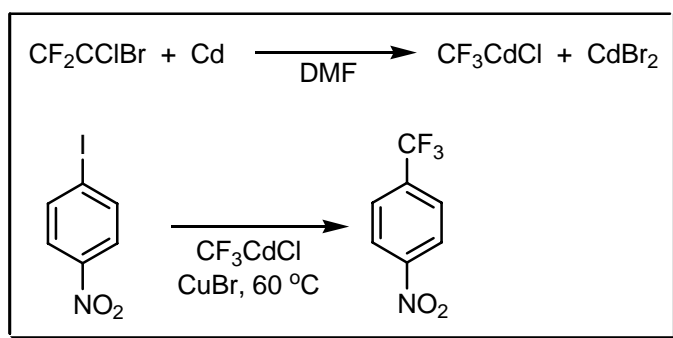
## BURTON – WIEMERS TRIFLUOROMETHYLATION

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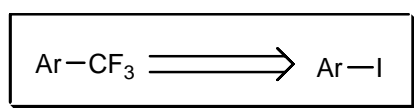
EXAMPLE :



MECHANISM :



DISCONNECTION :



**NOTES :**

The trifluoromethylation of aryl iodides with Cd(Cu) reagents, but mainly with CF<sub>3</sub>Cu (stabilised by HMPA), which is an excellent CF<sub>2</sub> transfer agent. Later work has extended the use of this reagent to a wide range of fluoroalkylated allenes and perfluorovinyl compounds.

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**REFERENCES :**

Houben – Weyl : E10, 465

Org. Synth. : 72, 225

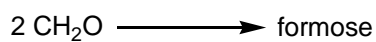
Org. Synth. Coll. Vol. : 9, 247

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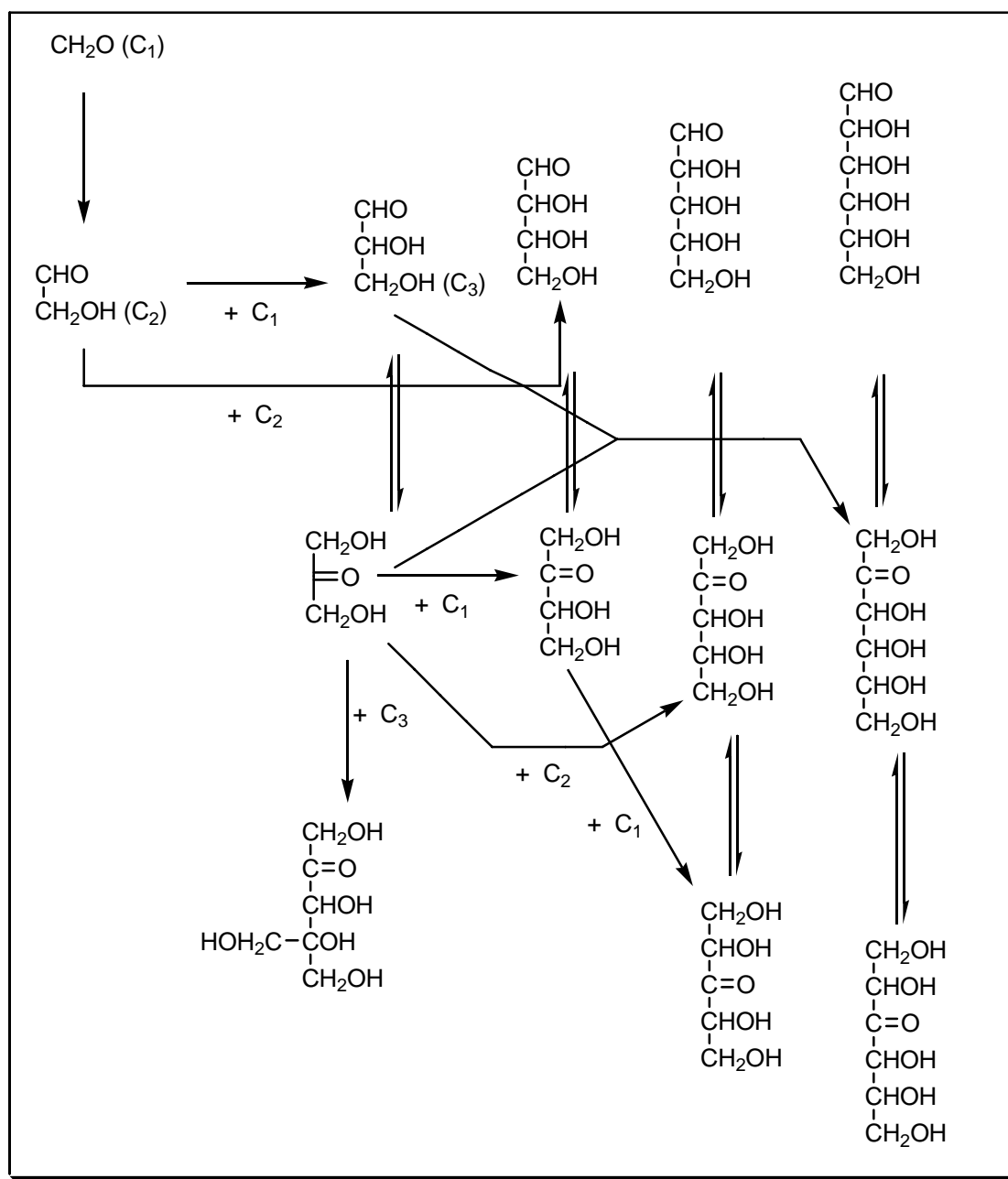
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- 

**COMMENTS :****BUTLEROW SUGAR SYNTHESIS**

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**EXAMPLE :**

## MECHANISM :



## NOTES :

Formaldehyde will give after several sequential aldol condensations a sugar mixture, called formose.

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**COMMENTS :**

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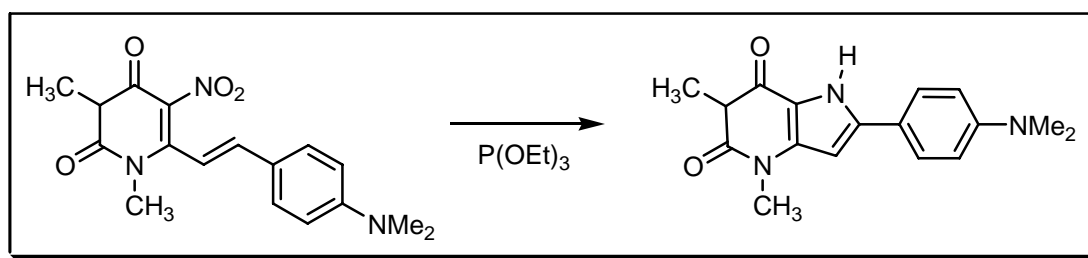
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***W***

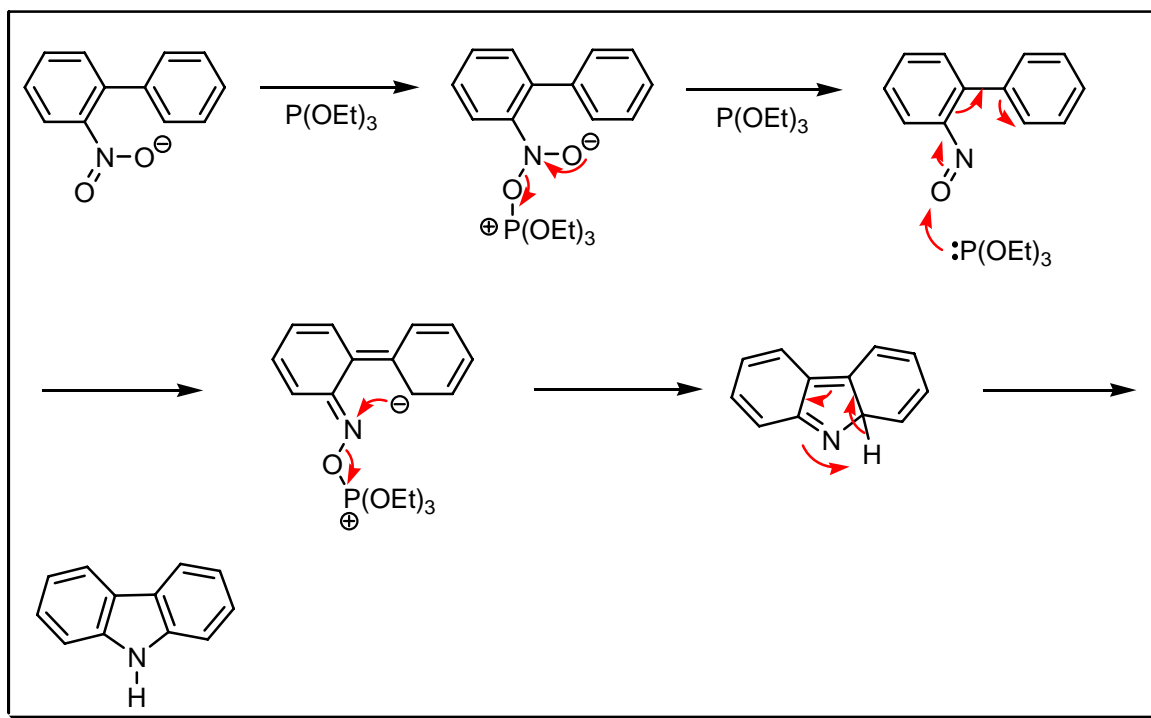
WURTZ AMINE SYNTHESIS · 446

## CADOGAN – CAMERON-WOOD CYCLISATION

### EXAMPLE :



### MECHANISM :



### NOTES :

The reduction of aromatic nitro compounds by triethyl phosphite leads to carbazoles, indoles, indazoles, triazoles and related compounds. Microwave-enhanced cyclisations have been reported. See also **Cadogan – Sundberg** indole reaction.

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**Org. Synth.** : 48, 113

**Org. Synth. Coll. Vol.** : 5, 941

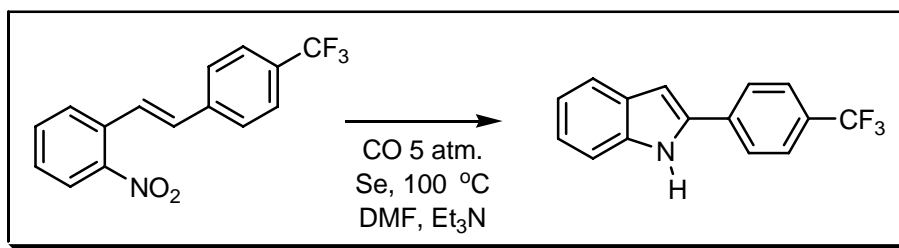
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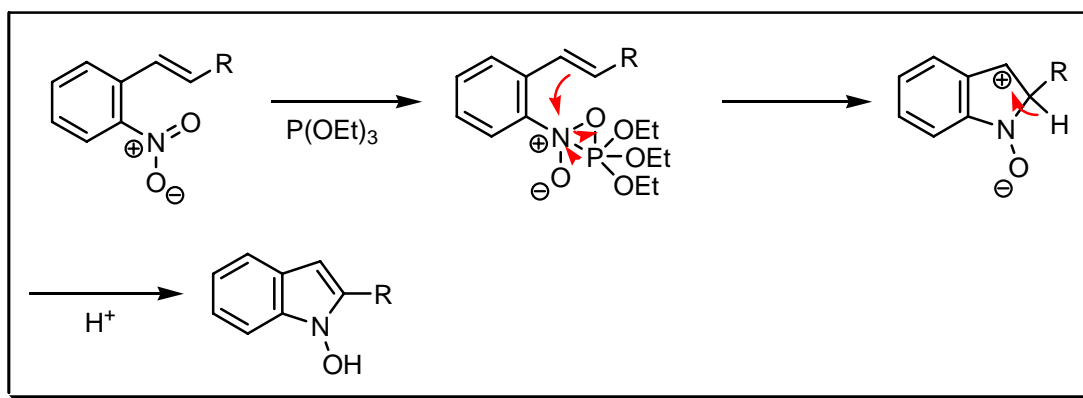
**COMMENTS :**

## CADOGAN – SUNDBERG INDOLE SYNTHESIS

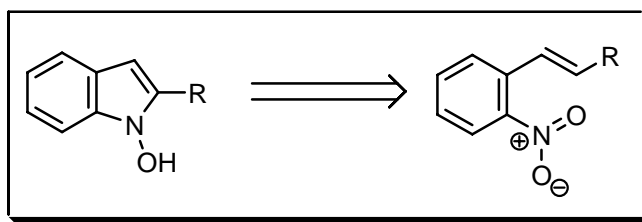
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

The deoxygenation of *ortho*-nitrostyrenes or *ortho*-nitrostilbenes with triethyl phosphate. Additional cyclisation of the nitrene or equivalent affords the indole. Instead of triethyl phosphite carbonyl selenide can be used. This reaction is very similar to the **von Baeyer – Emmerling**. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

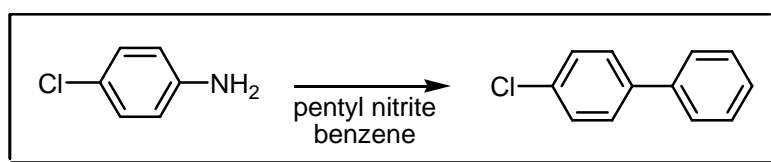
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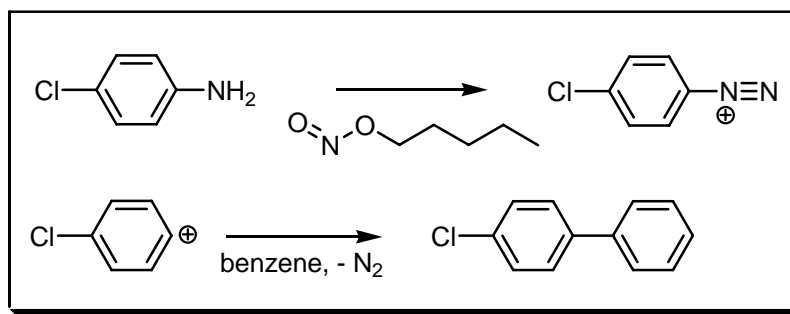
## COMMENTS :

## CADOGAN ARYLATION

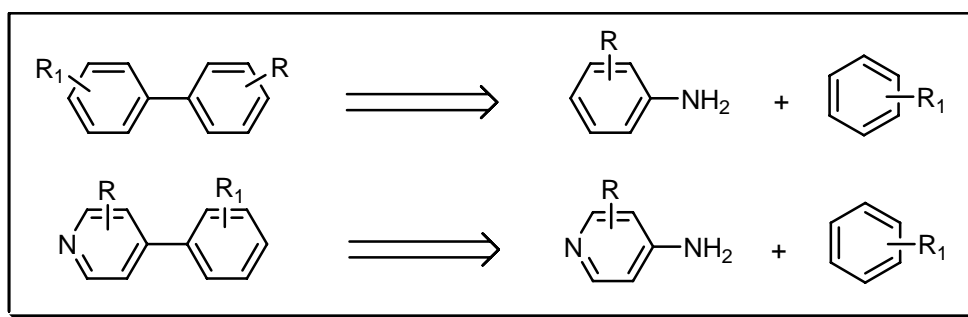
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Aminopyridines or aminobenzenes are diazotised with pentyl nitrite in refluxing benzene. The resulting diazonium compounds then couple with the solvent to give the desired phenylpyridines or biphenyls. A radical mechanism is also possible. See also **Balz – Schiemann**, **Craig** exchange, **Demjanov** rearrangement, **Gattermann** diazo, **Gattermann** sulphinic acid, **Griess** deamination, **Knoevenagel** diazotation, **Körner – Contardi**, **Meerwein** arylation, **Sandmeyer** diazonium, **Schwechten** and **Witt** diazotation reactions.

## REFERENCES :

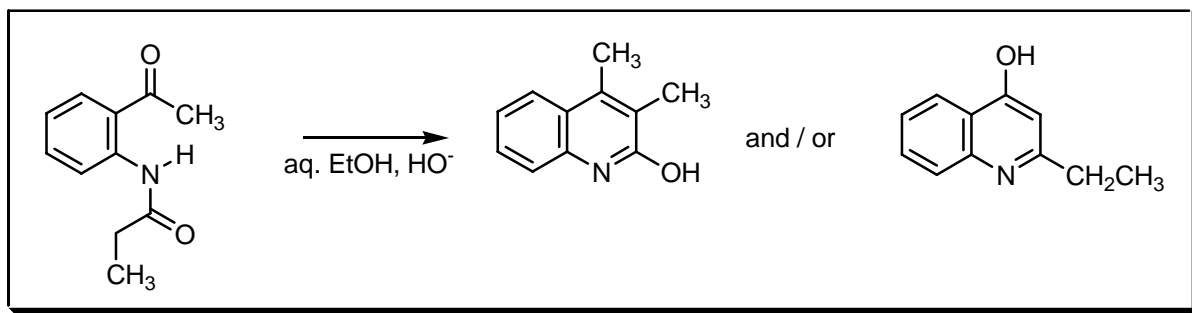
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## COMMENTS :

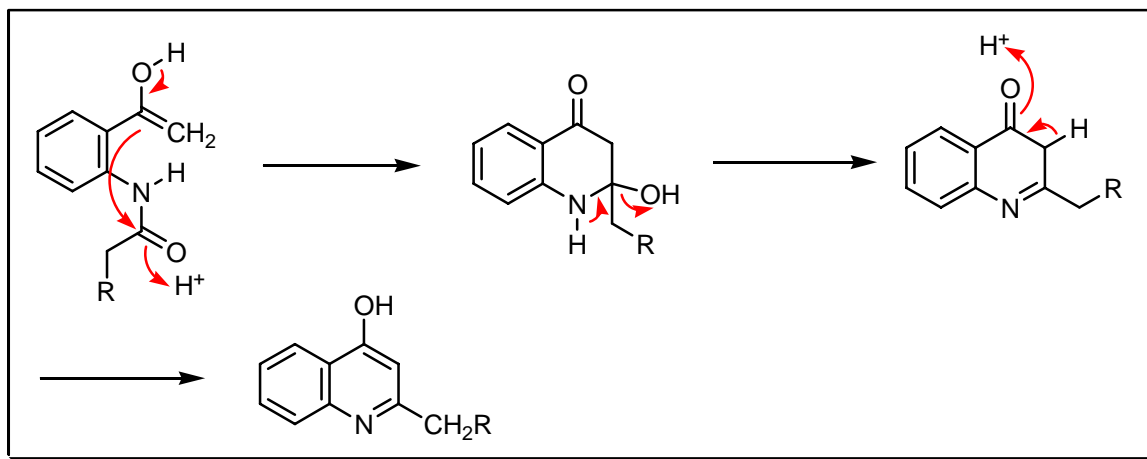
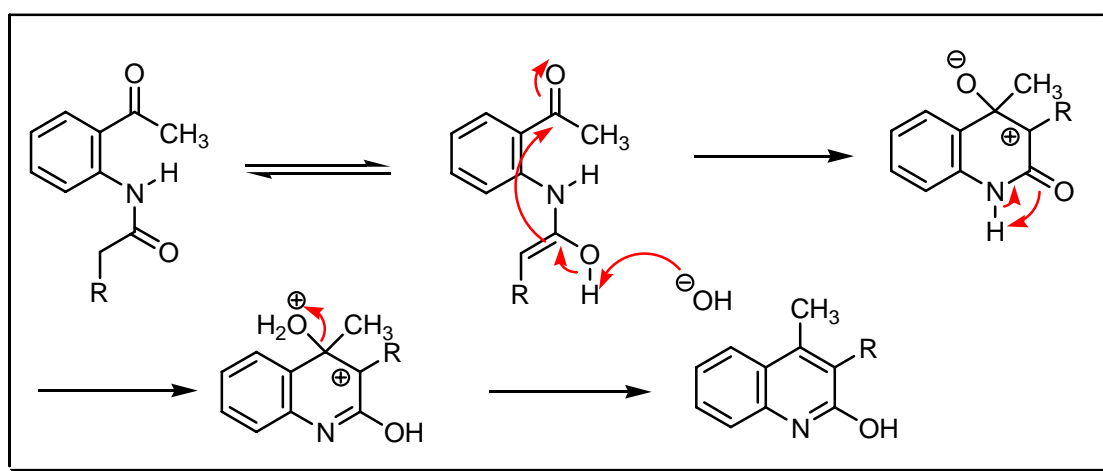


## CAMPS QUINOLINE SYNTHESIS

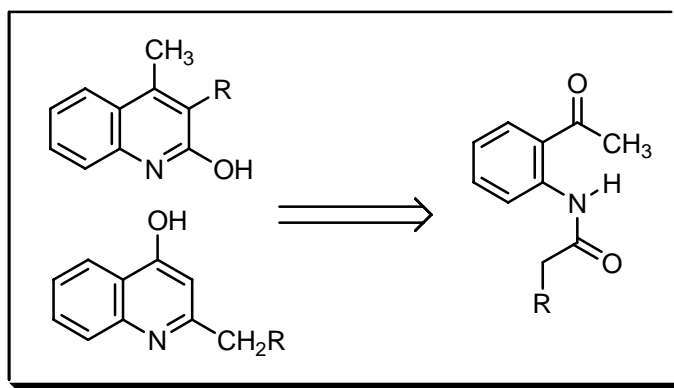
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

Hydroxyquinolines are obtained from *o*-acylaminoacetophenones by treatment with aqueous ethanolic alkali hydroxide. See also **Allan – Loudon**, **von Baeyer – Drewson** quinoline, **Combes** quinoline, **Conrad – Limpach**, **Doebner** quinoline, **Doebner – von Miller**, **Foulds – Robinson**, **Friedländer**, **Knorr** quinoline, **Meth–Cohn**, **von Niementowski** quinoline, **Pfitzinger – Borsche**, **Riehm** quinoline and **Skraup** quinoline reactions.

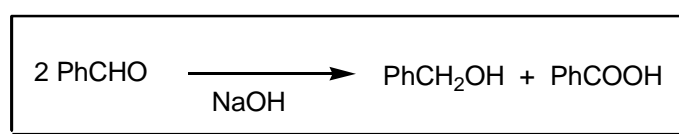
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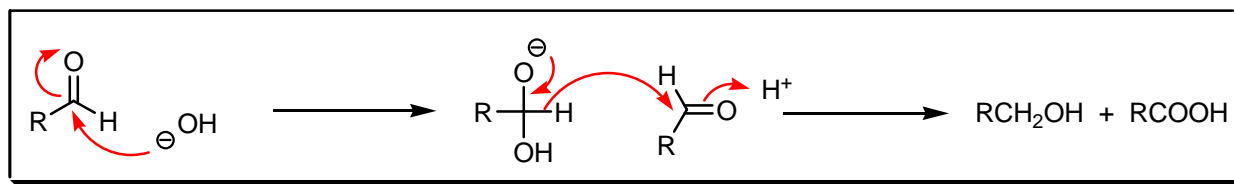
## COMMENTS :

## CANNIZZARO REACTION

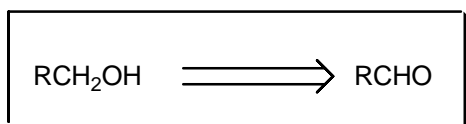
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

In the classic **Cannizzaro** reaction there are no  $\alpha$ -hydrogens present on the aldehyde. However, 1,4-dialdehydes are converted to  $\gamma$ -lactones using a rhodium phosphine complex, showing that  $\alpha$ -hydrogens do not pose a problem. **Crossed-Cannizzaro** reactions are also possible. A strong base is often necessary and the reaction can be carried out under solvent-free conditions. **Photo-Cannizzaro** reactions have also been reported. See also **Cheney**, **Nord**, **Tishchenko – Claisen** and **Tollens** reactions.

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**March** : 1234

**Smith – March** : 463, 1200, 1508, 1564

**Houben – Weyl** : **E3**, 636; **E5**, 274

**Org. React.** : **2**, 94

**Org. Synth.** : **18**, 79

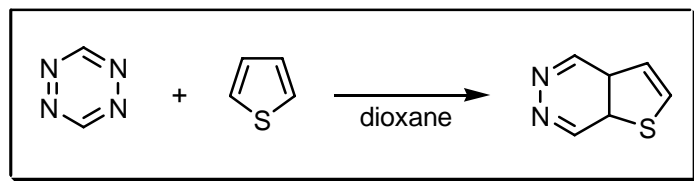
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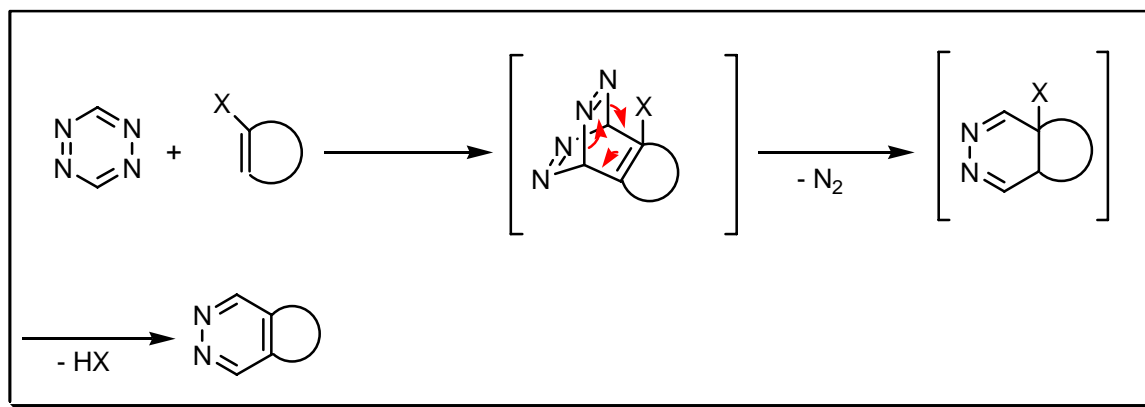
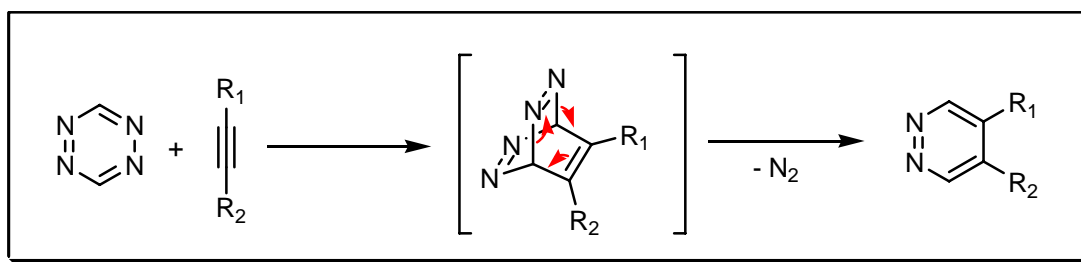
COMMENTS :

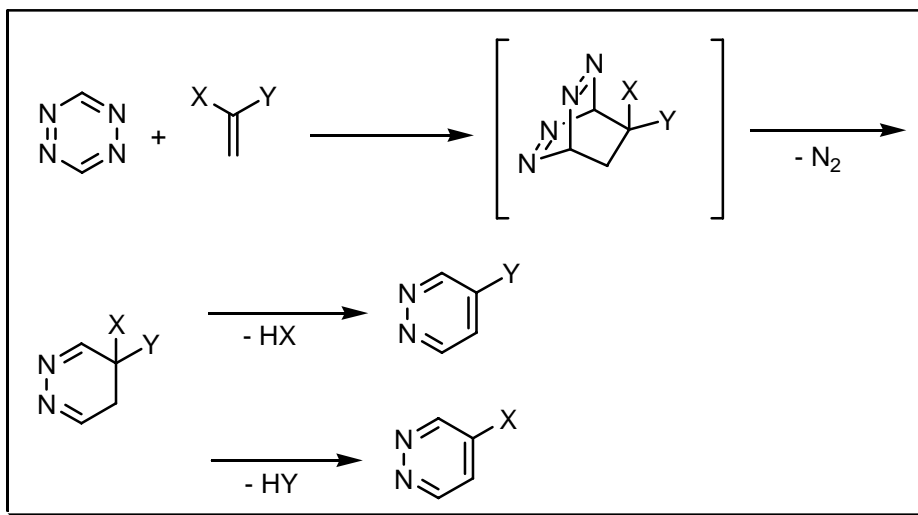
## CARBONI – LINDSEY SYNTHESIS

EXAMPLE :

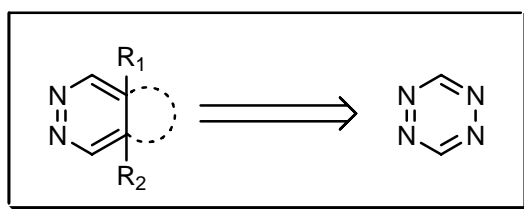


MECHANISM :





#### DISCONNECTION :



#### NOTES :

[4+2]-Cycloadditions are by far the most important reactions of 1,2,4,5-tetrazines. The cycloaddition of 1,2,4,5-tetrazines with simple alkenes and alkynes under mild thermal conditions affords 1:1 adducts, with the loss of nitrogen. See also **Boger – Panek** and **Diels – Alder** reactions.

#### REFERENCES :

Org. Synth. : 70, 79

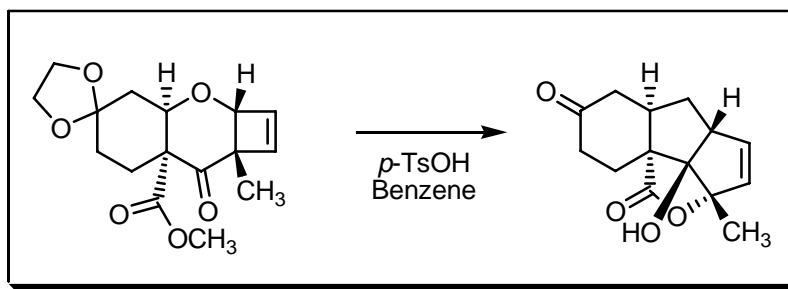
Org. Synth. Coll. Vol. : 9, 335

- 1) R.A. Carboni; R.V. Lindsey, *J. Am. Chem. Soc.*, 1959, **81**, 4342.
- 2) G. Seitz; L. Gorge, *Chem. -Ztg.*, 1984, **108**, 331.
- 3) D.L. Boger, *Chem. Rev.*, 1986, **86**, 781.
- 4) D.L. Boger, *Tetrahedron*, 1993, **39**, 2869.
- 5) J. Sauer; D.K. Heldmann; J. Hetzenegger; J. Krauthan; H. Sichert; J. Schuster, *Eur. J. Org. Chem.*, 1998, 2885.
- 6) G.L. Rusinov; R.I. Ishmetova; N.I. Latosh; I.N. Ganebnych; O.N. Chupakhin; V.A. Potemkin, *Russ. Chem. Bull.*, 2000, **49**, 355.
- 7) X.J. Zhou; E.G. Kovalev; J.T. Klug; V. Khordorkovsky, *Org. Lett.*, 2001, **3**, 1725.

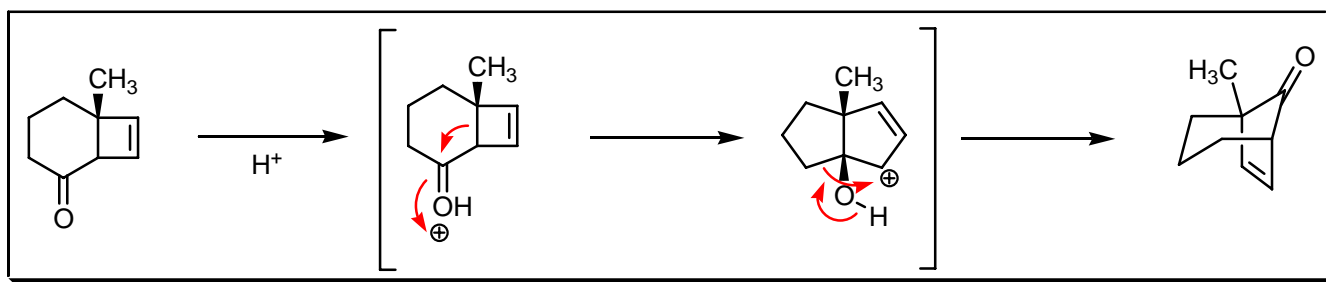
COMMENTS :

## CARGILL REARRANGEMENT

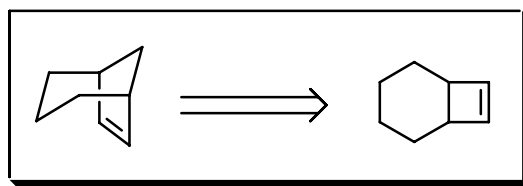
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

A practical method for the conversion of bicyclo[4.2.0]octene systems to bicycle[3.2.1]octene systems in the presence of an acid catalyst.

REFERENCES :

- 1) R.L. Cargill; J.W. Crawford, *Tetrahedron Lett.*, 1967, **8**, 169.
- 2) R.L. Cargill; J.W. Crawford, *J. Org. Chem.*, 1970, **35**, 356.
- 3) R.L. Cargill; D.M. Pond; S.O. LeGrand, *J. Org. Chem.*, 1970, **35**, 359.

4) R.L. Cargill; T.E. Jackson; N.P. Peet; D.M. Pond, *Acc. Chem. Res.*, 1974, **7**, 106.

5) K. Narasaka; H. Shimadzu; Y. Hayashi, *Chem. Lett.*, 1993, 621.

6) J.D. White; N.-S. Kim; D.E. Hill; J.A. Thomas, *Synthesis*, 1998, 619.

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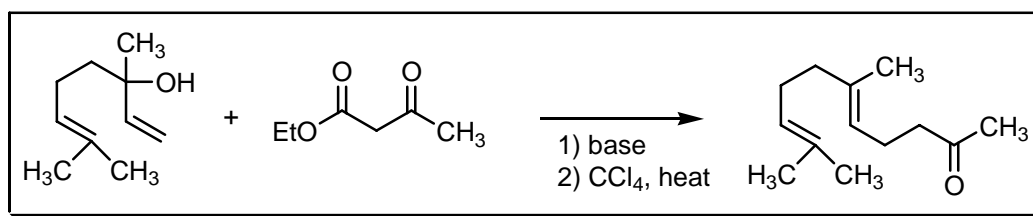
**COMMENTS :**

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**CARROLL METHYLENE ADDITION (KIMEL – COPE REARRANGEMENT)**

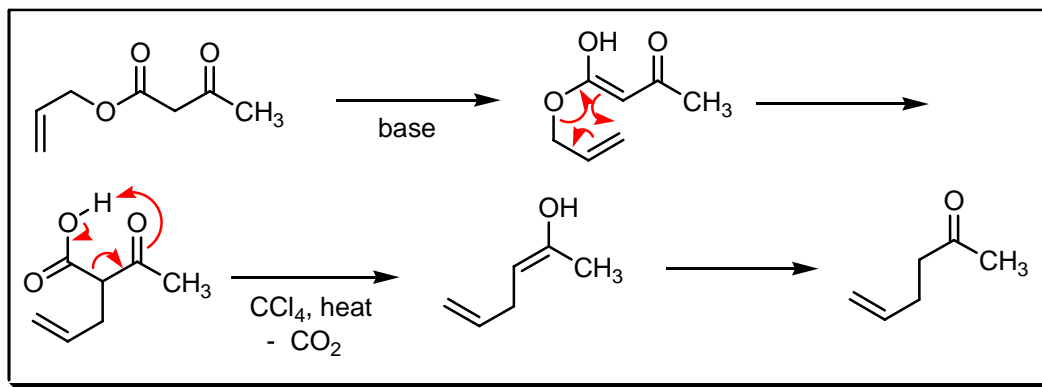
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**EXAMPLE :**



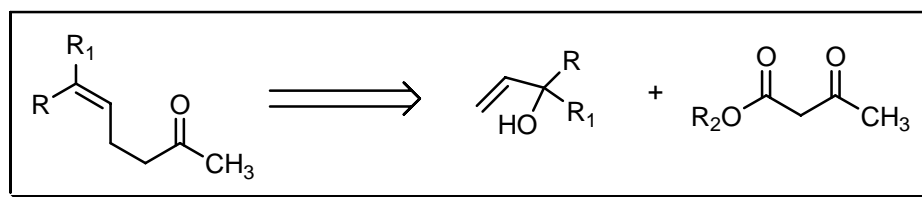
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**MECHANISM :**



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**DISCONNECTION :**



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**NOTES :**

$\beta,\gamma$ -Unsaturated alcohols react with active methylene compounds in the presence of an alkaline catalyst ( $\text{NaOAc}$ ,  $\text{NaOCH}_3$ ,  $\text{KOH}$ ) to yield an ethylenic ketone. The reaction involves the thermal rearrangement of allylic esters to  $\beta$ -

keto acids followed by decarboxylation to provide  $\gamma,\delta$ -unsaturated methylketones. An asymmetric **Carroll** rearrangement has been developed by **Enders** using the SAMP hydrazone method. See also **Belluš – Claisen** rearrangement, **Claisen** (**Claisen – Ireland**) rearrangement, **Cope**, **Eschenmoser – Meerwein – Claisen** rearrangement, **Ficini – Claisen**, **Johnson – Claisen**, **Marbet – Saucy** and **Overman** rearrangement reactions.

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#### REFERENCES :

**Smith** : 1241

**Smith 2<sup>nd</sup>** : 1023

**Houben – Weyl** : **E18**, 1061

**Org. React.** : **22**, 1; **41**, 1; **43**, 2

**Org. Synth.** : **47**, 87; **68**, 210

**Org. Synth. Coll. Vol.** : **5**, 767; **8**, 235

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  - 2) M.F. Carroll, *J. Chem. Soc.*, 1940, 1266.
  - 3) W. Kimel; A.C. Cope, *J. Am. Chem. Soc.*, 1943, **65**, 1992.
  - 4) M. Tanabe; K. Hayashi, *J. Am. Chem. Soc.*, 1980, **102**, 862.
  - 5) S.R. Wilson; M.F. Price, *J. Org. Chem.*, 1984, **49**, 722.
  - 6) D. Enders; M. Knopp; J. Runsink; G. Raabe, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 2278.
  - 7) J.L. Wood; B.M. Stolz; H.-J. Dietrich, *J. Am. Chem. Soc.*, 1995, **117**, 10413.
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  - 9) L.N. Sobenina; A.I. Mikhaleva; O.V. Petrova; R.I. Polovnikova; B.A. Trofimov, *Russ. J. Org. Chem.*, 1997, **33**, 1041.
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  - 11) A.M.M. Castro, *Chem. Rev.*, 2004, **104**, 2939.
  - 12) M.E. Jung; B.A. Duclos, *Tetrahedron Lett.*, 2004, **45**, 107.
  - 13) R. Kuwano; N. Ishida; M. Murakami, *Chem. Commun.*, 2005, 3951.
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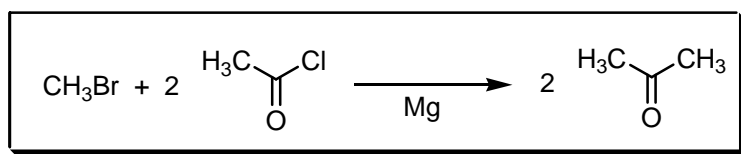
#### COMMENTS :



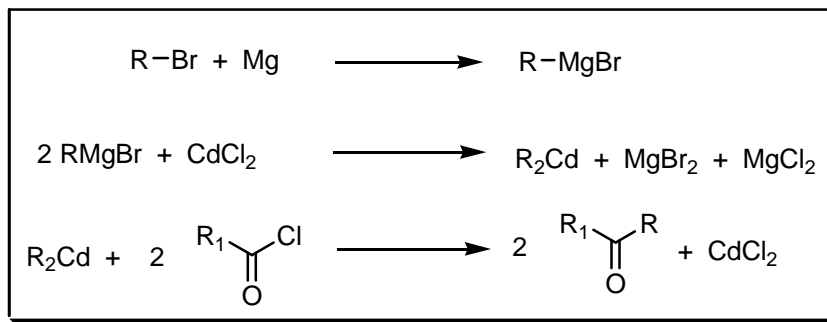
## CASON (GILMAN – NELSON) SYNTHESIS

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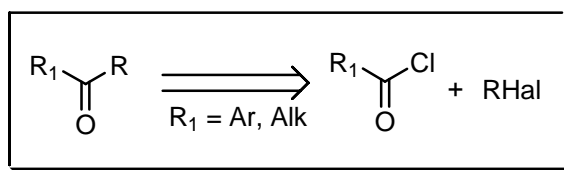
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The formation of ketones from aliphatic and aromatic acid chlorides and organometallic cadmium compounds. See also **Blaise**, **Blaise – Maire**, **Grignard** and **Reformatsky** reactions.

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### REFERENCES :

**Org. React.** : **8**, 28

**Org. Synth.** : **28**, 75

**Org. Synth. Coll. Vol.** : **3**, 601

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1) H. Gilman; J.F. Nelson, *Recl. Trav. Chim. Pays-Bas*, 1936, **55**, 518.

2) J. Cason, *J. Am. Chem. Soc.*, 1946, **68**, 2078.

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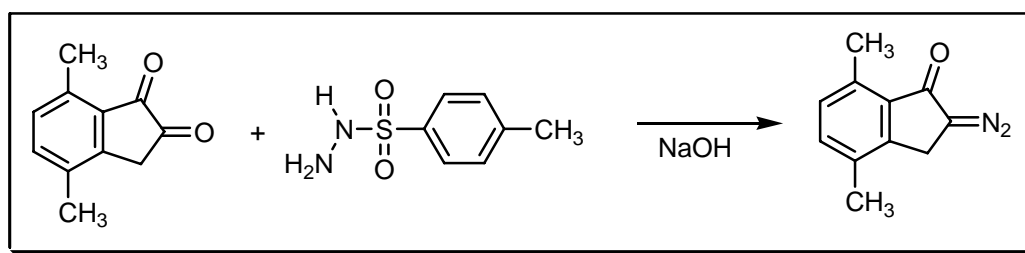
5) R.M. Shisla; W.C. Hammann, *J. Org. Chem.*, 1970, **35**, 3224.

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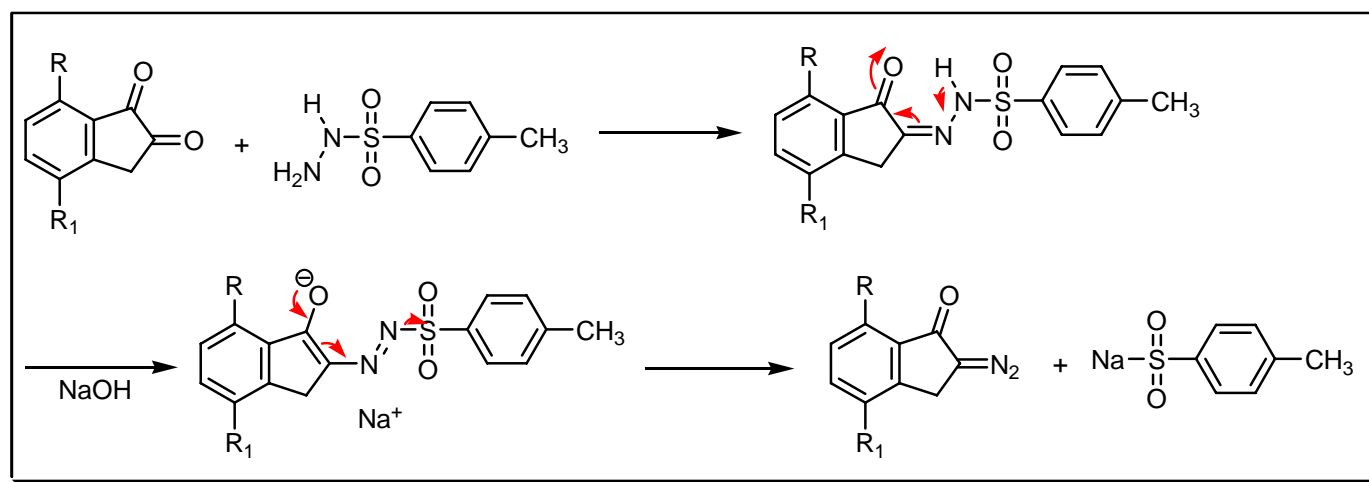
COMMENTS :

## CAVA REARRANGEMENT

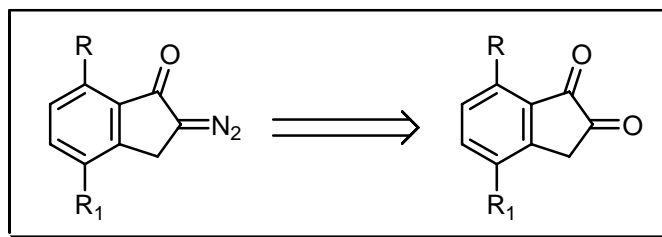
EXAMPLE :



MECHANISM :



DISCONNECTION :



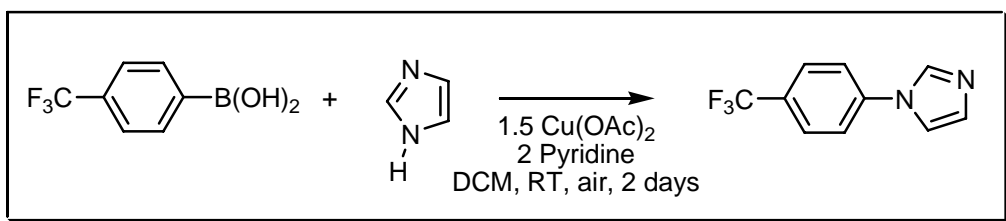
**NOTES :**

The formation of a diazoketone from an  $\alpha$ -diketone and *p*-toluenesulfonylhydrazide. See also **Bamford – Stevens** and **Forster** reactions.

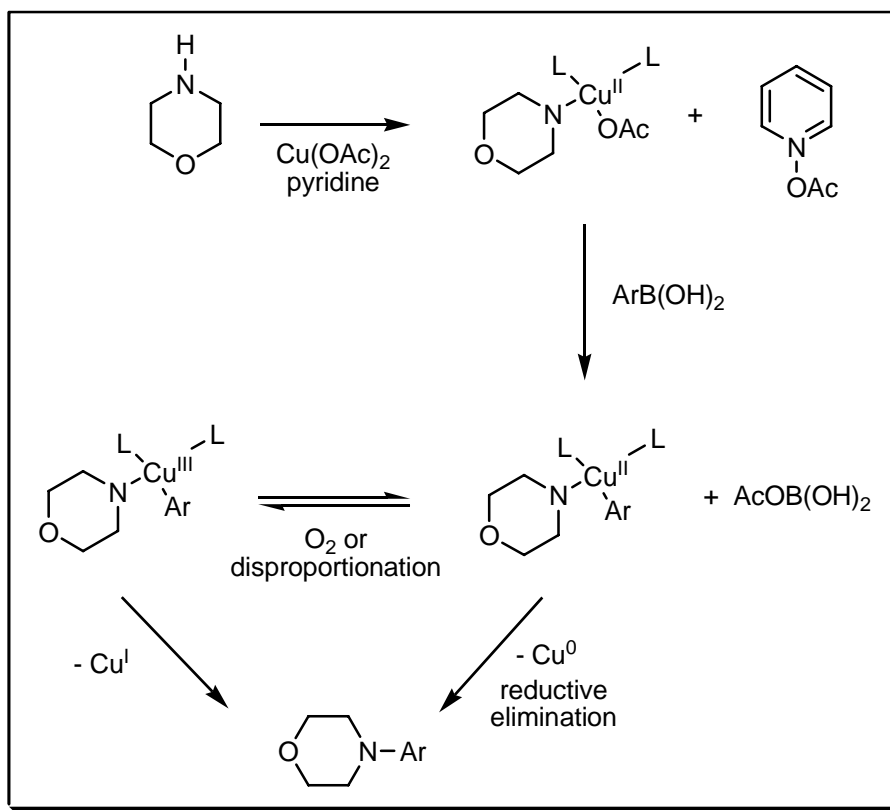
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**REFERENCES :**

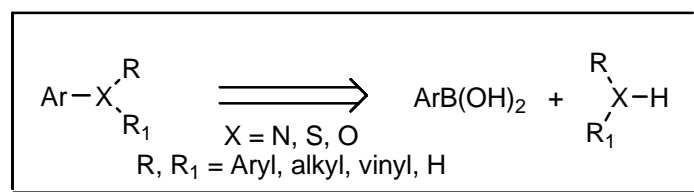
- 1) W. Borsche; R. Frank, *Liebigs Ann. Chem.*, 1926, **450**, 75.
  - 2) M.P. Cava; R.L. Little, *Chem. Ind. (London)*, 1957, 367.
  - 3) M.P. Cava; R.L. Little; D.R. Napier, *J. Am. Chem. Soc.*, 1958, **80**, 2257.
- 

**COMMENTS :****CHAN – LAM COUPLING****EXAMPLE :**

## MECHANISM :



## DISCONNECTION :



## NOTES :

An extremely versatile and powerful coupling method involving the formation of a carbon heteroatom bond by the copper mediated oxidative coupling of a boronic acid with an amine, alcohol or thiol. See also **Buchwald – Hartwig** and **Suzuki** reactions.

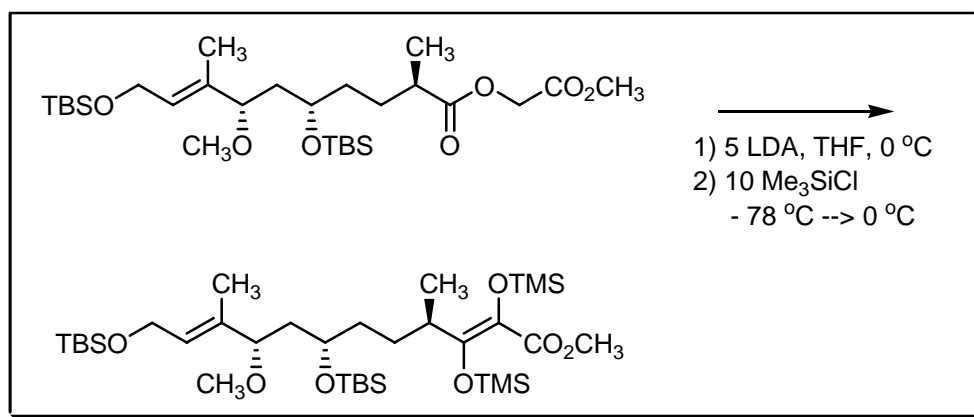
## REFERENCES :

- 1) P.Y.S. Lam; C.G. Clark; S. Saubern; J. Adams; M.P. Winters; D.M.T. Chan; A. Combs, *Tetrahedron Lett.*, 1998, **39**, 2941.
- 2) P.Y.S. Lam; S. Deudon; K.M. Averill; R. Li; M.Y. He; P. DeShong; C.G. Clark, *J. Am. Chem. Soc.*, 2000, **122**, 7600.
- 3) P.Y.S. Lam; G. Vincent; C.G. Clark; S. Deudon; P.K. Jadhav, *Tetrahedron Lett.*, 2001, **42**, 3415.
- 4) P.Y.S. Lam; C.G. Clark; S. Saubern; J. Adams; K.M. Averill; D.M.T. Chan; A. Combs, *Synlett*, 2002, 674.
- 5) P.Y.S. Lam; D. Bonne; G. Vincent; C.G. Clark; A.P. Combs, *Tetrahedron Lett.*, 2003, **44**, 1691.
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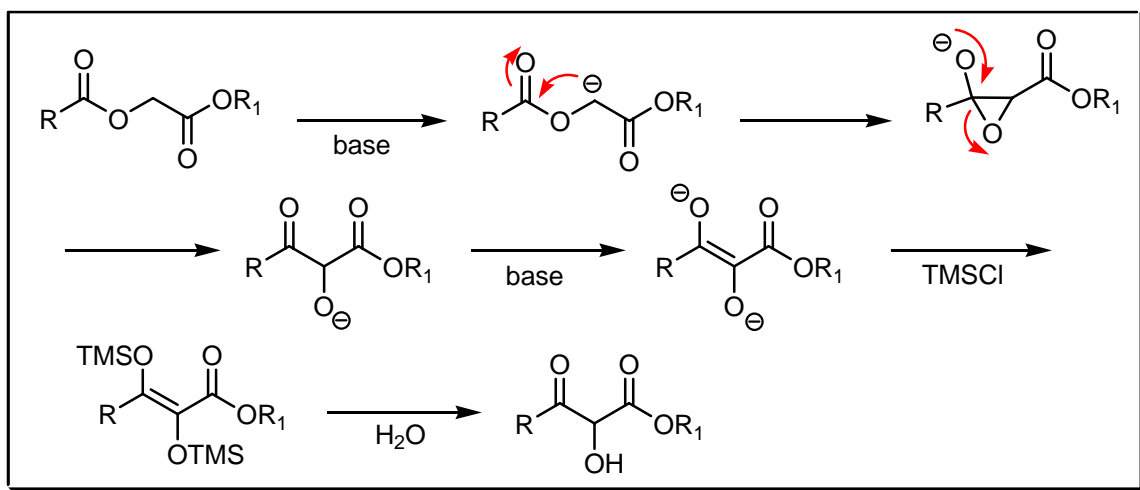
COMMENTS :

## CHAN REARRANGEMENT

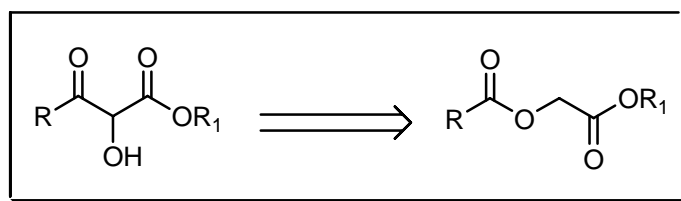
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

The base-induced rearrangement of  $\alpha$ -(acyloxy)acetates to  $\alpha$ -hydroxy- $\beta$ -keto esters. The rearrangement is believed to proceed *via* an epoxide.

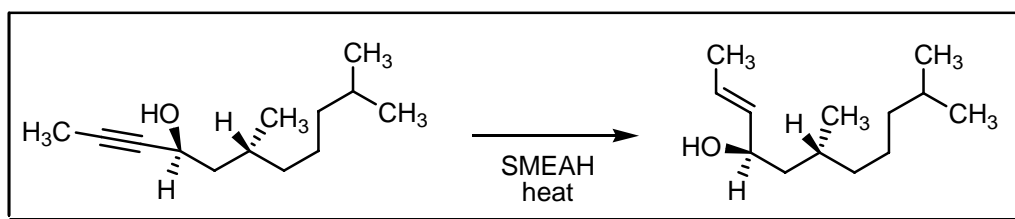
## REFERENCES :

- 1) S.D. Lee; T.H. Chan; K.S. Kwon, *Tetrahedron Lett.*, 1984, **24**, 3399.
- 2) J.D. White; S.C. Jeffrey, *J. Org. Chem.*, 1996, **61**, 2600.
- 3) P. Wipf; J.-L. Methot, *Org. Lett.*, 2001, **3**, 1261.

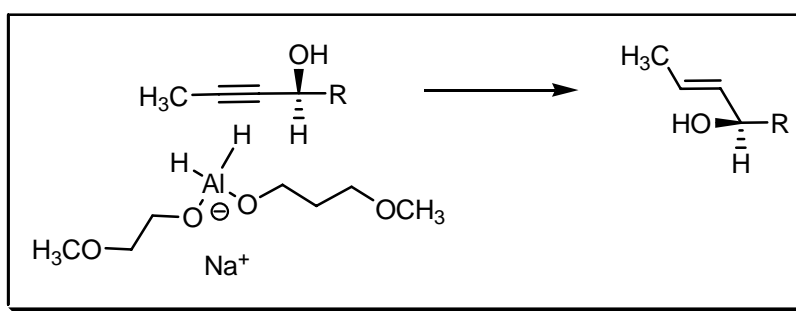
## COMMENTS :

## CHAN REDUCTION OF ACETYLENES

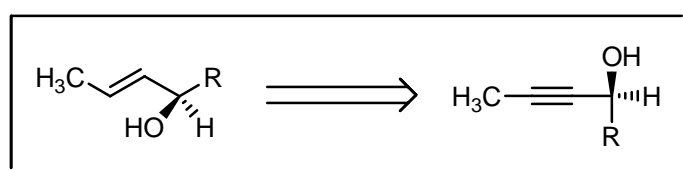
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The stereospecific reduction of  $\alpha$ -acetylenic alcohols to *E*-allylic alcohols using sodium bis(2-methoxyethoxy)aluminium hydride (SMEAH, Red-Al). The **Lindlar** catalyst gives (*Z*)-allylic alcohols.

## REFERENCES :

Org. Synth. : **64**, 182

Org. Synth. Coll. Vol. : **7**, 524

1) K.-K. Chan; N. Cohen; J.P. De Noble; A.C. Specian, jr.; G. Saucy, *J. Org. Chem.*, 1976, **41**, 3497.

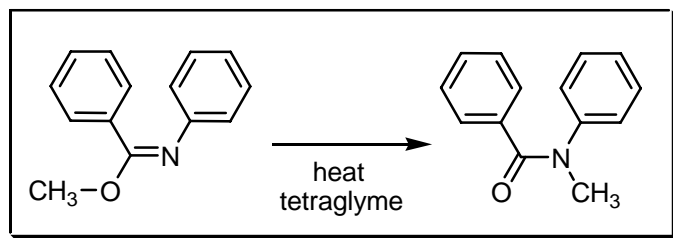
2) K.-K. Chan; A.C. Specian, jr.; G. Saucy, *J. Org. Chem.*, 1978, **43**, 3435.

3) B.M. Trost; M. Lautens, *J. Am. Chem. Soc.*, 1987, **109**, 1469.

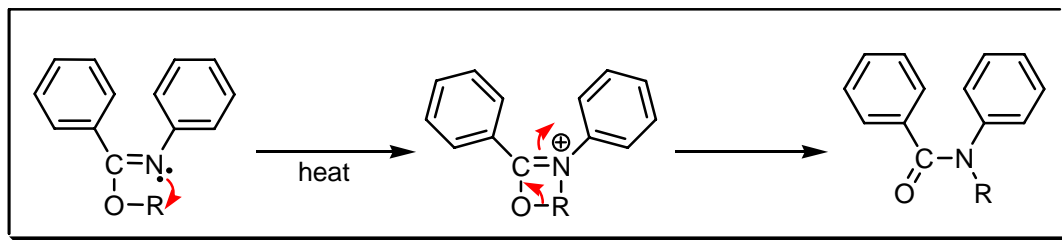
## COMMENTS :

## CHAPMAN REARRANGEMENT

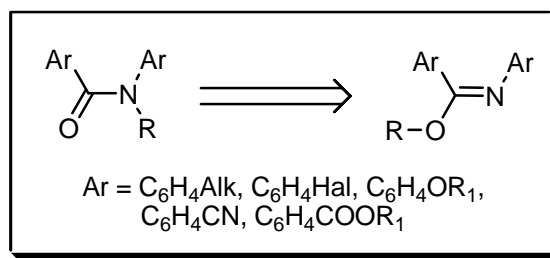
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

Arylimido esters when heated to 200 °C undergo an *intramolecular* rearrangement (1,3-oxygen to nitrogen shift) to give acylated diphenylamines. If R is electron-withdrawing then the reaction proceeds more quickly while with electron-donating groups on the aryl ring the reactivity is reduced. This reaction is sometimes called the **Beckmann – Chapman** rearrangement or the **Mumm** rearrangement. See also **Beckmann** rearrangement, **Hayashi** rearrangement, **Newman – Karnes – Kwart**, **Schönberg** and **Smiles** reactions.

## REFERENCES :

**March** : 1155

**Smith – March** : 1464

**Org. React.** : **14**, 1; **18**, 99

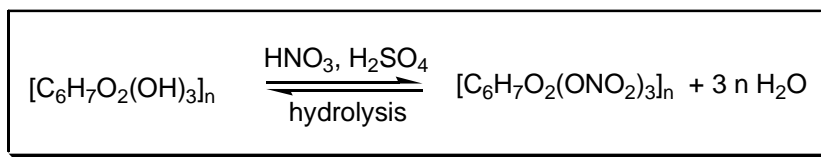
- 1) O. Mumm; H. Hesse; H. Volquartz, *Ber. Dtsch. Chem. Ges.*, 1915, **48**, 379.
- 2) A.W. Chapman, *J. Chem. Soc.*, 1925, **127**, 1992.
- 3) R. Roger; D.G. Nelson, *Chem. Rev.*, 1961, **61**, 179.
- 4) O.H. Wheeler; F. Roman; M.V. Santiago; F. Quiles, *Can. J. Chem.*, 1969, **47**, 503.
- 5) M.S. Newman, *Acc. Chem. Res.*, 1972, **5**, 354.
- 6) L.H. Peterson; A.W. Douglas; R.L. Tolman, *J. Heterocycl. Chem.*, 1981, **18**, 659.
- 7) X. Wang; Y. Cai; Z. Xu, *Zhongguo Yaoxue Zazhi*, 1997, **32**, 774.
- 8) K.-I. Shohda; T. Wada; M. Sekine, *Nucleosides, Nucleotides*, 1998, **17**, 2199.

## COMMENTS :



## de CHARDONNET CELLULOSE ESTERIFICATION

### EXAMPLE :



### NOTES :

The esterification of cellulose with nitric and sulfuric acid to silk. See also **Cross – Bevan – Beadle** reaction.

### REFERENCES :

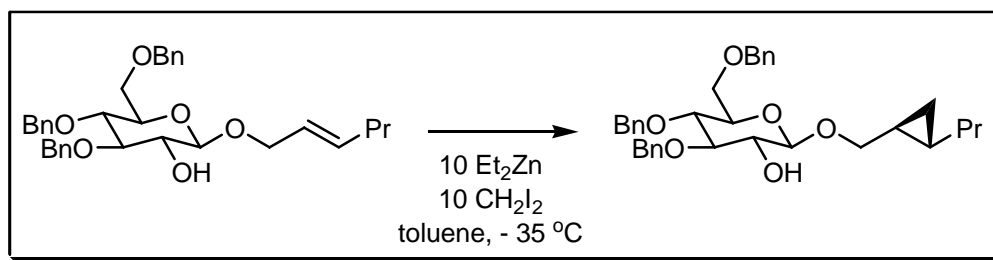
Houben – Weyl : 14/2, 868

H. de Chardonnet, *French patent*, 1884, 165349.

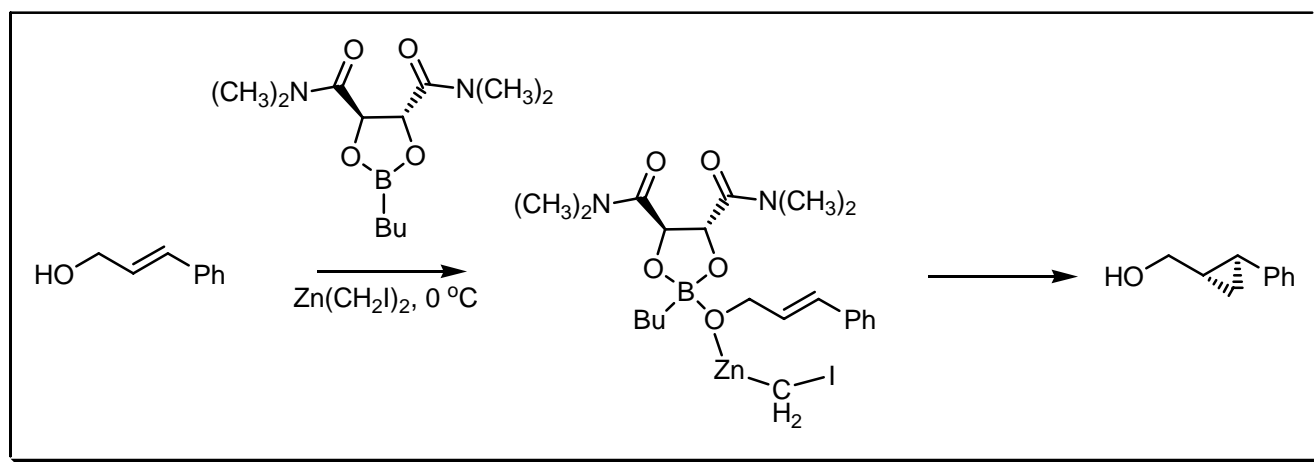
### COMMENTS :

## CHARETTE CYCLOPROPANATION

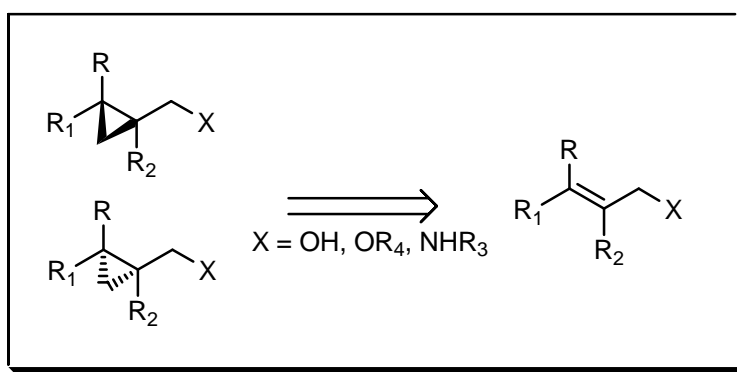
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The conversion of allylic alcohols, ethers, and carbamates into the corresponding enantiomerically enriched cyclopropanes using bis(iodomethyl)zinc and dioxaborolane derived ligands. Initial experiments used  $\alpha$ -D-glucopyranosides as chiral auxiliary. See also **Freund**, **Gustavson**, **Hass** cyclopropane, **Ipatiew** cyclopropane, **Kishner**, **Mousseron – Fraisse – McCoy**, **Nerdel** and **Simmons – Smith** reactions.

## REFERENCES :

**Smith – March** : 1084

**Smith 2<sup>nd</sup>** : 1212

**Org. React.** : **58**, 1

**Org. Synth.** : **76**, 86

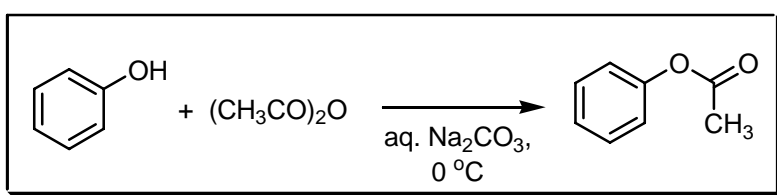
- 1) A.B. Charette; B. Côté; J.P. Marcoux, *J. Am. Chem. Soc.*, 1991, **113**, 8166.
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- 5) A.B. Charette; H. Juteau; H. Lebel; C. Molinaro, *J. Am. Chem. Soc.*, 1998, **120**, 11943.

6) K.C. Nicolaou; A. Ritzén; K. Namoto; R.M. Buey; J.F. Díaz; J.M. Andreu; M. Wartmann; K.-H. Altmann; A. O'Brate; P. Giannakakou, *Tetrahedron*, 2002, **58**, 6413.

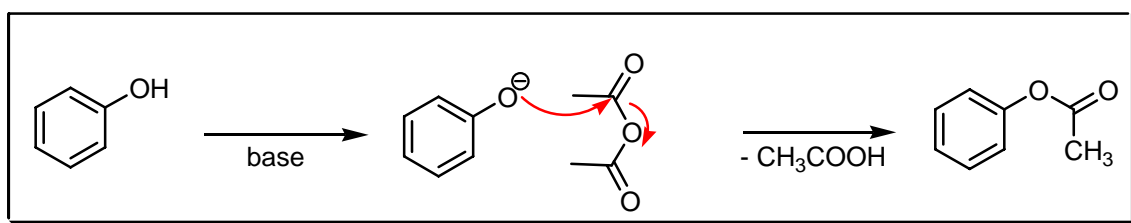
COMMENTS :

## CHATTAWAY ACETYLATION

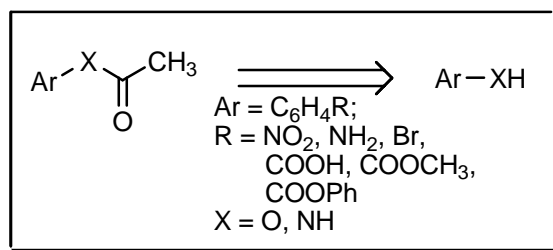
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

Aromatic hydroxyl- and amino-groups can be acetylated quantitatively by adding acetic anhydride to their dilute solutions in aqueous caustic alkali at  $0^\circ\text{C}$ . See also **Einhorn** acylation, **Galat – Elion**, **Lumière – Barbier**, **Schotten – Baumann** and **Weinreb** reactions.

REFERENCES :

March : 392

Smith – March : 483

Org. Synth. : 21, 22; 28, 68; 34, 1

Org. Synth. Coll. Vol. : 3, 281, 452; 4, 15

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1) F.D. Chattaway, *J. Chem. Soc.*, 1931, 2495.

2) E.R. Marshall; J.A. Luck; R.C. Elderfield, *J. Org. Chem.*, 1942, 7, 451.

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4) A.B. Maude; A. Williams, *J. Chem. Soc., Perkin Trans. 2*, 1997, 179.

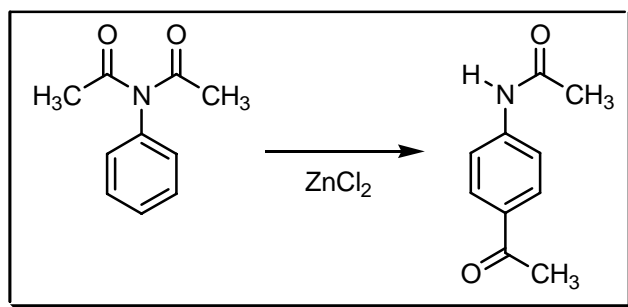
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COMMENTS :

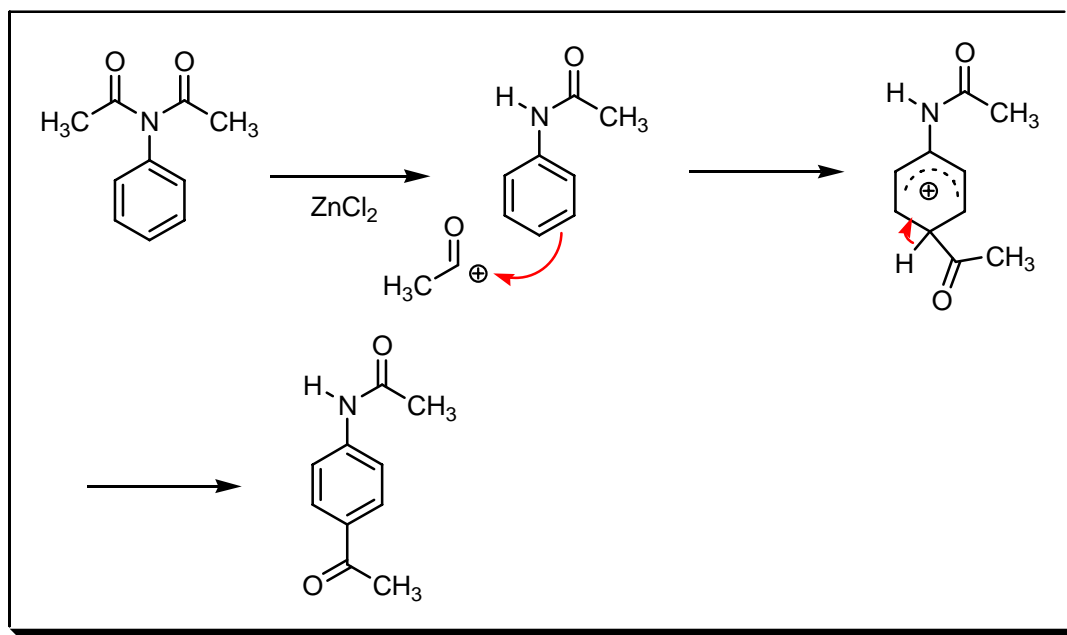
## CHATTAWAY REARRANGEMENT

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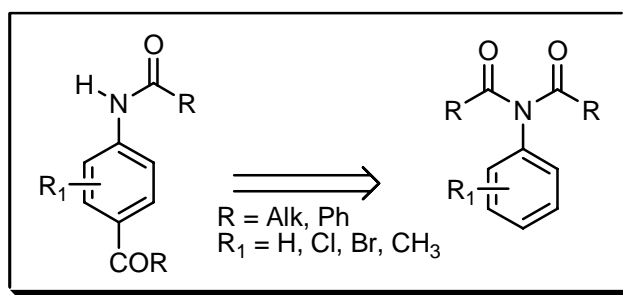
EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

*N,N*-Diacylanilines rearrange *intermolecularly* to acylamino-ketones when heated in the presence of freshly fused zinc chloride. See also **Bamberger** rearrangement, **Fischer – Hepp**, **Fries**, **Hofmann – Martius** and **Orton** reactions.

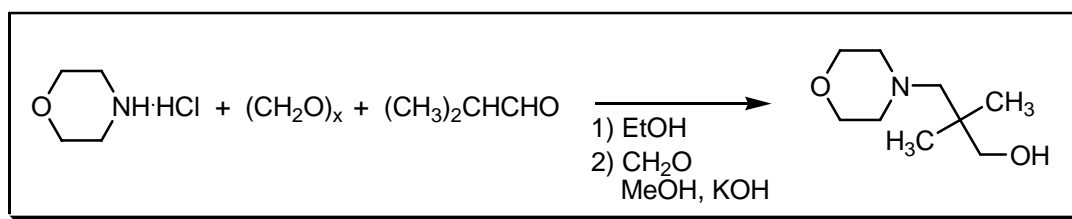
### REFERENCES :

- 1) F.D. Chattaway, *J. Chem. Soc.*, 1904, **85**, 386.
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- 3) J. Shorter, *Abstr. Pap. Am. Chem. Soc.*, 1987, **194**, 62.
- 4) B.I. Buzykin; L.P. Sysoeva, *Bull. Russ. Acad. Sci-Div. Chem. Sci.*, 1992, **41**, 1115.

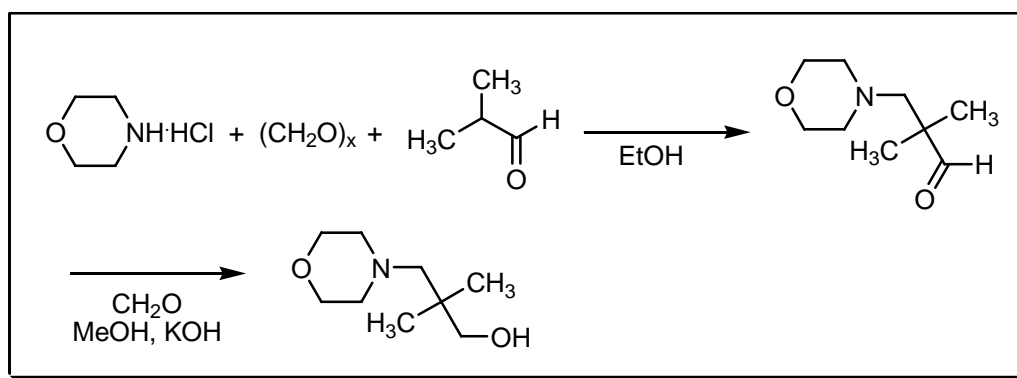
### COMMENTS :

## CHENEY SYNTHESIS

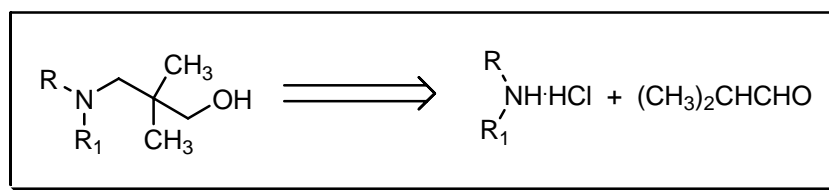
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This reaction involves a combination of the **Mannich** and the crossed **Cannizzaro** reactions. It affords a variety of 2,2-disubstituted amino-alcohols, analogous in constitution to 2,2-dimethyl-3-(4-morpholinyl)-1-propanol. Certain esters of these compounds exhibit physiological activity. See also **Cannizarro** and **Mannich** reactions.

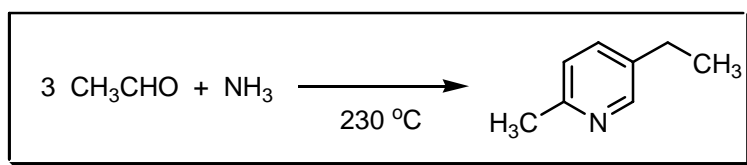
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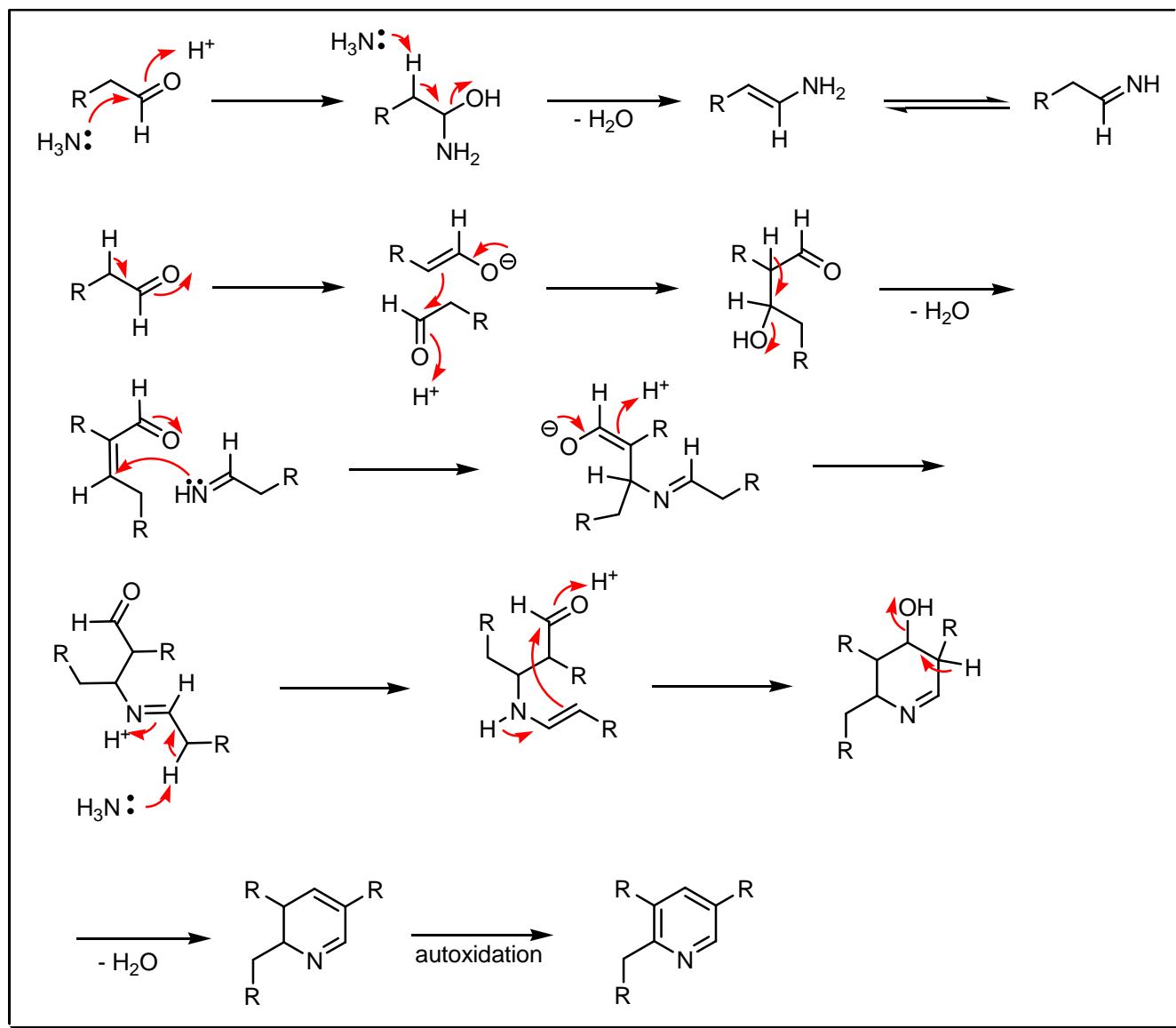
### COMMENTS :

## CHICHIBABIN PYRIDINE SYNTHESIS

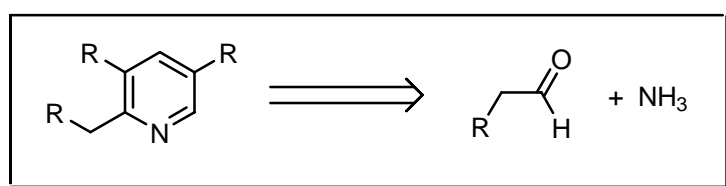
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The pyridine synthesis from aromatic acetaldehydes and ammonia. The mechanism of this reaction is still not clear, see **Sagitullin et al.** See also **Bohlmann – Rahtz**, **Gattermann – Skita**, **Guareschi – Thorpe**, **Hantzsch – Beyer**, **von Meyer – Mohr**, **Petrenko–Kritschenko**, **Riehm** pyridine and **Wakatsuki – Yamazaki – Bönnemann** reactions.

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## REFERENCES :

Houben – Weyl : **E7b**, 316

Org. Synth. : **30**, 41

Org. Synth. Coll. Vol. : **4**, 451

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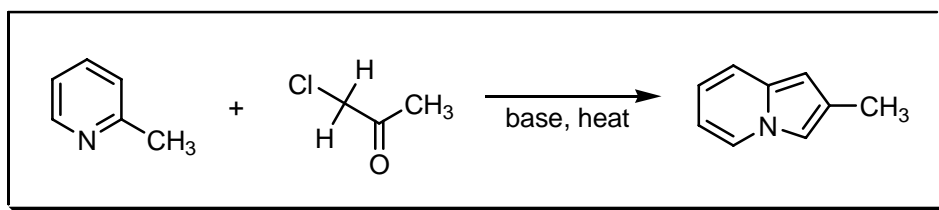
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## COMMENTS :

## CHICHIBABIN PYRROCOLINE (INDOLIZINE) SYNTHESIS

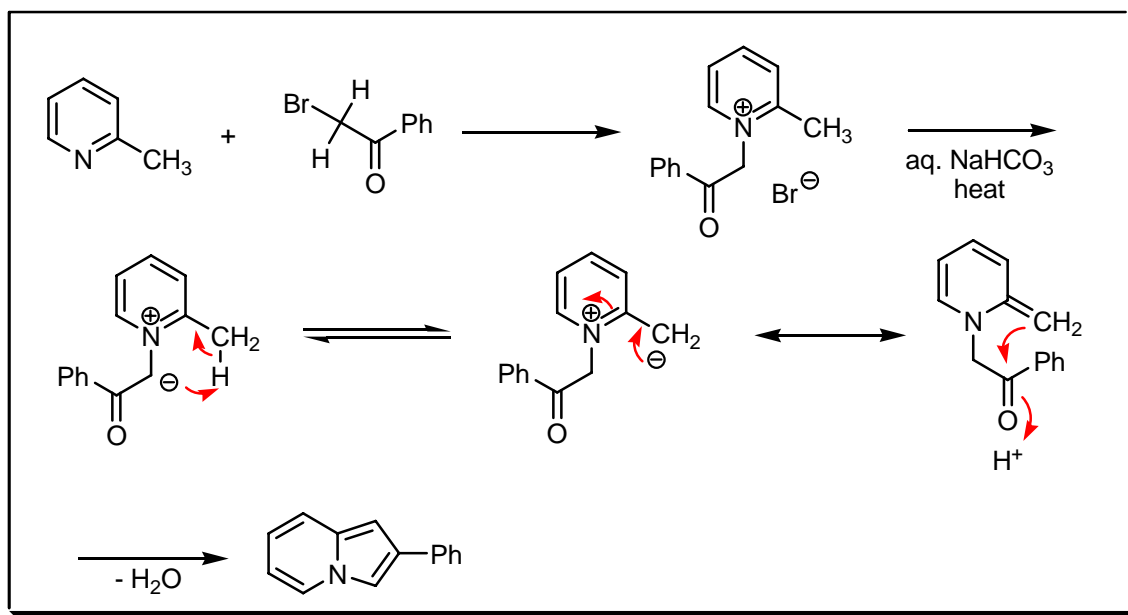
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### EXAMPLE :

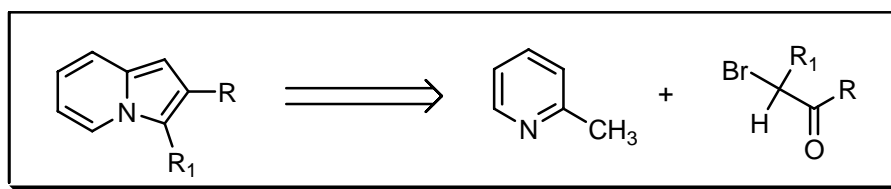




## MECHANISM :



## DISCONNECTION :



## NOTES :

Pyrrocolines are obtained by the cyclisation of the quaternary compounds formed from  $\alpha$ -picolines and  $\alpha$ -haloketones. See also **Scholtz** reaction.

## REFERENCES :

Houben – Weyl : E6/b1, 323

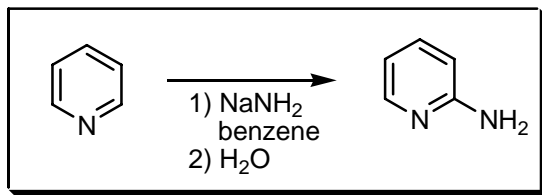
Science of Synthesis : 10, 765

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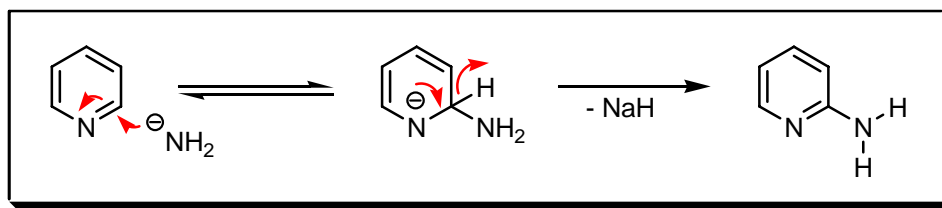
COMMENTS :

## CHICHIBABIN REACTION

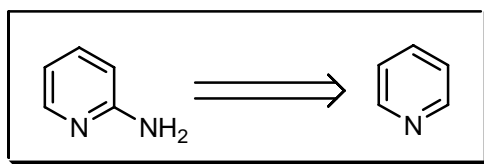
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

Heterocyclic bases, such as pyridine or quinoline or their derivatives, react with metal amides to yield amino derivatives. Intramolecular reactions are known. For a detailed reaction mechanism see **McGill** and **Rappa**.

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March : 668

Smith – March : 873

Houben – Weyl : **E7a**, 412, 765; **E7b**, 143, 187

Org. React. : 1, 91

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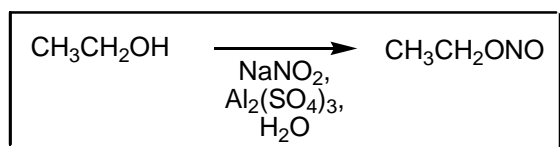
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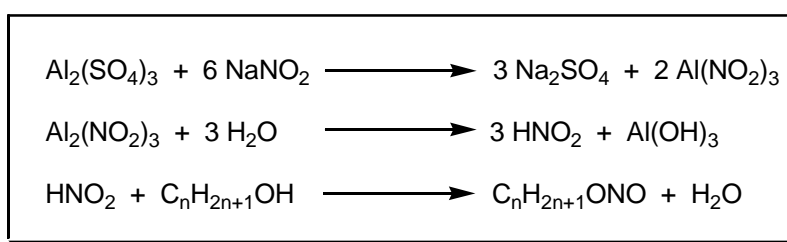
**COMMENTS :**

## CHRÉTIEN – LONGI NITROSATION

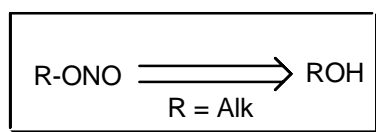
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**

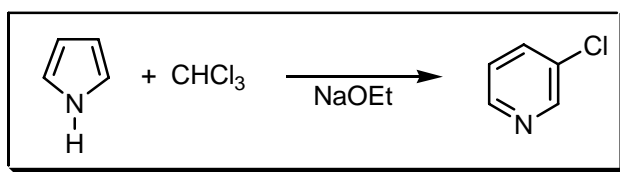
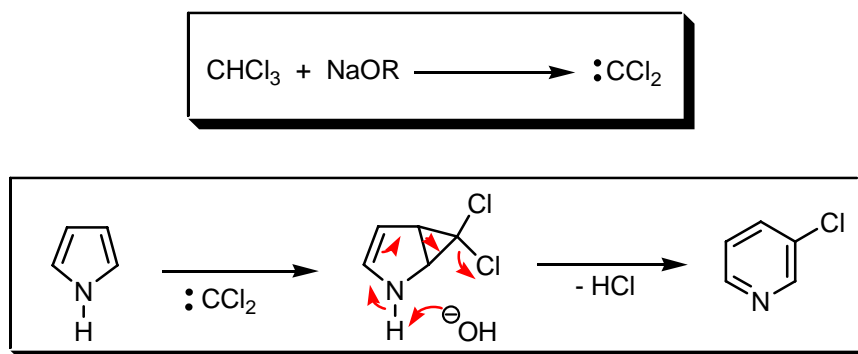
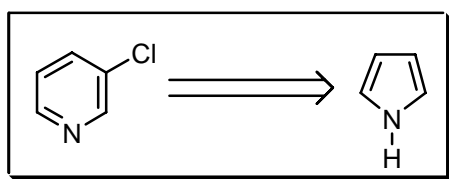


**NOTES :**

The aliphatic alcohol is treated with saturated aqueous sodium nitrite in the presence of aluminium sulfate to afford a nitroso compound.

**REFERENCES :**

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**COMMENTS :****CIAMICIAN – DENNSTEDT REARRANGEMENT****EXAMPLE :****MECHANISM :****DISCONNECTION :**

## NOTES :

The ring-expansion of pyrroles to pyridines by thermal methods or by the treatment of pyrroles with a variety of reagents, chloroform and sodium ethoxide. See also **Reimer – Tiemann** reactions.

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## REFERENCES :

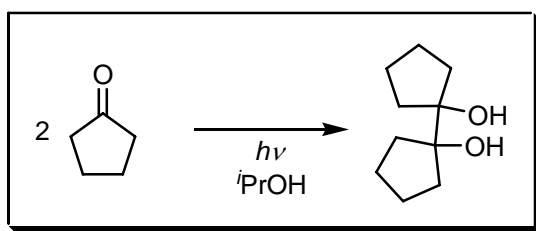
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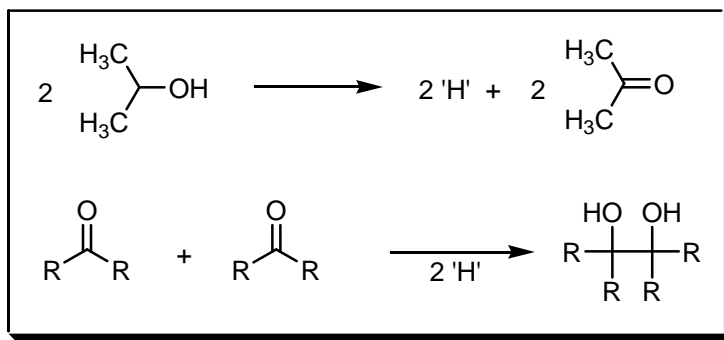
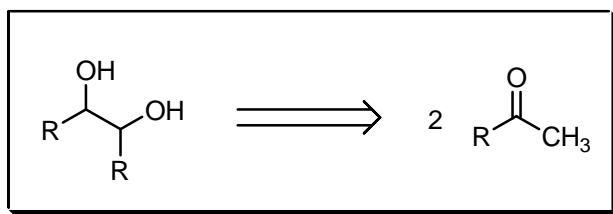
## COMMENTS :

## CIAMICIAN PHOTO COUPLING

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### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

The reductive coupling of ketones to diols. The isopropanol is the proton source. See also **Holleman** reaction.

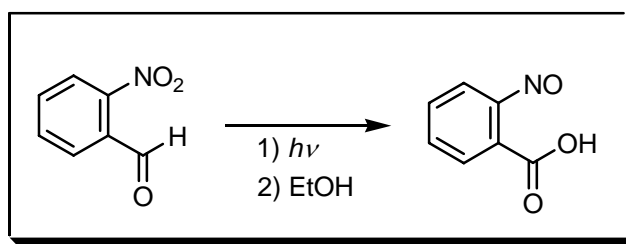
**REFERENCES :**

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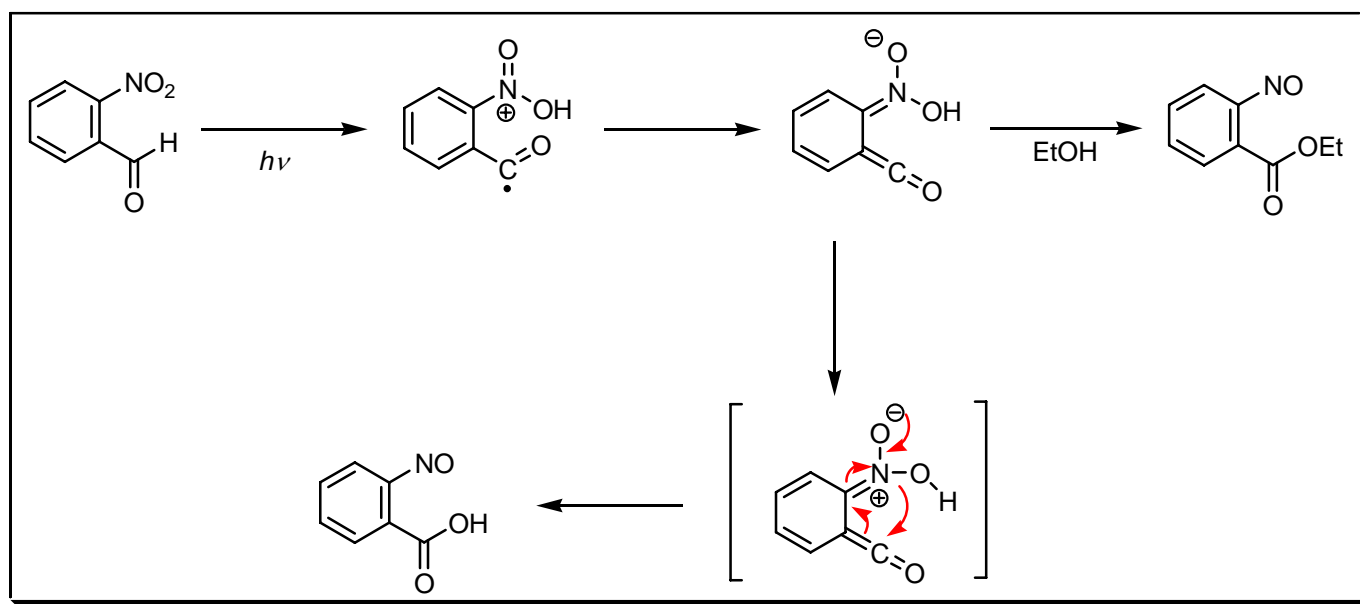
**COMMENTS :**

## CIAMICIAN PHOTO DISPROPORTIONATION

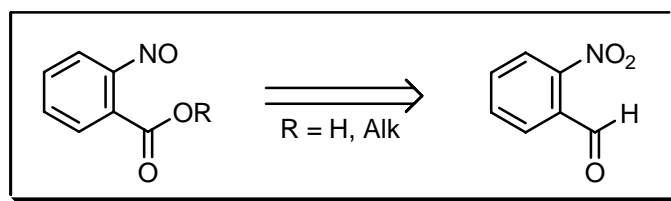
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The rearrangement from *o*-nitrobenzaldehyde to *o*-nitrosobenzoic acid in sun light, both in solution and solid state. The reaction is also possible using *o*-nitrophenylarsenicoxide.

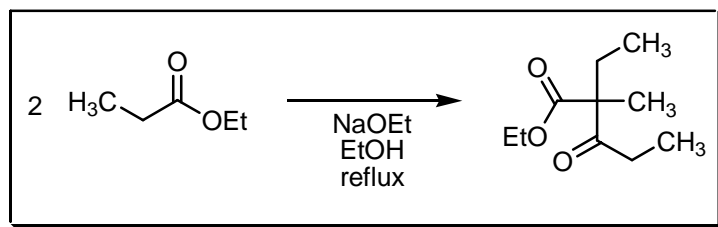
## REFERENCES :

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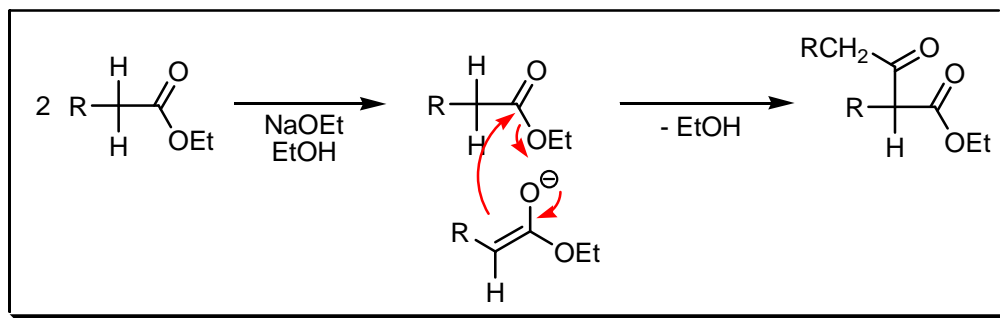
## COMMENTS :

## CLAISEN – GEUTHER CONDENSATION

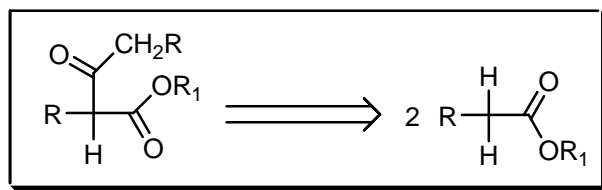
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The **Claisen – Geuther** condensation is the reaction of an ester containing an  $\alpha$ -hydrogen that can be removed by base with a second molecule of ester (acetoacetic ester condensation). The **Claisen – Schmidt** condensation is a



variation where the ester enolate anion reacts with an aldehyde. **Claisen** condensations are easier to carry out with thioesters. Solvent-free reactions are also possible. See also **Bouveault – Locquin**, **Claisen – Schmidt**, **Claisen – Wislicenus**, **Dieckmann**, **Erlenmeyer – Plöchl**, **Henry**, **Perkin** reaction and **Stobbe** reactions.

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#### REFERENCES :

**March** : 491

**Smith – March** : 1223

**Smith** : 892

**Smith 2<sup>nd</sup>** : 746

**Houben – Weyl** : **8**, 560

**Org. React.** : **1**, 266; **15**, 1

**Org. Synth.** : **30**, 43; **39**, 27

**Org. Synth. Coll. Vol.** : **4**, 461, 536

**Science of Synthesis** : **10**, 148, 601

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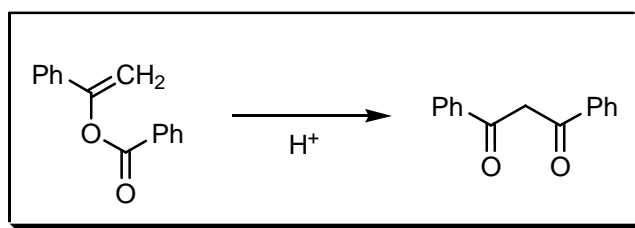
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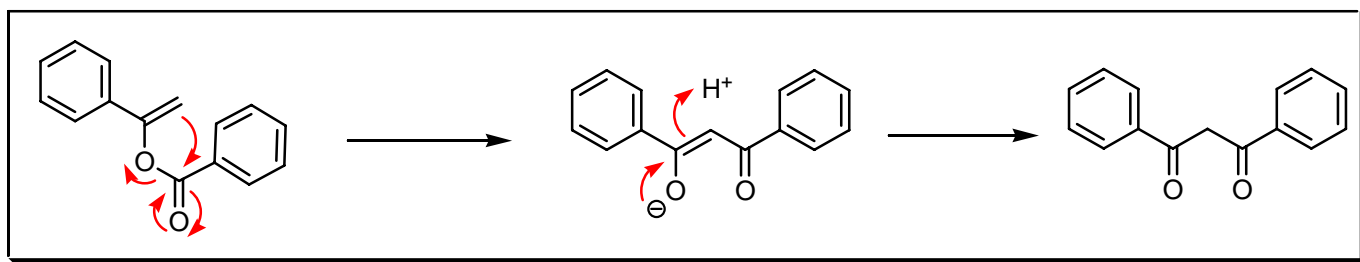
#### COMMENTS :

## CLAISEN – HAASE ENOL ESTER TRANSFORMATION

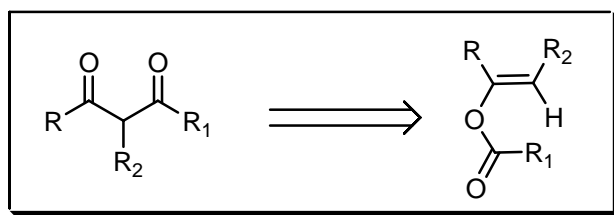
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The transformation of enol esters into C-acyl derivatives, under the influence of bases. Acid catalysts such as boron trifluoride are also effective. The reaction is *intermolecular* when base-catalysed and probably *intramolecular* when acid-catalysed. See also **Fries** rearrangement.

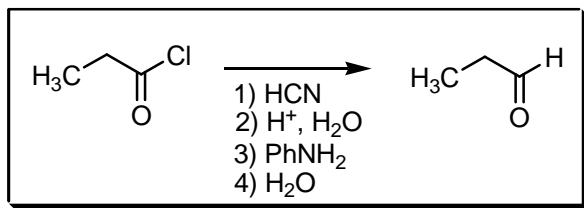
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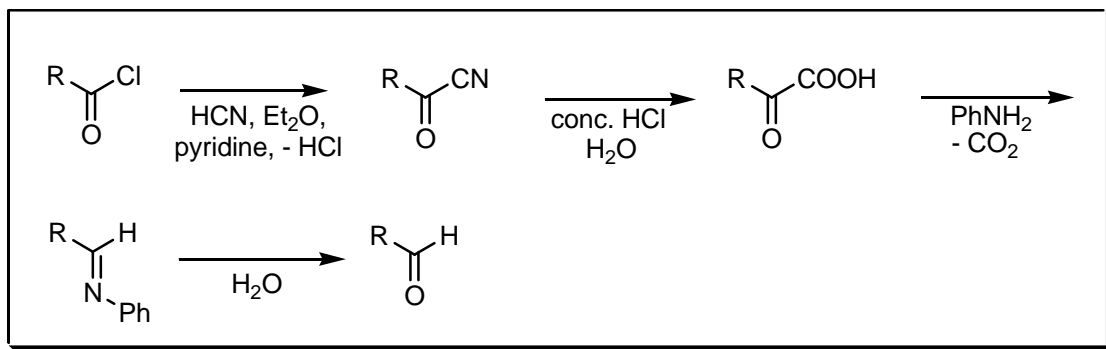
COMMENTS :

CLAISEN – MAUTHNER – BOUVEAULT SYNTHESIS

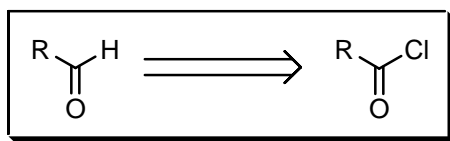
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

An acyl chloride is converted into the acyl cyanide by treatment with ethereal hydrogen cyanide in the presence of pyridine. The resulting nitrile when treated with cold concentrated hydrochloric acid yields the keto-acid which when treated with aniline gives the aldimine and then the aldehyde on hydrolysis. See also **Brandt**, **Guyot – Gry – Bouveault** and **Kolbe** aldehyde reactions.

REFERENCES :

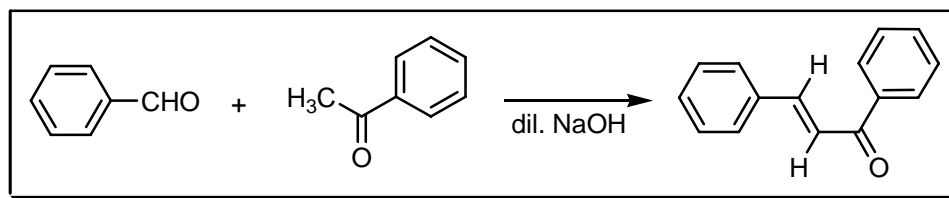
Houben – Weyl : 7/1, 292

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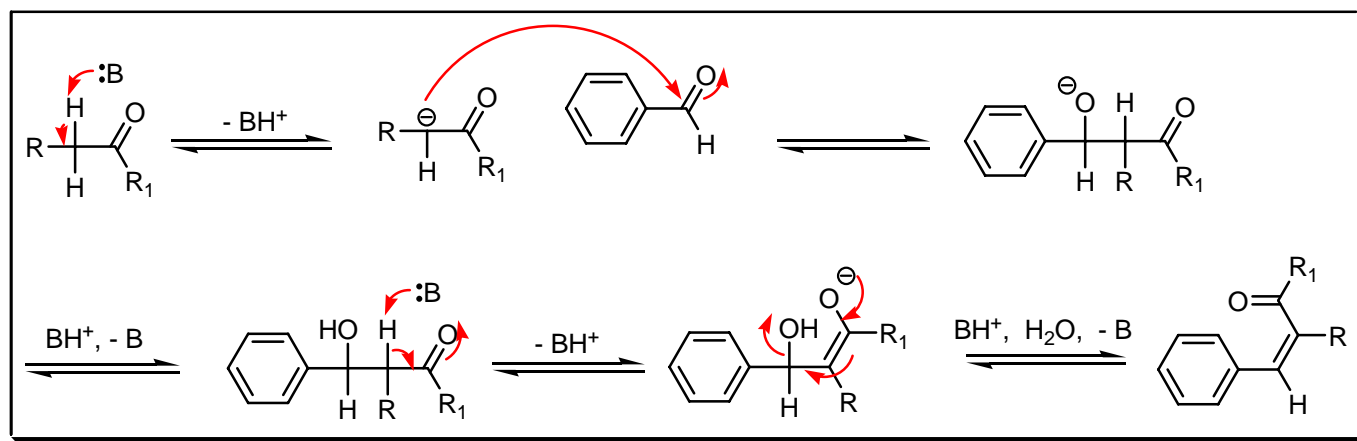
**COMMENTS :**

**CLAISEN – SCHMIDT CONDENSATION**

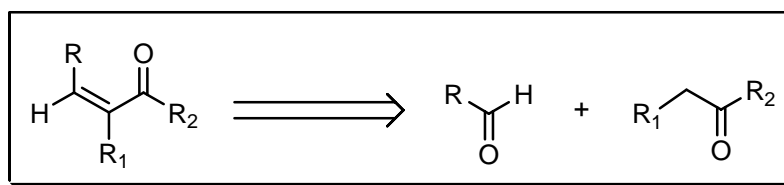
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

The reaction involves the room temperature condensation of an aldehyde or ketone with a compound containing a carbonyl-methylene group. The reaction requires dilute aqueous alkali or acid to occur and affords  $\alpha,\beta$ -unsaturated carbonyl compounds. See also **Claisen** cinnamic, **Claisen – Geuther** and **Perkin** reactions.

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## REFERENCES :

**March** : 940

**Smith – March** : 1221

**Smith** : 886

**Smith 2<sup>nd</sup>** : 740

**Houben – Weyl** : **E5**, 415

**Org. React.** : **16**, 3

**Org. Synth.** : **7**, 42; **12**, 22

**Org. Synth. Coll. Vol.** : **1**, 283; **2**, 167

**Science of Synthesis** : **10**, 101

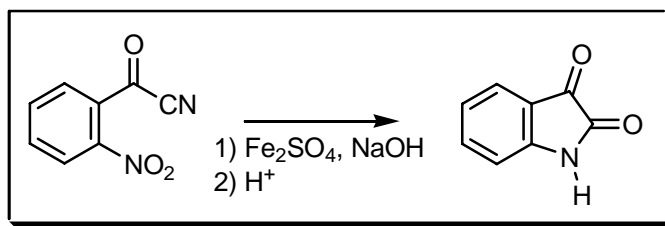
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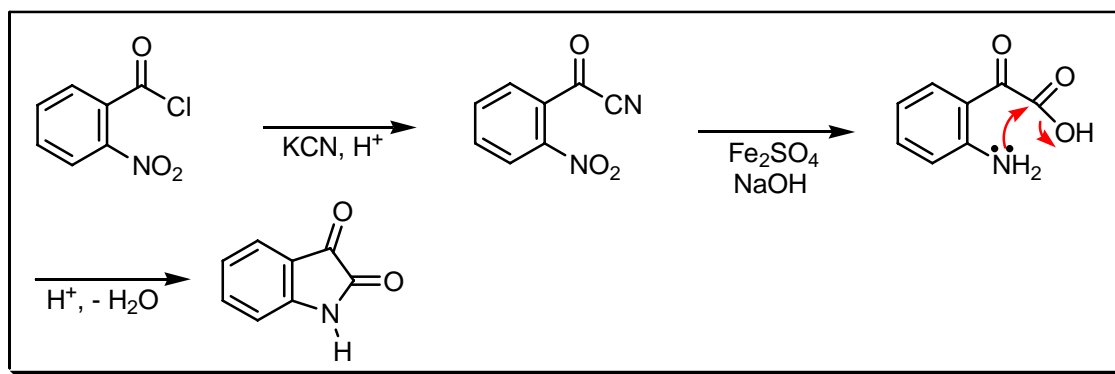
## COMMENTS :

## CLAISEN – SHADWELL SYNTHESIS

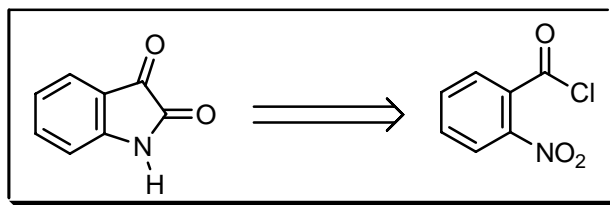
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

An *o*-nitrobenzoyl cyanide is hydrolysed to the acid which is reduced by ferrous hydroxide in alkaline solution to the corresponding *o*-aminophenylglyoxylic acid salt. Acidification yields an isatin derivative. See also **Sandmeyer** diphenylurea isatin and **Sandmeyer** isonitrosoacetanilide isatin reactions.

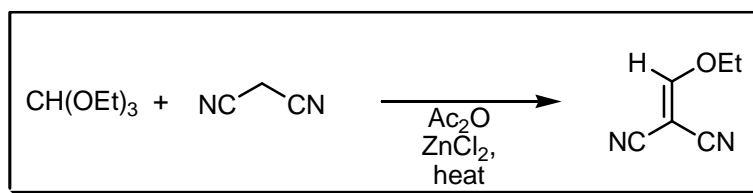
### REFERENCES :

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- 2) J. von Braun; G. Hahn, *Ber. Dtsch. Chem. Ges.*, 1923, **56**, 2343.
- 3) W.C. Sumpter, *Chem. Rev.*, 1944, **34**, 393.

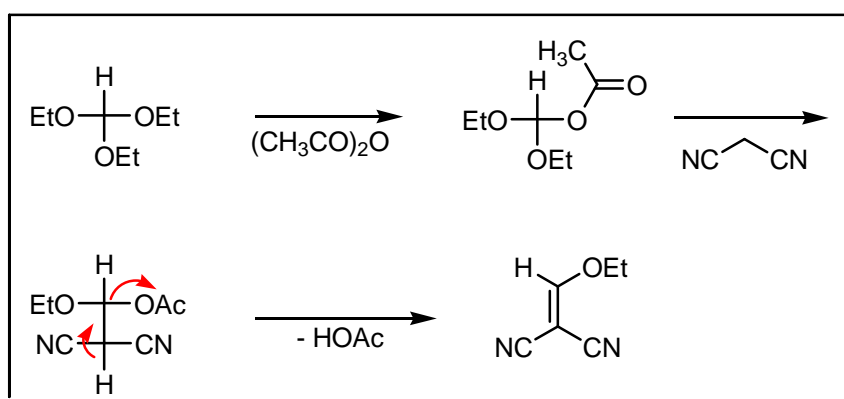
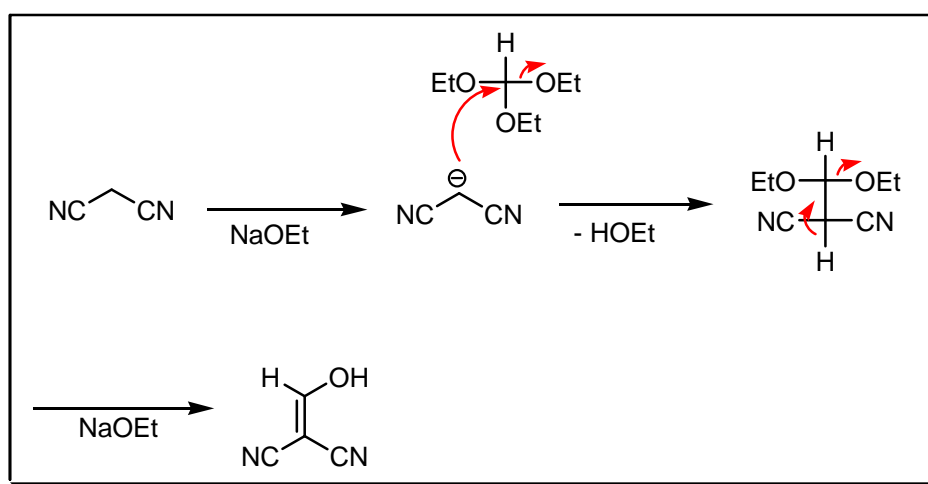
COMMENTS :

## CLAISEN – WISLICENUS CONDENSATION

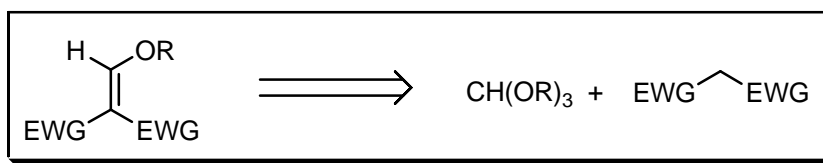
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

This reaction involves the condensation of ethyl formate with a compound containing an active hydrogen in the presence of sodium or sodium alkoxide to give a hydroxymethylene compound. A variation of this reaction involves the condensation of ethyl orthoformate in the presence of acetic anhydride with compounds containing active methylene groups to form ethoxymethylene derivatives. For the **Claisen** ortho ester rearrangement of indol-3-ylalkanols see Science of Synthesis. See also **Claisen** condensation and **Knoevenagel** condensation.

## REFERENCES :

Houben – Weyl : **7/1**, 44; **8**, 580

Org. React. : **1**, 266

Org. Synth. : **28**, 60

Org. Synth. Coll. Vol. : **3**, 395

Science of Synthesis : **10**, 593

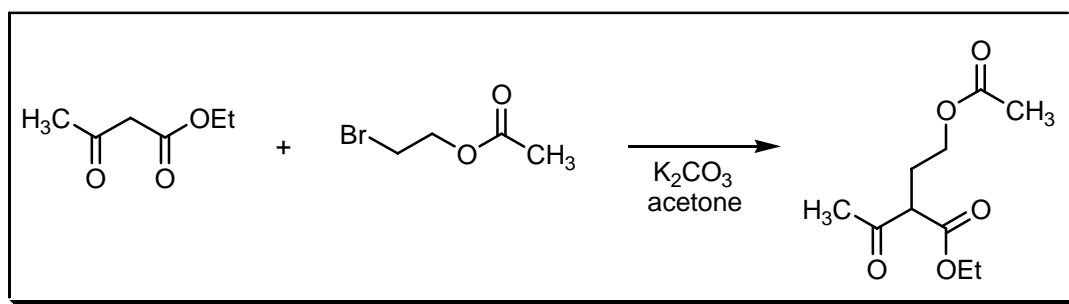
- 1) W. Wislicenus, *Ber. Dtsch. Chem. Ges.*, 1887, **20**, 2938.
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## COMMENTS :

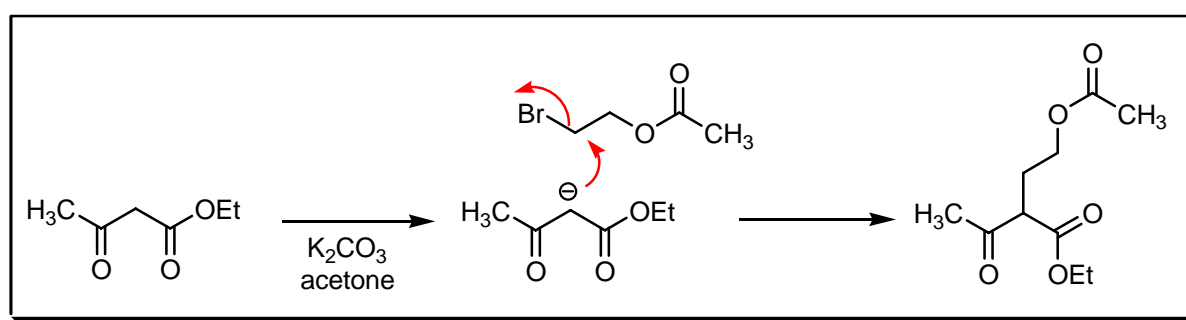


## CLAISEN CARBONATE ALKYLATION

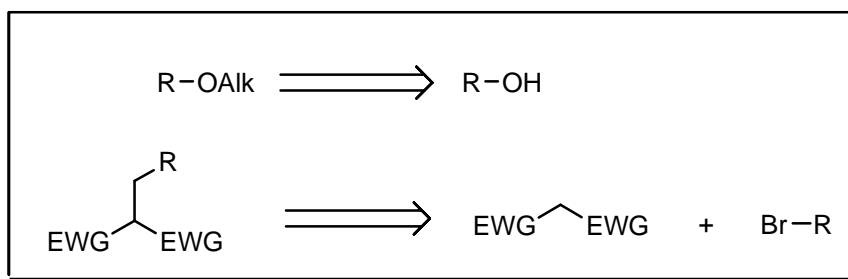
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

A widely used method for the alkylation of hydroxyl groups using an alkyl halide and potassium carbonate in acetone. The technique can also be applied to the C-alkylation of  $\beta$ -keto-carboxylic esters and O-alkyl derivatives are also formed. See also **Knoevenagel** condensation, **Perkin** alicyclic, **Robertson – Robinson** reactions.

## REFERENCES :

March : 464

Smith – March : 548

Smith : 875

Smith 2<sup>nd</sup> : 733

Houben – Weyl : 8, 603

Org. React. : 9, 107

Org. Synth. : 25, 9

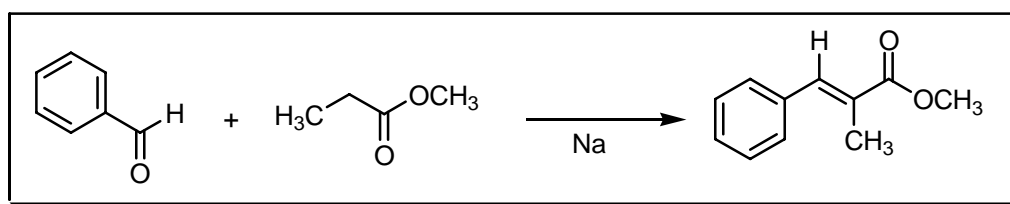
Org. Synth. Coll. Vol. : 3, 140

- 
- 1) L. Claisen, *Ber. Dtsch. Chem. Ges.*, 1890, **23**, 976.
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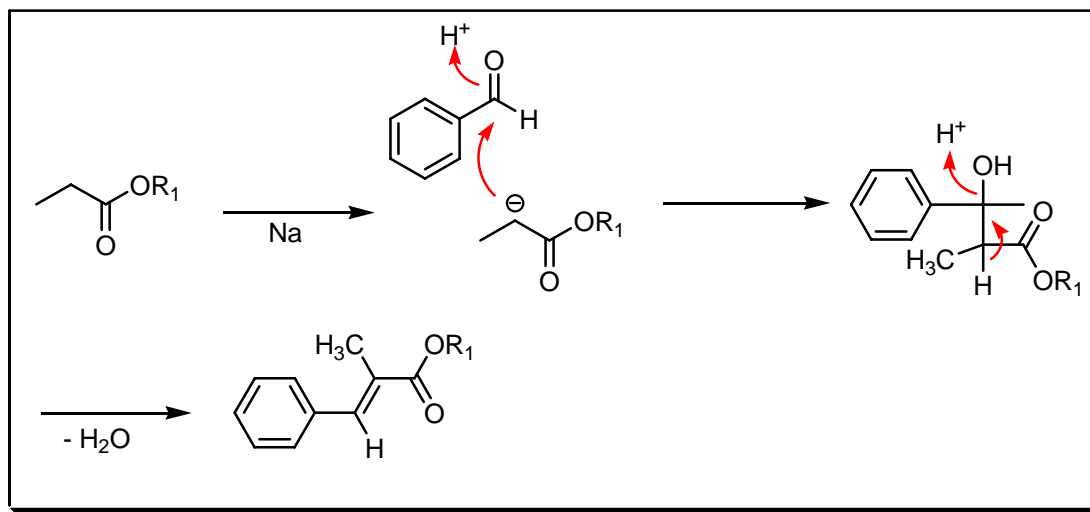
## COMMENTS :

## CLAISEN CINNAMIC ESTER SYNTHESIS

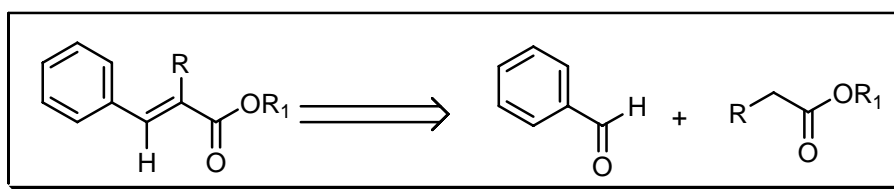
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Cinnamic esters are obtained by the condensation of aromatic aldehydes in the presence of sodium metal with esters of the type  $\text{RCH}_2\text{CO}_2\text{R}$ . See also **Claisen – Geuther** condensation, **Claisen – Schmidt**, **Knoevenagel** condensation, and **Perkin** reactions.

### REFERENCES :

Houben – Weyl : 4/2, 25; 8, 514; E3, 646

Org. Synth. : 9, 38

Org. Synth. Coll. Vol. : 1, 252

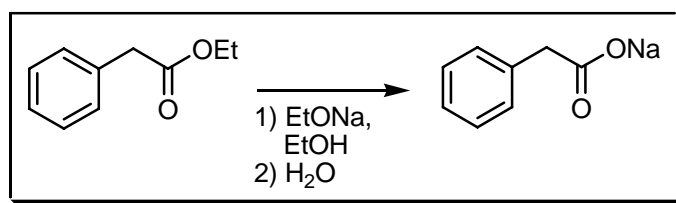
1) L. Claisen, *Ber. Dtsch. Chem. Ges.*, 1890, **23**, 976.

2) T.T. Howarth; A.J. Jackson; J. Judge; G.W. Kenner; D.J. Newman, *J. Chem. Soc., Perkin Trans. 1*, 1974, 490.

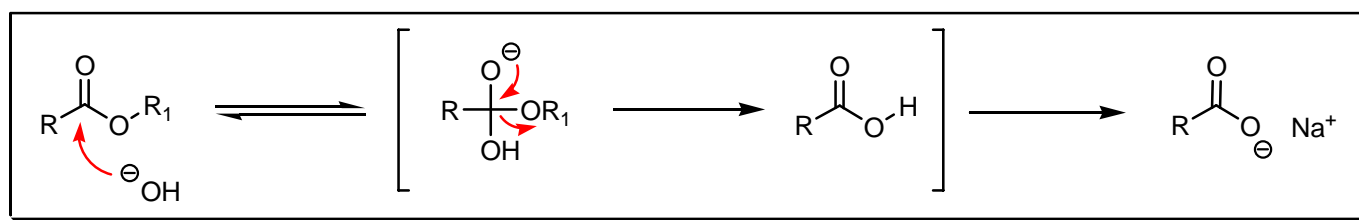
### COMMENTS :

## CLAISEN HYDROLYSIS

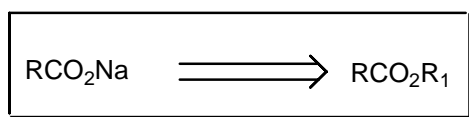
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This method which is suitable for the preparation of unstable acids from their esters involves the addition of the ester to a solution of one mole of sodium ethoxide in absolute ethanol followed by treatment of the solution with one mole of water. An ethereal solution of the ester can also be employed. See also **Twitchell** process.

### REFERENCES :

March : 378

Smith – March : 469

Houben – Weyl : 8, 423

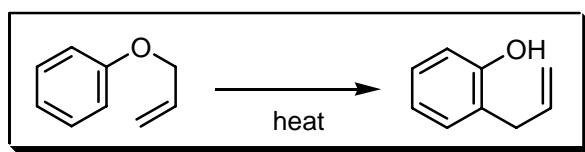
L. Claisen, *Ber. Dtsch. Chem. Ges.*, 1905, **38**, 693.

### COMMENTS :

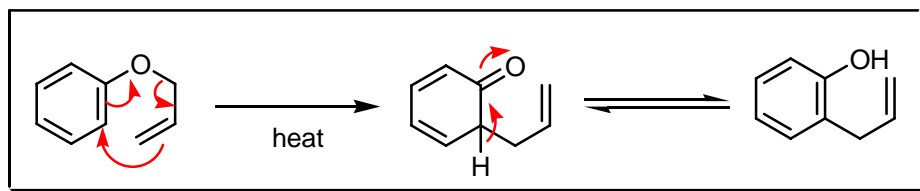
## CLAISEN REARRANGEMENT (CLAISEN – IRELAND REARRANGEMENT)

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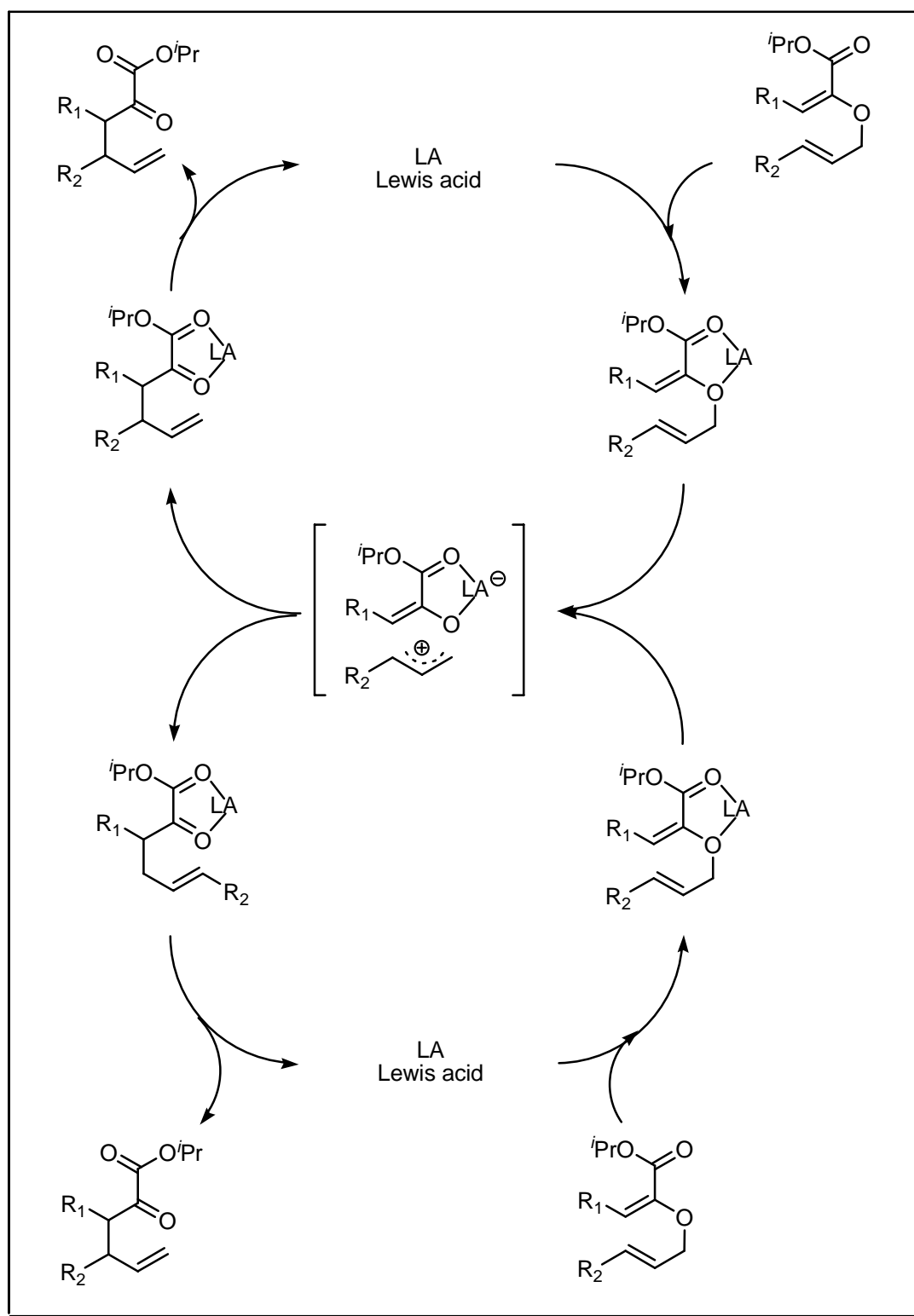
**EXAMPLE :**



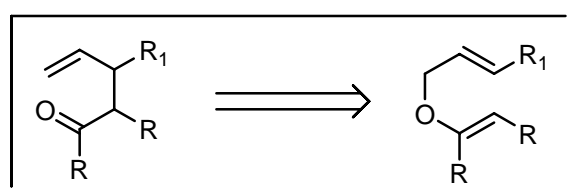
**MECHANISM :**



## Lewis acid catalysis :



## DISCONNECTION :



## NOTES :

The classic **Claisen** rearrangement ([3,3]-sigmatropic rearrangement) involves aromatic allyl ethers. The ester enolate reaction is very similar to the **Carroll (Kimel – Cope)** reaction and **Claisen – Ireland** rearrangement, *i.e.* the rearrangement of allyl esters as enolate anions to  $\gamma,\delta$ -unsaturated acids. By using boron enolates the reaction can be made enantioselective. A wide range of Lewis acids has also been used in this rearrangement. The **Arnold** variation uses strong base ( $^n\text{BuLi}$ ) to form the enolate. **Thio-Claisen** and **aza-Claisen** rearrangements are also known and have been reviewed. An anion-accelerated **Claisen** rearrangement has been reported by **Denmark *et al.*** Allyl aryl ethers undergo accelerated **Claisen** rearrangements in the presence of a mixture of water and trialkylalanes. Enzymatic rearrangements have also been reported. See also **Belluš – Claisen** rearrangement, **Carroll (Kimel – Cope)**, **Cope**, **Eschenmoser – Meerwein – Claisen** rearrangement, **Ficini – Claisen**, **Johnson – Claisen**, **Marbet – Saucy** and **Overman** rearrangement reactions.

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## REFERENCES :

**March** : 1136, 1140

**Smith – March** : 1449, 1452

**Smith** : 1238, 1243

**Smith 2<sup>nd</sup>** : 642, 848, 950, 1021, 1104

**Houben – Weyl** : **5/1b**, 920; **E3**, 306, 559, 572, 579; **E5**, 291, 877, 1097; **E6b**, 1147; **E7b**, 683; **E8a**, 124; **E8b**, 704; **E8d**, 761, 770; **E10/b2**, 198, 218; **E15**, 294, 3096, 3409; **E16d**, 411, 1157

**Org. React.** : **2**, 1; **22**, 1

**Org. Synth.** : **53**, 116; **66**, 29

**Org. Synth. Coll. Vol.** : **6**, 606; **8**, 536

**Science of Synthesis** : **1**, 367, 371, 374; **9**, 196; **10**, 32, 296

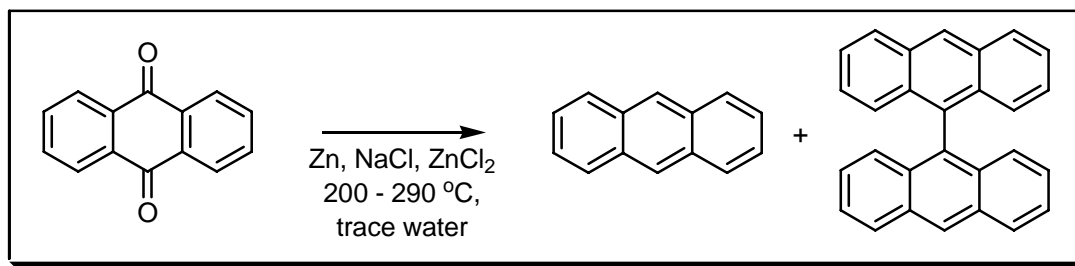
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  - 16) K. Hiratani; K. Kasuga; M. Goto; H. Uzawa, *J. Am. Chem. Soc.*, 1997, **119**, 12677.
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21) M. Hiersemann; L. Abraham, *Eur. J. Org. Chem.*, 2002, 1451.  
22) S.-P. Hong; H.A. Lindsay; T. Yaramasa; X. Zhang; M.C. McIntosh, *J. Org. Chem.*, 2002, **67**, 2042.  
23) K.C. Majumdar; S. Ghosh; M. Ghosh, *Tetrahedron*, 2003, **59**, 7251.  
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25) J.C. Gilbert; J. Yin; F.H. Fakhreddine; M.L. Karpinski, *Tetrahedron*, 2004, **60**, 51.
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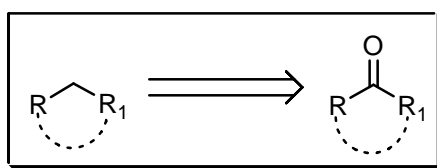
**COMMENTS :**

**CLAR REDUCTION**

**EXAMPLE :**



**DISCONNECTION :**



**NOTES :**

Zinc dust is used as the reducing agent in a molten mixture of sodium chloride and zinc chloride at 200 – 290 °C. The process is assisted by a small quantity of water. The method is of value for the reduction of quinones such as anthraquinone, but can also be applied to other carbonyls of carbocyclic and heterocyclic systems. See also **Clemmensen** reaction.

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- 2) E. Clar, *Ber. Dtsch. Chem. Ges.*, 1939, **72**, 1645.
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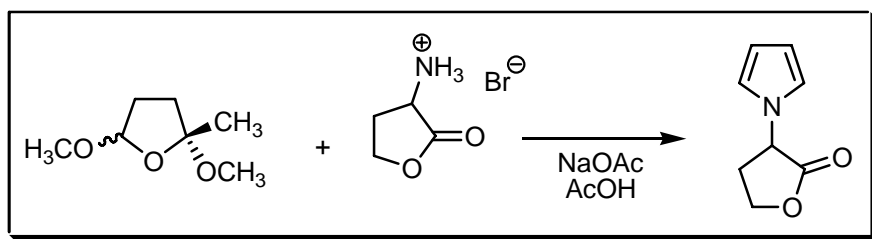
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**COMMENTS :**

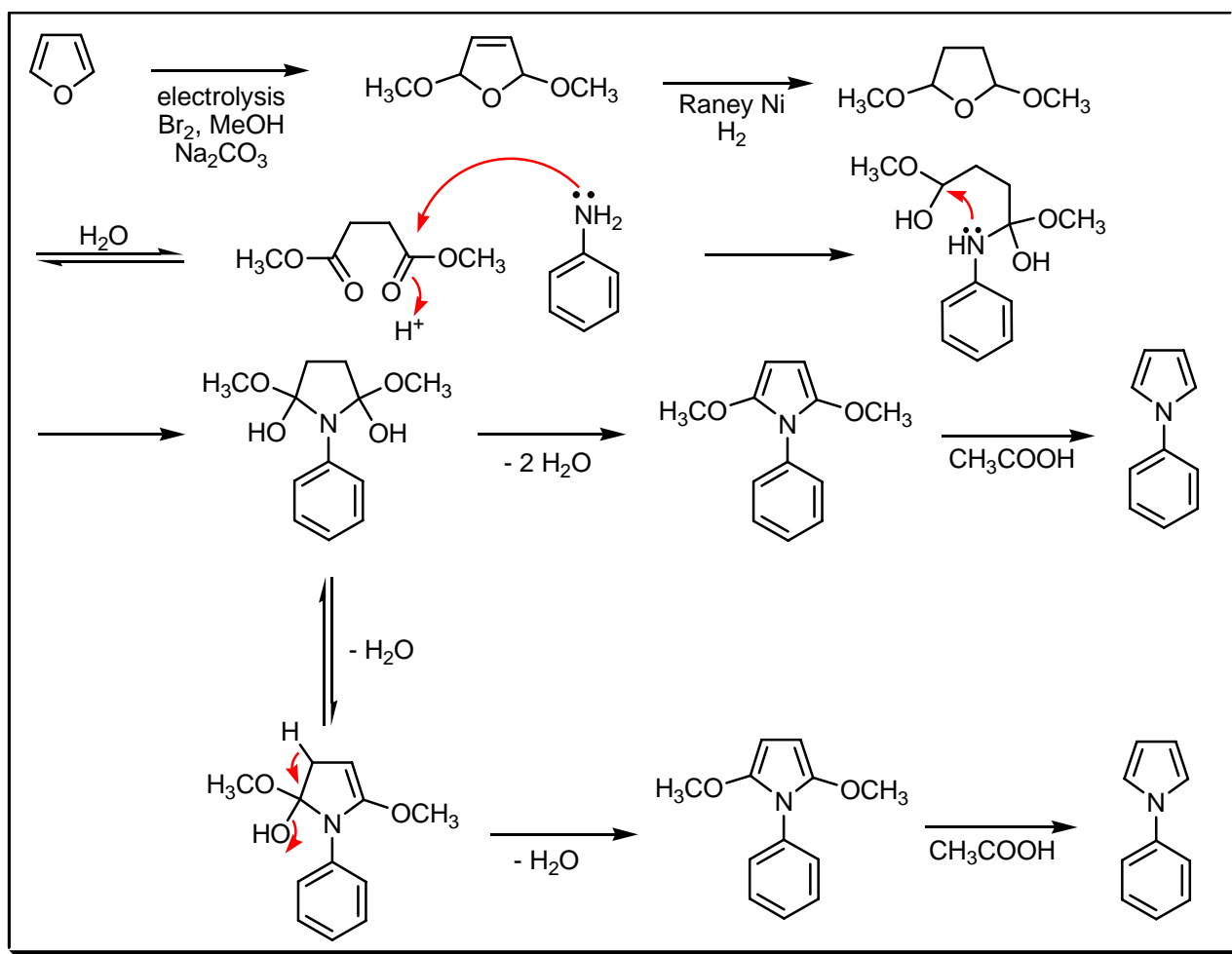
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**CLAUSON-KAAS REACTION**

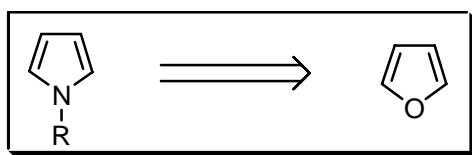
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**EXAMPLE :**

## MECHANISM :



## DISCONNECTION :



## NOTES :

The transformation of 2,5-dialkoxy substituted tetrahydrofurans into *N*-substituted pyrroles using primary amines or ammonia via the **Paal – Knorr** pyrrole reaction. A photo-oxidative analogue has been published by **Feringa** and **Butselaar**. See also **Achmatowicz**, **Barton – Zard**, **Fischer – Fink**, **Grob – Camenisch**, **Hantzsch** pyrrole, **Harries** pyrrole, **Kenner**, **Knorr** pyrrole, **Miller – Plöchl**, **Paal – Knorr**, **Padwa**, **Piloty – Robinson**, **Schwanert**, **Trofimov**, and **Zav'yalov** reactions.

## REFERENCES :

**Org. Synth.** : 40, 29

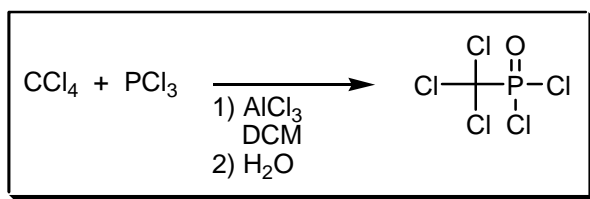
**Org. Synth. Coll. Vol.** : 5, 403

- 1) N. Clauson-Kaas; Z. Tyle, *Acta Chem. Scand.*, 1952, **6**, 667.
- 2) N. Elming; N. Clauson-Kaas, *Acta Chem. Scand.*, 1952, **6**, 867.
- 3) H. Gross, *Chem. Ber.*, 1962, **95**, 2270.
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- 7) M. van den Heuvel; A.D. Cuiper; H. van der Deen; R.M. Kellogg; B.L. Feringa, *Tetrahedron Lett.*, 1997, **38**, 1655.
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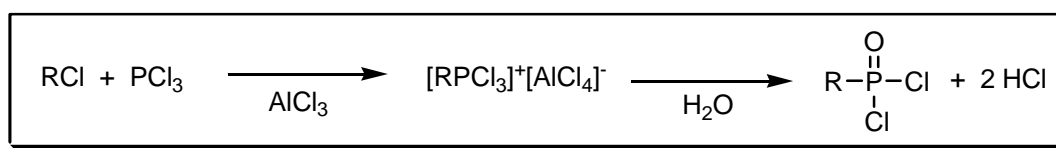
**COMMENTS :**

## CLAY – KINNEAR – PERREN PHOSPHONYL CHLORIDE SYNTHESIS

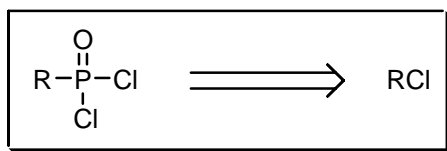
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

The synthesis of alkylphosphonyl dichloride by condensation of alkyl chloride with phosphorus trichloride and aluminium chloride, followed by hydrolysis. *N*-alkyl chlorides with more than 3 carbon atoms afford *sec*-alkyl phosphonyl dichlorides. A carbonium ion mechanism has been proposed. **Hoffmann** *et al.* has introduced a modification of this reaction. See also **Arbusov (Michaelis – Arbuzov)** and **Zinovev – Soborovskii** reactions.

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## REFERENCES :

**Org. Synth.** : **37**, 82

**Org. Synth. Coll. Vol.** : **4**, 950

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1) J.P. Clay, *J. Org. Chem.*, 1951, **16**, 892.

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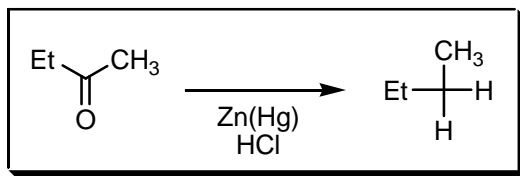
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## COMMENTS :

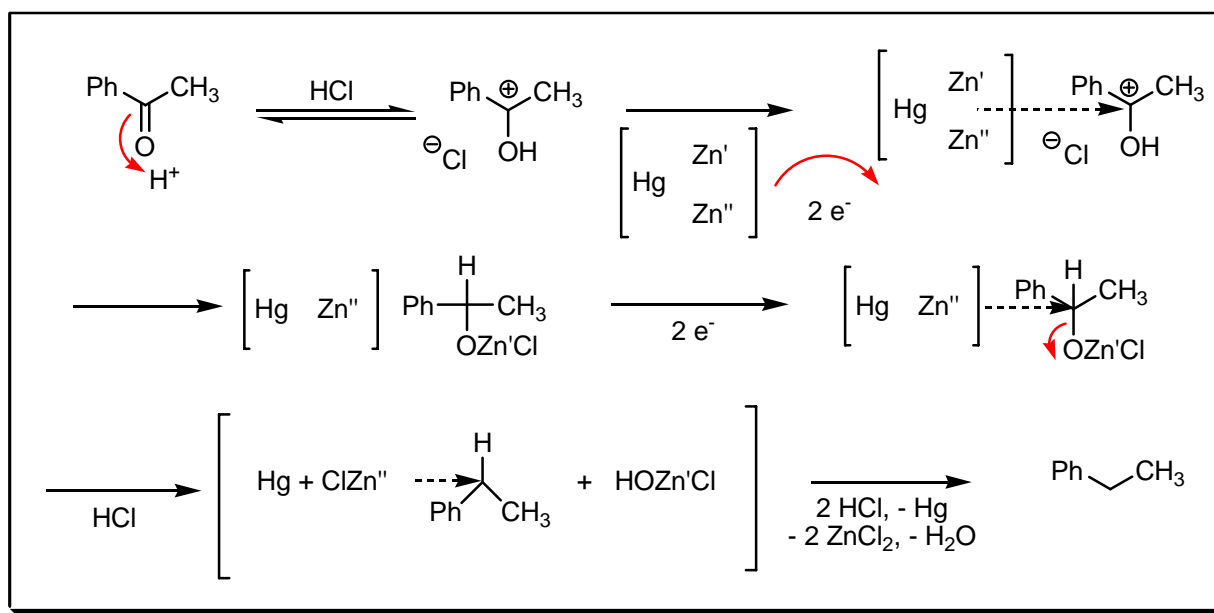
## CLEMMENSEN REDUCTION

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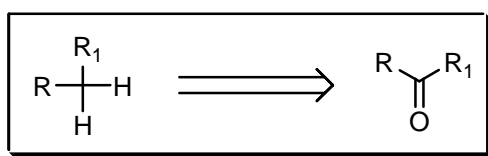
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The replacement of the carbonyl oxygen of the carbonyl group in an aldehyde or ketone by two hydrogen atoms using amalgamated zinc and hydrochloric acid. The reaction is subject to steric effects. Besides the mechanism shown, there is also, although somewhat contradictory, a heterogenous mechanism involving a zinc carbenoid. The **Martin – Sherman** modification gives improved yields and simplifies the work-up by adding a layer of toluene to the reaction mixture. See also **Wolff – Kishner – Staudinger** reaction.

## REFERENCES :

**March** : 1209

**Smith – March** : 1547

**Smith** : 469

**Smith 2<sup>nd</sup>** : 404, 411, 413, 1094, 1136

**Houben – Weyl** : **5/1a**, 244, 450; **E6b**, 437; **E7b**, 258; **E8d**, 469; **E15**, 1457

**Org. React.** : **1**, 155; **22**, 401

**Org. Synth.** : **20**, 57; **33**, 17

**Org. Synth. Coll. Vol.** : **3**, 444; **4**, 203

1) E. Clemmensen, *Ber. Dtsch. Chem. Ges.*, 1913, **46**, 1837.

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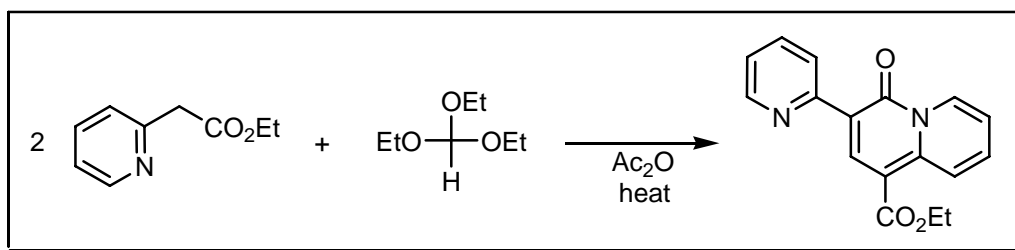
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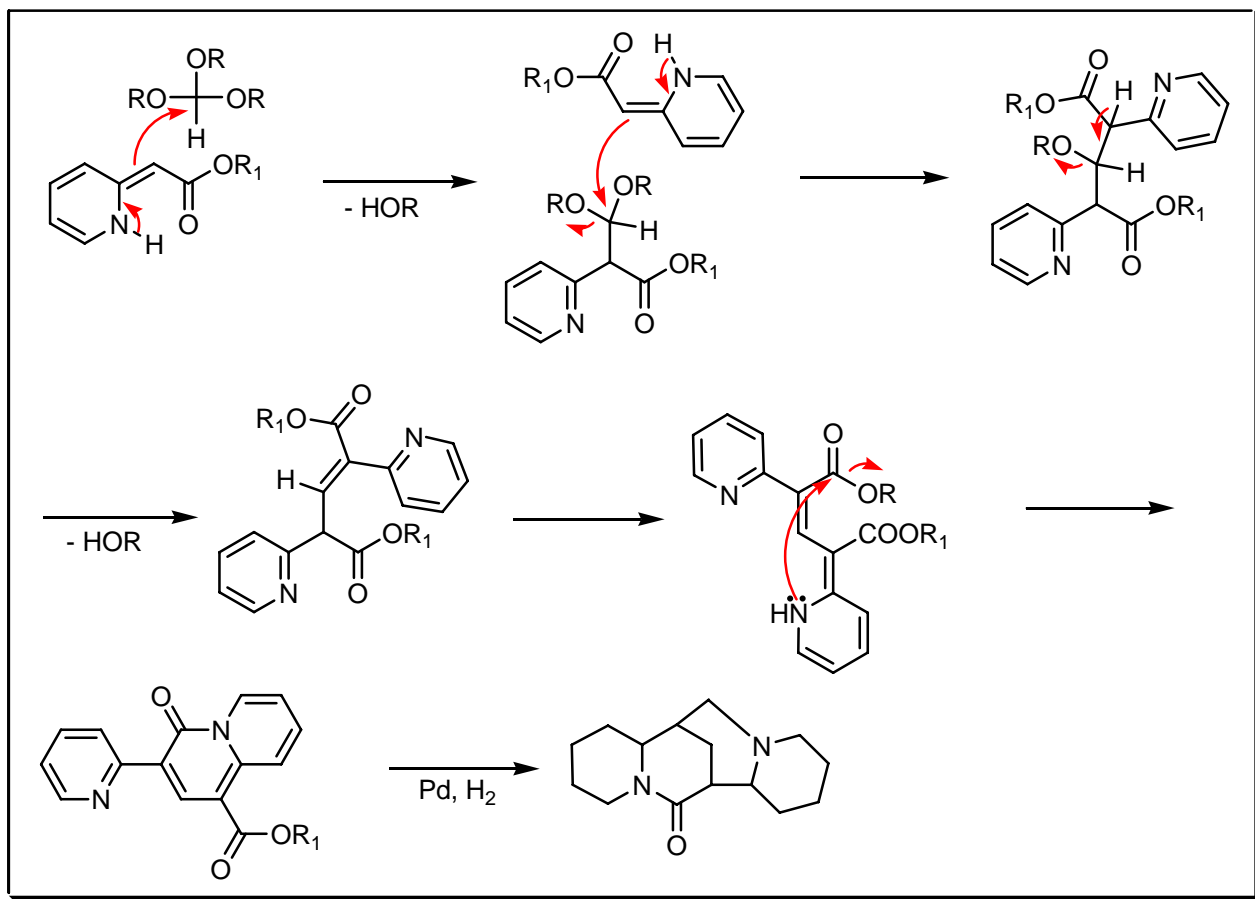
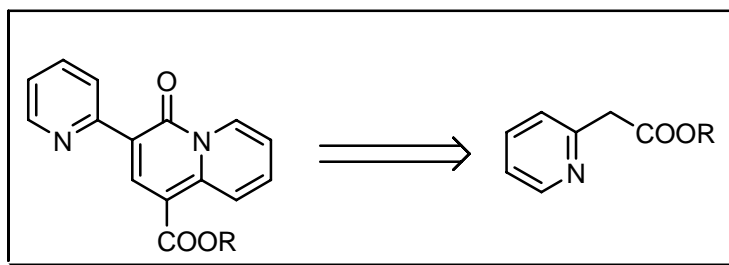
**COMMENTS :**

## CLEMO SYNTHESIS

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**EXAMPLE :**



**MECHANISM :****DISCONNECTION :****NOTES :**

This is a condensation between an orthoformic acid ester and the  $\alpha$ -methylene group of two  $\alpha$ -pyridyl-acetic acid ethyl esters. This method provides a synthetic route to sparteine alkaloids.

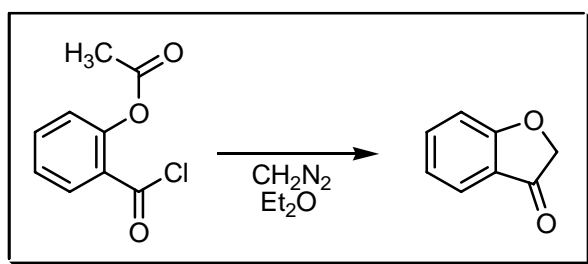
**REFERENCES :**

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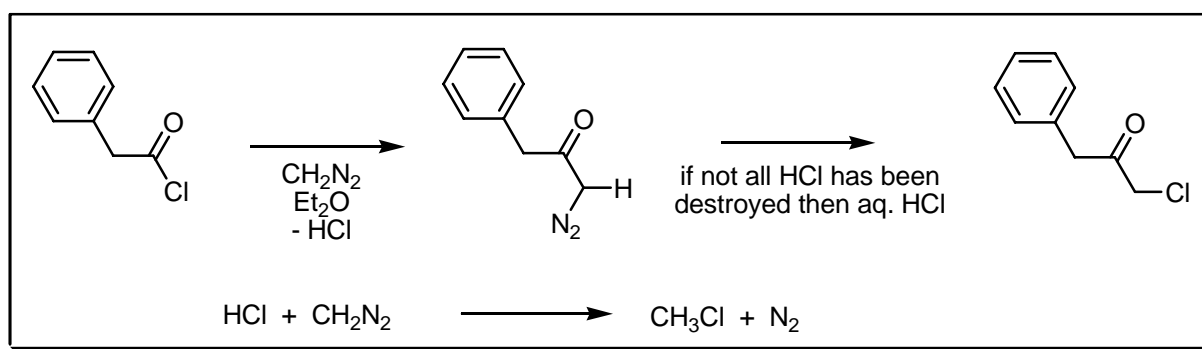
**COMMENTS :**

## CLIBBENS – NIERENSTEIN SYNTHESIS

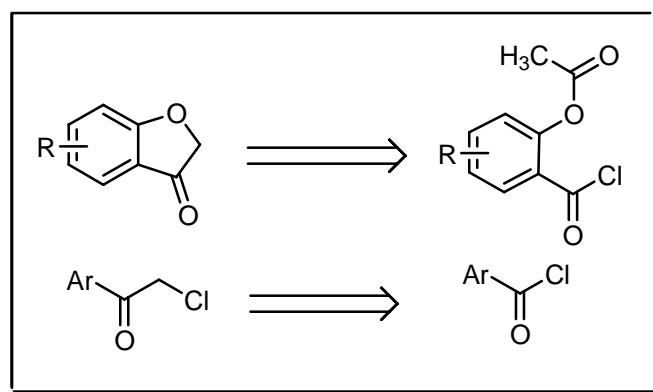
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Aroyl chlorides react with diazomethane in anhydrous diethyl ether to yield ω-chloroacetophenones. Coumaranones may be obtained if an *o*-hydroxyl group is present. This procedure (one mole diazomethane is added to the acid chloride) varied from **Arndt – Eistert**'s procedure where the acid chloride is added slowly to a cold solution of an excess diazomethane. See also **Arndt – Eistert**, **Büchner – Curtius – Schlotterbeck** and **Wolff** rearrangement reactions.



## REFERENCES :

Org. React. : 1, 38

Org. Synth. : 26, 13

Org. Synth. Coll. Vol. : 3, 119

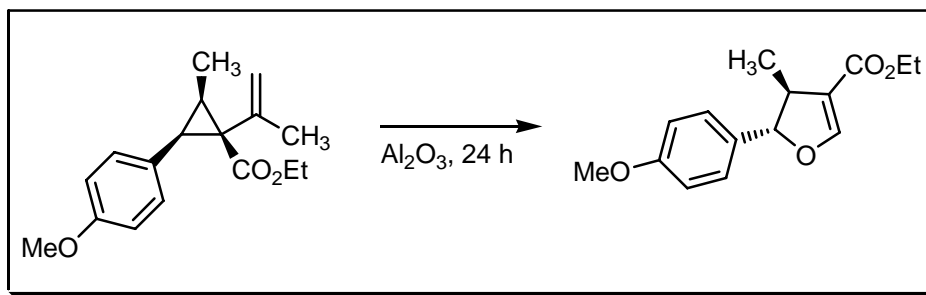
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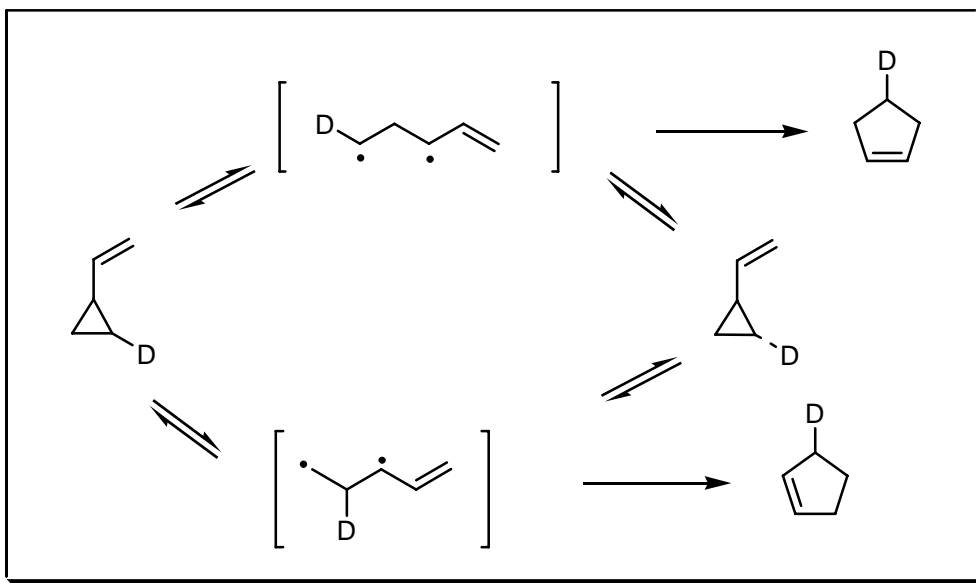
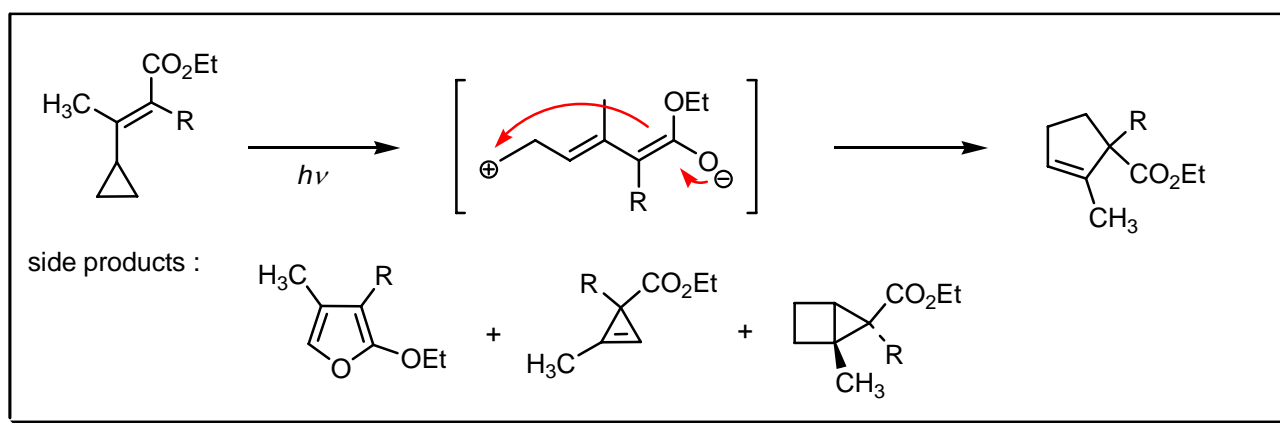
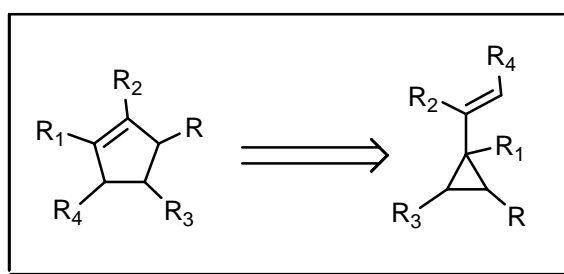
## COMMENTS :

## CLOKE – WILSON CYCLO PROPYL KETONE REARRANGEMENT

---

### EXAMPLE :



**MECHANISM :****Thermal :****Photochemical :****DISCONNECTION :****NOTES :**

The rearrangement of cyclopropyl ketones or imines to dihydrofurans or dihydropyrroles, either thermally (biradical or concerted), photochemically, or transition metal mediated (Rh(I), Rh(III), Ni(0)). The mechanisms are discussed in full in Organic Reactions.

## REFERENCES :

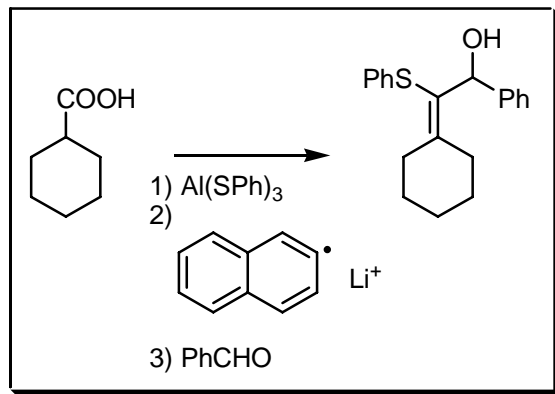
Org. React. : **33**, 247

- 1) J.B. Cloke, *J. Am. Chem. Soc.*, 1929, **51**, 1174.
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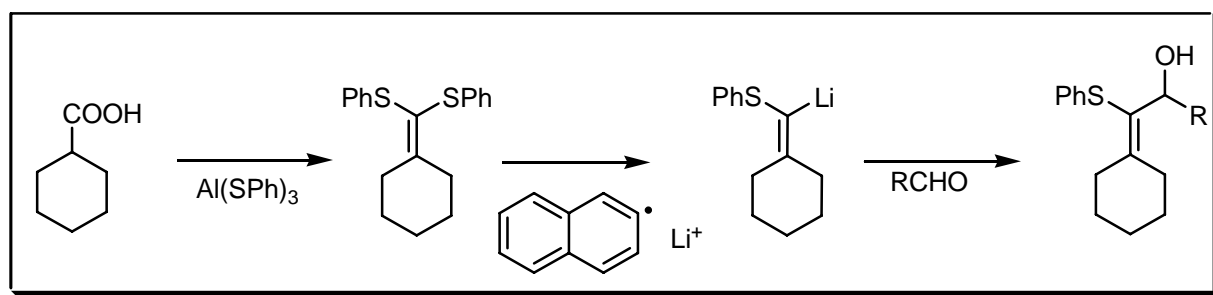
## COMMENTS :

## COHEN – DANIEWSKI PROCESS

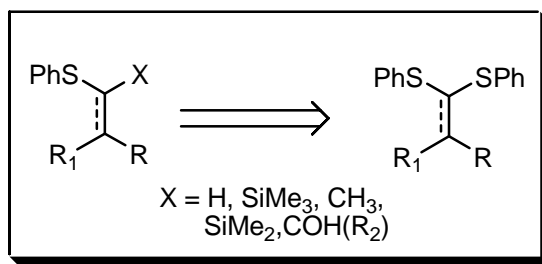
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

This is the reductive lithiation of alkyl phenyl sulfides, breaking the C<sub>sp</sub><sup>3</sup>-S bond. The dissolved radical anion is the source of the electrons. The reaction is useful in forming carbanions. See also **Rigby – Trost** reaction.

## REFERENCES :

March : 729

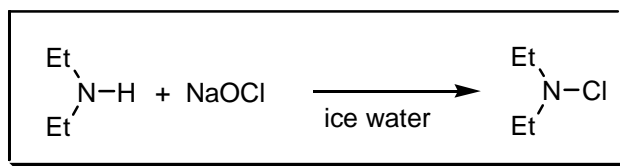
Smith – March : 941

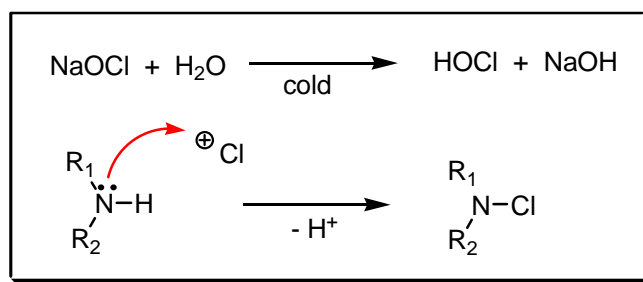
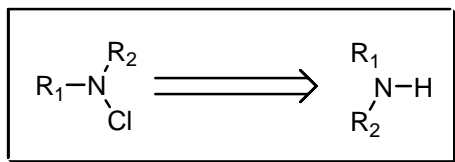
- 1) T. Cohen; W.M. Daniewski, *Tetrahedron Lett.*, 1978, **19**, 2991.
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- 4) T. Cohen; J.R. Matz, *Synth. Commun.*, 1980, **10**, 311.
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- 6) T. Cohen; M. Bhupathy, *Acc. Chem. Res.*, 1989, **22**, 152.

## COMMENTS :

## COLEMAN SYNTHESIS

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

The chlorination of secondary amines at low temperature. The hypochlorous acid is the source of the positive charged chlorine atoms.

**REFERENCES :**

Houben – Weyl : E16a, 878

Org. Synth. : 25, 14

Org. Synth. Coll. Vol. : 3, 159

1) A. Berg, *Ann. Chim. (Paris)*, 1894, **3**, 289.

2) G.H. Coleman, *J. Am. Chem. Soc.*, 1933, **55**, 3001.

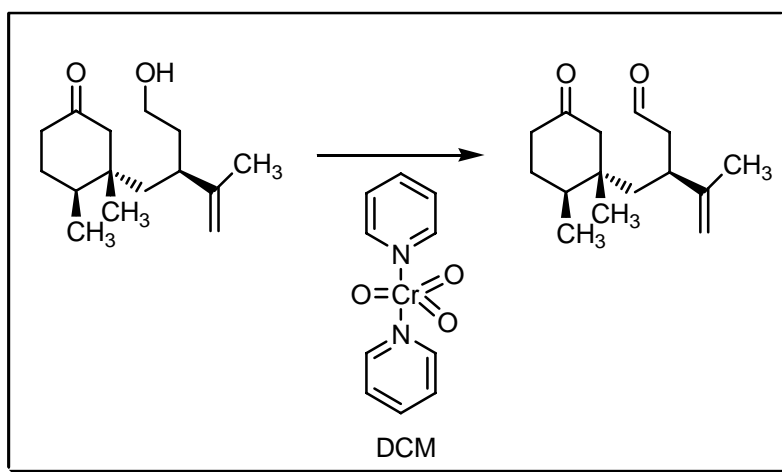
3) V.S. Heasley; P. Kovavic; R.M. Lange, *J. Org. Chem.*, 1966, **31**, 3050.

4) J.M. Antelo; F. Arce; J. Casado; R. Castro; M.E. Sanchez; A. Varela, *Bull. Soc. Chim. Belg.*, 1984, **93**, 35.

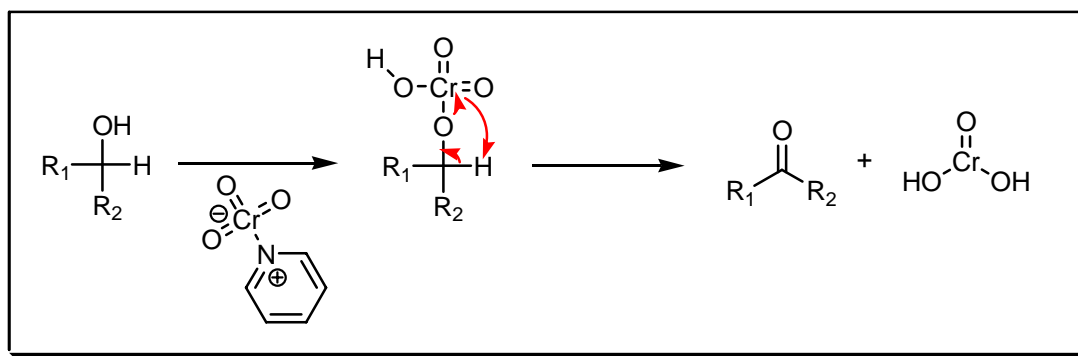
**COMMENTS :**

## COLLINS OXIDATION

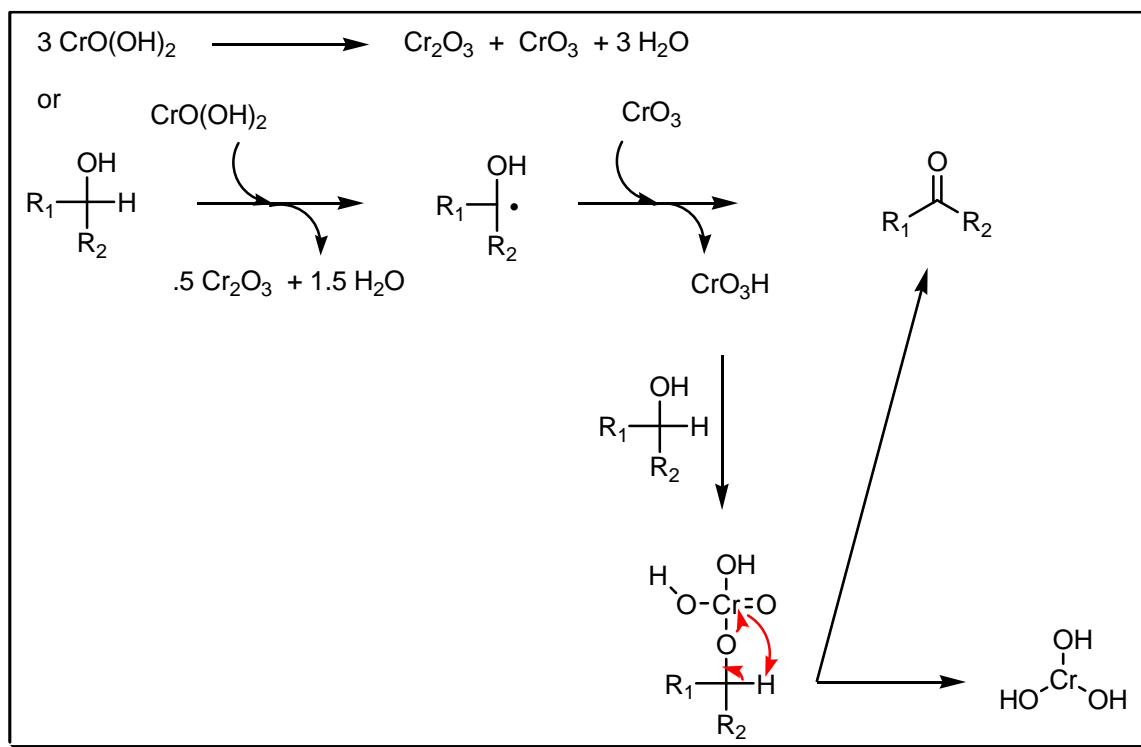
EXAMPLE :



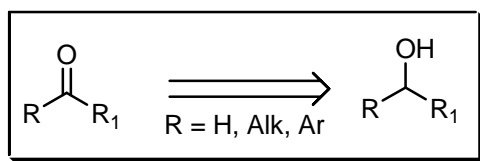
MECHANISM :



## Follow-up chemistry of Cr(IV) :



## DISCONNECTION :



## NOTES :

The reagent formed by the reaction of chromium trioxide and pyridine is first removed from the pyridine solvent and then dissolved in dichloromethane, and the alcohol is then added. There is a **Ratcliffe** modification; Chromium trioxide is added to the solution of pyridine and dichloromethane followed by the alcohol. Chromium-mediated oxidations have a competing pathway involving free-radical intermediates. See also **Anelli**, **Ball – Goodwin – Morton**, **Corey – Kim**, **Corey – Schmidt**, **Corey – Suggs**, **David – Thieffry**, **Delépine**, **Dess – Martin**, **Einhorn** oxidation, **Fétizon**, **Jones** oxidation, **Ley**, **Maurer – Drefahl**, **Mukaiyama** oxidation, **Nicolaou**, **Oppenauer**, **Parikh – von Doering**, **Pinnick**, **Pfitzner – Moffatt**, **Sarett**, **Swern** and **Uemura** reactions.

## REFERENCES :

**Smith – March** : 1514

**Smith** : 229

**Smith 2<sup>nd</sup>** : 199, 542

1) J.C. Collins; W.W. Hess; F.J. Frank, *Tetrahedron Lett.*, 1968, **9**, 3363.

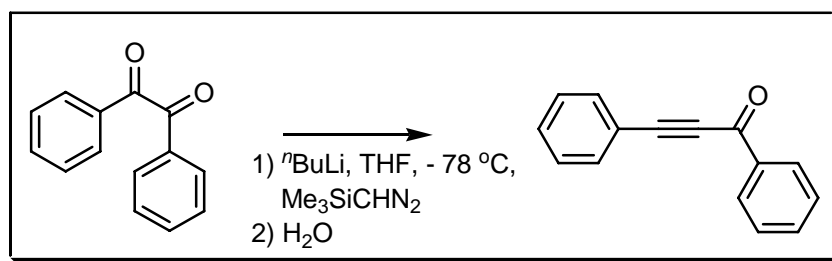
2) R. Ratcliffe; R. Rodehorst, *J. Org. Chem.*, 1970, **35**, 4000.

- 3) M. Li; M.E. Johnson, *Synth. Commun.*, 1995, **25**, 533.  
4) C. Provent; P. Chautemps; J.L. Pierre, *Synth. Commun.*, 1995, **25**, 1907.  
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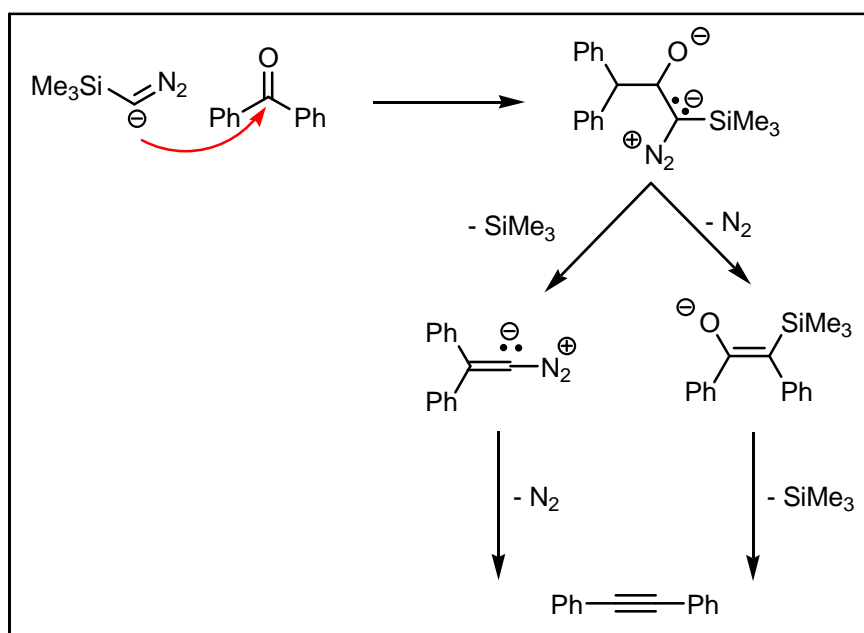
**COMMENTS :**

**COLVIN SYNTHESIS**

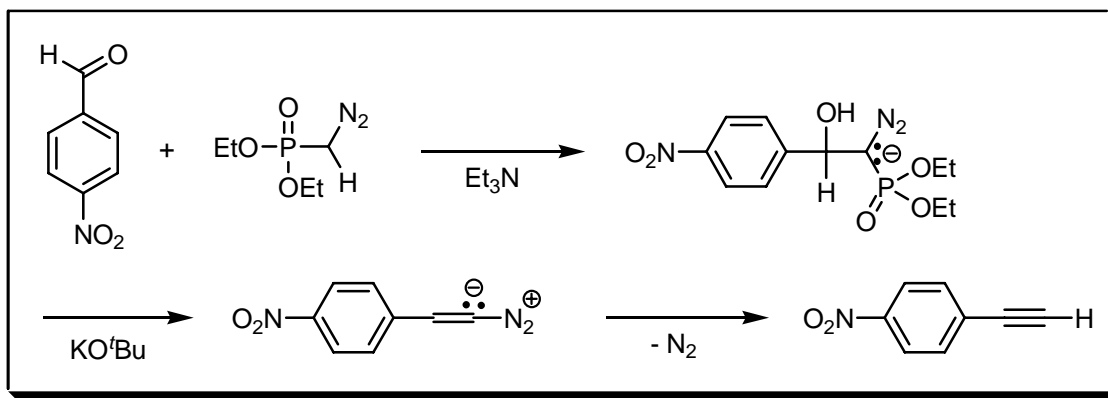
**EXAMPLE :**



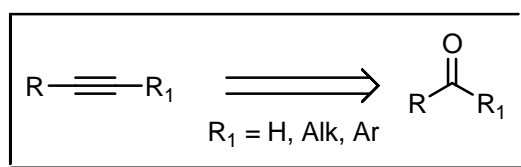
**MECHANISM :**







#### DISCONNECTION :



#### NOTES :

A simple one-step procedure of converting ketones and aldehydes into acetylenes using diazomethyltrimethylsilane or dialkyldiazomethylphosphonates. See also **Corey – Fuchs** and **Kowalski** reactions.

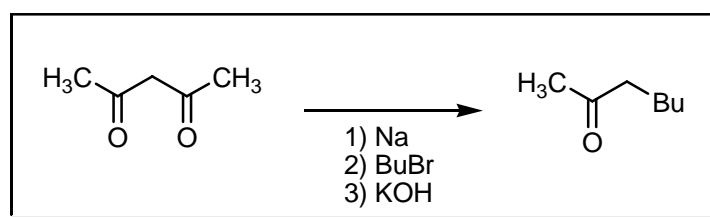
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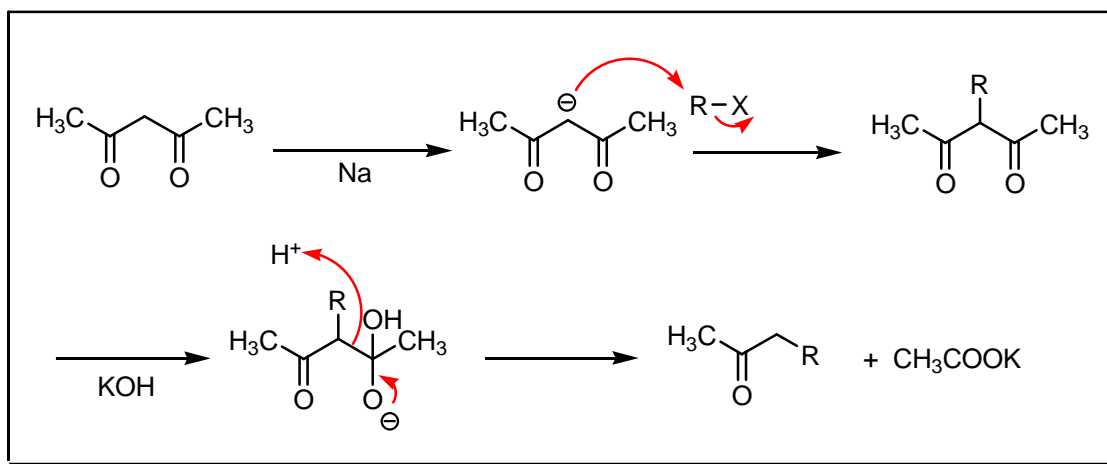
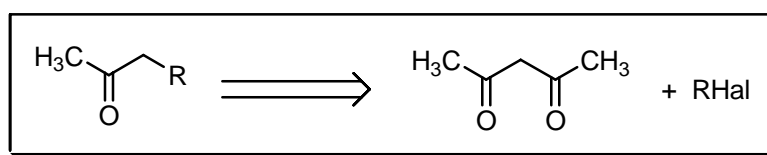
- 1) E.W. Colvin; B.J. Hamill, *J. Chem. Soc., Chem. Commun.*, 1973, 151.
- 2) E.W. Colvin; B.J. Hamill, *J. Chem. Soc., Perkin Trans. 1*, 1977, 869.
- 3) S. Ohira; K. Okai; T. Moritani, *J. Chem. Soc., Chem. Commun.*, 1992, 721.

#### COMMENTS :

### COMBES ACETYLACETONE SYNTHESIS

#### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

Acetylacetone is deprotonated with sodium and reacts with alkyl and aryl halides to yield a C-substituted derivative, which can be decomposed by alkali to a methyl ketone and an acetate.

**REFERENCES :**

Org. Synth. : 20, 6

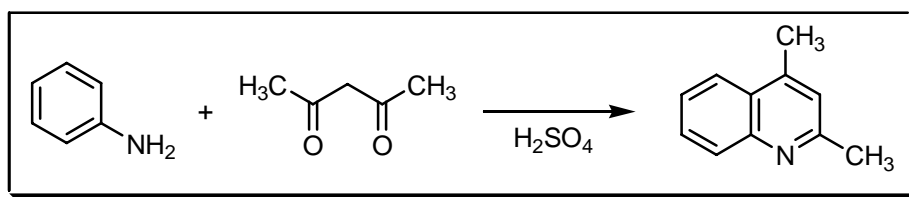
Org. Synth. Coll. Vol. : 3, 16

A. Combes, *C.R. Séances Acad. Sci.*, 1887, **104**, 920.

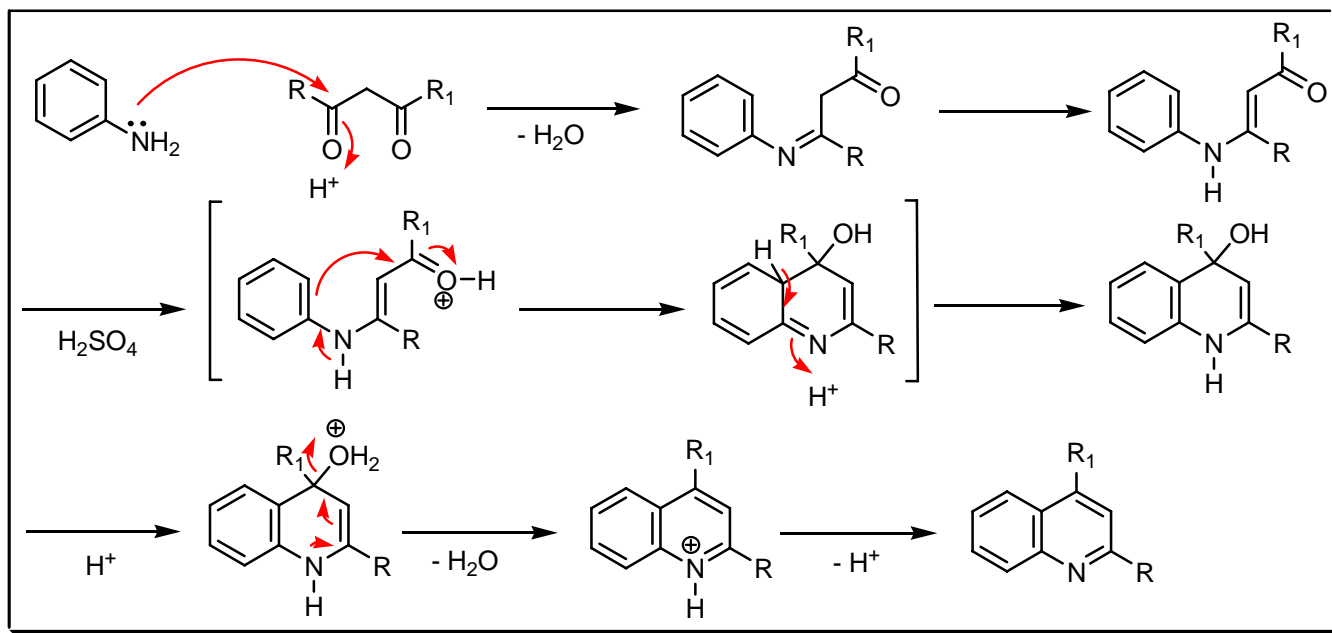
**COMMENTS :**

## COMBES QUINOLINE SYNTHESIS

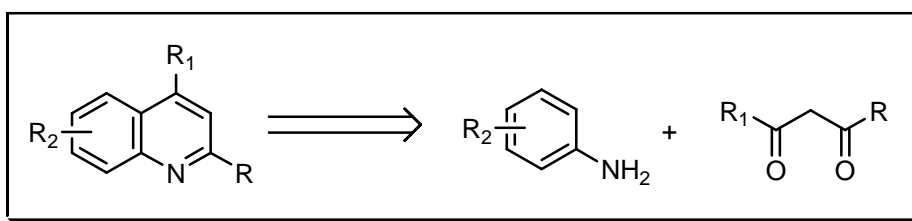
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

$\beta$ -Diketones react with primary arylamines to give  $\beta$ -amino-enone, which can be converted into 2,4-disubstituted quinolines using concentrated sulfuric acid. See also **Allan – Loudon**, **von Baeyer – Drewson** quinoline, **Camps**, **Conrad – Limpach**, **Doebner** quinoline, **Doebner – von Miller**, **Foulds – Robinson**, **Friedländer**, **Knorr** quinoline, **Meth–Cohn**, **von Niementowski** quinoline, **Pfitzinger – Borsche**, **Riehm** quinoline and **Skraup** quinoline reactions.

## REFERENCES :

Smith : 1336

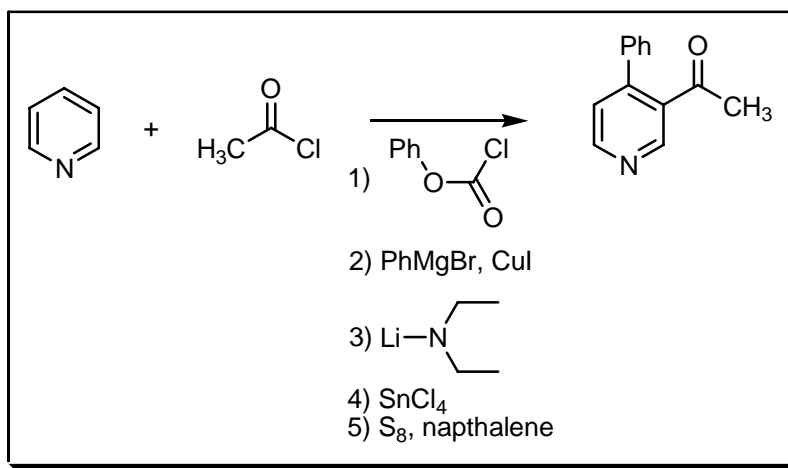
Smith 2<sup>nd</sup> : 1099

- 
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  - 2) F.W. Bergstrom, *Chem. Rev.*, 1944, **35**, 77.
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  - 7) E. Davioud-Charvet; S. Delarue; C. Biot; B. Schwoebel; C.C. Boehme; A. Müssigbrodt; L. Maes; C. Sergheraert; P. Grellier; R.H. Schirmer; K. Becker, *J. Med. Chem.*, 2001, **44**, 4268.
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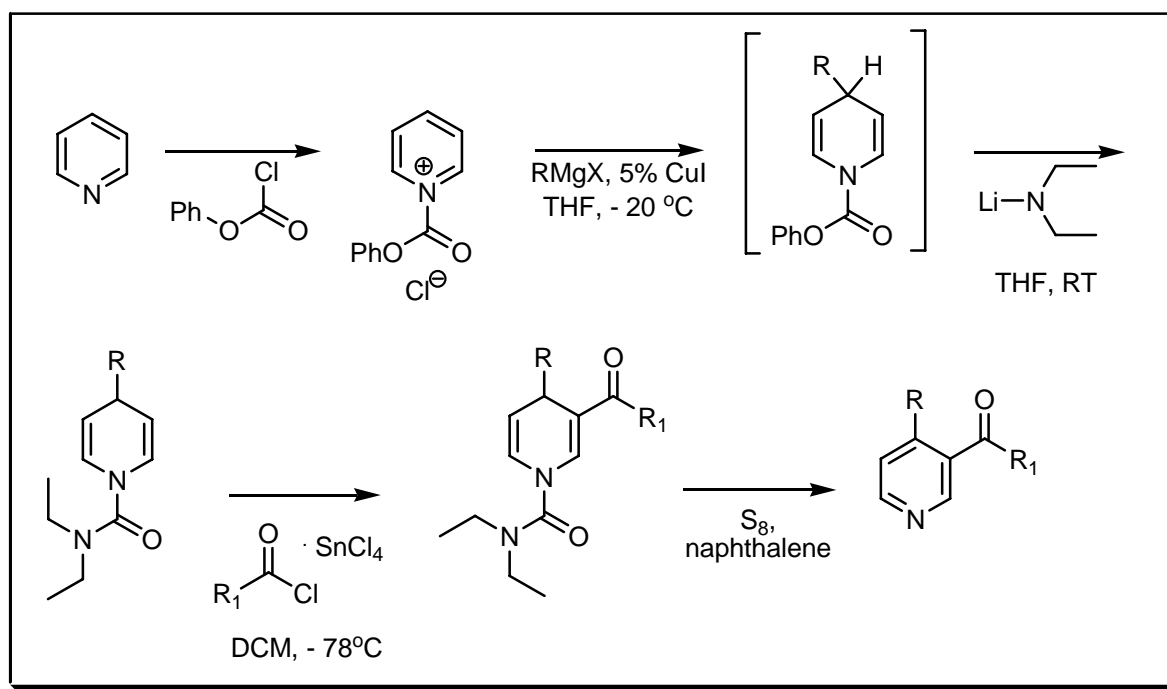
## COMMENTS :

## COMINS ADDITION

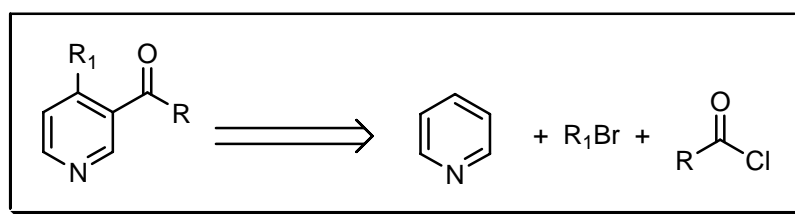
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The **Friedel – Crafts** acylation fails in the pyridine series, this is due to the basicity of the nitrogen atom. This reaction can also be used for the regioselective nucleophilic addition to substituted pyridines. See also **Emmert – Asendorf**, **Friedel – Crafts** and **Wibaut – Arens** reactions.

## REFERENCES :

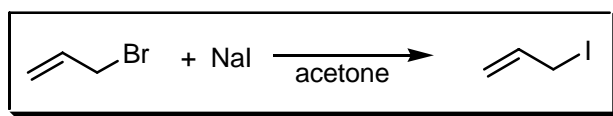
- 1) R.E. Lyle; D.L. Comins, *J. Org. Chem.*, 1976, **41**, 3250.
- 2) D.L. Comins; N.B. Mantlo, *Tetrahedron Lett.*, 1983, **24**, 3683.
- 3) I. Lantos; K. Gombatz; M. McGuire; L. Pridgen; J. Remich; S. Shilcrat, *J. Org. Chem.*, 1988, **53**, 4223.
- 4) D.L. Comins; M.M. Badawi, *Heterocycles*, 1991, **32**, 1869
- 5) B. Munoz; C. Chen; I.A. McDonald, *Biotechnol. Bioeng.*, 2000, **71**, 78.

## COMMENTS :

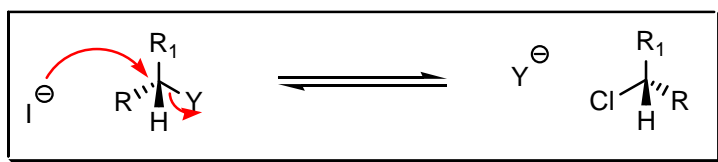
## CONANT – FINKELSTEIN HALOGEN EXCHANGE

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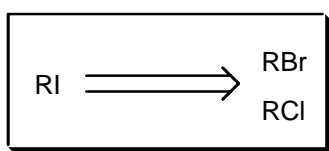
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The preparation of alkyl iodides from their corresponding bromides or chlorides by treatment with sodium iodide in acetone. In the case of 1,2-dihalides an ethylenic derivative is obtained. A mild and general method for the conversion of aryl, heteroaryl and vinyl bromides into their corresponding iodides has been developed by **Buchwald**.

### REFERENCES :

March : 430

Smith – March : 517

Smith : 154

Smith 2<sup>nd</sup> : 125, 1164

Houben – Weyl : 5/4, 595; E15, 1438; E19b, 1632

Org. Synth. : 30, 10

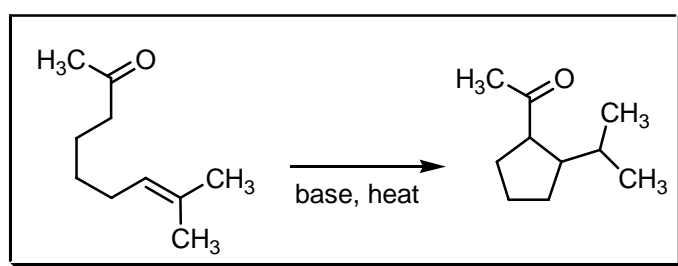
Org. Synth. Coll. Vol. : 4, 84

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- 3) J.B. Conant; W.R. Kirner, *J. Am. Chem. Soc.*, 1924, **46**, 232.
- 4) W.B. Smith; G.D. Branun, *Tetrahedron Lett.*, 1981, **22**, 2055.
- 5) S.D. Rychnovsky; G. Griesgraber, *J. Org. Chem.*, 1992, **57**, 559.
- 6) T.I. Richardson; S.D. Rychnovsky, *J. Am. Chem. Soc.*, 1997, **119**, 12360.
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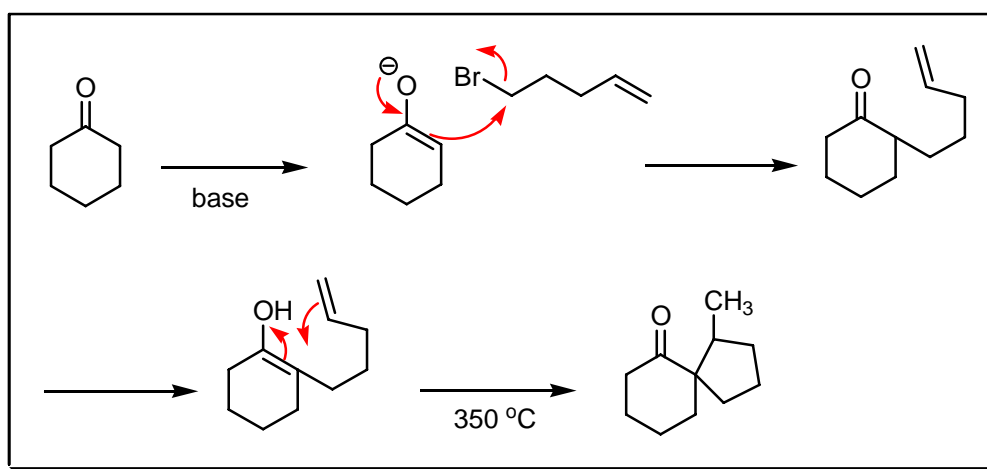
COMMENTS :

CONIA CYCLISATION

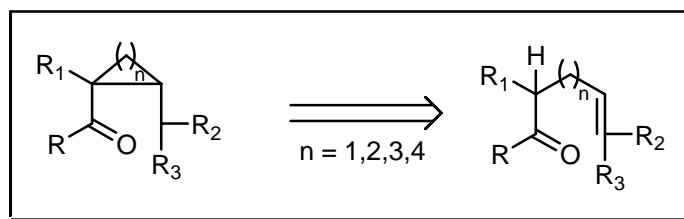
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

The thermal cyclisation (5-*exo*-trig) of dienones, ynones, diones, and ketoesters to monocyclic spirocyclic derivatives, *i.e.* an ene reaction of an unsaturated enol in which the carbonyl functionality serves as the ene component. Cobalt-mediated reactions are also known. See also **Alder** ene reaction.

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## REFERENCES :

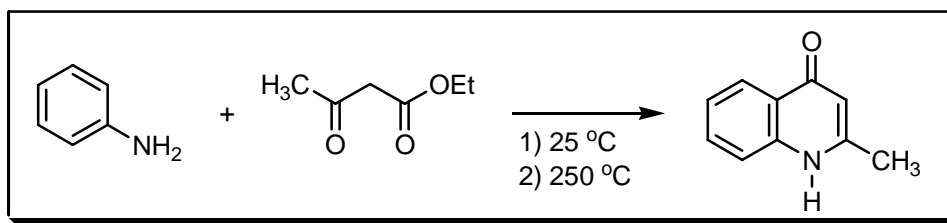
- 1) J.-M. Conia; P. Le Perche, *Tetrahedron Lett.*, 1965, **6**, 3305.
- 2) F. Rouessac; J.-M. Conia, *Tetrahedron Lett.*, 1965, **6**, 3313.
- 3) F. Rouessac; P. Belin; J.-M. Conia, *Tetrahedron Lett.*, 1965, **6**, 3319.
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- 5) G. Rousseau; P. Le Perche; J.-M. Conia, *Tetrahedron Lett.*, 1977, **18**, 45.
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## COMMENTS :

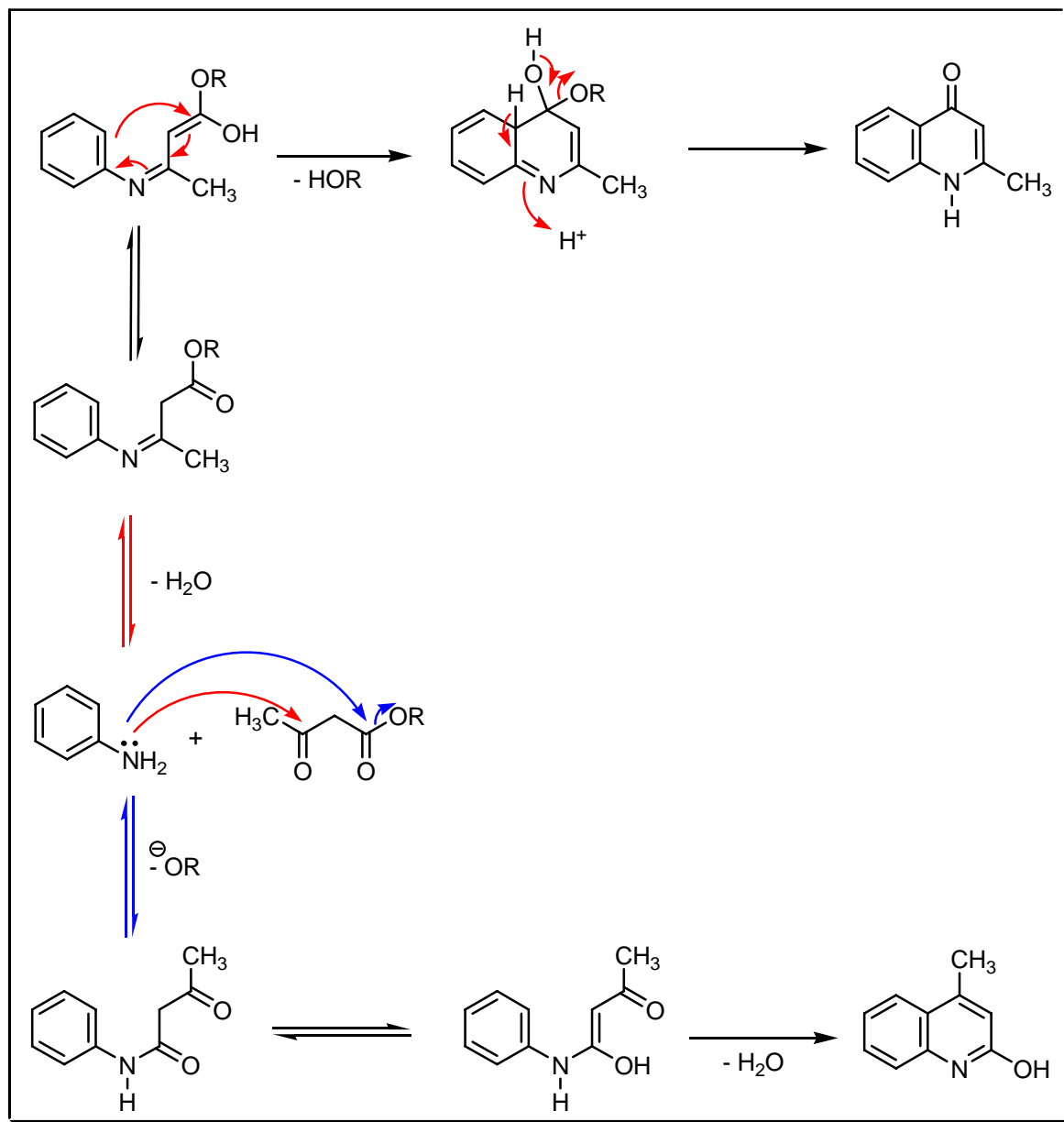
## CONRAD – LIMPACH SYNTHESIS

### EXAMPLE :

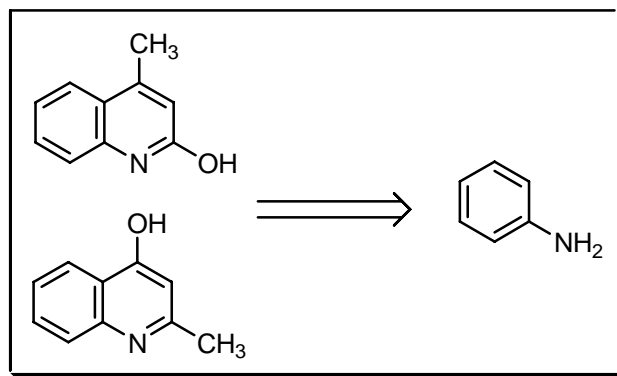




## MECHANISM :



## DISCONNECTION :



## NOTES :

The formation of 4-hydroxyquinolines by the condensation of  $\beta$ -keto-esters with arylamines under suitable conditions followed by high temperature cyclisation of the resulting  $\beta$ -anilinoacrylate derivative. See also **Allan – Loudon, von**

**Baeyer – Drewson** quinoline, **Camps, Combes** quinoline, **Doebner** quinoline, **Doebner – von Miller, Foulds – Robinson, Friedländer, Knorr** quinoline, **Meth–Cohn, von Niementowski** quinoline, **Pfitzinger – Borsche, Riehm** quinoline and **Skraup** quinoline reactions.

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#### REFERENCES :

**Smith** : 1335

**Smith 2<sup>nd</sup>** : 1098

**Houben – Weyl** : **8**, 627; **E7a**, 347, 355, 549

**Org. Synth.** : **24**, 68; **28**, 38; **29**, 70

**Org. Synth. Coll. Vol.** : **3**, 272, 580, 593

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1) M. Conrad; L. Limpach, *Ber. Dtsch. Chem. Ges.*, 1887, **20**, 944.

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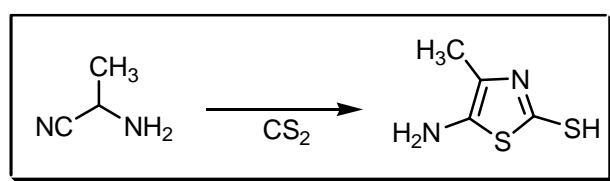
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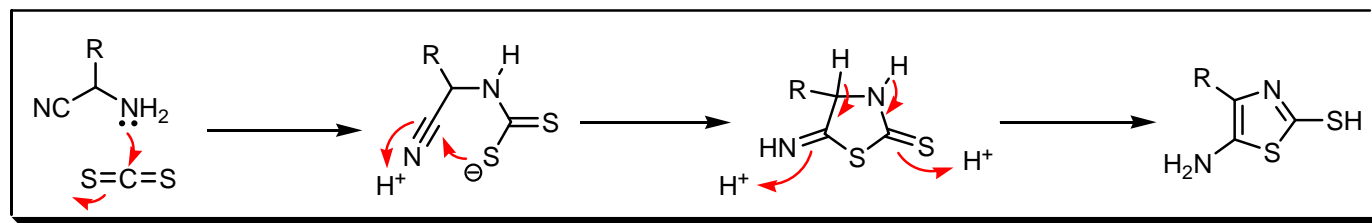
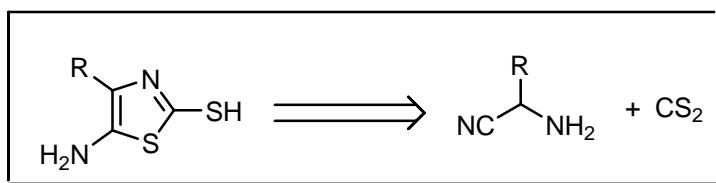
#### COMMENTS :

### COOK – HEILBRON THIAZOLE SYNTHESIS

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#### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

$\alpha$ -Aminonitriles react with  $\text{CS}_2$ , COS, isothiocyanates and dithiocarboxylic acid salts to afford 2,4-disubstituted-5-aminothiazoles.

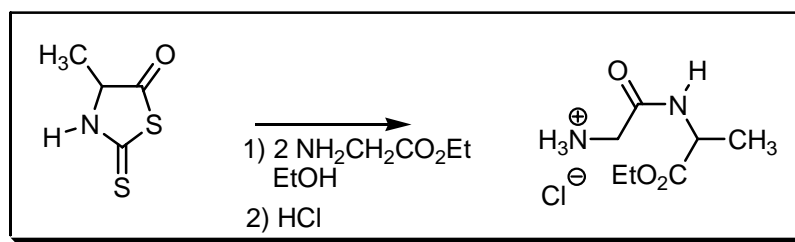
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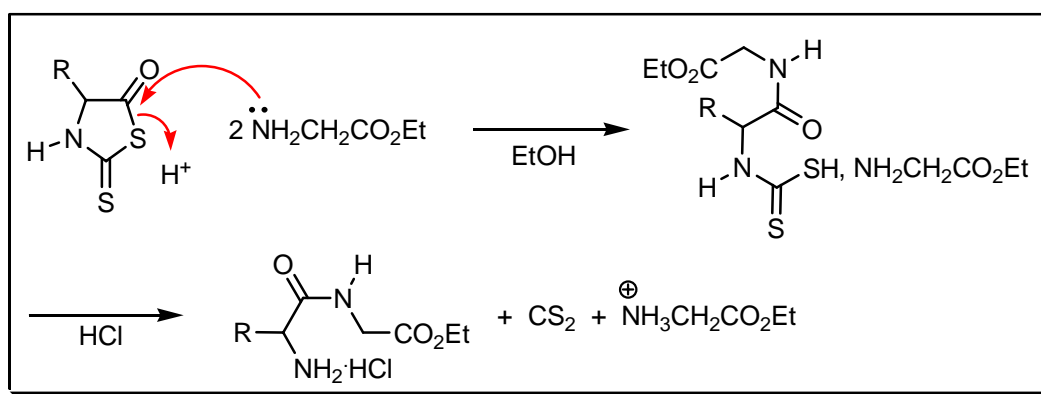
**COMMENTS :**

## COOK – LEVY PEPTIDE SYNTHESIS

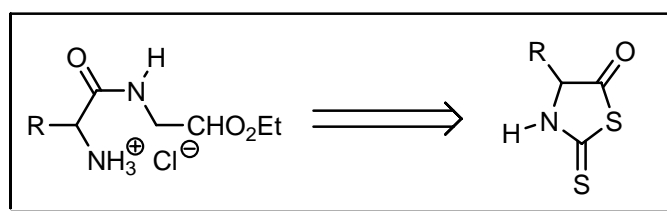
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

A 2-thio-5-thiazolidone is employed to achieve in a single operation the addition of a glycyl or similar residue to the ester of an  $\alpha$ -amino-acid or peptide. Coupling takes place in the presence of a tertiary base and the product is released by acidification. See also **Bailey** reaction.

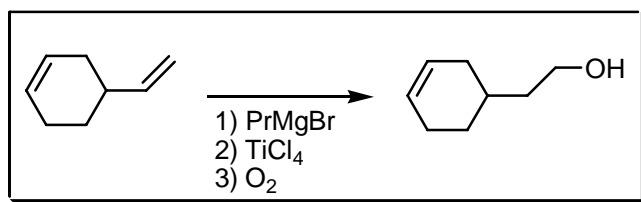
### REFERENCES :

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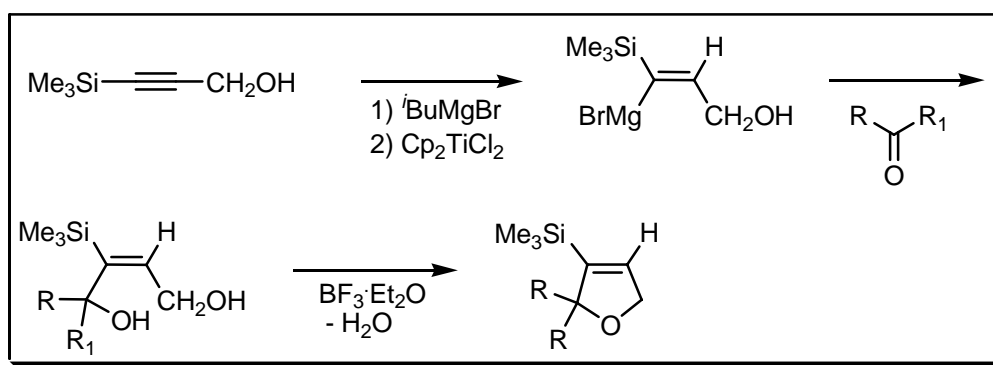
COMMENTS :

## COOPER – FINKBEINER HYDROMAGNESIATION

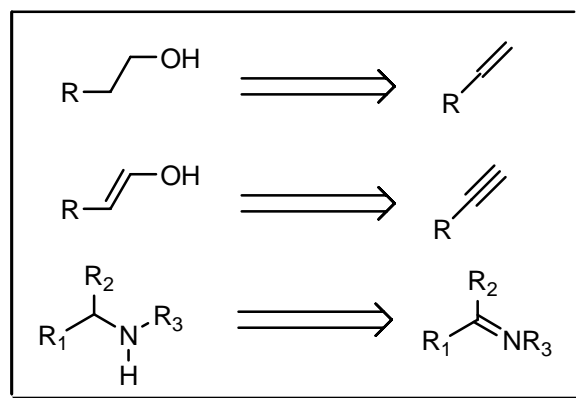
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

The titanium-catalysed exchange of HMgX between **Grignard** reagents and olefins, acetylenes (developed by **Sato et al.**) or imines (See **Crowe et al.**). The MgX of the **Grignard** reagent exchanges and migrates to the terminal position in the presence of titanium(IV).

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## REFERENCES :

**March** : 1089

**Smith – March** : 803

**Org. Synth.** : **69**, 106

**Org. Synth. Coll. Vol.** : **8**, 507

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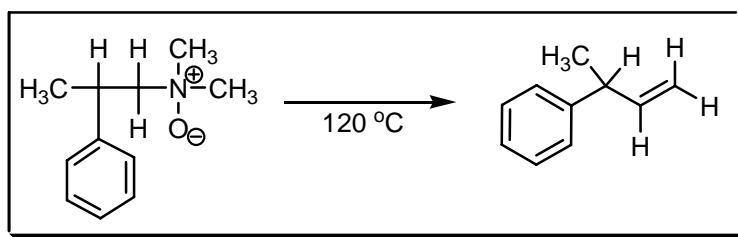
- 1) G.D. Cooper; H.L. Finkbeiner, *J. Org. Chem.*, 1962, **27**, 1493.
  - 2) G.D. Cooper; H.L. Finkbeiner, *J. Org. Chem.*, 1962, **27**, 3395.
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- 

## COMMENTS :

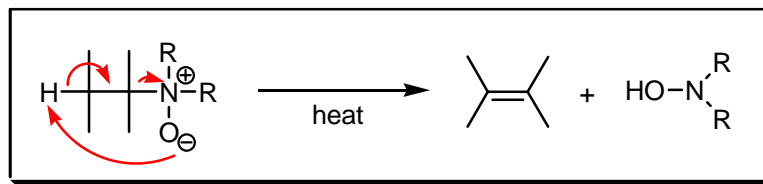
## COPE – MAMLOCK – WOLFFENSTEIN OLEFIN SYNTHESIS (COPE ELIMINATION)

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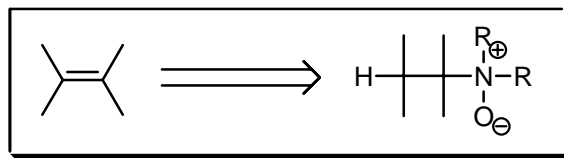
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The reaction is a thermal *syn* elimination of an amine oxide. Tertiary amines are readily converted to *N*-oxides by hydrogen peroxide or peroxyacids. Dehydrosulfenylation is a similar reaction. Selenoxides undergo a similar elimination reaction. See also **Hofmann** rearrangement and **Tschugaëff** reaction.

## REFERENCES :

**March** : 1018

**Smith – March** : 1333

**Smith** : 165

**Smith 2<sup>nd</sup>** : 137, 285

**Houben – Weyl** : 5/1b, 238

**Org. React.** : 11, 317

**Org. Synth.** : 39, 40

**Org. Synth. Coll. Vol.** : 4, 612

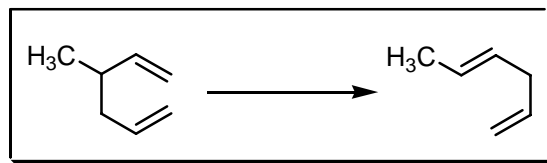
- 1) L. Mamlock; R. Wolffenstein, *Ber. Dtsch. Chem. Ges.*, 1900, **33**, 159.
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- 5) E.J. Corey; M.C. Desai, *Tetrahedron Lett.*, 1985, **26**, 5747.
- 6) E. Ciganek, *J. Org. Chem.*, 1990, **55**, 3007.
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- 8) I. Komaromi; J.M.J. Tronchet, *J. Phys. Chem. A.*, 1997, **101**, 3554.
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COMMENTS :

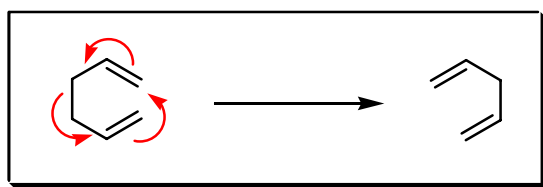
## COPE REARRANGEMENT

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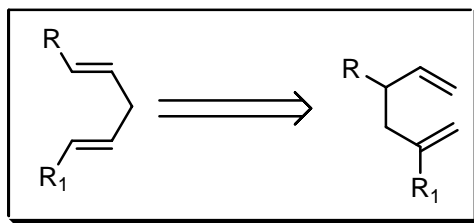
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The thermal isomerisation of 1,5-dienes in a [3,3]-sigmatropic rearrangement. The alcohol variant of the **Cope** rearrangement is called the **oxy-Cope** rearrangement. For the **aza-Cope** rearrangement see the **Overman** pyrrolidine synthesis. Catalytic amounts of palladium(II) enable the rearrangement to take place at about room temperature. See also **Claisen** (**Claisen – Ireland**) rearrangement and **Overman** pyrrolidine synthesis.

REFERENCES :

March : 1130

Smith – March : 1444

Smith : 1229, 1236

Smith 2<sup>nd</sup> : 950, 1006, 1014, 1210

Houben – Weyl : E3, 576; E5, 876; E6b, 234; E8b, 551; E10b2, 197; E15, 3080; E18, 1161



Org. React. : **22**, 1; **41**, 1; **43**, 93

Org. Synth. : **74**, 169; **76**, 199

Org. Synth. Coll. Vol. : **9**, 670; **10**, 2352

Science of Synthesis : **1**, 367; **9**, 447; **10**, 394

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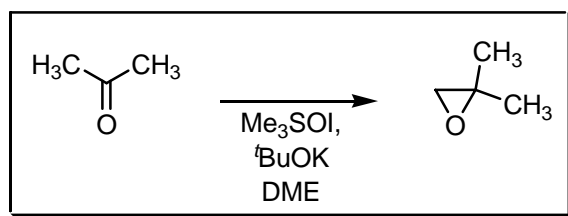
- 1) A.C. Cope; E.M. Hardy, *J. Am. Chem. Soc.*, 1940, **62**, 441.
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#### COMMENTS :

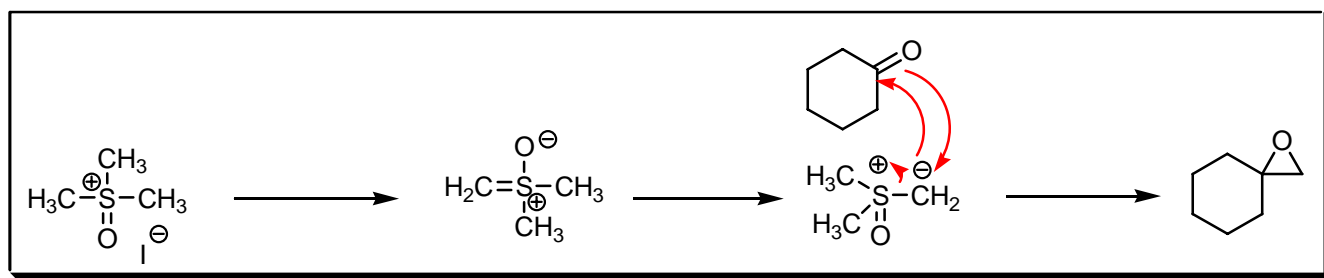
## COREY – CHAYKOVSKY EPOXIDATION

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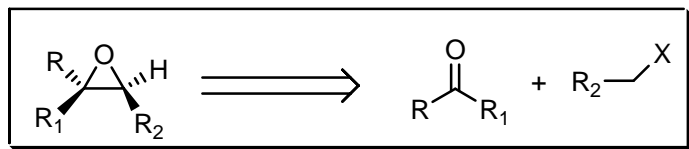
#### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The reaction of ketones with S-ylides derived from  $Me_3S^+I^-$  or  $Me_3SO^+I^-$  to give epoxides. However, the dimethylsulfoxonium methylide affords with  $\alpha,\beta$ -unsaturated carbonyl compounds, a conjugate addition takes place and the major product is the cyclopropane. If dimethylsulfonium methylide is used also the  $\alpha,\beta$ -unsaturated carbonyl compounds affords the epoxide. The aziridination of imines has also been published. See also **Büchner – Curtius – Schlotterbeck**, **Jacobsen – Katsuki**, **Juliá – Colonna**, **Katsuki – Sharpless**, **Mukaiyama – Yamada**, **Prileschajew**, **Shi** and **Weitz – Scheffer** reactions.

## REFERENCES :

**March** : 872, 974

**Smith – March** : 1089, 1247

**Smith 2<sup>nd</sup>** : 671

**Org. Synth.** : 49, 78

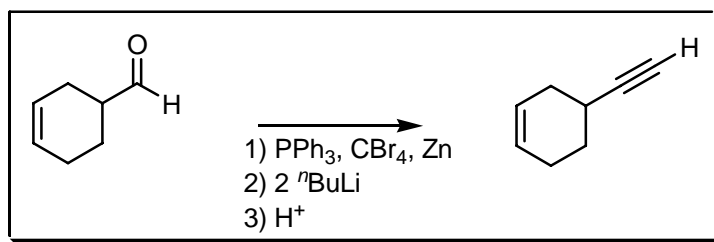
**Org. Synth. Coll. Vol.** : 5, 755

- 1) E.J. Corey; M. Chaykovsky, *J. Am. Chem. Soc.*, 1962, **84**, 867.
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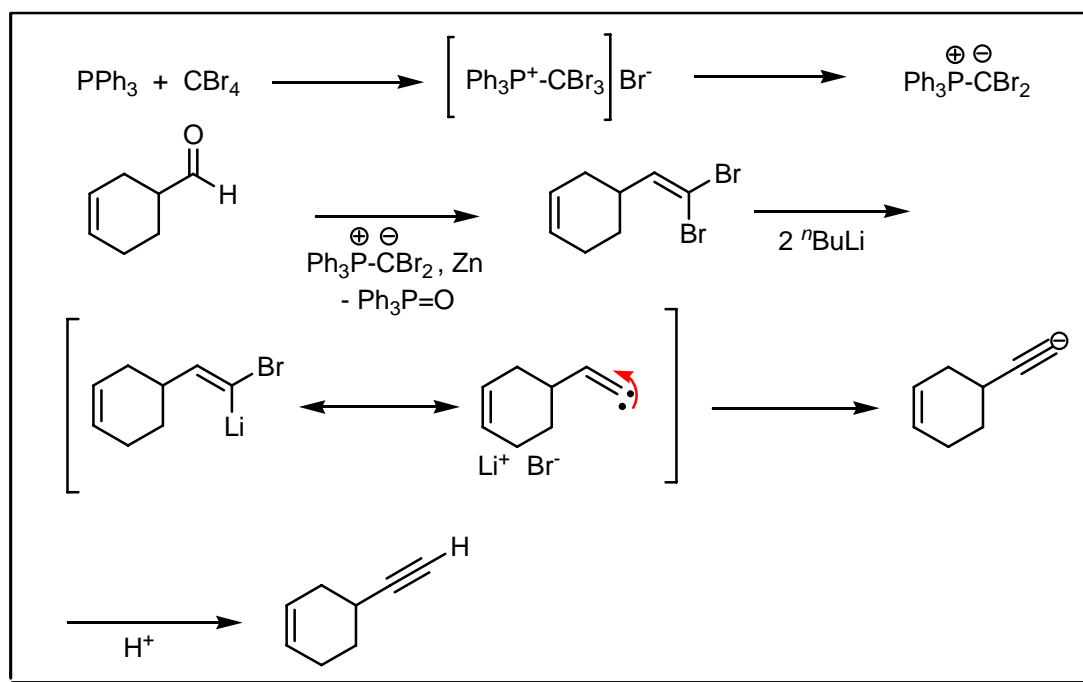
COMMENTS :

## COREY – FUCHS REACTION

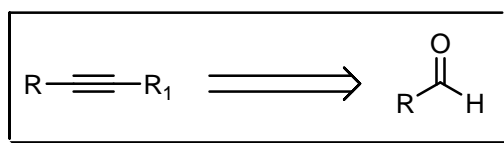
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

This is an alternative aldehyde alkyne elongation. The dibrominated phosphonium ylide is generated *in situ* by reaction of triphenylphosphine, carbon tetrabromide and zinc. A **Wittig** reaction between the ylide and an aldehyde gives the 1,1-dibromoalkene. This is treated with *n*-butyl lithium and forms the  $\alpha$ -lithiated bromoalkene, which is in resonance with the vinyl carbenoid, which undergoes H-migration to form an alkyne after acidic work-up. See also **Appel**, **Colvin**, **Kowalski**, **Seyferth – Gilbert** homologation and **Wittig** reactions.

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## REFERENCES :

Smith – March : 1233

Smith 2<sup>nd</sup> : 660

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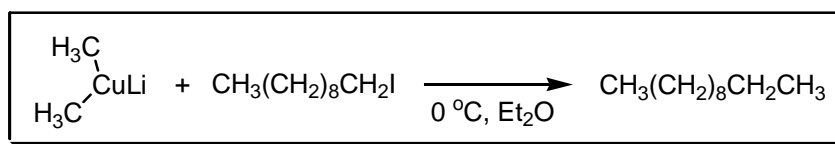
- 1) E.J. Corey, P.L. Fuchs, *Tetrahedron Lett.*, 1972, **13**, 3769.
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## COMMENTS :

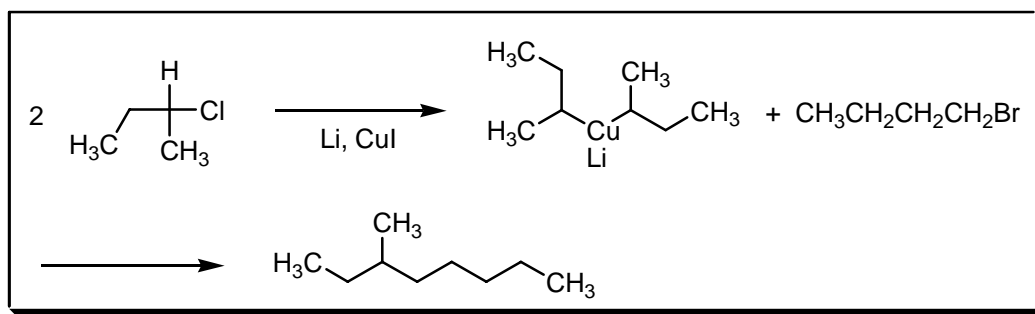
## COREY – HOUSE REACTION

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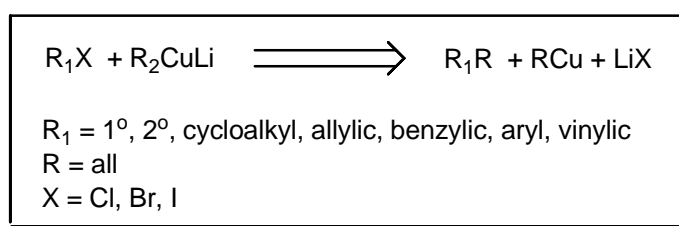
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The lithium dialkylcuprate (**Gilman** reagent) is formed using the alkyl lithium reagent and copper(I) iodide. These reagents are rather unstable but have the ability of to undergo organometallic coupling reactions with alkyl bromides and alkyl iodides. See also **Knochel** and **Ullmann** diaryl reactions.

## REFERENCES :

**March** : 451

**Smith – March** : 538

**Smith** : 761

**Smith 2<sup>nd</sup>** : 642

**Org. React.** : **22**, 253

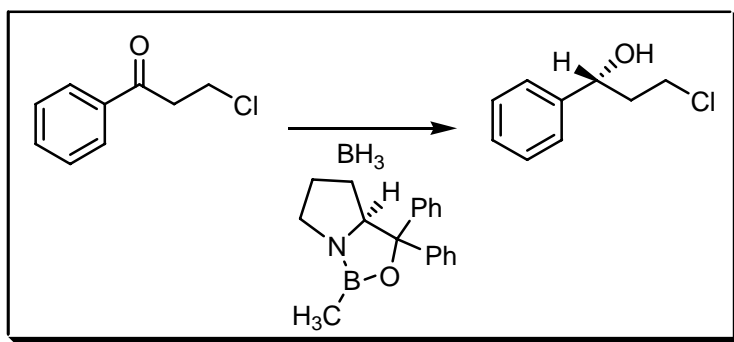
**Org. Synth. Coll. Vol.** : **6**, 248

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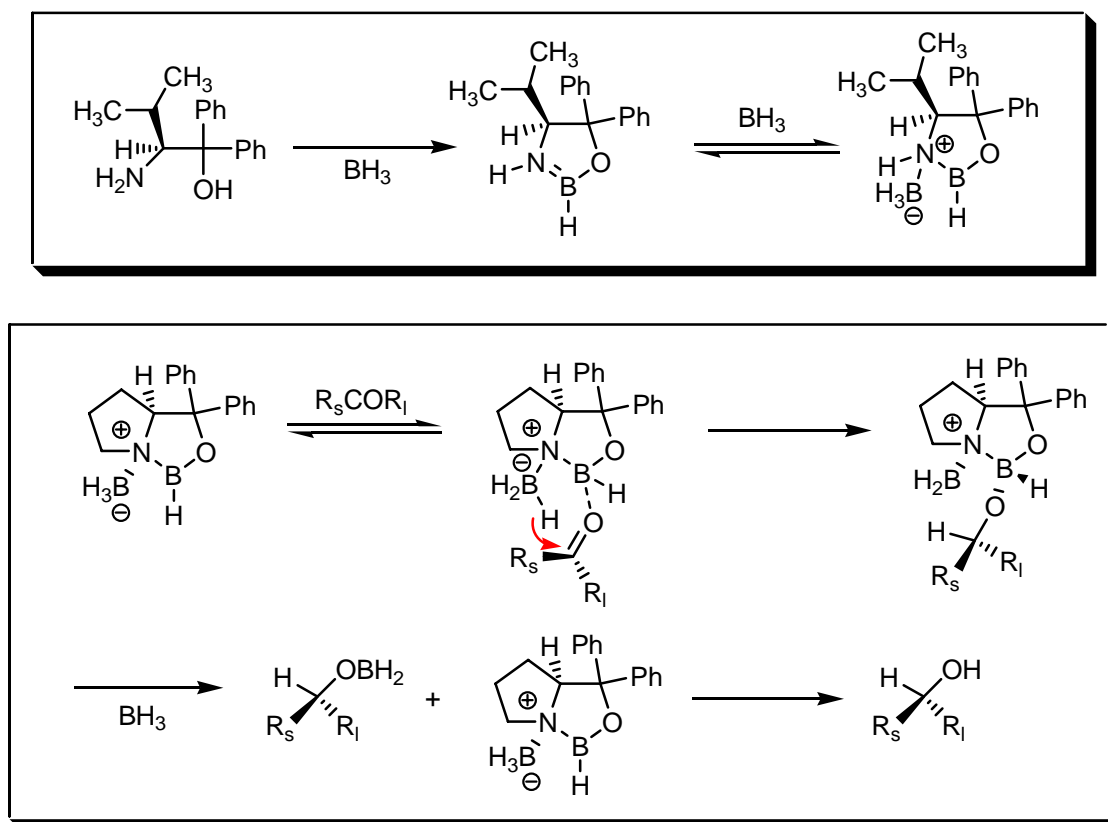
COMMENTS :

## COREY – ITSUNO – BAKSHI – SHIBATA ENANTIOSELECTIVE BORANE REDUCTION

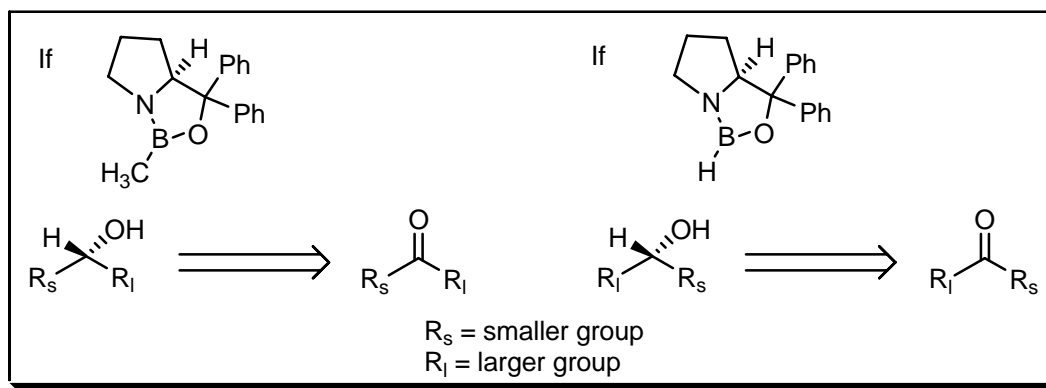
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The enantioselective reduction of prochiral ketones by borane or catecholborane catalysed by oxazaborolidine. The limitation of **Itsuno's** approach was the use of stoichiometric amounts of chiral oxazaborolidine. **Corey** demonstrated the catalytic enantioselective reduction. The oxazaborolidines can be polymer supported. See also **Midland** reduction and **Noyori** hydrogenation.

## REFERENCES :

**March** : 915

**Smith – March** : 1201

**Org. React.** : **52**, 395

**Org. Synth.** : **74**, 50

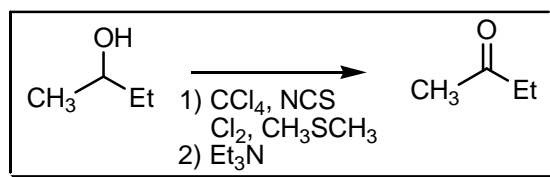
**Org. Synth. Coll. Vol.** : **9**, 676

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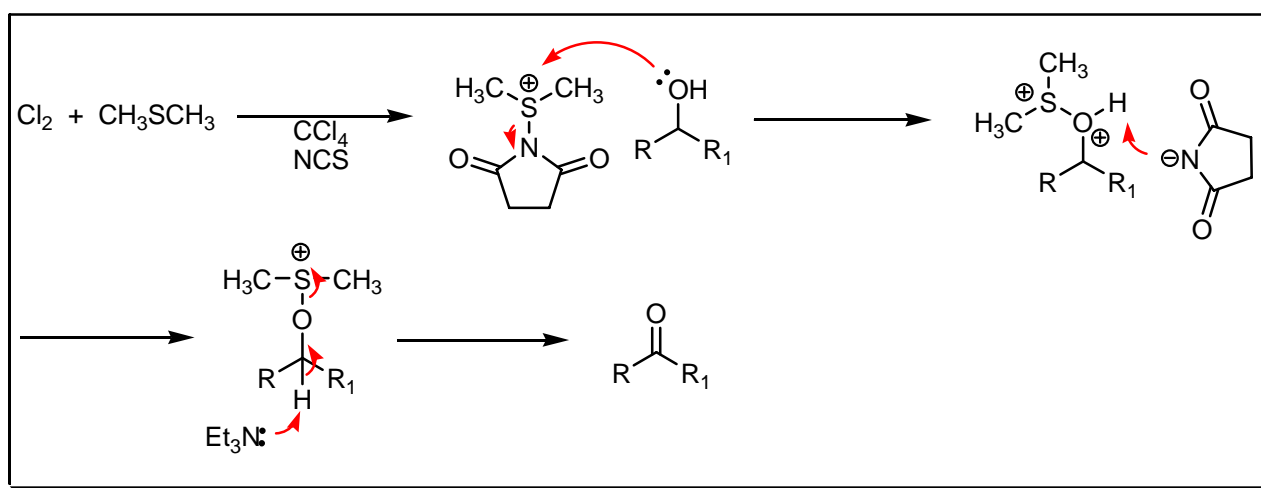
COMMENTS :

COREY – KIM OXIDATION

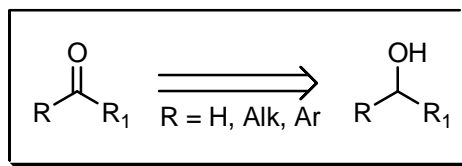
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The oxidation of primary and secondary alcohols to aldehydes and ketones using NCS or NBS and  $\text{Me}_2\text{S}$ . Allylic and dibenzylic compounds give halides as products. An odourless method has been introduced. See also **Anelli**, **Ball – Goodwin – Morton**, **Collins**, **Corey – Schmidt**, **Corey – Suggs**, **David – Thieffry**, **Delépine**, **Dess – Martin**, **Einhorn** oxidation, **Fétizon**, **Jones** oxidation, **Ley**, **Maurer – Drefahl**, **Mukaiyama** oxidation, **Nicolaou**, **Oppenauer**, **Parikh – von Doering**, **Pfitzner – Moffatt**, **Sarett**, **Swern** and **Uemura** reactions.



## REFERENCES :

March : 433

Smith – March : 519, 1536

Org. Synth. : 58, 122

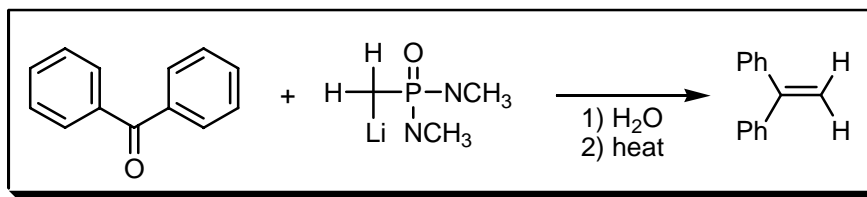
Org. Synth. Coll. Vol. : 6, 220

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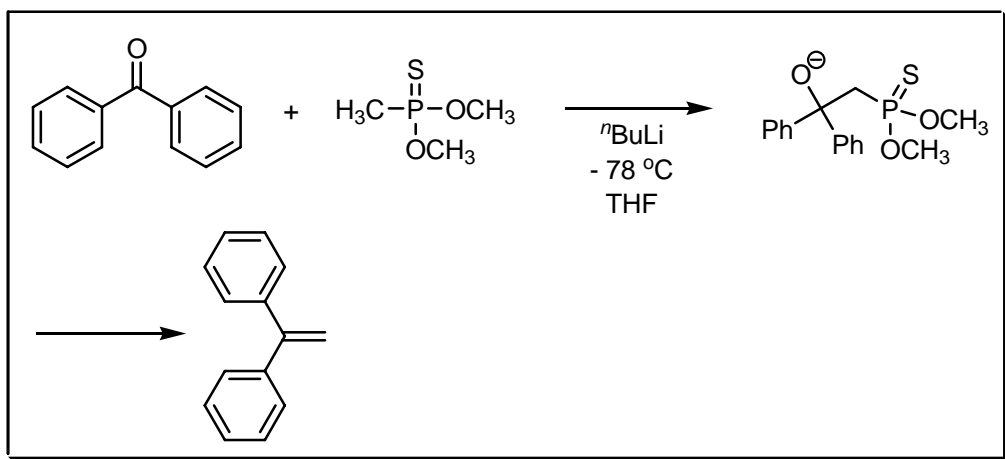
## COMMENTS :

## COREY – KWIATKOWSKI REACTION

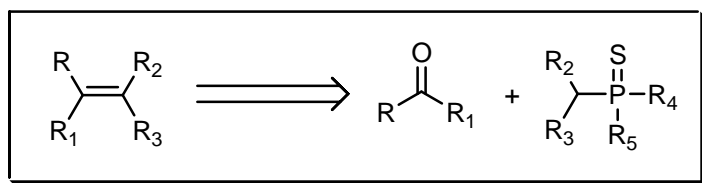
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of *cis* and *trans* olefins via  $\beta$ -keto and  $\beta$ -hydroxy phosphonamides. See also **Eastwood**, **Horner – Wadsworth – Emmons**, **Julia – Paris – Kocienski – Lythgoe**, **Krief – Reich – Chow**, **Nozaki – Hiyama – Kishi** (**Takai – Utimoto**), **Nysted**, **Paquette**, **Petasis** reaction, **Peterson**, **Ramberg – Bäcklund**, **Still – Gennari**, **Takeda**, **Tebbe** and **Wittig** reactions.

## REFERENCES :

**March** : 956

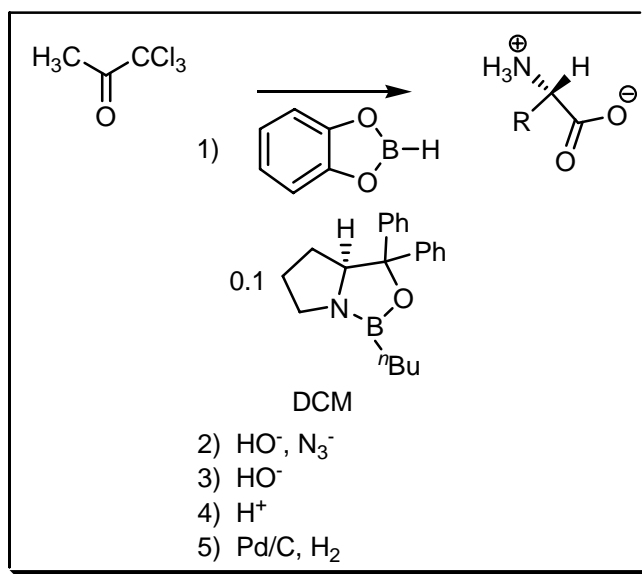
**Smith – March** : 1231

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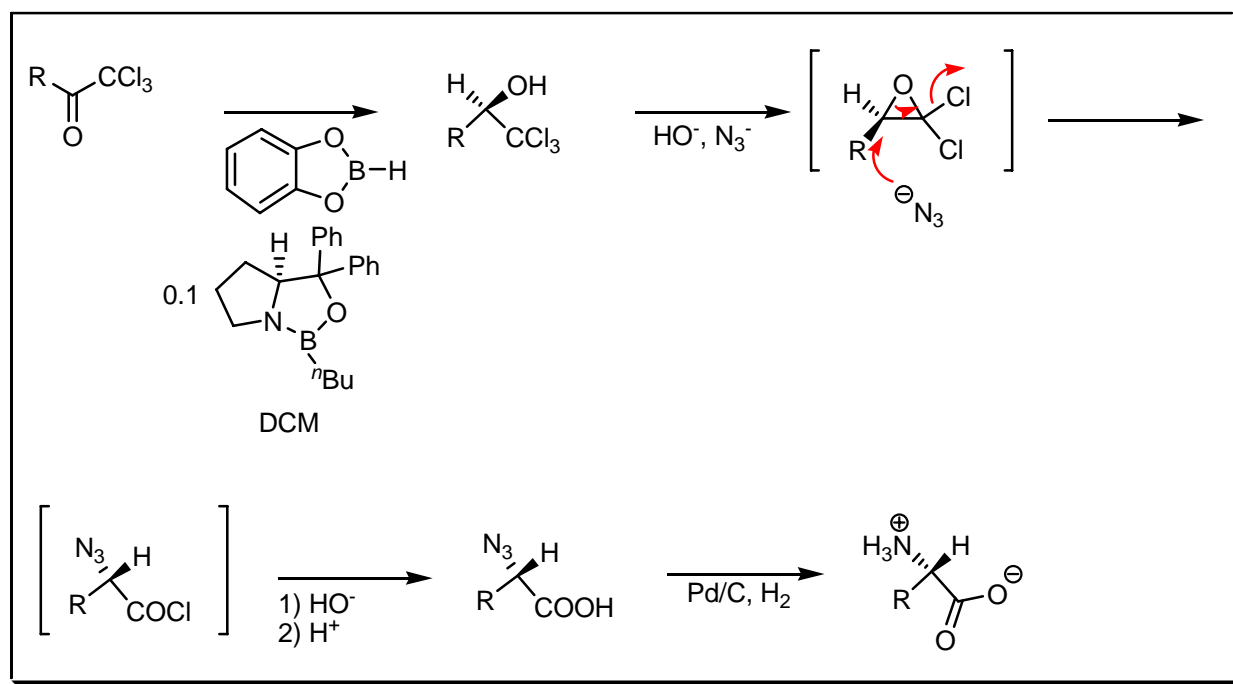
## COMMENTS :

## COREY – LINK REACTION

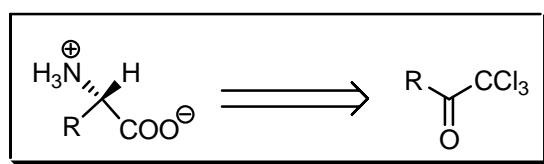
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The one-pot conversion of (trichloromethyl)carbinols, generated by oxazaborolidine-catalysed asymmetric reduction of trichloromethyl ketones, into  $\alpha$ -azido and  $\alpha$ -hydroxy acids. Deprotonation of the carbinol generates the chiral *gem*-dichlorooxirane. The *in-situ* nucleophile provides the functional group. The azide attacks from the more hindered face, rather than from the less sterically hindered face as in the **Bucherer – Bergs** and **Strecker** amino acid reactions. See also **Bouveault – Locquin** amino acid, **von Braun** amino acid synthesis, **Bucherer – Bergs**, **Darapsky**, **Herbst – Engel**, **Knoop – Oosterlin**, **O'Donnell**, **Reeve** synthesis, **Schöllkopf**, **Sorensen**, **Strecker** amino acid, **Tiemann** amination, **Ultee**, **Urech** and **Zelinksy – Stadnikoff** reactions.

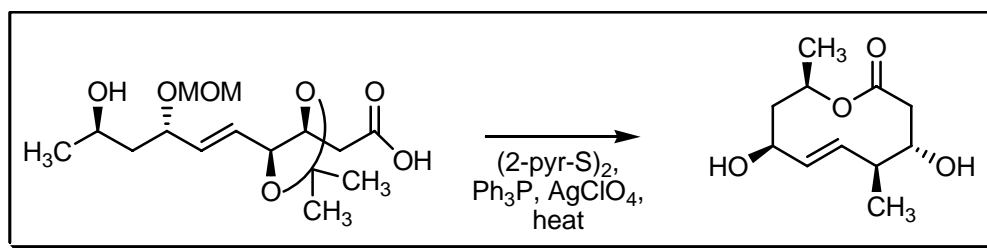
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- 4) V.K. Aggarwal; J.K. Barrell; J.M. Worrall; R. Alexander, *J. Org. Chem.*, 1998, **63**, 7128.
- 5) C. Domínguez; J. Ezquerra; S.R. Baker; S. Borrelly; L. Prieto; M. Espada; C. Pedregal, *Tetrahedron Lett.*, 1998, **39**, 9305.
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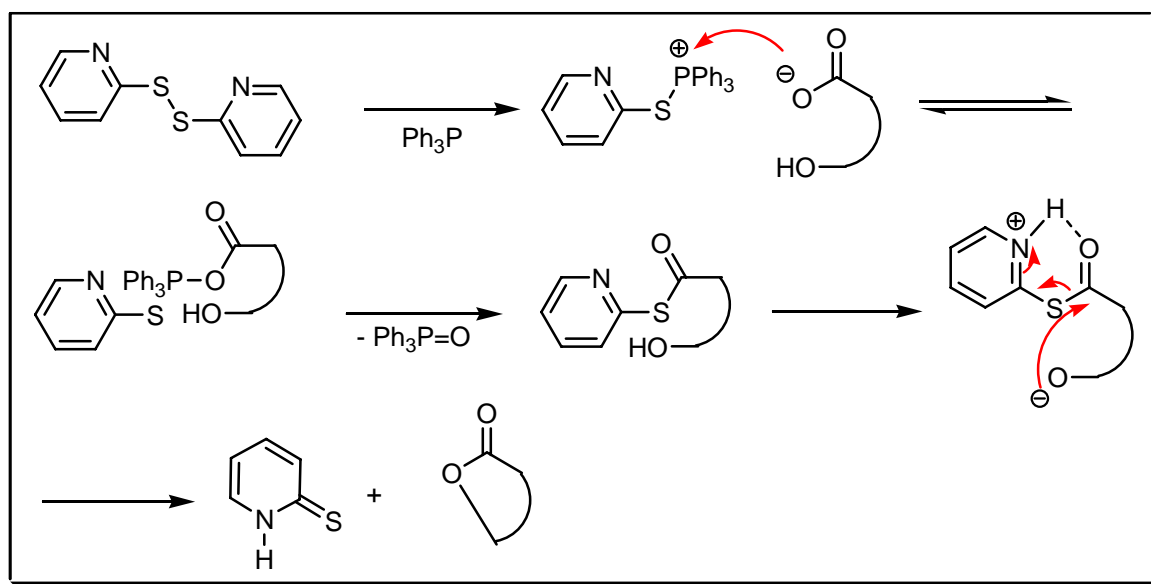
## COMMENTS :

## COREY – NICOLAOU MACROLACTONISATION

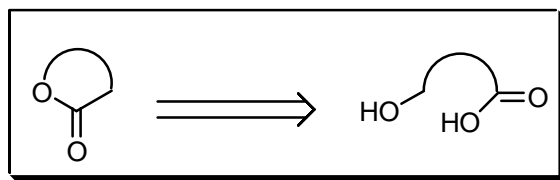
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

This reaction allows the lactonisation of hydroxy acids under mild conditions using 2,2'-dipyridyl disulfide and triphenylphosphine (**Gerlach – Thalmann** modification uses silver perchlorate). Alternative disulfides have also been used by **Corey**. See also **Diels – Alder**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Kita**, **Masamune**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi** (**Takai – Utimoto**), **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Venkatraman – Wagle**, **Vorbrüggen – Krolikiewicz**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

## REFERENCES :

Smith 2<sup>nd</sup> : 528

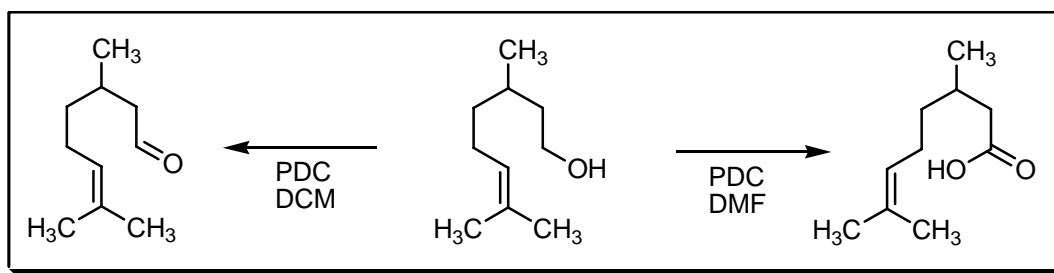
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- 13) T. Sasaki; M. Inoue; M. Hirama, *Tetrahedron Lett.*, 2001, **42**, 5299.

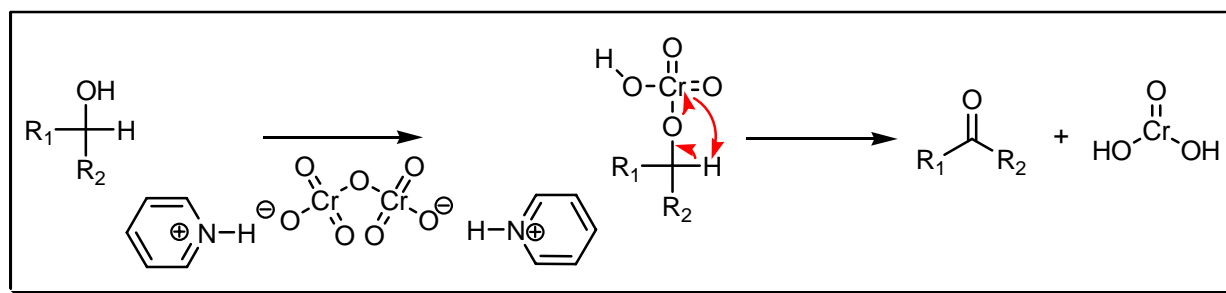
**COMMENTS :**

**COREY – SCHMIDT OXIDATION**

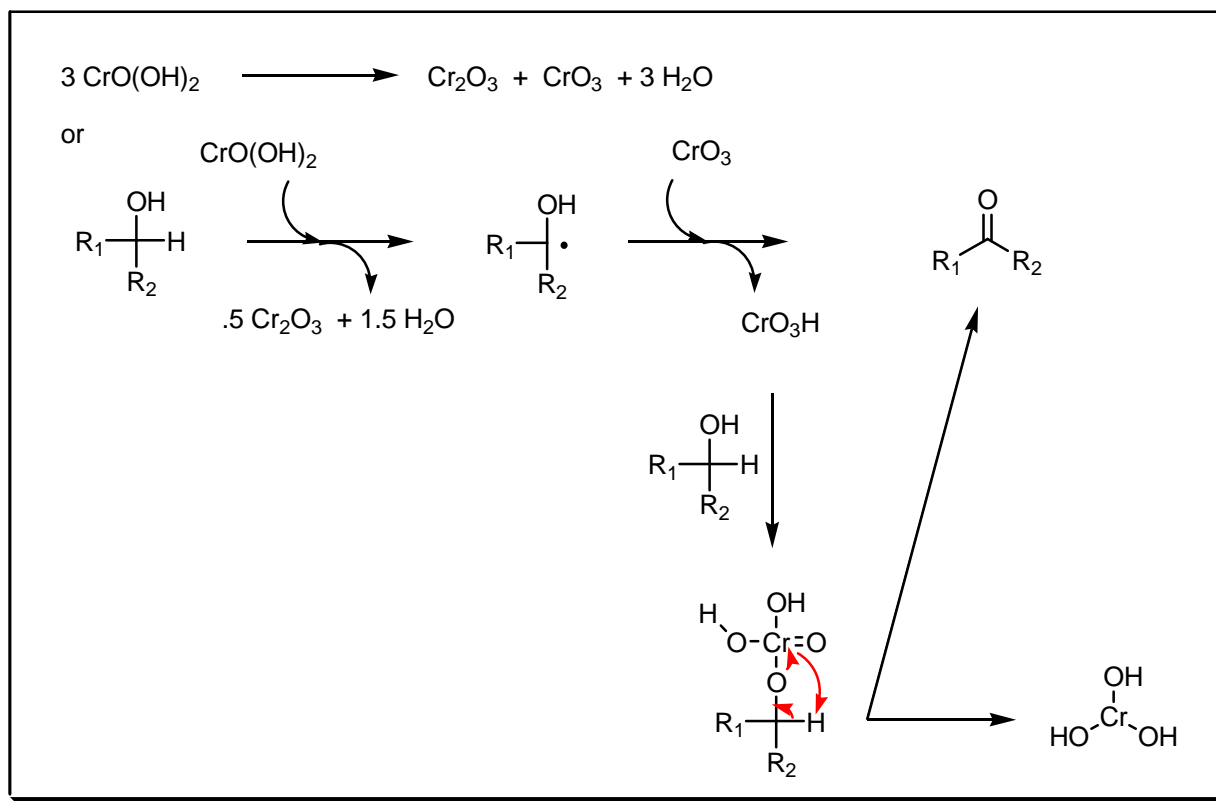
**EXAMPLE :**



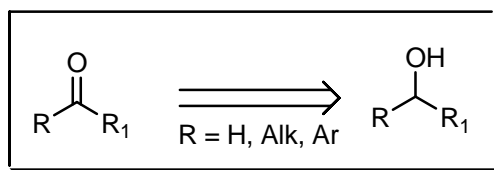
**MECHANISM :**



### Follow-up chemistry of Cr(IV) :



### DISCONNECTION :



### NOTES :

The oxidation of alcohols, to aldehydes, ketones and carboxylic acids using pyridinium dichromate, a less acidic oxidising agent than PCC. See also **Anelli**, **Ball – Goodwin – Morton**, **Collins**, **Corey – Kim**, **Corey – Suggs**, **David – Thieffry**, **Delépine**, **Dess – Martin**, **Einhorn** oxidation, **Fétizon**, **Jones** oxidation, **Ley**, **Maurer – Drefahl**, **Mukaiyama** oxidation, **Nicolaou**, **Oppenauer**, **Parikh – von Doering**, **Pinnick**, **Pfitzner – Moffatt**, **Sarett**, **Swern** and **Uemura** reactions.

### REFERENCES :

**March** : 884, 1168

**Smith – March** : 1514

**Smith** : 231

**Smith 2<sup>nd</sup>** : 201

**Org. Synth.** : **52**, 5; **55**, 84; **67**, 114; **68**, 175; **73**, 36; **80**, 1

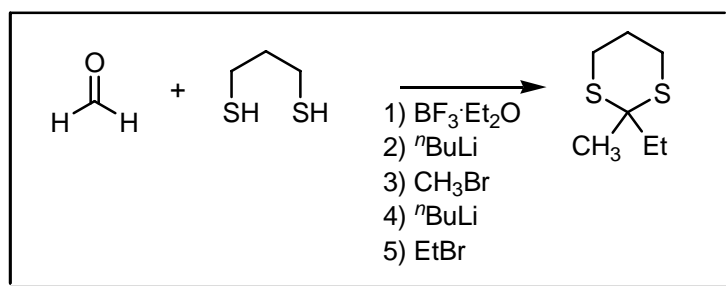
**Org. Synth. Coll. Vol.** : **6**, 373, 644; **8**, 13, 43; **9**, 132

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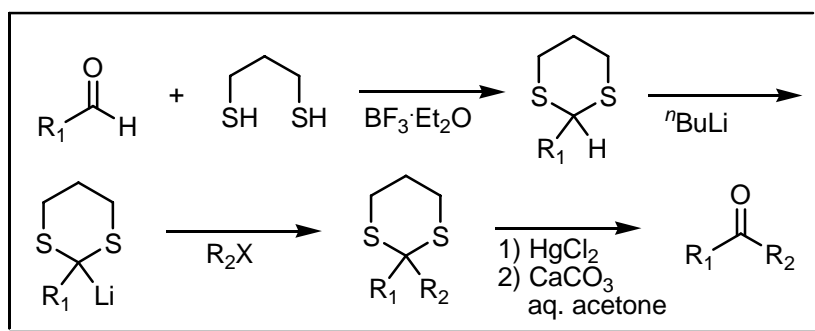
COMMENTS :

## COREY – SEEBACH PROCEDURE

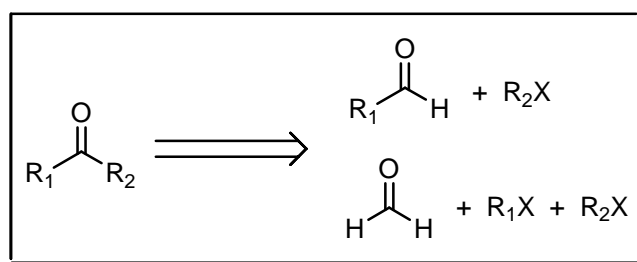
EXAMPLE :



MECHANISM :



DISCONNECTION :





## NOTES :

The carbonyl group is converted into a cyclic thioacetal that can be easily deprotonated due to the stabilisation effect of the sulfur carbanion. By reversing the polarity (*umpolung*) of the acyl carbon nucleophilic acylation can take place. These reagents can be used in the synthesis of aldehydes, silyl and germyl ketones, cyclic carbonyl compounds, carbohydrates and  $\alpha$ -keto acids.

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## REFERENCES :

Smith – March : 556

Smith : 658

Smith 2<sup>nd</sup> : 557

Org. Synth. : 50, 72

Org. Synth. Coll. Vol. : 6, 556

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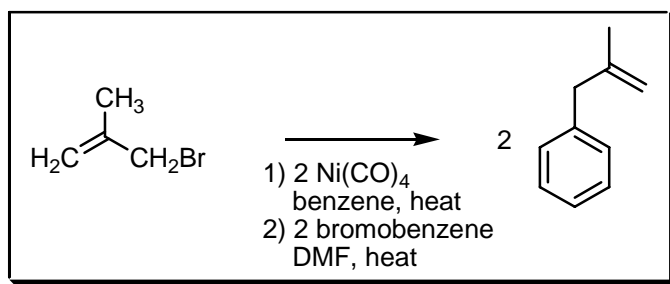
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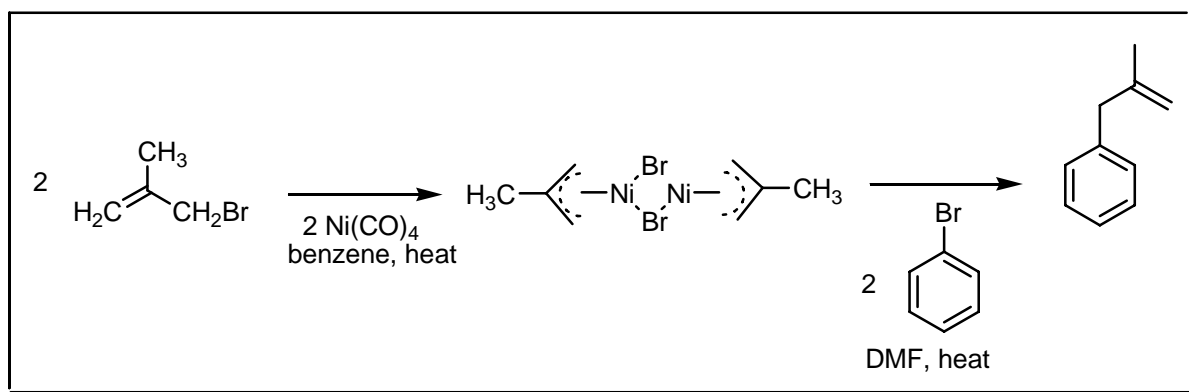
## COMMENTS :

## COREY – SEMMELHACK MODIFICATION

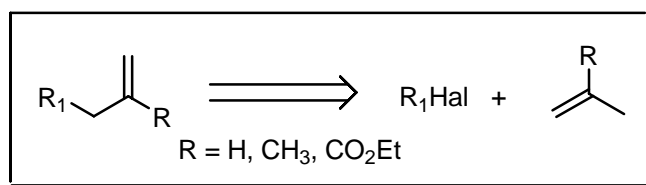
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Zero-valent nickel complexes such as  $\text{Ni}(\text{COD})_2$  and  $\text{Ni}(\text{PPh}_3)_4$  react readily with aryl and vinyl halides, tosylates and acetates *via* a  $\pi$ -allyl nickel complex to give symmetrical coupling products. The reaction is a low-temperature analogue of the **Ullmann** reaction. See also **Ullmann** reaction.

### REFERENCES :

Smith – March : 541

Smith 2<sup>nd</sup> : 1125

Org. React. : 19, 119

Org. Synth. : 52, 115

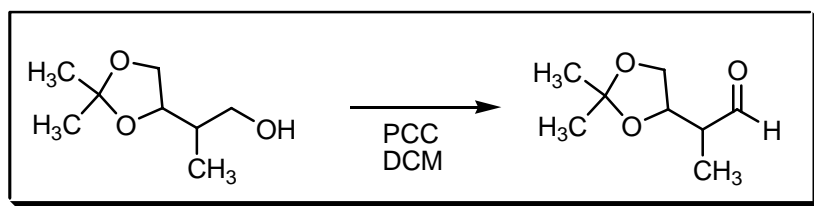
Org. Synth. Coll. Vol. : 6, 722

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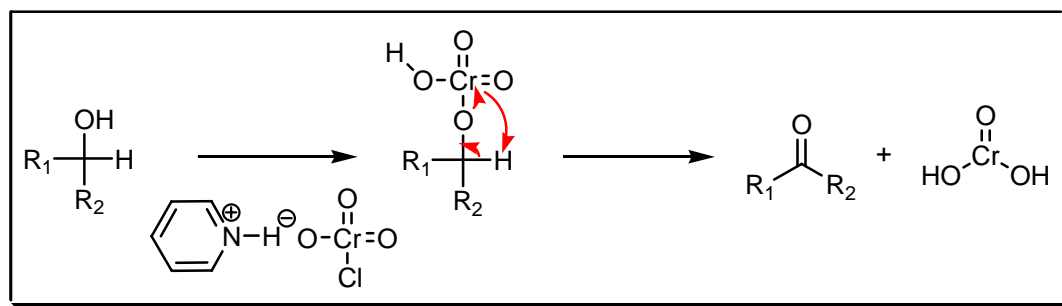
**COMMENTS :**

**COREY – SUGGS OXIDATION**

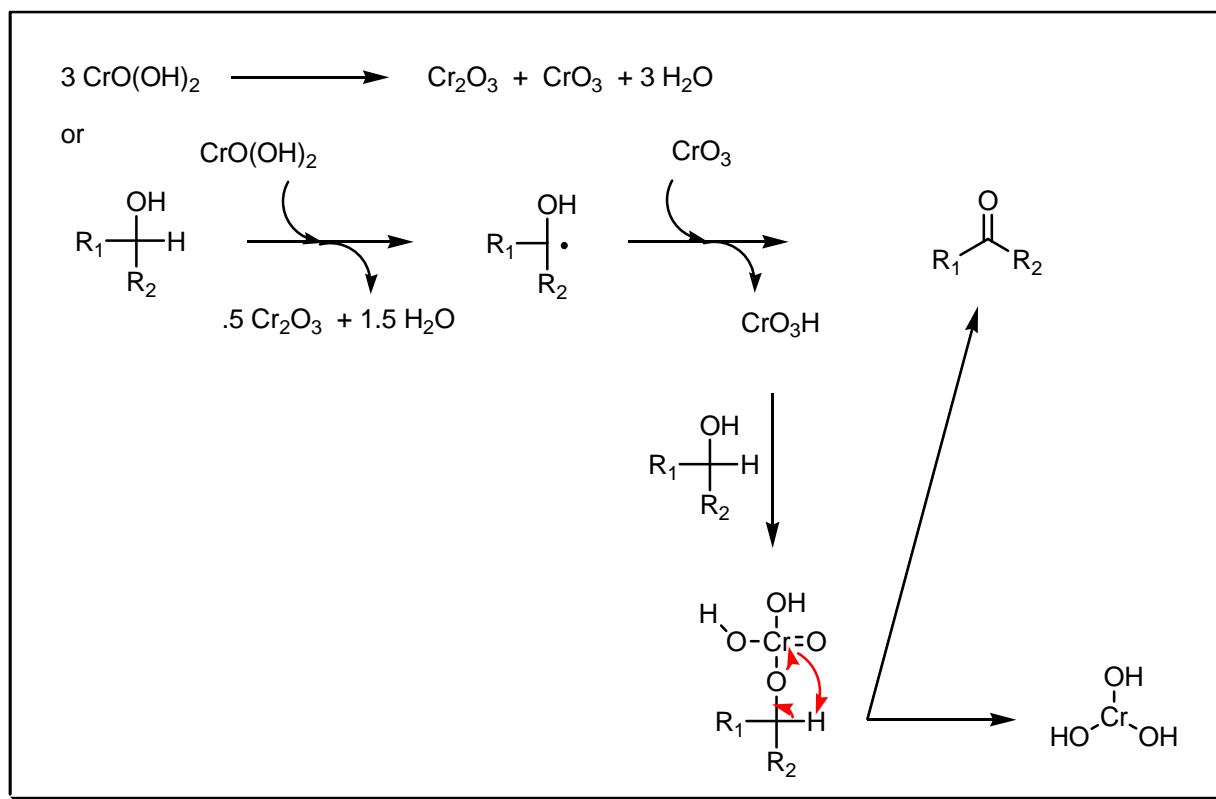
**EXAMPLE :**



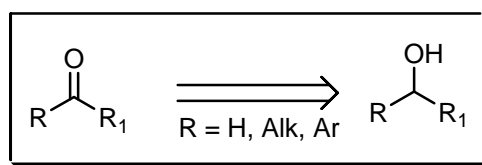
**MECHANISM :**



## Follow-up chemistry of Cr(IV) :



## DISCONNECTION :



## NOTES :

The oxidation of primary and secondary alcohols using pyridinium chlorochromate (slightly more acidic than pyridinium dichromate). See also **Anelli**, **Ball – Goodwin – Morton**, **Collins**, **Corey – Kim**, **Corey – Schmidt**, **David – Thieffry**, **Delépine**, **Dess – Martin**, **Einhorn** oxidation, **Fétizon**, **Jones** oxidation, **Ley**, **Maurer – Drefahl**, **Mukaiyama** oxidation, **Nicolaou**, **Oppenauer**, **Parikh – von Doering**, **Pinnick**, **Pfitzner – Moffatt**, **Sarett**, **Swern** and **Uemura** reactions.

## REFERENCES :

**March** : 447, 1174, 1188, 1196

**Smith – March** : 1514, 1531

**Smith** : 230, 549, 1302

**Smith 2<sup>nd</sup>** : 200

**Org. Synth.** : **52**, 5; **55**, 84; **72**, 189; **75**, 69; **76**, 110

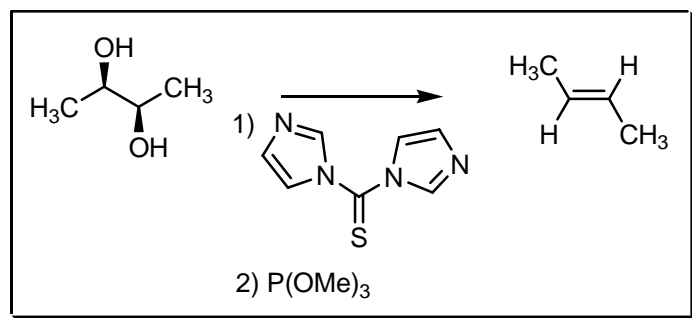
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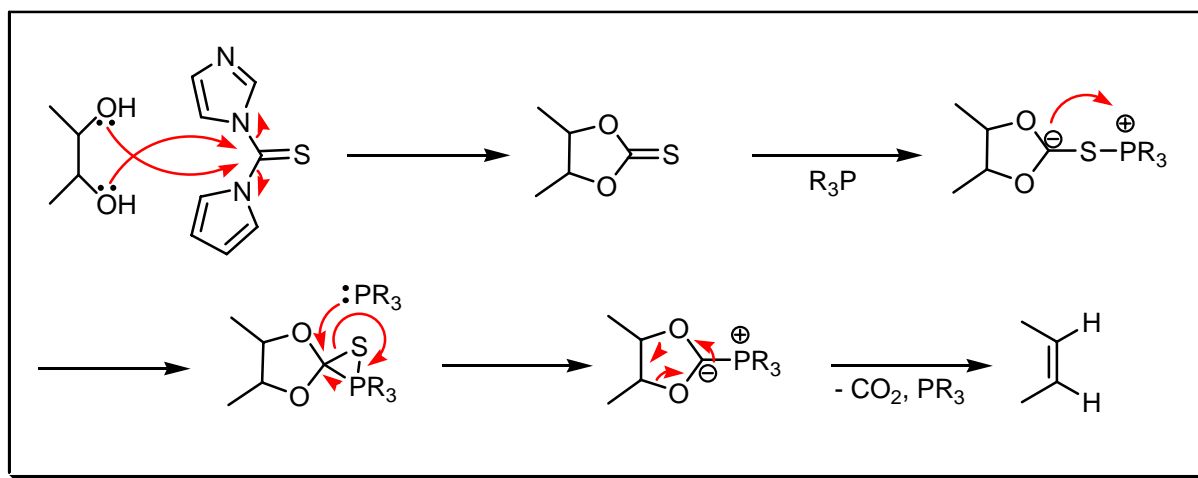
COMMENTS :

## COREY – WINTER ALKENE SYNTHESIS

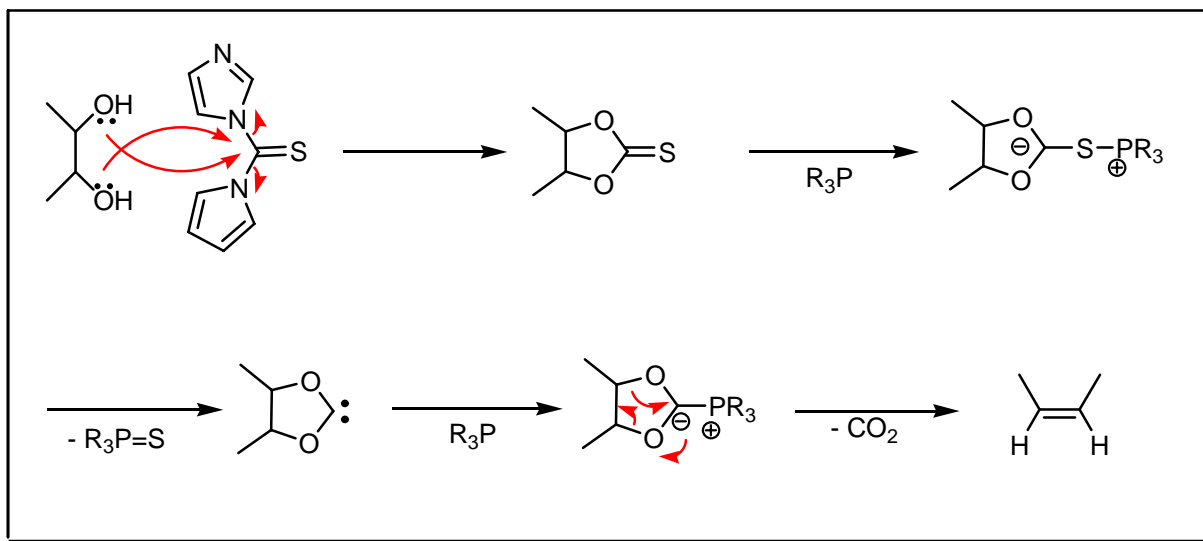
EXAMPLE :



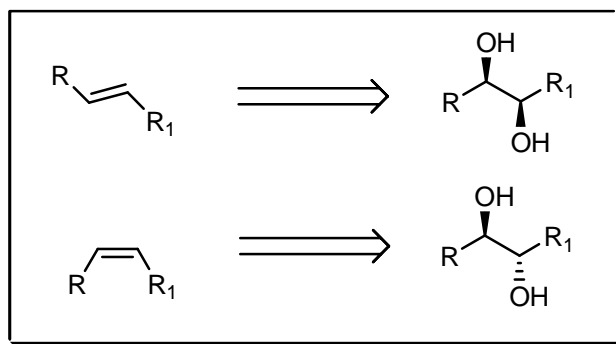
MECHANISM :



### Carbene intermediate mechanism :



### DISCONNECTION :



### NOTES :

The formation of olefins from *vicinal* diols. Thiocarbonyldiimidazole (TCDI) was originally suggested by **Corey**, but other reagents can be used (e.g. thiophosgene). The intermediate can be cleaved with an alkyl phosphite or with bis(1,5-cyclooctadiene) nickel. See also **Corey – Kwiatkowski**, **Eastwood**, **Garegg – Samuelsson**, **Horner – Wadsworth – Emmons**, **Julia – Paris – Kocienski – Lythgoe**, **Krief – Reich – Chow**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Nysted**, **Paquette**, **Petasis** reaction, **Peterson**, **Ramberg – Bäcklund**, **Still – Gennari**, **Takeda**, **Tebbe** and **Wittig** reactions.

### REFERENCES :

March : 1028

Smith – March : 1340

Houben – Weyl : E19b, 1696

Org. React. : 30, 457

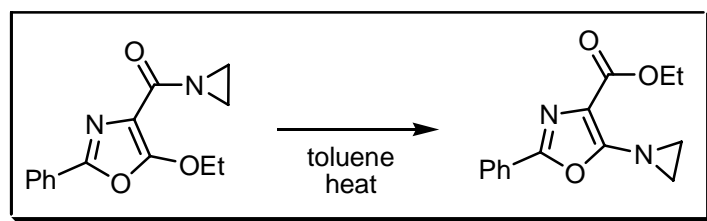
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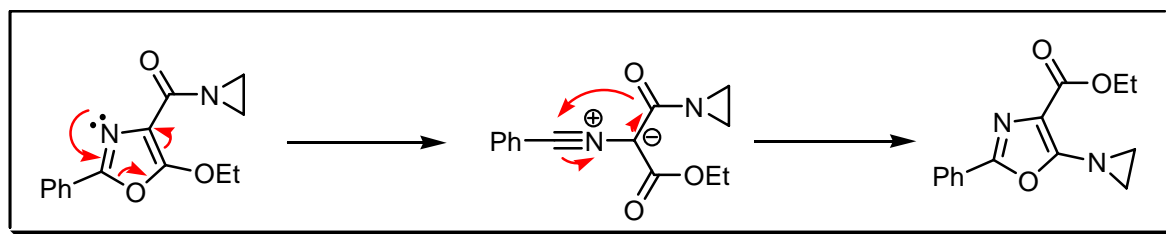
**COMMENTS :**

## CORNFORTH REARRANGEMENT

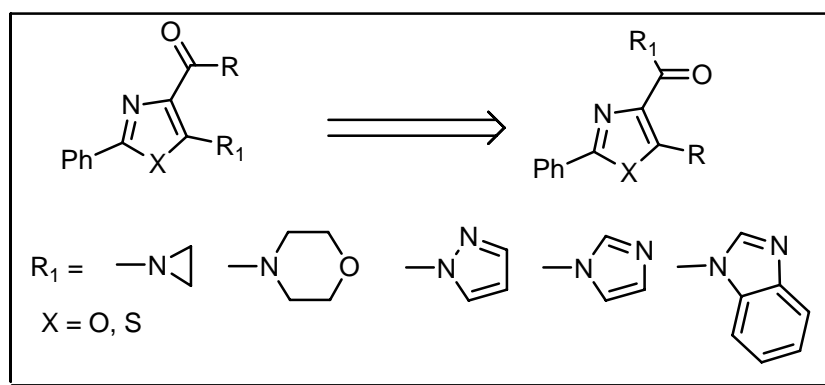
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

The thermal rearrangement of 4-carbonyl substituted oxazoles *via* nitrilium ylids.

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## REFERENCES :

Houben – Weyl : **E8a**, 998; **E8b**, 60, 182, 325

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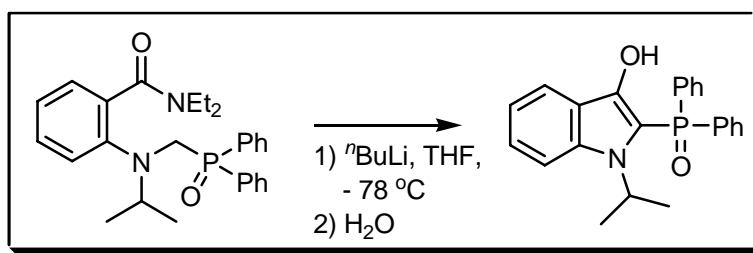
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## COMMENTS :

## COUTURE INDOLE SYNTHESIS

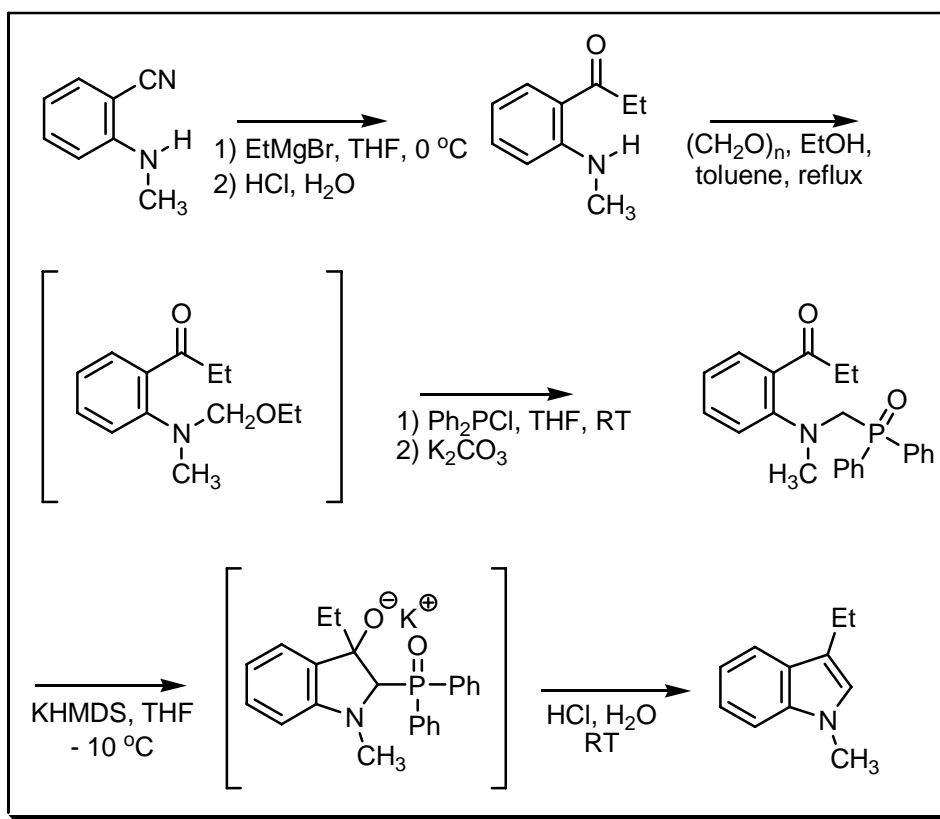
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### EXAMPLE :

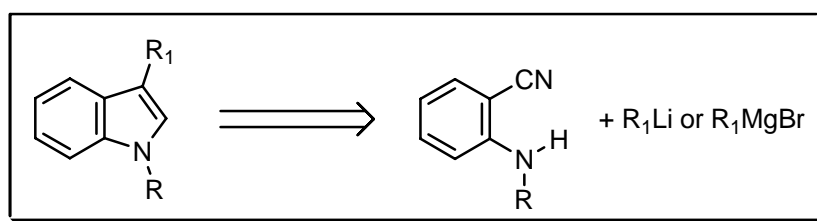




## MECHANISM :



## DISCONNECTION :



## NOTES :

This is a simple indole synthesis based on the *intramolecular* **Horner – Wadsworth – Emmons** reaction. The nature of the base dramatically affects the outcome of the reaction. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Horner – Wadsworth – Emmons**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

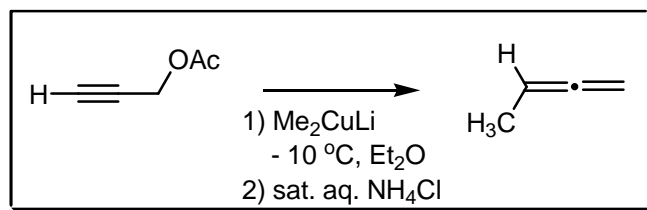
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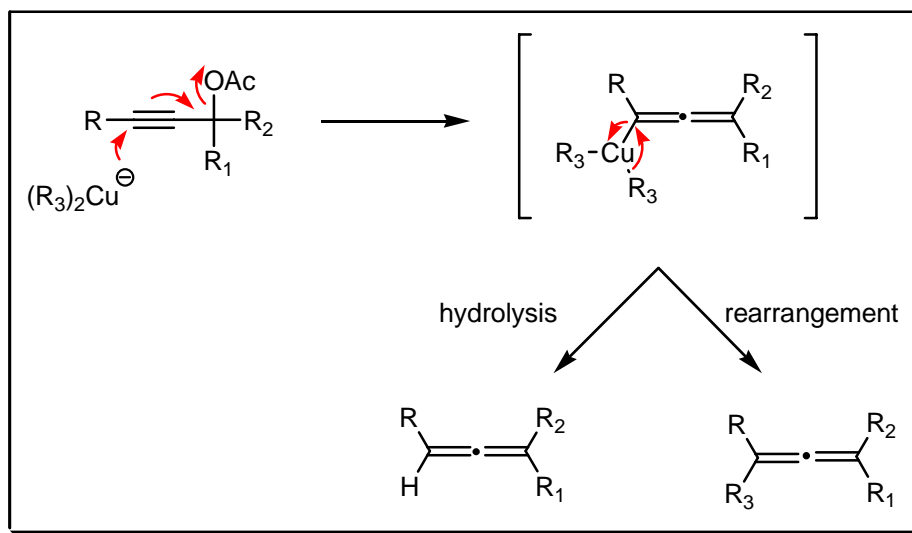
## COMMENTS :

## CRABBÉ SYNTHESIS

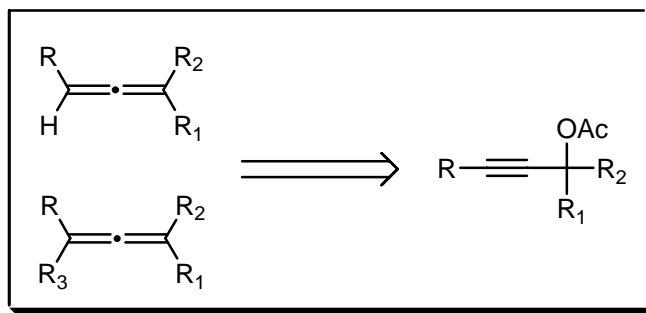
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The formation of allenes by the reaction of lithium diorganocuprates on propargylic acetates via hydrolysis or rearrangement.

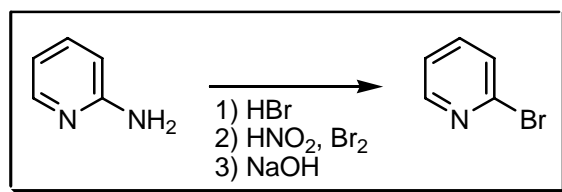
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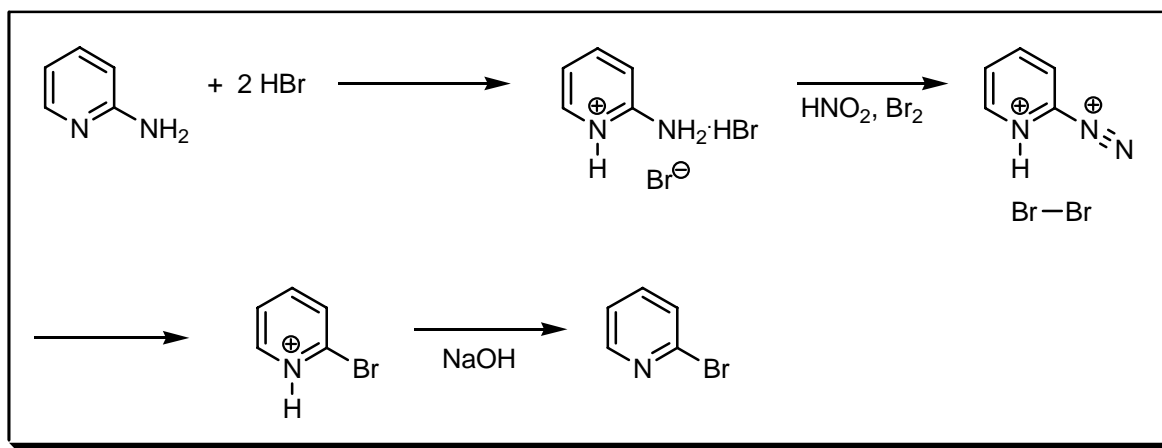
## COMMENTS :

## CRAIG EXCHANGE

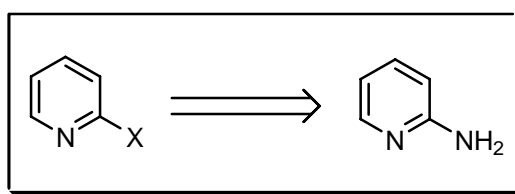
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

$\alpha$ -Halide substituted pyridines are prepared by the diazotisation of an  $\alpha$ -aminopyridine in hydrohalogenic acid solution in the presence of excess halogen. This method gives much higher yields than the more common **Sandmeyer** arylamine halogenation reaction. See also **Balz – Schiemann**, **Cadogan** arylation, **Demjanov** rearrangement, **Gattermann** diazo, **Gattermann** sulphinic acid, **Griess** deamination, **Knoevenagel** diazotation, **Körner – Contardi**, **Meerwein** arylation, **Sandmeyer** diazonium, **Schwechten** and **Witt** diazotation reactions.

## REFERENCES :

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Org. Synth. Coll. Vol. : 3, 136

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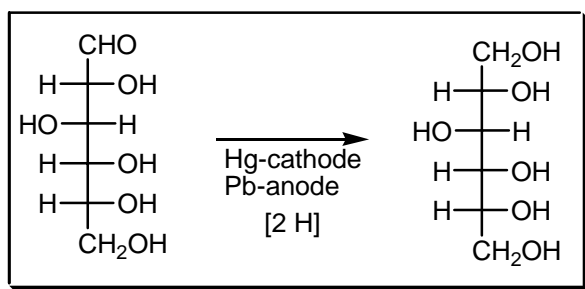
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## COMMENTS :

## CREIGHTON PROCESS

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### EXAMPLE :



### NOTES :

The electrolytic sugar reduction (mainly glucose) to the corresponding alcohols (sorbitol) using mercury and lead electrodes.

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### REFERENCES :

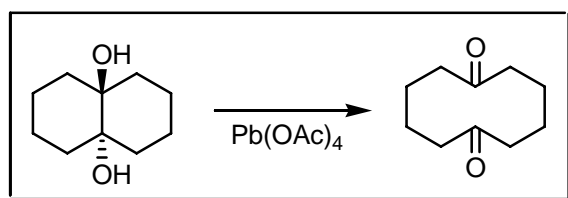
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### COMMENTS :

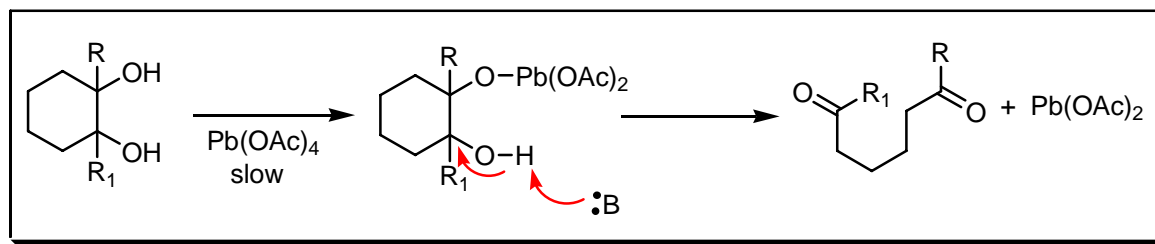
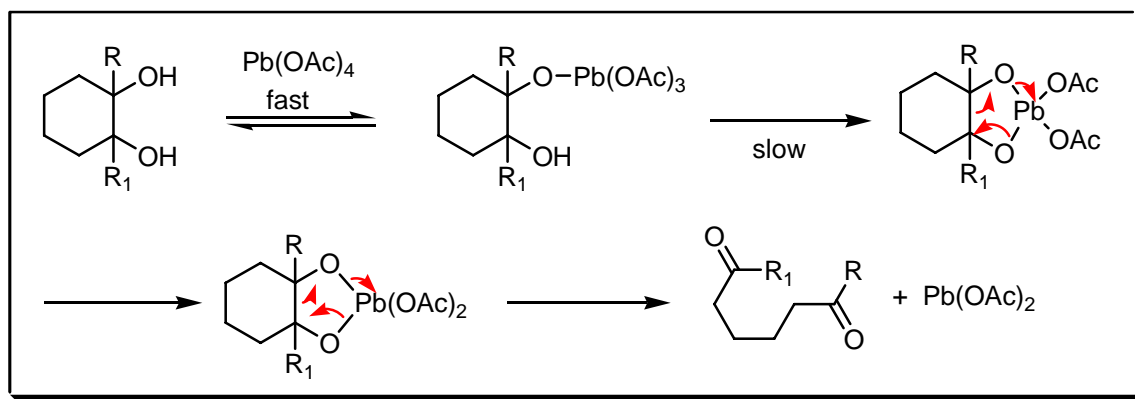
## CRIEGEE GLYCOL CLEAVAGE

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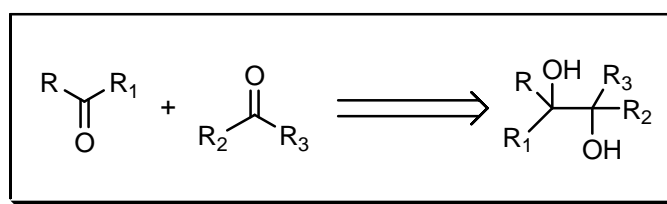
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Lead tetraacetate is used for the cleavage of  $\alpha$ -glycols. The reaction has a variety of applications including the determination of ring structures in sugars. Also works on  $\beta$ -amino alcohols, glyoxals and  $\alpha$ -hydroxy aldehydes or ketones. The cleavage preferentially takes place *via* a five-membered lead(IV) acid diester. If the OH-groups are fixed in a *trans* orientation the reaction proceeds slowly *via* the mono-ester. See also **Hudson – Jackson**, **Lemieux – Johnson**, **Malprade**, **Milas**, **Rigby** and **Ruff – Fenton** reactions.

## REFERENCES :

**March** : 1175

**Smith – March** : 1520

**Smith** : 304

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**Houben – Weyl** : E3, 510

**Org. React.** : 2, 341

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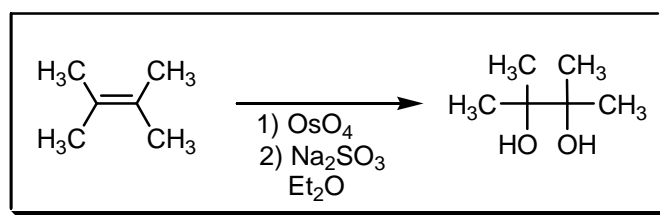
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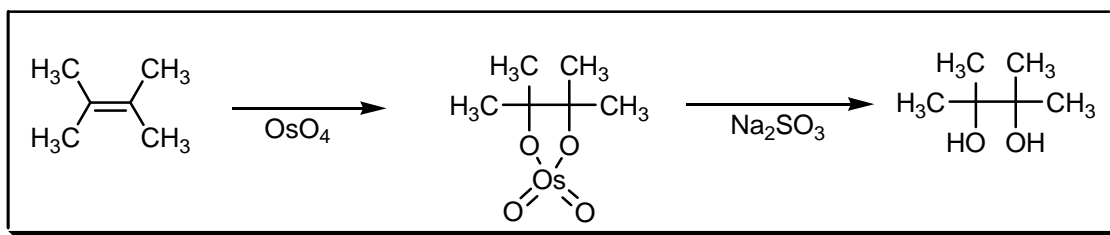
**COMMENTS :**

## CRIEGEE OSMIUM TETROXIDE REACTION

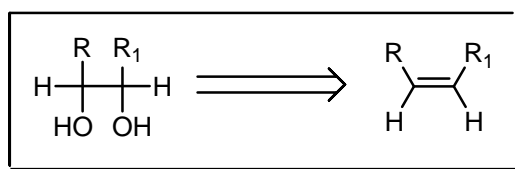
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

Alkenes react with osmium tetroxide in dry ether to form a cyclic osmic ester, which can be isolated and is subsequently cleaved to the *cis*-glycol using sodium sulfite. See also **Milas**, **Prévost**, **Sharpless** dihydroxylation and **Woodward** *cis*-hydroxylation reactions.

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## REFERENCES :

**March** : 822

**Smith – March** : 1048

**Smith** : 284

**Smith 2<sup>nd</sup>** : 248

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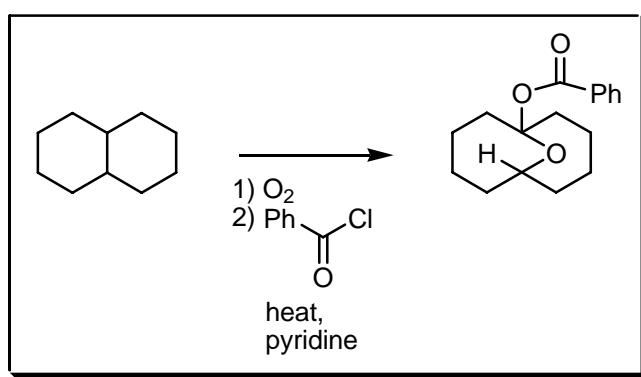
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## COMMENTS :

## CRIEGEE REARRANGEMENT

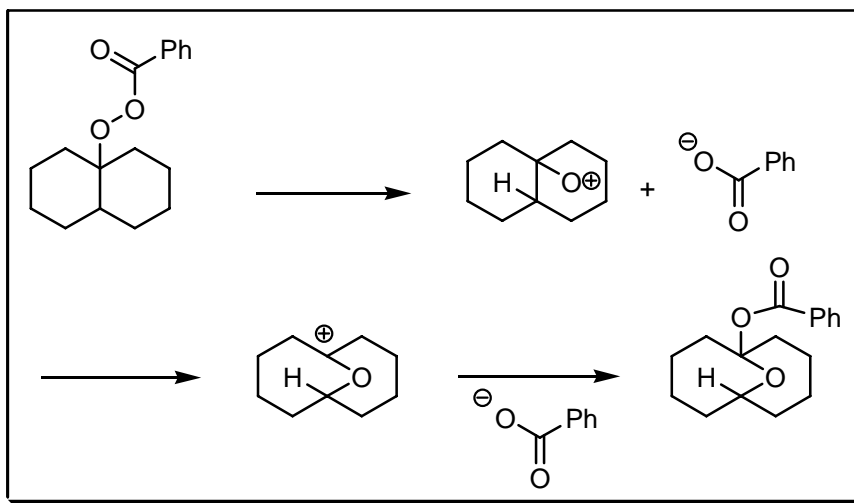
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### EXAMPLE :

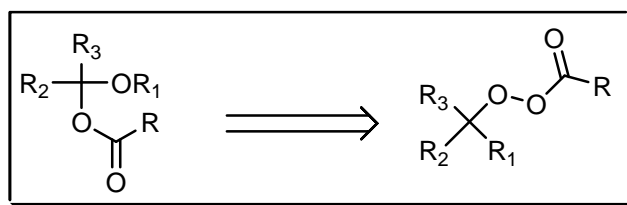




## MECHANISM :



## DISCONNECTION :



## NOTES :

In the original paper by **Criegee**, 9-decalyl peresters rearrange rapidly (in solvents of high ionising power) with ionic fission of the oxygen-oxygen link to form the corresponding esters of 1-hydroxy-1,6-epoxycyclodecane. This reaction has been extended to secondary allylic hydroperoxides. See also **von Baeyer – Villiger** and **Wagner – Meerwein** reactions.

## REFERENCES :

**Org. React.** : **43**, 251

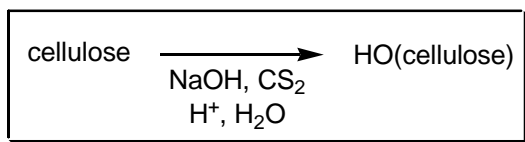
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COMMENTS :

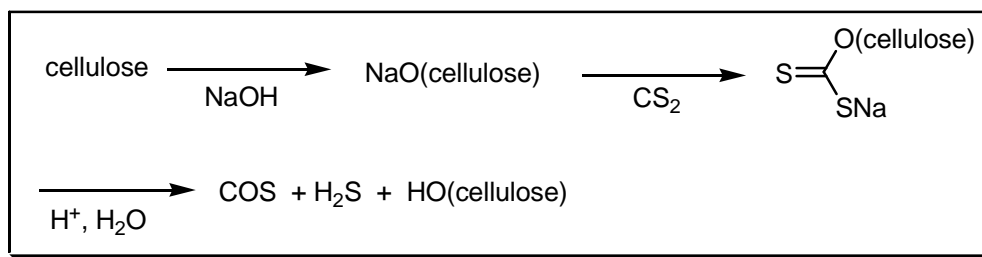
## CROSS – BEVAN – BEADLE REACTION

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EXAMPLE :



MECHANISM :



NOTES :

The formation of artificial silk from cellulose. See also **Chardonnet** reaction.

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REFERENCES :

Houben – Weyl : 14/2, 882

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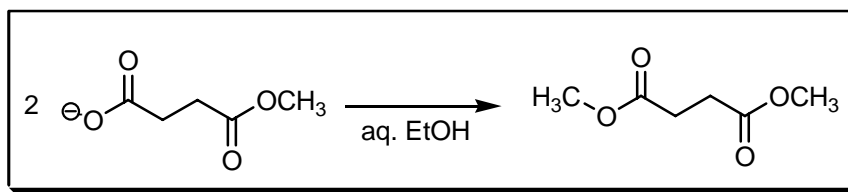
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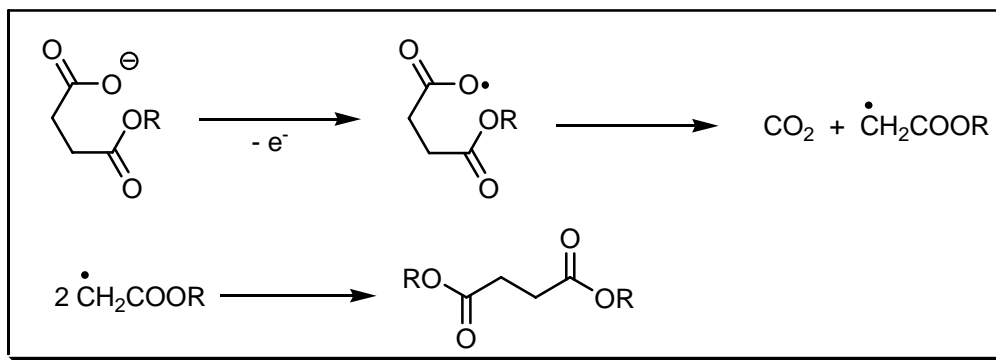
COMMENTS :

## CRUM BROWN – WALKER ELECTROLYSIS

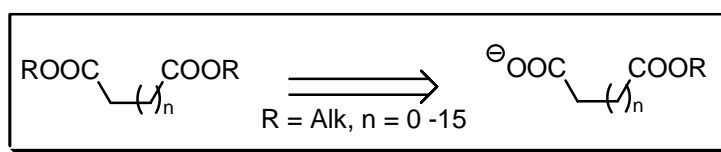
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The formation of  $\omega,\omega'$ -dicarboxylic acid esters starting from the mono ester with an ionised carboxylic acid under the **Kolbe** electrolysis conditions. See also **Hofer – Moest** and **Kolbe** electrolytic reactions.

### REFERENCES :

Houben – Weyl : 8, 500, 599

Org. Synth. : 21, 48; 60, 1

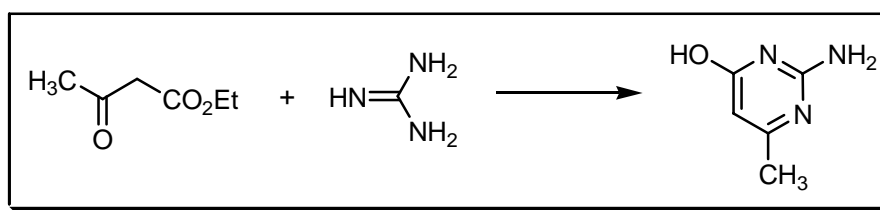
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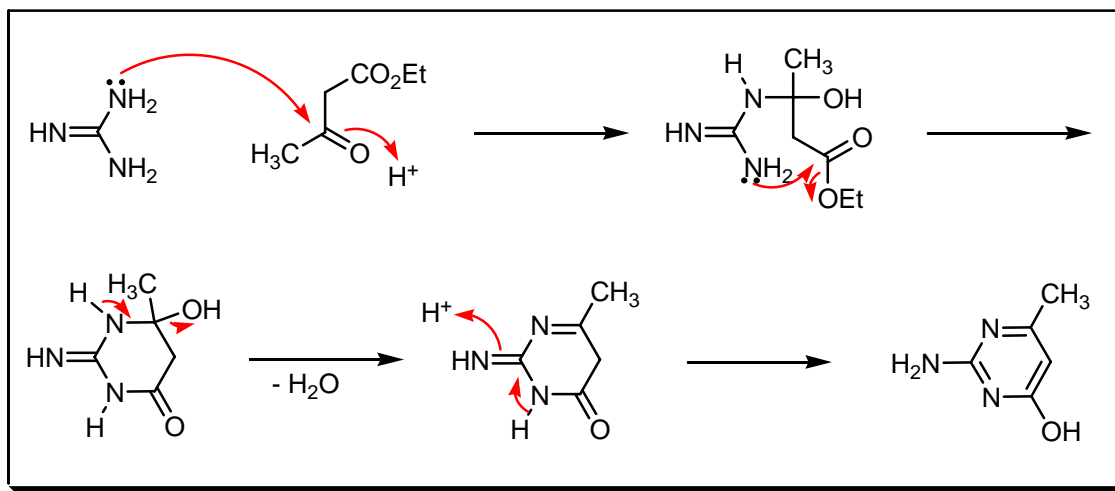
COMMENTS :

CURATOLO SYNTHESIS

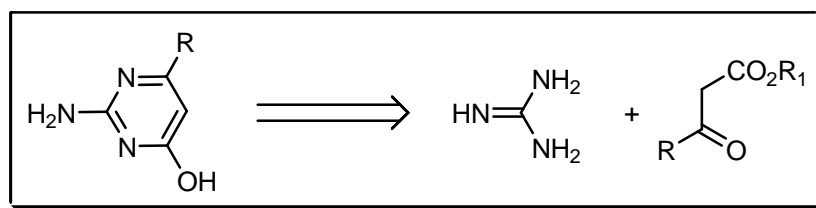
EXAMPLE :



MECHANISM :



DISCONNECTION :



**NOTES :**

The synthesis of 2-amino-6-hydroxypyrimidines by heating guanidine carbonate with  $\beta$ -ketoesters. See also **Traube purine** reaction.

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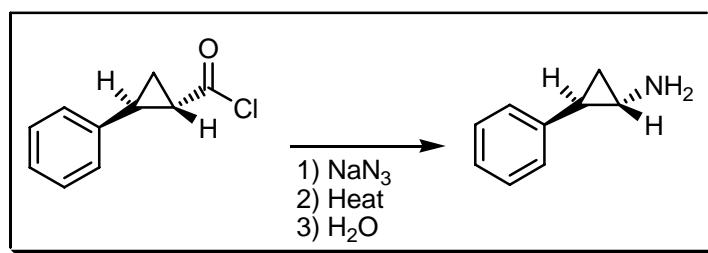
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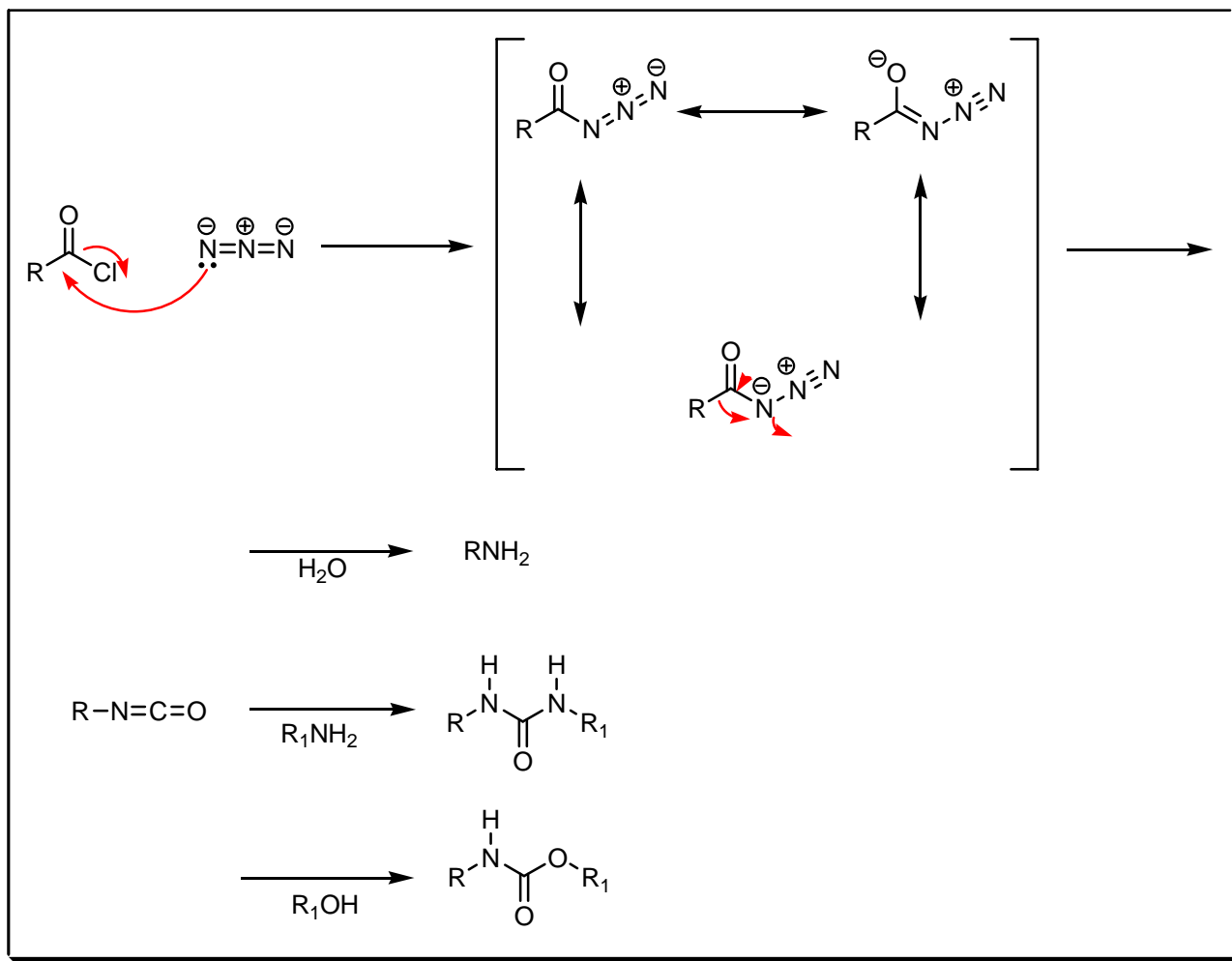
**COMMENTS :**

## CURTIUS REARRANGEMENT

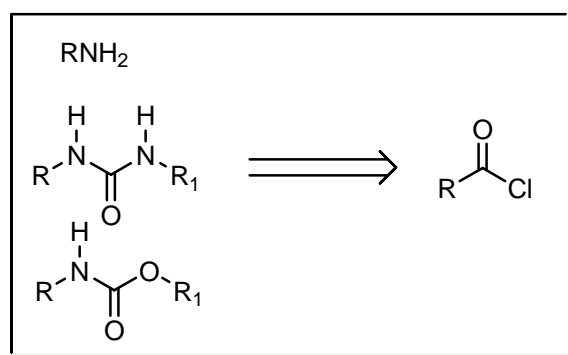
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**EXAMPLE :**

# MECHANISM :



# DISCONNECTION :



## NOTES :

The rearrangement of acid azides to isocyanates with evolution of nitrogen. The isocyanates can be converted into urethanes, ureas, amides and amines. The reaction is carried out in ethanolic solution so that the isocyanate formed first reacts with the alcohol to produce an urethane from which a primary amine can be obtained by hydrolysis. When the azide contains halogen or hydroxyl groups in the  $\alpha$ -position, or  $\alpha,\beta$ -unsaturation, the product is an aldehyde or ketone. The alkaline hydrolysis of the isocyanate to sometimes called **Wurtz** amine synthesis. The **photochemical Curtius** rearrangement is also known as the **Harggar** reaction. See also **Beckmann**, **Hofmann** degradation, **Lossen**, **Schmidt** rearrangement, **Tiemann** rearrangement and **Wolff** reactions.

---

## REFERENCES :

**March** : 886, 1091

**Smith – March** : 1178, 1380, 1384, 1406, 1412

**Smith** : 1147

**Smith 2<sup>nd</sup>** : 862, 955

**Houben – Weyl** : **11/1**, 862; **E3**, 527; **E5**, 554; **E6b**, 140; **E8a**, 759, 838; **E8c**, 677; **E8d**, 79; **E16a**, 596; **E16d**, 627; **E19c**, 408

**Org. React.** : **3**, 337

**Org. Synth.** : **18**, 5; **36**, 69; **51**, 48

**Org. Synth. Coll. Vol.** : **2**, 24, **4**, 819; **6**, 910

**Science of Synthesis** : **10**, 75, 177, 258

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## COMMENTS :

D



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**B**

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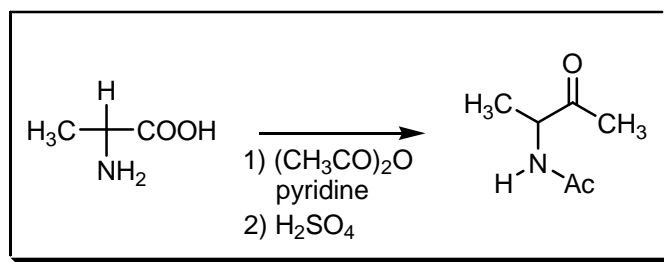
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**W**

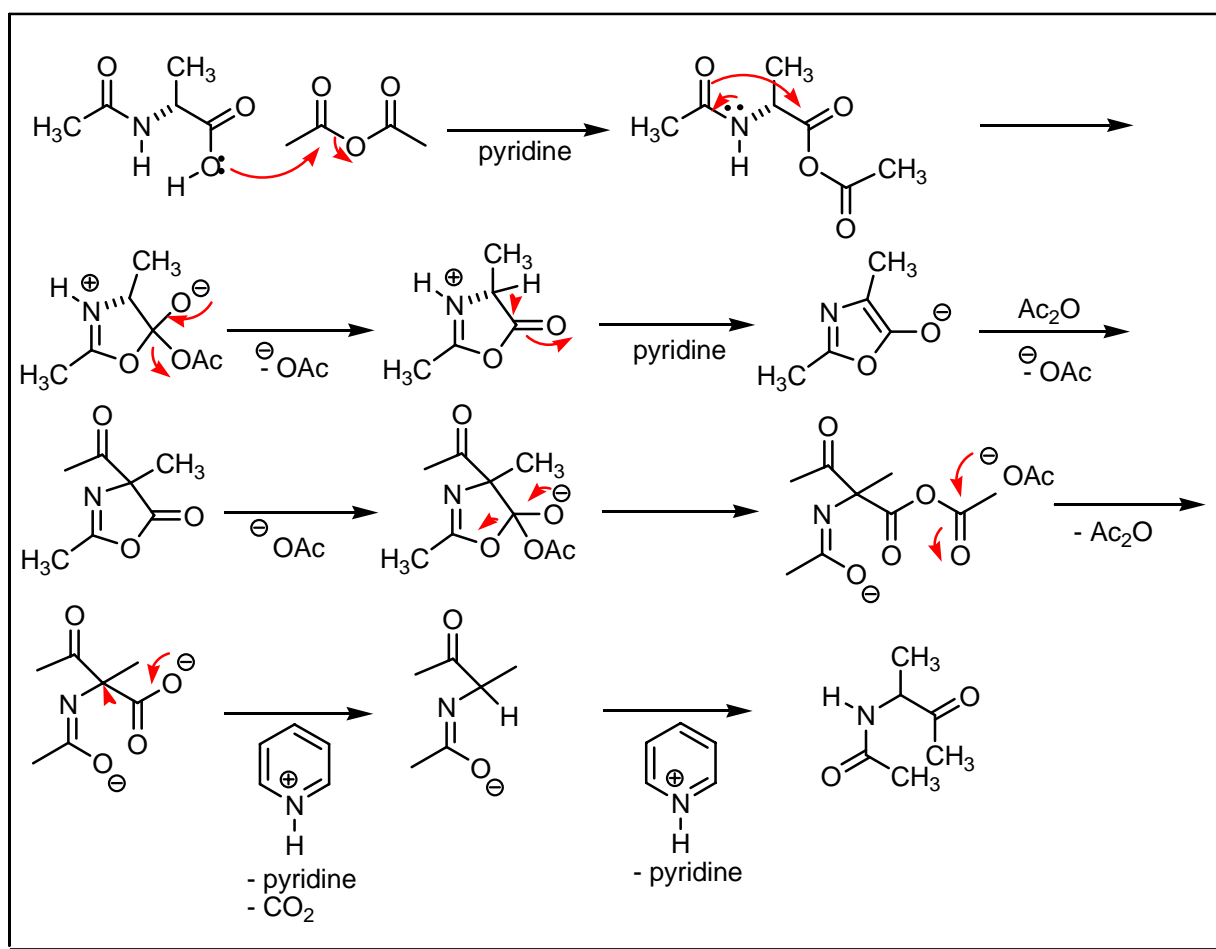
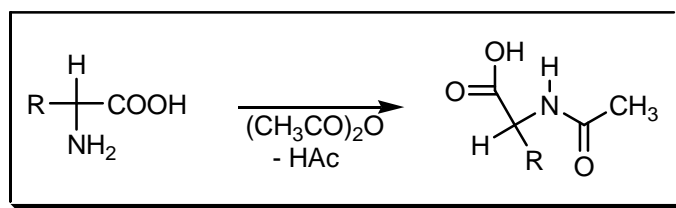
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## DAKIN – WEST REACTION

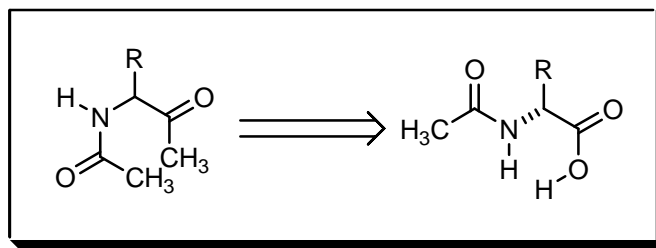
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

Amino acids, when heated with aliphatic acid anhydrides under the catalytic influence of a base such as pyridine, undergo decarboxylative C-acylation with formation of the corresponding acylamino-ketones. The corresponding acyl halide may replace the anhydride. See also **Dakin** azlactone, **Erlenmeyer – Plöchl** and **Kawase** rearrangement reactions.

## REFERENCES :

**March** : 631

**Smith – March** : 812

**Houben – Weyl** : **E8a**, 927, 1006; **E15**, 678

**Org. Synth.** : **33**, 1; **45**, 1

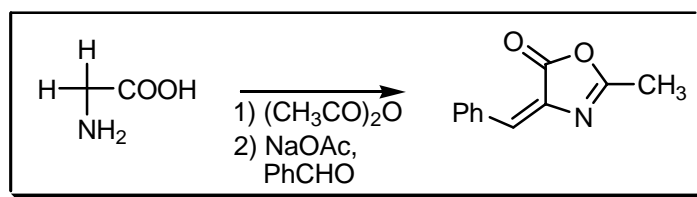
**Org. Synth. Coll. Vol.** : **4**, 5; **5**, 27

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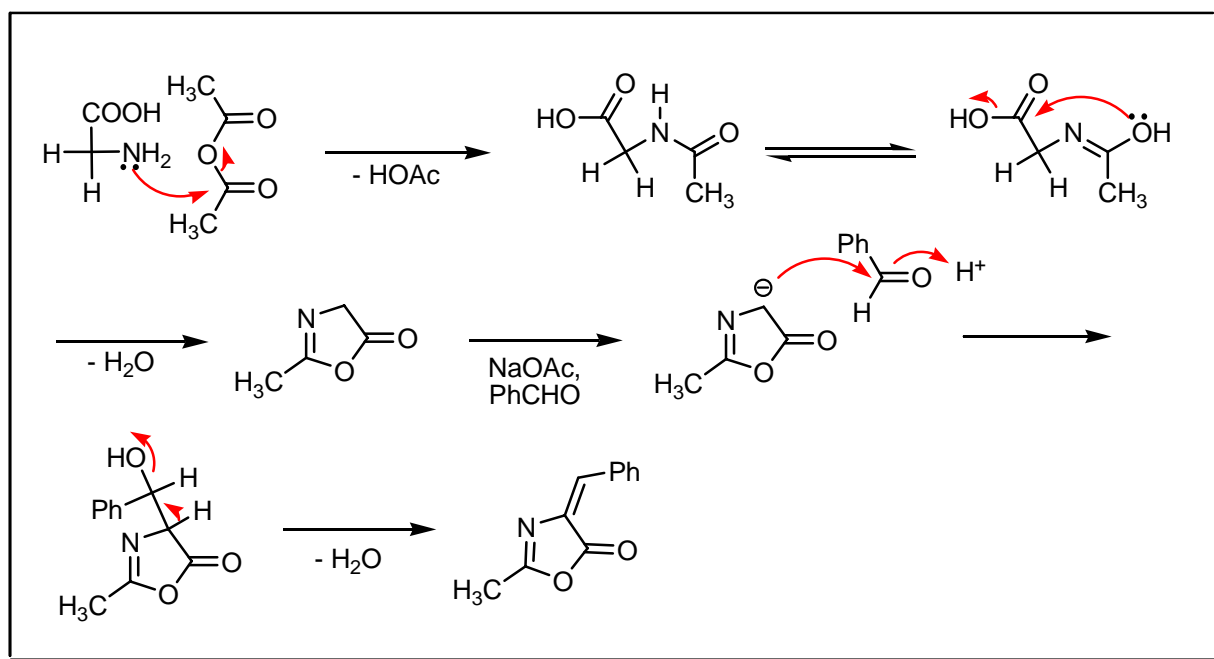
## COMMENTS :

## DAKIN AZLACTONE REACTION

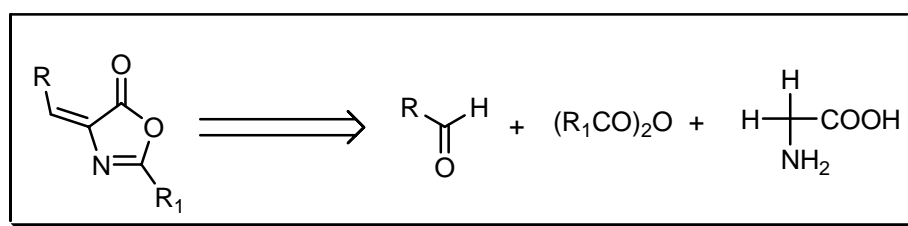
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :

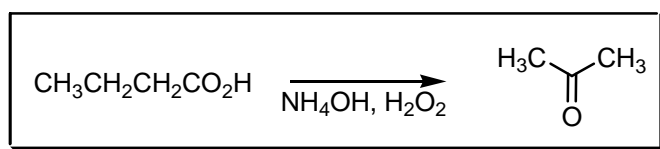


### NOTES :

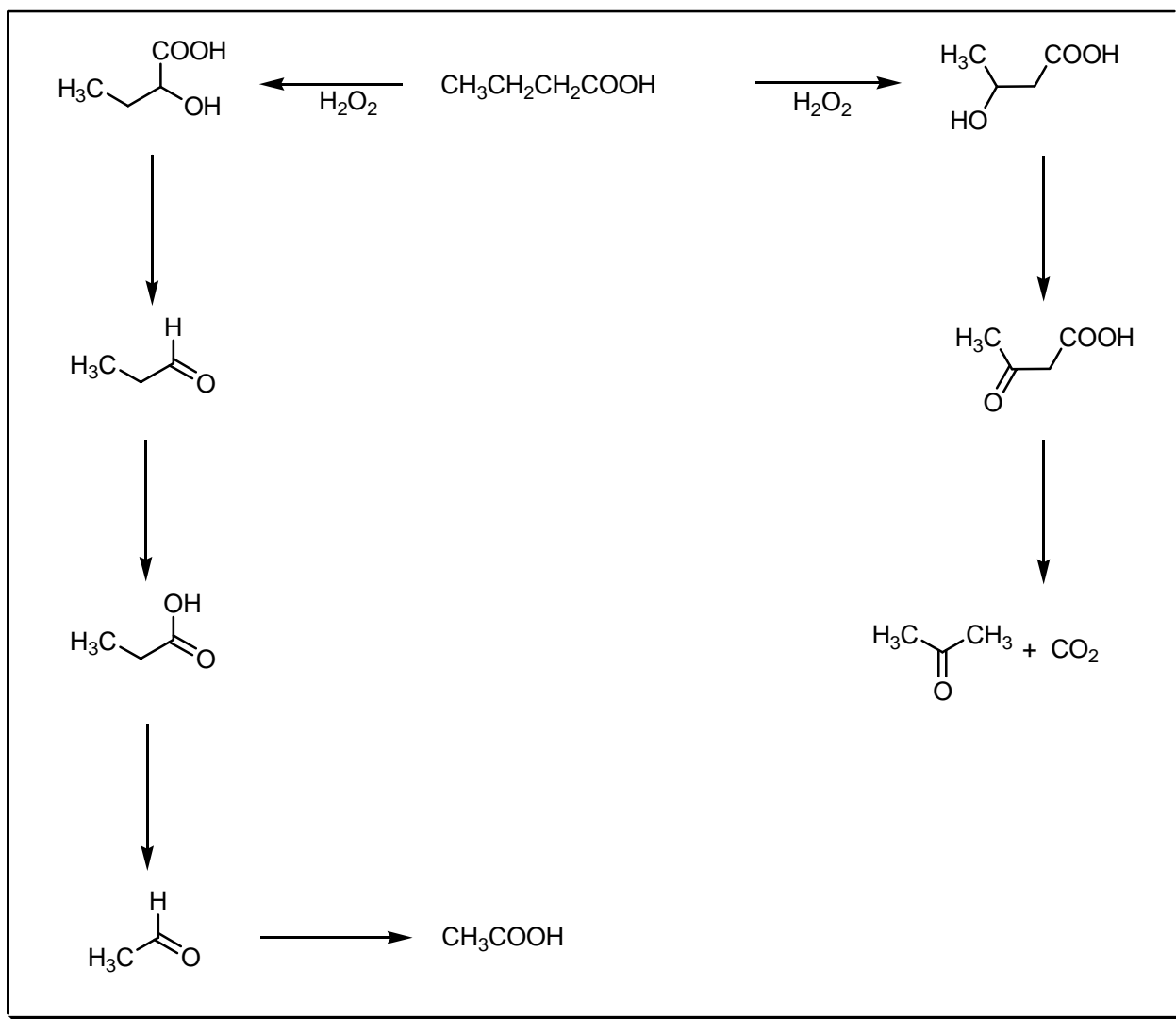
A variant of the **Erlenmeyer – Plöchl** 5-oxazolone synthesis in which glycine is treated with one mole of acetic anhydride and then with an aldehyde, sodium acetate and more acetic anhydride. See also **Dakin – West** and **Erlenmeyer – Plöchl** reactions.

**REFERENCES :**

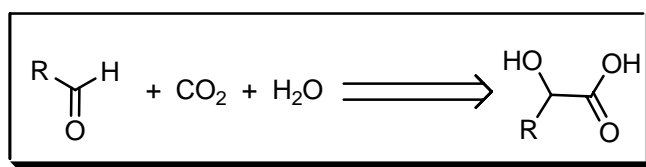
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2) E. Baltazzi, *J. Chem. Soc., Quat. Rev.*, 1955, **9**, 153.
- 

**COMMENTS :****DAKIN OXIDATION OF BUTYRIC ACID****EXAMPLE :**

**MECHANISM :**



### DISCONNECTION :



**NOTES :**

The ammonium salts of butyric, glycolic, lactic,  $\alpha$ -oxybutyric,  $\beta$ -oxybutyric,  $\alpha$ -oxyisovaleric acids are oxidised by hydrogen peroxide at 37 °C to yield aldehydes with exception of glycolic,  $\beta$ -oxybutyric and butyric acids.

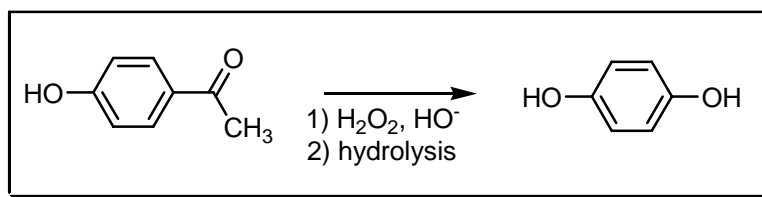
## REFERENCES :

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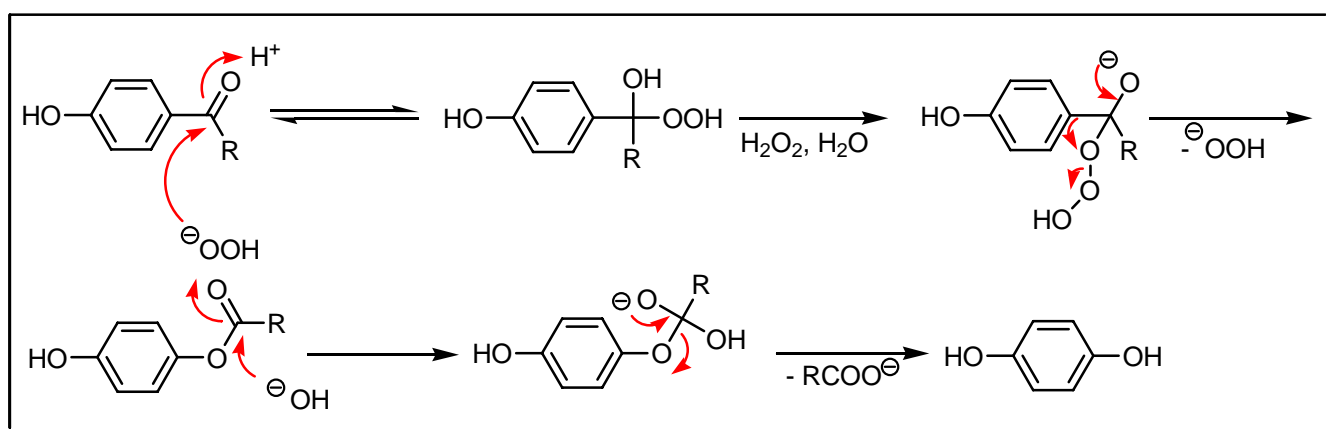
COMMENTS :

DAKIN PHENOL ALDEHYDE OXIDATION

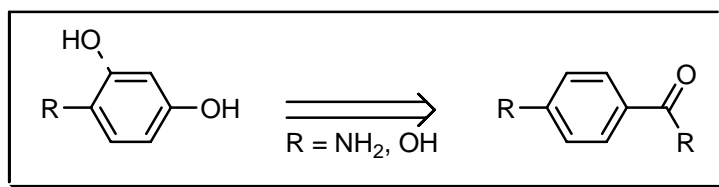
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The use of peroxide to replace an *o*- or *p*-formyl or -acetyl group in phenols or amines with a hydroxyl group. The amine or hydroxyl group must be *ortho* or *para* to the carbonyl group. The mechanism is essentially the same as for the **von Baeyer – Villiger** reaction. Some other unlikely mechanisms including a spirocyclic epoxide intermediate or phenoxide radical mechanism have been proposed. See also **Böeseken – Ballio**, **Bohn – Schmidt**, **Boyland – Sims** and **Elbs** persulfate oxidation reactions.

## REFERENCES :

March : 1184

Smith – March : 1528

Smith : 297

Smith 2<sup>nd</sup> : 261

Houben – Weyl : 7/1, 489

Org. Synth. : 3, 28; 26, 90

Org. Synth. Coll. Vol. : 1, 149; 3, 759

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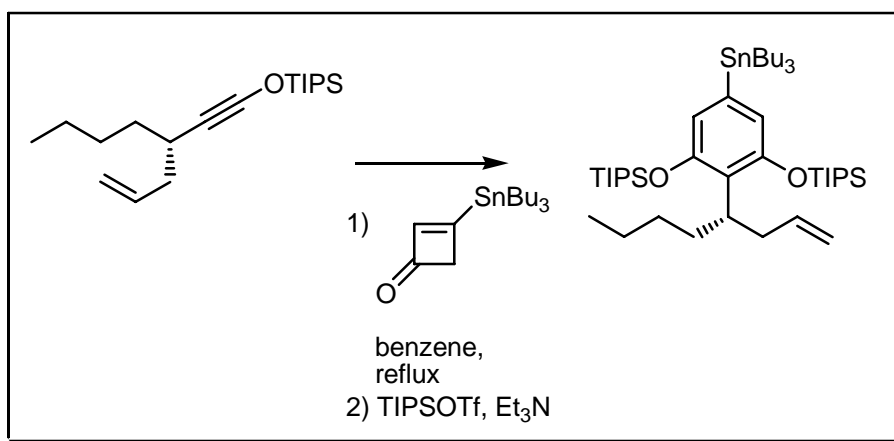
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## COMMENTS :

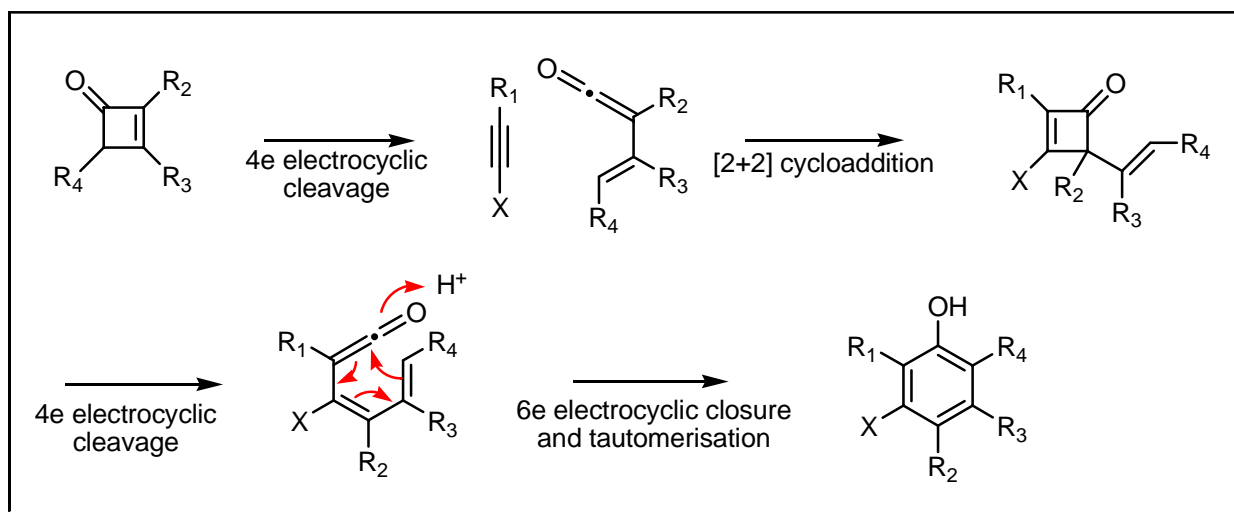


## DANHEISER ANNULATION

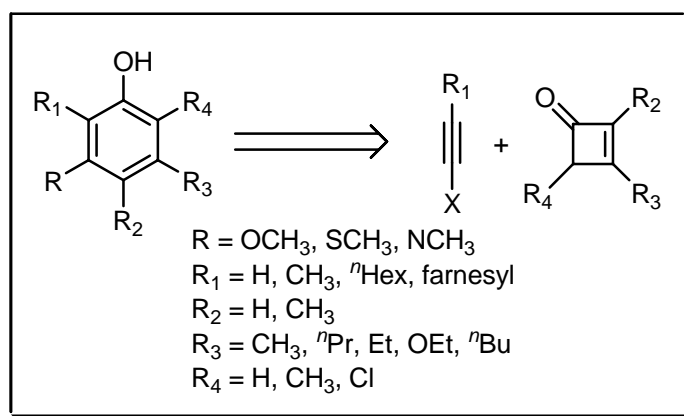
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



**NOTES :**

The one-step thermal combination of a heterosubstituted alkyne with a cyclobutenone derivative. The reaction proceeds *via* a cascade of four pericyclic reactions.

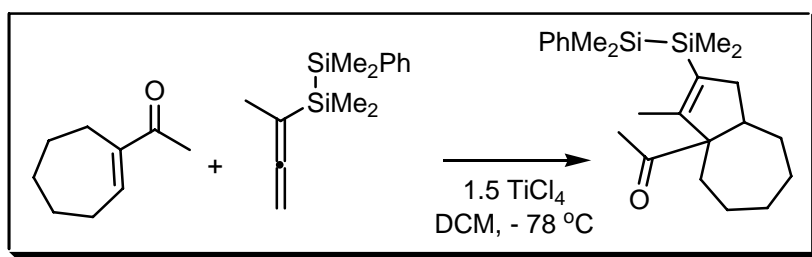
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**REFERENCES :**

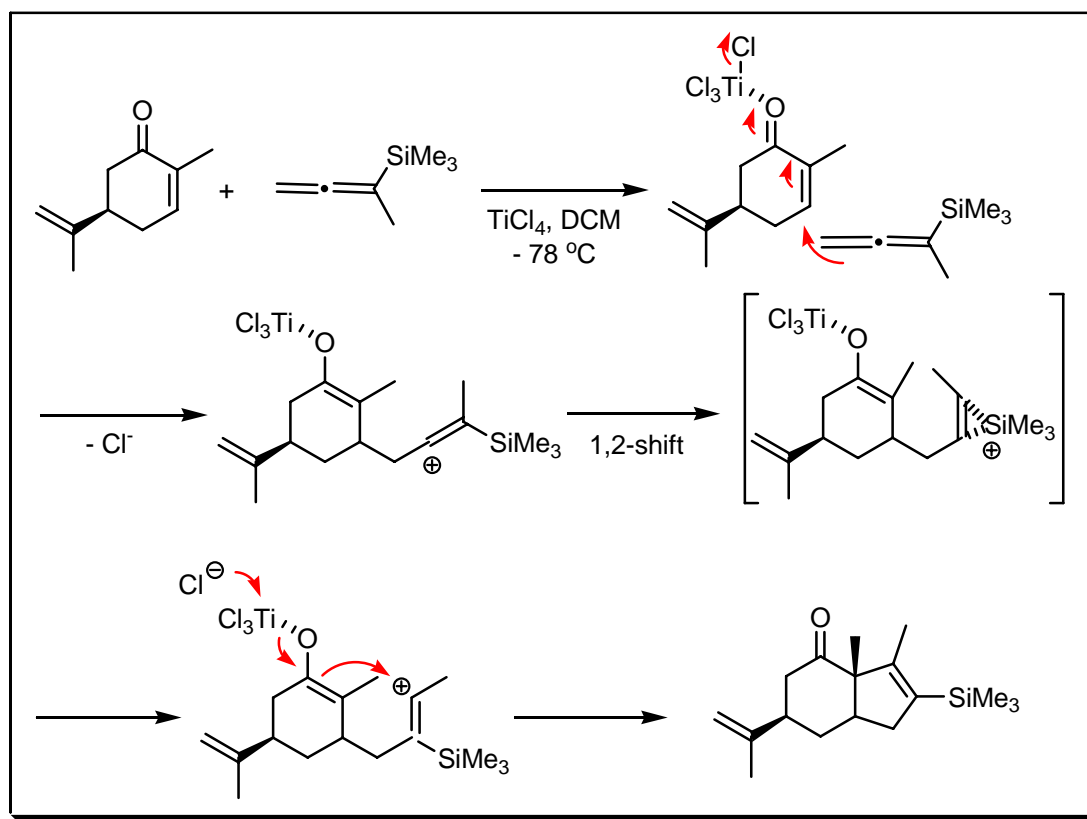
Smith 2<sup>nd</sup> : 982

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- 

**COMMENTS :****DANHEISER CYCLOPENTENE ANNULATION****EXAMPLE :**

## MECHANISM :



## NOTES :

In the presence of a Lewis acid an  $\alpha,\beta$ -unsaturated ketone reacts with an alkylsilylallene to afford an alkylsilyl cyclopentene.

## REFERENCES :

Org. Synth. : 66, 8

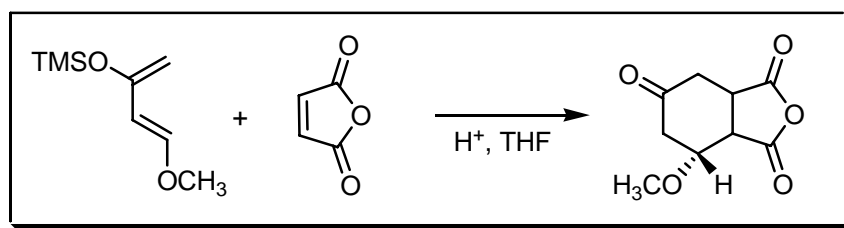
Org. Synth. Coll. Vol. : 8, 347

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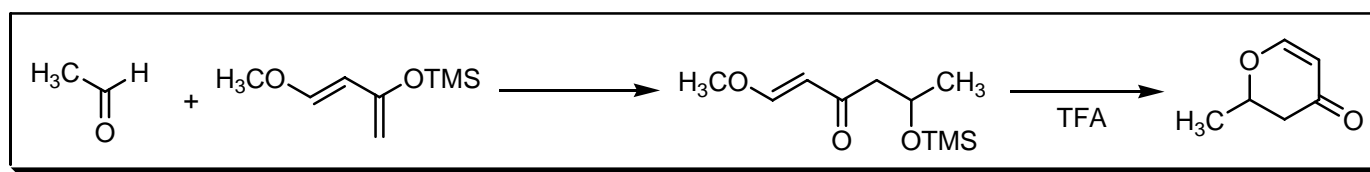
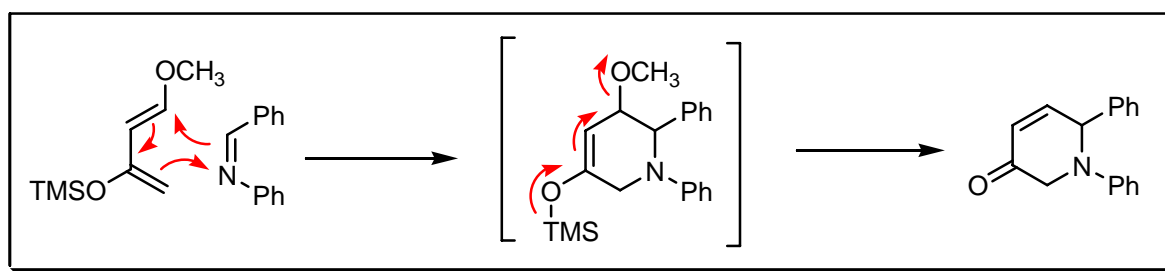
## COMMENTS :

## DANISHEFSKY REACTION

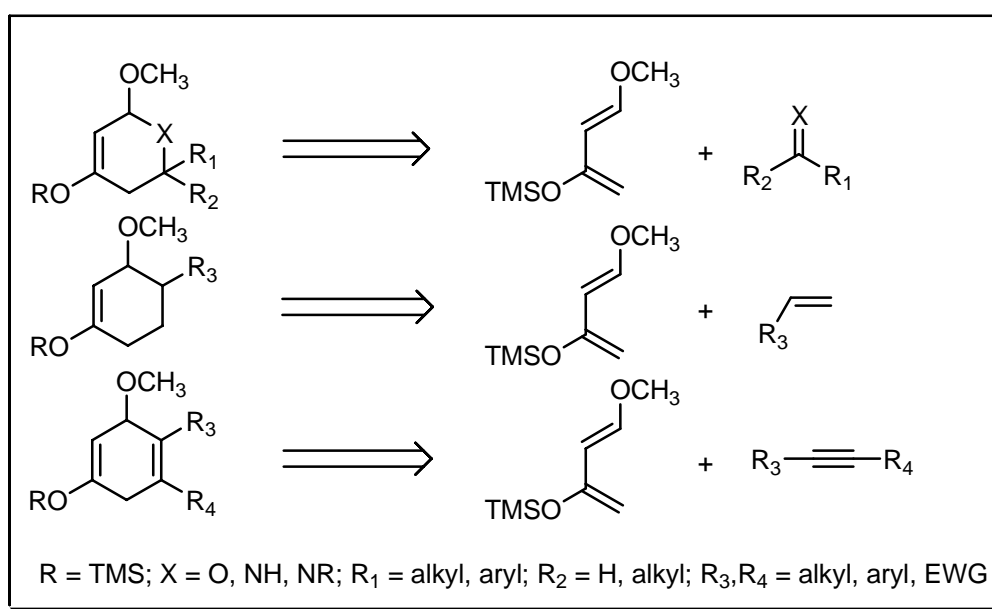
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The use of *trans*-4-methoxybutene-2-one as the diene (**Danishefsky** diene), giving both high reactivity and high orientational specificity in reactions with unsymmetrical dienophiles, where Y is an electron withdrawing group. There is a step-wise pathway proposed, this is often referred to as **Mukaiyama** aldol reaction pathway. See also **Diels – Alder** and **Wagner–Jauregg** reactions.

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## REFERENCES :

March : 839

Smith – March : 1062

Smith : 1113, 1130

Smith 2<sup>nd</sup> : 928

Org. Synth. : **61**, 147

Org. Synth. Coll. Vol. : **7**, 312

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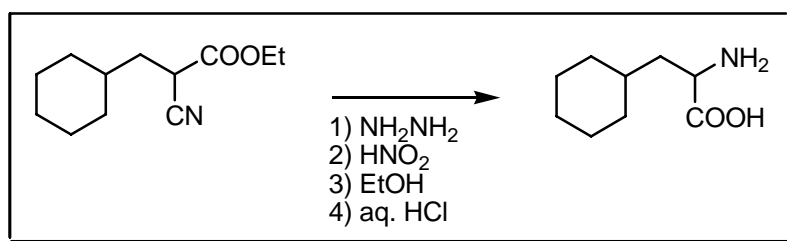
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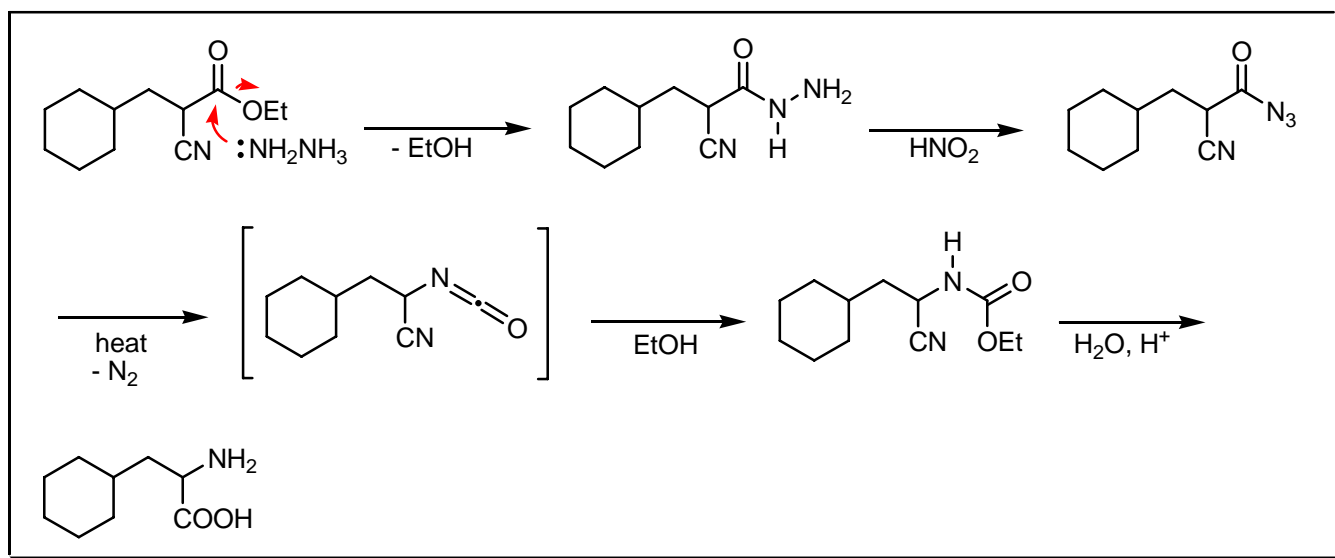
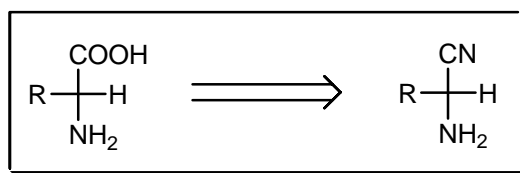
## COMMENTS :

## DARAPSKY AMINO ACID REACTION

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### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

Ethyl alkylcyanoacetate is converted into acylazide *via* the hydrazide. The azide is treated with alcohol and the resulting cyanourethane hydrolysed to the corresponding  $\alpha$ -amino acid. The alkyl cyanoacetate is conveniently prepared by the condensation of ethyl cyanoacetate with an aldehyde to give the corresponding alkylidene compound which is simultaneously hydrogenated. Many amino acids have been prepared this way.

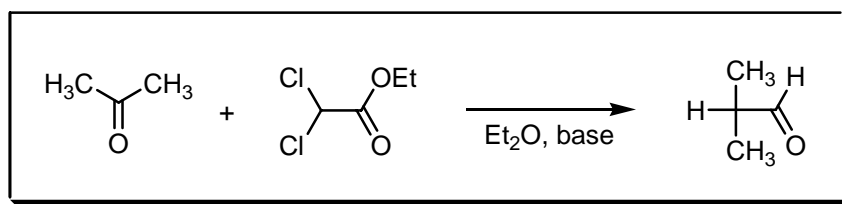
**REFERENCES :**

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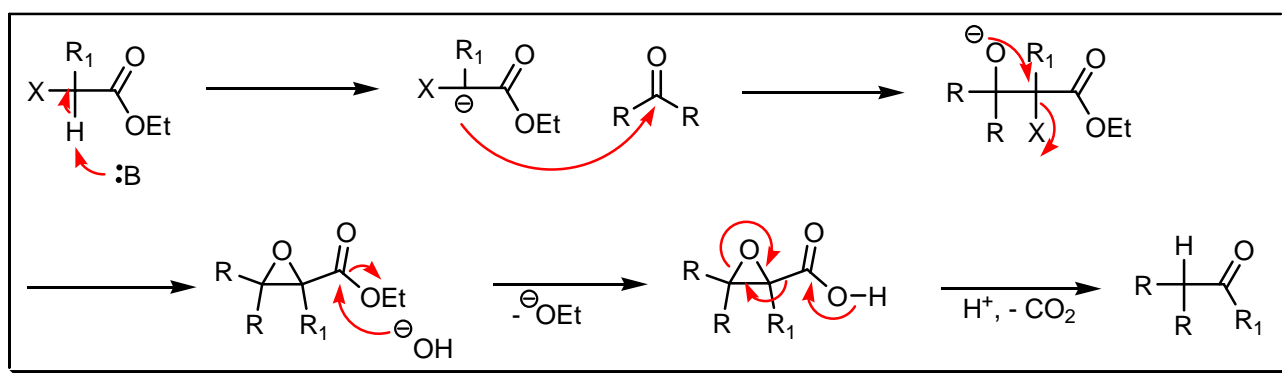
**COMMENTS :**

## DARZENS – ERLLENMEYER – CLAISEN CONDENSATION

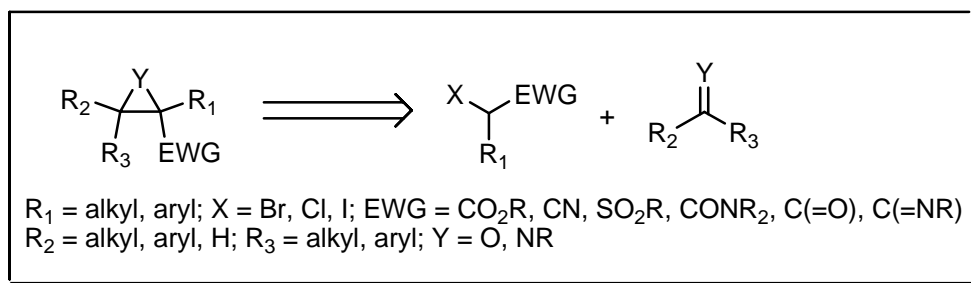
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Ethyl dichloroacetate combines with aldehydes and ketones in the presence of base to yield an  $\alpha$ -chloro- $\beta$ -hydroxyester. (The initial step is a **Knoevenagel**-type reaction.) This can be converted into a glycidic ester or an  $\alpha$ -chloro acrylic ester. Enantioselective **Darzens** reactions are also known. The reaction can be carried out on  $\alpha$ -halo ketones,  $\alpha$ -halo nitriles,  $\alpha$ -halo sulfoxides,  $\alpha$ -halo sulfones,  $\alpha$ -halo *N,N*-disubstituted amides and  $\alpha$ -halo-ketimines. See also **Arndt – Eistert**, **Büchner – Curtius – Schlotterbeck**, **Clibbens – Nierenstein**, **Corey – Chaykovsky**, **Jacobsen – Katsuki**, **Juliá – Colonna**, **Katsuki – Sharpless**, **Mukaiyama – Yamada**, **Prileschajew**, **Shi**, **Weitz – Scheffer** and **Wolff** reactions.

### REFERENCES :

March : 954

Smith – March : 809, 1219

Smith : 902

Smith 2<sup>nd</sup> : 753

Houben – Weyl : 6/3, 406; 7/1, 326; 8, 513; E6a, 49; E14b, 1194

Org. React. : 5, 413; 31, 1

Org. Synth. : 24, 82; 34, 54

Org. Synth. Coll. Vol. : 3, 727; 4, 459

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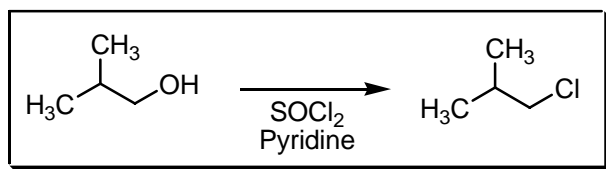
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#### COMMENTS :

## DARZENS METHOD

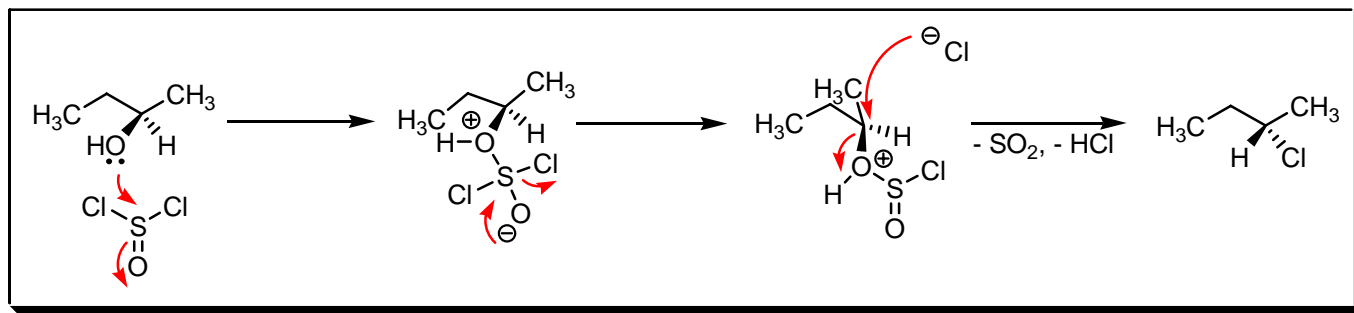
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#### EXAMPLE :

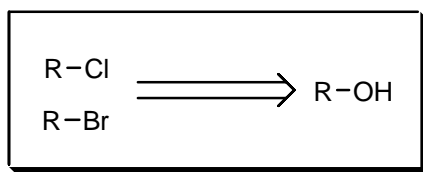




## MECHANISM :



## DISCONNECTION :



## NOTES :

An alcohol is treated with thionyl chloride or thionyl bromide in the presence of a tertiary base. See also **Appel**, **Blum** and **Landauer – Rydon** reactions.

## REFERENCES :

**March** : 327

**Smith – March** : 518

**Smith** : 151

**Smith 2<sup>nd</sup>** : 122

**Org. Synth.** : **12**, 20; **14**, 18; **25**, 84; **31**, 37; **36**, 3; **53**, 13, 70

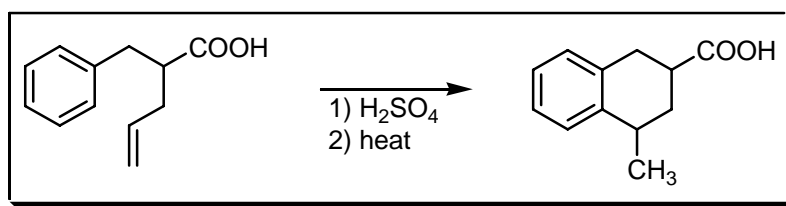
**Org. Synth. Coll. Vol.** : **2**, 136, 159; **3**, 698; **4**, 169, 333; **6**, 75, 781

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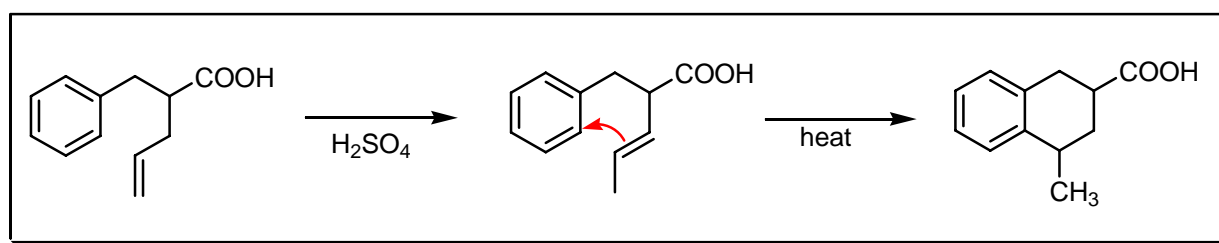
## COMMENTS :

## DARZENS SYNTHESIS OF TETRALIN

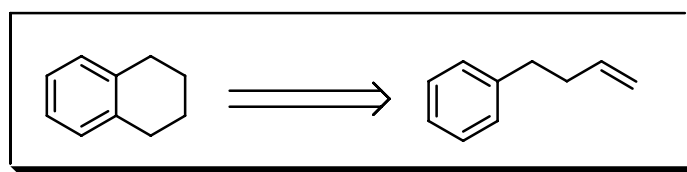
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

A method for the synthesis of tetralin and other tetrahydro-aromatic carboxylic acids. The reaction is typified by the cyclo-isomerisation of allylbenzylacetic acid using sulfuric acid. See also **Bardhan – Sengupta** and **Bogert – Cook** reactions.

### REFERENCES :

Smith : 1332

Smith 2<sup>nd</sup> : 1096

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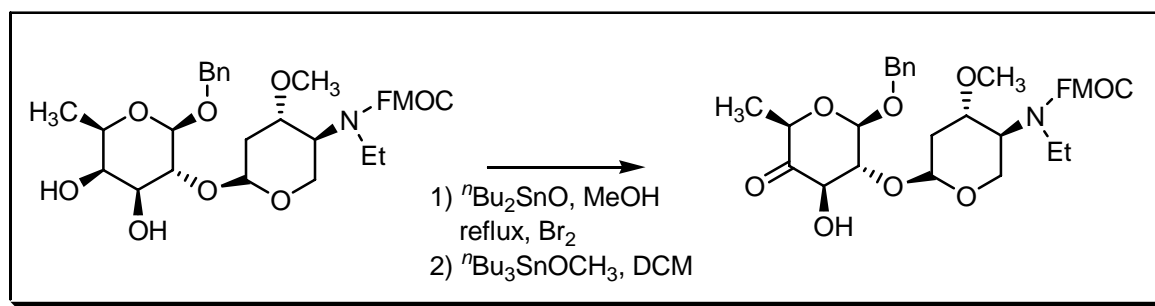
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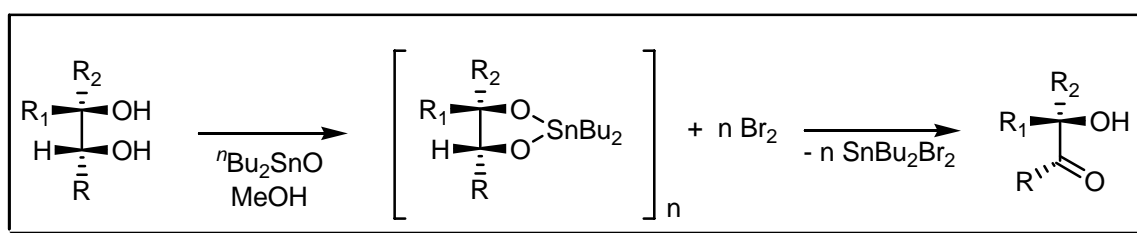
### COMMENTS :

## DAVID – THIEFFRY OXIDATION

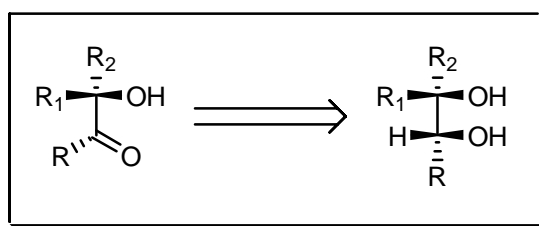
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The oxidation of a sugar diol to a hydroxyl and a carbonyl.  $n\text{Bu}_3\text{SnOCH}_3$  is used to quench the  $\text{HBr}$  formed. The bromine oxidises the oxygen-tin bond to give the carbonyl. See also **Anelli**, **Ball – Goodwin – Morton**, **Collins**, **Corey – Kim**, **Corey – Schmidt**, **Corey – Suggs**, **Delépine**, **Dess – Martin**, **Einhorn** oxidation, **Fétizon**, **Jones** oxidation, **Ley**, **Maurer – Drefahl**, **Mukaiyama** oxidation, **Nicolaou**, **Oppenauer**, **Parikh – von Doering**, **Pfitzner – Moffatt**, **Sarett**, **Swern** and **Uemura** reactions.

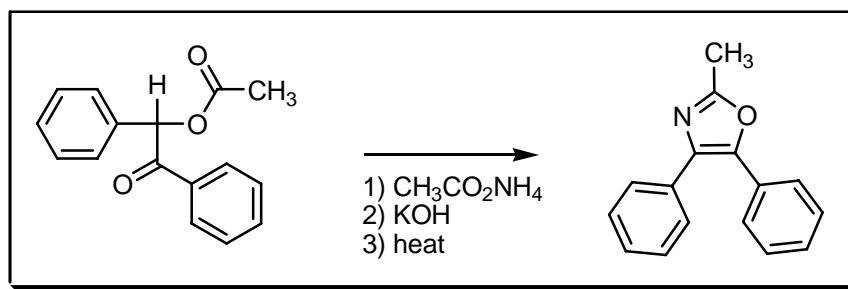
### REFERENCES :

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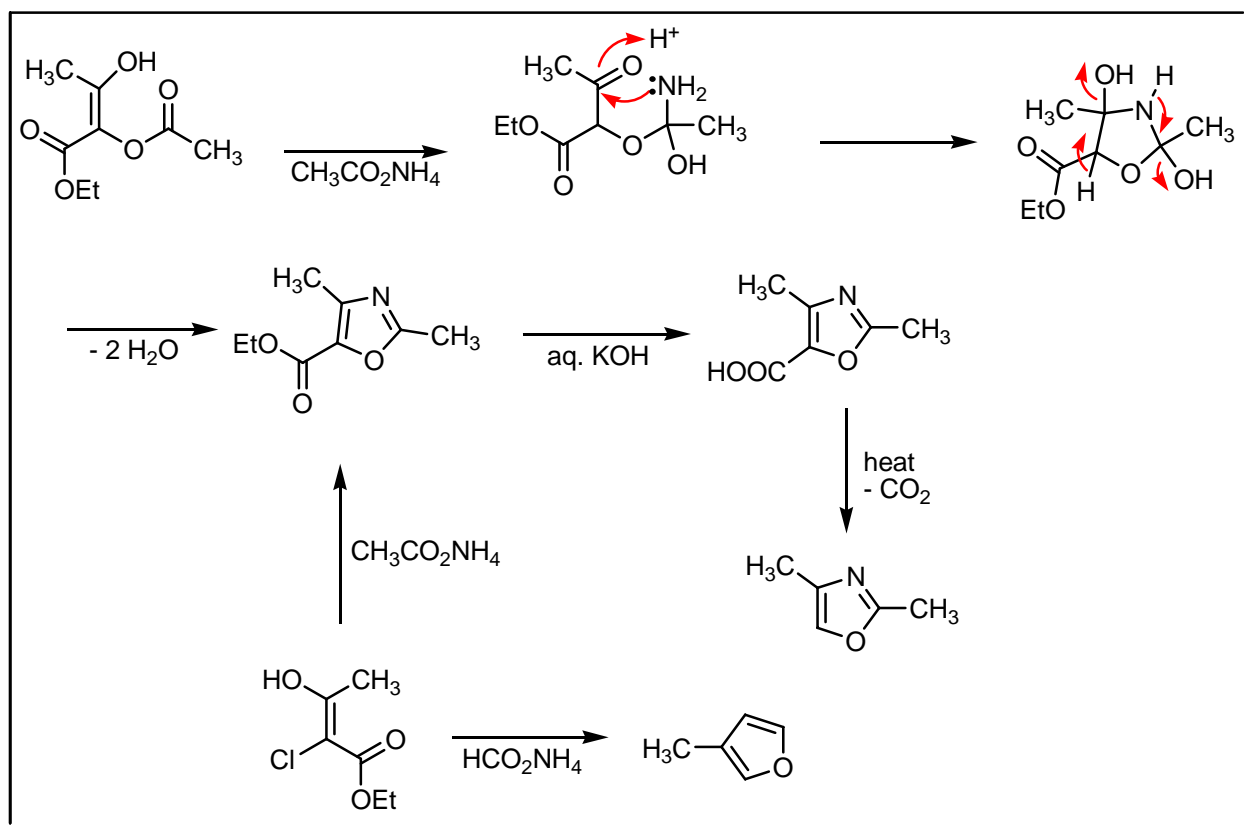
COMMENTS :

## DAVIDSON OXAZOLE SYNTHESIS

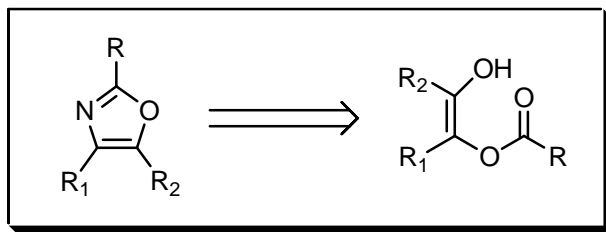
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

*o*-Acyloins when treated with ammonium acetate in acetic acid give oxazole derivatives. See also **Fischer** oxazole, **Japp** oxazole and **Robinson – Gabriel** reactions.

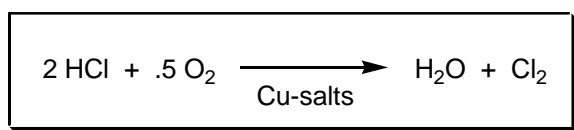
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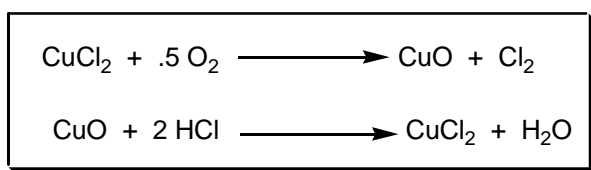
## COMMENTS :

## DEACON REACTION

### EXAMPLE :



### MECHANISM :



## NOTES :

Hydrogen chloride is oxidised with oxygen in the presence of copper salts to chlorine. Other catalysts can also be used.

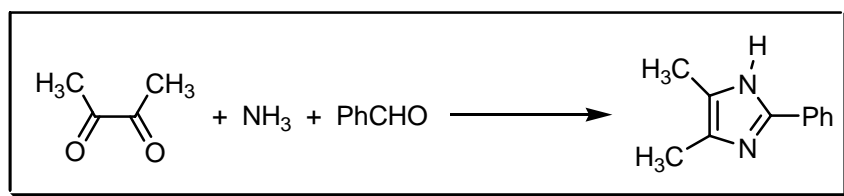
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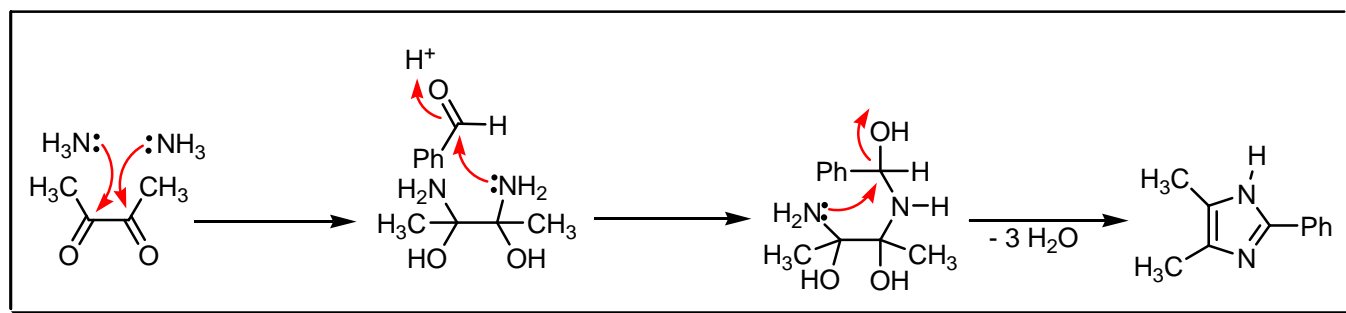
## COMMENTS :

## DEBUS – RADZISZEWSKI IMIDAZOLE SYNTHESIS

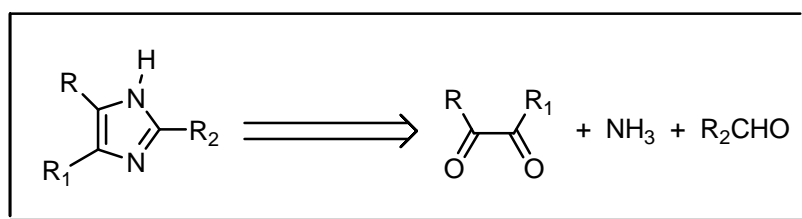
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

This reaction is one of a number of similar imidazole syntheses. The **Debus – Radziszewski** reaction forms the imidazole ring by condensing  $\alpha$ -dicarboxylic compounds with aldehydes and ammonia. There are two modifications by **Weidenhagen** and **Maquenne**, each using slightly different conditions. See also **Akabori – Neuberg – Fischer**, **Brackeen**, **Bredereck**, **Maquenne**, **Wallach** imidazole and **Weidenhagen** reactions.

## REFERENCES :

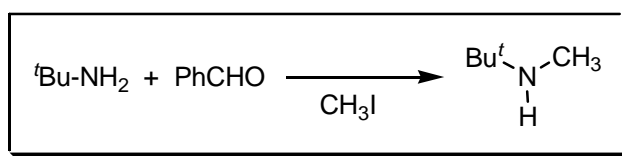
Houben – Weyl : E8c, 9, 13, 97

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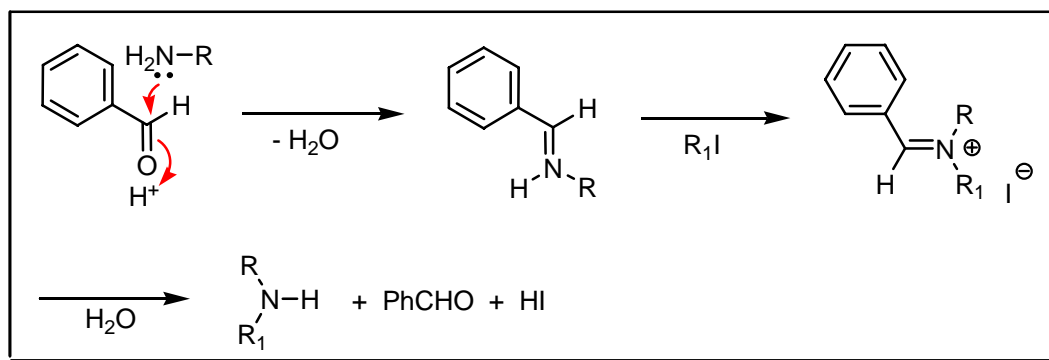
## COMMENTS :

## DECKER – FORSTER AMINATION

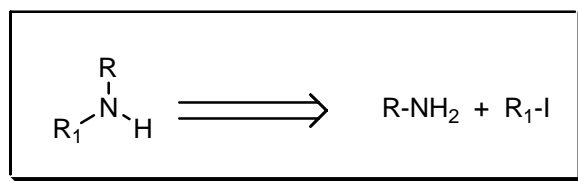
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The conversion of a primary amine to a secondary amine by condensation with an aldehyde, followed by the addition of alkyl halide to a Schiff's base and followed by subsequent hydrolysis. See also **Eschweiler – Clarke**, **Henze – Humphries**, **Leuckart** and **Schiff** reactions.

## REFERENCES :

Houben – Weyl : 11/1, 108, 956; **E14b**, 994, 1129

Org. Synth. : 44, 72

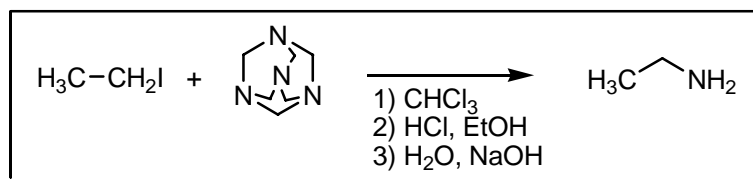
Org. Synth. Coll. Vol. : 5, 736

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## COMMENTS :

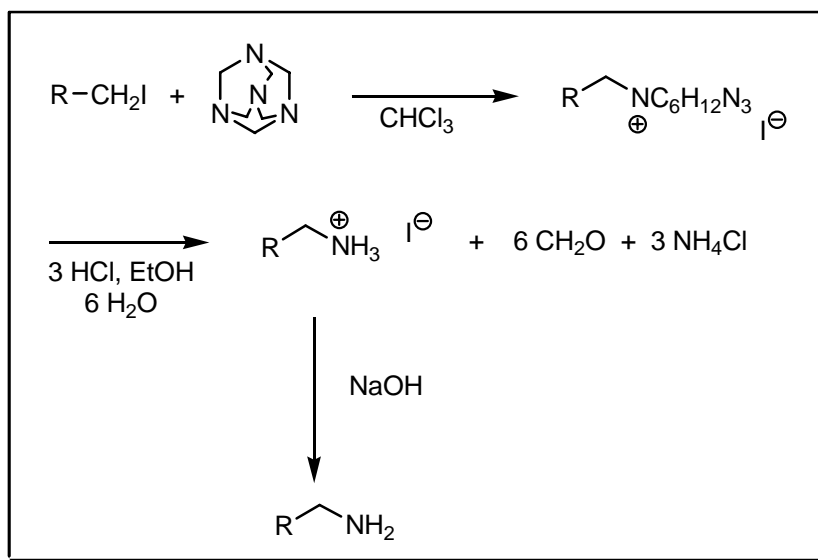
## DELÉPINE AMINE SYNTHESIS

### EXAMPLE :

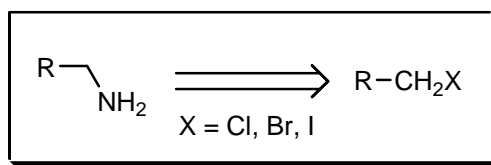




## MECHANISM :



## DISCONNECTION :



## NOTES :

Organic halides with hexamethylenetetramine form quaternary compounds, which on treatment with ethanolic hydrogen chloride yield primary amines. See also **Gabriel** and **Sommelet** aldehyde reactions.

## REFERENCES :

Houben – Weyl : E16d, 713

Org. React. : 8, 197

Org. Synth. : 43, 6

Org. Synth. Coll. Vol. : 5, 121

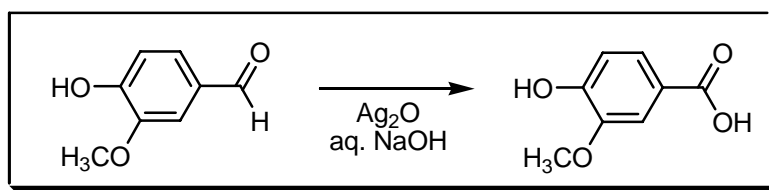
- 1) M. Delépine, *C.R. Séances Acad. Sci.*, 1895, **120**, 501.
- 2) N.L. Wendler, *J. Am. Chem. Soc.*, 1949, **71**, 375.
- 3) N. Blazevic; D. Kolbah; B. Belin; V. Sunjic; F. Kafjez, *Synthesis*, 1979, 161.
- 4) R.A. Henry; R.A. Hollins; C. Lowe–Ma; D.W. Moore; R.A. Nissan, *J. Org. Chem.*, 1990, **55**, 1796.

## COMMENTS :

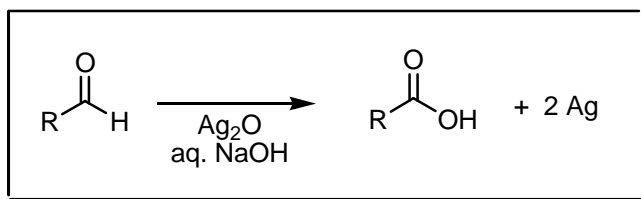
## DELÉPINE OXIDATION

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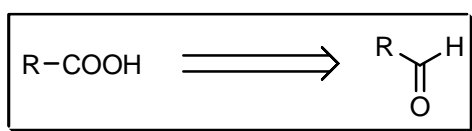
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The use of silver oxide in the presence of alkali for the oxidation of aldehydes to acids. Under similar conditions with acetic acid and phosphoric acid aromatic hydrocarbons can be oxidised to the corresponding aldehydes and ketones. See also **Anelli**, **Ball – Goodwin – Morton**, **Collins**, **Corey – Kim**, **Corey – Schmidt**, **Corey – Suggs**, **David – Thieffry**, **Dess – Martin**, **Einhorn** oxidation, **Fétizon**, **Jones** oxidation, **Ley**, **Maurer – Drefahl**, **Mukaiyama** oxidation, **Nicolaou**, **Oppenauer**, **Parikh – von Doering**, **Pfitzner – Moffatt**, **Pinnick**, **Sarett**, **Swern** and **Uemura** reactions.

### REFERENCES :

Smith : 254

Smith 2<sup>nd</sup> : 218

Org. Synth. : 30, 101; 33, 94; 36, 36

Org. Synth. Coll. Vol. : 4, 493, 919, 972

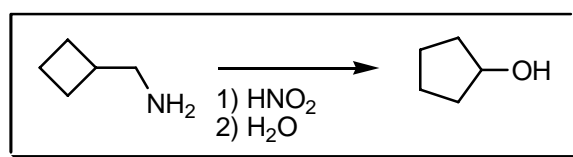
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- 3) R.N. Hammer; J. Klemberg, *Inorg. Synth.*, 1953, **4**, 12.
- 4) L. Syper, *Tetrahedron Lett.*, 1967, **8**, 4193.
- 5) S.C. Thomason; D.G. Kubler, *J. Chem. Educ.*, 1968, **45**, 546.

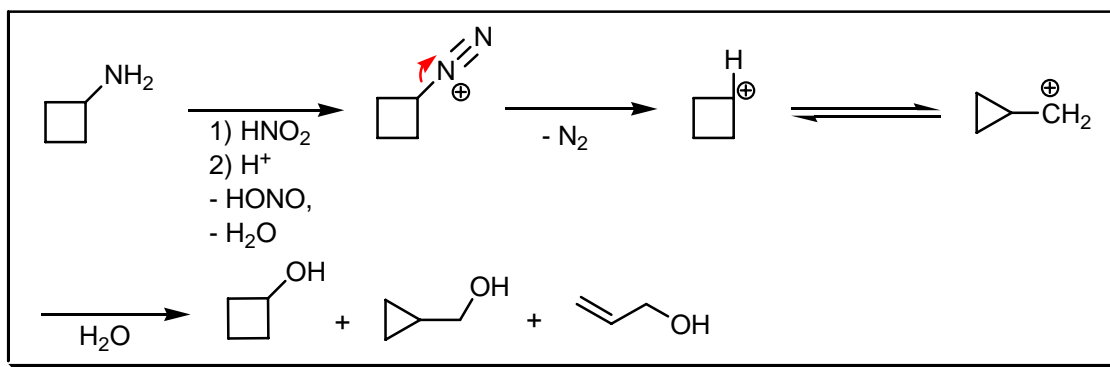
## COMMENTS :

## DEMJANOV REARRANGEMENT

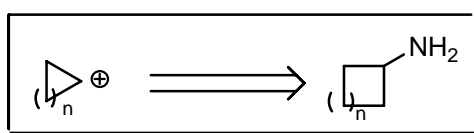
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This rearrangement by diazotation frequently occurs when a primary amine is treated with nitrous acid and proceeds as shown. Ring expansion or contraction occurs with cyclic amines. See also **Balz – Schiemann**, **Cadogan** arylation,

**Craig** exchange, **Gattermann** diazo, **Gattermann** sulphinic acid, **Godchot – Mousseron**, **Griess** deamination, **Knoevenagel** diazotation, **Körner – Contardi**, **Meerwein** arylation, **Sandmeyer** diazonium, **Schwechten**, **Tiffeneau** – **Demjanov** rearrangement, **Wagner – Meerwein** and **Witt** diazotation reactions.

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#### REFERENCES :

**March** : 1074

**Smith – March** : 1398

**Smith** : 1293

**Smith 2<sup>nd</sup>** : 1067

**Houben – Weyl** : **E19b**, 389; **E19c**, 404

**Org. React.** : **11**, 157

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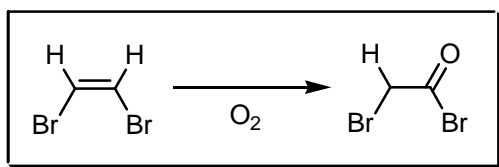
- 1) E. Linnemann, *Liebigs Ann. Chem.*, 1867, **144**, 129.
  - 2) N.J. Demjanov; M. Lushnikov, *J. Russ. Physik. Chem. Ges.*, 1903, **35**, 26.
  - 3) P.A.S. Smith; D.R. Baer; S.N. Ege, *J. Am. Chem. Soc.*, 1954, **76**, 4564.
  - 4) R. Kotani, *J. Org. Chem.*, 1965, **30**, 350.
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  - 7) D. Fattori; S. Henry; P. Vogel, *Tetrahedron*, 1993, **49**, 1649.
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#### COMMENTS :

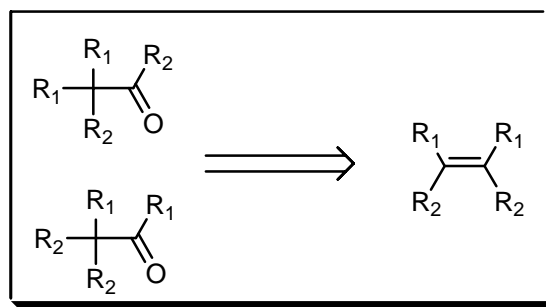
### DEMOLE SYNTHESIS

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#### EXAMPLE :



## DISCONNECTION :



## NOTES :

Di-, tri- and tetrahalogenated ethylenes are autoxidised to halogenated acids with wandering of a proton. The mechanism is not fully understood, initial formation of the epoxide has been proposed.

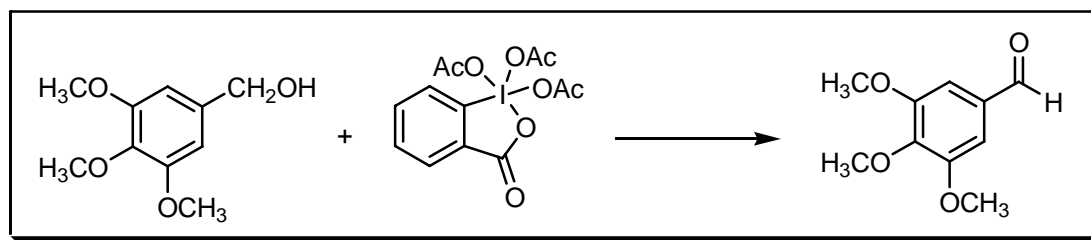
## REFERENCES :

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- 5) E. Erdmann, *J. Prakt. Chem.*, 1912, **85**, 78.
- 6) N. Prileschajew, *Ber. Dtsch. Chem. Ges.*, 1926, **59**, 194.
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- 8) H. Cohn; E.D. Bergmann, *Isr. J. Chem.*, 1964, **2**, 355.

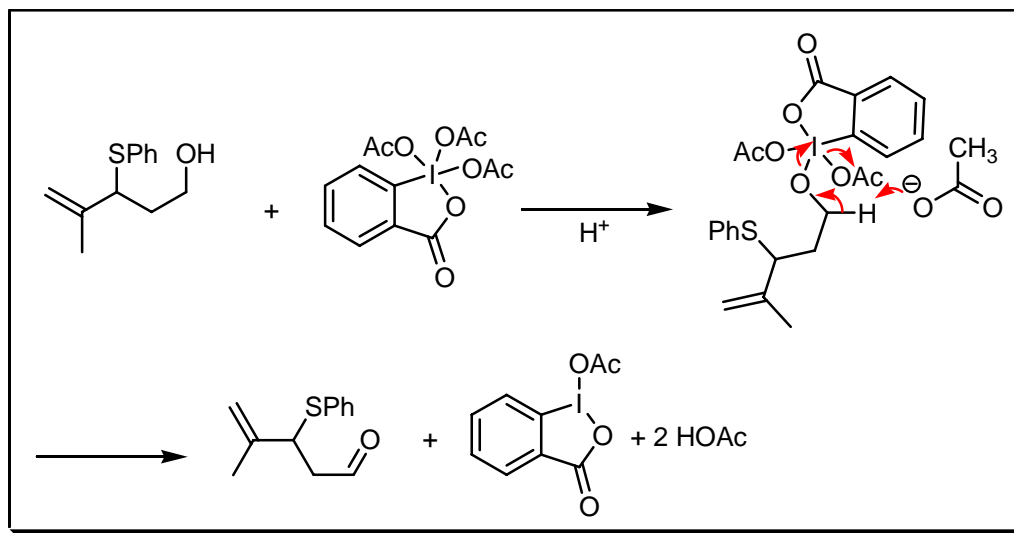
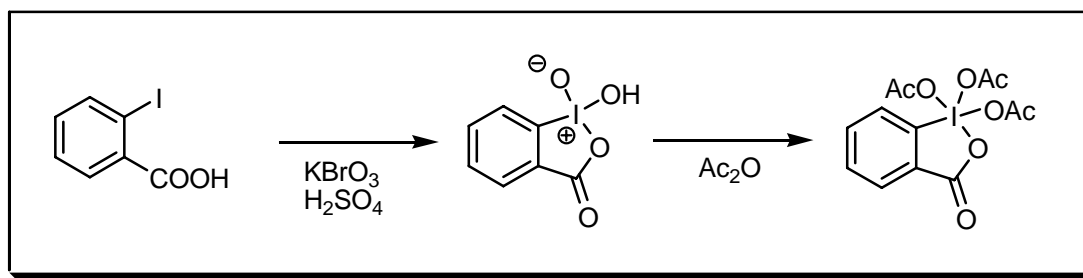
## COMMENTS :

## DESS – MARTIN PERIODINANE REACTION

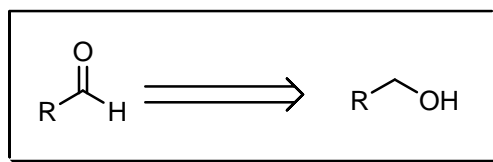
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The oxidation of alcohols to aldehydes or ketones using periodinanes. The arylidiodo ester is formed from the **Dess – Martin** reagent and the alcohol. This ester undergoes a  $\beta$ -elimination and forms the aldehyde. Basic work-up removes the arylidiodo compound. The addition of one equivalent of water has been found to accelerate the reaction. This reagent can furthermore induce cyclisation reactions and has been used for the removal of thioacetals and thioketals. See also **Anelli**, **Ball – Goodwin – Morton**, **Collins**, **Corey – Kim**, **Corey – Schmidt**, **Corey – Suggs**, **David – Thieffry**, **Delépine**, **Einhorn** oxidation, **Fétizon**, **Jones** oxidation, **Ley**, **Maurer – Drefahl**, **Mukaiyama** oxidation, **Nicolaou**, **Oppenauer**, **Parikh – von Doering**, **Pfitzner – Moffatt**, **Pinnick**, **Sarett**, **Swern** and **Uemura** reactions.

## REFERENCES :

Smith – March : 1516

Smith : 241

Smith 2<sup>nd</sup> : 209

Houben – Weyl : E10b2, 39

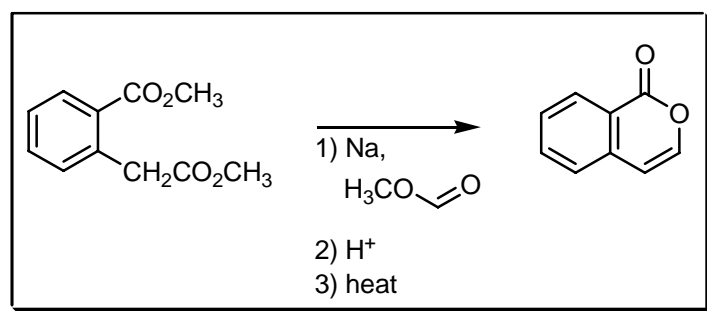
Org. React. : 53, 1

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  - 6) T. Kitamura; Y. Fujiwara, *Org. prep. Proced. Int.*, 1997, **29**, 409.
  - 7) K.-Y. Akiba, *Chemistry of Hypervalent Compounds*, 1999, 9.
  - 8) D.S. Bose; A.V. Narsaiah, *Synth. Commun.*, 1999, **29**, 937.
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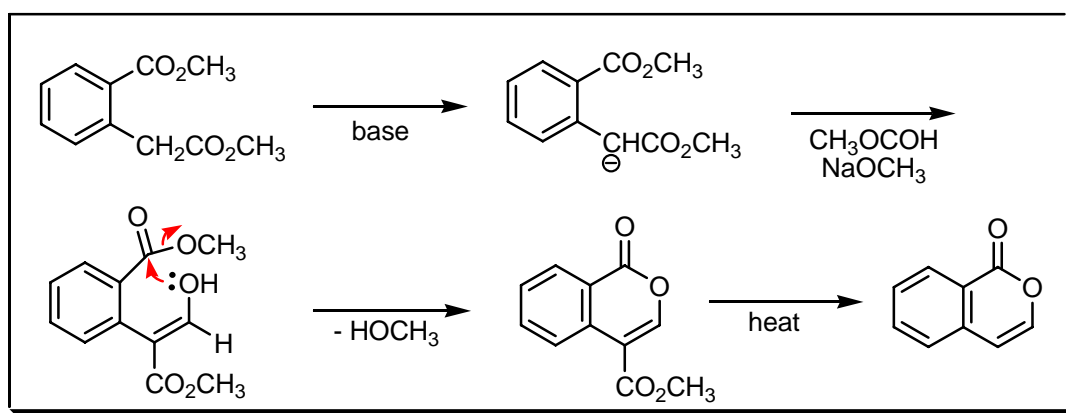
**COMMENTS :**

# DIECKMANN – MEISER SYNTHESIS

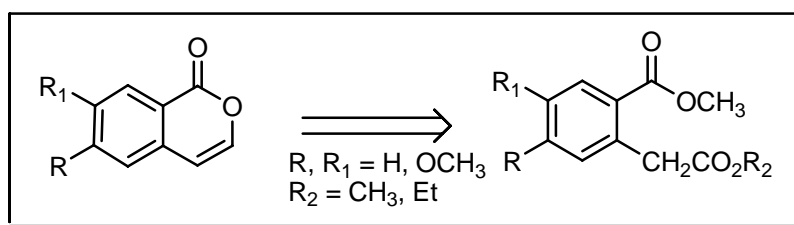
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Isocoumarins devoid of substituents in the 3- and 4-position are obtained by the base-catalysed condensation of ethyl formate with an ester of homophthalic acid. The resulting hydroxymethylene derivative is cyclised and the carbomethoxy group in the 4-position is eliminated, e.g. by heat.

## REFERENCES :

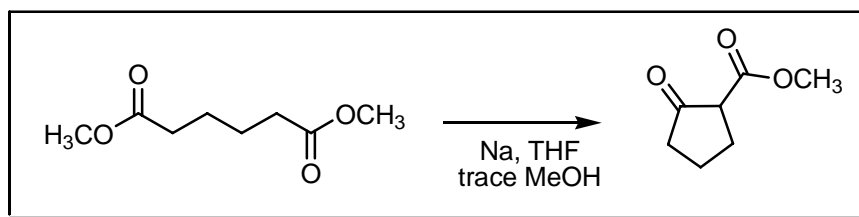
- 1) W. Dieckmann; W. Meiser, *Ber. Dtsch. Chem. Ges.*, 1908, **41**, 3253.
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- 3) A. Kamal; A. Robertson; E.T. Tittensor, *J. Chem. Soc.*, 1950, 3375.



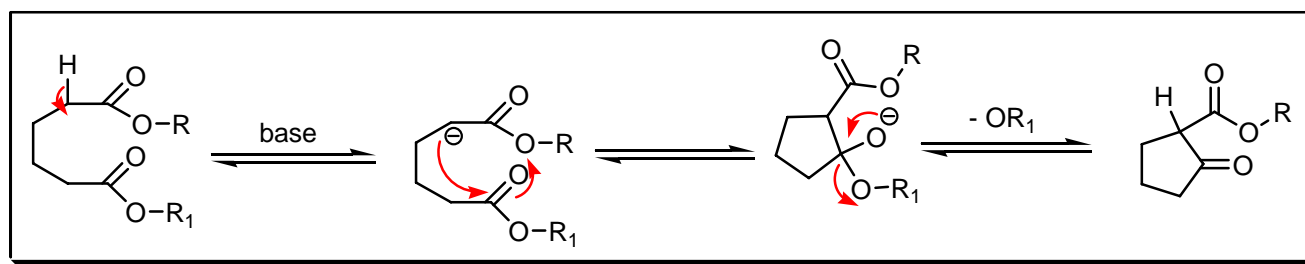
COMMENTS :

## DIECKMANN CONDENSATION

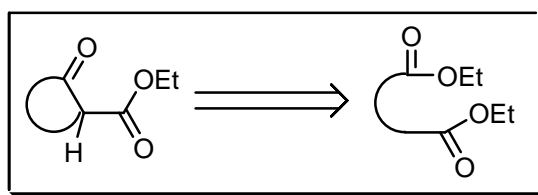
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

Esters having hydrogen on the  $\delta$ - or  $\epsilon$ -carbon atom, which is activated by a carbonyl group undergo base-catalysed *intramolecular Claisen – Geuther* condensation. The **Dieckmann – Komppa** modification is the condensation between oxalic acid esters and the esters of glutamic acid, followed by the cyclisation to produce  $\alpha$ -diketones. The **House – Babad** method uses phosphonium salts to synthesis cyclic ketones. Solvent-free conditions have also been reported in the literature. See also **Claisen – Geuther** reaction.

REFERENCES :

March : 492, 1228

Smith – March : 569

Smith : 895

Smith 2<sup>nd</sup> : 749

Houben – Weyl : **8**, 574; **E6a**, 252, 312; **E6b**, 1212; **E7a**, 319; 1994, **E8b**, 518

Org. React. : **1**, 1; **6**, 410; **15**, 1

Org. Synth. : **57**, 1; **66**, 52

Org. Synth. Coll. Vol. : **6**, 167; **8**, 112

Science of Synthesis : **9**, 314, 318; **10**, 58, 166, 281, 673

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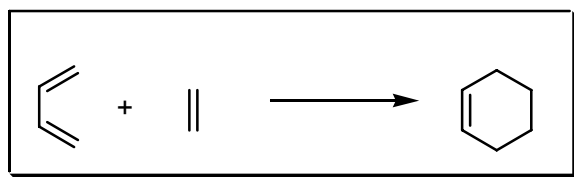
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COMMENTS :

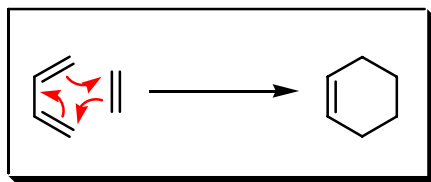
## DIELS – ALDER REACTION

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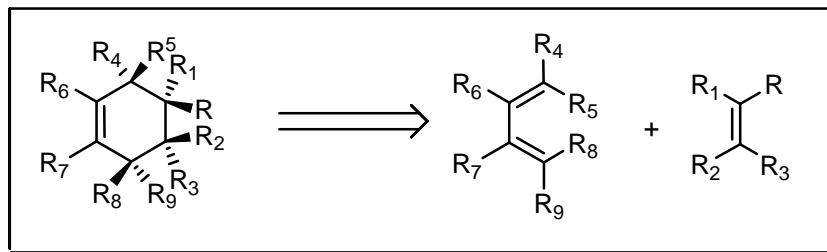
EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

This reaction, of which there are many variations, involves the addition of a compound containing a double or triple bond (dienophile) across the 1,4-positions of a conjugated system (diene), with the formation of a six membered ring. See also **Boger – Panek**, **Bradsher** cycloaddition, **Carboni – Lindsey**, **Corey – Nicolaou**, **Danishefsky**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Masamune**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Staab**, **Stacey**, **Steglich – Hassner**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolkiewicz**, **Wagner–Jauregg**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

## REFERENCES :

**March** : 839

**Smith – March** : 1062

**Smith** : 1113, 1130

**Smith 2<sup>nd</sup>** : 928

**Houben – Weyl** : **E3**, 639; **E5**, 428, 772; **E8a**, 449, 786, 1007, 1010; **E16a**, 319; **E19c**, 85

**Org. React.** : **4**, 1; **5**, 136; **32**, 1; **52**, 1; **53**, 223

**Org. Synth.** : **17**, 25; **30**, 93; **43**, 27; **46**, 44; **48**, 68; **49**, 1; **50**, 24, 36, 43; **53**, 48; **58**, 163; **59**, 71; **60**, 41; **61**, 147; **62**, 149; **65**, 32, 98; **66**, 142; **68**, 198, 206; **69**, 31; **71**, 30, 181; **72**, 86; **73**, 253; **77**, 254; **78**, 160, 202

**Org. Synth. Coll. Vol.** : **2**, 102; **4**, 890; **5**, 96, 424, 459, 604; **6**, 82, 196, 422, 445, 454, 496; **7**, 4, 312, 485; **8**, 31, 173, 298, 353, 444, 597; **9**, 67; 186, 396, 722; **10**, 2390, 2621, 2625

**Science of Synthesis** : **1**, 57, 519, 990; **9**, 54, 130, 222, 258, 328; **10**, 61, 87, 107, 147, 167, 193, 231, 243, 245, 303, 344, 474, 587, 700, 703, 813, 827

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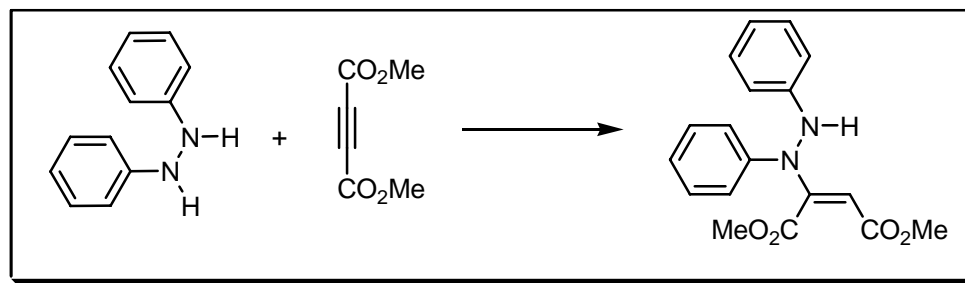
- 2) J.A. Norton, *Chem. Rev.*, 1942, **31**, 319.
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**COMMENTS :**

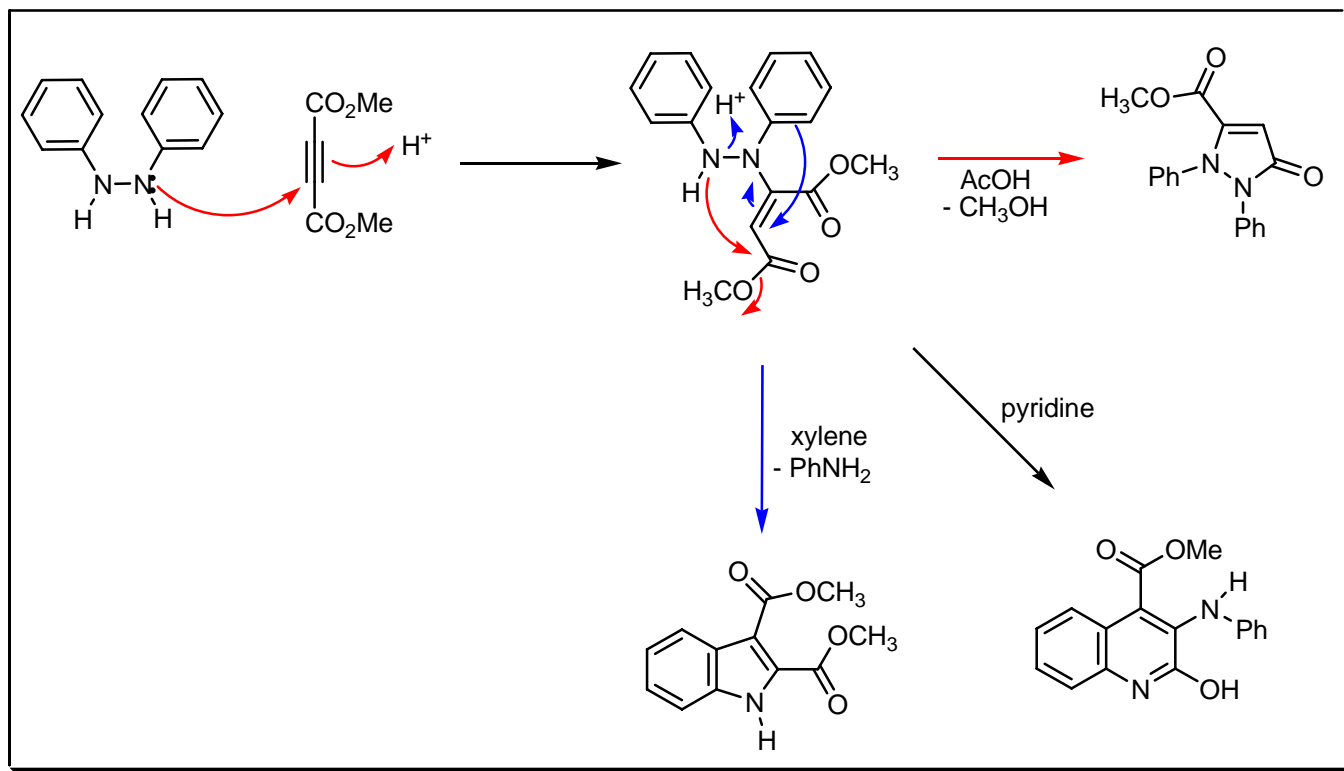
## DIELS – REESE REACTION

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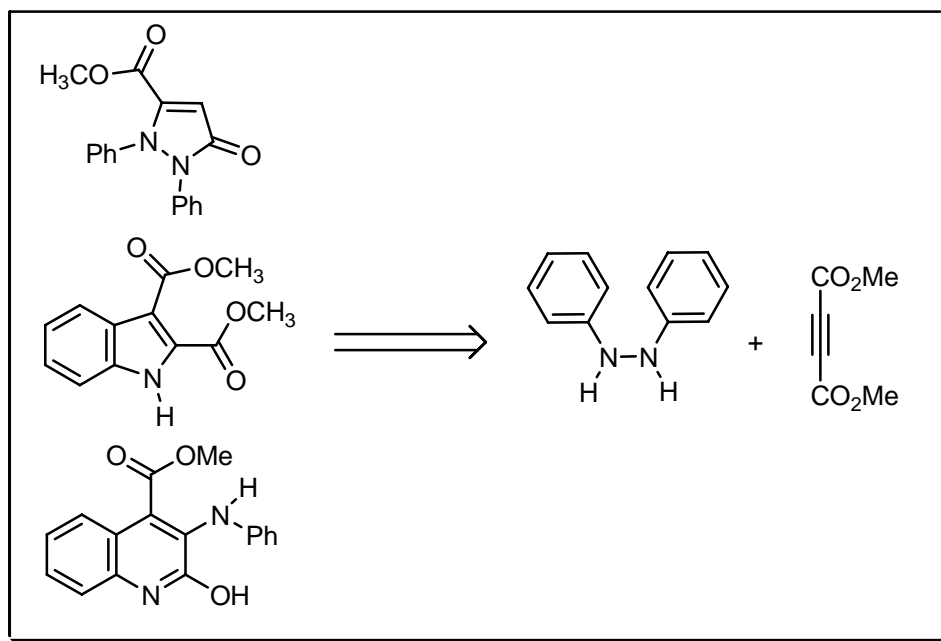
**EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

Dimethyl acetylenedicarboxylate reacts with hydrazobenzenes to yield an adduct which can be cyclised, under suitable conditions, to heterocyclic compounds.

## REFERENCES :

1) O. Diels; J. Reese, *Liebigs Ann. Chem.*, 1934, **511**, 168.

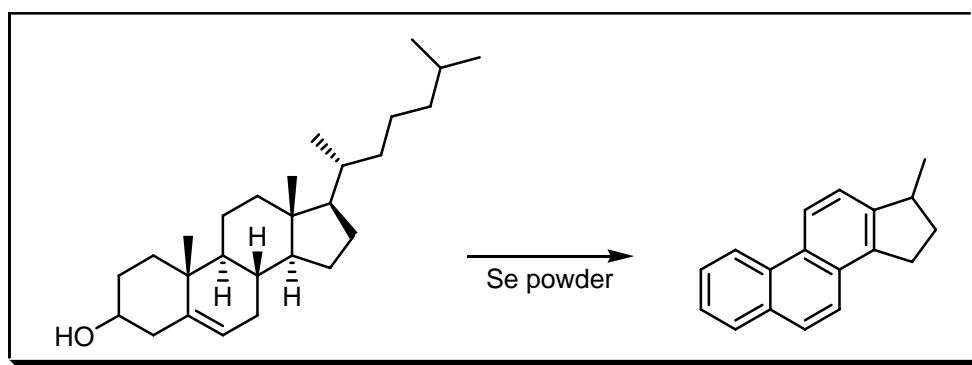
- 2) O. Diels; J. Reese, *Liebigs Ann. Chem.*, 1935, **519**, 147.  
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- 

**COMMENTS :**

## DIELS DEHYDRATION

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**EXAMPLE :**



**NOTES :**

The compound to be dehydrated is heated with finely divided selenium. All the dehydrated compounds e.g. cholesterol, hormones, vitamins form  $\gamma$ -methylcyclopentenophenanthrene.

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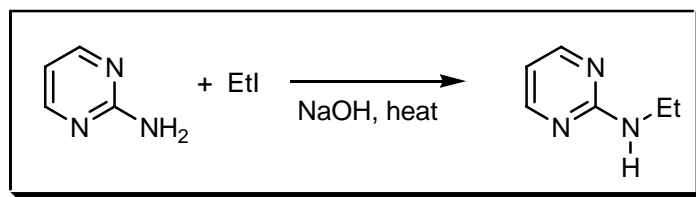
**REFERENCES :**

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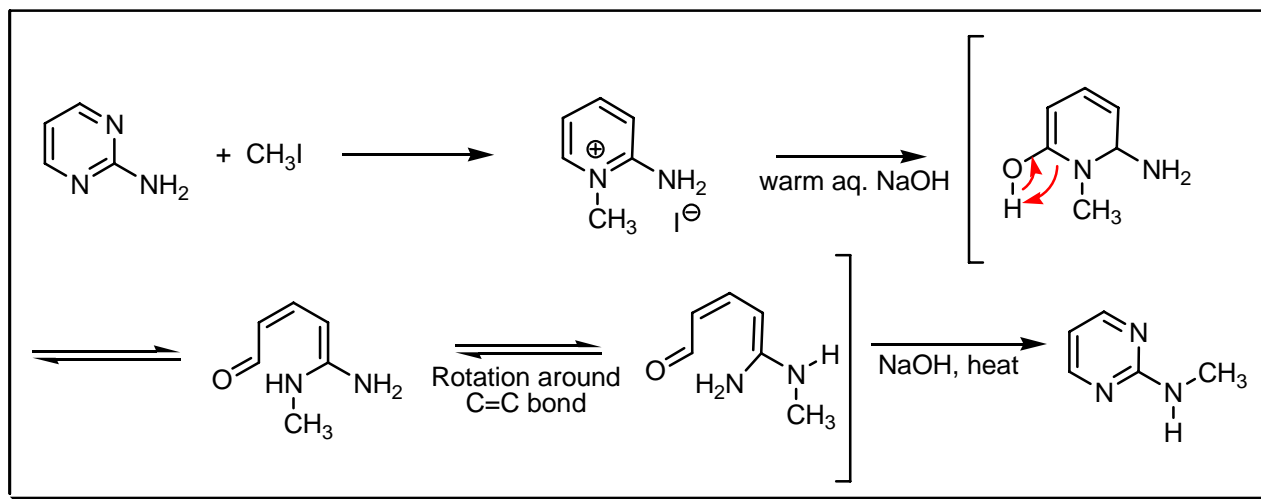
**COMMENTS :**

## DIMROTH REARRANGEMENT

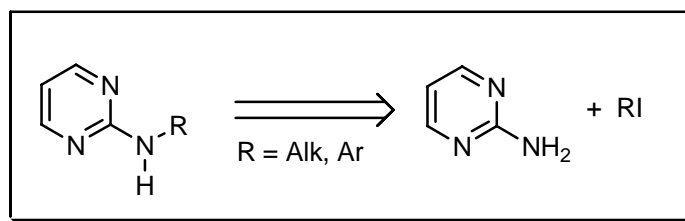
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The migration of an alkyl or aryl group from a heterocyclic to an *exocyclic* nitrogen atom. The reaction has been modified by **Katritzky** *et al.* Some authors also include the translocation of heteroatoms within rings of fused systems as a type 1 **Dimroth** rearrangement.

### REFERENCES :

**Houben – Weyl** : **E7b**, 453; **E8a**, 337; 784; **E8c**, 184; **E8d**, 90, 134, 190, 210, 289, 346

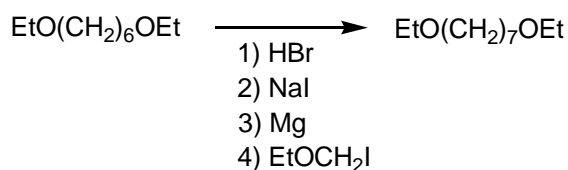
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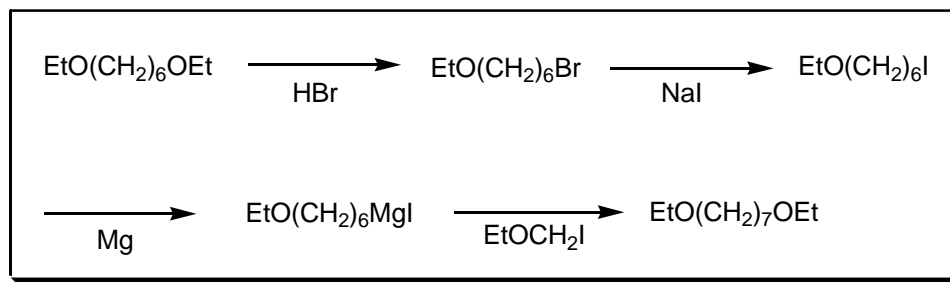
**COMMENTS :**

**DIONNEAU METHOD**

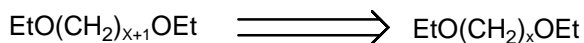
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



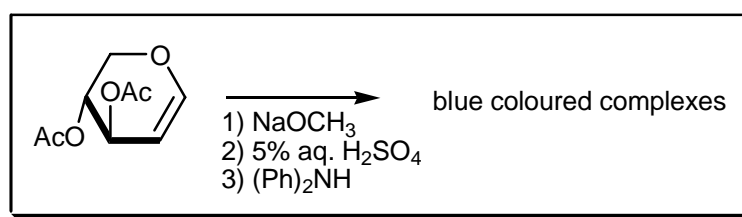
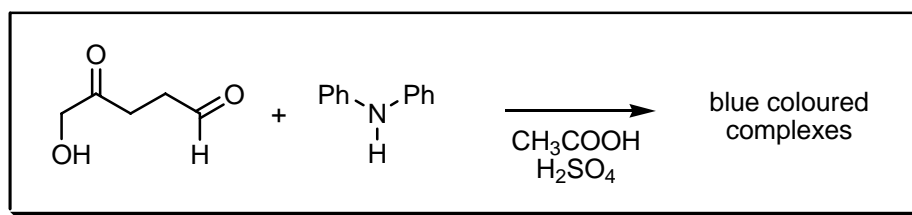


**NOTES :**

The diethyl ether of the alcohol when reacted with hydrogen bromide yields an  $\alpha$ -bromo- $\omega$ -ethoxyalkane, which with sodium iodide gives the corresponding iodo-compound. The **Grignard** reagent of this compound reacts with ethyl iodomethyl ether yielding the higher homologue of the starting ether.

**REFERENCES :**

M.R. Dionneau, *C.R. Séances Acad. Sci.*, 1906, **142**, 91.

**COMMENTS :****DISCHE REACTION****EXAMPLE :****MECHANISM :****NOTES :**

The reaction between the **Dische** reagent (diphenylamine, acetic acid and sulfuric acid) and 2-deoxypentoses resulting in the development of a blue colour. The reaction depends on the conversion of the pentose to  $\omega$ -hydroxylevulaldehyde which then reacts with diphenylamine to give a mixture of blue coloured complexes.

**REFERENCES :**

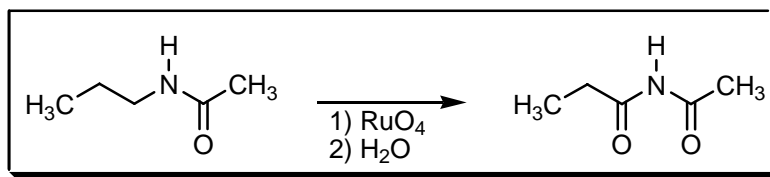
Houben – Weyl : E3, 678

- 1) J. Knop, *J. Am. Chem. Soc.*, 1924, **46**, 263.
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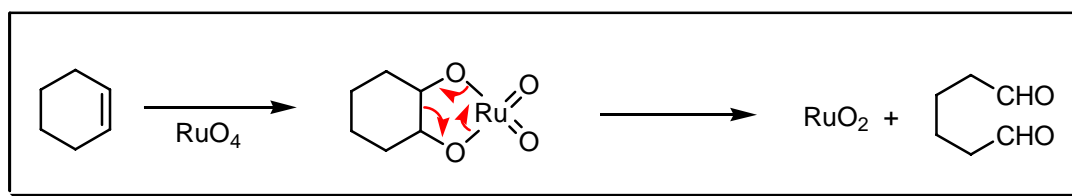
**COMMENTS :**

## DJERASSI – RYLANDER OXIDATION

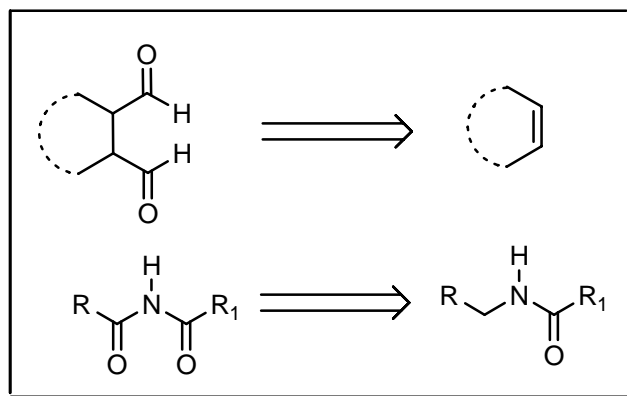
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

The oxidative cleavage of phenols, alkenes, alkynes, oxidation of aromatics to quinones, oxidation of alkyl amides to imides or of ethers to esters using  $\text{RuO}_4$  or  $\text{NaIO}_4$ . See also **Barry, Hudson – Jackson, Lemieux – Johnson, Lemieux – von Rudloff** and **Malaprade** reactions.

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## REFERENCES :

**March** : 1181, 1200

**Smith – March** : 1534, 1540

**Smith** : 301

**Smith 2<sup>nd</sup>** : 265

**Org. Synth.** : **46**, 78; **68**, 41; **70**, 29; **74**, 1; **72**, 1, 6

**Org. Synth. Coll. Vol.** : **5**, 791; **8**, 377; **9**, 39, 63, 450, 454

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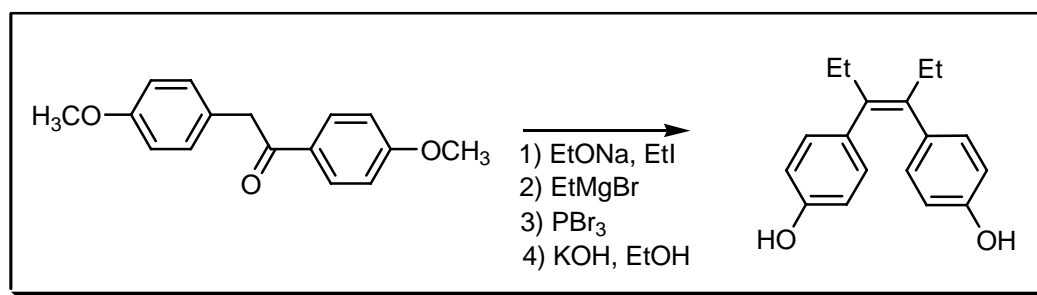
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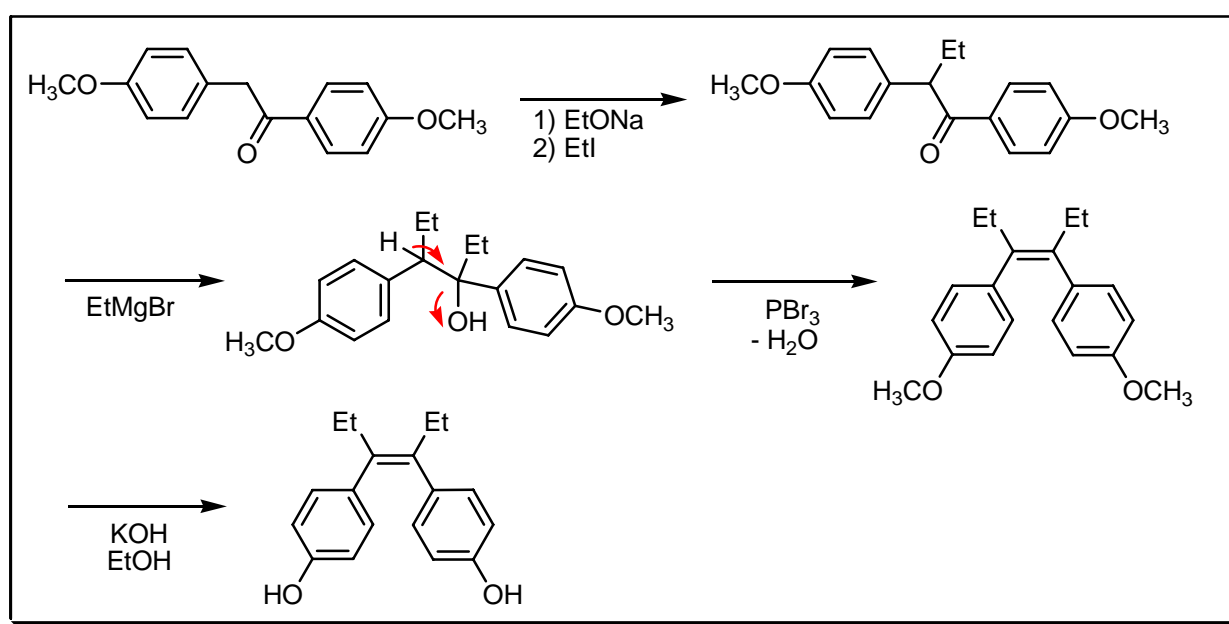
## COMMENTS :

## DODDS – ROBINSON SYNTHESIS

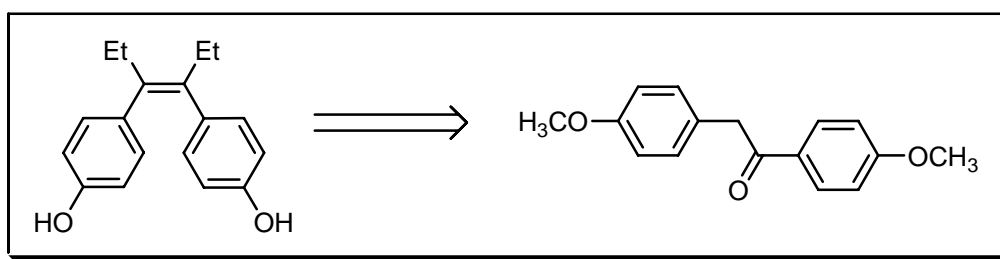
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This is the synthesis of substituted 1,2-diphenyl ethenes. Various modifications of this synthesis have been proposed. These compounds possess *anti*-oestrogenic properties. See also **Kharasch – Kleimann** reaction.

### REFERENCES :

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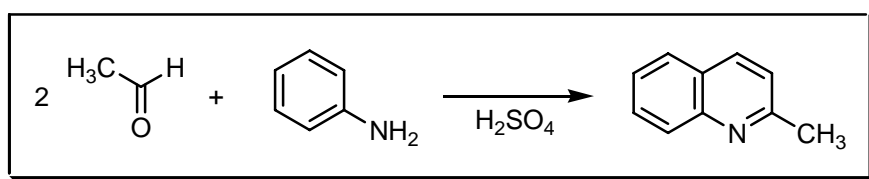
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**COMMENTS :**

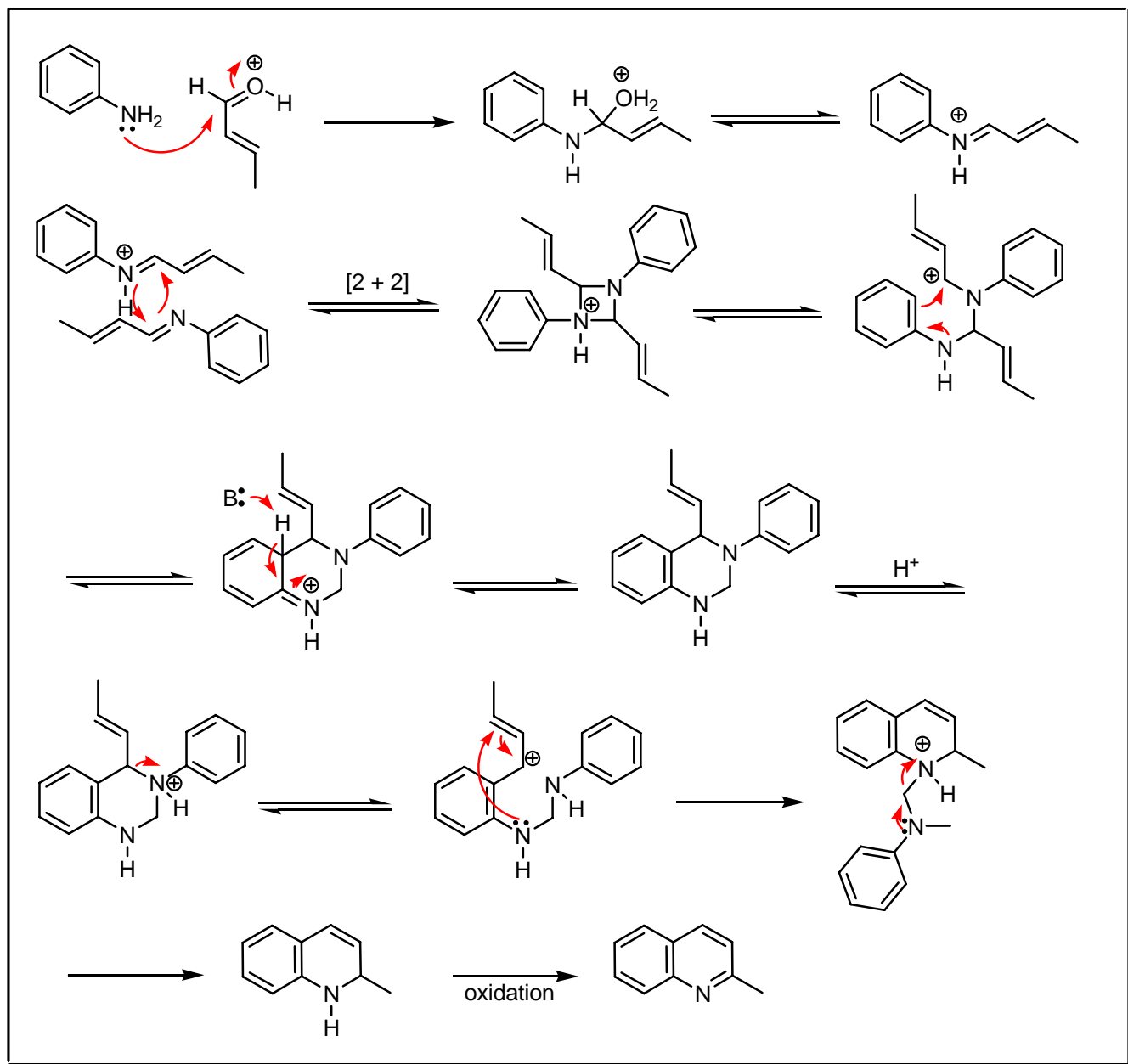
## DOEBNER – von MILLER SYNTHESIS

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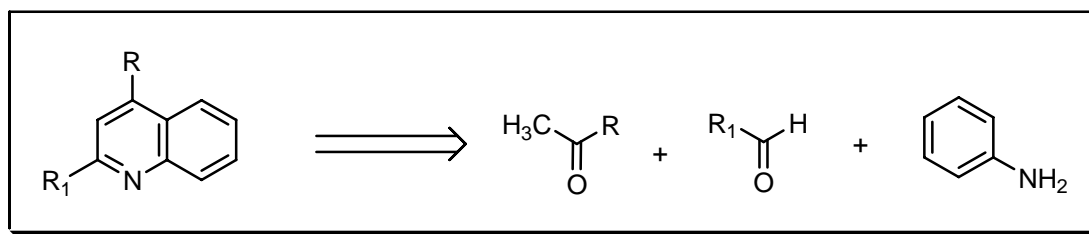
**EXAMPLE :**



## MECHANISM :



## DISCONNECTION :

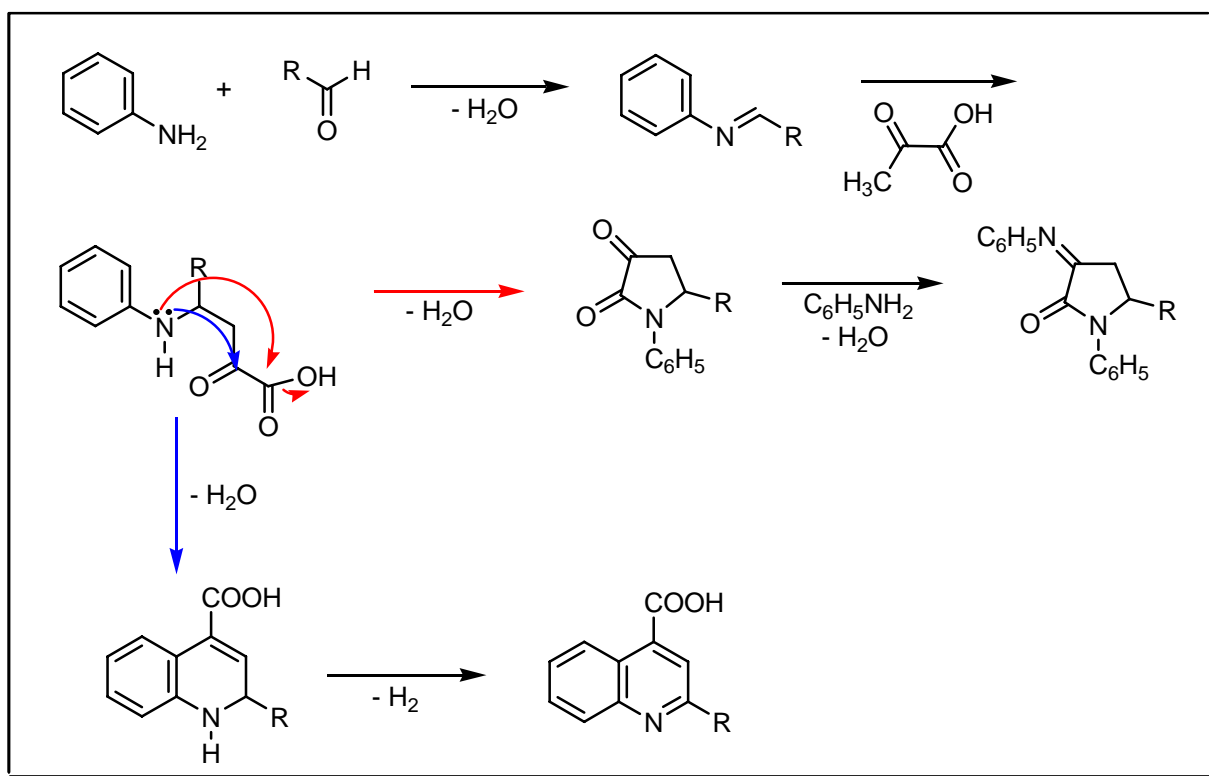


## NOTES :

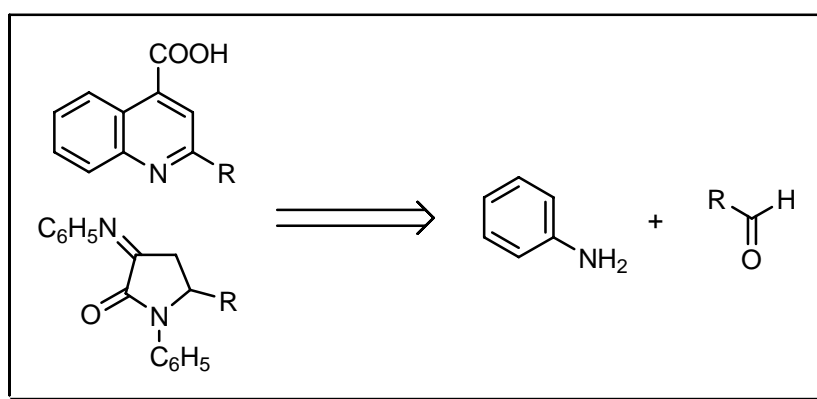
The synthesis of quinoline derivatives by condensation, in the presence of sulfuric or hydrochloric acid, of an aromatic amine with (i) an unsaturated aldehyde, or (ii) two molecules of an aldehyde  $RCH_2CHO$  or (iii) one molecule of  $RCH_2CHO$  and one molecule of  $R_1CHO$ . Addition of zinc chloride promotes the reaction. The mechanism is the same as for the **Skraup** reaction. Although an alternative mechanism has been proposed and is shown here. The **Beyer**



## MECHANISM :



## DISCONNECTION :



## NOTES :

An aromatic amine is condensed with pyruvic acid and an aldehyde to give a 2-substituted quinoline-4-carboxylic acid or a 1-aryl-3-(arylimino)pyrrolidinone. See also **Allan – Loudon**, **von Baeyer – Drewson** quinoline, **Camps**, **Combes** quinoline, **Conrad – Limpach**, **Doebner – von Miller**, **Foulds – Robinson**, **Friedländer**, **Knorr** quinoline, **Meth-Cohn**, **von Niementowski** quinoline, **Pfitzinger – Borsche**, **Riehm** quinoline and **Skraup** quinoline reactions.



## REFERENCES :

Smith : 1338

Smith 2<sup>nd</sup> : 1100

Houben – Weyl : 2, 444; E7a, 359

Org. React. : 1, 210

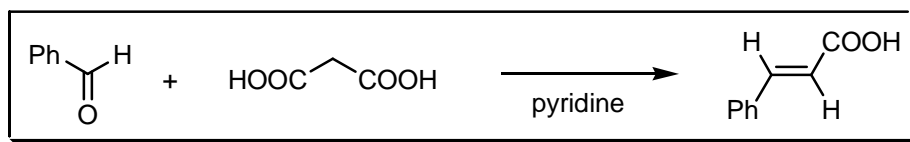
- 
- 1) C. Böttiger, *Liebigs Ann. Chem.*, 1876, **188**, 336.
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## COMMENTS :

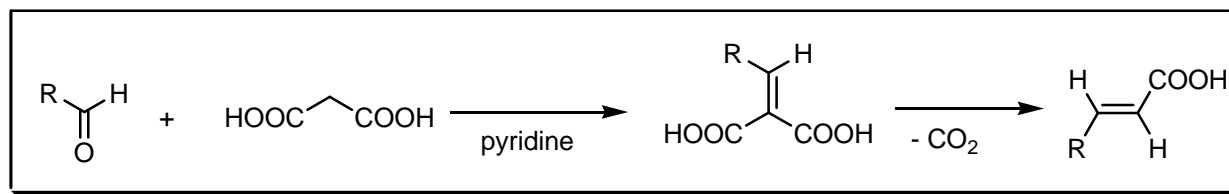
## DOEBNER MODIFICATION

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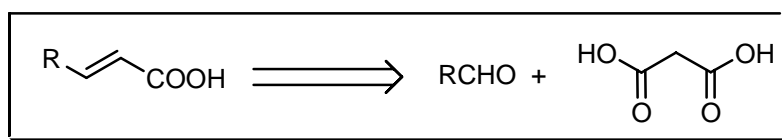
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The **Knoevenagel** condensation of malonic acid or ester with aldehydes in the presence of pyridine, usually with the addition of a little piperidine, to give unsaturated acids is known as the **Doebner** modification. See also **Knoevenagel** condensation and **Perkin** reaction.

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## REFERENCES :

**March** : 948

**Smith – March** : 1226

**Smith** : 898

**Smith 2<sup>nd</sup>** : 750

**Org. React.** : **1**, 266

**Org. Synth.** : **24**, 92; **25**, 51; **31**, 35; **33**, 62; **59**, 1

**Org. Synth. Coll. Vol.** : **3**, 425, 783; **4**, 327, 731; **6**, 95

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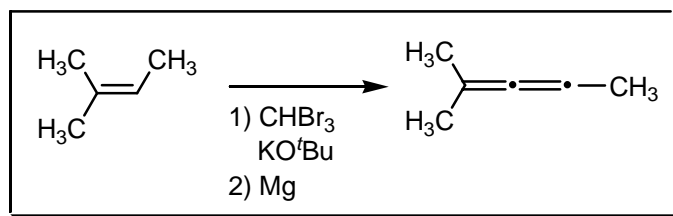
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## COMMENTS :

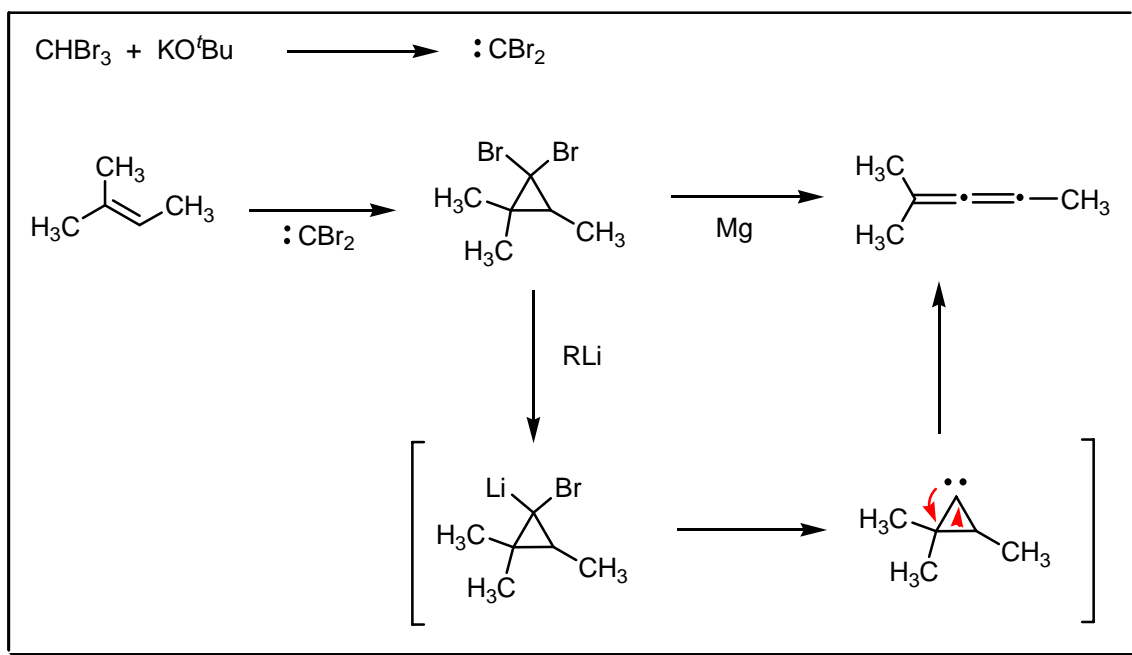
## von DOERING – LA FLAMME – MOORE ALLENE SYNTHESIS

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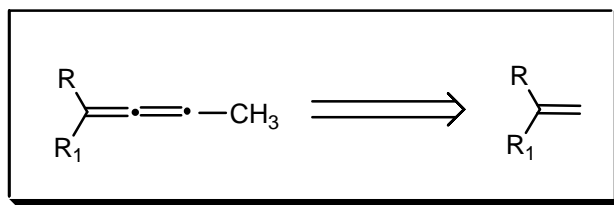
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The allene synthesis from olefins *via gem*-dihalocyclopropanes. **von Doering** and **La Flamme** used magnesium while **Moore** and **Skattebøl** used an organolithium species. **Grignard** reagents can also be used. See also **Skattebøl** reaction.

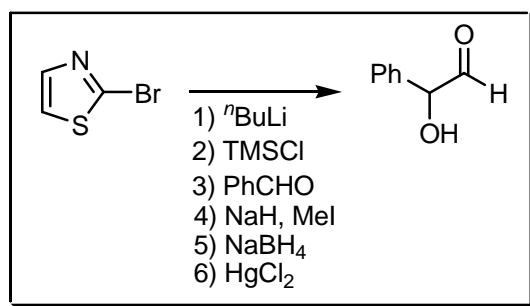
## REFERENCES :

- 1) W. von E. Doering; A.K. Hoffmann, *J. Am. Chem. Soc.*, 1954, **76**, 6162.
- 2) W. von E. Doering; P.M. LaFlamme, *Tetrahedron*, 1958, **2**, 75.
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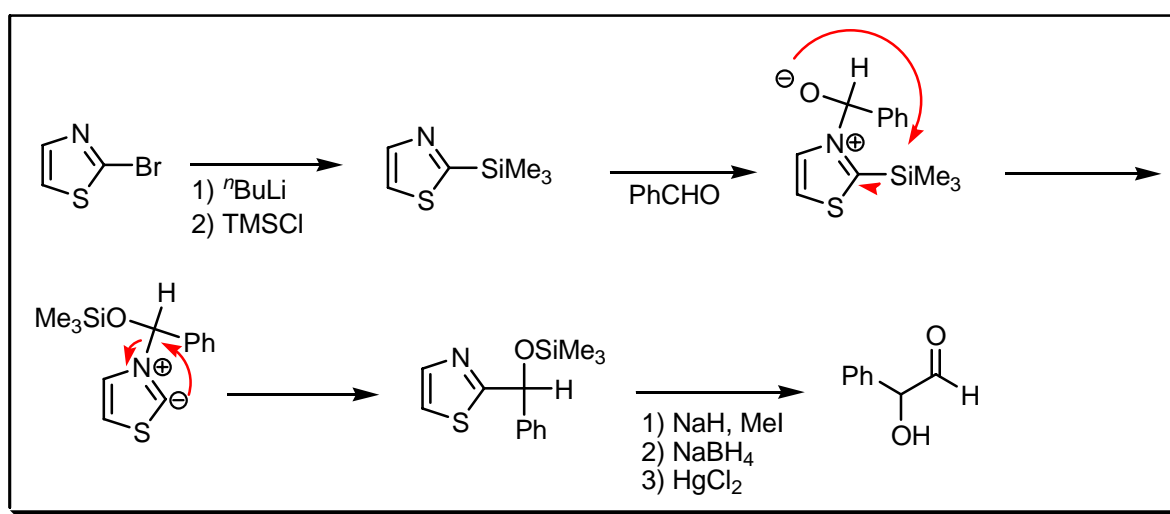
## COMMENTS :

## DONDONI HOMOLOGATION

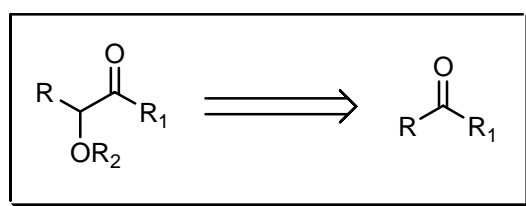
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The homologation of aldehydes, ketones, acyl chlorides, ketenes, two carbon homologation *via* 2-(trimethylsilyl)thiazole, acting as a formyl anion synthon. See also **Hodges – Vedejs** reaction.

### REFERENCES :

Org. Synth. : 72, 21; 77, 78

Org. Synth. Coll. Vol. : 9, 52

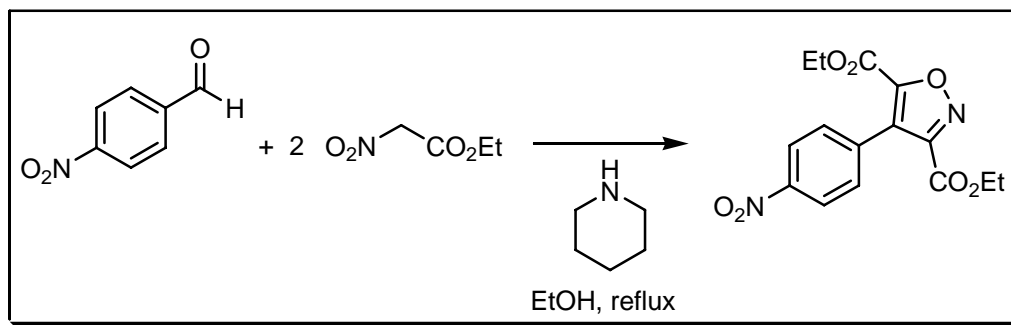
- 1) A. Dondoni; T. Dall'Occo; G. Fautin; M. Fogagnolo; A. Medici; P. Pedrini, *J. Chem. Soc., Chem. Commun.*, 1984, 258.
  - 2) A. Dondoni; G. Fautin; M. Fogagnolo; A. Medici; P. Pedrini, *J. Org. Chem.*, 1988, **53**, 1748.
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**COMMENTS :**

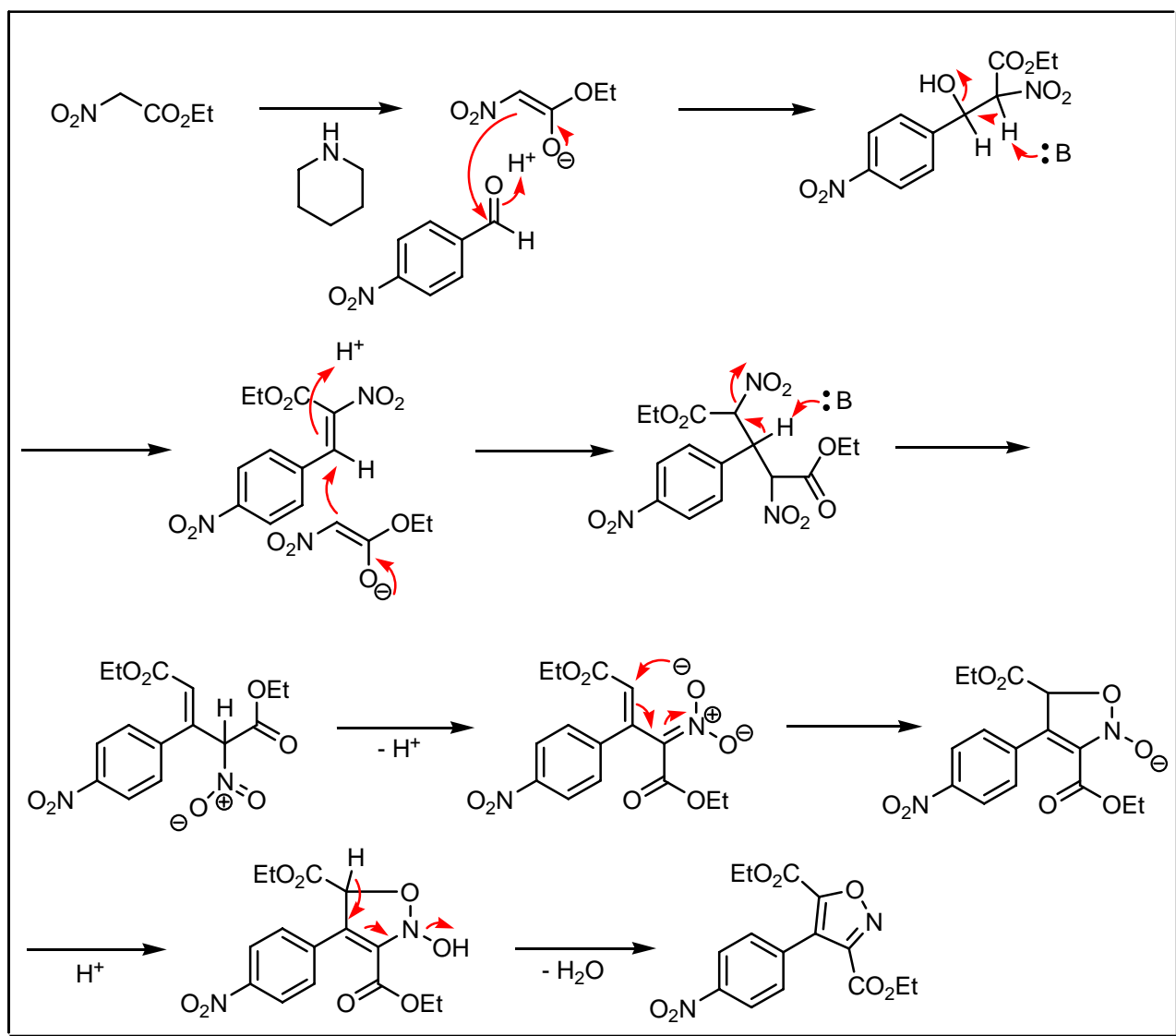
## DORNOW – WIEHLER ISOXAZOLE REACTION

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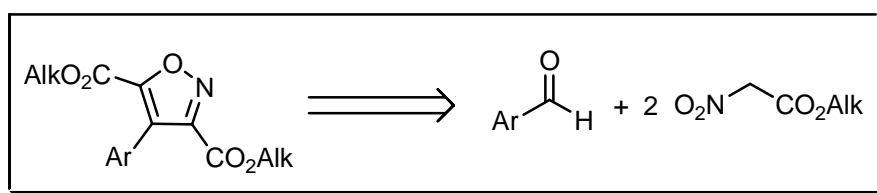
**EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

Aryl aldehydes and  $\alpha$ -nitroesters condense to afford isoxazoles.

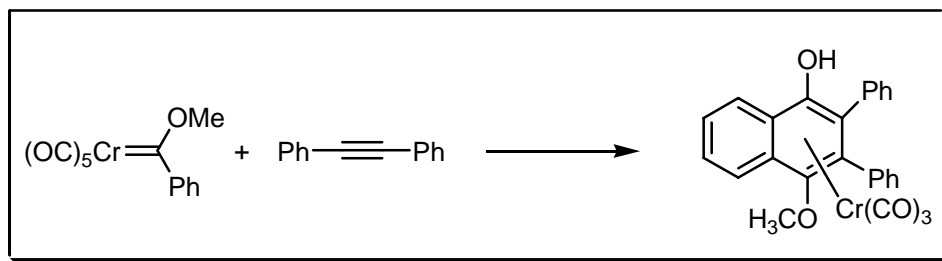
## REFERENCES :

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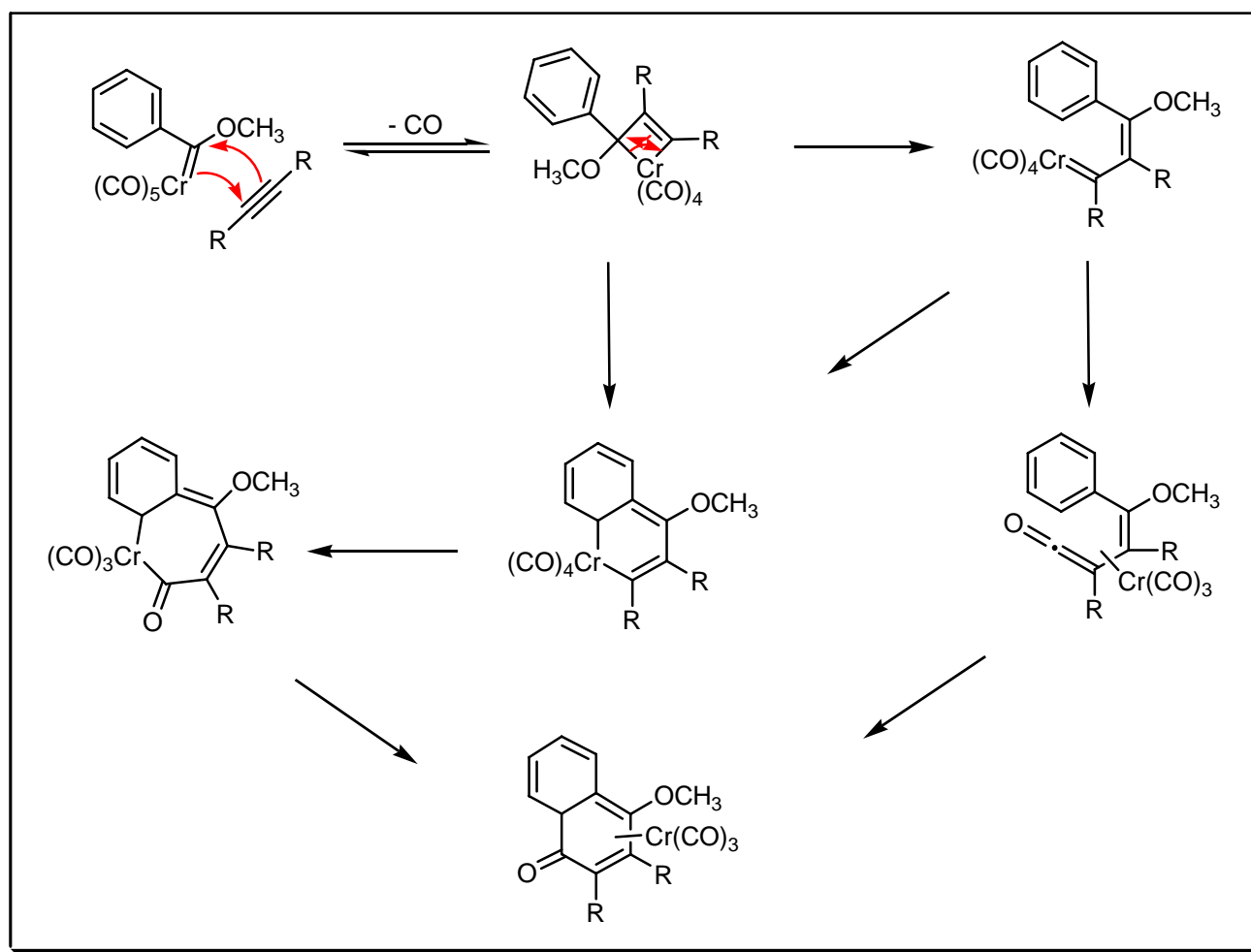
**COMMENTS :**

## DÖTZ HYDROQUINONE SYNTHESIS

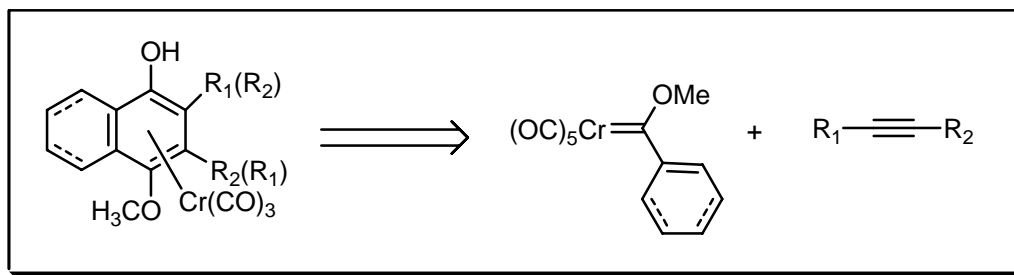
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

The (regiospecific) hydroquinone synthesis from alkynes and **Fischer** carbonyl carbene chromium complexes. Microwave-assisted reactions are also known. The reactions involving chromium alkynyl carbene complexes is sometimes called **Wulff** cyclisation.

## REFERENCES :

**Science of Synthesis** : 1, 852

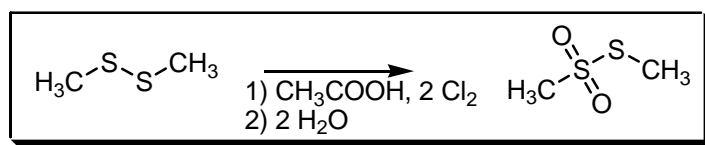
- 1) K.H. Dötz, *Angew. Chem., Int. Ed. Engl.*, 1975, **14**, 644.
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## COMMENTS :

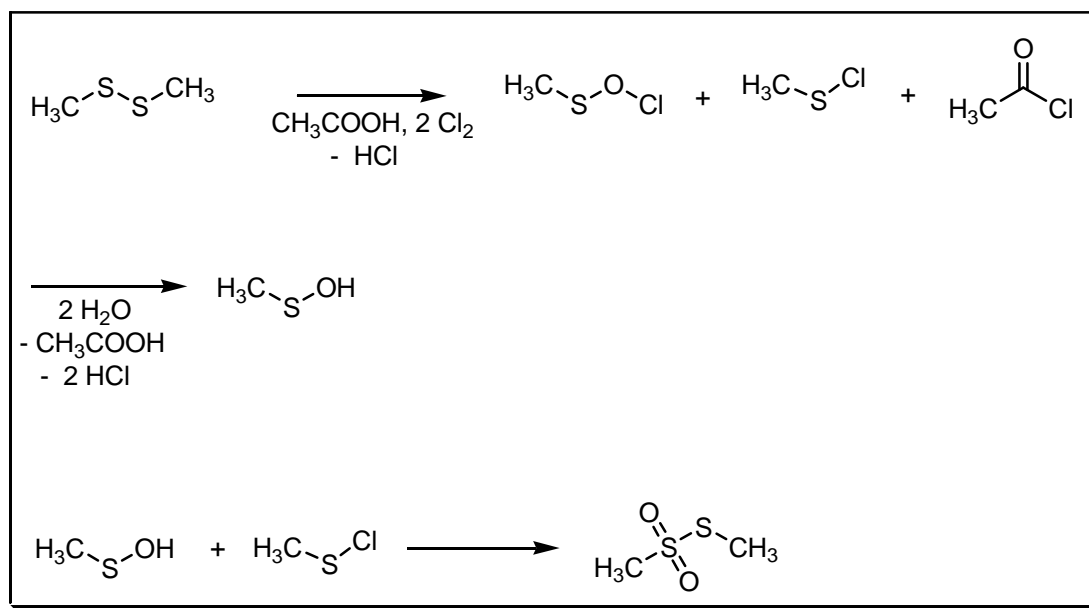


## DOUGLAS – FARAH REACTION

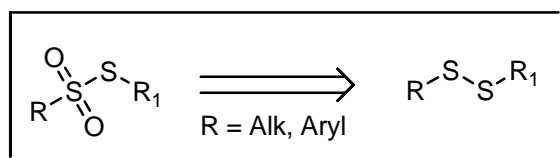
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Thiosulfonate esters can be prepared by the addition of chlorine to a cold mixture of alkyl disulfides and acetic acid, followed by the addition of water. During the chlorination, alkylsulfenyl, acetyl and alkylsulfinyl chlorides are formed. Hydrolysis of the latter gives alkylsulfinic acid and reacts with alkylsulfenyl chloride to form the thiosulfonate ester. This procedure is very general for the synthesis of thiosulfonates.

### REFERENCES :

Houben – Weyl : E11, 145

1) I.B. Douglas; B.S. Farah, *J. Org. Chem.*, 1958, **23**, 330.

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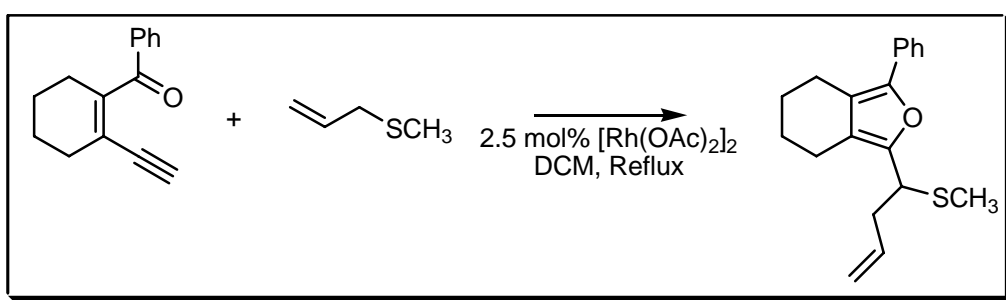
**COMMENTS :**

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**DOYLE – KIRMSE REACTION**

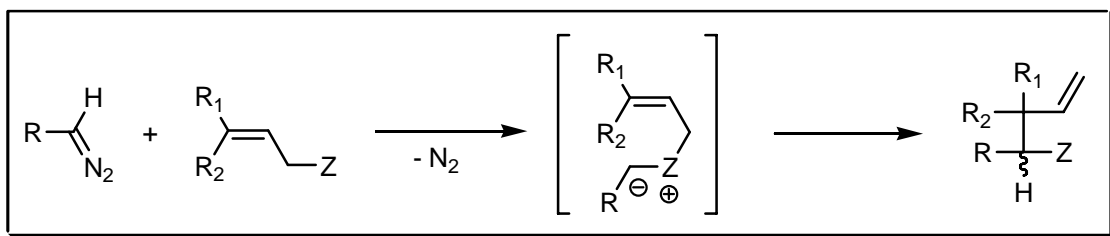
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**EXAMPLE :**



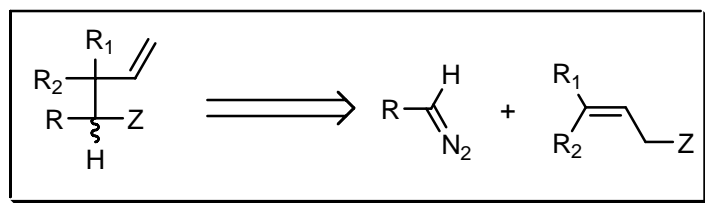
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**MECHANISM :**



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**DISCONNECTION :**



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**NOTES :**

The reaction between allylic compounds and diazo compounds, iron, copper or rhodium-catalysed. The reaction involves a [2,3]-sigmatropic rearrangement and is a powerful method for the formation of C-C bonds. **Uemura *et al.*** has published a rhodium(II)-catalysed reaction without the use of a diazoalkane.

## REFERENCES :

March : 1142

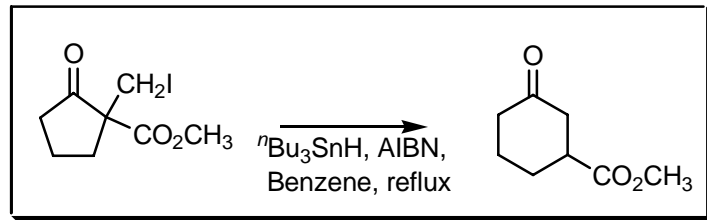
Smith – March : 1453

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- 1) W. Kirmse; M. Kapps, *Chem. Ber.*, 1968, **101**, 994.
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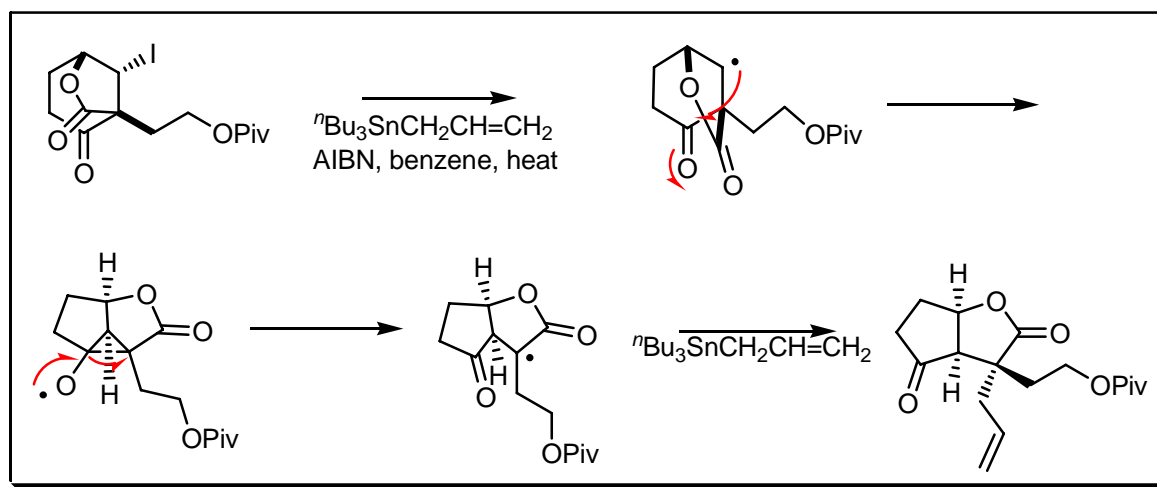
## COMMENTS :

## DOWD – BECKWITH REACTION

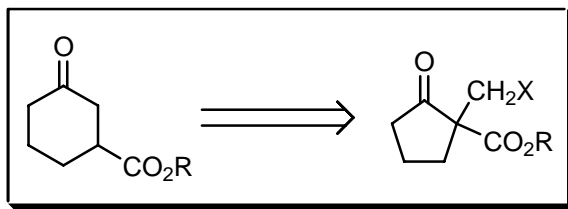
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



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## NOTES :

The free radical mediated ring expansion of haloalkyl  $\beta$ -ketoesters. See also **Ciamician – Dennstedt** rearrangement and **Reimer – Tiemann** rearrangement.

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**Org. Synth.** : **69**, 188

**Org. Synth. Coll. Vol.** : **8**, 562

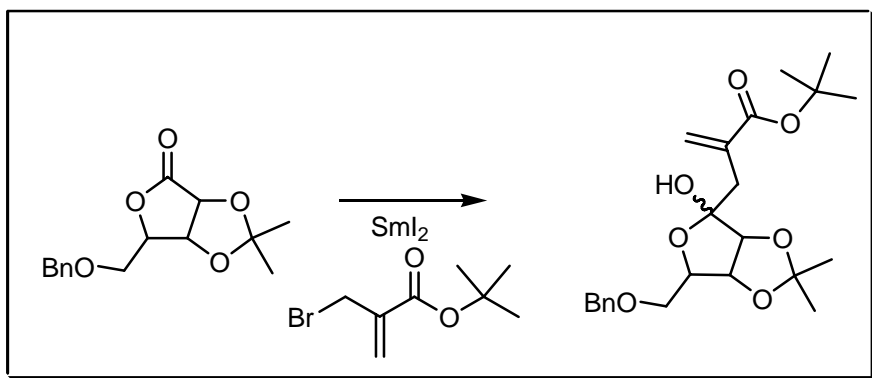
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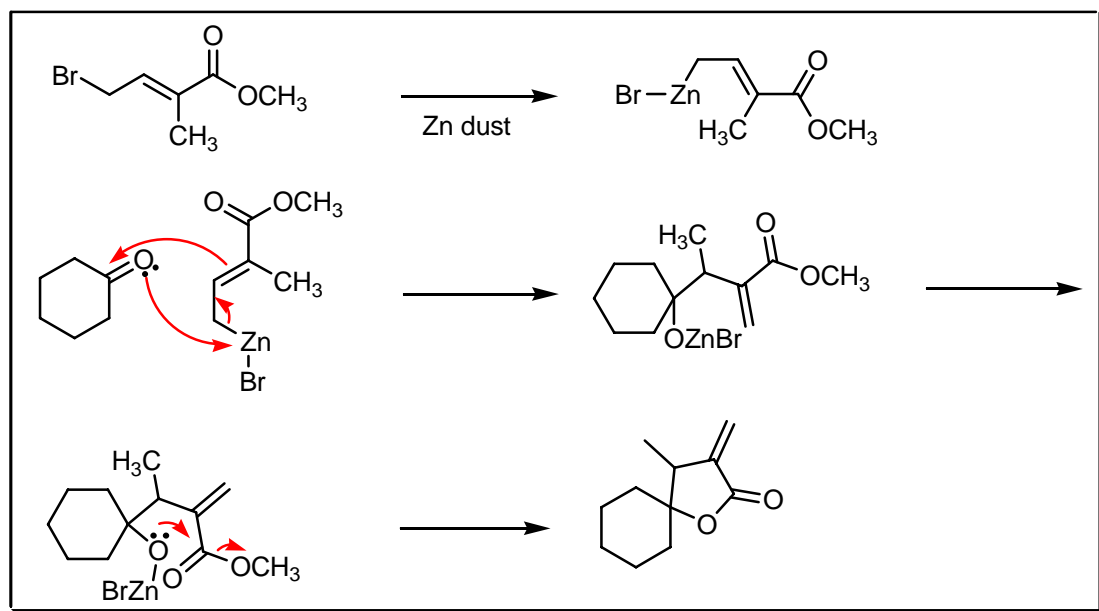
## COMMENTS :

## DREIDING – SCHMIDT REACTION

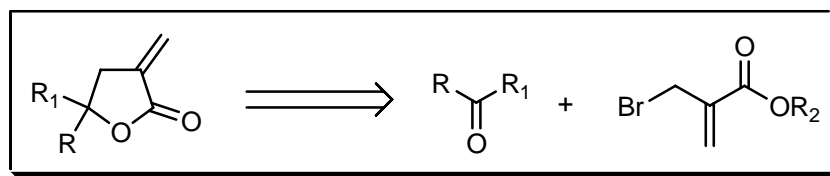
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The methylene lactone formation starting from ketones or aldehydes and  $\alpha$ -(bromoalkyl)acrylic esters. See also **Blaise, Gilman – Speeter** and **Reformatsky** reactions.

### REFERENCES :

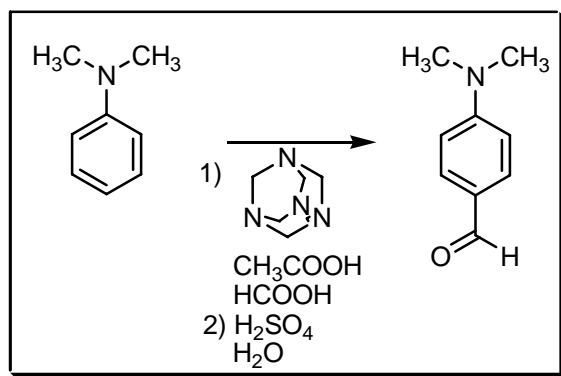
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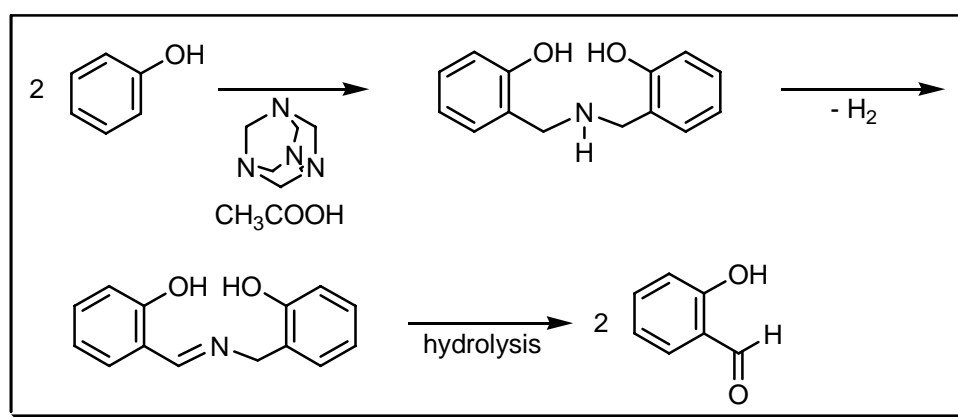
COMMENTS :

## DUFF REACTION

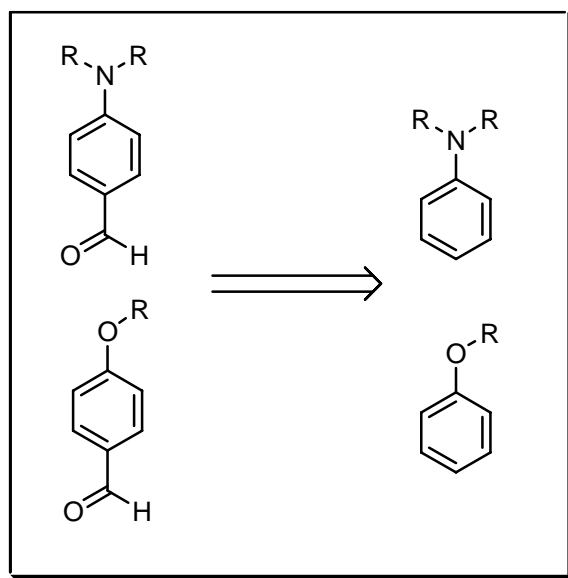
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

A mixture of *N,N*-dialkylaniline or a phenol, hexamethylenetetramine, acetic and formic acids, is heated and the aminoalkylated product is treated with mineral acid and water. If the *o*-position is blocked the *p*-substituted compound is formed. See also **Ciamician – Dennstedt**, **Reimer – Tiemann** and **Sommelet** reactions.

## REFERENCES :

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**Smith – March** : 717

**Houben – Weyl** : **7/1**, 43, 198; **E6b**, 1074

**Org. Synth.** : **31**, 92; **75**, 1

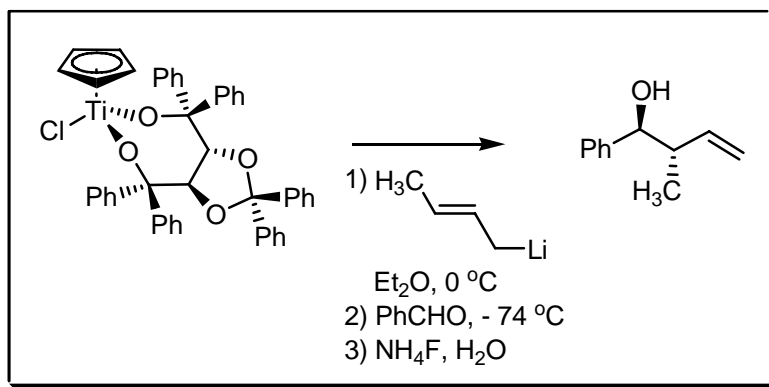
**Org. Synth. Coll. Vol.** : **4**, 866; **10**, 96

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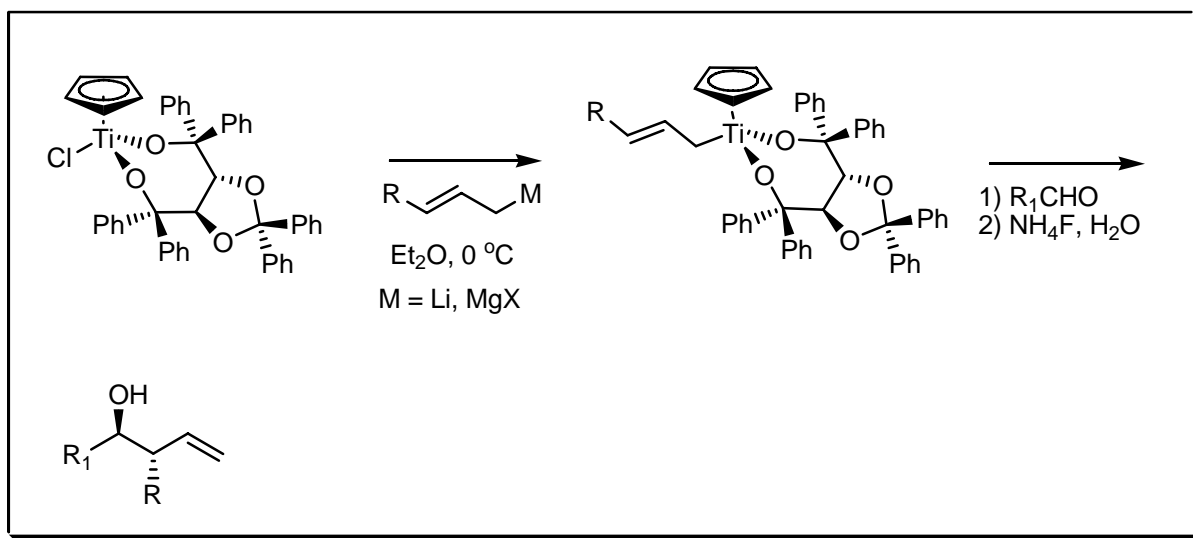
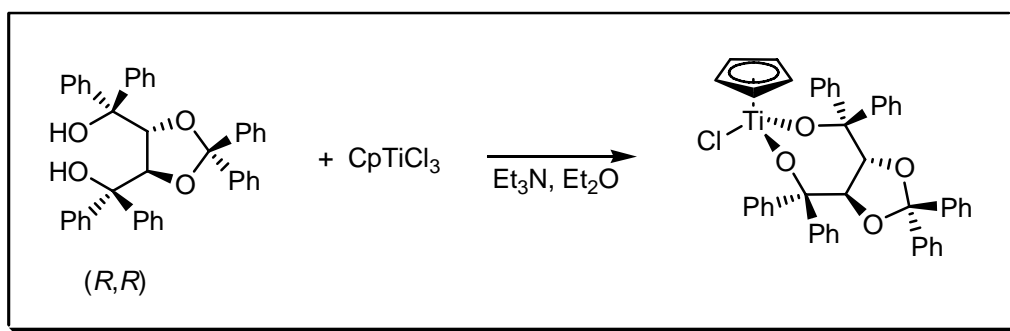
## COMMENTS :

## DUTHALER – HAFNER ALLYLATION

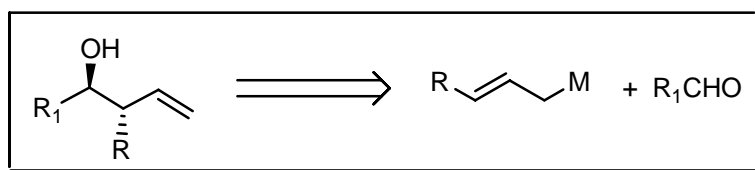
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :





## NOTES :

The chiral TADDOL titanium complex is used for asymmetric allylation reactions. The chiral diol is available in both enantiomeric forms. The titanium complex may be used in crude form. See also **Ibuka – Yamamoto**, **Matteson**, **Roush – Hoffmann – Yamamoto** and **Thomas** reactions.

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## REFERENCES :

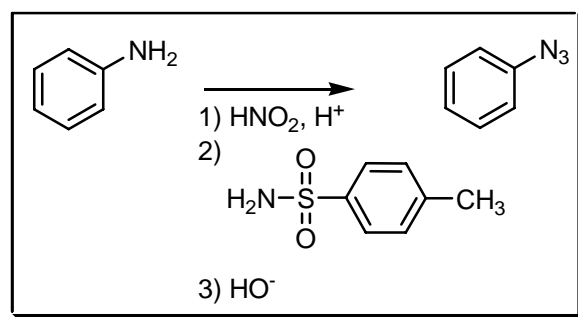
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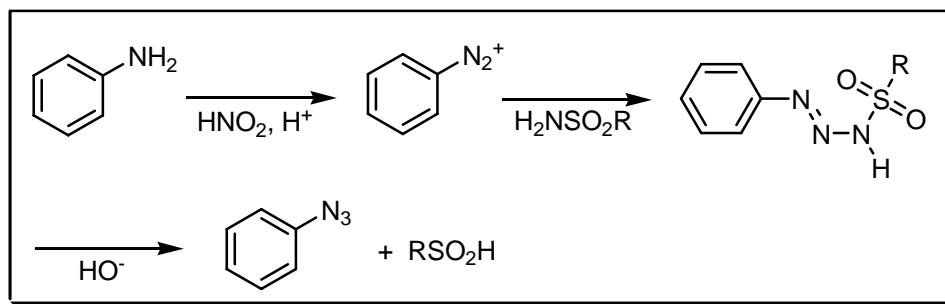
## COMMENTS :

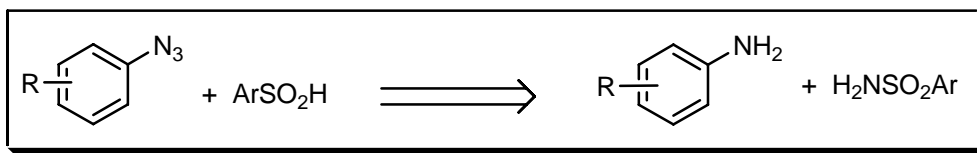
## DUTT – WORMALL REACTION

### EXAMPLE :



### MECHANISM :



**DISCONNECTION :**

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**NOTES :**

Aromatic azides and sulfonic acids are obtained by the action of aromatic diazonium salts on aliphatic or aromatic sulfonamides in the presence of alkali.

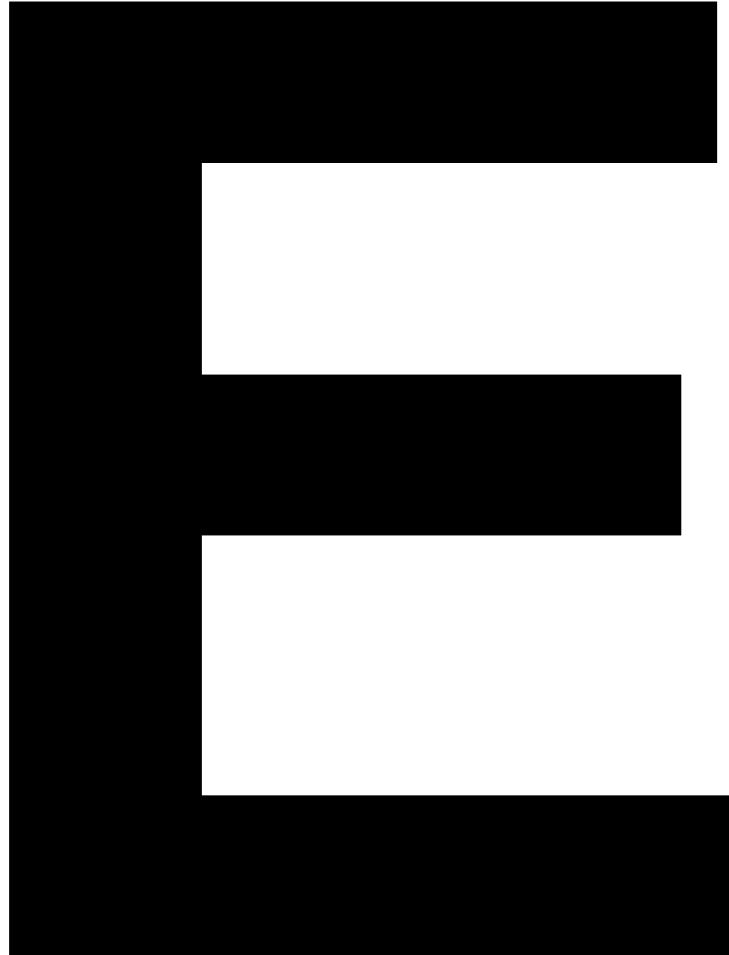
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**COMMENTS :**



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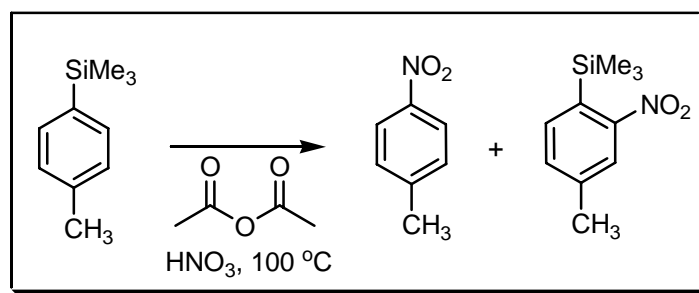
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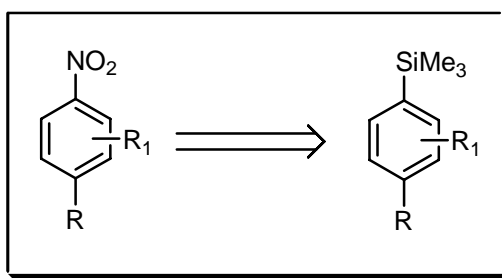
## EABORN – CHVALOVSKÝ REACTION

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### EXAMPLE :



### DISCONNECTION :



### NOTES :

The cleavage of aryl-trimethylsilyl bonds using nitrating agents in acetic anhydride. The reaction most likely proceeds *via* nitrosodesilylation followed by oxidation. It is not known what the exact dominant nitrating entity is, it is assumed that it is a lower nitrogen oxide.

### REFERENCES :

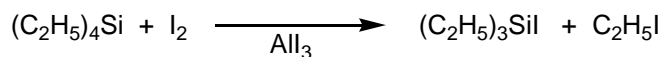
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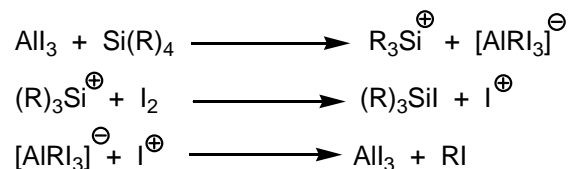
## EABORN REACTION

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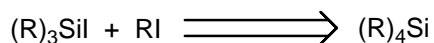
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The formation of alkyl iodide silanes from tetraalkylsilane and iodine in the presence of aluminium iodide. Further reactions are possible, and the product can transhalogenate to give the corresponding fluoro compound. The ease of displacement varies from phenyl >> methyl > ethyl > *n*/*i* propyl. See also **Ruff** reaction.

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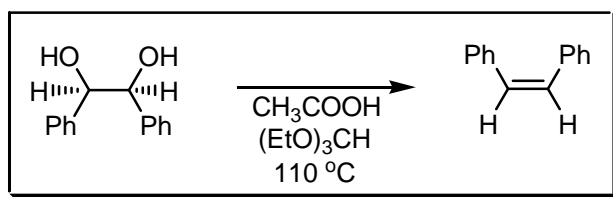
### REFERENCES :

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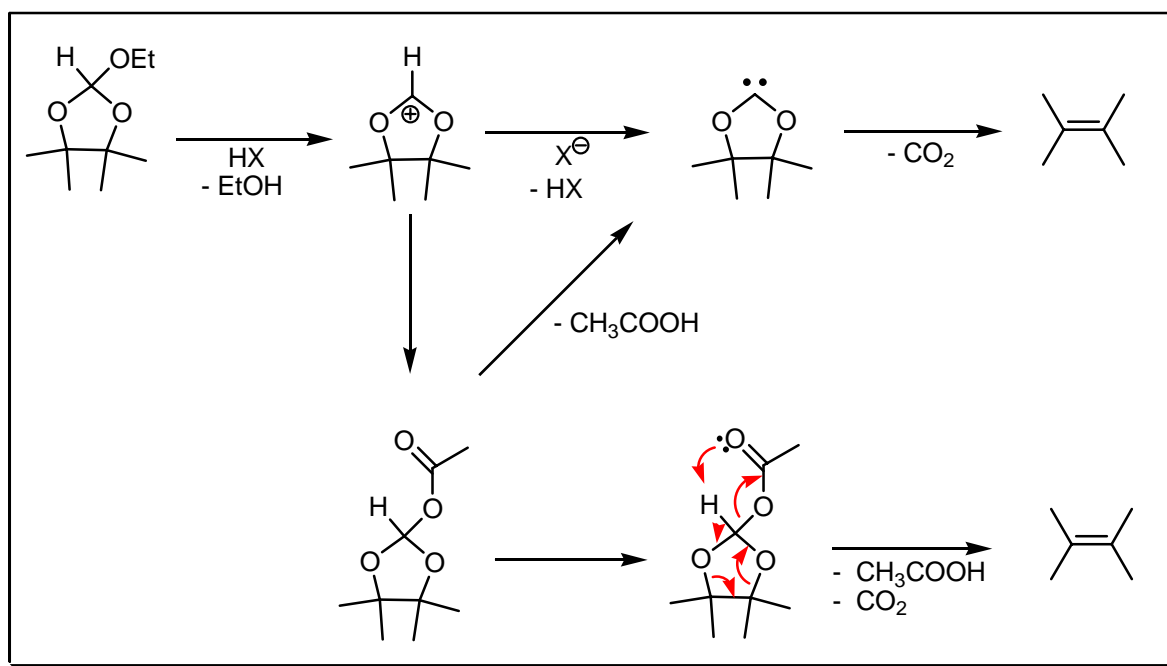
### COMMENTS :

## EASTWOOD REACTION

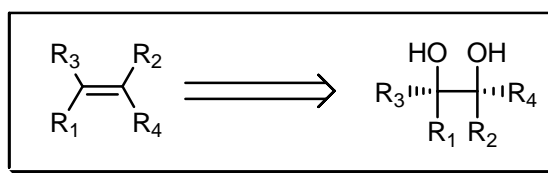
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The treatment of *vicinal* diols with ethyl orthoformate at elevated temperatures, followed by continued heating at somewhat higher temperatures ( $160 - 220^\circ\text{C}$ ) in the presence of a carboxylic acid leads to olefin formation (one-pot, one-reagent olefin synthesis). See also **Corey – Kwiatkowski**, **Horner – Wadsworth – Emmons**, **Julia – Paris – Kocienski** – **Lythgoe**, **Krief – Reich – Chow**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Nysted**, **Paquette**, **Petasis** reaction, **Peterson**, **Ramberg – Bäcklund**, **Still – Gennari**, **Takeda**, **Tebbe** and **Wittig** reactions.

## REFERENCES :

March : 1029

Smith – March : 1341

Org. React. : 30, 457

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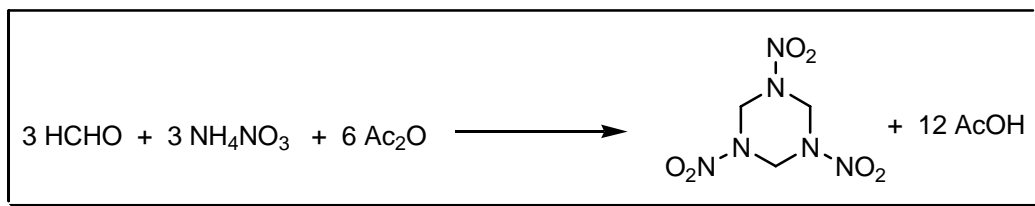
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- 

## COMMENTS :

## EBELE – SCHIESSLER – ROSS CYCLONITE SYNTHESIS

---

### EXAMPLE :



### NOTES :

Cyclonite is obtained (60% yield based on formaldehyde) by the addition of paraformaldehyde and ammonium nitrate to acetic anhydride at 70 °C. See also **Hale**, **Knoffler – Bachmann** and **Wolfram** reactions.

---

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- 

## COMMENTS :



## ECKEY PROCESS

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### NOTES :

This process involves the direct esterification of glycidyl fatty acid esters with fatty acids. **Eckey's** process of low-temperature directed *interesterification* of fats has been modified by **Eckey** and **Formo** to include simultaneous alcoholysis as well as ester-ester interchange. In the modified process, in the presence of catalysts (e.g. NaOCH<sub>3</sub>), melted fats and glycerol interesterify to produce an equilibrium mixture of monoglycerides, diglycerides, triglycerides and free glycerol. Crystallisation of high melting monoglycerides or diglycerides takes place when the temperature of the liquid product is lowered sufficiently. This lowering of the temperature and subsequent crystallisation of a component from the liquid phase disturbs the equilibrium, whose re-establishment is continuously promoted by the rearrangement catalyst. The desired glyceride continues to crystallise out until the supply of its constituent groups is no longer sufficient to maintain the super saturation of the liquid phase with respect to the precipitated solid. The pure single-fatty acid diglycerides were isolated from the crystalline products by tedious solvent crystallisation. A radical pathway is most likely.

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### REFERENCES :

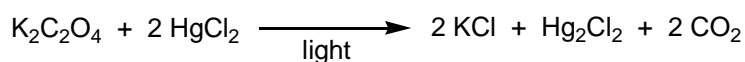
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### COMMENTS :

## EDER REACTION

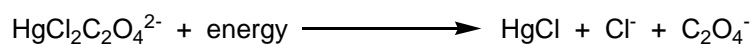
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### EXAMPLE :



### MECHANISM :

primary step :



## NOTES :

**Eder** published this reaction as a new chemical way to measure the intensity of UV radiation in daylight. The great energy efficiency indicates that the reaction is most probably a chain reaction.

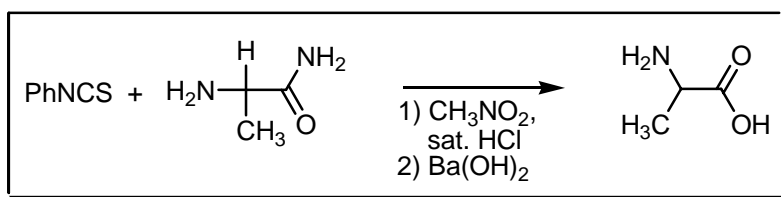
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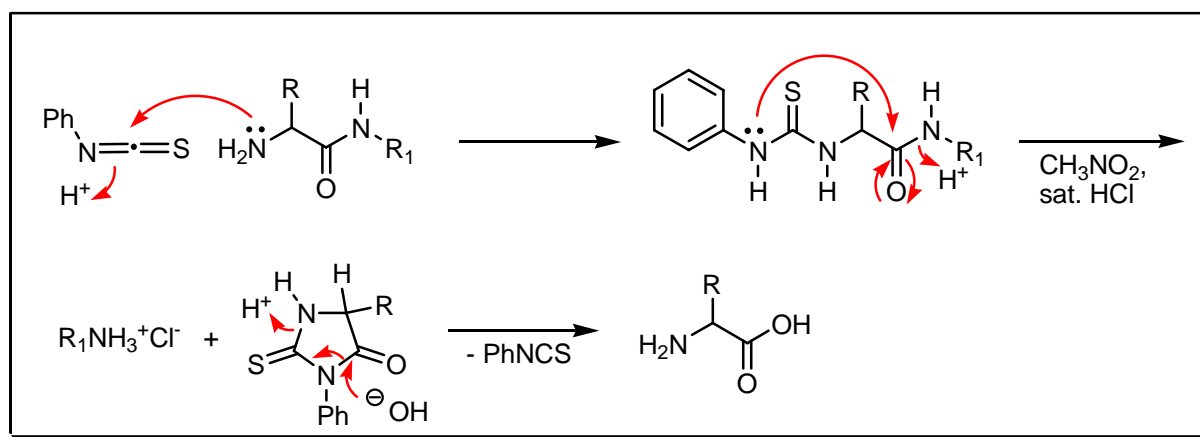
## COMMENTS :

## EDMAN DEGRADATION

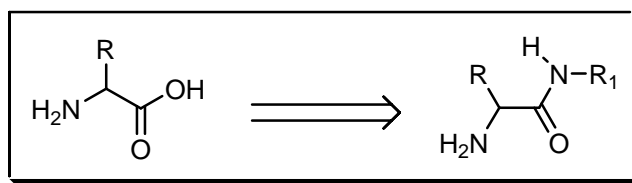
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

This degradation involves the reaction of phenyl isothiocyanate with an amino-group of a peptide at a controlled pH (pH 9) to form the phenyl thiocarbamyl derivative. Cleavage of this derivative in anhydrous nitromethane saturated with hydrogen chloride affords the phenylthiohydantoin and the hydrochloride of the amino-acid or peptide lacking the terminal amino-acid. The process can be repeated. See also **Schlack – Kumpf** reaction.

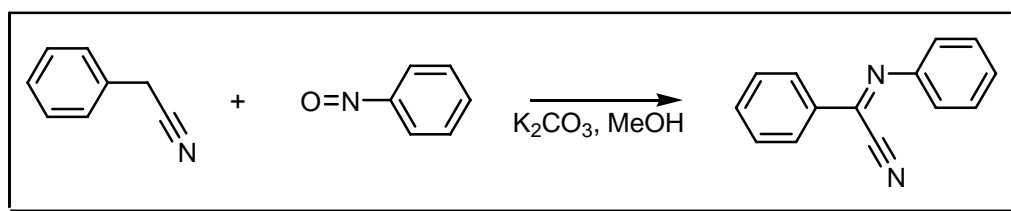
## REFERENCES :

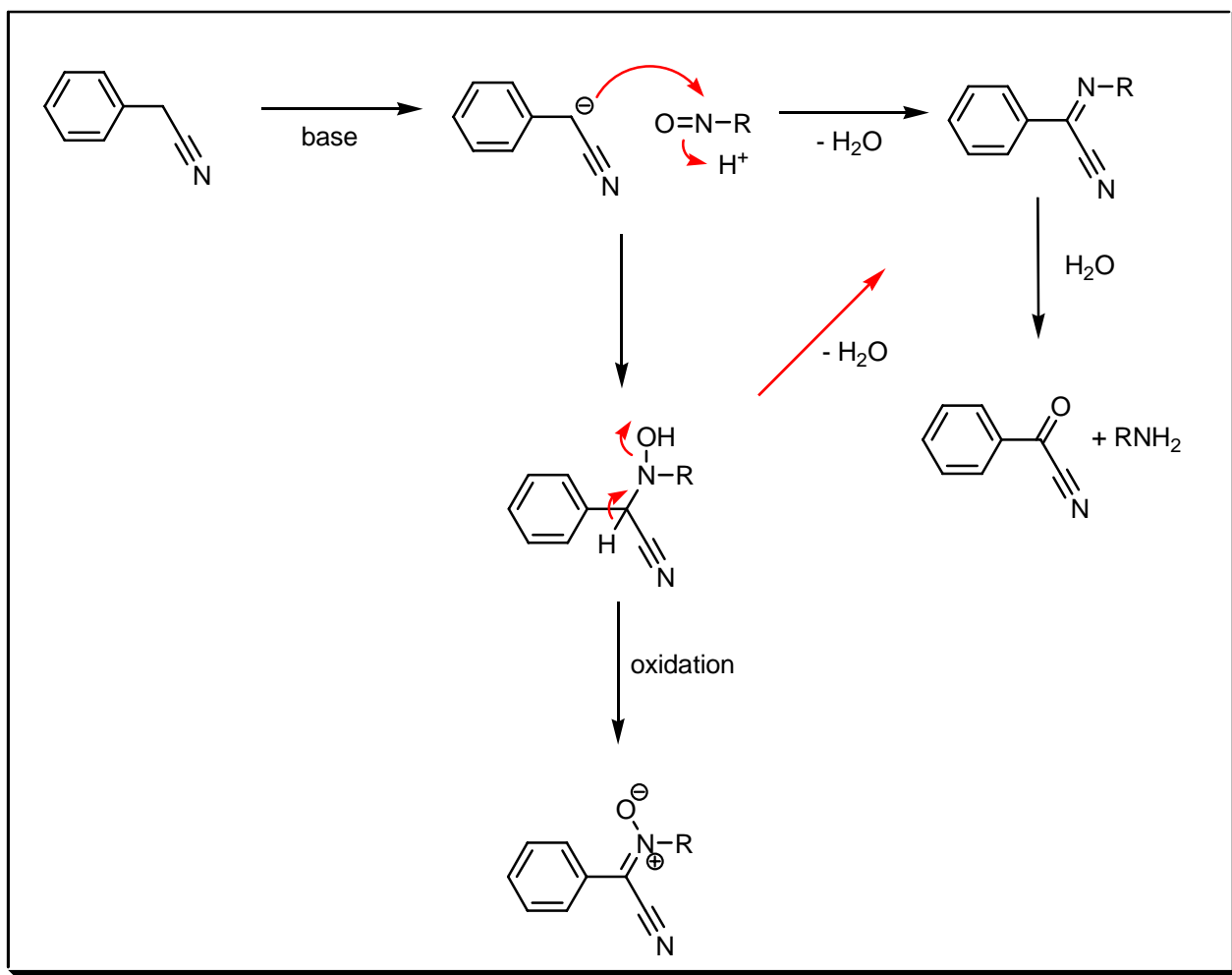
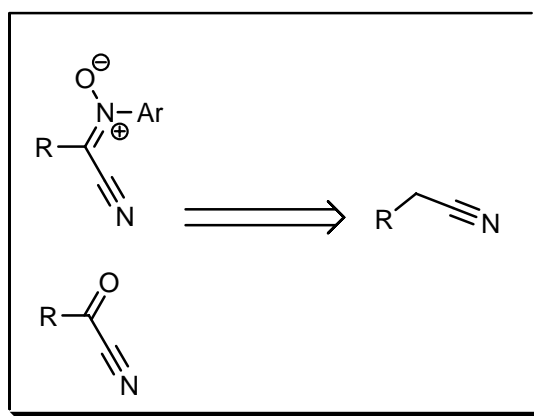
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## COMMENTS :

## EHRlich – SACHS REACTION

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

Compounds containing a reactive methylene group undergo condensation in aqueous ethanolic base with aromatic nitroso compounds yielding a mixture of azomethines, *N*-oximino ethers and azoxy compounds. The formation of azomethines is promoted by using absolute methanol as a solvent, anhydrous potassium carbonate as condensing agent and by employing equimolar proportions of the reactants. The azomethines may be hydrolysed to the corresponding ketones or aldehydes and amines.

## REFERENCES :

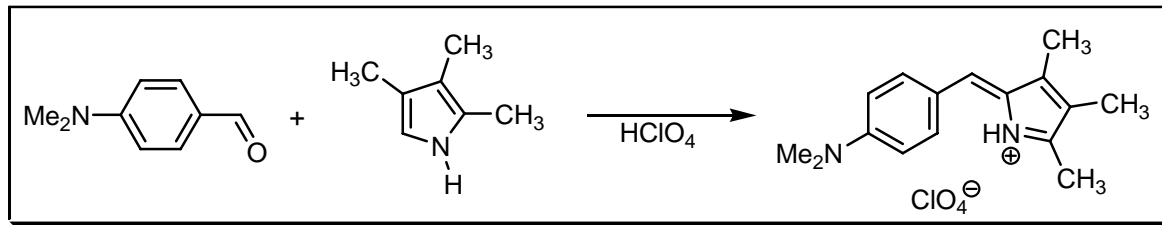
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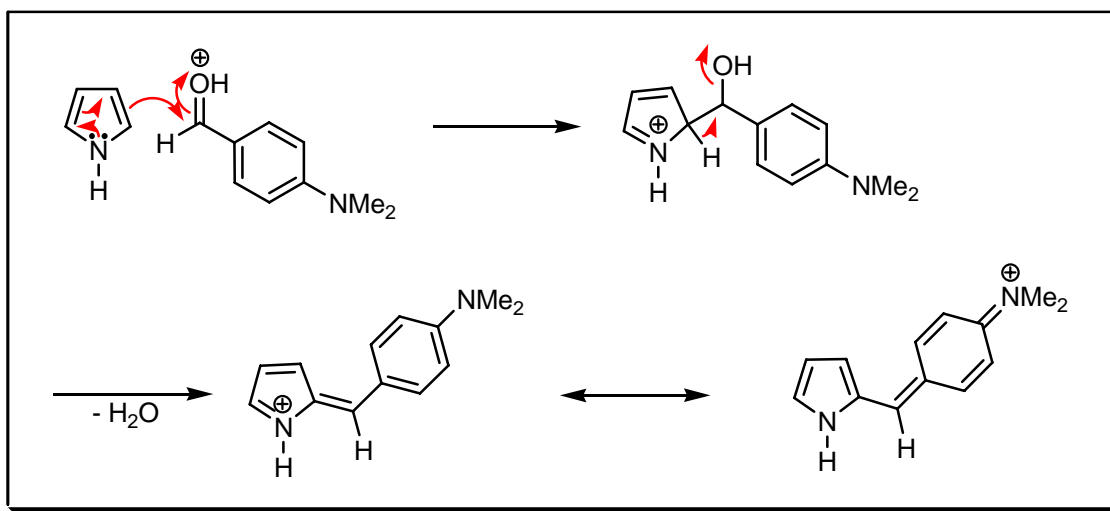
## COMMENTS :

## EHRlich PYRROLE REACTION

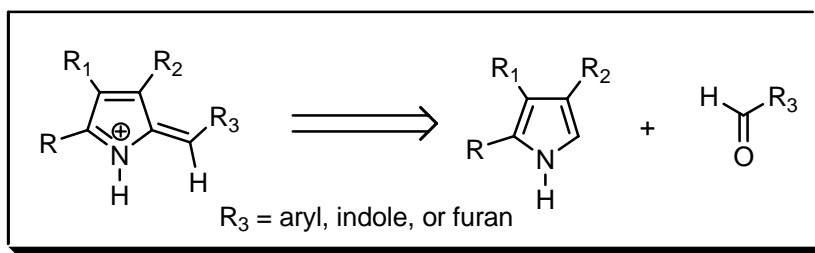
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

Pyrroles, unsubstituted in the  $\alpha$ -position, condense with aldehydes *e.g.* *p*-dimethylaminocinnamic aldehyde in the presence of acid, to give the corresponding derivative. The reaction has been extended to a variety of aldehydes and to indole ( $\beta$ -position) and furan derivatives. The **Ehrlich** test uses *p*-dimethylaminocinnamic aldehyde.

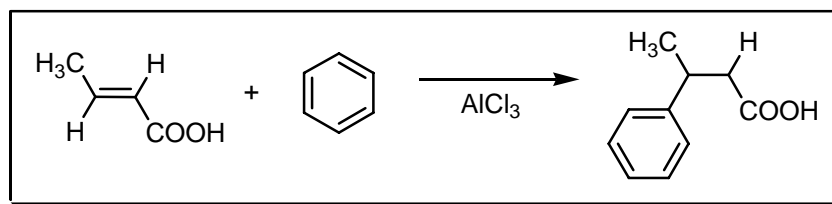
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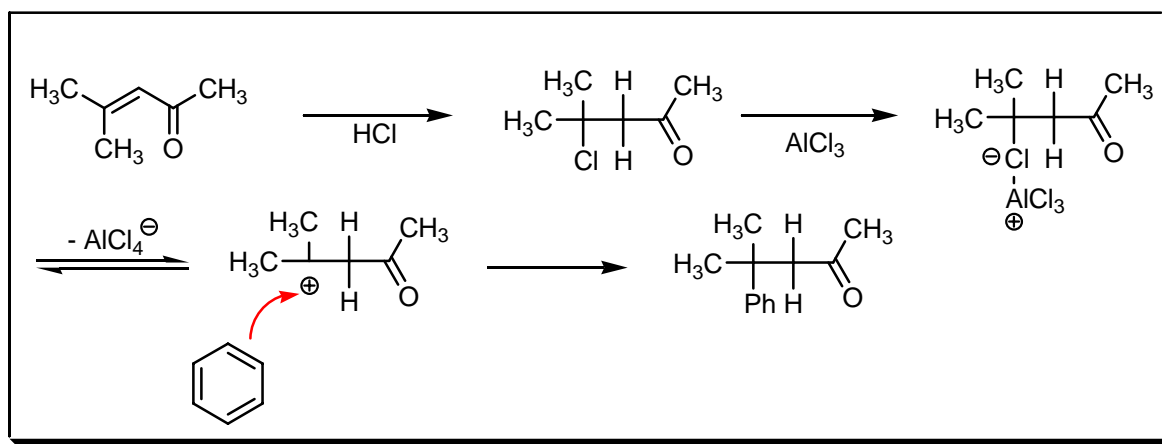
## COMMENTS :

## EIJKMAN ADDITION

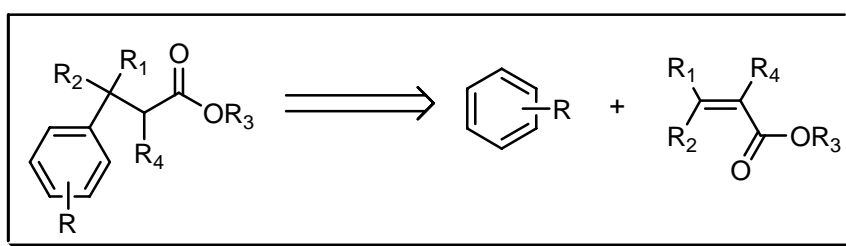
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The interaction of an aromatic hydrocarbon with an α,β-unsaturated carboxylic acid or ester in the presence of aluminium chloride yields the β-aryl acid. Mesityl oxide reacts similarly with fluorobenzene. See also **Friedel – Crafts** and **Michael** reactions.

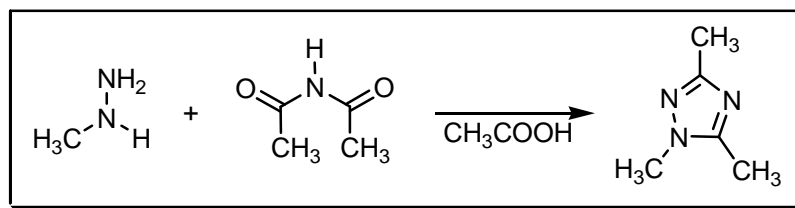
## REFERENCES :

- 1) J.F. Eijkman, *Chem. Weekblad*, 1904, **1**, 421.
- 2) J.F. Eijkman, *Chem. Weekblad*, 1908, **5**, 655.
- 3) E.J. King, *J. Am. Chem. Soc.*, 1927, **49**, 562.
- 4) A. Hoffman, *J. Am. Chem. Soc.*, 1929, **51**, 2542.
- 5) L.I. Smith; C.-P. Lo, *J. Am. Chem. Soc.*, 1948, **70**, 2215.
- 6) J. Colonge; L. Pichat, *Bull. Soc. Chim. Fr.*, 1949, 177.
- 7) R.V. Christian, jr., *J. Am. Chem. Soc.*, 1952, **74**, 1591.
- 8) A. Mustafa; W. Asker; A.H. Harhash; N.A.L. Kassab, *Tetrahedron*, 1963, **19**, 1577.
- 9) H.E. Zimmerman; C.J. Samuel, *J. Am. Chem. Soc.*, 1975, **97**, 4025.
- 10) P.S. Hillery; L.A. Cohen, *J. Am. Chem. Soc.*, 1983, **105**, 2760.
- 11) A.R. Maguire; N.R. Buckley; P. O'Leary; G. Ferguson, *J. Chem. Soc., Perkin Trans. 1*, 1998, 4077.

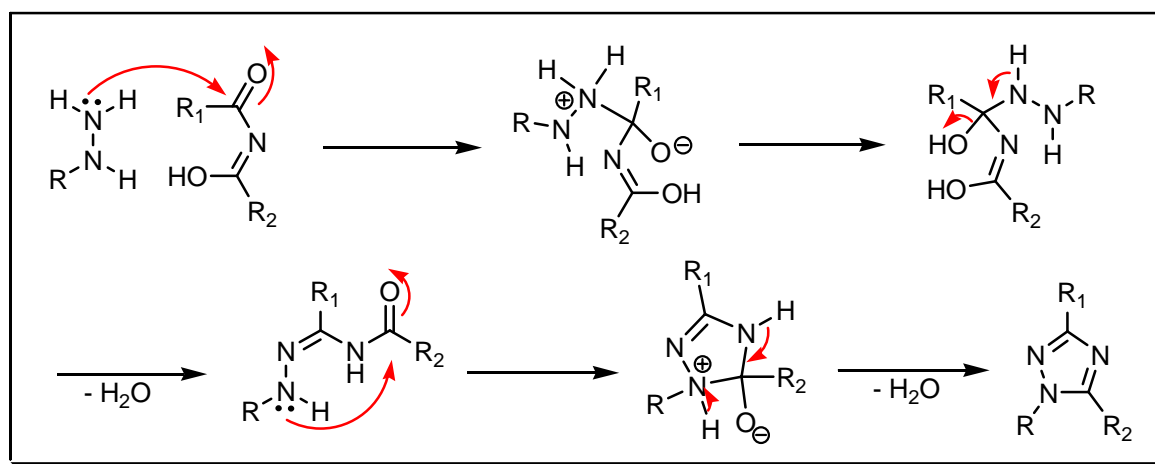
COMMENTS :

## EINHORN – BRUNNER REACTION

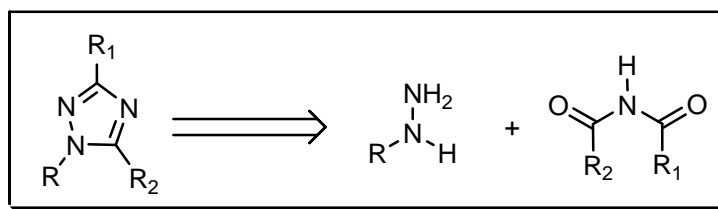
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The synthesis of substituted 1,2,4-triazoles by the condensation of a hydrazine with a diacylamine. See also **Kaiser** triazole and **Pellizzari** reactions.



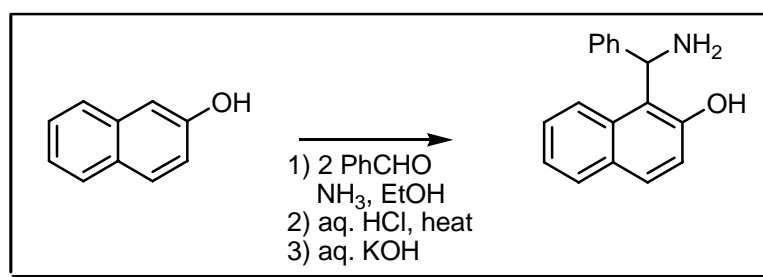
## REFERENCES :

- 1) A. Einhorn; E. Bischkopff; B. Szelinski, *Liebigs Ann. Chem.*, 1905, **343**, 229.
- 2) K. Brunner, *Ber. Dtsch. Chem. Ges.*, 1914, **47**, 2671.
- 3) M.R. Atkinson; J.B. Polya, *J. Chem. Soc.*, 1952, 3418.
- 4) M.R. Atkinson; J.B. Polya, *J. Chem. Soc.*, 1954, 141.
- 5) K.T. Potts, *Chem. Rev.*, 1961, **61**, 87.

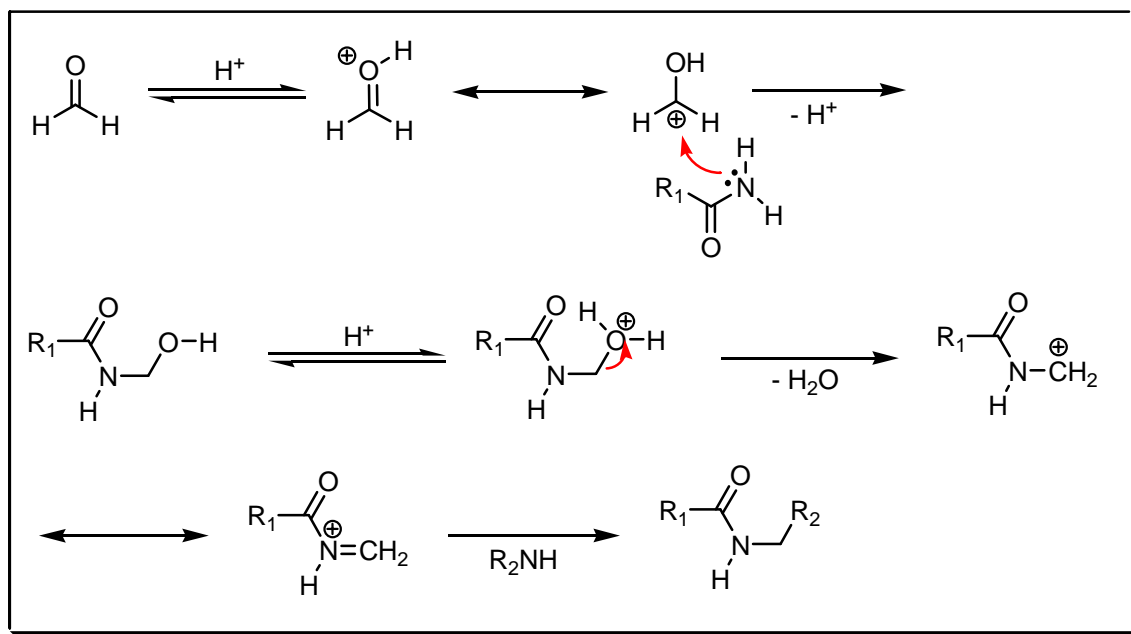
## COMMENTS :

## EINHORN – TSCHERNIAC AMIDOMETHYLATION

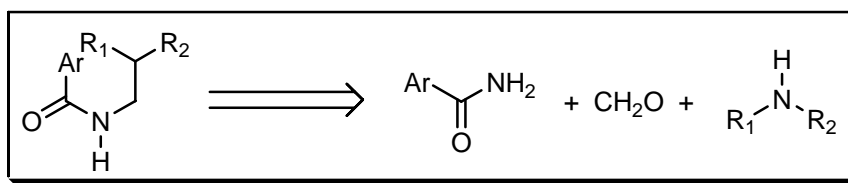
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The preparation of amidomethyl derivatives of aromatic compounds (Phenols, secondary and tertiary aromatic amines, pyrroles and indoles) or activated methylene groups by treatment of an ethanolic or methanolic mixture of the compound and an amide with hydrogen chloride or chloric acid. See also **Mannich** reaction.

## REFERENCES :

**March** : 550

**Smith – March** : 722

**Houben – Weyl** : 11/1, 795

**Org. React.** : 14, 63

**Org. Synth.** : 9, 60; 35, 78; 40, 31

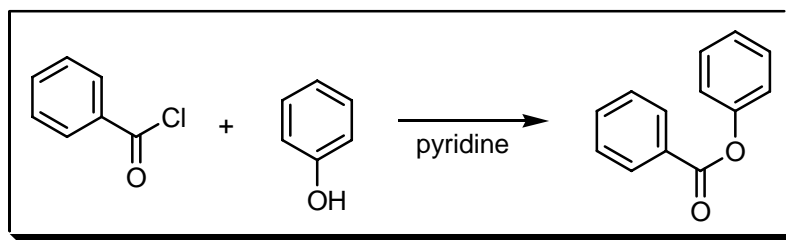
**Org. Synth. Coll. Vol.** : 1, 381; 4, 626; 5, 434

- 1) A. Einhorn, *Liebigs Ann. Chem.*, 1905, **343**, 207.
- 2) H. Hellmann, *Angew. Chem.*, 1957, **69**, 463.
- 3) F. Lauria; C. Bernardelli; G. Tosolini; W. Logemann, *Liebigs Ann. Chem.*, 1967, **706**, 233.
- 4) I.H. Sanchez; F.J. Lopez; J.J. Soria; M.I. Larraza; H.J. Flores, *J. Am. Chem. Soc.*, 1983, **105**, 7640.
- 5) K.J. Hu; J.S. Bradshaw; V.N. Pastuhok; K.E. Krakowiak; N.K. Dalley; X.X. Zhang; R.M. Izatt, *J. Org. Chem.*, 1998, **63**, 4786.
- 6) K.J.C. van Bommel; F. Westerhof; W. Verboom; D.N. Reinhoudt; R. Hulst, *J. Prakt. Chem.*, 1999, **341**, 284.

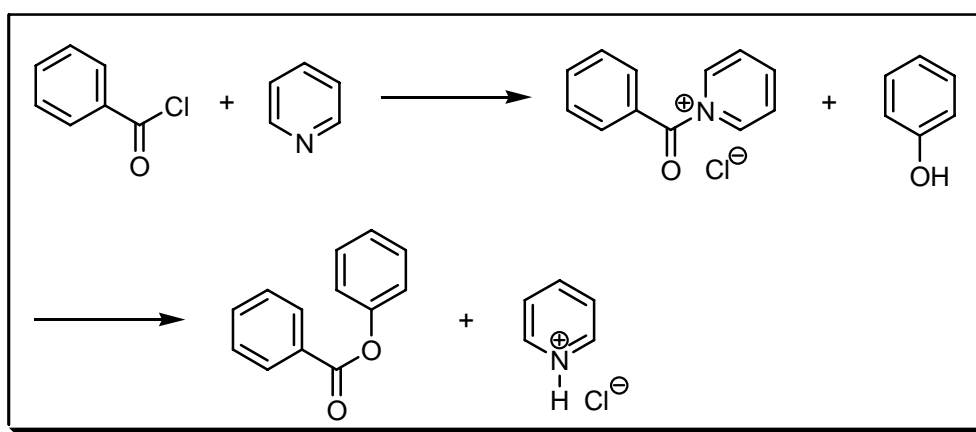
## COMMENTS :

## EINHORN ACYLATION

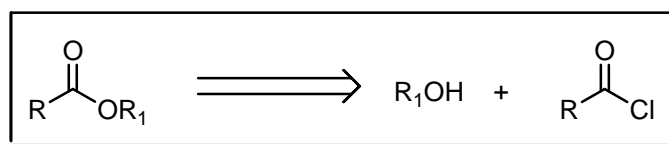
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The acylating mixture for alcohols consists of an acyl chloride and pyridine or other tertiary base. See also **Chattaway** acylation, **Galat – Elion**, **Lumière – Barbier**, **Schotten – Baumann** and **Weinreb** reactions.

### REFERENCES :

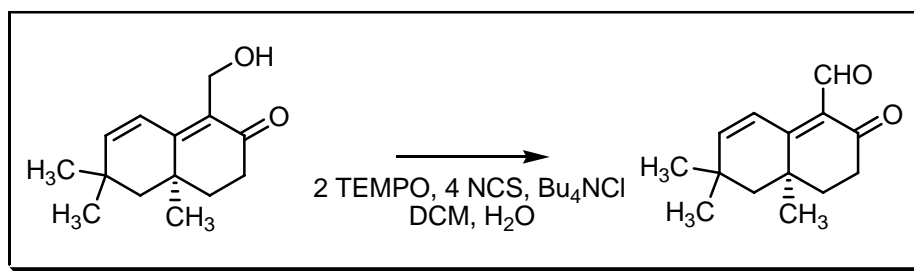
**Houben – Weyl** : 2, 332; 8, 545

- 1) M. Dennstedt; J. Zimmermann, *Ber. Dtsch. Chem. Ges.*, 1886, **19**, 75.
- 2) A. Einhorn; F. Hollandt, *Liebigs Ann. Chem.*, 1898, **301**, 95.
- 3) F. Ullmann; G. Nadai, *Ber. Dtsch. Chem. Ges.*, 1908, **41**, 1870.
- 4) J.A. Mills, *J. Chem. Soc.*, 1951, 2332.
- 5) I. Bauerova; M. Ludwig, *Coll. Czech. Chem. Commun.*, 2000, **65**, 1777.
- 6) A.C. Spivey; A. Maddaford; D.P. Leese; A.J. Redgrave, *J. Chem. Soc., Perkin Trans. 1*, 2001, 1785.

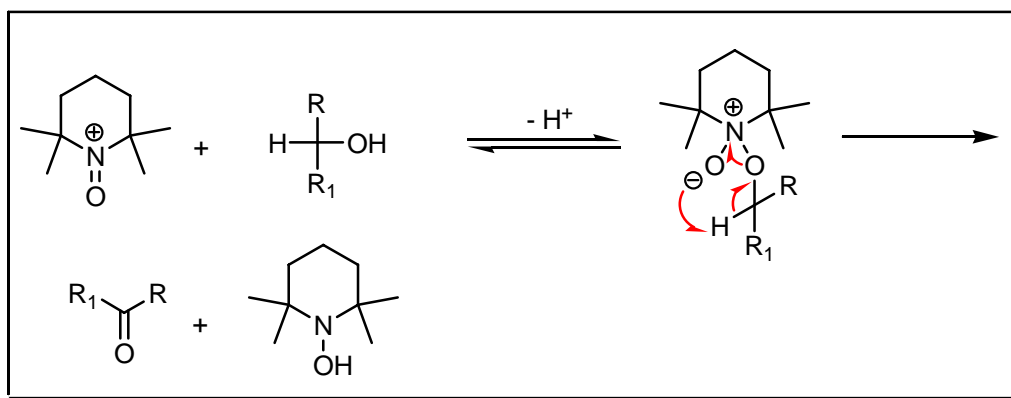
COMMENTS :

## EINHORN OXIDATION

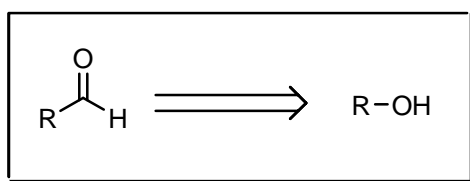
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

TEMPO catalyses the oxidation of primary alcohols to aldehydes by *N*-chlorosuccinimide (NCS), in a biphasic dichloromethane – aqueous buffer system ( $\text{NaHCO}_3$ ,  $\text{K}_2\text{CO}_3$ , pH 8.6) in the presence of  $t\text{Bu}_4\text{NCl}$  (The phase transfer catalyst). The proton abstraction may occur *intra*- or *intermolecularly*. Aliphatic, benzylic and allylic alcohols are readily oxidised without any over-oxidation to the carboxylic acid. Secondary alcohols are oxidised to ketones but in a much lower efficiency. See also **Anelli, Ball – Goodwin – Morton, Collins, Corey – Kim, Corey – Schmidt, Corey – Suggs, David – Thieffry, Delépine, Dess – Martin, Fétizon, Jones oxidation, Ley, Maurer – Drefahl, Mukaiyama oxidation, Nicolaou, Oppenauer, Parikh – von Doering, Pfitzner – Moffatt, Pinnick, Sarett, Swern and Uemura reactions.**

## REFERENCES :

**Smith – March** : 1515

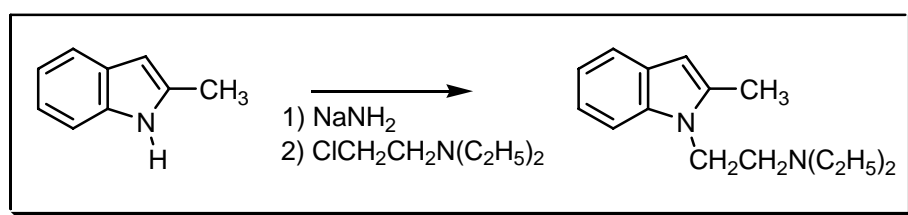
1) J. Einhorn; C. Einhorn; F. Ratajczak; J.-L. Pierre, *J. Org. Chem.*, 1996, **61**, 7452.

2) B.B. Snider; B. Shi, *Tetrahedron Lett.*, 2001, **42**, 9123.

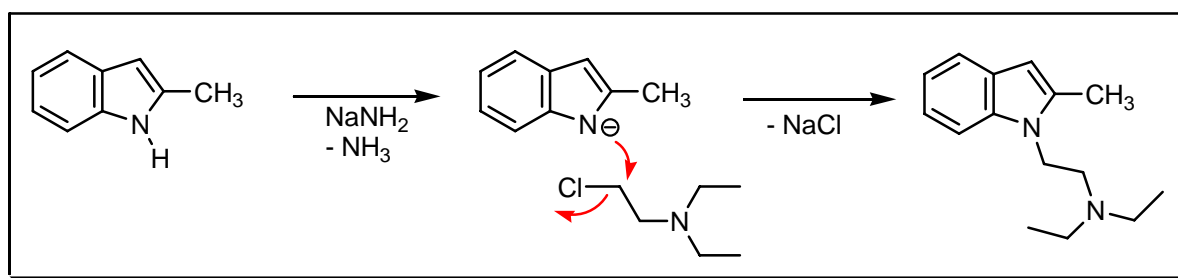
## COMMENTS :

## EISLEB AMINOALKYLATION

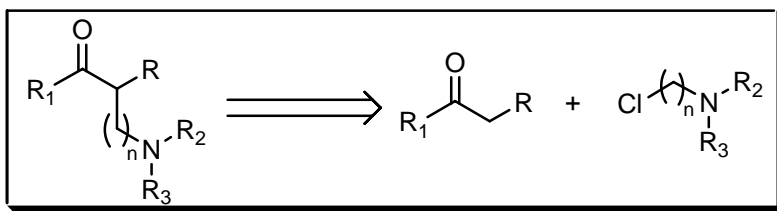
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

Active hydrogen atoms can be replaced by *tert*-aminoalkyl groups by treatment of the *tert*-aminoalkyl chloride with the compound in the presence of sodamide and a suitable solvent. Compounds like  $\beta$ -dichloroethyl ether react similarly. This chemistry is used in the synthesis of pethidine-based analgesics.

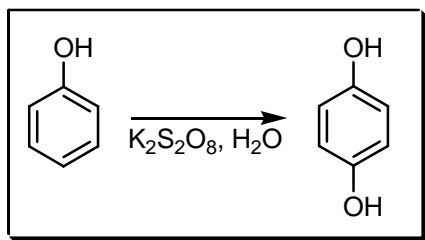
## REFERENCES :

- 1) O. Eisleb, *Ber. Dtsch. Chem. Ges.*, 1941, **74**, 1433.
- 2) J.A. Barltrop, *J. Chem. Soc.*, 1946, 958.
- 3) R.L. Clark; A.A. Pessolano; J. Weijlard; K. Pfister, *J. Am. Chem. Soc.*, 1953, **75**, 4963.
- 4) J. Diamond; W.F. Bruce; F.T. Tyson, *J. Org. Chem.*, 1957, **22**, 399.

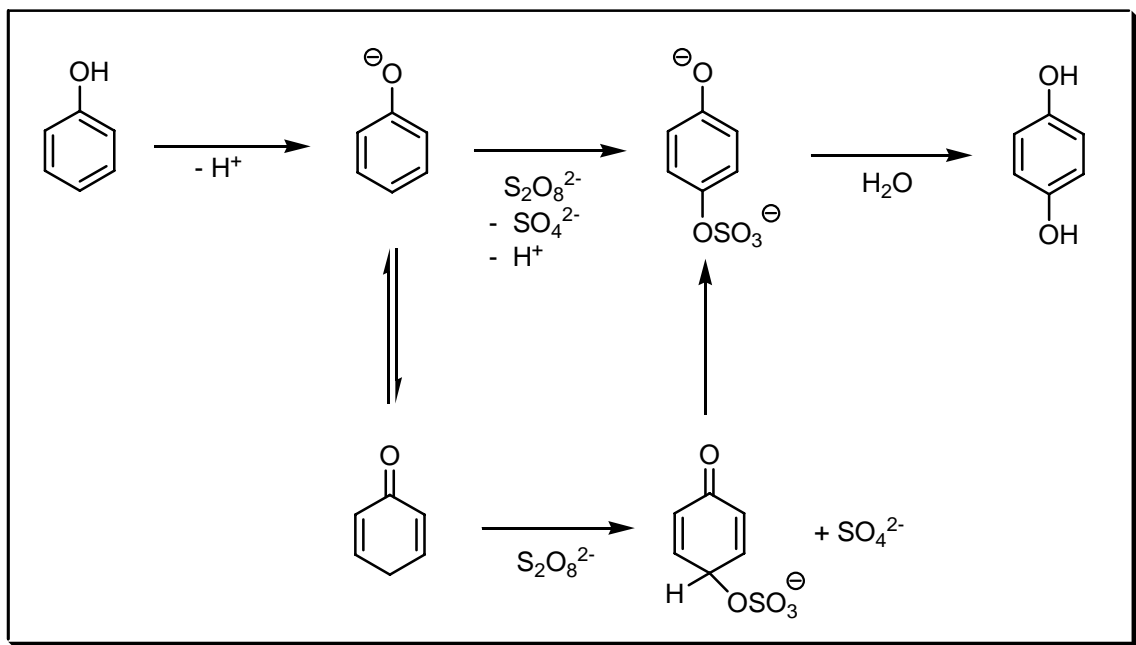
## COMMENTS :

## ELBS PERSULFATE OXIDATION

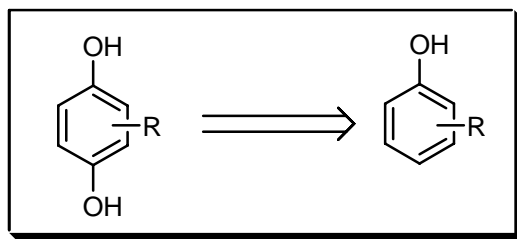
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

This reaction involves the oxidation of monohydric phenols to dihydric phenols or aromatic amines using potassium persulfate in alkaline solution (**Boyland – Sims** reaction). The second hydroxyl group enters *ortho* to that already present but if that position is blocked, the *para* position is favoured. See also **Boyland – Sims** reaction.

## REFERENCES :

March : 554

Smith – March : 724

Smith : 261

Smith 2<sup>nd</sup> : 226

Houben – Weyl : E7b, 572; E11, 1003

Org. React. : 5, 421; 35, 421

1) K. Elbs, *J. Prakt. Chem.*, 1893, **48**, 179.

2) S.M. Setha, *Chem. Rev.*, 1951, **49**, 91.

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4) D.T. Hurst, *Aust. J. Chem.*, 1983, **36**, 1285.

5) K.G. Watson; A. Serban, *Aust. J. Chem.*, 1995, **48**, 1503.

6) E.C. Behrman; S. Chen; E.J. Behrman, *Tetrahedron Lett.*, 2002, **43**, 3221.

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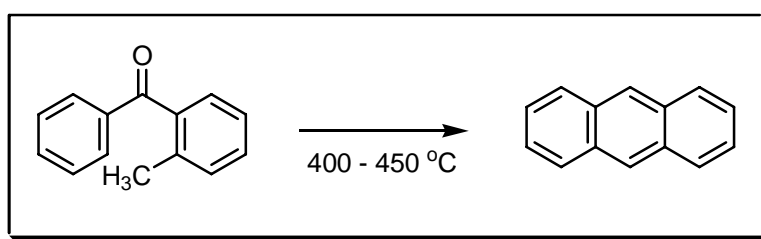
**COMMENTS :**

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**ELBS REACTION**

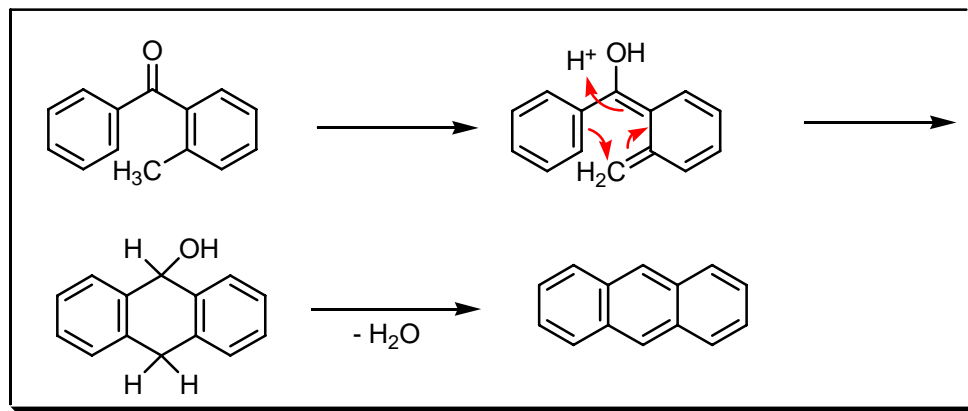
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**EXAMPLE :**



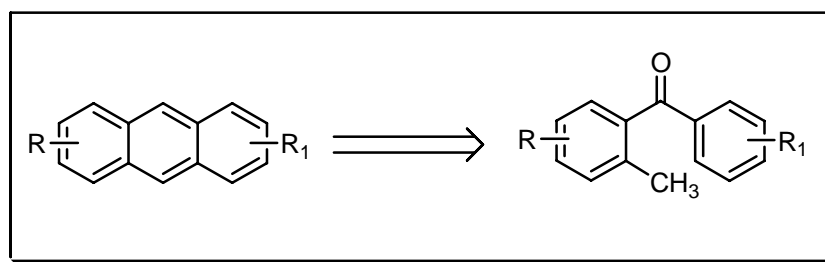
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**MECHANISM :**



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**DISCONNECTION :**





## NOTES :

Diaryl ketones with a methyl or methylene substituent adjacent to the carbonyl group undergo cyclodehydration to the corresponding anthracene derivative when pyrolysed. See also **Scholl** reaction.

## REFERENCES :

**Org. React.** : **1**, 129

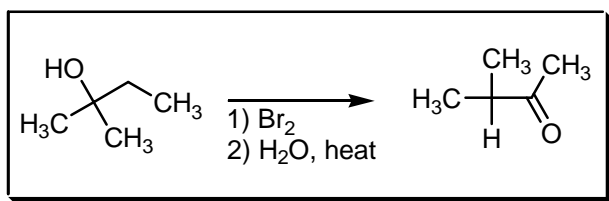
**Science of Synthesis** : **10**, 241

- 1) A. Behr; W.A. van Dorp, *Ber. Dtsch. Chem. Ges.*, 1873, **6**, 753.
- 2) K. Elbs; E. Larsen, *Ber. Dtsch. Chem. Ges.*, 1884, **17**, 2847.
- 3) E.D. Bergman; J. Blum, *J. Org. Chem.*, 1960, **25**, 474.
- 4) M.S. Newman; V.K. Khanna, *J. Org. Chem.*, 1980, **45**, 4507.
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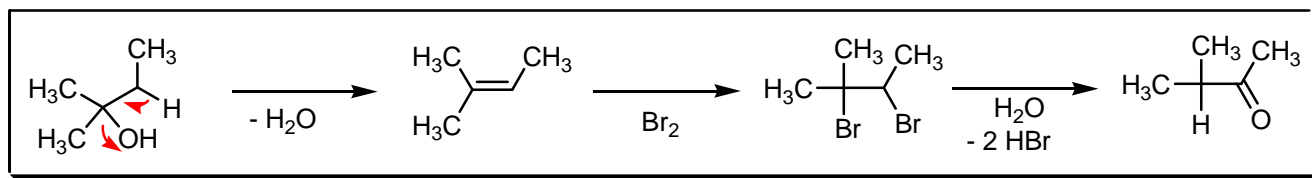
## COMMENTS :

## ELTEKOFF KETONE SYNTHESIS

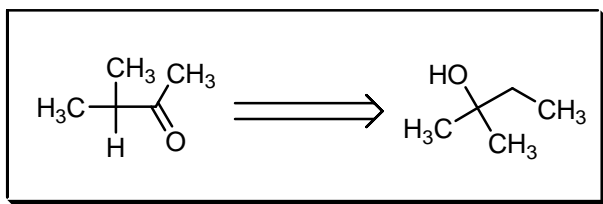
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The formation of a ketone from *tert*-amylalcohol *via* an olefin and a dibromide.

## REFERENCES :

Houben – Weyl : 5/4, 162

Org. Synth. : 13, 68

Org. Synth. Coll. Vol. : 2, 408

1) A. Eltekoff, *Ber. Dtsch. Chem. Ges.*, 1878, **11**, 989.

2) W.L. Evers; H.S. Rothrock; H.M. Woodburn; E.E. Stahly; F.C. Whitmore, *J. Am. Chem. Soc.*, 1933, **55**, 1136.

3) C.M. Suter; H.D. Zook, *J. Am. Chem. Soc.*, 1944, **66**, 738.

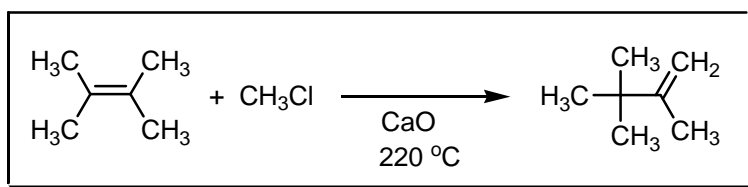
4) L.J. Andrews; R.M. Kiefer, *J. Am. Chem. Soc.*, 1953, **75**, 3547.

5) E.A. Braude; E.A. Evans, *J. Chem. Soc.*, 1955, 3332.

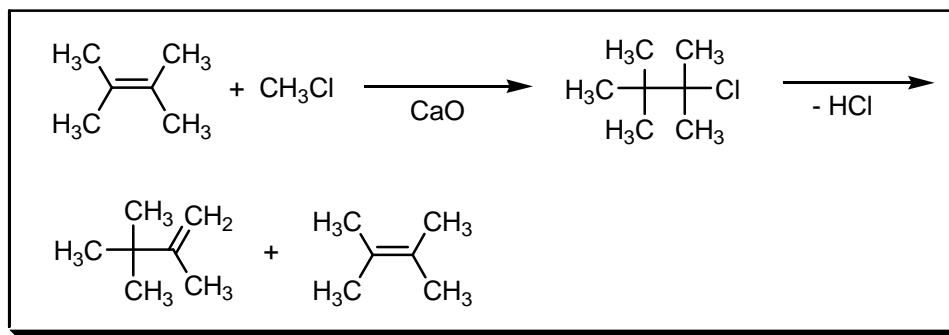
## COMMENTS :

## ELTEKOFF METHYLATION

### EXAMPLE :



### MECHANISM :



### NOTES :

Olefins when treated with methyl halide in the presence of catalysts ( $\text{CaO}$  or  $\text{PbO}$ ) yield a complex mixture of methylated olefins.

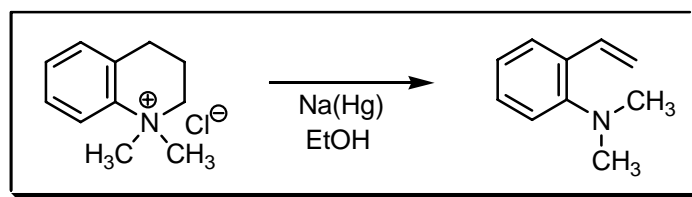
### REFERENCES :

- 1) A. Eltekoff, *J. Russ. Physik. Chem. Ges.*, 1878, **10**, 86.
- 2) A. Eltekoff, *J. Russ. Physik. Chem. Ges.*, 1878, **11**, 412.
- 3) V.A. Miller; W.G. Lovell, *Ind. Eng. Chem.*, 1948, **40**, 138.

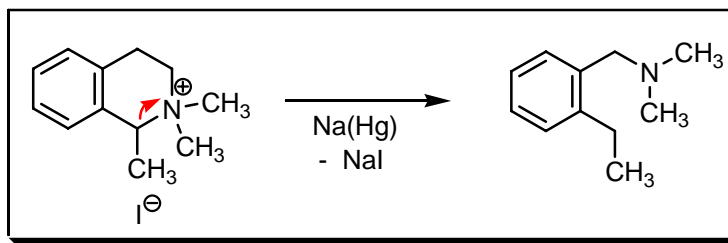
### COMMENTS :

## EMDE DEGRADATION

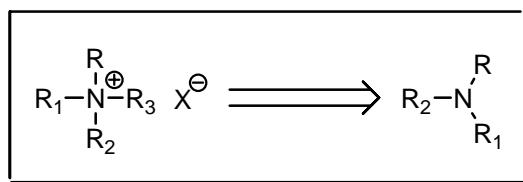
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

A modification of the **Hofmann** degradation which involves treating an alcoholic or aqueous solution of a quaternary ammonium halide with sodium amalgam. The method can be successful where the **Hofmann** method fails, but cannot be used for the cleavage of ammonium salts with four saturated alkyl substituents. Photochemical **Emde** reactions are known. See also the **von Braun** amide and **Hofmann** degradation reactions.

## REFERENCES :

**March** : 446

**Smith – March** : 530

**Houben – Weyl**: 11/1, 973; **E7b**, 202

**Org. React.** : 7, 143, 278

1) H. Emde, *Ber. Dtsch. Chem. Ges.*, 1909, **42**, 2590.

2) H. Emde, *Liebigs Ann. Chem.*, 1912, **391**, 88.

3) H. Emde, *Helv. Chim. Acta*, 1932, **15**, 1330.

4) A.J. Birch, *J. Chem. Soc., Quat. Rev.*, 1950, **4**, 78.

5) J.G. Cannon; P.R. Khonje; J.P. Long, *J. Med. Chem.*, 1975, **18**, 110.

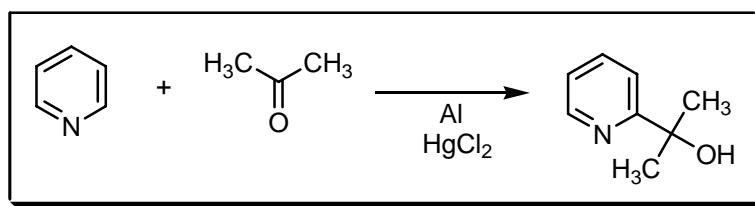
6) V. Partali; S. Jolidon; H.J. Hansen, *Helv. Chim. Acta*, 1985, **68**, 1952.

7) J. Lévy; M. Soufyane; C. Mirand; M.D. de Maindreville; D. Royer, *Tetrahedron: Asymmetry*, 1997, **8**, 4127.

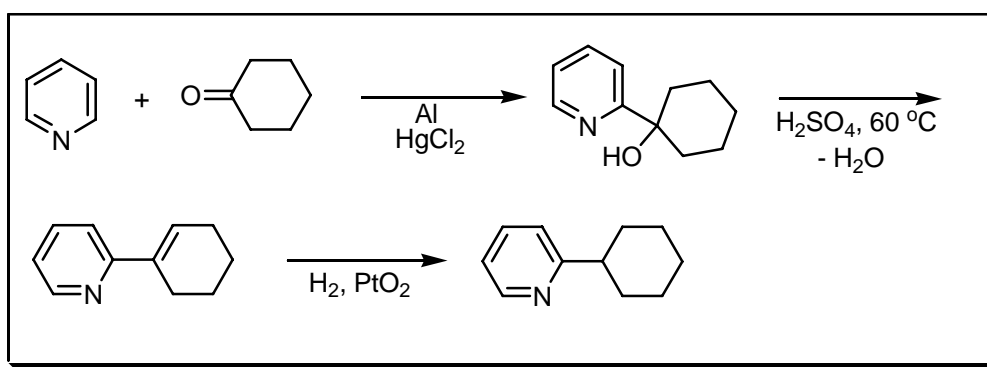
## COMMENTS :

## EMMERT – ASENDORF REACTION

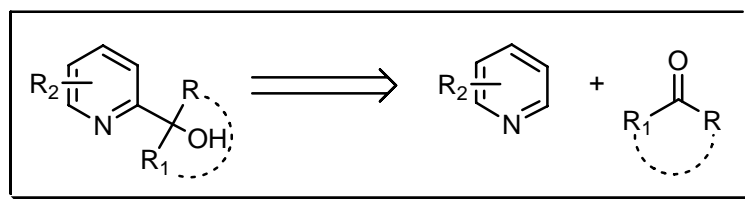
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

2-Pyridyldialkylcarbinols are prepared by the condensation of aldehydes or ketones with pyridine or its homologues in the presence of aluminium or magnesium, mercuric chloride and iodine. Small amounts of the 4-pyridyl compound are also formed. Besides open chain aliphatic and aromatic ketones, cyclic ketones can also be used. See also **Comins** and **Friedel – Crafts** reactions.

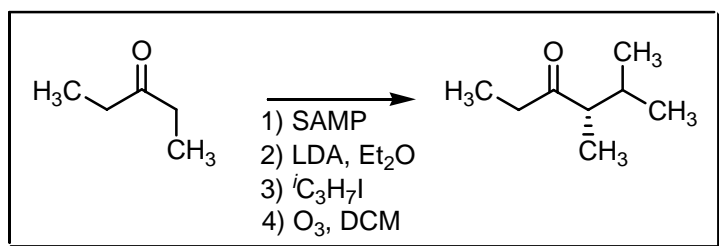
### REFERENCES :

- 1) B. Emmert; E. Asendorf, *Ber. Dtsch. Chem. Ges.*, 1939, **72A**, 1188.
- 2) B. Emmert; E. Pirot, *Ber. Dtsch. Chem. Ges.*, 1941, **74**, 714.
- 3) G.B. Bachmann; M. Hamer; E. Dunning; R.M. Schisla, *J. Org. Chem.*, 1957, **22**, 1296.
- 4) C.E. Crawforth; C.A. Russell; O. Meth-Cohn, *J. Chem. Soc., Chem. Commun.*, 1970, 1406.
- 5) R. Tschesche; W. Führer, *Chem. Ber.*, 1978, **111**, 3502.

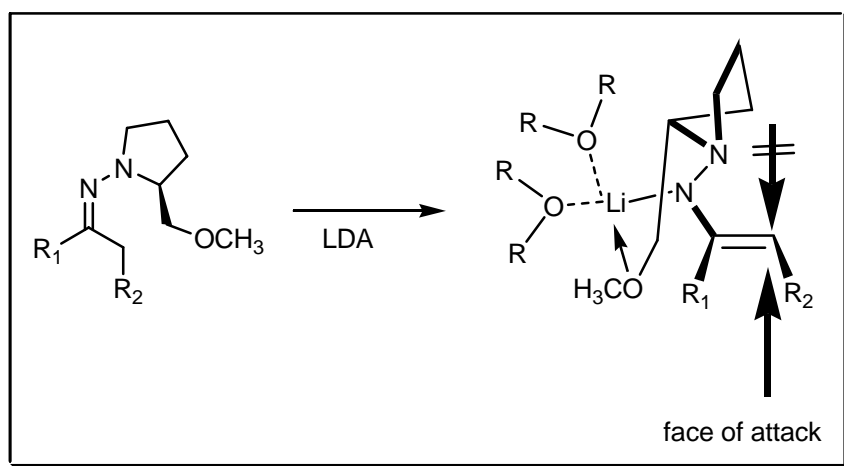
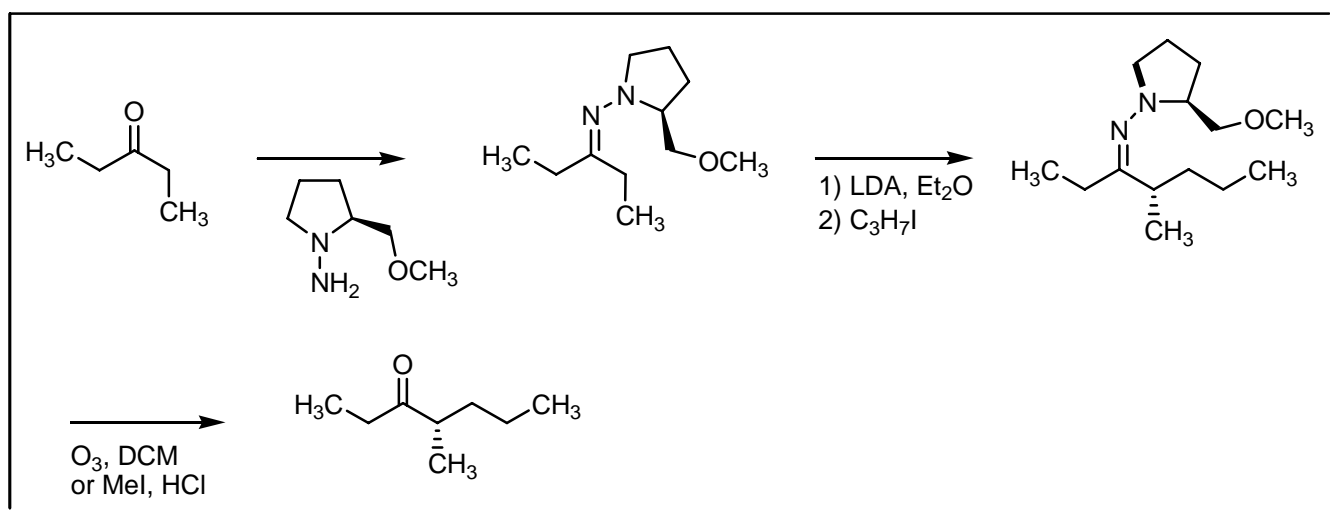
COMMENTS :

## ENDERS REACTION

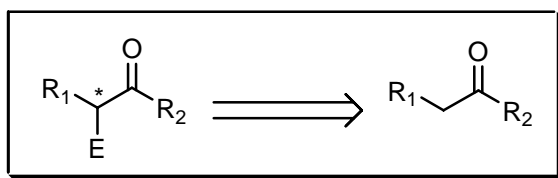
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The asymmetric electrophilic substitution of aldehydes and ketones via (S) or (R)-1-amino-2-methoxymethylpyrrolidine (SAMP or RAMP) hydrazones. Even more sterically hindered auxiliary have been prepared (SAMBO, RAMBO, SADP, SAEP, SAPP). See also **Evans** reaction.

## REFERENCES :

Smith : 945

Smith 2<sup>nd</sup> : 787

Org. Synth. : 65, 173, 183

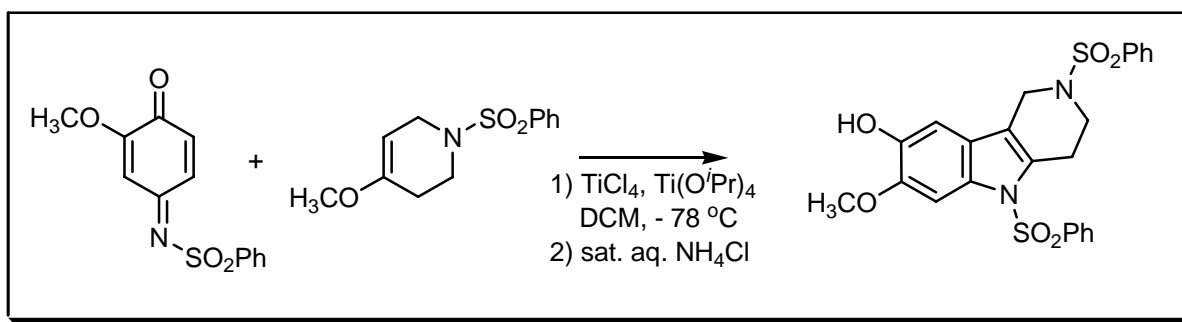
Org. Synth. Coll. Vol. : 8, 26, 403

- 1) D. Enders; H. Eichenauer, *Angew. Chem., Int. Ed. Engl.*, 1976, **15**, 549.
- 2) D. Enders; H. Eichenauer; U. Baus; H. Schubert; K.A.M. Kremer, *Tetrahedron*, 1984, **40**, 1345.
- 3) D. Enders; P. Fey; H. Kipphardt, *Org. Prep. Proced. Int.*, 1985, **17**, 1.
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- 6) D. Enders; L. Wortmann; R. Peters, *Acc. Chem. Res.*, 2000, **33**, 157.
- 7) D. Enders; K. Funabiki, *Org. Lett.*, 2001, **3**, 1575.
- 8) A. Job; C.F. Janeck; W. Bettray; R. Peters; D. Enders, *Tetrahedron*, 2002, **58**, 2253.

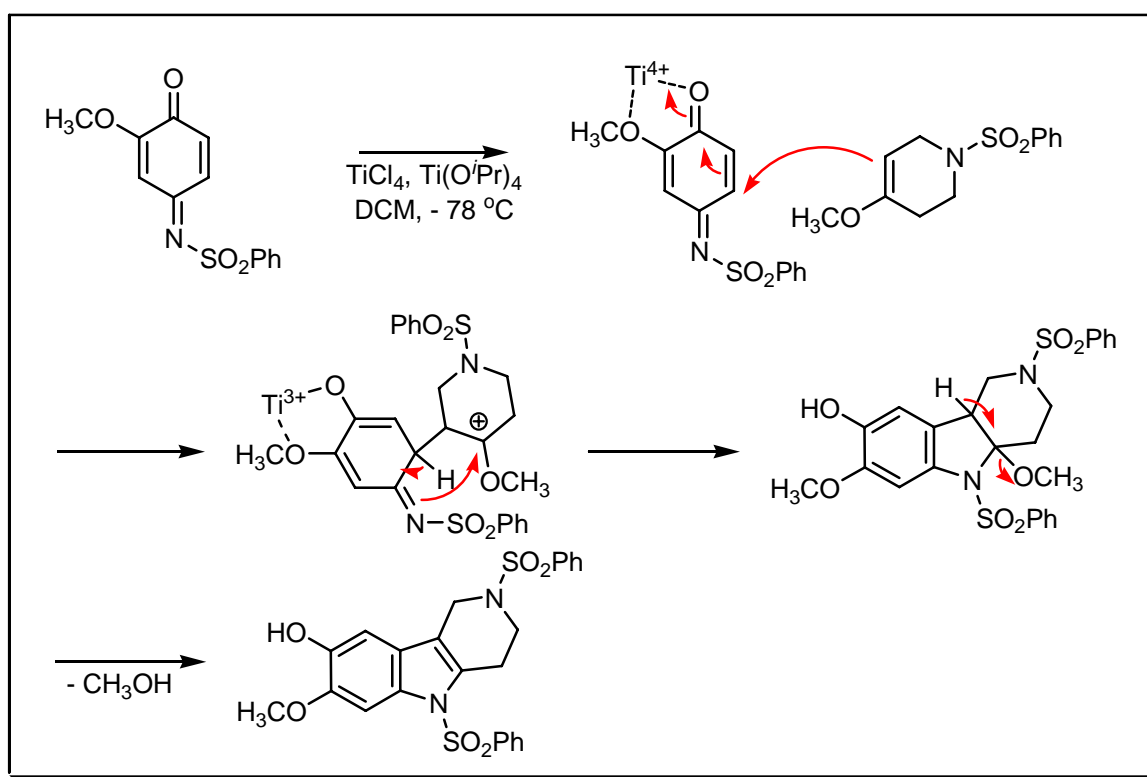
## COMMENTS :

## ENGLER INDOLE SYNTHESIS

### EXAMPLE :



### MECHANISM :





## NOTES :

2-Alkoxy-4-(*N*-phenylsulfonyl)imino-1,4-benzoquinones react with allyl-silane or stannanes, enol ethers, styrenes and simple  $\pi$ -systems in the presence of a regioselective Lewis acid. If  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  is used benzofurans are obtained. However when  $\text{TiCl}_4$  is used indoles and dihydro indoles are obtained. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

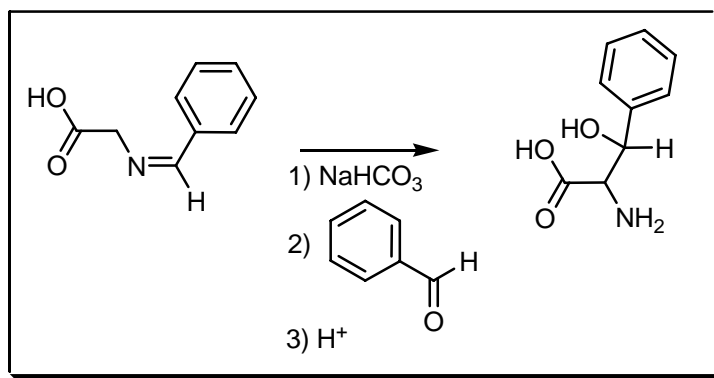
## REFERENCES :

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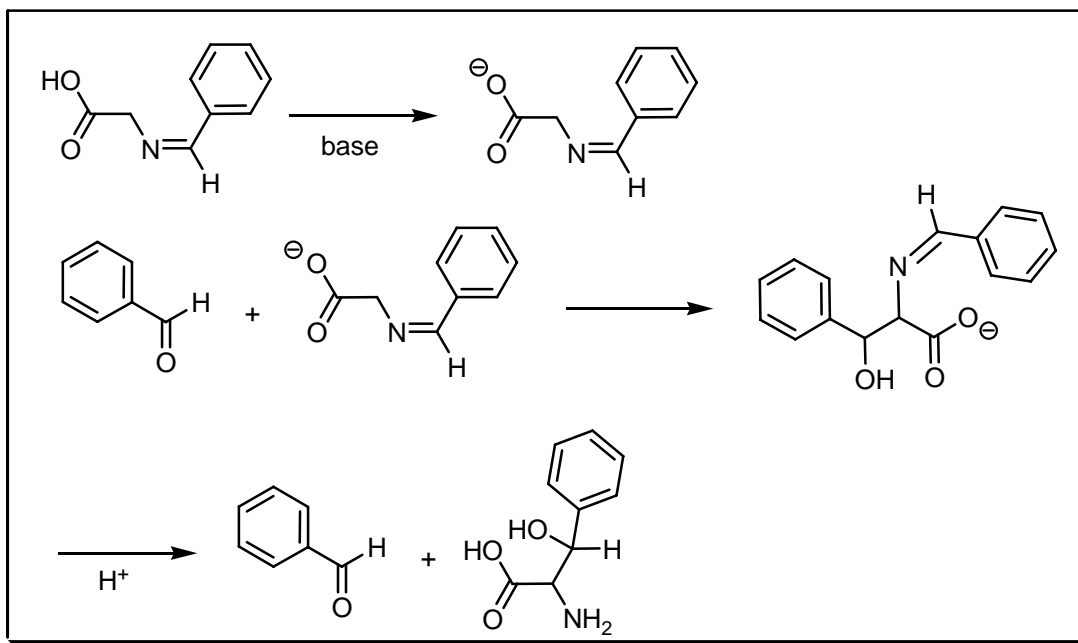
## COMMENTS :

## ERLENMEYER – FRÜSTÜCK SYNTHESIS

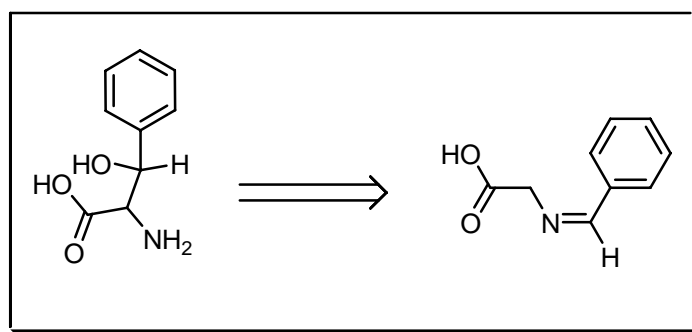
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The formation of phenyl serine by aldol addition of benzaldehyde and benzylideneglycine in weak alkaline solution followed by acidic hydrolysis. See also **Erlenmeyer – Plöchl** reaction.

## REFERENCES :

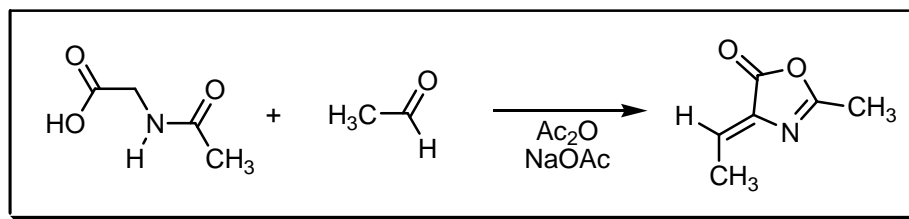
Houben – Weyl : 11/2, 427; E5, 583

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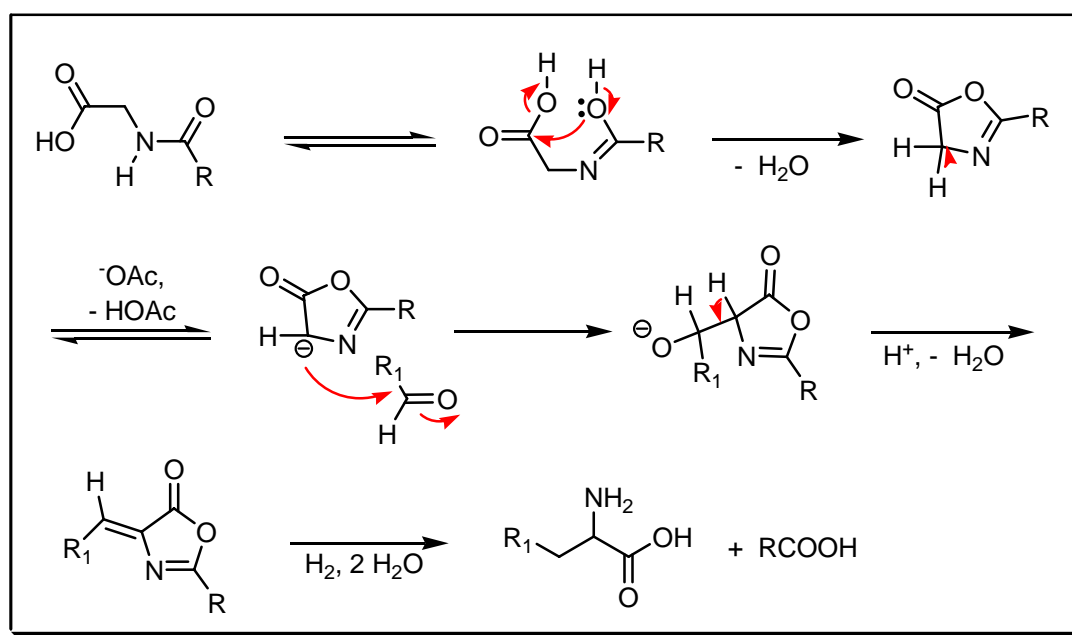
COMMENTS :

## ERLENMEYER – PLÖCHL AZLACTONE SYNTHESIS

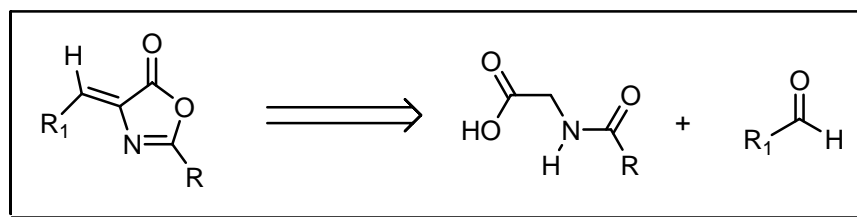
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

Saturated azlactones are obtained by the action of acetic anhydride on  $\alpha$ -acylamino acids. Unsaturated azlactones are obtained by the condensation of an aldehyde with an  $\alpha$ -acylglycine in the presence of acetic anhydride and usually sodium acetate. Reduction and hydrolysis of these compounds yields amino acids. Ketones like cyclohexanone can also be employed. The reaction is one of the key steps in Monsanto's *L*-DOPA synthesis. The reaction of an aldehyde with hippuric acid is often called the **Erlenmeyer** azlactone synthesis. See also **Bergmann** azlactone peptide synthesis, **Dakin** azlactone, **Dakin – West** and **Erlenmeyer – Früstück** reactions.

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## REFERENCES :

**Houben – Weyl** : **11/2**, 306, 373; **E5**, 406, 822

**Org. React.** : **1**, 231; **3**, 198

**Org. Synth.** : **19**, 1

**Org. Synth. Coll. Vol.** : **2**, 1

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- 1) J. Plöchl, *Ber. Dtsch. Chem. Ges.*, 1883, **16**, 2815.
  - 2) E. Erlenmeyer, jr., *Liebigs Ann. Chem.*, 1893, **275**, 1.
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  - 4) R.K. Griffith; H.J. Harwood, *J. Org. Chem.*, 1964, **29**, 2658.
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  - 7) K.L. Bailey; T.F. Molinski, *J. Org. Chem.*, 1999, **64**, 2500.
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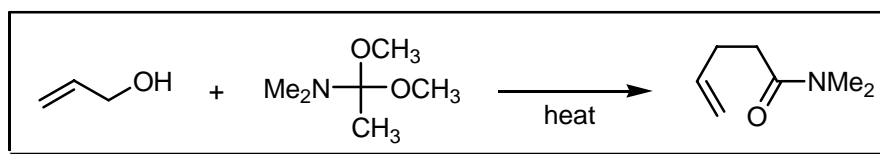
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## COMMENTS :

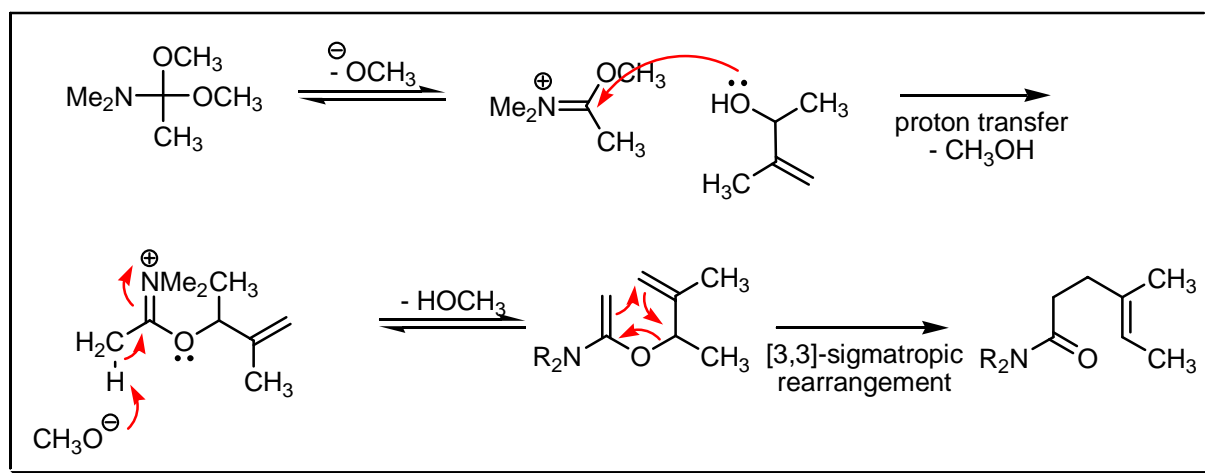
## ESCHENMOSER – MEERWEIN – CLAISEN REARRANGEMENT

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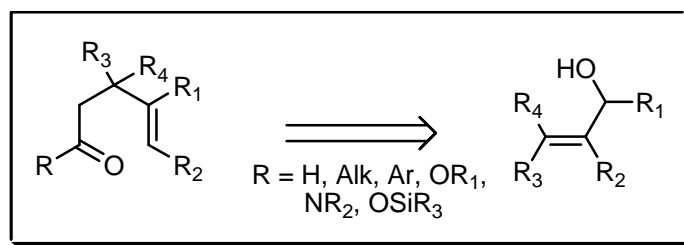
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The **Claisen** rearrangement has been adapted in recent years to provide a viable synthetic sequence for the preparation of functional groups other than aldehydes and ketones. Ester and amide syntheses have been reported which proceed through the **Claisen** intermediate. The **Claisen** rearrangement has also been used to generate transubstituted double bonds stereoselectively, angularly-functionalised derivatives, substituted cyclohexenes, acids, and furans. The rearrangement proceeds with very high *E*-selectivity due to the destabilising 1,3-diaxial interactions in the transition state that would give the *Z*-isomer. See also **Belluš – Claisen** rearrangement, **Carroll (Kimel – Cope)**, **Claisen (Claisen – Ireland)** rearrangement, **Cope**, **Ficini – Claisen**, **Johnson – Claisen**, **Marbet – Saucy** and **Overman** rearrangement reactions.

## REFERENCES :

Smith : 1243

Smith 2<sup>nd</sup> : 1025

Houben – Weyl : E10b2, 225

Org. Synth. : 54, 71, 77

Org. Synth. Coll. Vol. : 6, 298, 491

- 1) A. Eschenmoser; K. Steen; D. Felix; A.E. Wick, *Helv. Chim. Acta*, 1964, **47**, 2425.
- 2) W. Fleischhacker; B. Richter, *Monatsh. Chem.*, 1992, **123**, 837.
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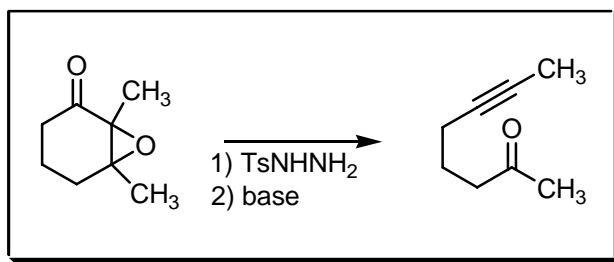
**COMMENTS :**

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**ESCHENMOSER – TANABE RING CLEAVAGE**

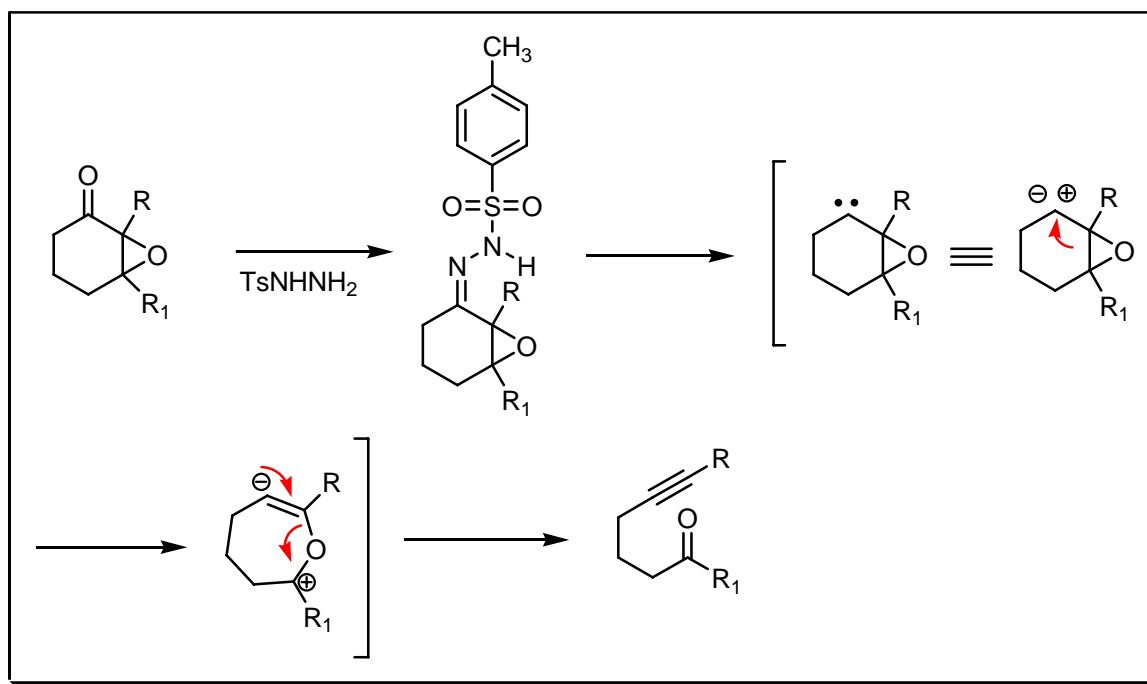
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**EXAMPLE :**

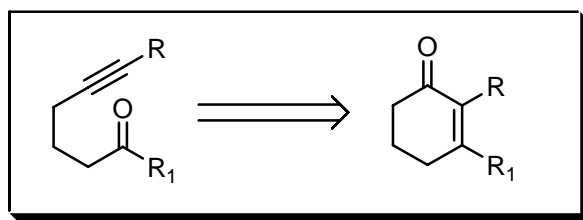


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**MECHANISM :**



## DISCONNECTION :



## NOTES :

The cleavage of  $\alpha,\beta$ -epoxy ketones to an acetylene and a carbonyl compound *via* a sulfonylhydrazone and a base. The *N*-aminoaziridine version of the  $\alpha,\beta$ -epoxyketone to alkynone fragmentation is a possible alternative in situations where the simple tosylhydrazone version fails. The tosylhydrazone method often gives good yields at low reaction temperatures, but it tends to be unsuccessful with the epoxides of acyclic enones or those not fully substituted at the  $\beta$ -carbon atom. Basically the reaction is a seven-centre **Grob**-type fragmentation. See also **Grob** fragmentation and **Wharton** reaction.

## REFERENCES :

March : 1037

Smith – March : 1347

Smith : 600

Smith 2<sup>nd</sup> : 516

Org. Synth. : 55, 52

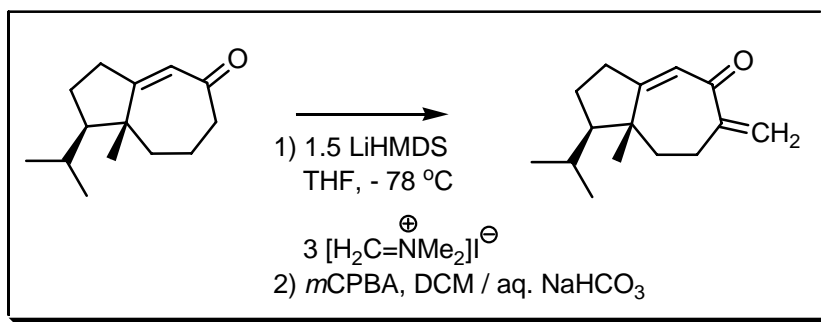
Org. Synth. Coll. Vol. : 6, 679

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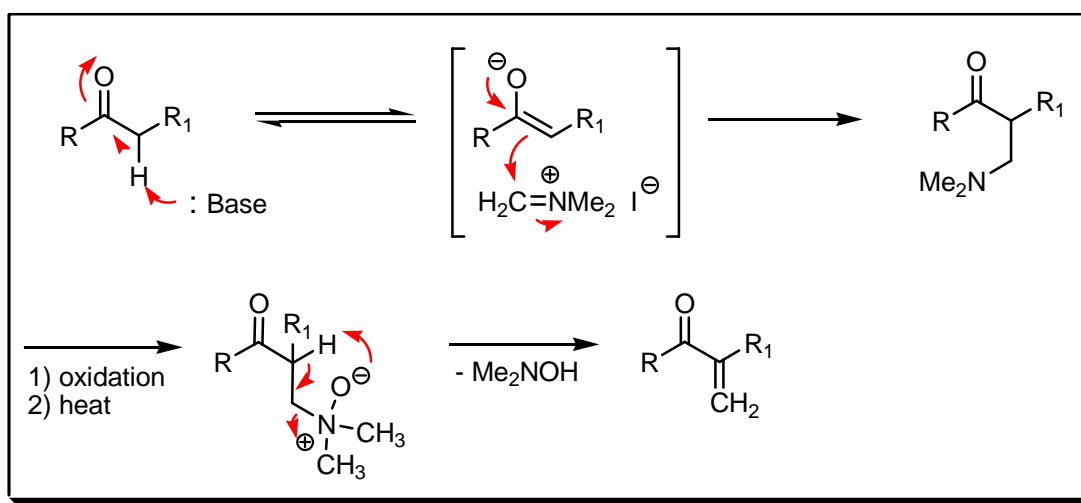
## COMMENTS :

## ESCHENMOSER METHENYLATION

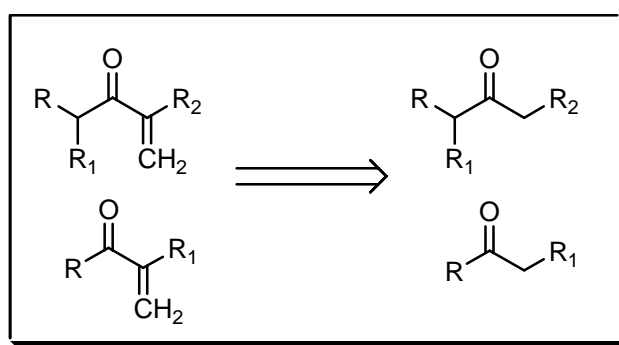
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The introduction of a (dimethylamino)methyl group into the  $\alpha$ -position of a carbonyl group using dimethyl(methylene)ammonium iodide.



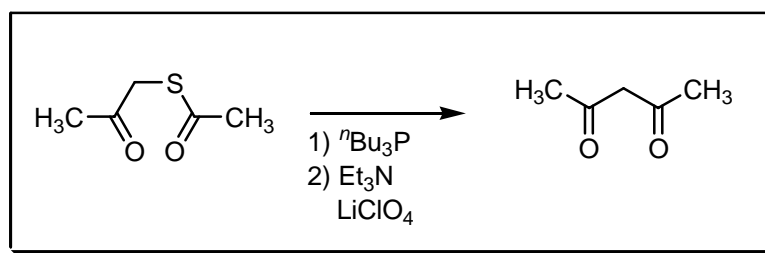
## REFERENCES :

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## COMMENTS :

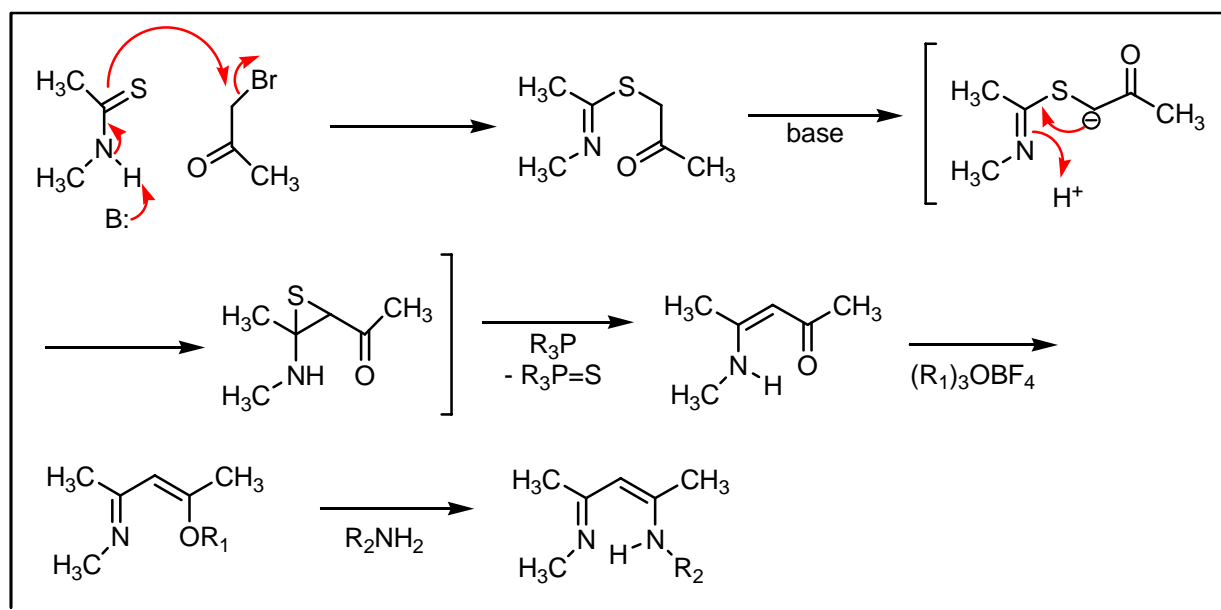
## ESCHENMOSER SULFIDE CONTRACTION

### EXAMPLE :

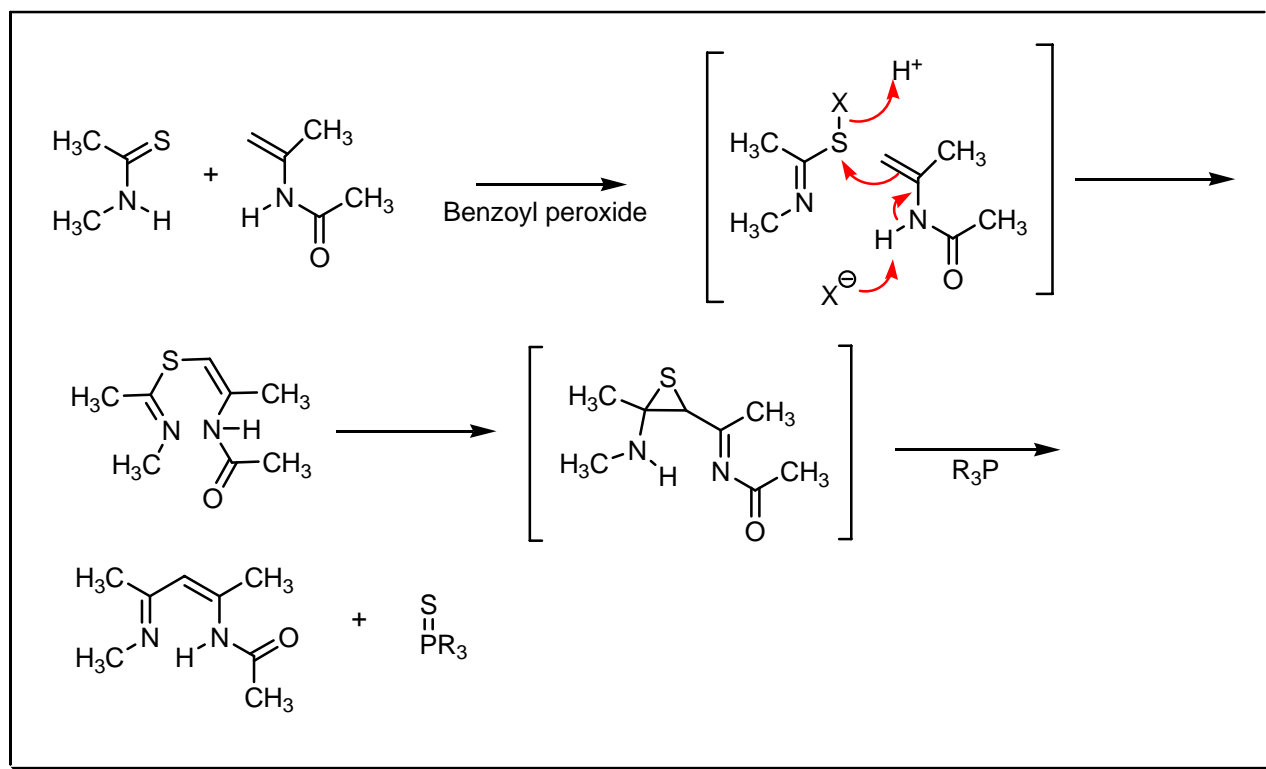


### MECHANISM :

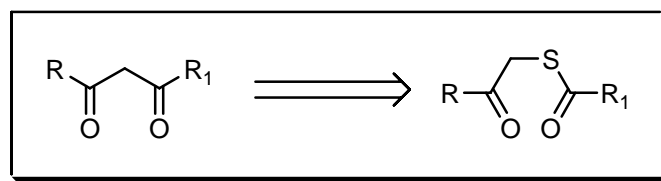
#### Alkylative :



## Oxidative :



## DISCONNECTION :



## NOTES :

In both versions, one of the two coupling partners is a thioamide. In the alkylative **Eschenmoser** sulfide contraction the nucleophilic sulfur atom of the thioamide initiates an  $\text{S}_{\text{N}}2$  displacement of a suitable leaving group to give the thioiminoester. In the presence of an enolising base, the nucleophilic character of the carbon atom situated between the sulfur atom and the carbonyl group is unveiled and it obligingly attacks the proximal electrophilic thioiminoester carbon. The formation of an episulfide which subsequently collapses in the presence of a phosphine or a phosphite thiophile affords a vinylogous amide. In the oxidative **Eschenmoser** sulfide contraction the thioamide is oxidised by benzoylperoxide to give either the O-benzoate of the thiolactam-S-oxide or a symmetrical disulfide. The sulfur atom of the thioamide behaves as an electrophile. The nucleophilic enamide attacks the sulfur atom affording a sulfur-bridged intermediate. The vinylogous amidine is obtained after the action of a phosphine on the episulfide.

## REFERENCES :

March : 1049

Org. Synth. : 55, 127

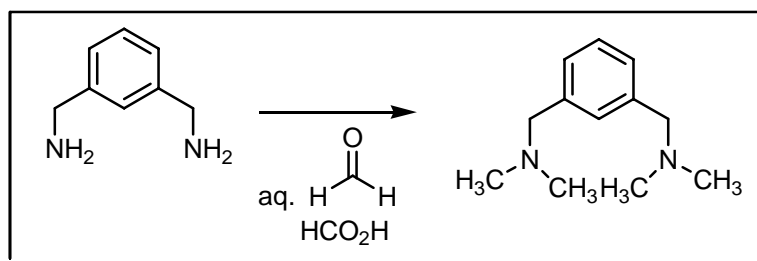
Org. Synth. Coll. Vol. : 6, 776

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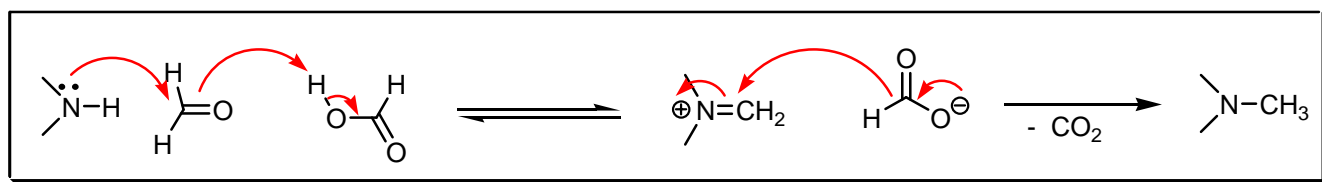
## COMMENTS :

## ESCHWEILER – CLARKE REACTION

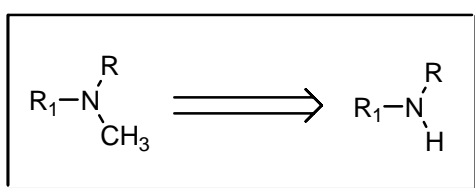
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

A method for the methylation of primary and secondary amines in which the amine is heated with formaldehyde and an excess of formic acid (hydride source) at 100 °C (microwave-enhanced methylation reactions are also known.) See also **Foster – Decker**, **Leuckart – Wallach**, **Pictet – Spengler** and **Plöchl** reactions.

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## REFERENCES :

**March** : 899

**Smith – March** : 1188

**Houben – Weyl** : **E16c**, 848

**Org. React.** : **5**, 301

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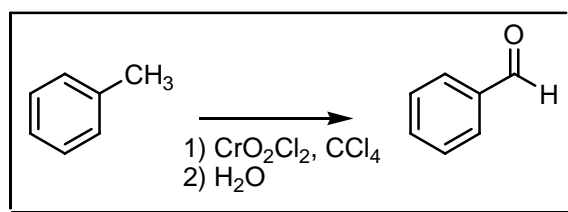
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  - 2) H.T. Clarke; H.B. Gillespie; S.Z. Weisshaus, *J. Am. Chem. Soc.*, 1933, **55**, 4571.
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## COMMENTS :

## ÉTARD REACTION

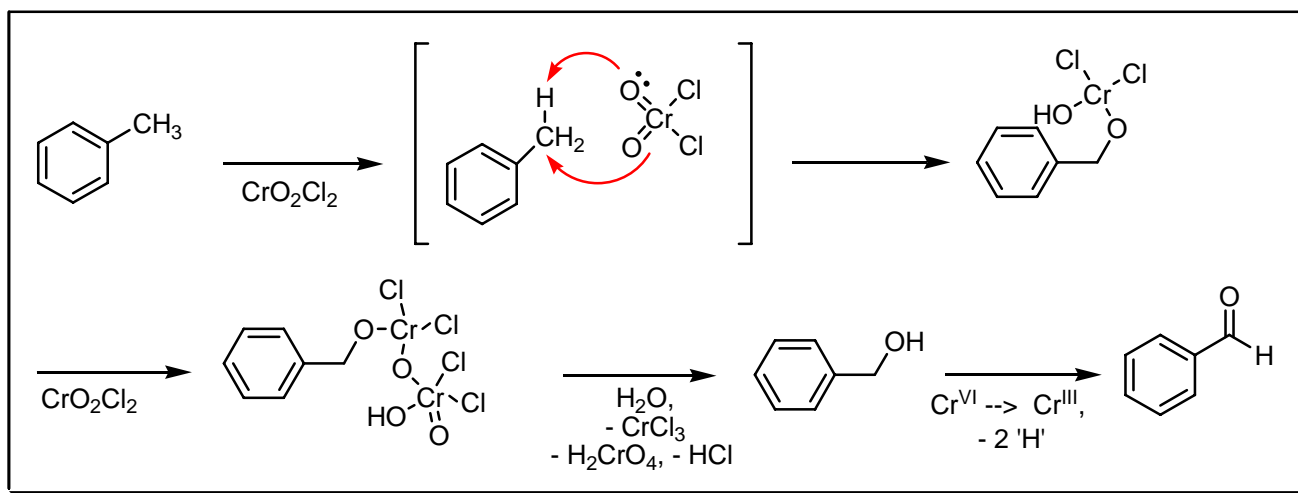
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### EXAMPLE :

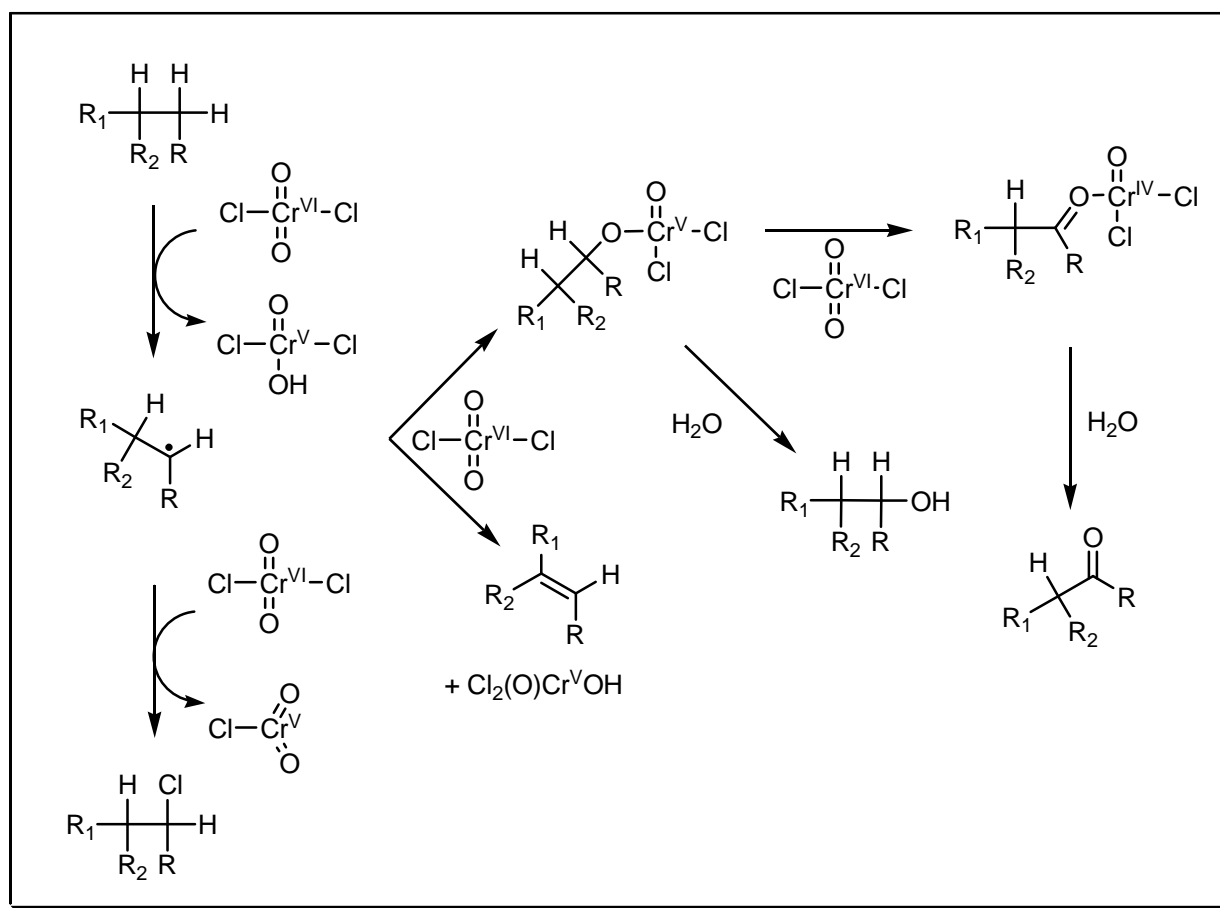


# MECHANISM :

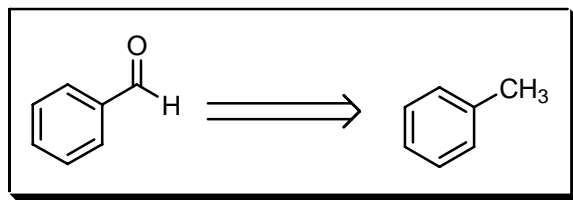
## Nenitzescu :



## Cook :



## DISCONNECTION :



## NOTES :

The oxidation of side-chain aryl or cycloalkyl methyl groups to aldehydes using chromyl chloride. There is still a major debate over the mechanism of the oxidation, the proposed mechanisms by **Nenitzescu et al.** and **Cook et al.** are presented here.

## REFERENCES :

**March** : 1190

**Smith – March** : 1534

**Smith** : 316

**Smith 2<sup>nd</sup>** : 276

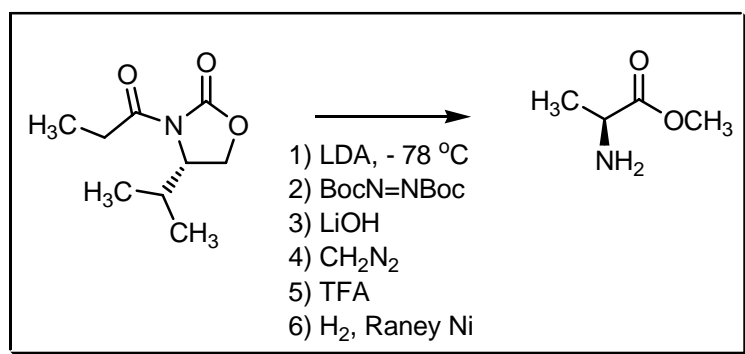
**Houben – Weyl** : 7/1, 143; **E3**, 242

- 1) A. Étard, *C.R. Séances Acad. Sci.*, 1877, **84**, 127.
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- 3) L.N. Ferguson, *Chem. Rev.*, 1946, **38**, 237.
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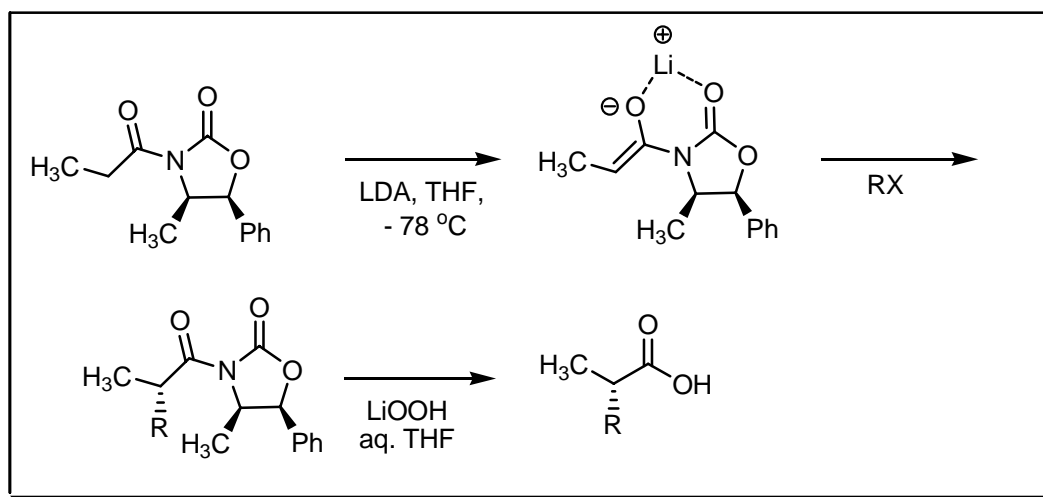
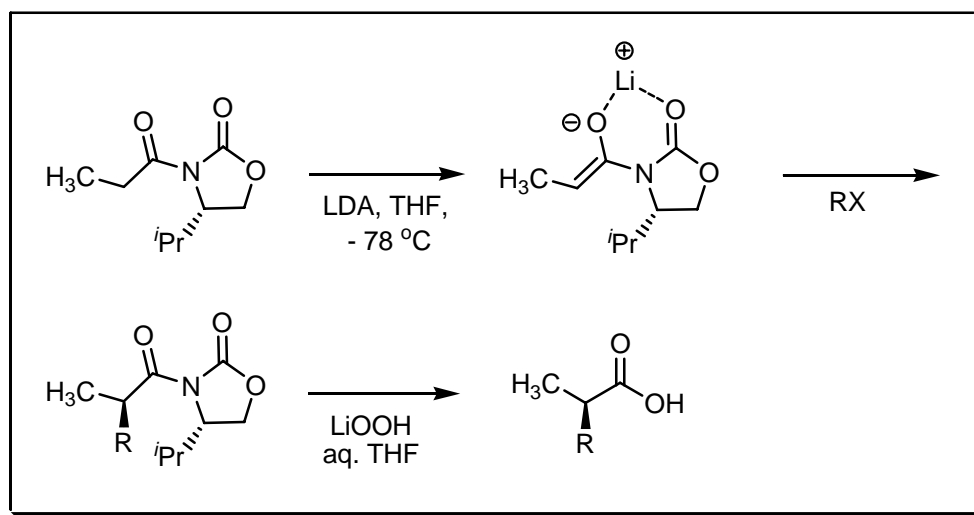
## COMMENTS :

## EVANS REACTION

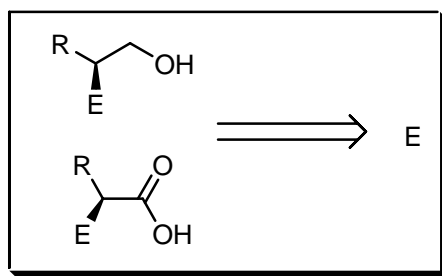
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



Product	Reagents
RCOOH	KOH, LiOH, LiOH/H <sub>2</sub> O
RCH <sub>2</sub> OH	LiBH <sub>4</sub> , LiAlH <sub>4</sub>
RCOOR <sub>1</sub>	LiOR, NaOR, BrMgOR, Ti(OR) <sub>4</sub>
RCOSR	LiSR, BnSAlMe <sub>3</sub> Li
RCONR <sub>2</sub>	N <sub>2</sub> H <sub>4</sub> , n-amylONO, NH <sub>4</sub> Cl, Cp <sub>2</sub> Ti(Zr)Cl <sub>2</sub>
Weinreb amide	MeONHMe·HCl, AlMe <sub>3</sub>

## NOTES :

The use of a temporary template for chiral induction. There are two auxiliaries based on *L*-valine and norephedrine which are of opposite absolute stereochemistry at the inducing group (<sup>i</sup>Pr and CH<sub>3</sub>). Almost any acyl chloride can be attached *via* the nitrogen atom. Chelation between the two carbonyl oxygens fixes the conformation of the auxiliary and alkylation then occurs from the least hindered face. The enolate geometry is always *Z*-(O). Cleavage can be accomplished by hydrolysis, reduction, esterification or amidation. The so-called **non-Evans** (still *syn*) products can be obtained by using a titanium enolate. In this case the oxazolidinone carbonyl is also chelated. See also **Enders** and **Mukaiyama** reactions.

## REFERENCES :

Smith – March : 1221

Smith : 1172

Smith 2<sup>nd</sup> : 972

Org. Synth. : 68, 77, 83; 80, 57

Org. Synth. Coll. Vol. : 8, 339, 528

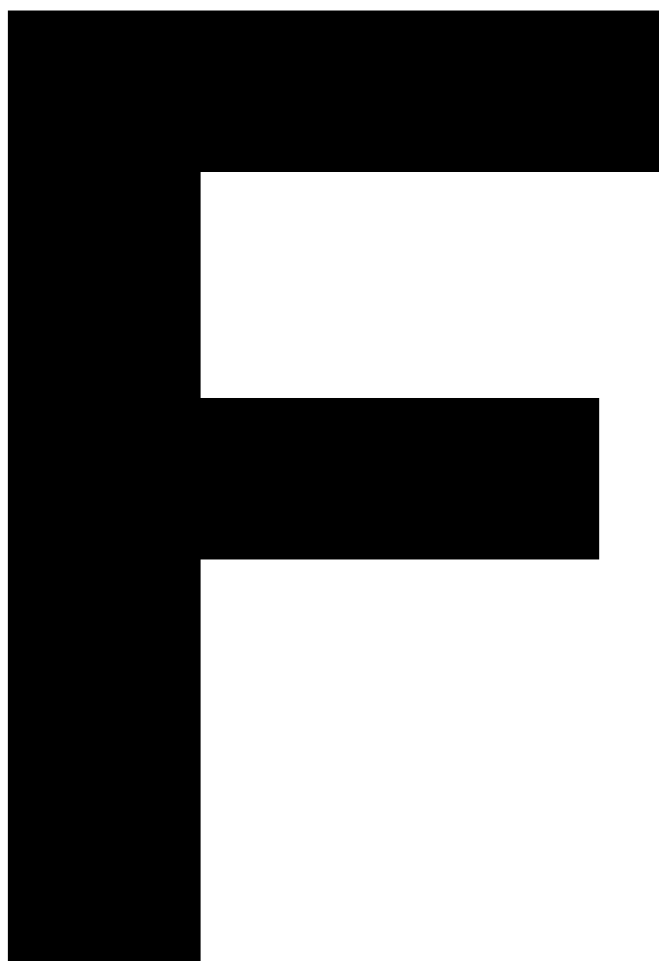
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**COMMENTS :**



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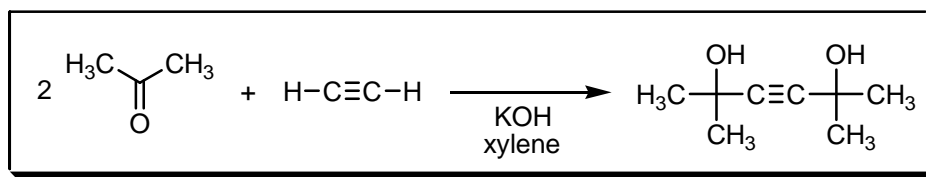
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**W**

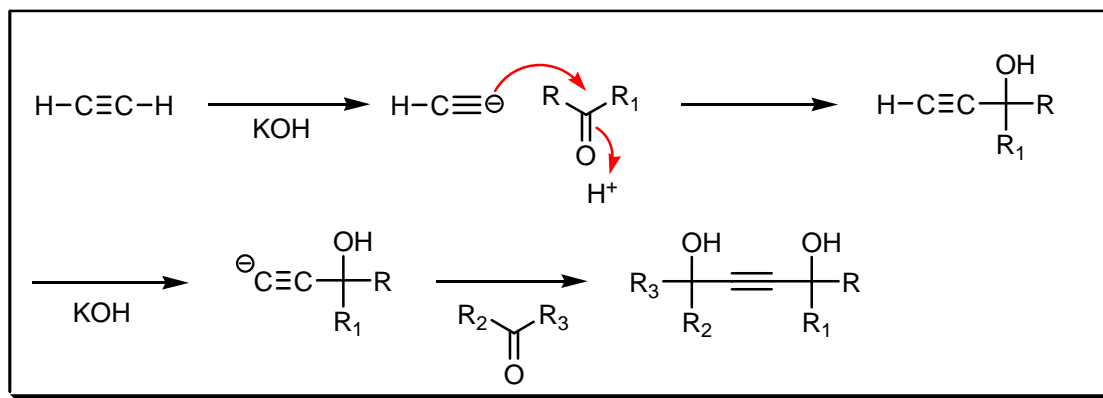
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## FAVORSKII – BABAYAN SYNTHESIS

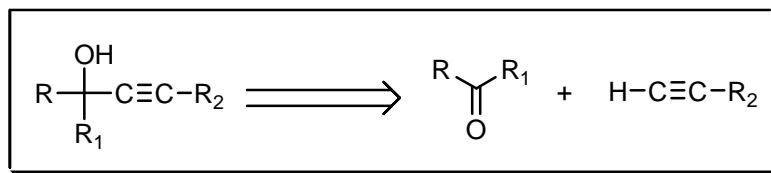
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The synthesis of acetylenic alcohols by addition of ketones with terminal acetylenic hydrocarbons in the presence of anhydrous potassium hydroxide and a solvent like THF, liquid ammonia, DMSO or xylene. Acetylenic  $\gamma$ -glycols may be obtained from acetylene. See also **Arens – van Dorp**, **Carroll (Kimel – Cope)** rearrangement, **Nef**, **Reppe** acetylene synthesis and **Whiting – Nayler** reactions.

### REFERENCES :

**March** : 948

**Smith – March** : 1225

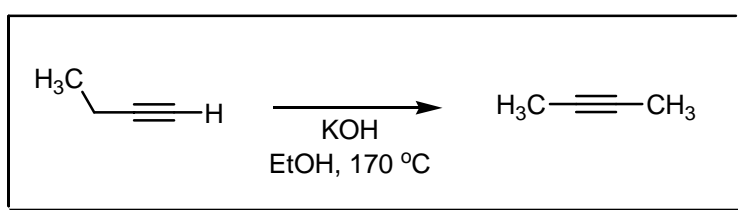
**Houben – Weyl** : E15, 1387

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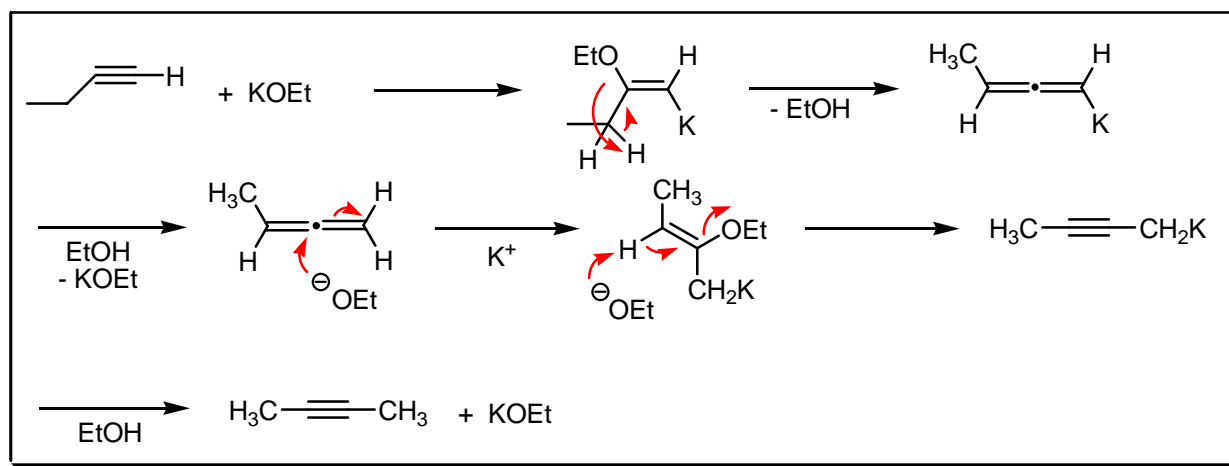
**COMMENTS :**

**FAVORSKII ACETYLENE REARRANGEMENT**

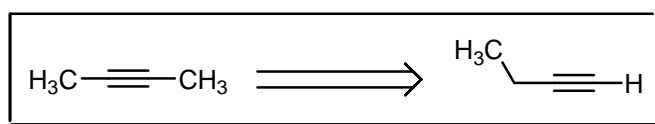
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

Alkyl substituted acetylenes rearrange by heating with ethanolic potassium hydroxide, e.g. *n*-propylacetylene gives ethyl methyl acetylene on treatment with ethanolic potassium hydroxide at about 170 °C.

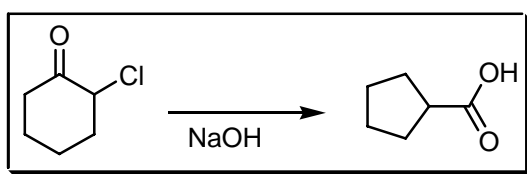
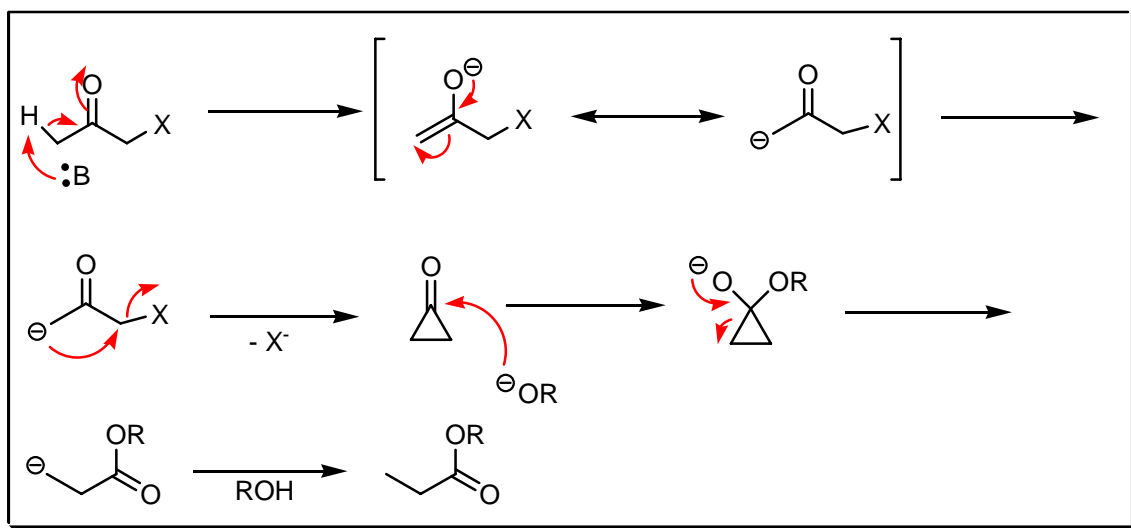
**REFERENCES :**

Houben – Weyl : 7/1, 227

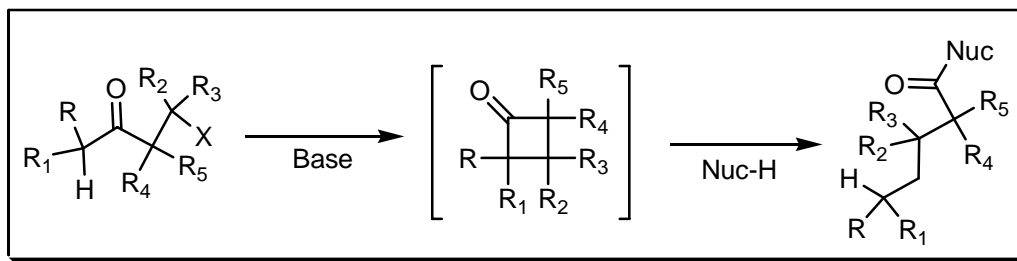
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A. Favorskii, *J. Prakt. Chem.*, 1888, **37**, 382.

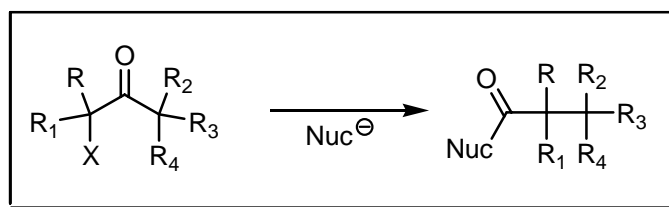
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**COMMENTS :****FAVORSKII REARRANGEMENT****EXAMPLE :****MECHANISM :**

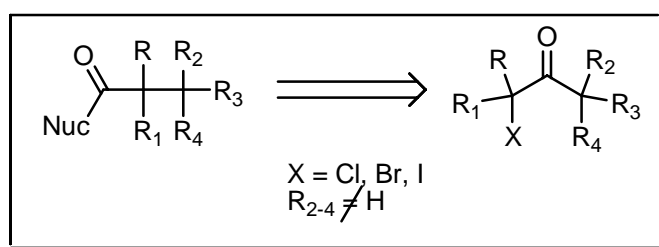
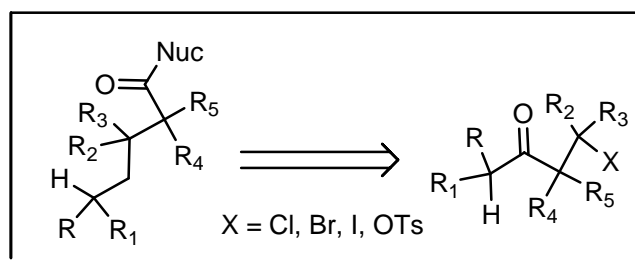
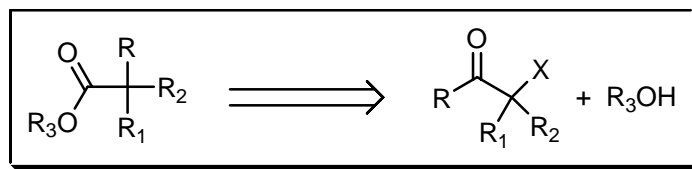
### Homo-Favorskii :



### Quasi-Favorskii :



### DISCONNECTION :



### NOTES :

$\alpha$ -Halogenoketones rearrange with loss of halogen by bases into carboxylic acids or their derivatives, with the same number of carbon atoms in the rearranged starting material. Depending on whether the base is hydroxide ion, alkoxide ion or amine, the product is an acid salt, an ester or an amide. The reaction is sometimes called the **Wallach** degradation, but the classical **Wallach** degradation is the rearrangement of certain terpene dibromoketones. Many of these products are of uncertain purity and structure. There are two important variants, the **homo-Favorskii** rearrangement and the **quasi-Favorskii** rearrangement. The first one takes place when  $\beta$ -halo ketones are treated

with base in the presence of a nucleophile, the second one takes place when the  $\alpha$ -halo ketone does not have any enolisable hydrogens.

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#### REFERENCES :

**March** : 1080

**Smith – March** : 1403

**Smith 2<sup>nd</sup>** : 802

**Houben – Weyl** : 4/2, 811; 8, 456; **E15**, 2862; **E16b**, 12

**Org. React.** : 11, 261

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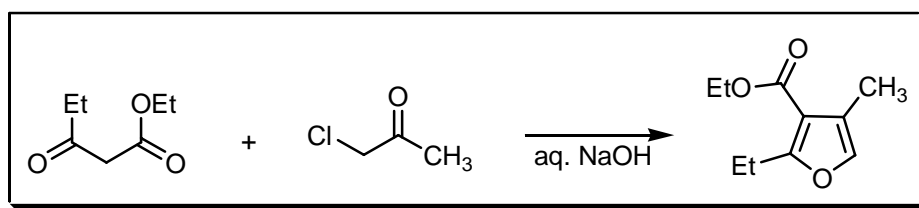
- 1) A. Favorskii; K. Desboud, *J. Prakt. Chem.*, 1895, **51**, 533.
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#### COMMENTS :

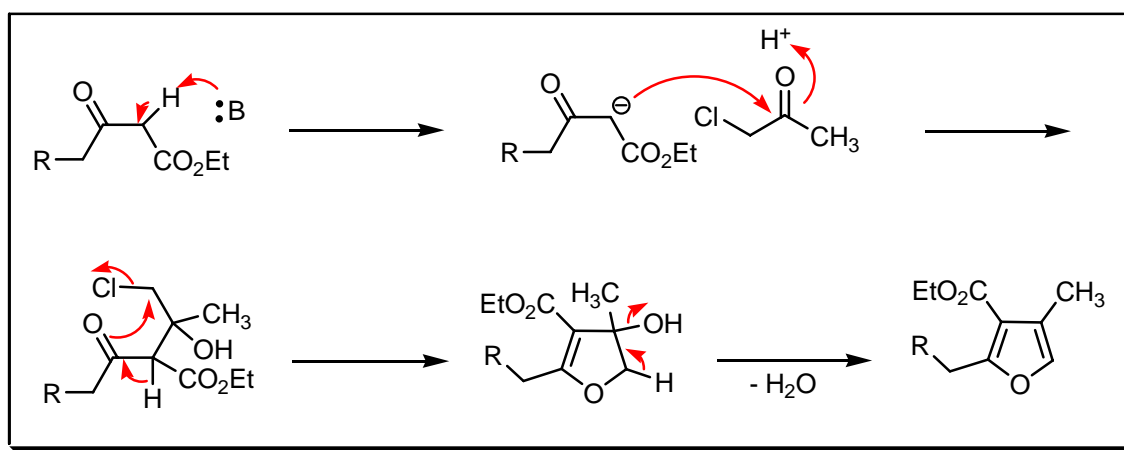


## FEIST – BÉNARY FURAN SYNTHESIS

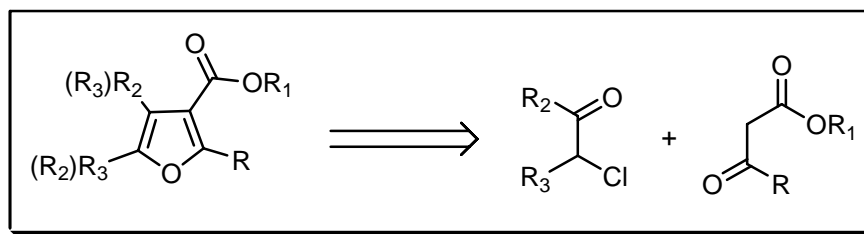
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This is an initial aldol condensation at the carbonyl carbon of an  $\alpha$ -halocarbonyl compound. *Intramolecular* displacement of the halide by the enolate oxygen atom gives ring-closure. The orientation of  $R_2$  and  $R_3$  depends if O- or C-alkylation takes place. When ammonia is used as condensing agent pyrrole derivatives are always obtained as secondary products. The chloroketone can be replaced by a 1,2-dichloro-ether, which decomposes in the presence of ammonia to form a monochloroketone or aldehyde. See also **Knorr** pyrrole reaction.

### REFERENCES :

Houben – Weyl : E6a, 51, 54, 64

Science of Synthesis : 9, 188; 10, 135

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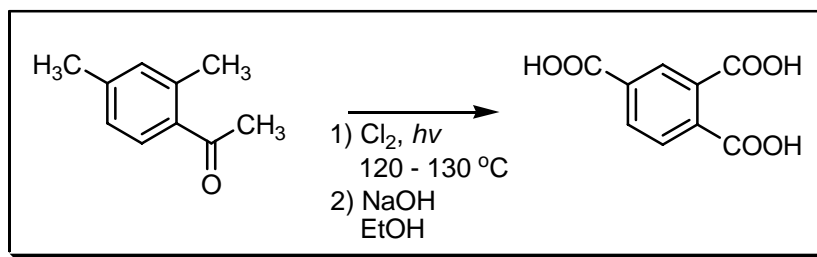
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**COMMENTS :**

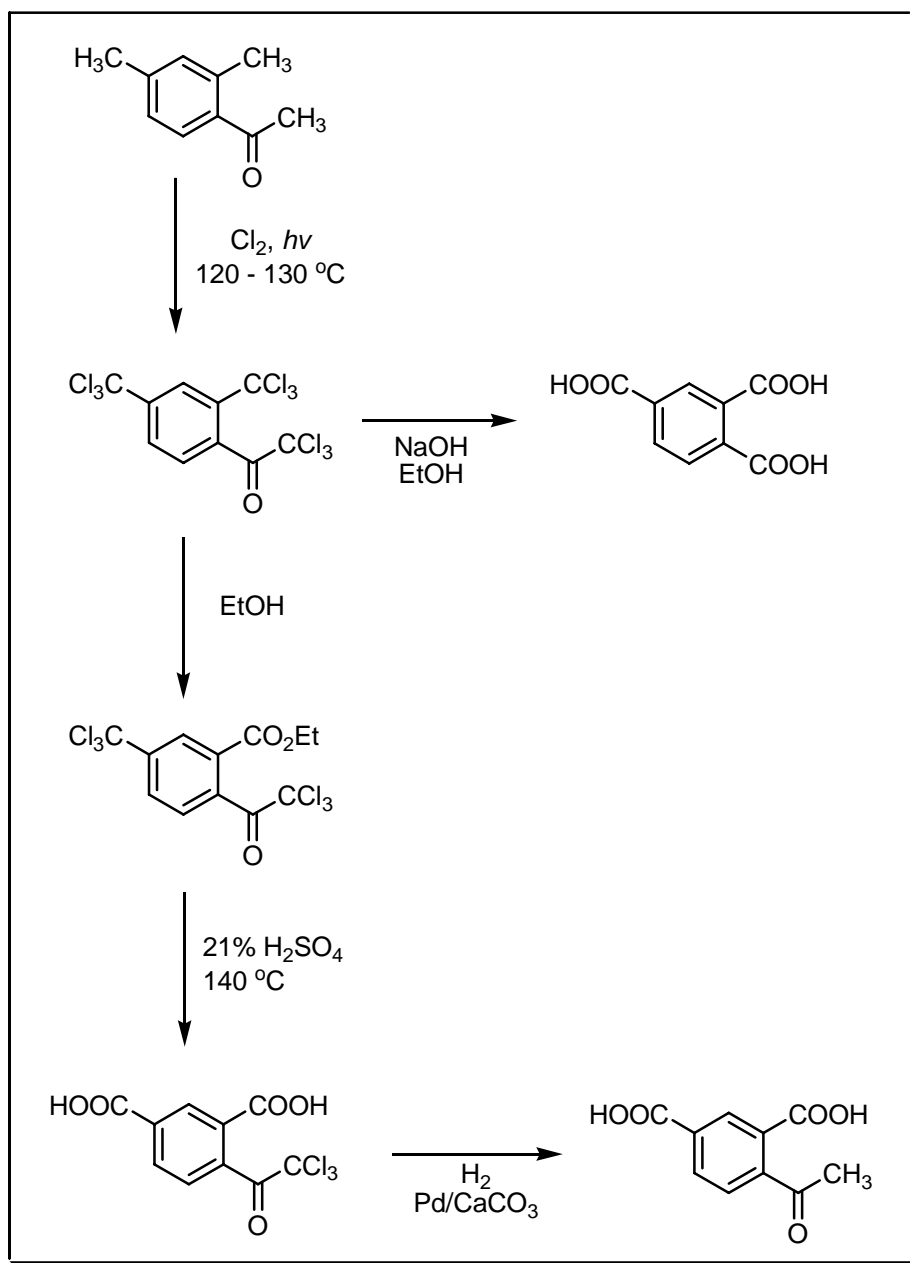
## FEIST CARBOXYLIC ACID SYNTHESIS

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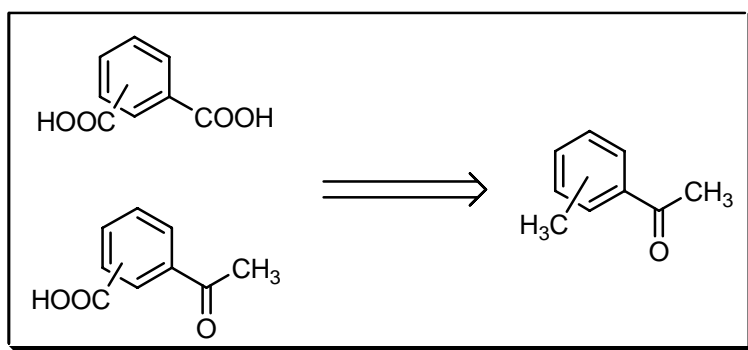
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**

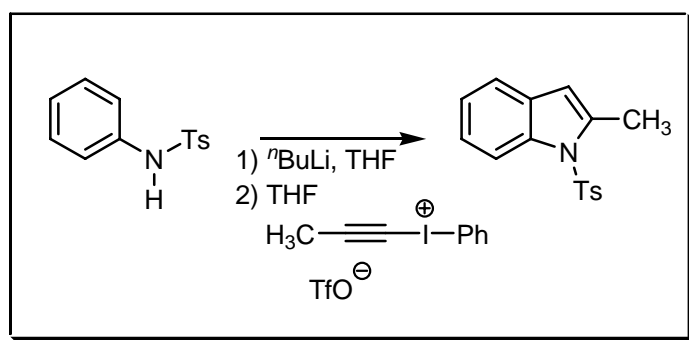
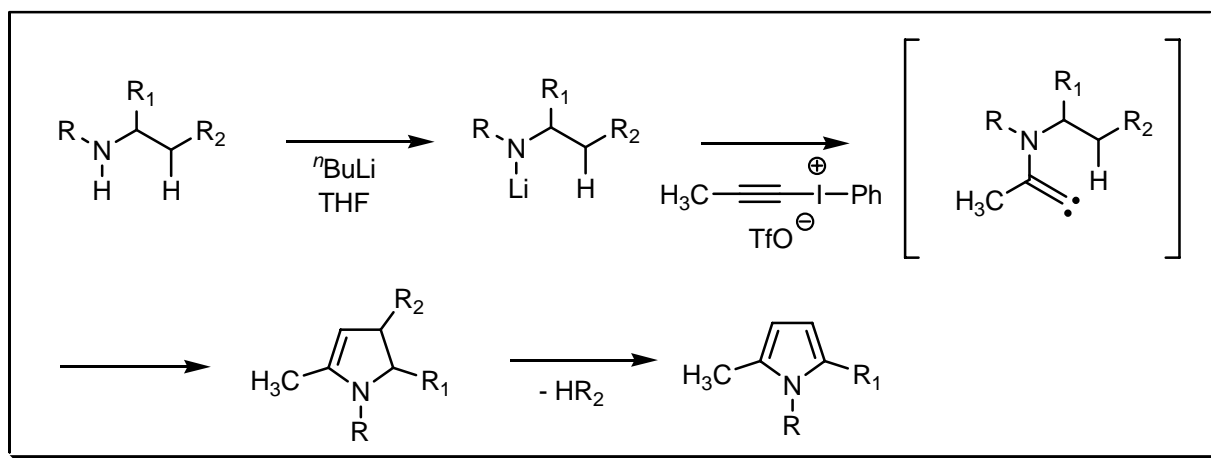


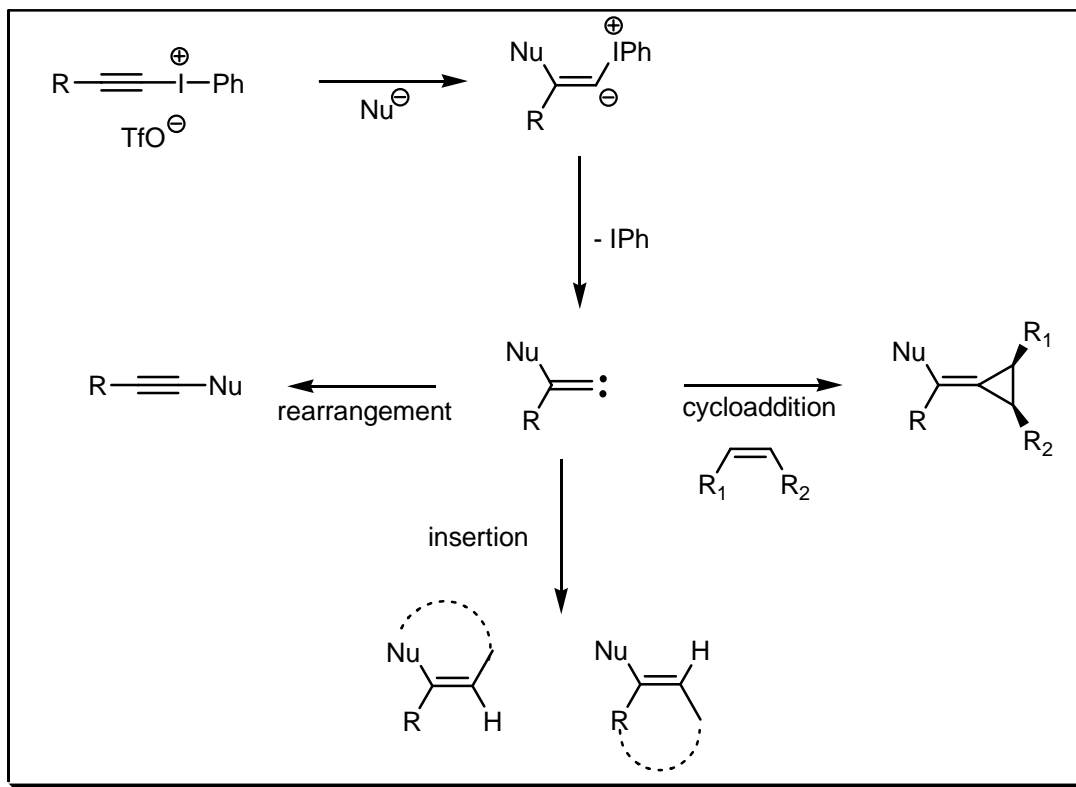
**NOTES :**

Benzene-polycarboxylic acids are prepared by chlorinating acetylpolymethylbenzenes at high temperatures and hydrolysing the chlorinated product. The acetyl group facilitates the chlorination of the methyl groups.

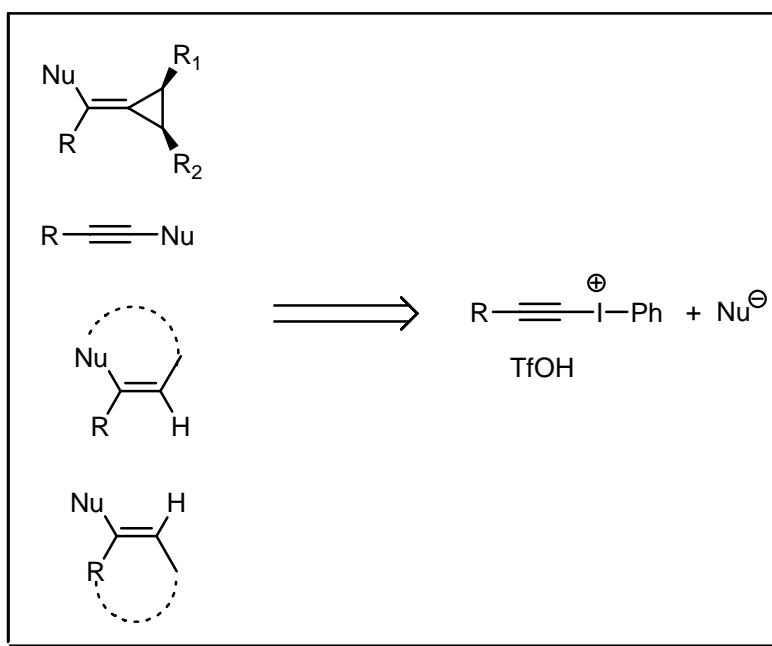
**REFERENCES :**

F. Feist, *Liebigs Ann. Chem.*, 1932, **496**, 99.

**COMMENTS :****FELDMAN INDOLE SYNTHESIS****EXAMPLE :****MECHANISM :**



#### DISCONNECTION :



#### NOTES :

Five-membered nitrogen-containing heterocycles are prepared by *inter*- or *intramolecular* [3 atom + 2 atom] combination of sulfonamide anions with alkynylidonium triflates *via* vinylidene carbene C-H insertion. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**,

**Smith, Sugawara** indole, **Sundberg, Thiele – Dimroth, Thyagarajan, Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender, Widman, Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

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#### REFERENCES :

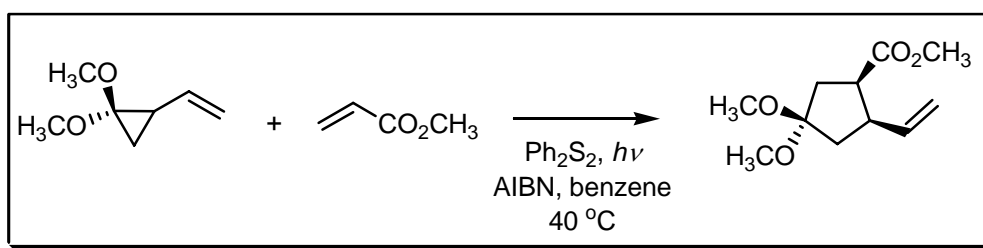
- 1) K.S. Feldman; M.M. Bruendl; K. Schildknecht, *J. Org. Chem.*, 1995, **60**, 7722.
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#### COMMENTS :

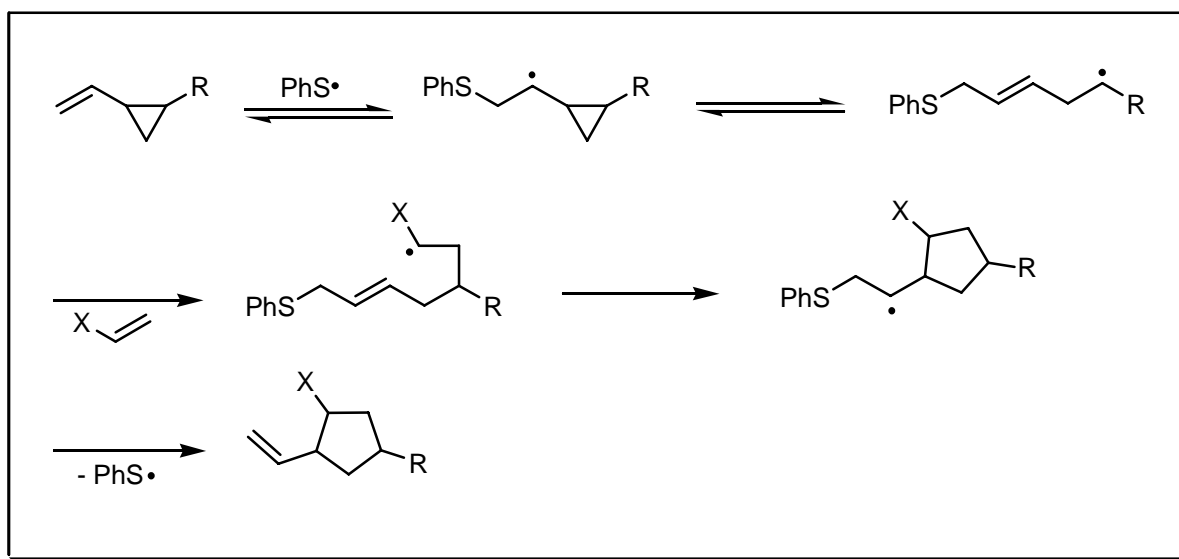
### FELDMAN SYNTHESIS

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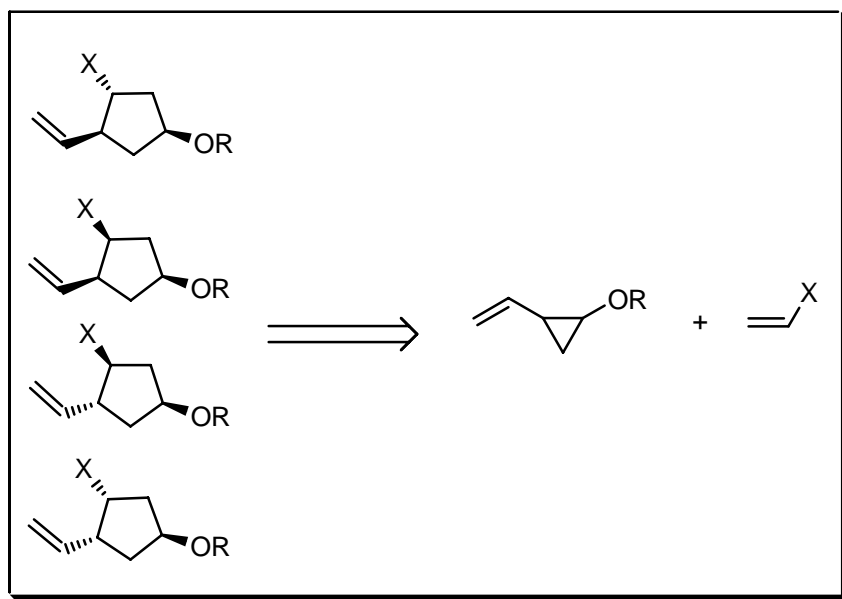
#### EXAMPLE :



#### MECHANISM :



## DISCONNECTION :



## NOTES :

The phenylthio radical-catalysed alkenylation of vinylcyclopropanes to give vinylcyclopentanes with high stereoselectivity.

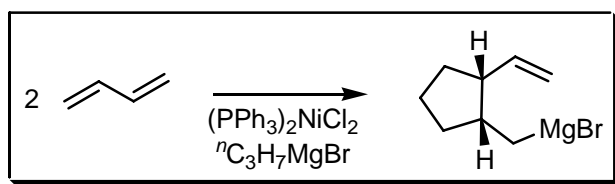
## REFERENCES :

- 1) K.S. Feldman; R.E. Simpson; M. Parvez, *J. Am. Chem. Soc.*, 1986, **108**, 1328.
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- 6) C.C. Huval; K.M. Church; D.A. Singleton, *Synlett*, 1994, 273.

## COMMENTS :

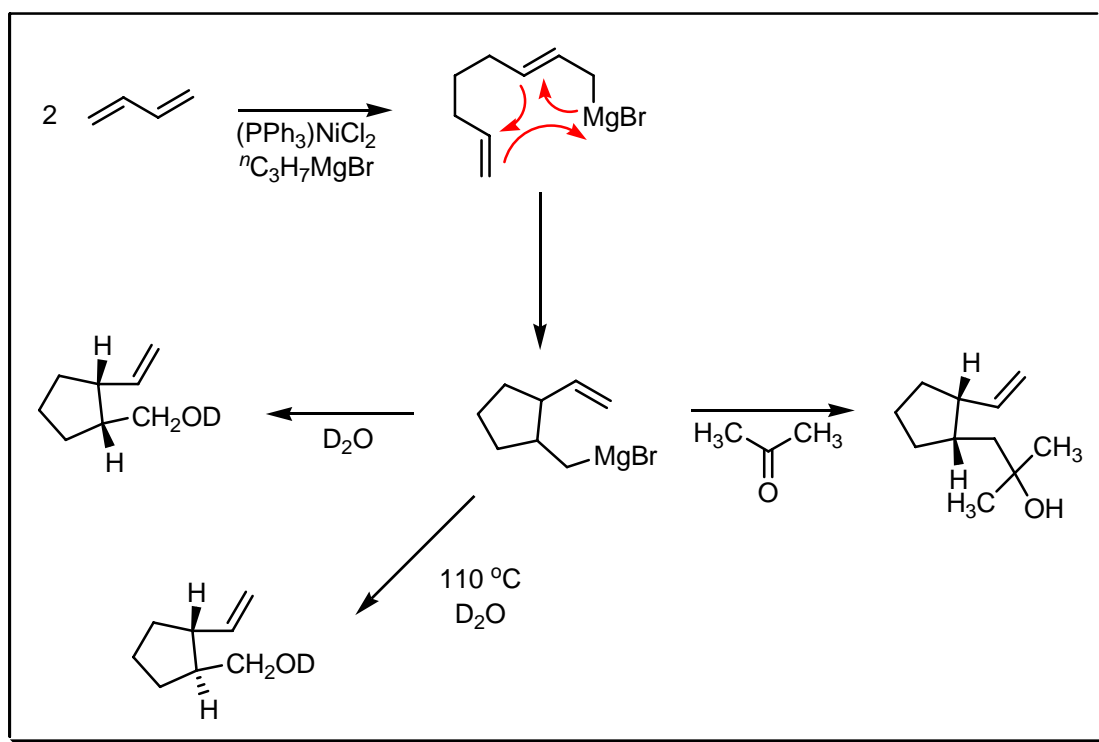
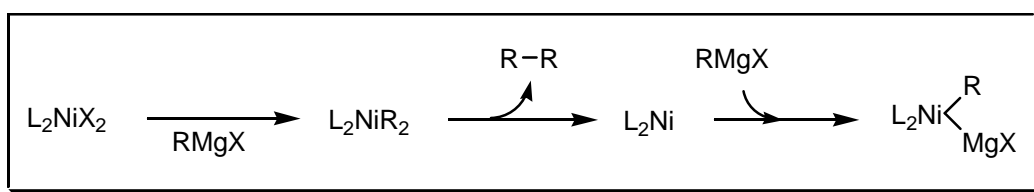
## FELKIN CYCLISATION

### EXAMPLE :



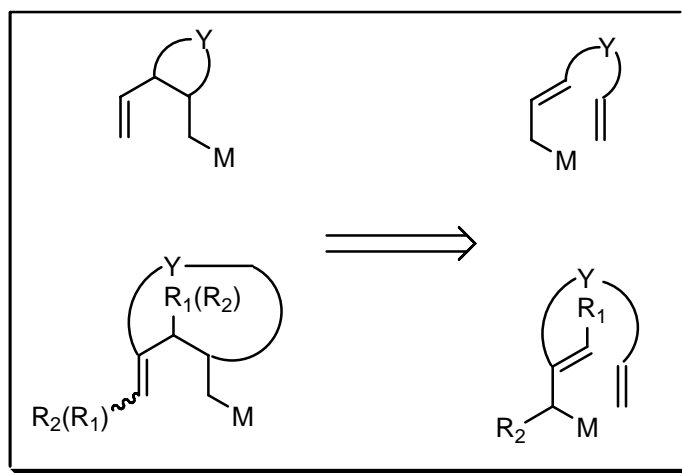
### MECHANISM :

Activation of **Grignard** reagent :





## DISCONNECTION :



## NOTES :

The *intramolecular* magnesium-ene reaction. The **Grignard** reagent has to be activated in the presence of a phosphine nickel complex. There are two types of reactions. See also **Alder ene**, **Tsuji – Trost** and **Tsuji – Wacker** reactions.

## REFERENCES :

**March** : 794

**Smith – March** : 1021

**Smith** : 1249

**Smith 2<sup>nd</sup>** : 1030

**Org. React.** : **20**, 133

**Org. Synth.** : **31**, 85; **43**, 27; **65**, 159

**Org. Synth. Coll. Vol.** : **4**, 766; **5**, 459; **8**, 427

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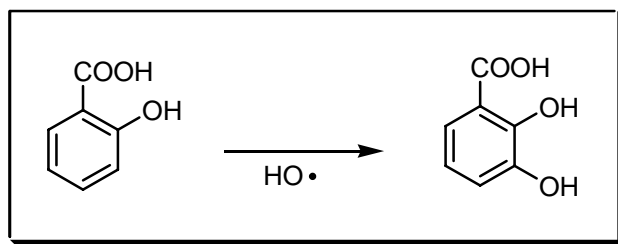
3) W. Oppolzer, *Angew. Chem., Int. Ed. Engl.*, 1989, **28**, 38.

## COMMENTS :

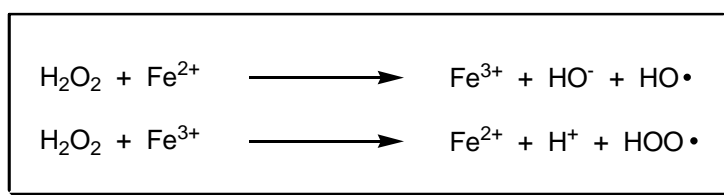
## FENTON REACTION

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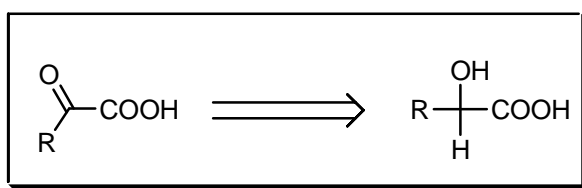
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The reaction is named after the method for the oxidation of  $\alpha$ -hydroxy acids and 1,2-glycols, using hydrogen peroxide in the presence of a ferrous salt. **Fenton** discovered in 1894 that several metals have a special oxygen transfer properties which improve the use of hydrogen peroxide. Actually, some metals have a strong catalytic power to generate highly reactive hydroxyl radicals. Nowadays, the **Fenton's** reaction is used to treat a large variety of water pollution such as phenols, formaldehyde, pesticides, rubber chemicals and so on. See also **Haber – Weiss (Haber – Willstätter)**, **Milas** and **Ruff – Fenton** reactions.

### REFERENCES :

**March** : 700, 713, 721

**Smith – March** : 916

**Smith** : 260, 1433

**Smith 2<sup>nd</sup>** : 225, 1182

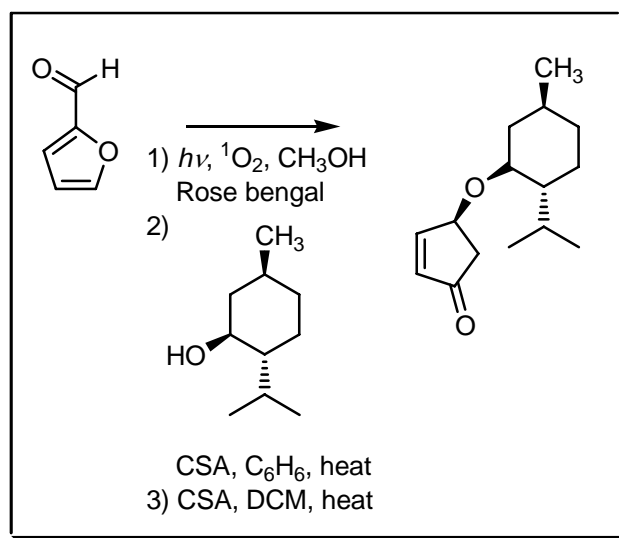
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**COMMENTS :**

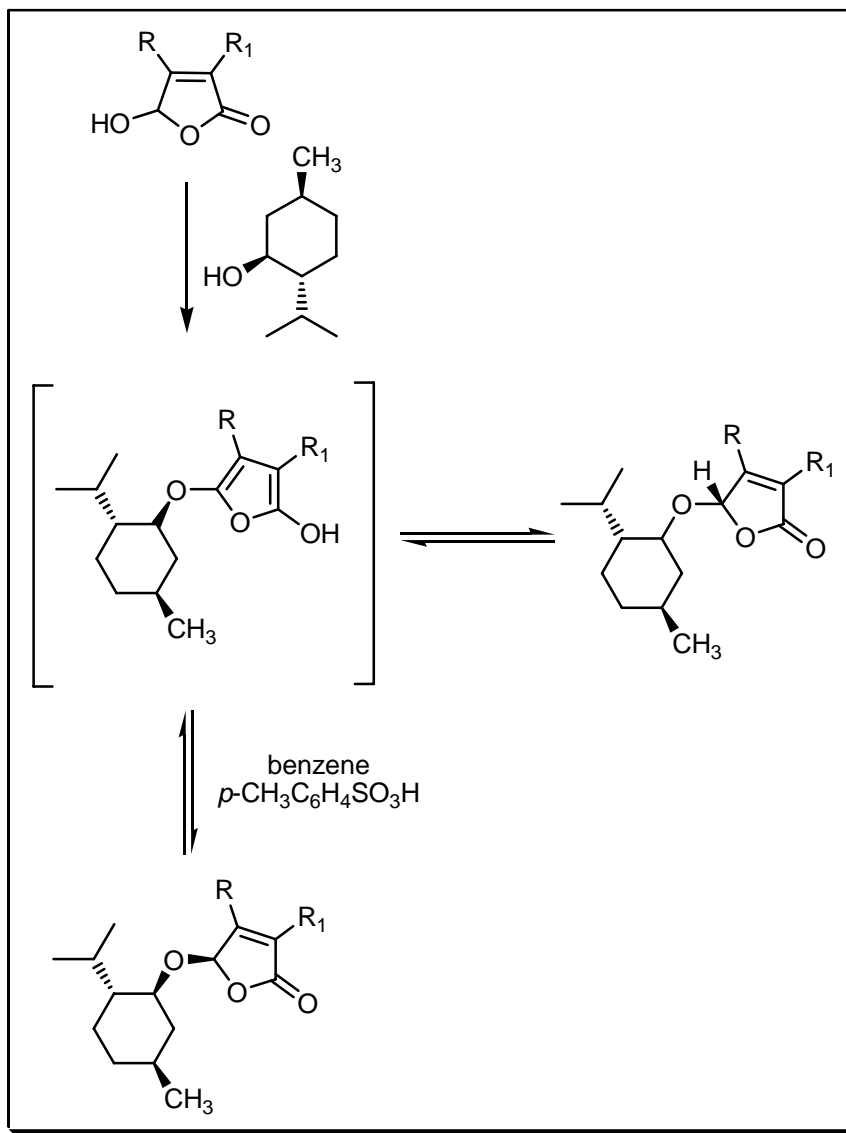
## FERINGA CHIRAL BUTENOLIDE SYNTHESIS

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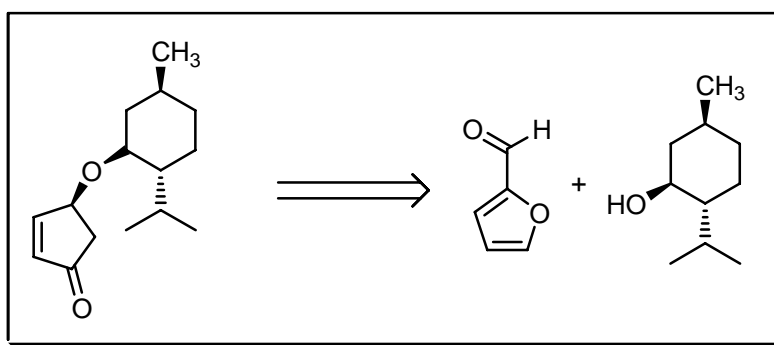
**EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

These valuable chiral building blocks (butenolides) are prepared *via* the reaction of 5-hydroxy-2(5H)-furanones with *d*- or *l*-menthol followed by recrystallisation or *via* the single photooxygenation of furfural. These routes are good alternatives for the carbohydrate-derived chiral butenolides. The double bond of these butenolides participates in diastereoselective dihydroxylation, 1,4-conjugate addition, [2+2] photochemical reactions, asymmetric **Diels – Alder**

reactions, 1,3-dipolar cycloadditions and tandem double **Michael** addition / *intramolecular* nucleophilic substitution reactions.

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**REFERENCES :**

**Org. Synth. : 80, 66**

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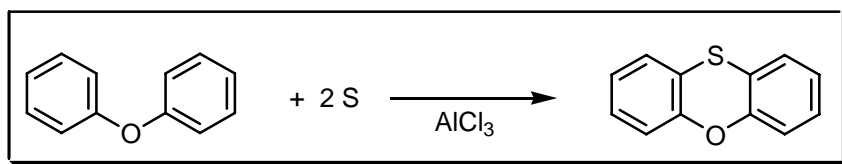
- 1) B.L. Feringa; J.C. de Jong, *J. Org. Chem.*, 1988, **53**, 1125.
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  - 7) H. Huang; Q. Chen, *Tetrahedron: Asymmetry*, 1999, **10**, 1295.
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**COMMENTS :**

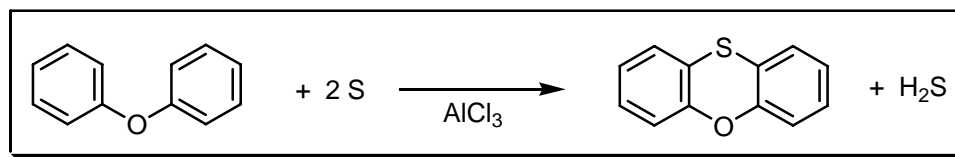
## FERRARIO – ACKERMAN REACTION

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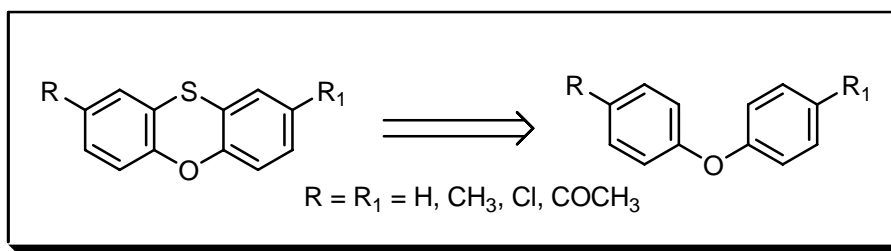
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

Phenoxathiines are obtained by the reaction between diphenyl ethers, sulfur and anhydrous aluminium chloride. The reaction can also be done electrochemically with a carbon-sulfur electrode.

## REFERENCES :

**Org. Synth.** : **18**, 64

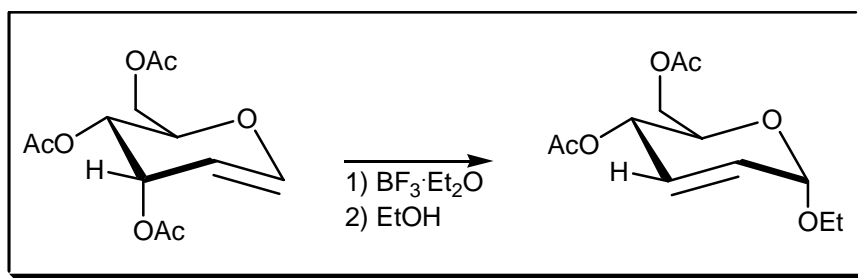
**Org. Synth. Coll. Vol.** : **2**, 485

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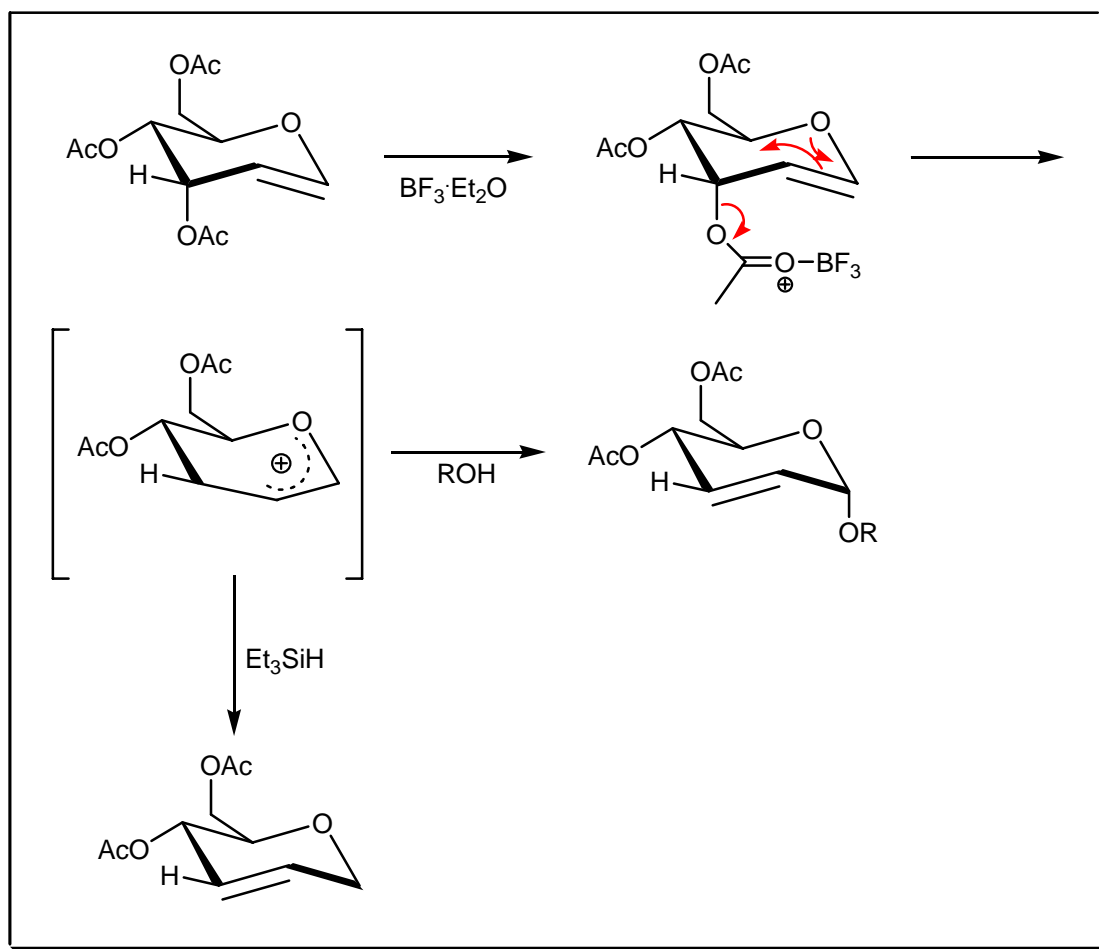
## COMMENTS :

## FERRIER REARRANGEMENT I

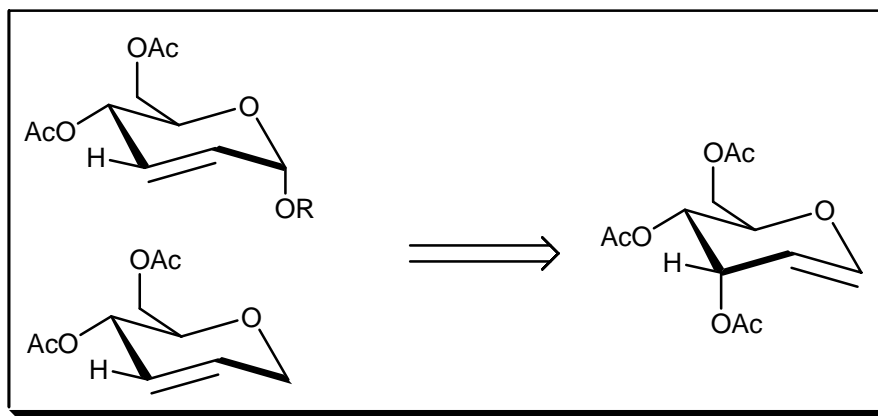
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The rearrangement of 2,3-unsaturated sugars using boron trifluoride etherate to form the delocalised allyloxocarbenium ion. This ion can be trapped with an alcohol or triethylsilane.

## REFERENCES :

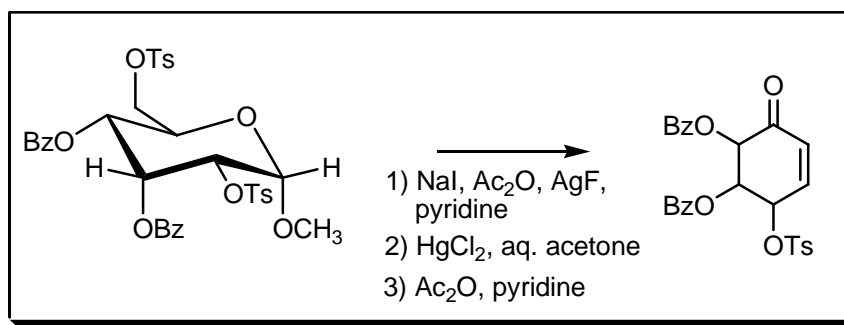
- 1) R.J. Ferrier, *Adv. Carbohydr. Chem.*, 1965, **20**, 67.
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- 3) J.C. López; A.M. Gomez; S. Valverde; B. Fraser-Reid, *J. Org. Chem.*, 1995, **60**, 3851.
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## COMMENTS :

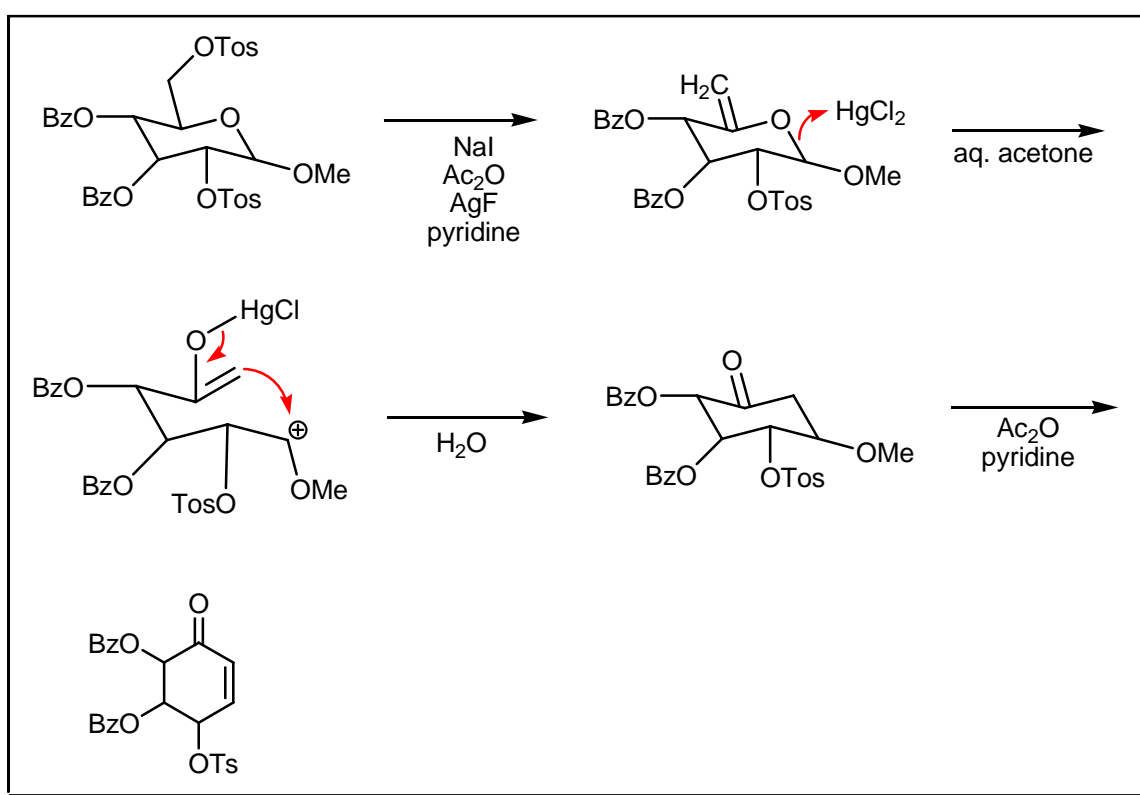


## FERRIER REARRANGEMENT II

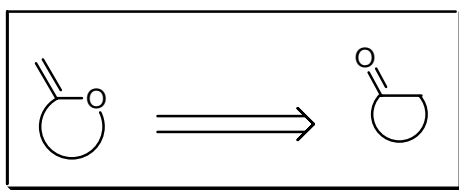
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The transformation of unsaturated glycosides into cyclohexanone derivatives by heating in aqueous acetone with mercury(II) salts. The 5-hydroxyl and the 3-substituent of the product are predominately in a *trans* relationship. The **Petasis** modification better known as the **Petasis – Ferrier** rearrangement uses  $\text{Cp}_2\text{TiMe}_2$ , followed by  $t\text{Bu}_3\text{Al}$ , and proceeds through a similar oxocarbenium intermediate.

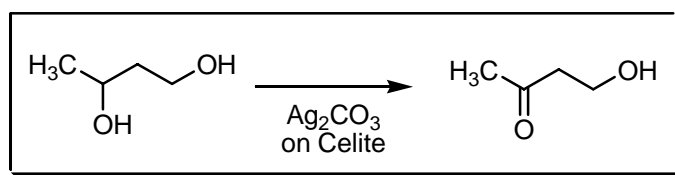
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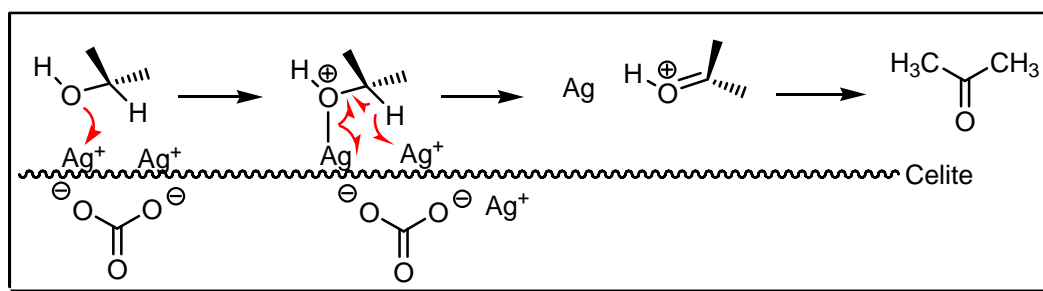
## COMMENTS :

## FÉTIZON OXIDATION

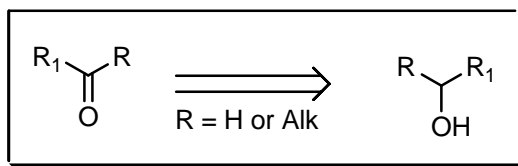
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



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## NOTES :

The oxidation of primary and secondary alcohols using silver carbonate and Celite. The alcohol is reversibly chemisorbed on the Celite surface. In the second irreversible step electron transfer takes place involving a second silver cation. See also **Anelli**, **Ball – Goodwin – Morton**, **Collins**, **Corey – Kim**, **Corey – Schmidt**, **Corey – Suggs**, **David – Thieffry**, **Delépine**, **Dess – Martin**, **Einhorn** oxidation, **Jones** oxidation, **Ley**, **Maurer – Drefahl**, **Mukaiyama** oxidation, **Nicolaou**, **Oppenauer**, **Parikh – von Doering**, **Pfitzner – Moffatt**, **Pinnick**, **Sarett**, **Swern** and **Uemura** reactions.

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## REFERENCES :

**March** : 1168

**Smith** : 250

**Smith 2<sup>nd</sup>** : 217

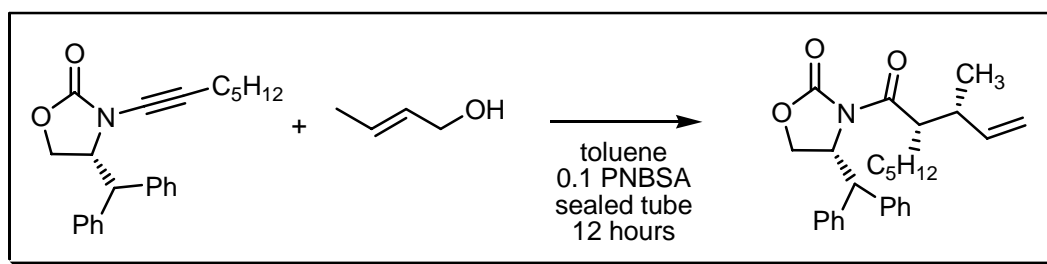
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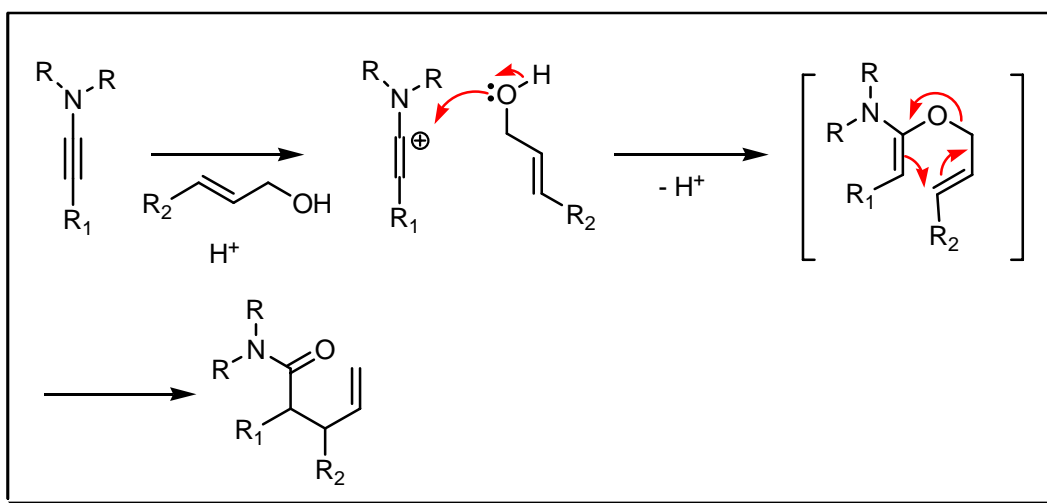
## COMMENTS :

## FICINI – CLAISEN REARRANGEMENT

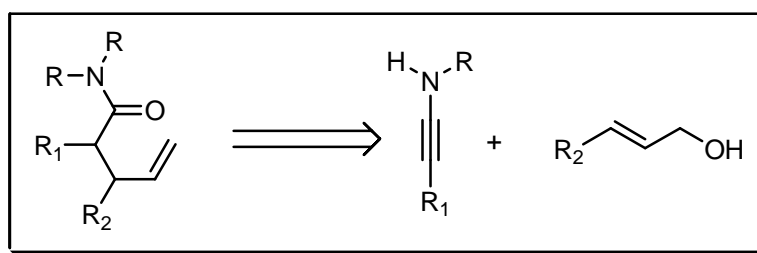
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The **Claisen** rearrangement of ynamine and ynamides. See also **Belluš – Claisen** rearrangement, **Carroll (Kimmel – Cope)**, **Claisen (Claisen – Ireland)** rearrangement, **Cope**, **Eschenmoser – Meerwein – Claisen** rearrangement, **Johnson – Claisen**, **Marbet – Saucy** and **Overman** rearrangement reactions.

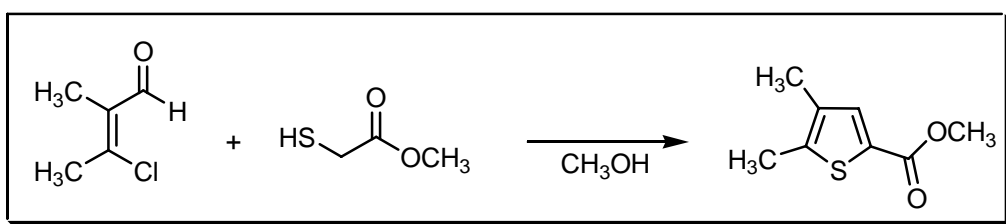
### REFERENCES :

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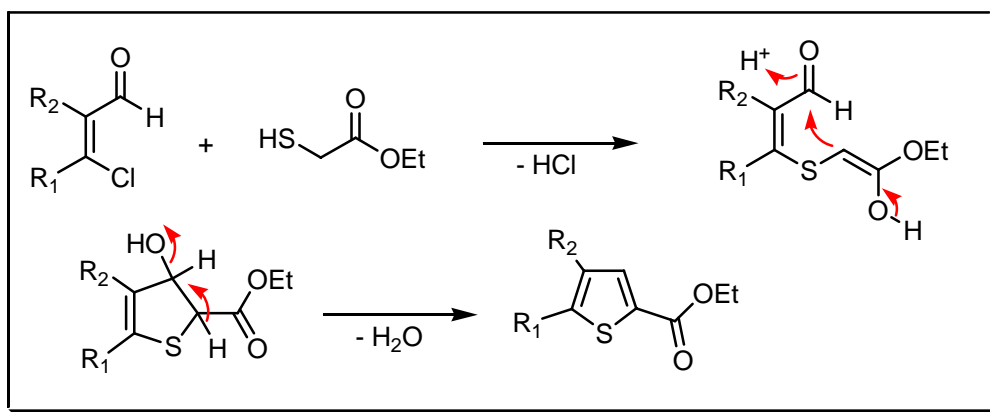
**COMMENTS :**

**FIESSELMANN THIOPHENE SYNTHESIS**

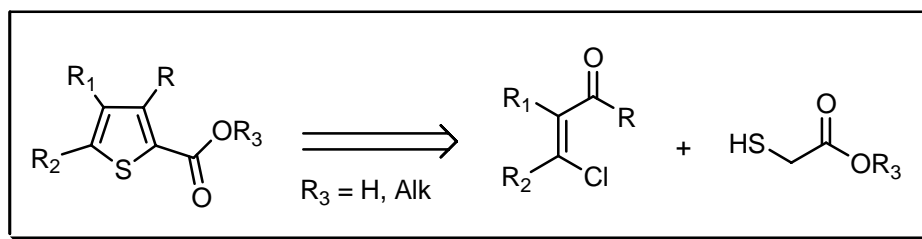
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

1,3-Dicarbonyl compounds or  $\beta$ -chlorovinyl aldehydes react with thioglycolates or other thiols possessing a reactive methylene group (*intramolecular aldol condensation*) to give thiophene-2-carboxylic esters. Many selenophene are

prepared by a modified **Fiesselmann** synthesis. See also **Baumann – Fromm**, **Bogert – Herrera**, **Hinsberg** thiophene, **Volhard – Erdmann** and **Willgerodt – Kindler** reactions.

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#### REFERENCES :

**Science of Synthesis** : 9, 315

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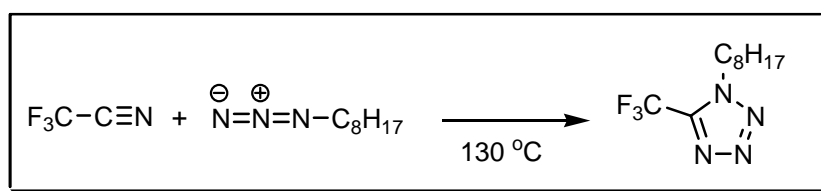
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#### COMMENTS :

### FINEGAN TETRAZOLE SYNTHESIS

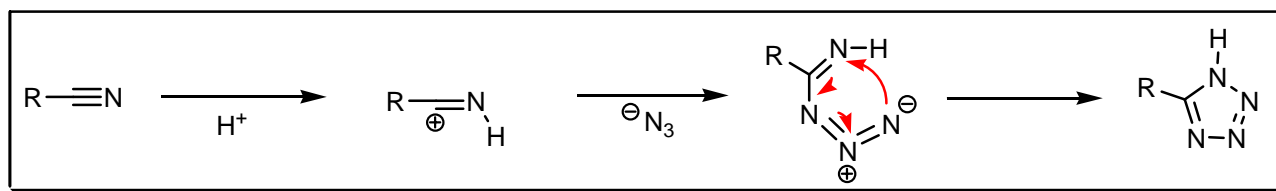
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#### EXAMPLE :

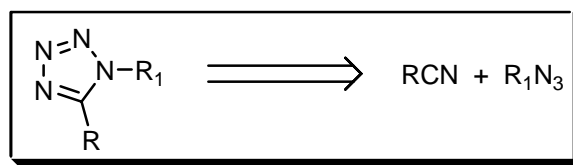


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#### MECHANISM :



## DISCONNECTION :



## NOTES :

The tetrazole synthesis from azides by dipolar cycloaddition with Lewis acid activated nitriles or *intramolecularly* with nitriles in the presence of acids. See also **Huisgen** reaction.

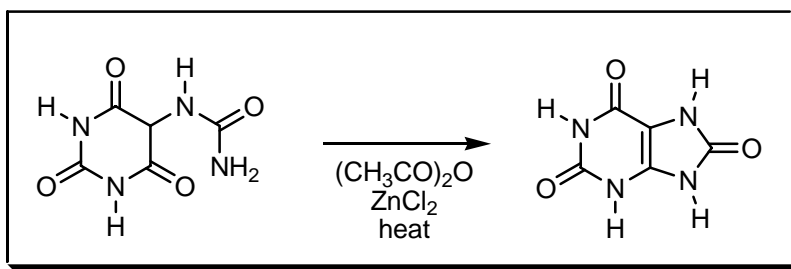
## REFERENCES :

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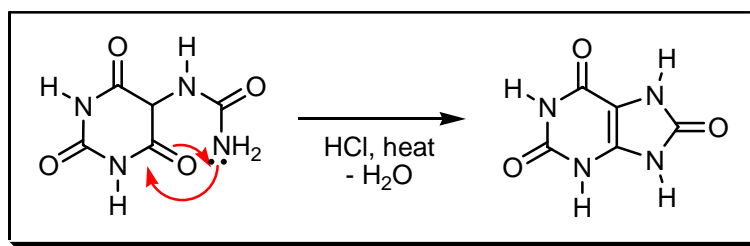
## COMMENTS :

## FISCHER – ACH URIC ACID SYNTHESIS

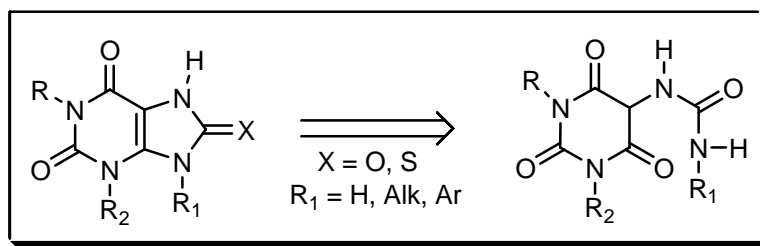
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

Pseudouric acid dehydrates and cyclises with oxalic acid or hydrochloric acid or with zinc chloride in acetic anhydride. The method can be applied to the synthesis of alkylated uric acids and of aminodihydroxypurines. See also **Behrend** – **Roosen**, **Horbaczewski** and **Traube** reactions.

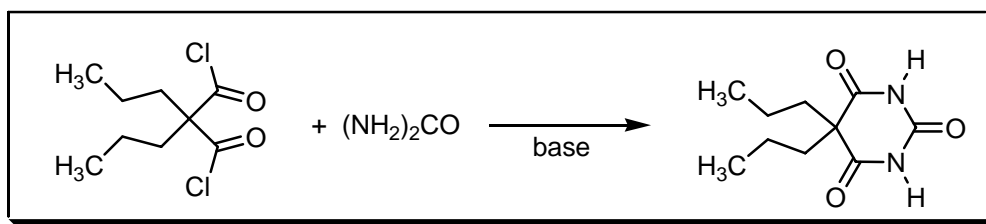
## REFERENCES :

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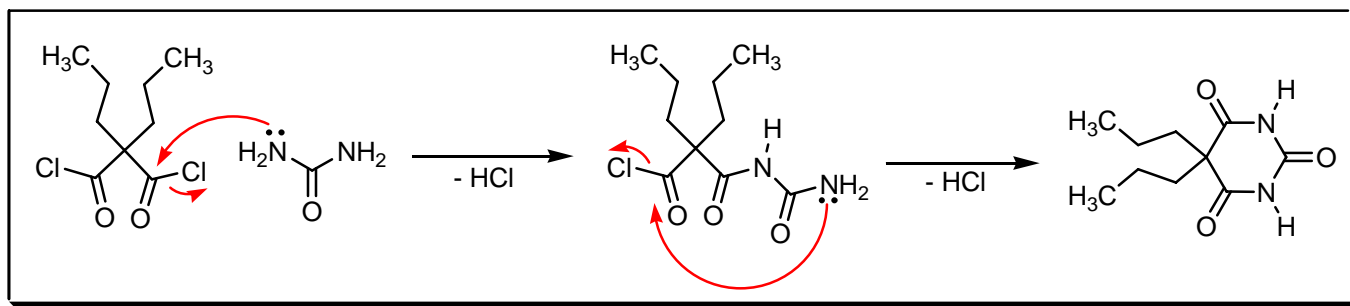
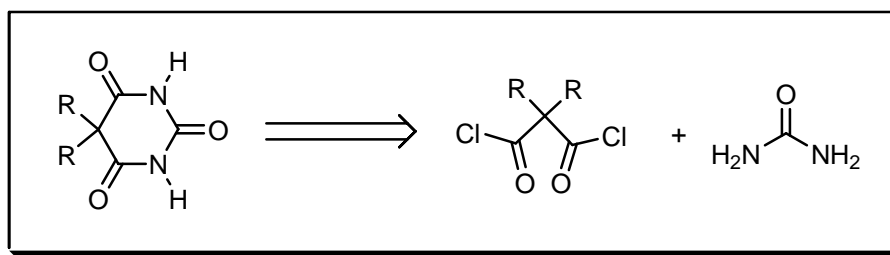
## COMMENTS :

## FISCHER – DILTHEY CONDENSATION

### EXAMPLE :





**MECHANISM :****DISCONNECTION :****NOTES :**

C,C-Dialkylbarbituric acids are obtained by the reaction of a dialkyl malonyl chloride with urea. A similar condensation occurs with guanidine.

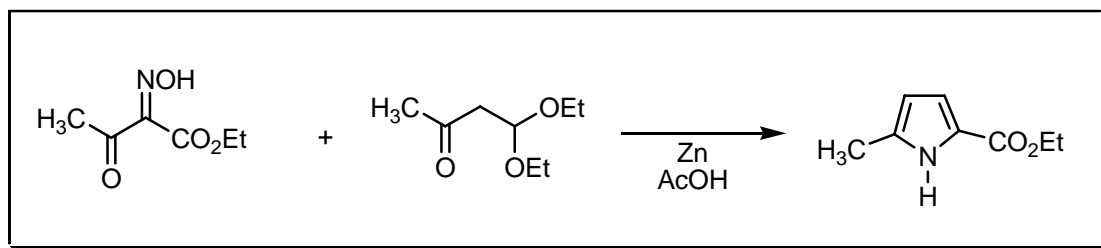
**REFERENCES :**

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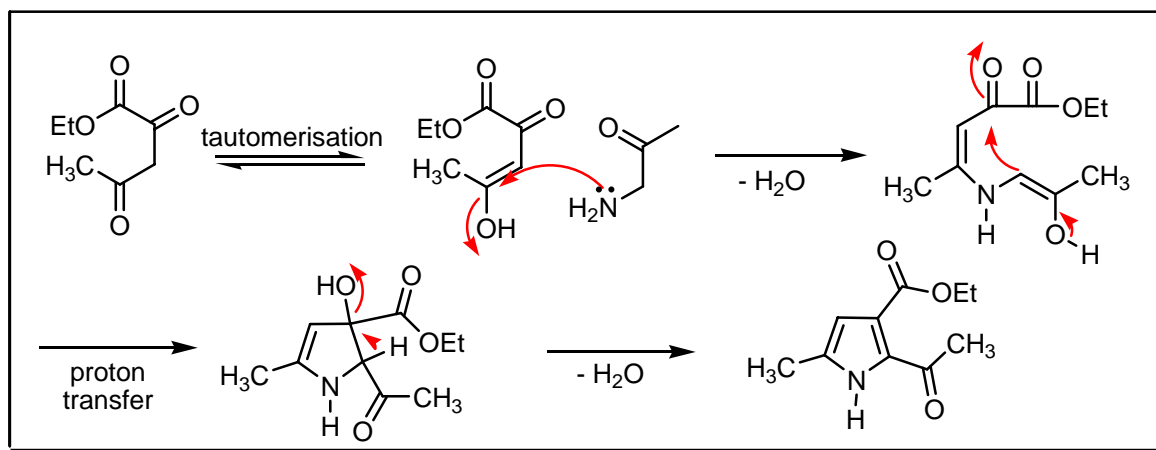
**COMMENTS :**

## FISCHER – FINK PYRROLE SYNTHESIS

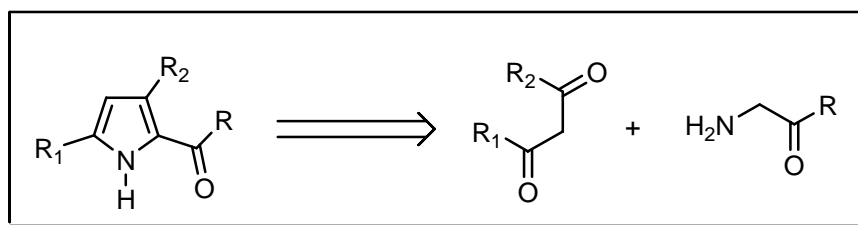
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The interaction of the diethylacetal of acetylacetaldehyde with ethyl isonitrosoacetate and zinc dust in acetic acid gives ethyl 2-methyl-pyrrole-5-carboxylate. This compound is also obtained when isonitrosobutyrylacetate is employed. The zinc reduces the NOH to NH<sub>2</sub>. In some systems mixtures of **Fischer – Fink** and **Paal – Knorr** products are obtained. See also **Barton – Zard**, **Clauson-Kaas**, **Grob – Camenisch**, **Hantzsch** pyrrole, **Harries** pyrrole, **Kenner**, **Knorr** pyrrole, **Miller – Plöchl**, **Paal – Knorr**, **Padwa**, **Piloty – Robinson**, **Schwanert**, **Trofimov** and **Zav'yalov** reactions.

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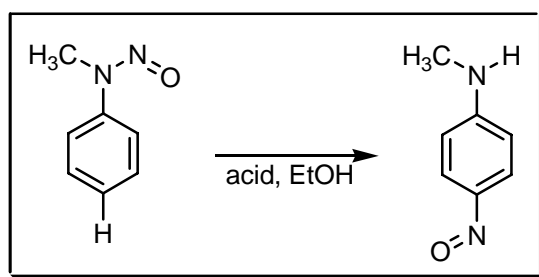
**COMMENTS :**

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**FISCHER – HEPP REARRANGEMENT**

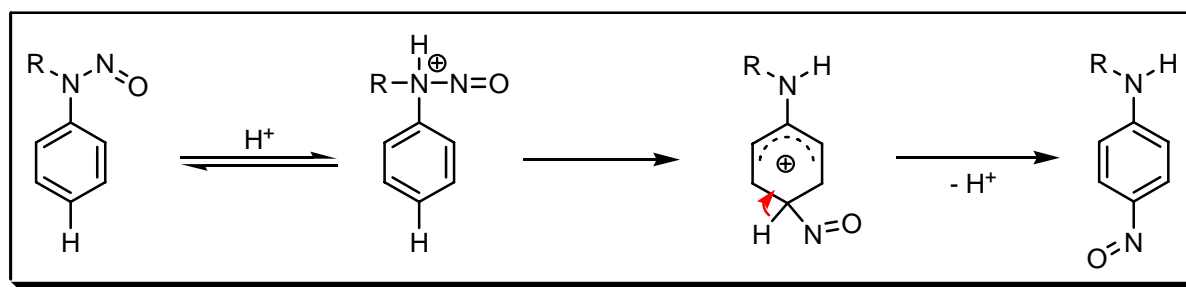
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**EXAMPLE :**



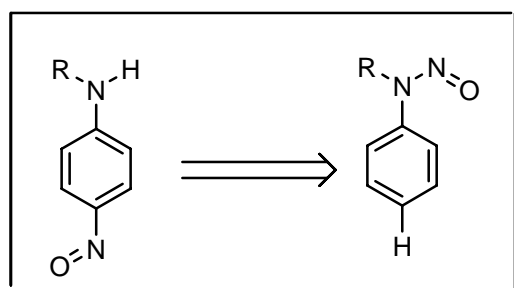
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**MECHANISM :**



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**DISCONNECTION :**



## NOTES :

*N*-Nitroso derivatives of secondary *N*-alkyl or aryl anilines undergo *intramolecular* rearrangement in acid solution to form the corresponding (usually *p*-) nitroso-*N*-alkyl or aryl anilines. See also **Orton** rearrangement.

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## REFERENCES :

March : 558

Smith – March : 728

Houben – Weyl : 4/2, 57; 11/1, 834

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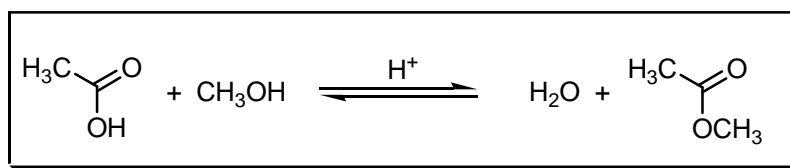
- 1) O. Fischer; E. Hepp, *Ber. Dtsch. Chem. Ges.*, 1886, **19**, 2991.
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## COMMENTS :

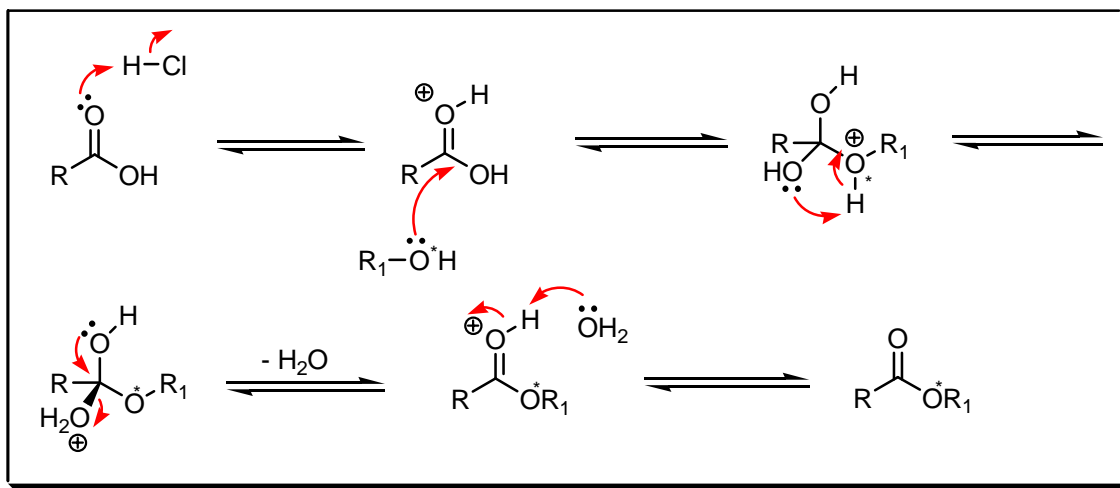
## FISCHER – SPEIER ESTERIFICATION

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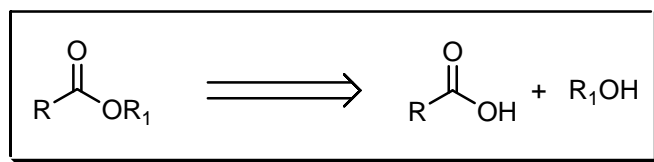
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The use of mineral acids as catalysts in esterification of carboxylic acids with alcohols.

## REFERENCES :

March : 393

Smith – March : 484

Org. Synth. : 5, 53; 36, 3

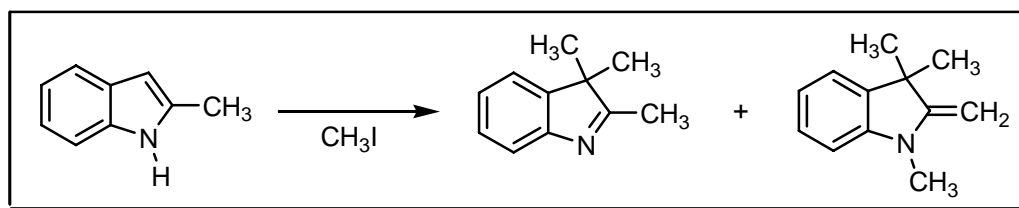
Org. Synth. Coll. Vol. : 1, 237; 4, 169

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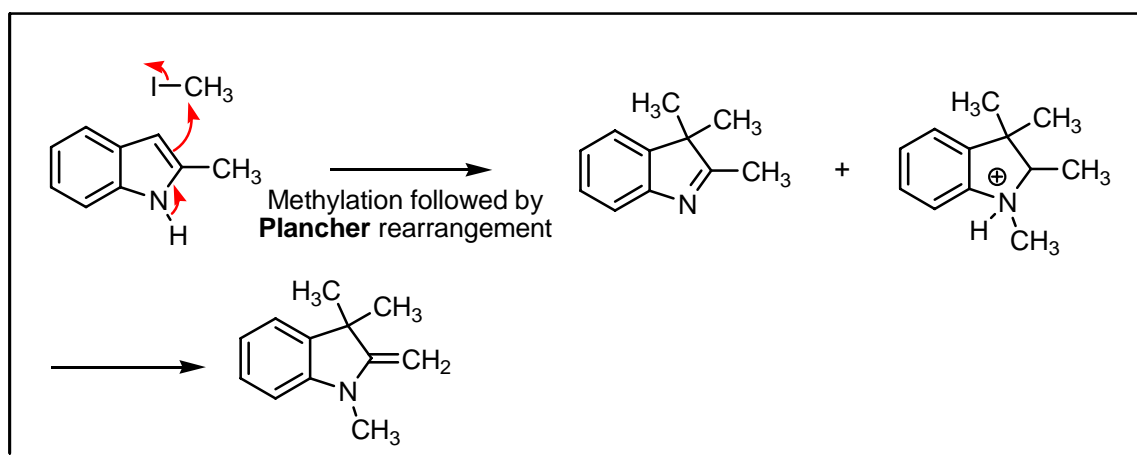
COMMENTS :

## FISCHER – STECHE SYNTHESIS

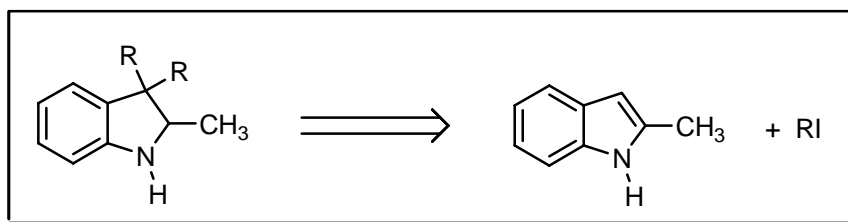
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

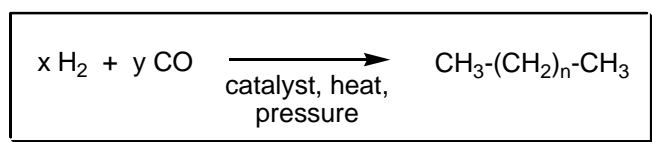
The formation of indolenines (pseudoindoles) by heating indoles with an alkyl iodide. The migration of an alkyl group of the indole from C-2 to C-3 during methylation with methyl iodide is the **Plancher** rearrangement. See also **Plancher** rearrangement.

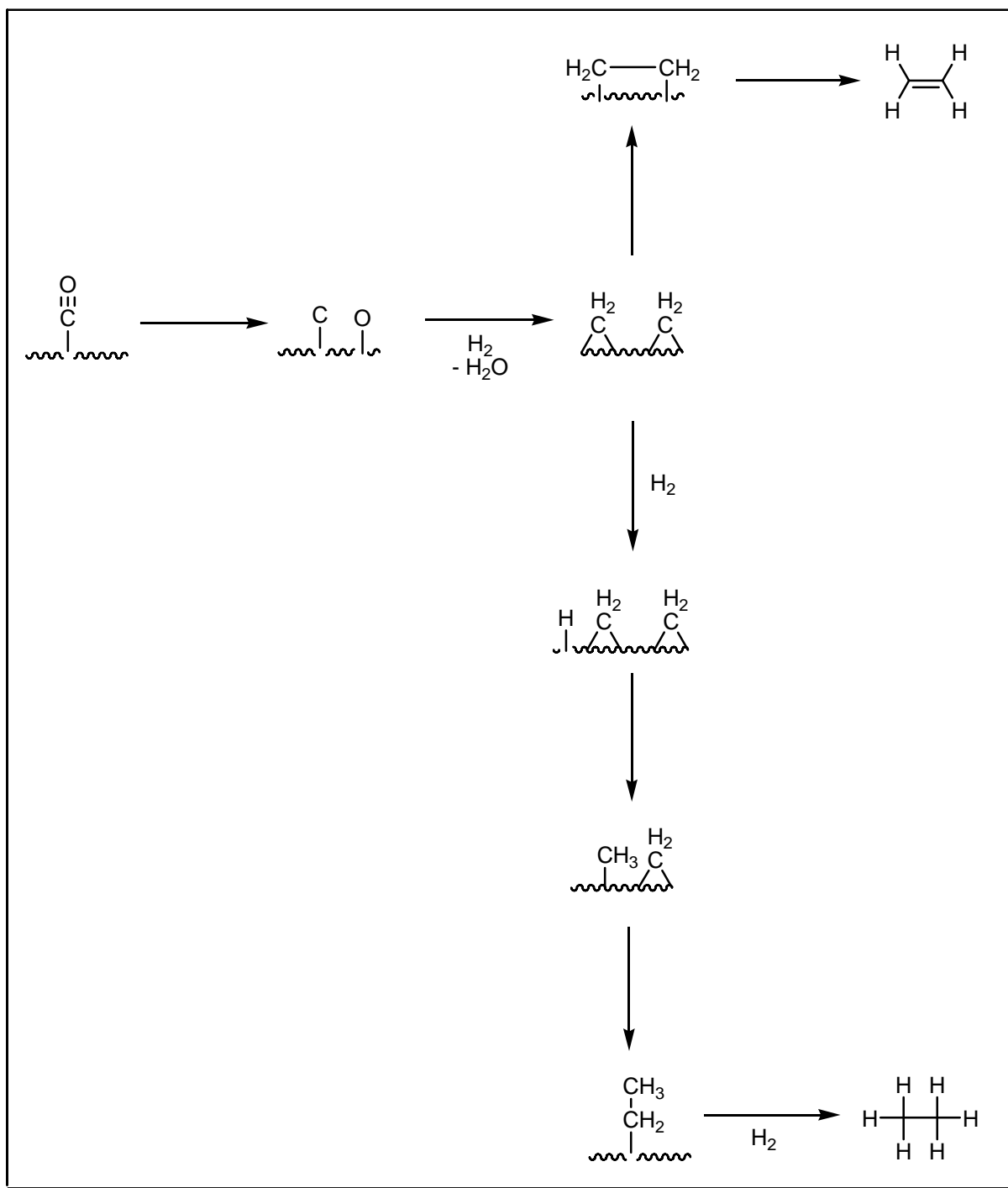
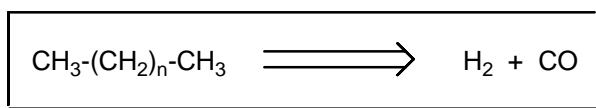
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**COMMENTS :****FISCHER – TROPSCH SYNTHESIS****EXAMPLE :**

**MECHANISM :****DISCONNECTION :****NOTES :**

The catalytic hydrogenation of carbon monoxide using enriched synthesis gas from passage of steam over heated coke will afford hydrocarbons, aliphatic alcohols, aldehydes and ketones. The product ratio varies with conditions. The high pressure Synthol process gives mainly oxygenated products and addition of olefins in the presence of cobalt



catalyst, while the Oxo synthesis, produces aldehydes. Normal pressure synthesis leads mainly to petroleum-like hydrocarbons. A similar process is the **Bergius** process.

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**Houben – Weyl** : 4/2, 164, 183, 184, 186, 254, 332

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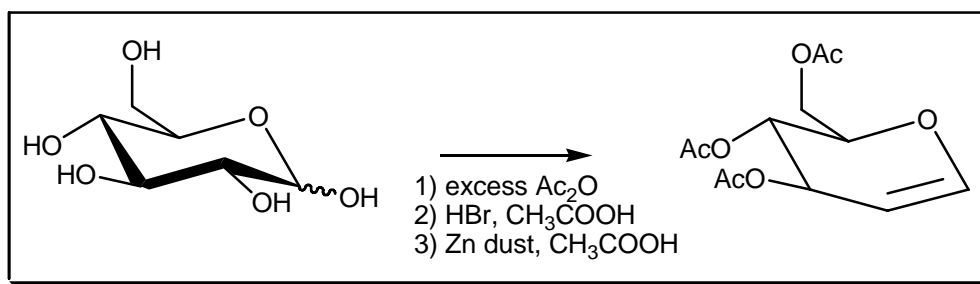
## COMMENTS :

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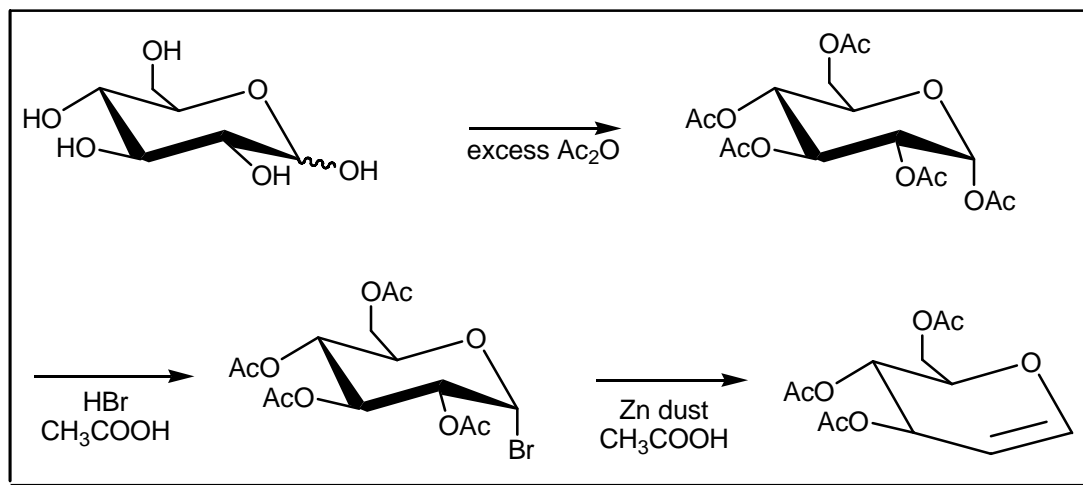
## FISCHER – ZACH REACTION

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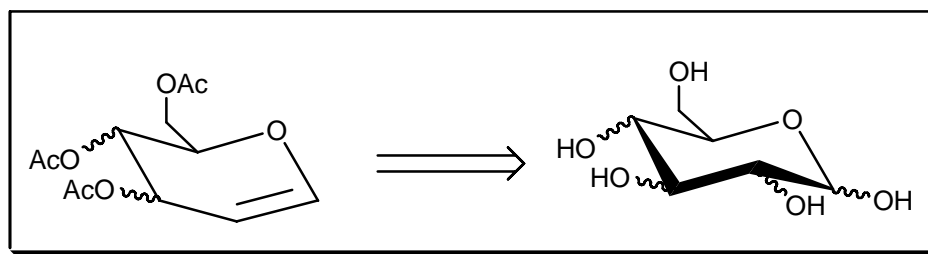
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The classic synthesis of glucals under acidic conditions. However, this reaction fails in the furanoid glycal synthesis. A modification is based on the reductive elimination work by **Scheffold**. Vitamin B-12, ammonium chloride and zinc dust in methanol can catalyse the reduction, although it also fails again with the furanoid glycals. For a preparation of these compounds see **Ireland et al.**

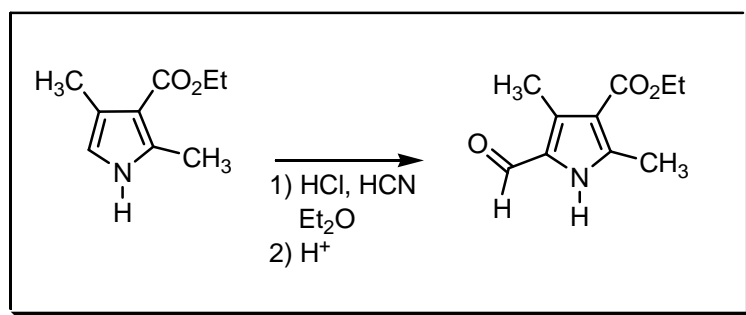
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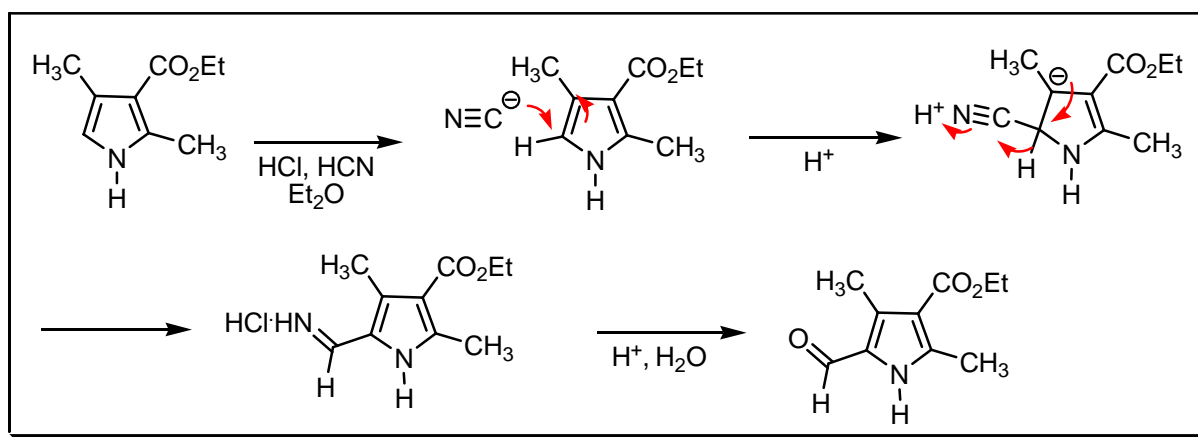
## COMMENTS :

## FISCHER – ZERWECK PYRROLE ALDEHYDE SYNTHESIS

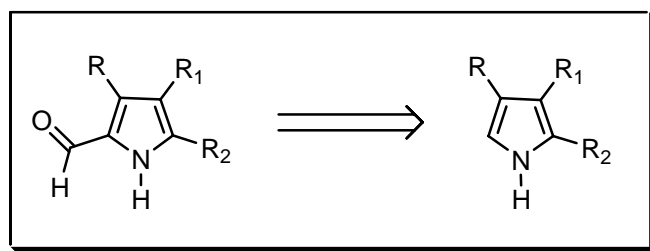
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

An ethereal or chloroform solution of a pyrrole and hydrogen cyanide on treatment with hydrogen chloride yields an  $\alpha$ -alkimine hydrochloride, which on hydrolysis forms an  $\alpha$ -pyrrole aldehyde. If the  $\alpha$ -position is already substituted, the  $\beta$ -compound is obtained. See also **Gattermann** formylation and **Hoesch – Houben** reactions.

### REFERENCES :

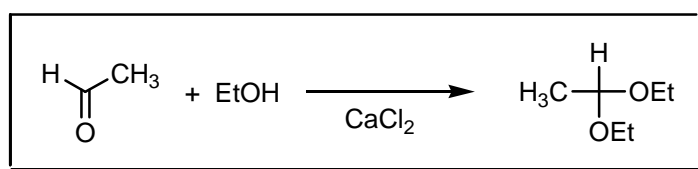
Houben – Weyl : 7/1, 27

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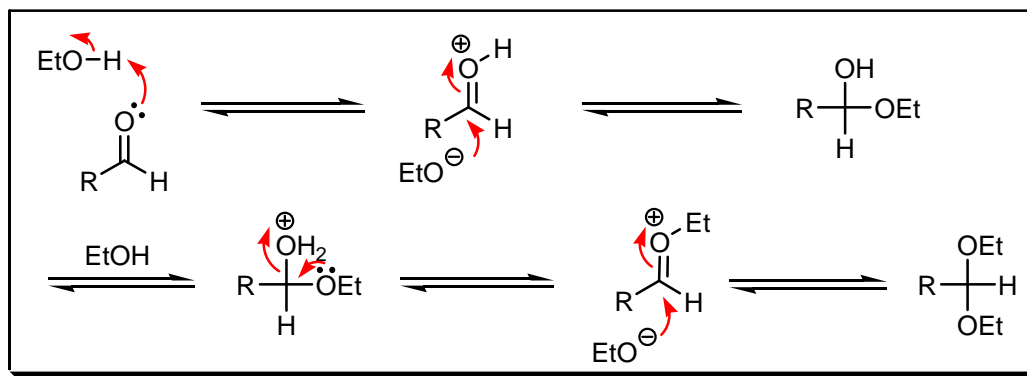
**COMMENTS :**

## FISCHER ACETAL SYNTHESIS

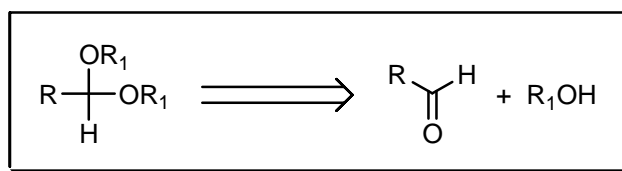
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

Acetals are obtained by the action of excess of an alcohol on an aldehyde with e.g. calcium chloride as catalyst.

## REFERENCES :

March : 889

Smith – March : 1180

Smith : 655

Smith 2<sup>nd</sup> : 554

Houben – Weyl : 7/1, 419

Org. Synth. : 3, 1; 74, 1

Org. Synth. Coll. Vol. : 1, 1; 9, 39

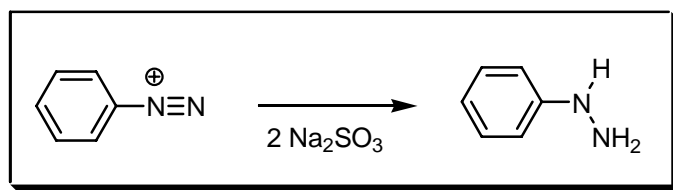
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## COMMENTS :

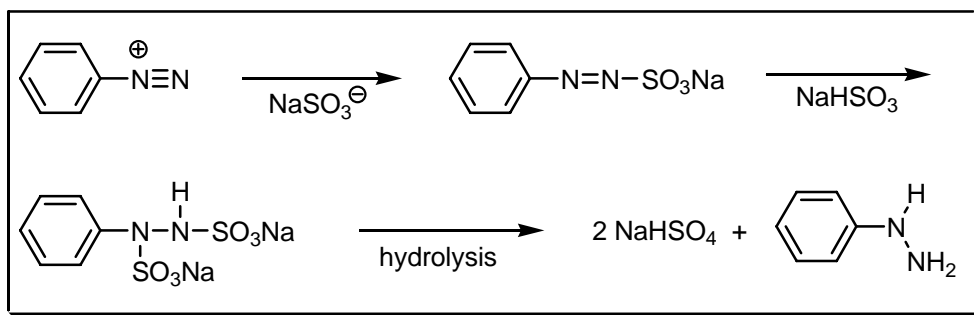
## FISCHER ARYLHYDRAZINE SYNTHESIS

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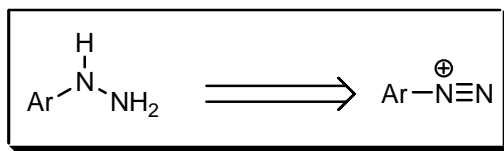
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

Aromatic diazo-compounds on reduction with alkali sulfite yield arylhydrazine sulfonates, which on acid hydrolysis form arylhydrazine salts.

## REFERENCES :

Org. Synth. : 2, 71

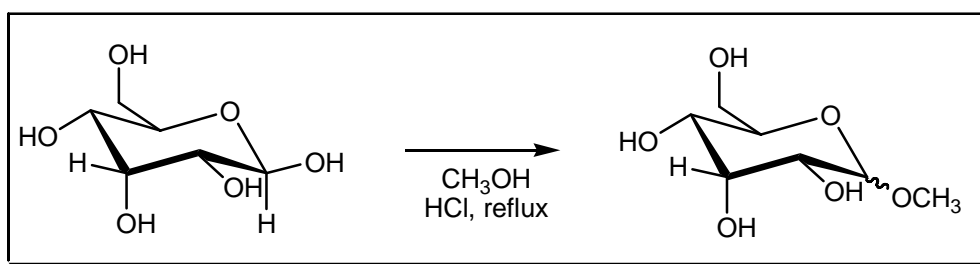
Org. Synth. Coll. Vol. : 1, 432

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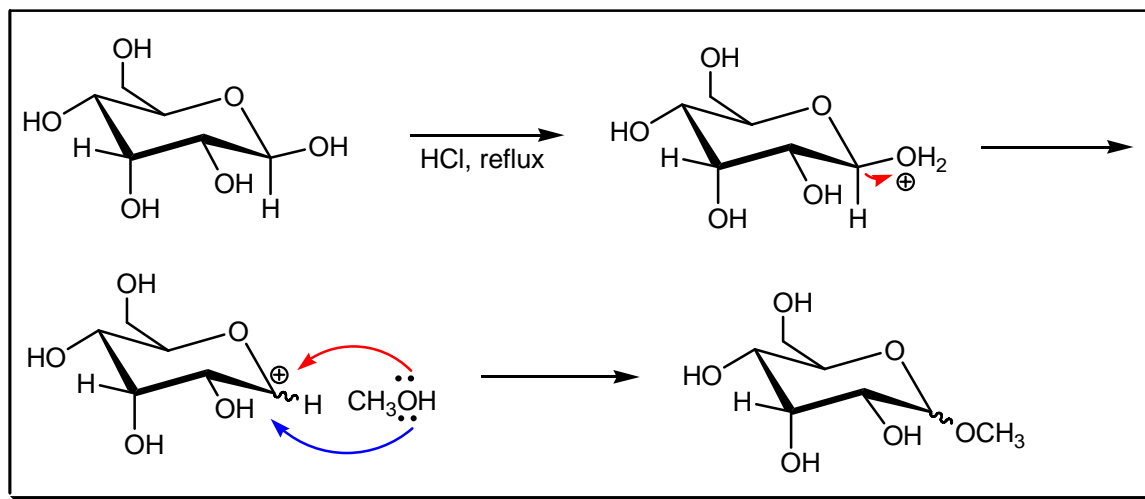
## COMMENTS :

## FISCHER GLYCOSIDATION

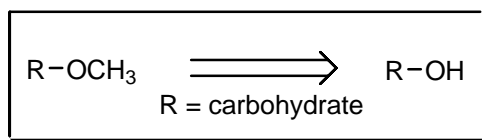
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The glycosidation of sugars in boiling acidified alcohol. See also **Kahne** glycosidation, **Koenigs – Knorr**, **Michael** glycosidation and **Schmidt** glycosidation reactions.

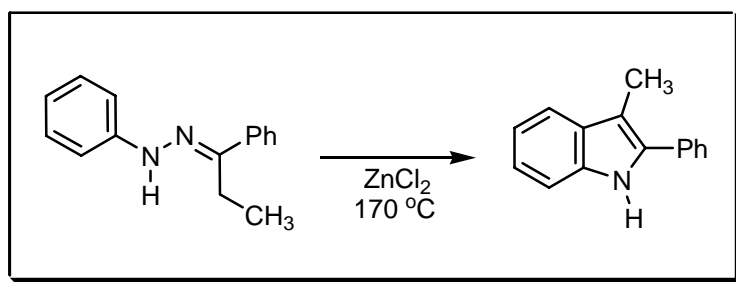
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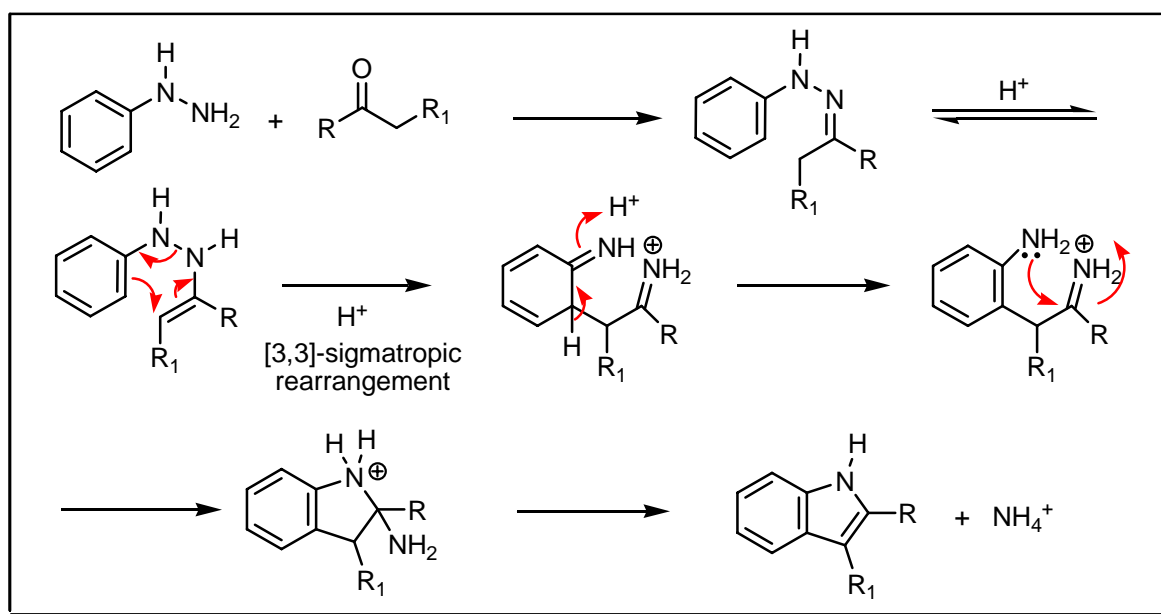
## COMMENTS :

# FISCHER INDOLE SYNTHESIS

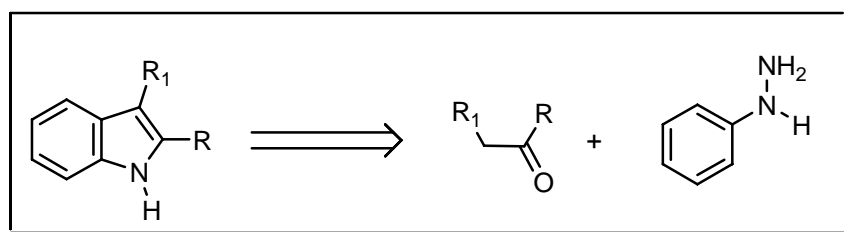
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

An aldehyde or ketone hydrazone from an arylhydrazine with a free *ortho* position, is heated at 180 – 200 °C with e.g. anhydrous zinc chloride, polyphosphoric acid or a Lewis acid catalyst. It is the second step which is technically the named reaction, the formation of an indole from an arylhydrazone of an aldehyde or ketone. The main step in the mechanism is a [3,3]-sigmatropic rearrangement. A palladium-catalysed reaction has been reported by **Buchwald *et al.*** See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber –**



**Batcho, Lipp, Madelung** indole, **Magnus, Martin, Montecchi, Mori – Ban, Murphy, Naito, Nenitzescu** indole, **Piloty – Robinson, Pschorr – Hoppe, Reissert** indole, **Saegusa** indole, **Schmid, Smith, Sugawara** indole, **Sundberg, Thiele – Dimroth, Thyagarajan, Watanabe, Weerman** indole, **Wender, Widman, Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

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#### REFERENCES :

**March** : 1141

**Smith – March** : 1452

**Smith** : 1343

**Smith 2<sup>nd</sup>** : 847, 1104

**Org. React.** : **10**, 143

**Houben – Weyl** : **10/2**, 546; **E6b**, 692; **E15**, 1017; **E16a**, 815

**Org. Synth.** : **22**, 98

**Org. Synth. Coll. Vol.** : **3**, 725

**Science of Synthesis** : **10**, 288, 316, 339, 366, 370, 698, 723

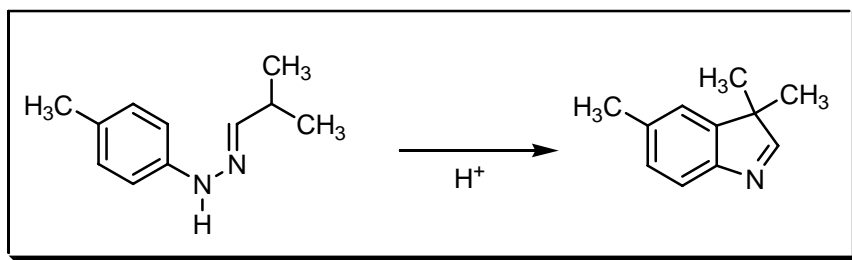
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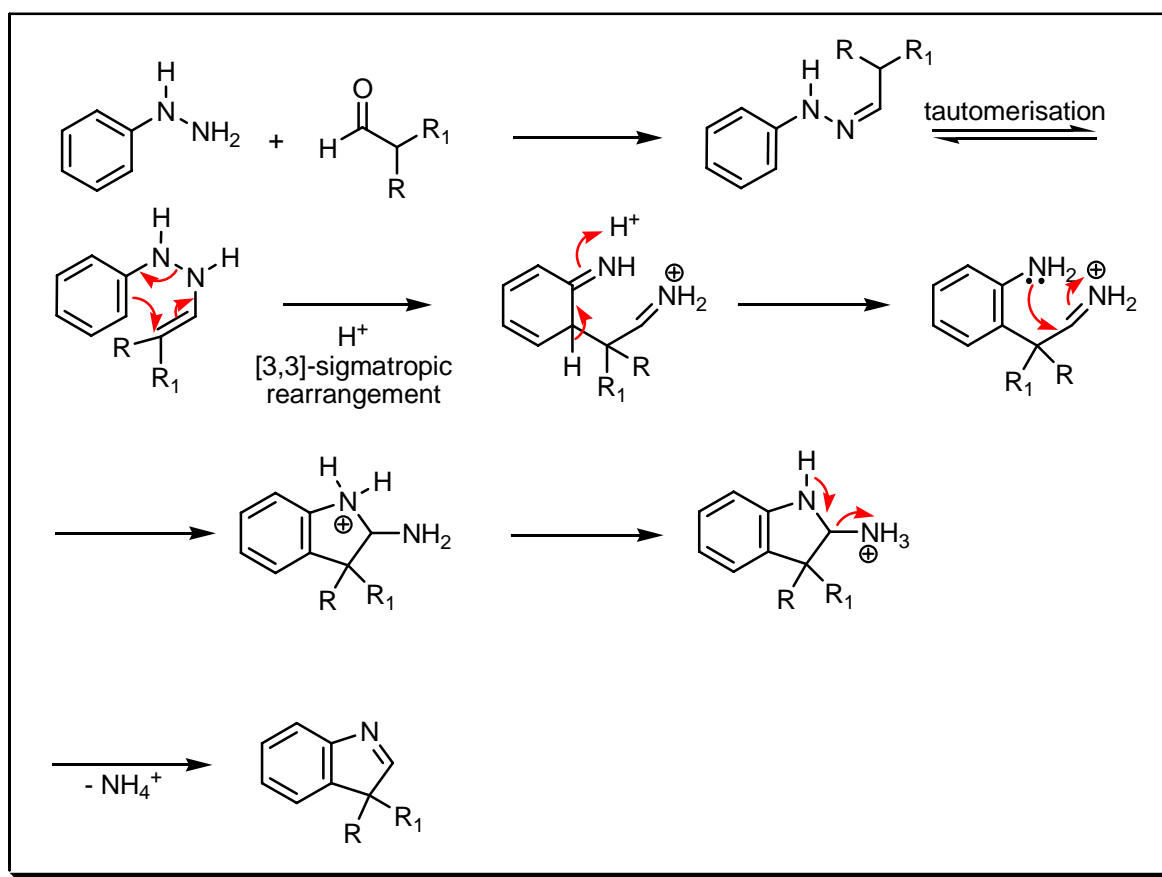
#### COMMENTS :

## FISCHER INDOLENINES SYNTHESIS

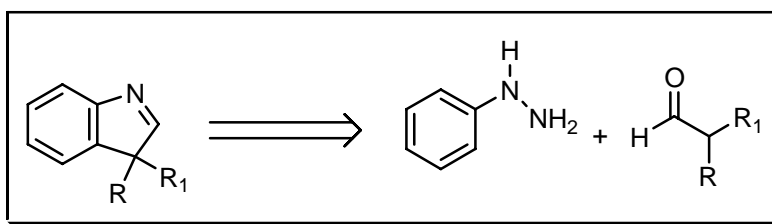
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The **Fischer** indole synthesis when applied to arylhydrazones of aldehydes and ketones containing a methylene group adjoining the carbonyl group yields 3,3-disubstituted indolenines. See also **Fischer** indole reaction.

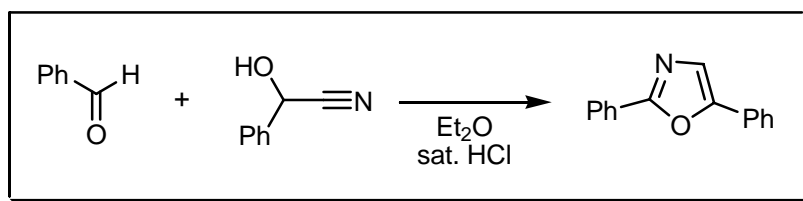
## REFERENCES :

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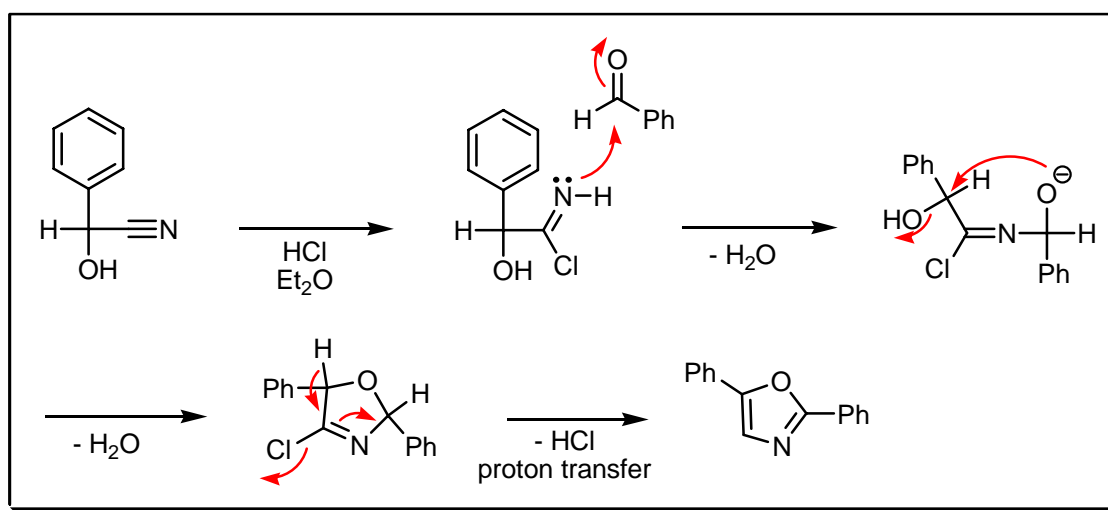
## COMMENTS :

## FISCHER OXAZOLE SYNTHESIS

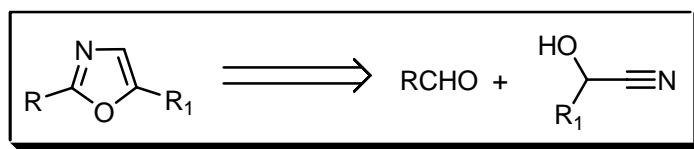
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

This synthesis involves the condensation in dry hydrogen chloride of an aldehyde with an aldehyde cyanohydrin. The reaction only works in the aromatic series. If however an  $\alpha$ -hydroxyamide is used some aliphatic derivatives can be prepared. See also **Davidson, Japp, Robinson – Gabriel** and **Witte – Seeliger** reactions.

## REFERENCES :

Houben – Weyl : E8a, 899

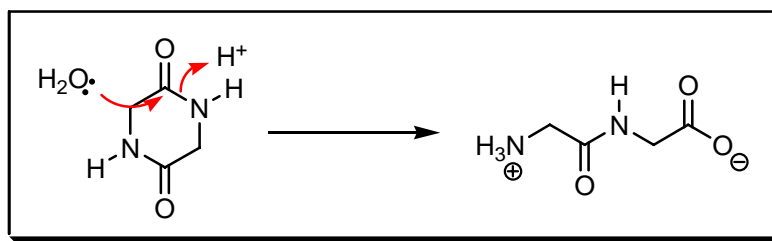
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## COMMENTS :

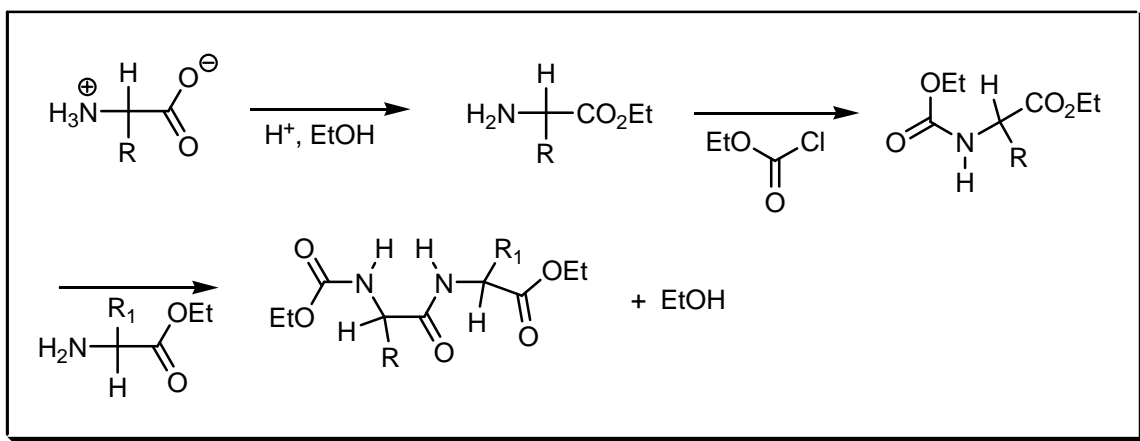
## FISCHER PEPTIDE SYNTHESIS

### MECHANISM :

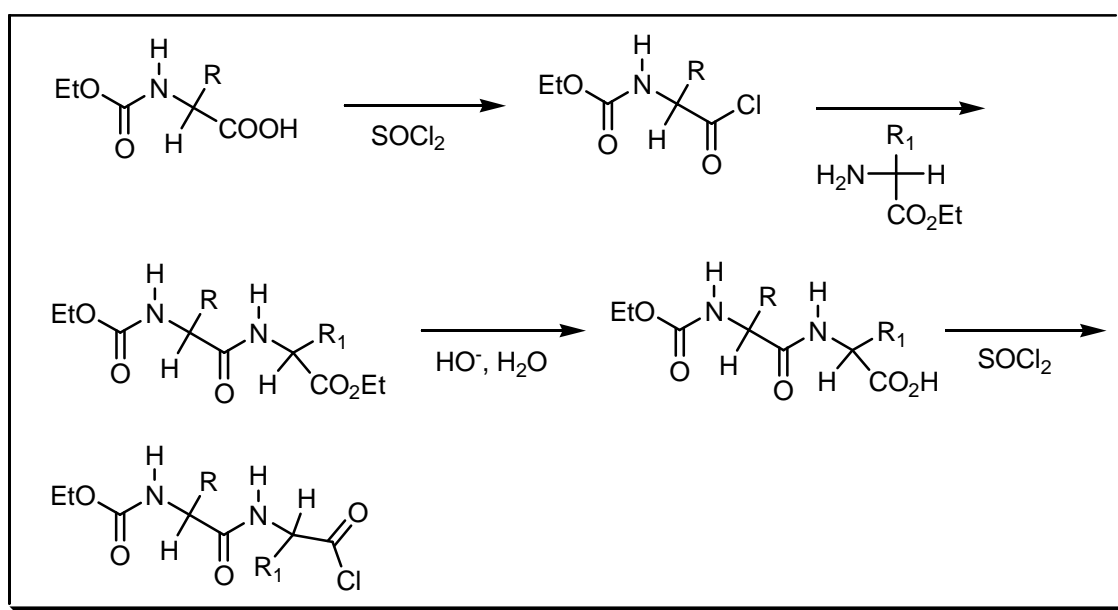
#### Method 1 :



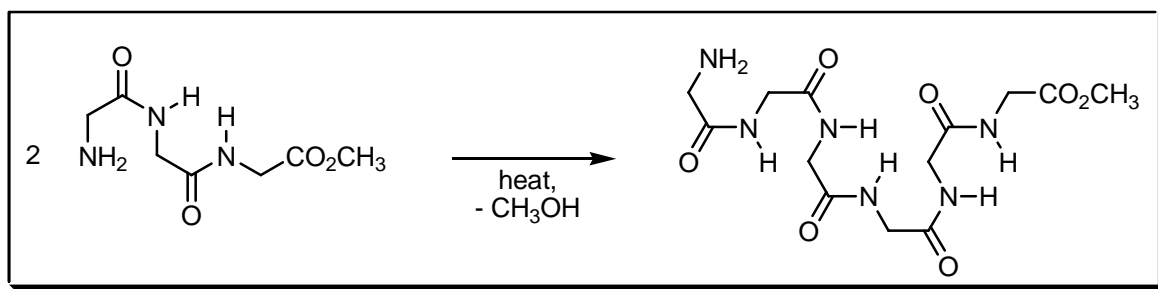
**Method 2 :**

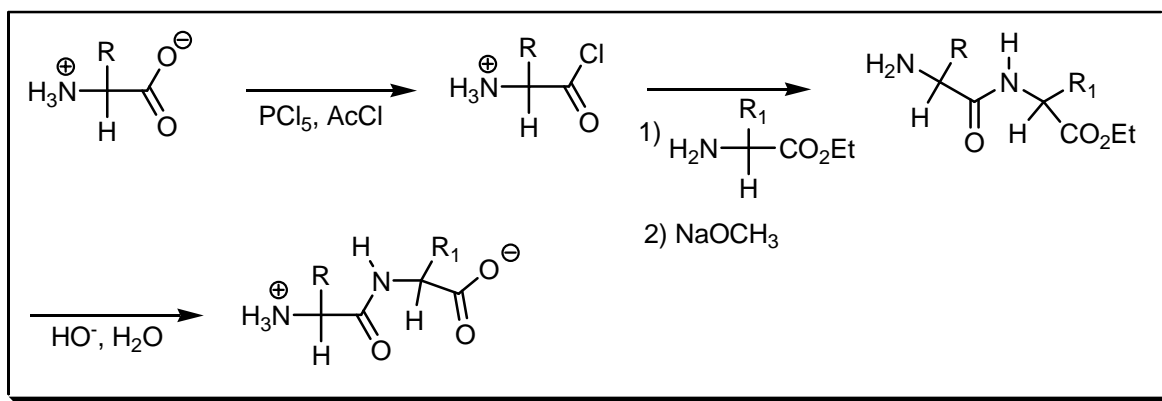
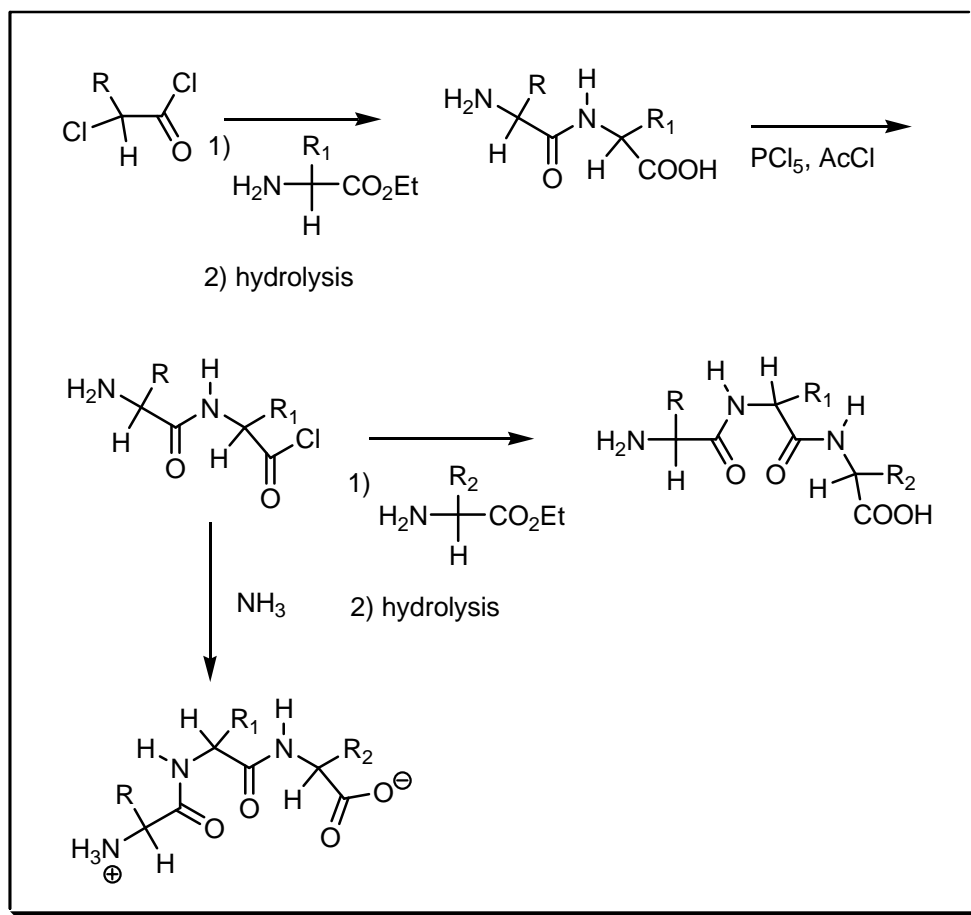


**Method 3 :**



**Method 4 :**



**Method 5 :****Method 6 :****NOTES :**

**Method 1 :** The amino acid esters on heating yield 2,5-diketopiperazines which on partial hydrolysis give dipeptides.

**Method 2 :** The amino group of an amino acid is activated by forming the methyl or ethyl ester. It is then protected by formation of the ethoxy carbonyl derivative. This derivative on treatment with a second amino acid ester forms a dipeptide with the loss of ethanol. The method becomes increasingly difficult as the peptide chain is increased in length.

**Method 3 :** Alternatively, the ethoxycarbonyl-amino acid is converted by thionyl chloride into the acid chloride, which is condensed with a second amino acid ester. The peptide ester thus formed can in turn be saponified and converted into the acid chloride and condensed with a second amino acid ester and so on. It is impossible to remove the ethoxycarbonyl group.

**Method 4 :** Esters of tripeptides lose alcohol on heating and form hexapeptide esters.

**Method 5 :** An amino acid is converted into the acid chloride with phosphorous pentachloride in acetyl chloride. This gives a peptide ester on treatment with an amino acid ethyl ester followed by neutralisation with sodium methoxide. The peptide ester can be saponified.

**Method 6 :** An  $\alpha$ -chloro- or bromo-acyl chloride is treated with an amino acid ester and the condensation product is hydrolysed to the acid and converted to the acid chloride with phosphorous pentachloride in acetyl chloride. This is then condensed with a second amino acid ester and so on. The terminal chlorine can be replaced by  $\text{NH}_2$  with the use of ammonia.

See also **Bergmann – Zervars**, **Leuchs – Bergmann** and **Sheehan – Frank** reactions.

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#### REFERENCES :

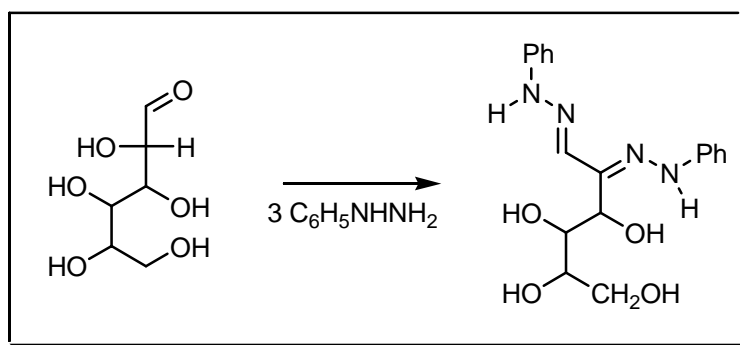
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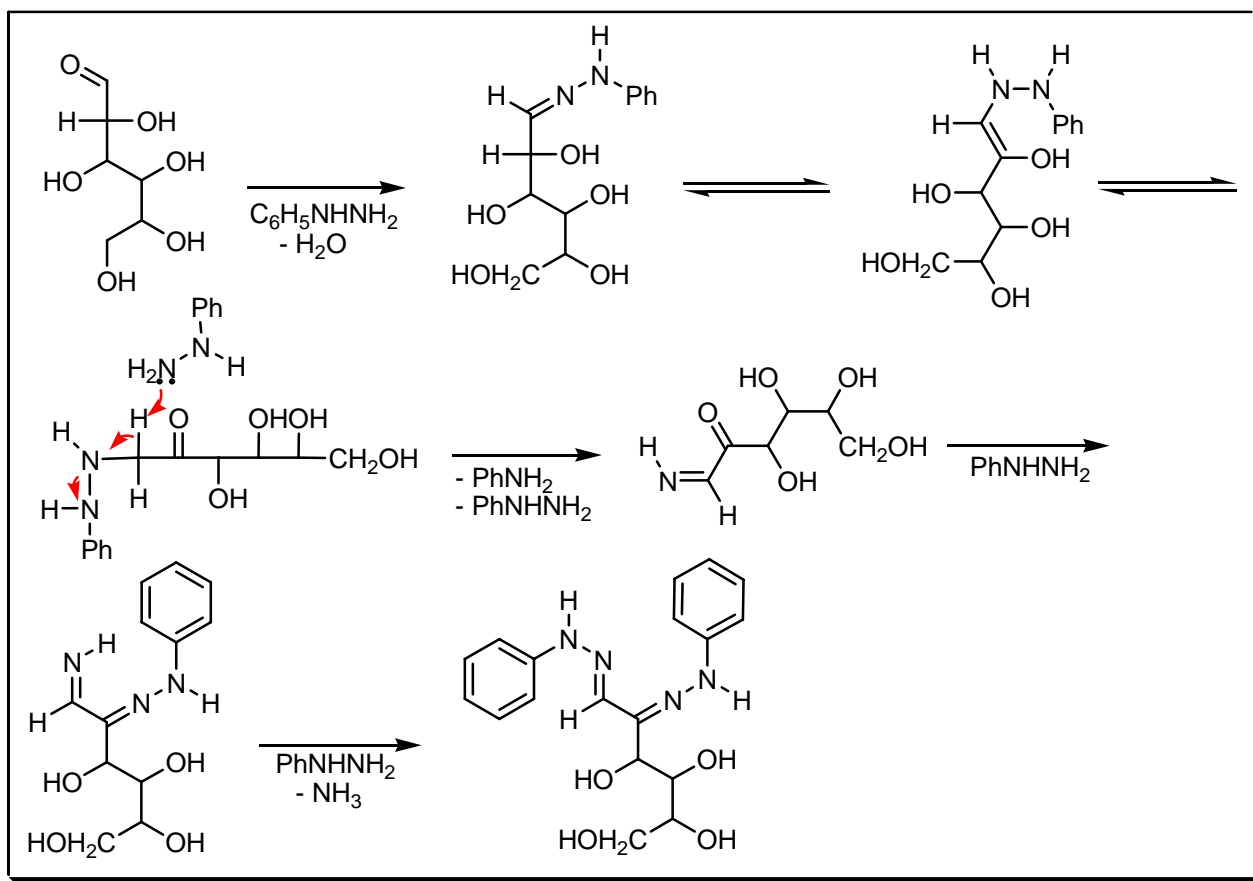
#### COMMENTS :

## FISCHER PHENYLHYDRAZINE AND OXAZONE REACTION

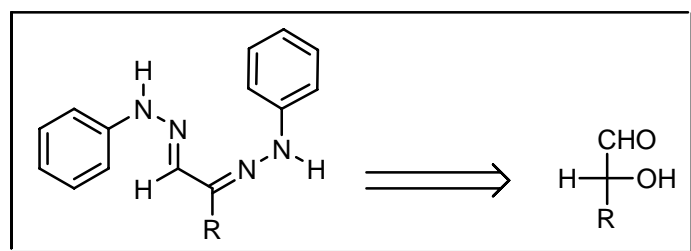
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :





## NOTES :

When one molecule of phenyl hydrazine acts upon one molecule of an aldose or ketose a hydrazone results which in most cases is very soluble in water, but if three molecules of the hydrazine react (one of which is reduced to ammonia and aniline) insoluble crystalline substances result, termed osazones, which readily characterises the sugar from which they are obtained. An electron-attracting group in the phenyl hydrazine promotes osazone formation. See also **Barry** degradation and **Ohle** cleavage.

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## REFERENCES :

- 1) E. Fischer, *Ber. Dtsch. Chem. Ges.*, 1884, **17**, 579.
- 2) F. Weygand, *Ber. Dtsch. Chem. Ges.*, 1940, **73**, 1284.
- 3) H.H. Stroh; A. Arnold; H.G. Scharnow, *Chem. Ber.*, 1965, **98**, 1404.

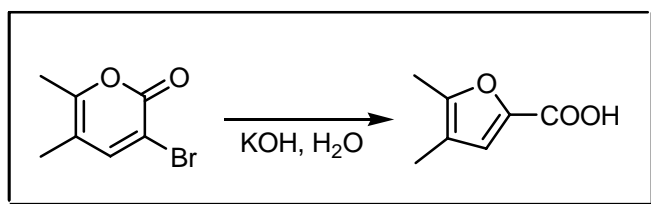
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## COMMENTS :

## FITTIG – EGBERT REARRANGEMENT

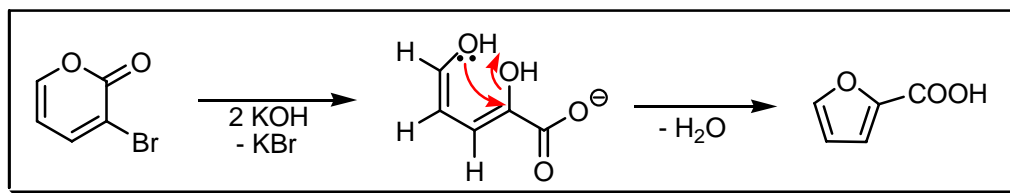
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### EXAMPLE :

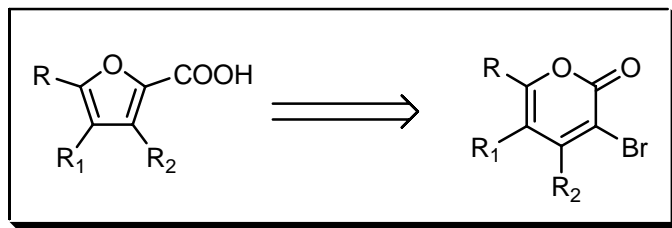


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### MECHANISM :



## DISCONNECTION :



## NOTES :

3-Bromo-2H-pyran-2-ones on treatment with alkali rearrange to form furan-2-carboxylic acids.

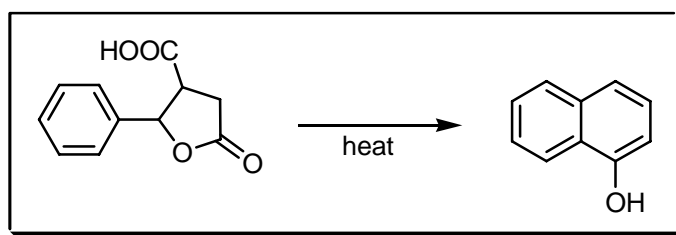
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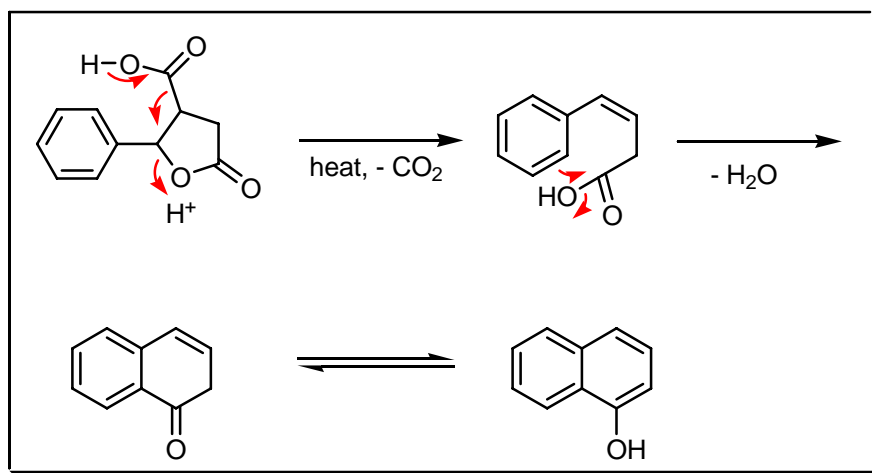
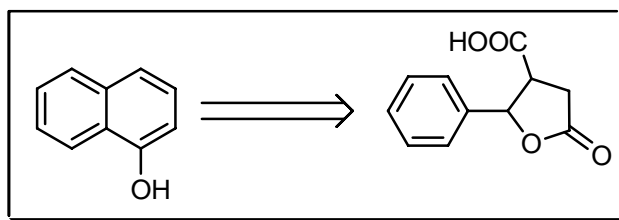
- 1) R. Fittig; G. Egbert, *Liebigs Ann. Chem.*, 1883, **216**, 162.
- 2) W. Will; P. Beck, *Ber. Dtsch. Chem. Ges.*, 1886, **19**, 1777.
- 3) F. Feist, *Ber. Dtsch. Chem. Ges.*, 1901, **32**, 1992.

## COMMENTS :

## FITTIG – ERDMANN SYNTHESIS

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

Phenylisocrotonic acids when heated yield  $\alpha$ -naphthols. Phenylparaconic acids react in a similar way.

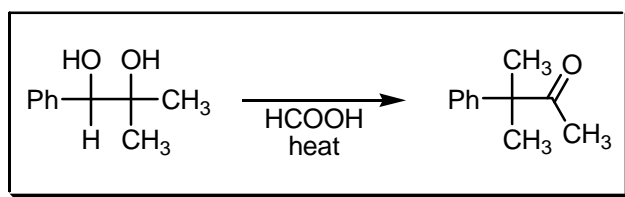
**REFERENCES :**

- 1) R. Fittig; H. Erdmann, *Ber. Dtsch. Chem. Ges.*, 1883, **16**, 43.
- 2) R. Fittig; H. Erdmann, *Liebigs Ann. Chem.*, 1885, **227**, 242.
- 3) A. Kreutz, *Liebigs Ann. Chem.*, 1902, **321**, 130.
- 4) R. Fittig, *Liebigs Ann. Chem.*, 1904, **330**, 292.

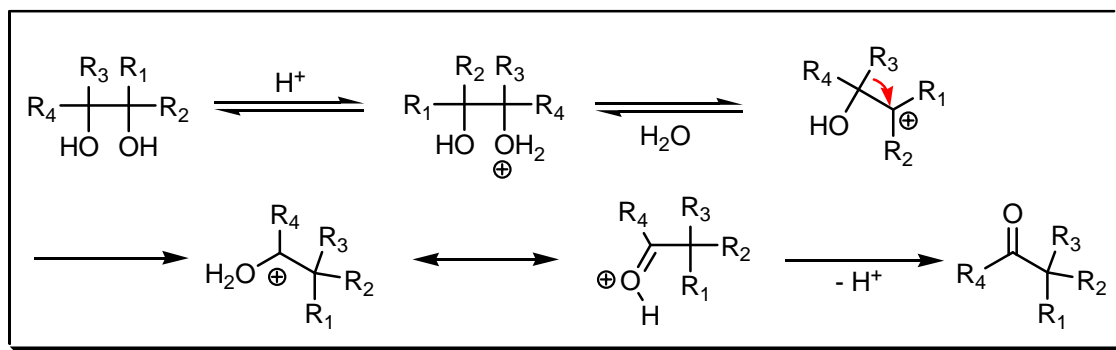
**COMMENTS :**

## FITTIG PINACOLONE REARRANGEMENT

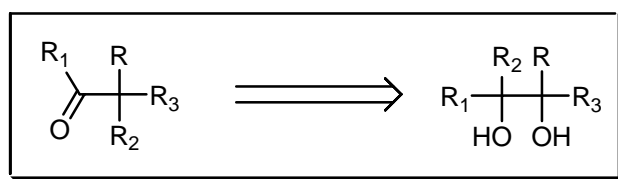
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The acid-catalysed carbocation rearrangement of 1,2-diols to ketones. See also **Wagner – Meerwein** rearrangement.

### REFERENCES :

March : 1072

Smith – March : 1396

Org. Synth. : 5, 91; 14, 12; 42, 38

Org. Synth. Coll. Vol. : 1, 462; 2, 73; 5, 326

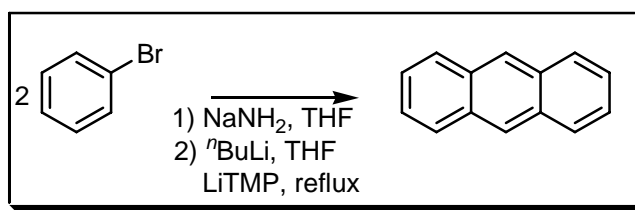
- 1) R. Fittig, *Liebigs Ann. Chem.*, 1860, **114**, 54.
  - 2) T. Zincke, *Ber. Dtsch. Chem. Ges.*, 1876, **9**, 1761.
  - 3) N.C. Dens; C. Perizzolo, *J. Org. Chem.*, 1957, **22**, 836.
  - 4) R.D. Sands; D.G. Botteron, *J. Org. Chem.*, 1963, **28**, 2690.
  - 5) K. Suzuki; E. Katayama; G.-I. Tsuchihashi, *Tetrahedron Lett.*, 1983, **24**, 4997.
  - 6) M. de Lezaeta; W. Sattar; P. Svoronos; S. Karimi; G. Subramaniam, *Tetrahedron Lett.*, 2002, **43**, 9307.
- 

**COMMENTS :**

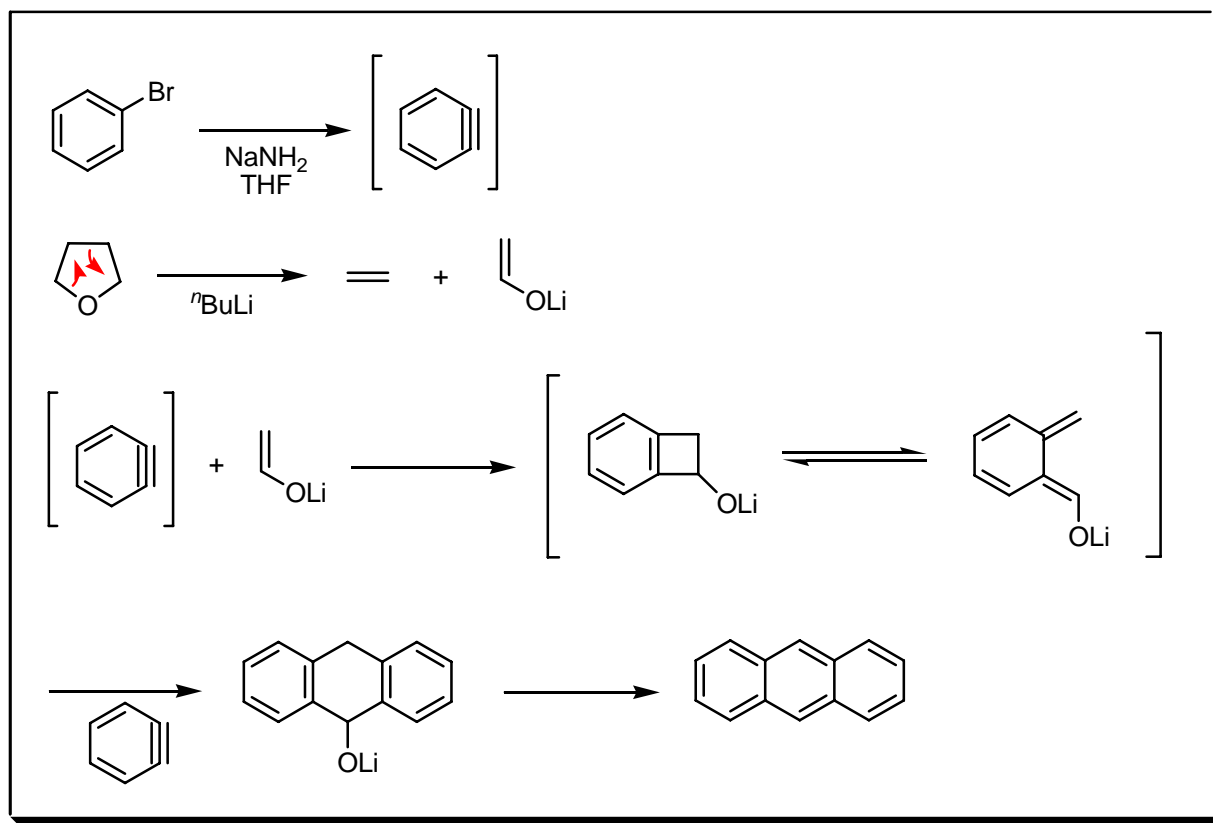
## FLEMING – MAH ANTHRACENE SYNTHESIS

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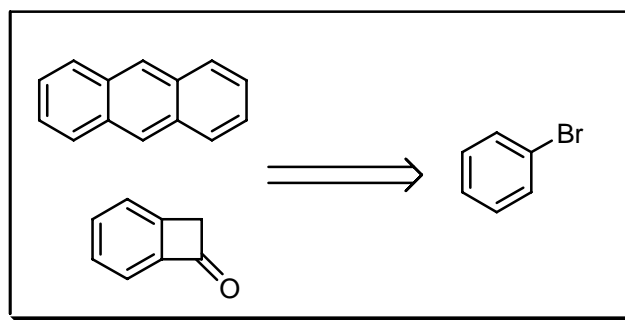
**EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

In the classic example anthracene is easily prepared in one-step from bromobenzene by using *N*-lithio-2,2,6,6-tetramethylpiperidine in THF. This reaction has been extended to the formation of benzocyclobutenones.

## REFERENCES :

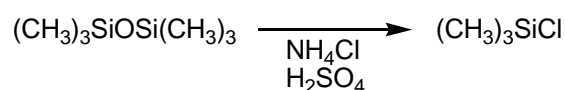
- 1) I. Fleming; T. Mah, *J. Chem. Soc., Perkin Trans. 1*, 1975, 964.
- 2) R.V. Stevens; G.S. Bisacchi, *J. Org. Chem.*, 1982, **47**, 2393.
- 3) R.V. Stevens; G.S. Bisacchi, *J. Org. Chem.*, 1982, **47**, 2396.
- 4) L.S. Liebeskind; L.J. Lescosky; C.M. McSwain, jr., *J. Org. Chem.*, 1989, **54**, 1435.
- 5) J.J. Fitzgerald; N.E. Drysdale; R.A. Olofson, *J. Org. Chem.*, 1992, **57**, 7122.

**COMMENTS :**

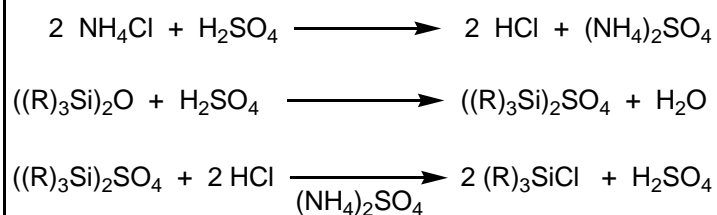
**FLOOD REACTION**

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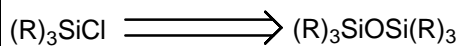
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

Trialkylhalogenosilanes are obtained by treatment of a concentrated sulfuric acid solution of a hexa-alkyldisiloxane with an ammonium halide or by treatment of the intermediate trialkylsilyl sulfate with hydrogen chloride in the presence of ammonium bisulfate (prevents reversal of last step). See also **Eaborn** reaction.

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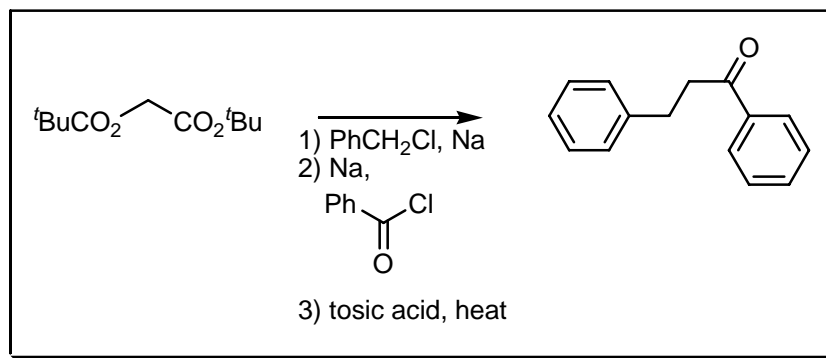
**REFERENCES :**

- 1) E.A. Flood, *J. Am. Chem. Soc.*, 1933, **55**, 1735.
  - 2) L.H. Sommer; G.T. Kerr; F.C. Whitmore, *J. Am. Chem. Soc.*, 1948, **70**, 445.
  - 3) L. Birkofer; O. Stuhl, *Top. Curr. Chem.*, 1980, **88**, 33.
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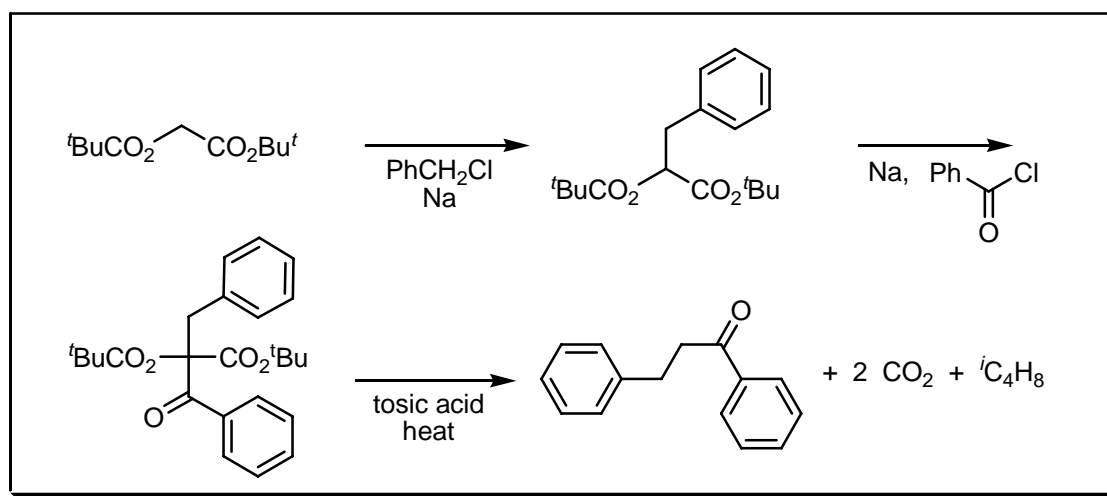
COMMENTS :

## FONKEN – JOHNSON SYNTHESIS

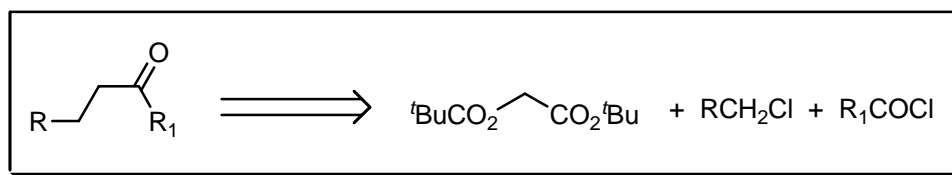
EXAMPLE :



MECHANISM :



DISCONNECTION :





## NOTES :

Di-*tert*-butyl acylalkylmalonates, when heated with *p*-toluenesulfonic acid or anhydrous acetic acid give isobutylene, carbon dioxide and a ketone. This is a modification of the **Bowman debenzylation** reaction. See also **Baudart**, **Bowman** debenzylation, **Kapp – Knoll** and **Robinson – Robinson** reactions.

## REFERENCES :

Org. Synth. : 34, 26

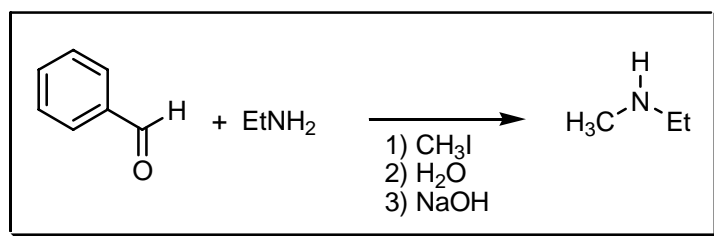
Org. Synth. Coll. Vol. : 4, 261

G.S. Fonken; W.S. Johnson, *J. Am. Chem. Soc.*, 1952, **74**, 831.

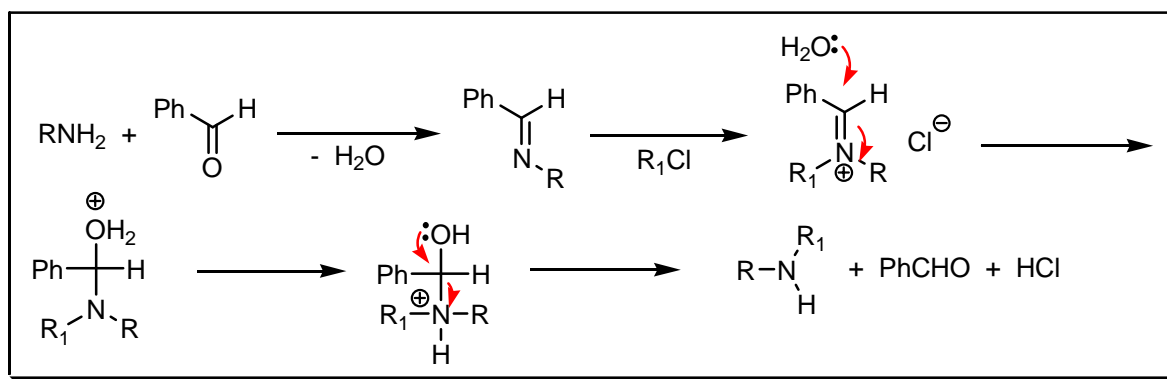
## COMMENTS :

## FORSTER – DECKER REACTION

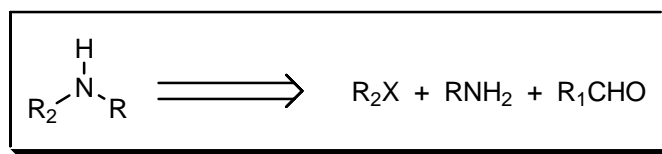
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The conversion of a primary amine into a secondary amine by condensation with an aldehyde, followed by the addition of alkyl halide to the **Schiff's** base and subsequent hydrolysis. See also **Eschweiler – Clarke**, **Henze – Humphries** and **Schiff** reactions.

## REFERENCES :

Houben – Weyl : 11/1, 108, 956

Org. Synth. : 44, 75

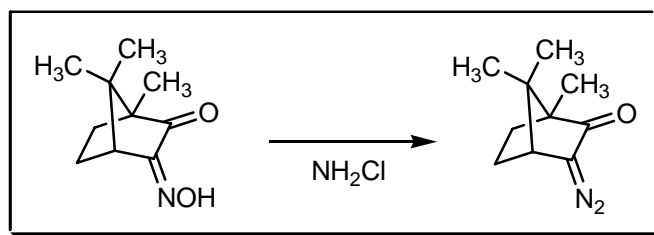
Org. Synth. Coll. Vol. : 5, 758

- 1) M.O.J. Forster, *J. Chem. Soc.*, 1899, **75**, 934.
- 2) H. Decker; P. Becker, *Liebigs Ann. Chem.*, 1913, **395**, 362.
- 3) H.G. Reiber; T.D. Stewart, *J. Am. Chem. Soc.*, 1940, **62**, 3026.
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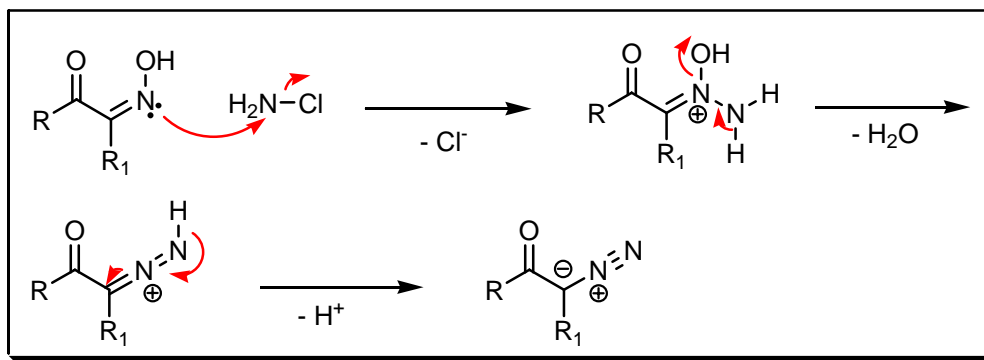
## COMMENTS :

## FORSTER REACTION

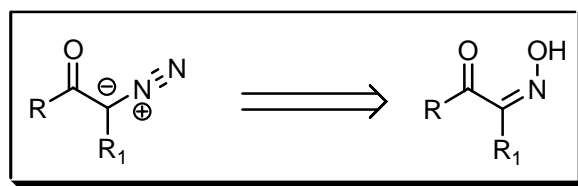
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The formation of diazo derivatives from oximes. See also **Bamford – Stevens** and **Cava** reactions.

### REFERENCES :

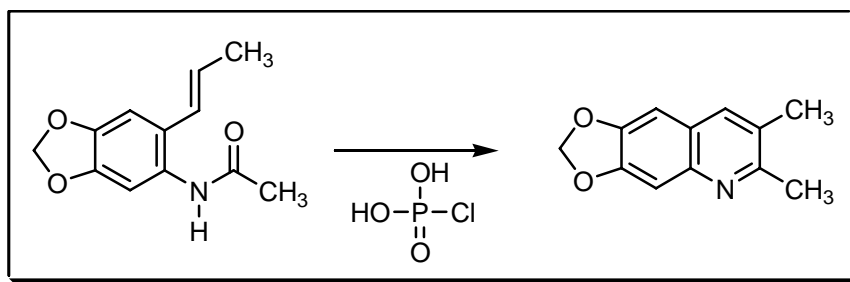
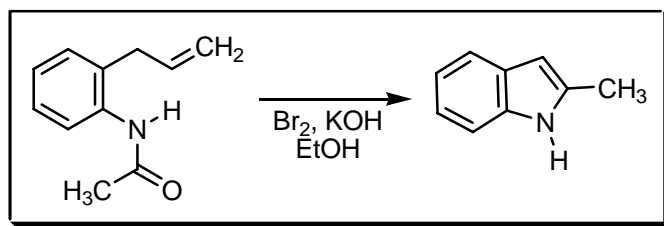
**Houben – Weyl** : 10/4, 582

- 1) M.O.J. Forster, *J. Chem. Soc.*, 1915, **107**, 260.
- 2) M.P. Cava; R.L. Little, *Chem. Ind. (London)*, 1957, 367.
- 3) W. Rundel, *Angew. Chem.*, 1962, **74**, 469.
- 4) M.P. Cava; B.R. Vogt, *J. Org. Chem.*, 1965, **30**, 3776.
- 5) A.M. van Leusen; J. Strating; D. van Leusen, *Tetrahedron Lett.*, 1973, **14**, 5207.
- 6) G. L'Abbe; J.P. Dekerk; M. Deketele, *J. Chem. Soc., Chem. Commun.*, 1983, 588.
- 7) G. L'Abbe; I. Luyten; S. Toppet, *J. Heterocycl. Chem.*, 1992, **29**, 713.

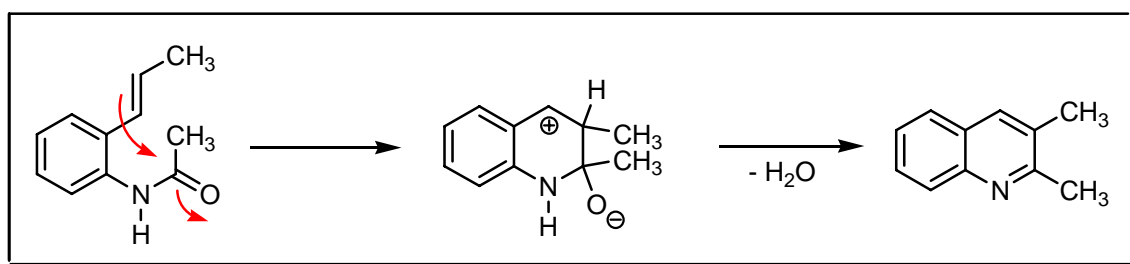
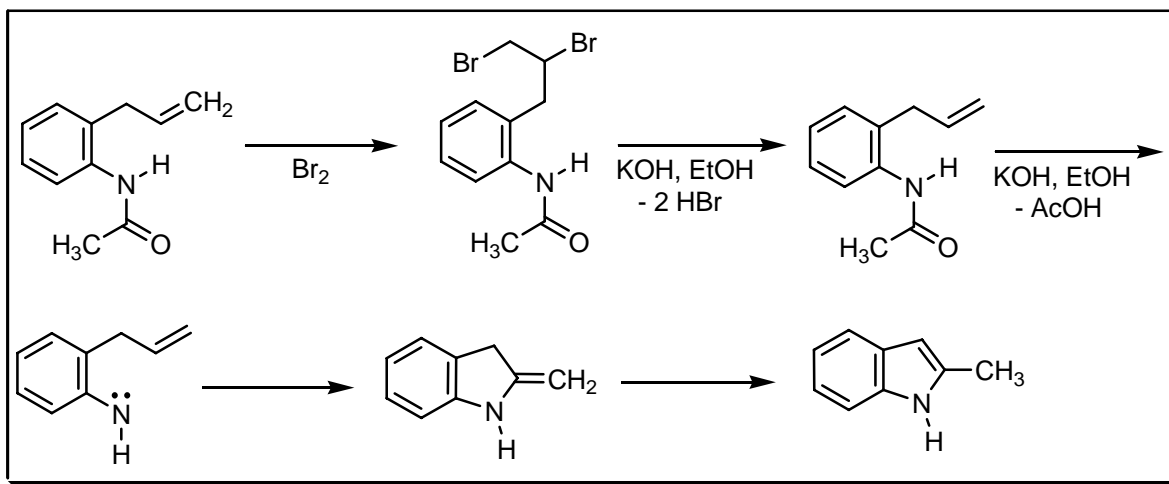
### COMMENTS :

## FOULDS – ROBINSON INDOLE / QUINOLINE SYNTHESIS

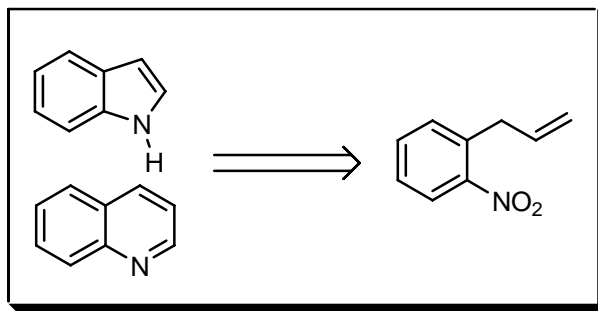
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

2-Allyl- or 2-vinyl-anilides on treatment with alcoholic alkali yield indoles, while on treatment with phosphoryl chloride quinoline derivatives are obtained. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

## REFERENCES :

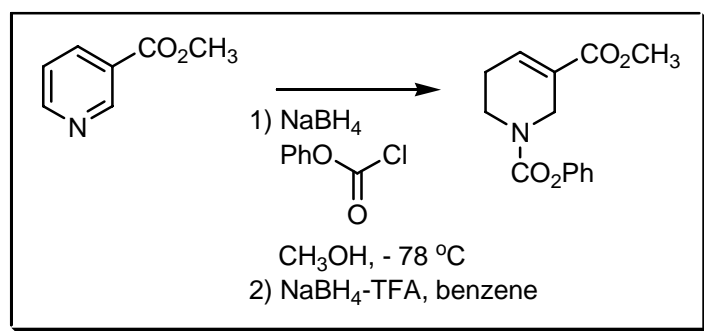
**Houben – Weyl** : **E7a**, 343

- 1) R.P. Foulds; R. Robinson, *J. Chem. Soc.*, 1914, **105**, 1963.
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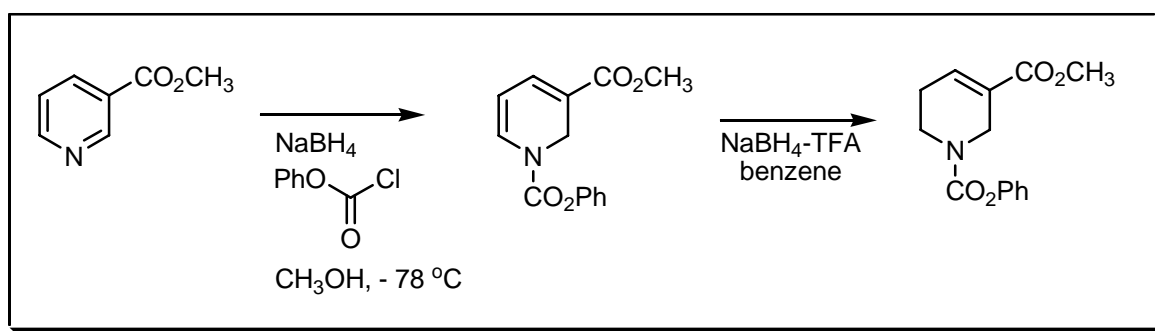
## COMMENTS :

## FOWLER SYNTHESIS

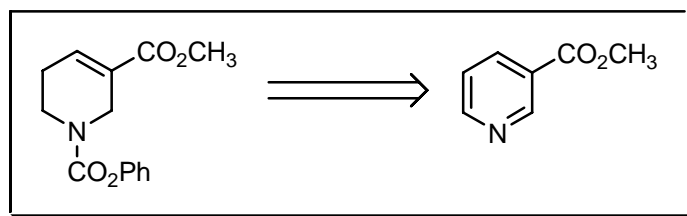
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This is the partial reduction of pyridines using a hydride source, sodium borohydride and sodium borohydride-trifluoroacetic acid.

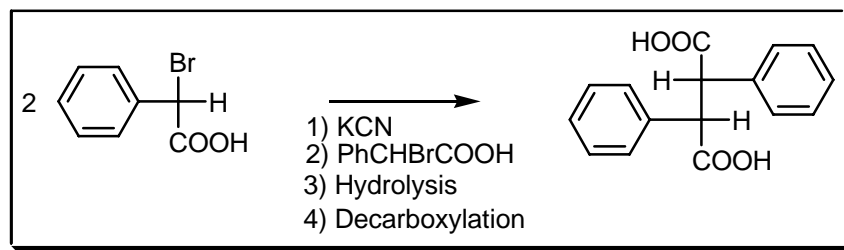
### REFERENCES :

- 1) F.W. Fowler, *J. Org. Chem.*, 1972, **37**, 1321.
- 2) R.J. Sundberg; J.D. Bloom, *J. Org. Chem.*, 1981, **46**, 4836.
- 3) R.J. Sundberg; G. Hamilton; C. Trindle, *J. Org. Chem.*, 1986, **51**, 3672.
- 4) G. Zhao; U.C. Deo; B. Ganem, *Org. Lett.*, 2001, **3**, 201.

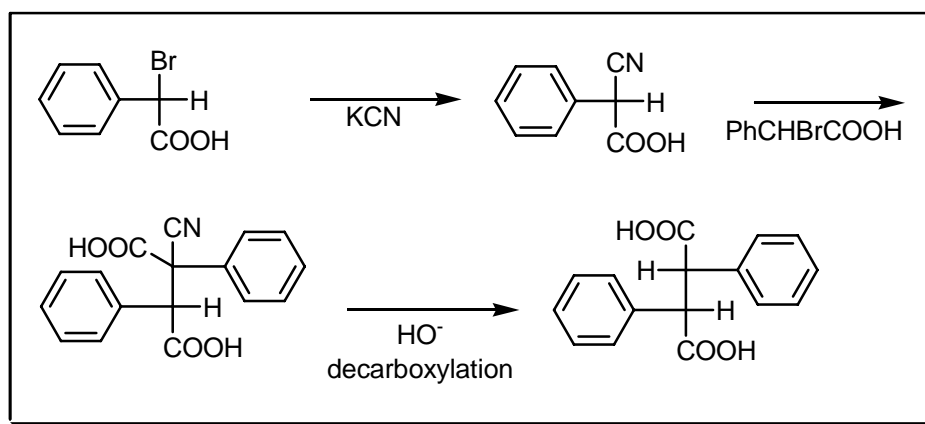
**COMMENTS :**

**FRANCHIMONT DICARBOXYLIC ACID SYNTHESIS**

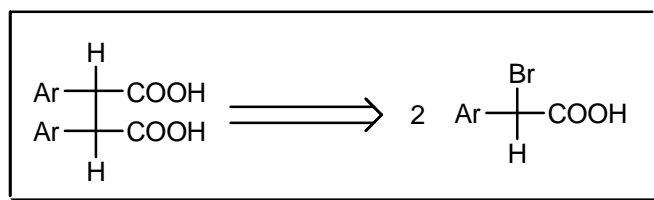
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

$\alpha$ -Bromo-acids or -esters react with potassium cyanide to yield cyanodicarboxylic acid derivatives, which can be hydrolysed and partially decarboxylated to give  $\alpha,\beta$ -dicarboxylic acids.

**REFERENCES :**

1) A.P.N. Franchimont, *Ber. Dtsch. Chem. Ges.*, 1872, **5**, 1048.

2) R.C. Fuson; O.R. Kreimeier; G.L. Nimmo, *J. Am. Chem. Soc.*, 1930, **52**, 4074.

3) H.N. Rydon, *J. Chem. Soc.*, 1936, 593.

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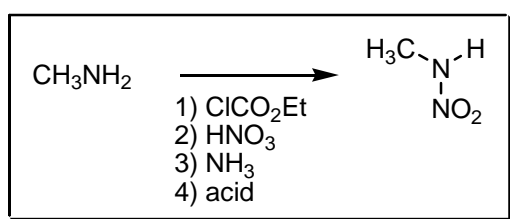
**COMMENTS :**

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**FRANCHIMONT NITRAMINE REACTION**

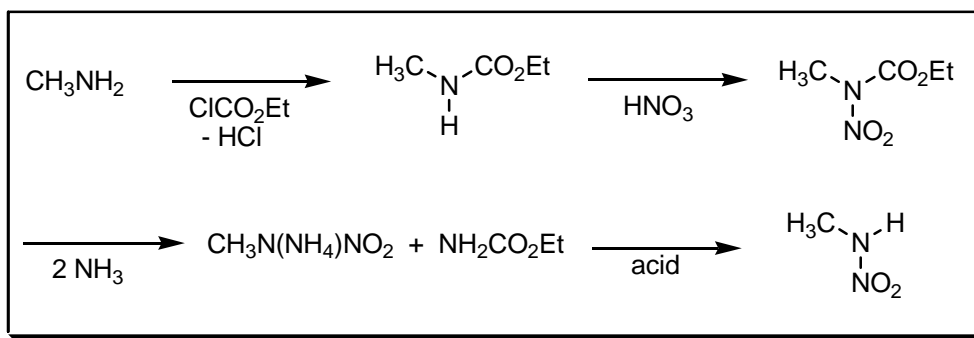
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**EXAMPLE :**



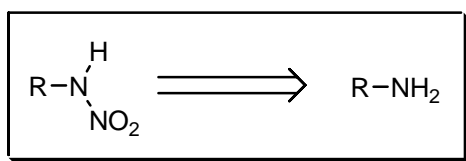
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**MECHANISM :**



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**DISCONNECTION :**



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**NOTES :**

The amine is condensed with e.g. ethyl chloroformate and the product nitrated to the secondary nitramide which is decomposed using alkali to yield the salt of the required nitramine.

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**REFERENCES :**

1) E.A. Klobbie, *Recl. Trav. Chim. Pays-Bas*, 1887, **7**, 31.



2) A.P.N. Franchimont; E.A. Klobbie, *Recl. Trav. Chim. Pays-Bas*, 1888, **8**, 17.

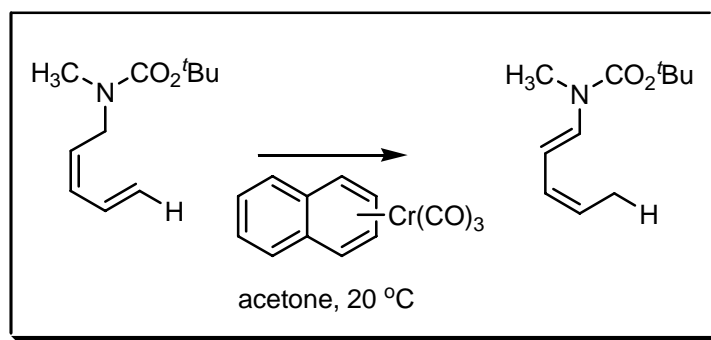
3) A.P.N. Franchimont, *Recl. Trav. Chim. Pays-Bas*, 1894, **13**, 308.

4) A.H. Lamberton, *J. Chem. Soc., Quat. Rev.*, 1951, **5**, 75.

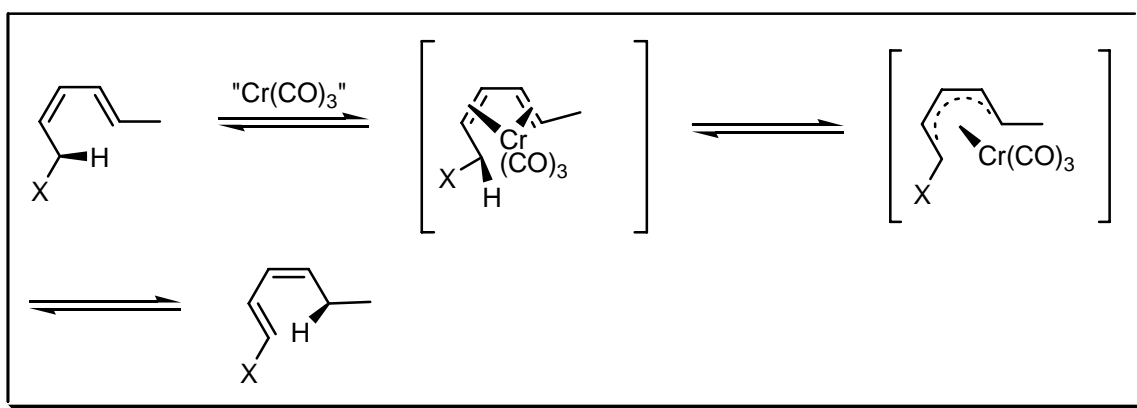
COMMENTS :

## FRANKEL – SHIBASAKI REARRANGEMENT

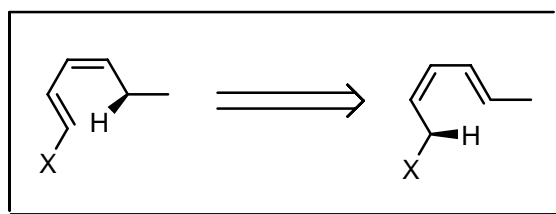
EXAMPLE :



MECHANISM :



DISCONNECTION :

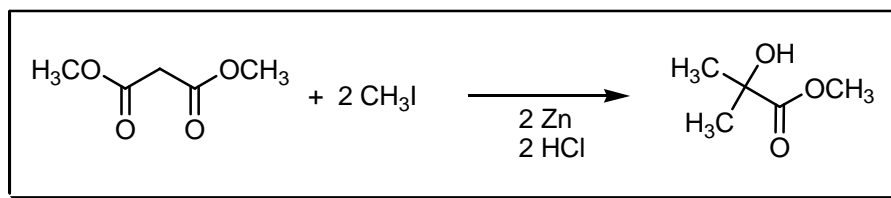
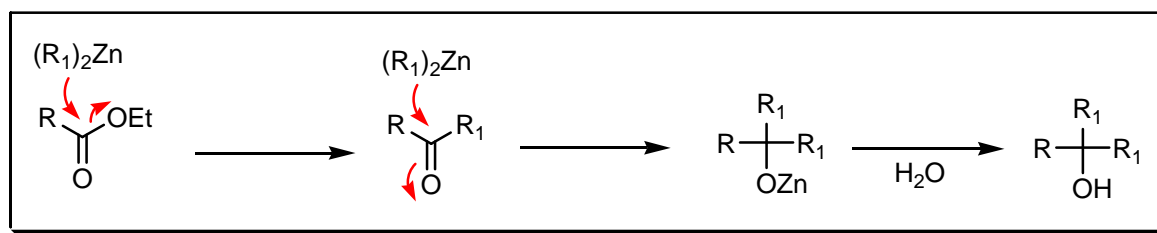
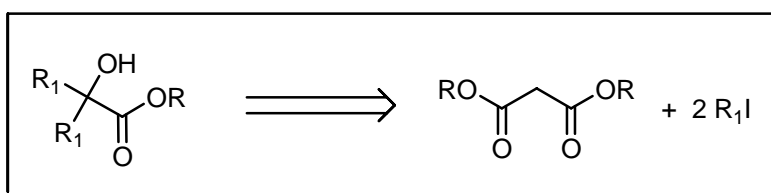


**NOTES :**

Arene tricarbonyl chromium complexes have the ability to catalyse the isomerisation (1,5-sigmatropic rearrangement) of conjugated dienes or dienamides.

**REFERENCES :**

- 1) E.N. Frankel; E. Selke; C.A. Glass, *J. Am. Chem. Soc.*, 1968, **90**, 2446.
- 2) M. Sodeoka; M. Shibasaki, *Chem. Lett.*, 1984, 579.
- 3) R. Noyori; H. Takaya, *Acc. Chem. Res.*, 1990, **23**, 345.
- 4) M. Sodeoka; H. Yamada; M. Shibasaki, *J. Am. Chem. Soc.*, 1990, **112**, 4906.
- 5) M. Sodeoka; M. Shibasaki, *Synthesis*, 1993, 643.

**COMMENTS :****FRANKLAND – DUPPA REACTION****EXAMPLE :****MECHANISM :****DISCONNECTION :**

**NOTES :**

The condensation of dialkyl oxalate with alkyl halides in the presence of zinc to give derivatives of glycolic acid. See also **Frankland**, **Reformatsky** and **Schorigin – Wanklyn** reactions.

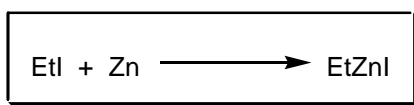
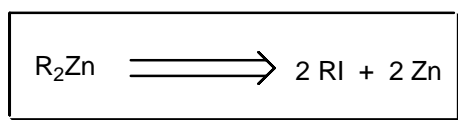
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**REFERENCES :**

Houben – Weyl : 13/2a, 741

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- 1) E. Frankland, *Liebigs Ann. Chem.*, 1863, **126**, 109.
  - 2) E. Frankland; D.F. Duppa, *Liebigs Ann. Chem.*, 1865, **135**, 25.
- 

**COMMENTS :****FRANKLAND SYNTHESIS****EXAMPLE :****DISCONNECTION :****NOTES :**

Alkyl zinc halides or dialkyl zinc compounds are obtained by treating alkyl halides with zinc. The process can also be applied to aryl radicals. See also **Grignard** reaction.

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**REFERENCES :**

Houben – Weyl : 13/2a, 570  
Org. Synth. : 12, 86  
Org. Synth. Coll. Vol. : 2, 184

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- 1) E. Frankland, *Liebigs Ann. Chem.*, 1849, **71**, 171.

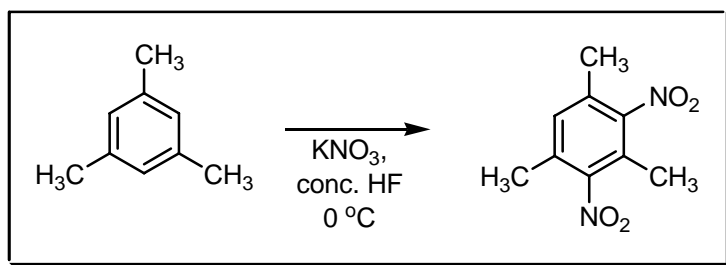
- 2) E. Frankland, *Liebigs Ann. Chem.*, 1853, **85**, 329.  
3) E. Frankland, *Liebigs Ann. Chem.*, 1853, **85**, 3641.  
4) W.H. Broch, *Nature*, 1996, **383**, 591.  
5) D. Seyferth, *Organometallics*, 2001, **20**, 2940.
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**COMMENTS :**

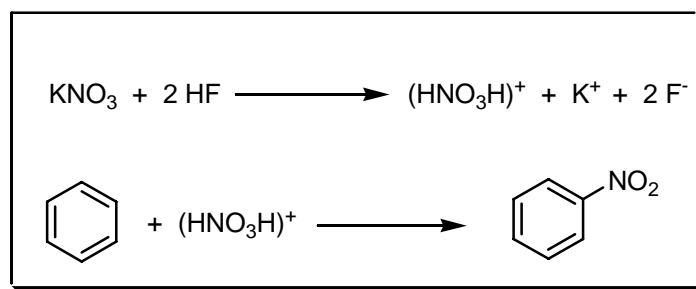
## FREDENHAGEN PROCESS

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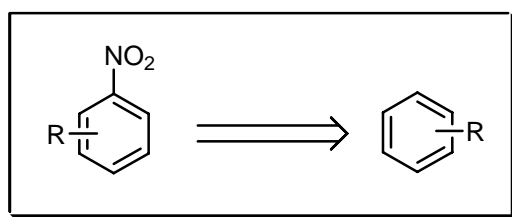
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



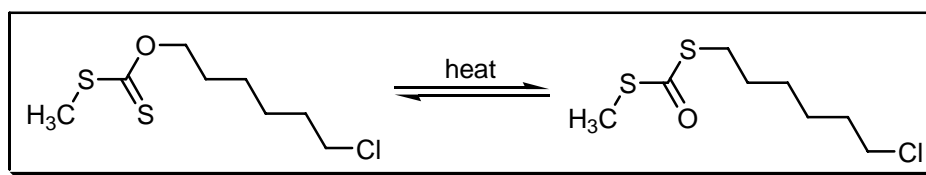
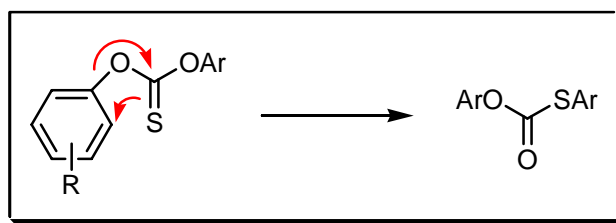
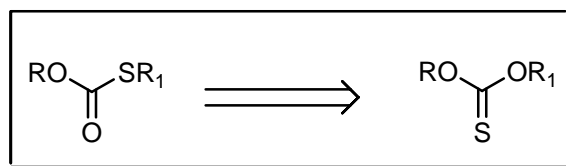
**NOTES :**

The nitration agent consists of a nitrate, e.g. potassium nitrate in anhydrous or highly concentrated hydrogen fluoride. This is one of the several methods of nitrating aromatic compounds.

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- 

**COMMENTS :****FREUDENBERG – SCHÖNBERG XANTHATE REARRANGEMENT****EXAMPLE :****MECHANISM :****DISCONNECTION :**

## NOTES :

The rearrangement of S-methyl xanthates to S-methyldithiocarbonates (conversion of alcohols to thiols *via* xanthates, also phenols to thiophenols *via* thiocarbamates.) See also **Beckmann** rearrangement, **Hayashi** rearrangement, **Newman – Karnes – Kwart** and **Smiles** reactions.

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## REFERENCES :

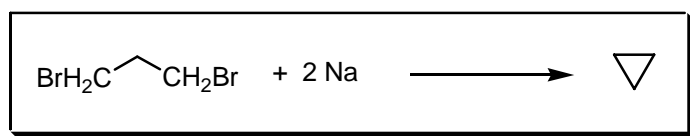
Org. React. : 14, 1

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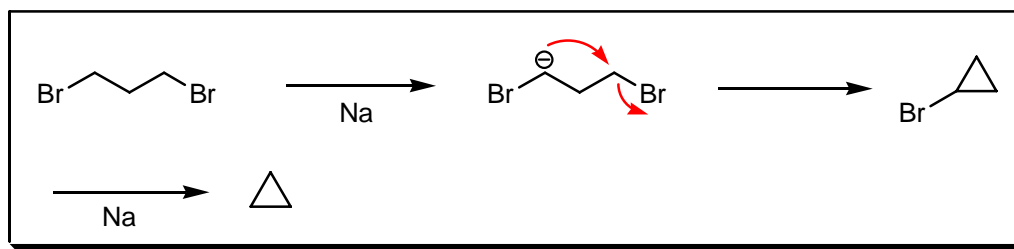
## COMMENTS :

## FREUND REACTION

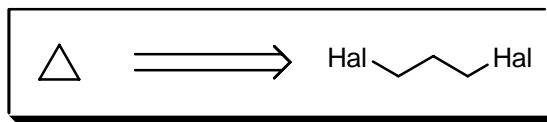
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The production of cyclic hydrocarbons by the internal condensation of dihalogenohydrocarbons with sodium. This method can also be used for 3-, 4-, 5- and 6-membered rings but it best for 3-membered. See also **Charette**, **Gustavson**, **Hass** cyclopropane, **Ipatiew** cyclopropane, **Kishner**, **Mousseron – Fraisse – McCoy**, **Nerdel**, **Perkin**, **Simmons – Smith** and **Wurtz – Fittig** reactions.

## REFERENCES :

Houben – Weyl : 13/1, 492

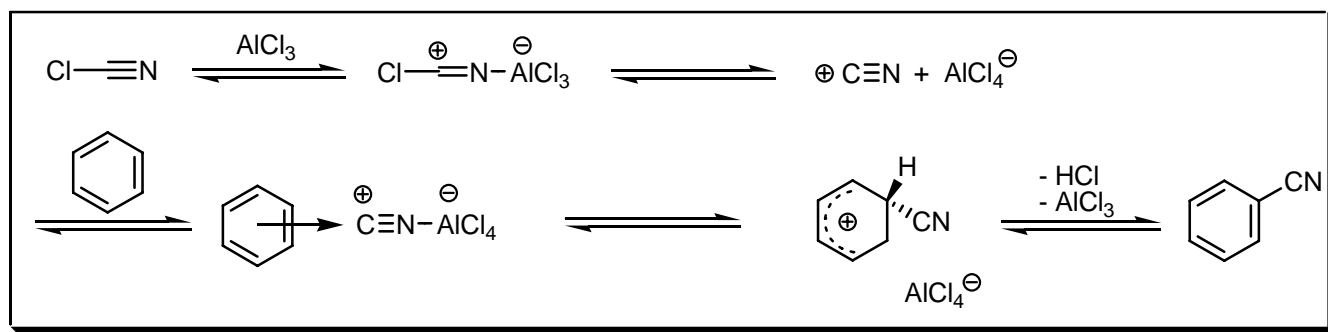
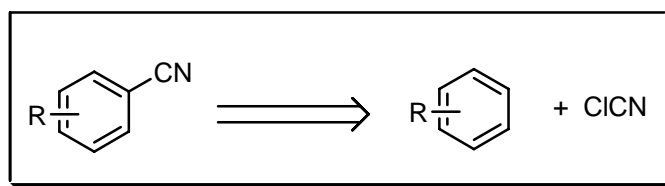
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## COMMENTS :

## FRIEDEL – CRAFTS – KARRER REACTION

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

The formation of aromatic nitriles by the action of cyanogens halide on aromatic hydrocarbons in the presence of finely divided aluminium chloride. The exact mechanism is not clear. Double aluminium chloride activation has been proposed.

**REFERENCES :**

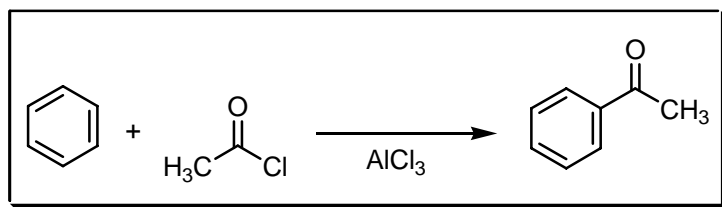
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- 5) V.P. Wystrach, 1952, US patent 2584409
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**COMMENTS :**

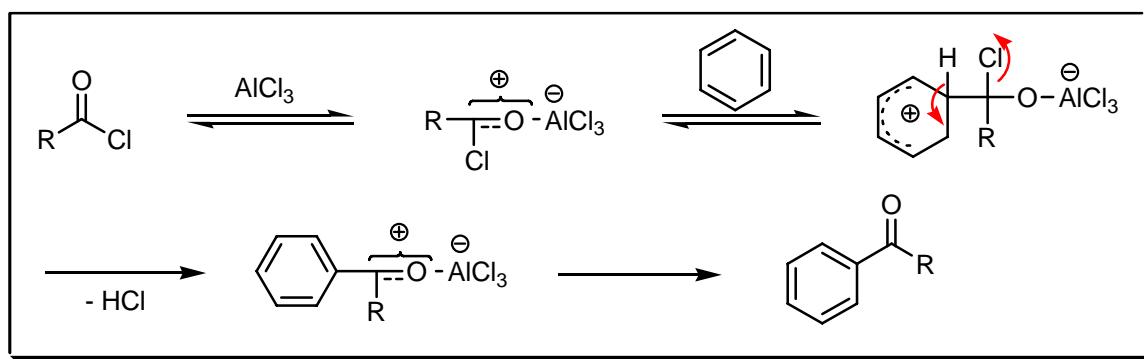
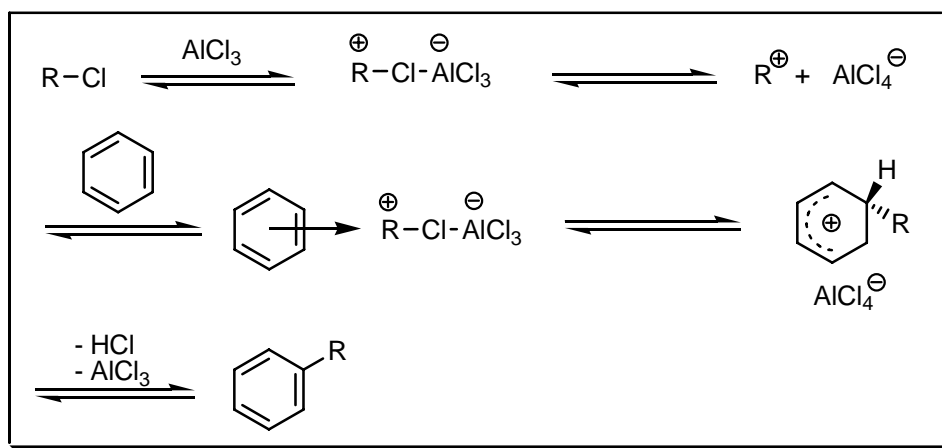


## FRIEDEL – CRAFTS REACTION

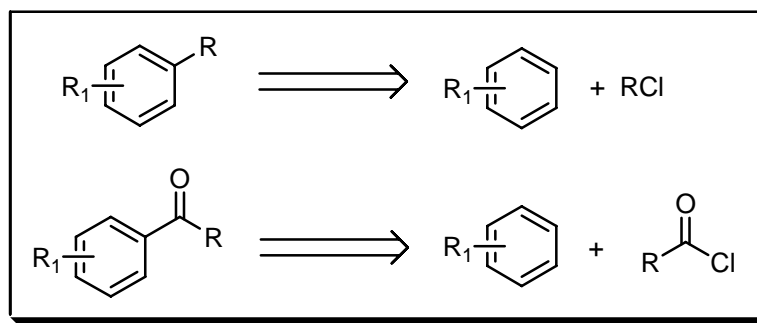
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The condensation of alkyl and acyl halides with aromatic compounds in the presence of aluminium chloride or a related acid catalyst to give hydrocarbons or ketones. The scope of the reaction is wide and comprises of many types of organic condensation reactions promoted by aluminium chloride or similar catalysts. During the recent few decades the term has been freely used to include olefins, alcohols, anhydrides, esters, cyclic and open chain ethers and polymethylenes, e.g. cyclopropane as reactants, and such diverse substances as zinc chloride, ferric chloride, titanium tetrachloride, boron trifluoride, hydrogen fluoride, phosphoric oxide and sulfuric acid as reagents. Some open or cyclic alkanes have been found to react. If the acid chloride and aluminium chloride complex is formed first and then the hydrocarbon is added the reaction is known under the **Perrier** modification. The use of nitrobenzene as the solvent in the application to phenols is known as the **Behn** reaction. The **Vilsmeier – Haack** modification involves the use of an anilide in the presence of phosphorous oxychloride. The use of anhydrous ferric chloride in the **Friedel – Crafts** reaction is known as the **Nencki** modification. It is a milder catalyst than aluminium chloride and can be employed with reactive molecules when the latter is too drastic. The **Radziewanowski** modification is the alkylation and arylation of aromatics with alkyl and arylhalogens in the presence of aluminium and hydrogen chloride to circumvent the use of the moisture sensitive aluminium chloride. Photo-**Friedel – Crafts** acylation of 1,4-naphthoquinones has been reported and also alkylations with silicon compounds. See also **Balshohn, Comins, Eijkman, Emmert – Asendorf, Gattermann – Ehrhardt, Haworth, Prins** and **Vilsmeier – Haack** reactions.

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**March** : 536

**Smith – March** : 712

**Smith** : 1313, 1324

**Smith 2<sup>nd</sup>** : 6, 847, 1080, 1090

**Houben – Weyl** : **4/2**, 61, 767; **8**, 377; **E5**, 1447; **E6a**, 439, 852, 977; **E7b**, 290; **E8a**, 750, 986; **E19c**, 362

**Houben – Weyl** : **7/2a**, 284

**Org. Synth.** : **14**, 40; **21**, 103

**Org. Synth. Coll. Vol.** : **2**, 304; **3**, 761

**Org. React.** : **2**, 114; **3**, 1; **5**, 229; **18**, 1

**Org. Synth.** : **4**, 73, 81; **8**, 26; **10**, 32; **12**, 16; **23**, 100; **29**, 38

**Org. Synth. Coll. Vol.** : **1**, 95, 157, 548; **2**, 156, 248; **3**, 343, 841

**Science of Synthesis** : **1**, 757, 799, 947; **9**, 248, 352, 356, 510, 567; **10**, 45, 132, 148, 171, 212, 240, 252, 287, 318, 335, 407, 438, 534, 537, 592, 602, 725

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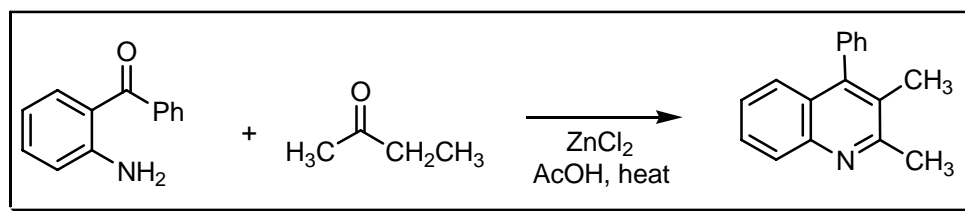
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**COMMENTS :**

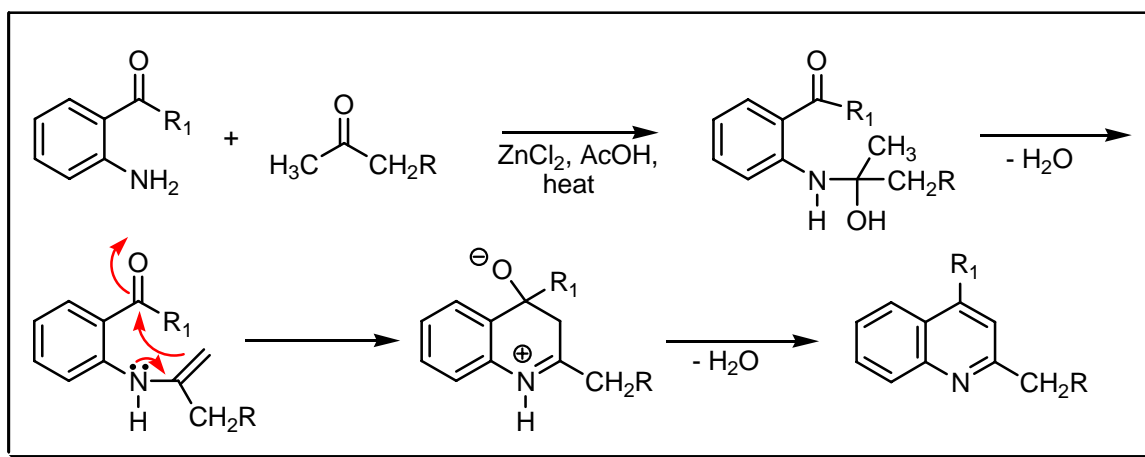
## FRIEDLÄNDER QUINOLINE SYNTHESIS

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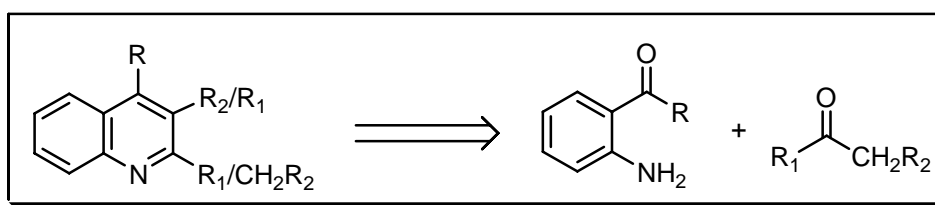
**EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

This reaction involves the condensation, acid- or base-catalysed, of an aromatic *o*-amino carbonyl derivative with a compound containing a methylene group  $\alpha$ - to the carbonyl. The orientation of the condensation depends on the orientation of the formed enolate or enol. The use of this reaction has been limited due to the limited availability of the *o*-aminobenzaldehydes. The **Borsche – Ried** modification uses **Schiff** bases instead of *o*-aminoarylcarbonyls. See also **Allan – Loudon**, **von Baeyer – Drewson** quinoline, **Camps**, **Combes** quinoline, **Conrad – Limpach**, **Doebner** quinoline, **Doebner – von Miller**, **Foulds – Robinson**, **Knorr** quinoline, **Meth–Cohn**, **von Niementowski** quinoline, **Pfitzinger – Borsche**, **Riehm** quinoline and **Skraup** quinoline reactions.

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**March** : 897

**Smith – March** : 1186

**Houben – Weyl** : **E8a**, 267, 278

**Org. React.** : **28**, 37

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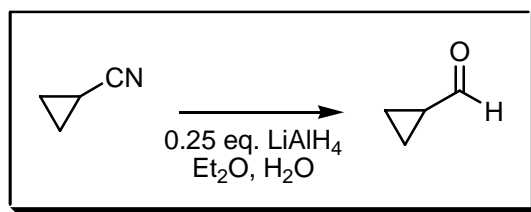
**COMMENTS :**

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**FRIEDMAN SYNTHESIS**

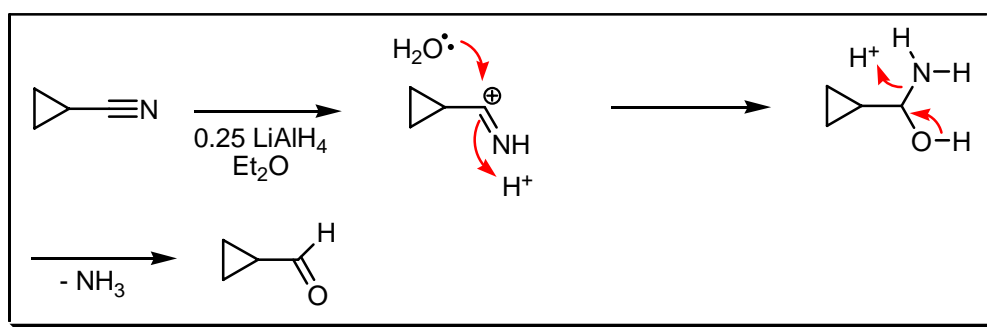
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**EXAMPLE :**



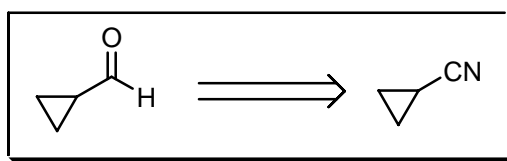
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**MECHANISM :**



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**DISCONNECTION :**

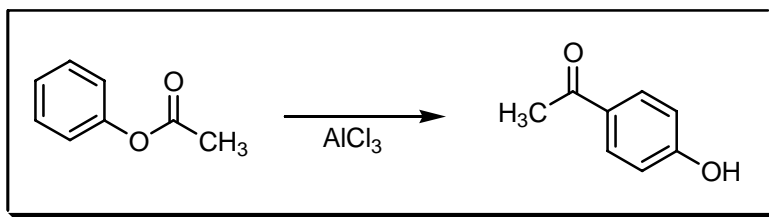
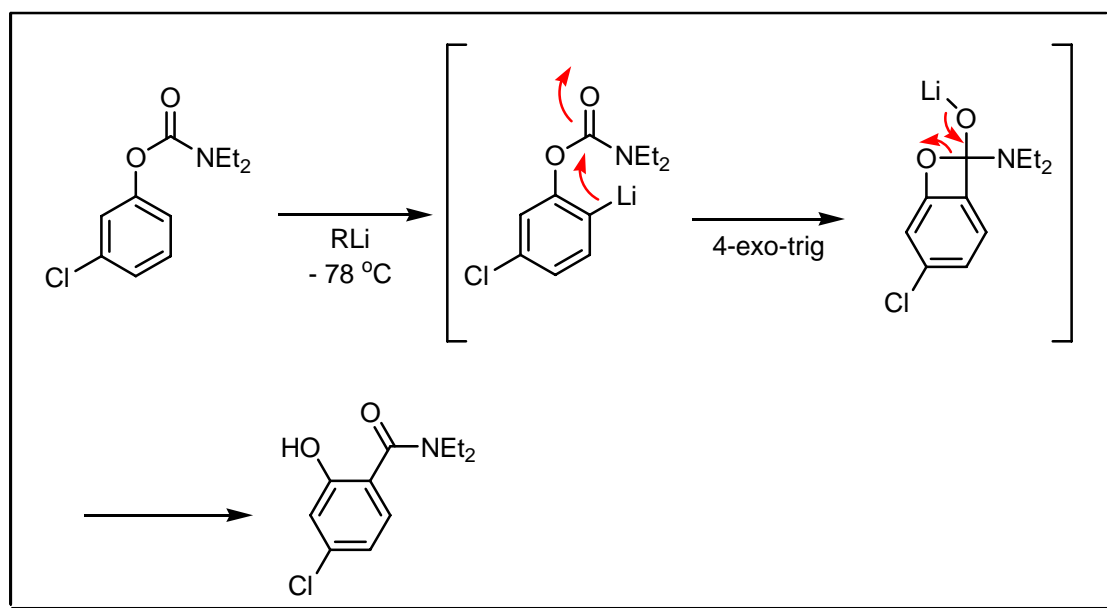


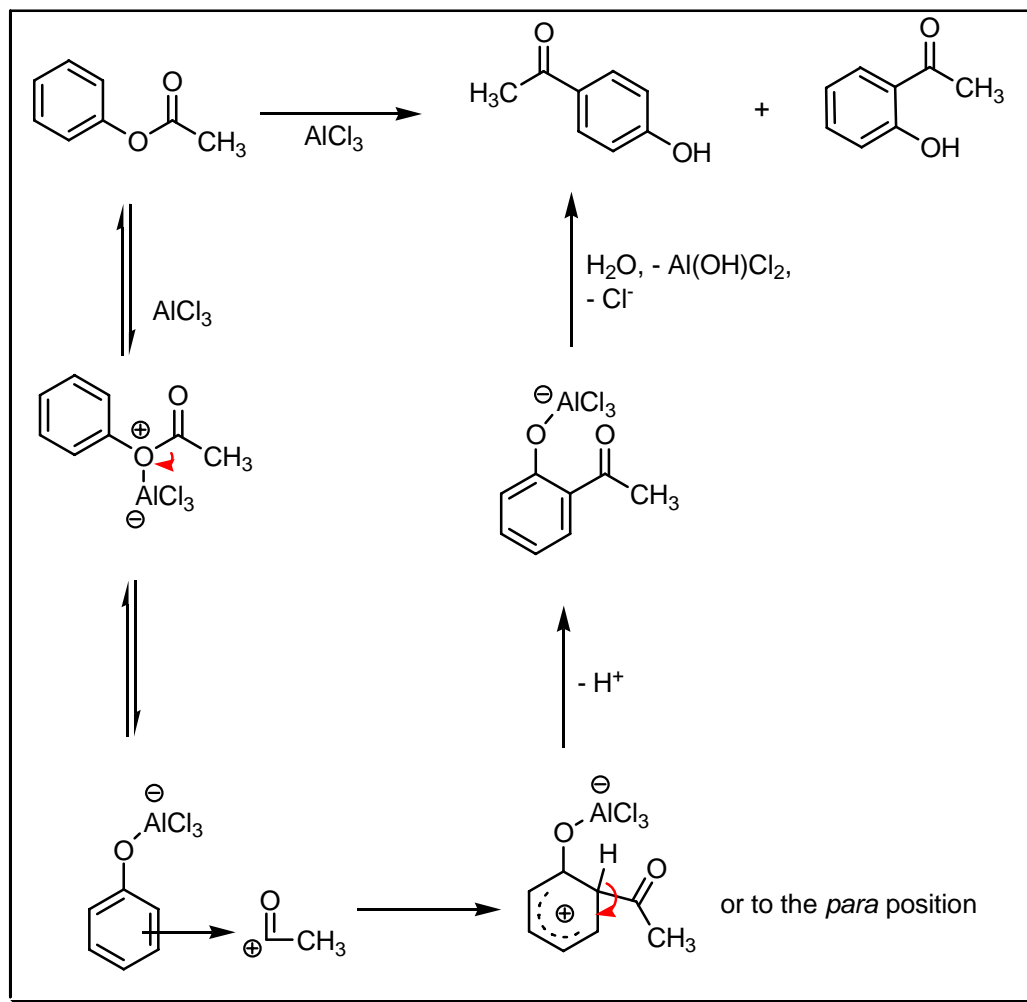
**NOTES :**

This reaction is exemplified by the treatment of an ethereal solution of cyclopropyl cyanide with lithium aluminium hydride to yield cyclopropane aldehyde.

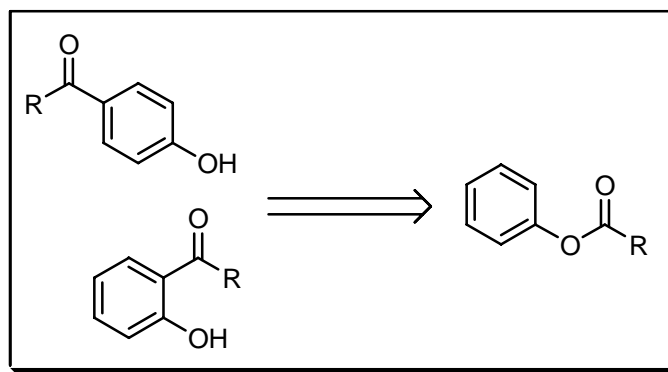
**REFERENCES :**

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**COMMENTS :****FRIES REARRANGEMENT****EXAMPLE :****MECHANISM :****Anionic Fries-rearrangement :**



#### DISCONNECTION :



#### NOTES :

Lewis-acid catalysed ( $\text{AlCl}_3$ ,  $\text{BF}_3$ ,  $\text{ZnCl}_2$ ,  $\text{TiCl}_4$ ,  $\text{FeCl}_3$ ,  $\text{ZrCl}_4$ ) rearrangement of phenols to *ortho*- or *para*-ketophenols. *Meta*-directing groups can interfere. The mechanism is still in question. There is also a photo-Fries, an anionic Fries and thia-Fries rearrangement. See also **von Auwers** indane-1-one, **Claisen – Haase**, **Hoesch – Houben**, **Limaye** and **Snieckus** rearrangement reactions.

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March : 555

Smith – March : 725

Smith : 1348

Smith 2<sup>nd</sup> : 1108

Houben – Weyl : 4/2, 127; 7/2a, 379; 8, 634; E6a, 484, 983; E6b, 436; E7a, 95; E8a, 303; E10b2, 234; E11, 105;  
E19c, 382

Org. React. : 1, 342

Org. Synth. : 13, 90

Org. Synth. Coll. Vol. : 2, 543

Science of Synthesis : 10, 45, 93, 95

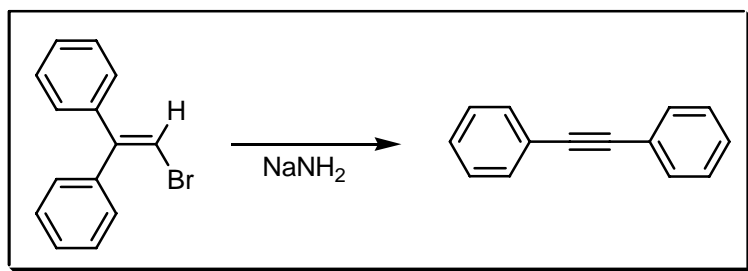
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COMMENTS :

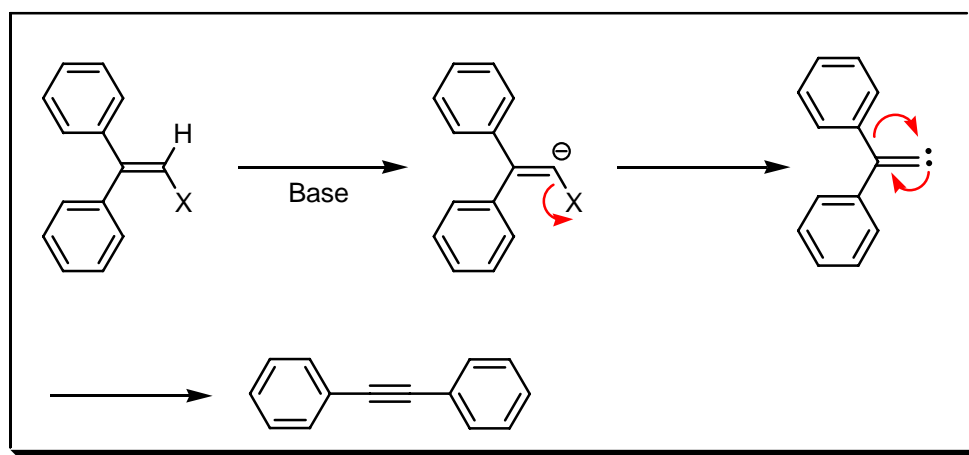


# FRITSCH – BUTTENBERG – WIECHELL REARRANGEMENT

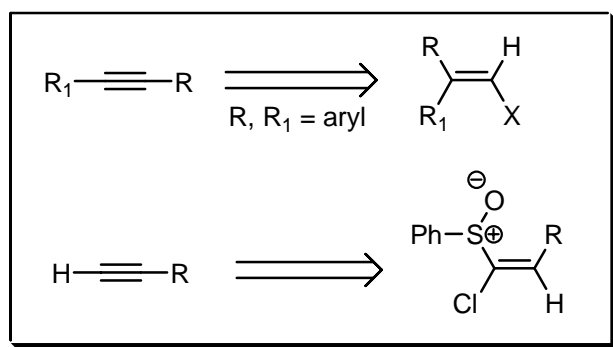
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

$\alpha$ -Elimination from 1,1'-diaryl-2-haloethylenes leading via carbene rearrangement to alkynes. Typical bases include sodium amide, alkoxide ion, and organolithium reagents. The reaction is inhibited by electron-withdrawing groups on the aromatic rings. **Tykwinski** *et al.* has reported a modification of this reaction. See also **Murahashi** cross-coupling.

## REFERENCES :

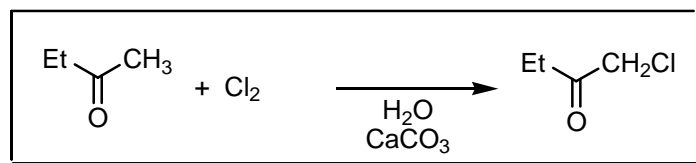
Smith 2<sup>nd</sup> : 632

- 1) P. Fritsch, *Liebigs Ann. Chem.*, 1894, **279**, 319.
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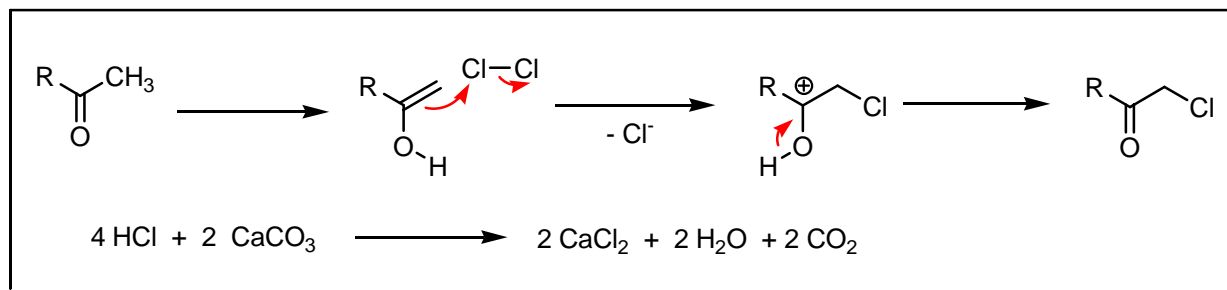
**COMMENTS :**

**FRITSCH – KLING CHLORINATION**

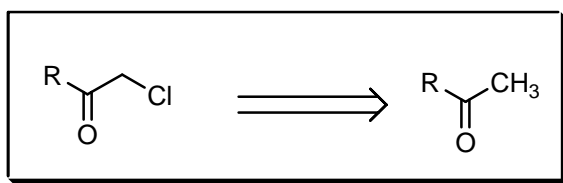
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

The reaction is effected by passing chlorine into the ketone in the presence of water and calcium carbonate. Aqueous calcium chloride may also be added. See also **Bedoukian** and **Hell – Volhard – Zelinsky** reactions.

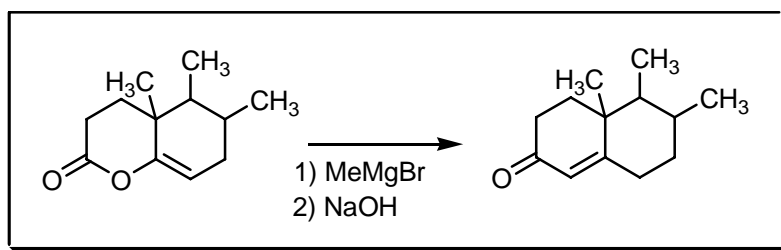
## REFERENCES :

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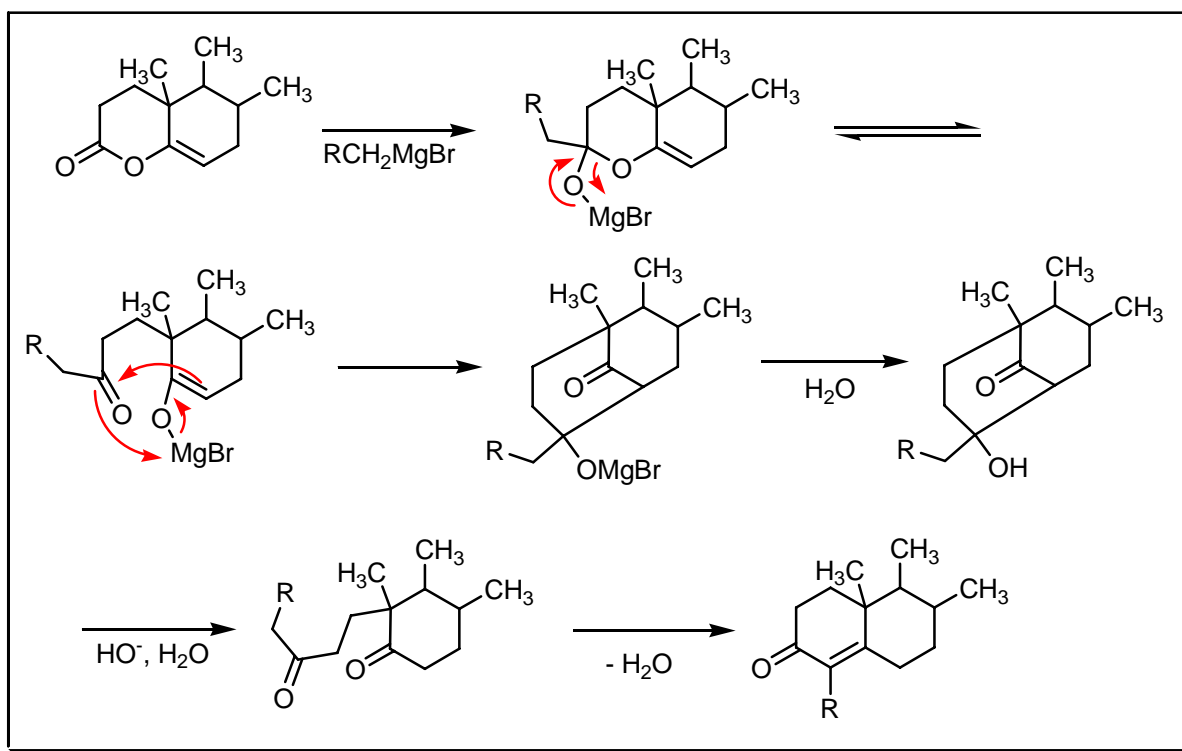
## COMMENTS :

## FUJIMOTO – BELLEAU REACTION

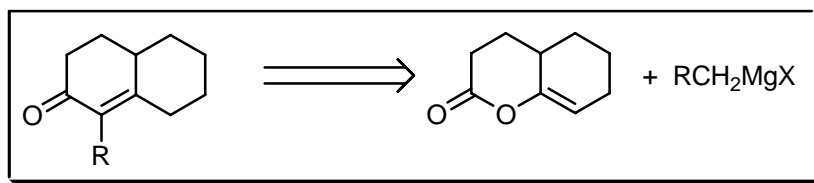
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of fused cyclohexenones from lactones (an alternative to the **Robinson** reaction). **Lygo et al.** introduced a **Horner – Wadsworth – Emmons** modification of this reaction as an alternative approach to the classical **Ferrier** cyclisation, which is normally carried out under acidic instead of basic conditions. See also **Robinson – Mannich** annulation.

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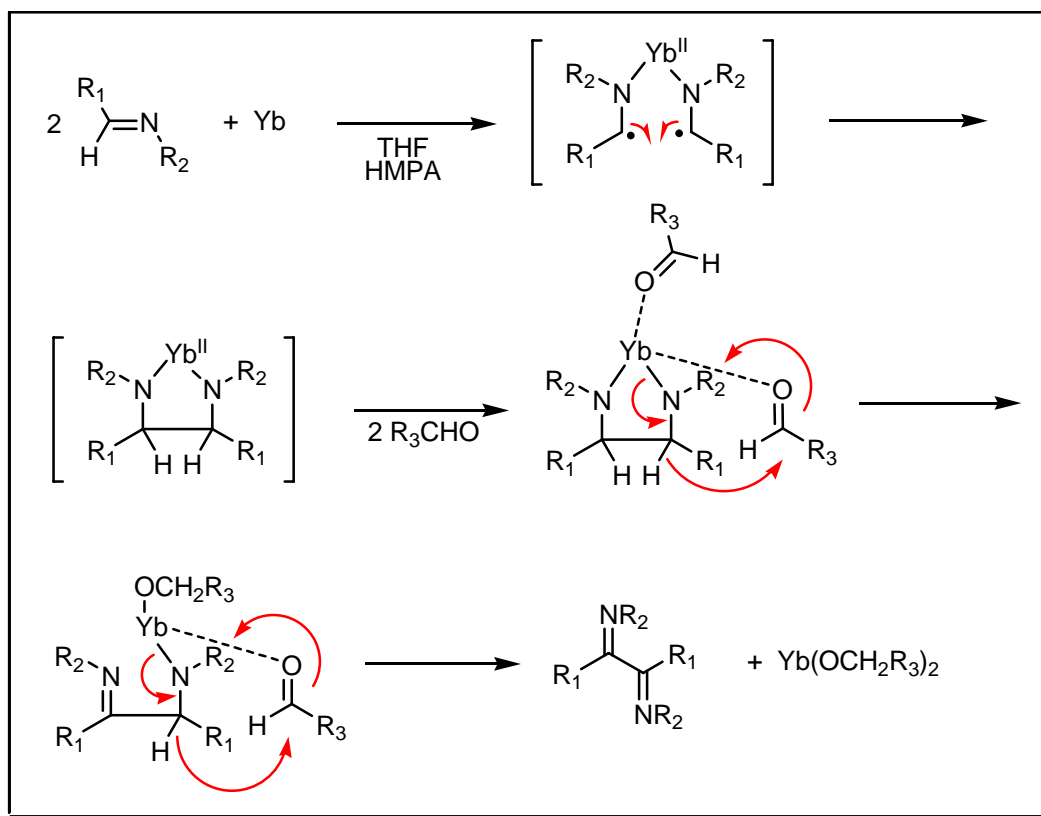
## COMMENTS :

## FUJIWARA LANTHANIDE REACTION

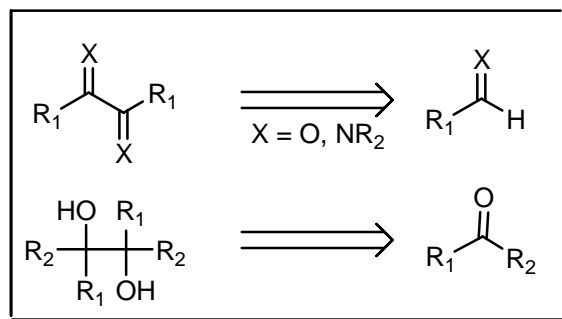
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Lanthanide metals have been utilised for various transformations of organic functional groups or C-C bond formations *via* coupling reactions. Ytterbium metal causes the coupling reaction of carbonyl and thiocarbonyl compounds, and

imines, but also aldimines undergo similar reactions. Other metals than lanthanides are also used. See also **Holleman** and **Pedersen** reactions.

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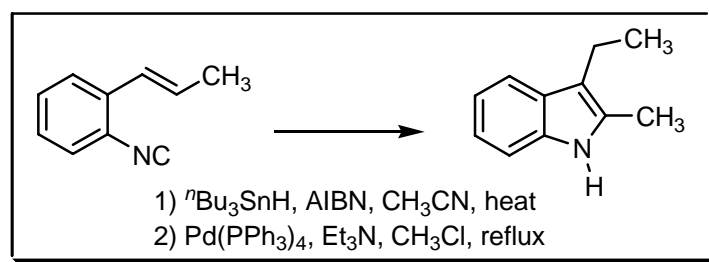
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#### COMMENTS :

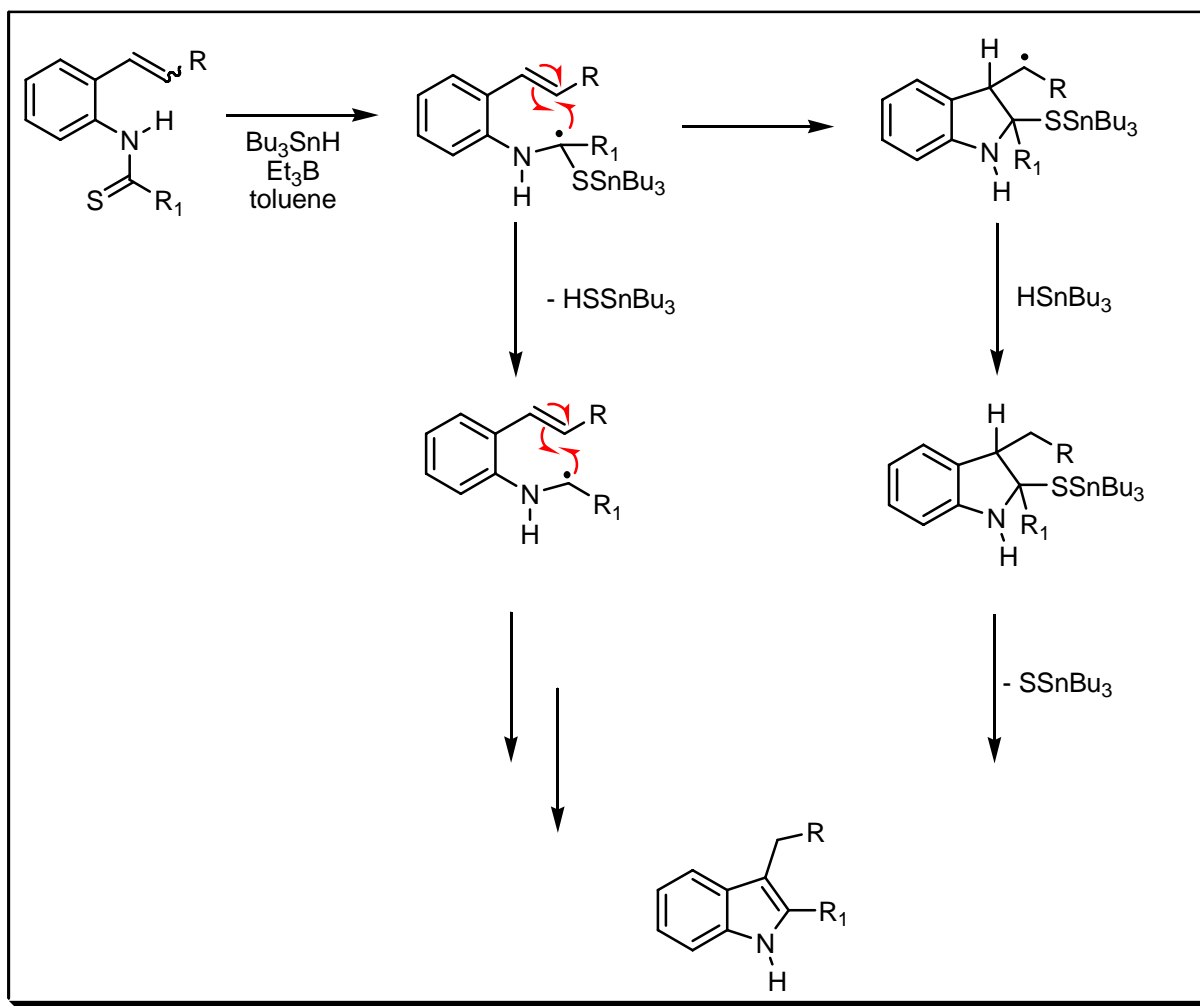
### FUKUYAMA INDOLE SYNTHESIS

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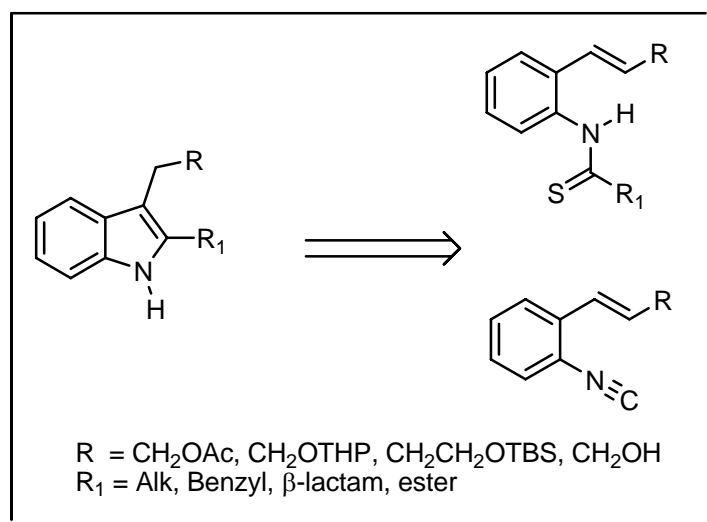
#### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of substituted indoles using an arylisothioamide- or arylthioamide-alkene system *via* a tin mediated free radical cyclisation. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fürstner**, **Gassman**

indole, **Grandberg**, **Hegedus**, **Hemetsberger** – **Knittel**, **Inanaga**, **Iwao**, **Japp** – **Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber** – **Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori** – **Ban**, **Murphy**, **Naito**, **Nenitzescu** indole, **Piloty** – **Robinson**, **Pschorr** – **Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele** – **Dimroth**, **Thyagarajan**, **Watanabe**, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

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## REFERENCES :

**Science of Synthesis** : **10**, 455

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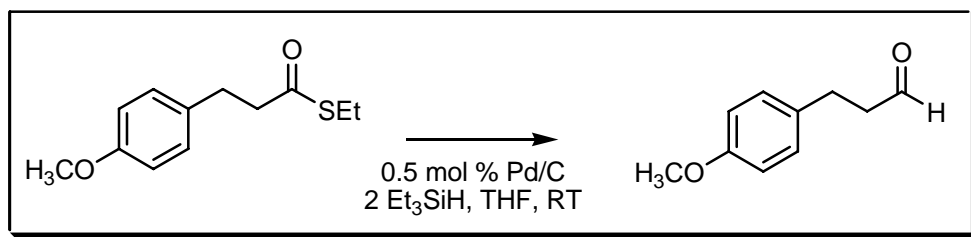
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## COMMENTS :

## FUKUYAMA REDUCTION

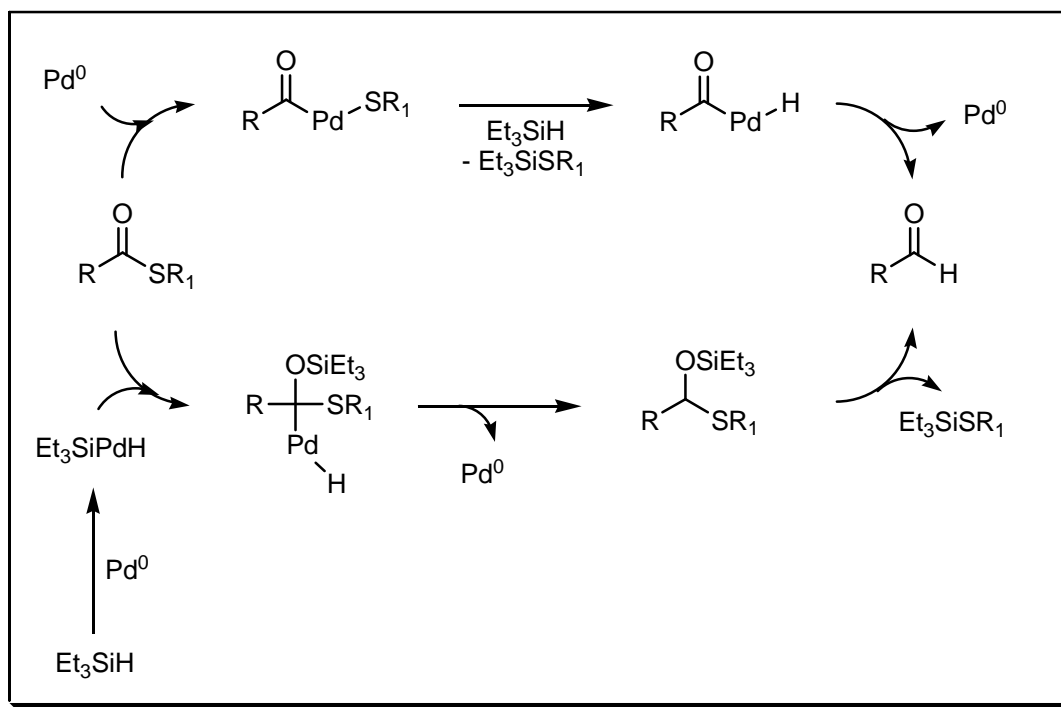
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### EXAMPLE :

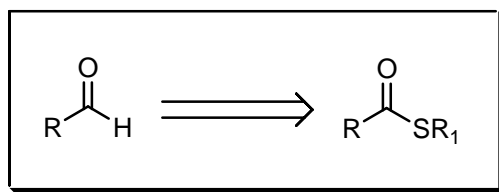




## MECHANISM :



## DISCONNECTION :



## NOTES :

Thiol esters are reduced with  $\text{Et}_3\text{SiH}$  in the presence of palladium on coal to afford aldehydes. The mechanism is not completely understood. **Seki** has improved the reaction conditions, so that multifunctional ketones can be prepared employing dialkylzincs.

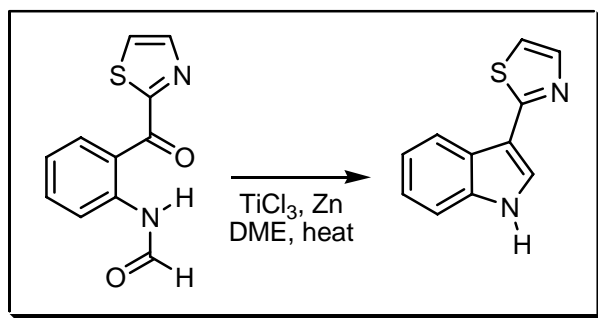
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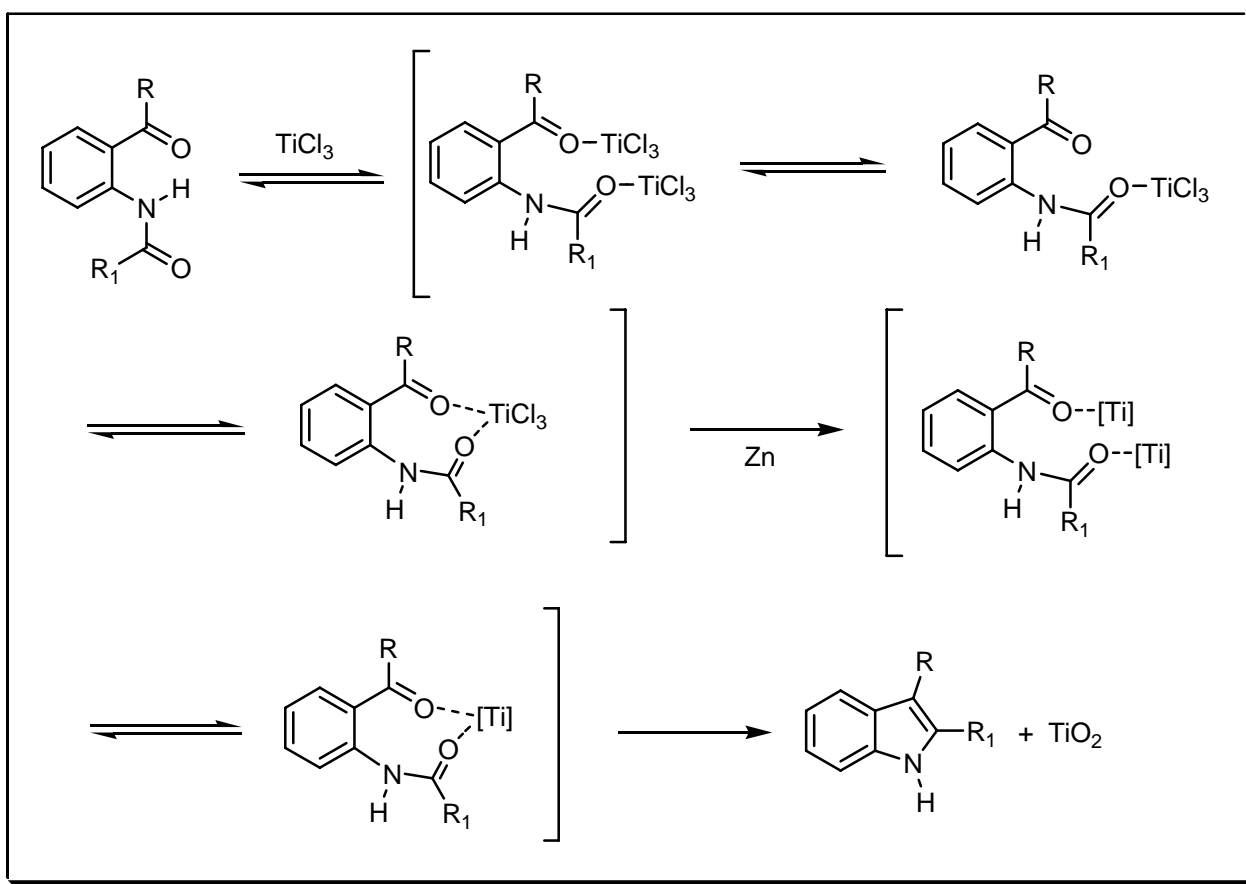
## COMMENTS :

# FÜRSTNER INDOLE SYNTHESIS

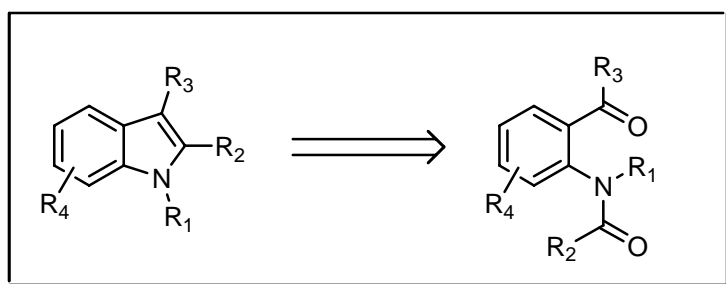
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Indoles are prepared by an *intramolecular McMurry* reaction. The zinc reduces the titanium cation to zerovalent titanium. The reaction can be made catalytic. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **McMurry**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe**, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

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## COMMENTS :

**G**

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**C**

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**E**

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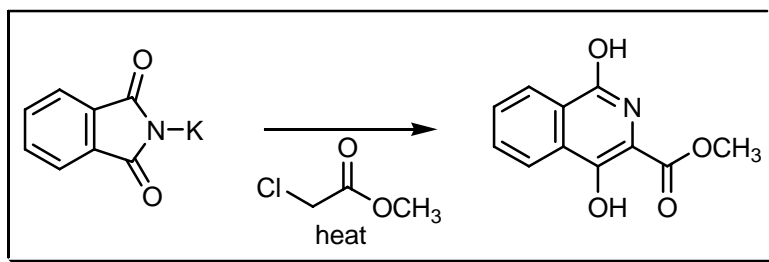
**H**

HAY REACTION · 695

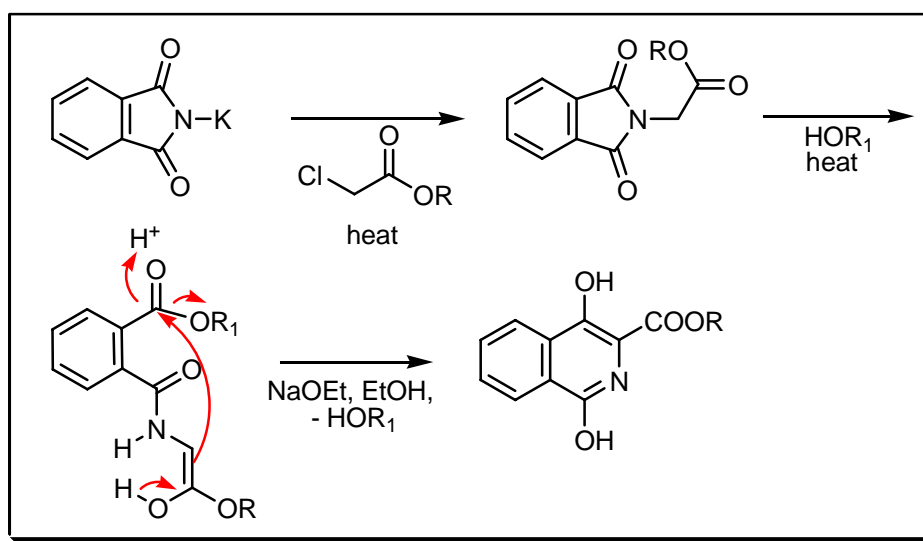
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## GABRIEL – COLMAN REARRANGEMENT

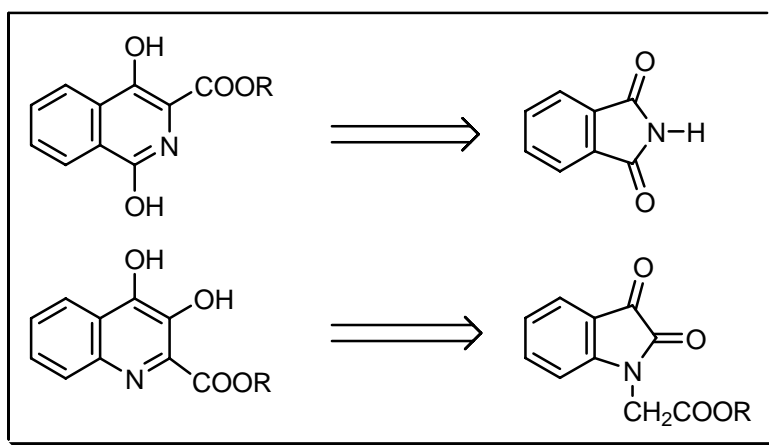
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Phthalimidoacetic esters and phthalimide ketones on treatment with ethanolic sodium ethoxide undergo ring-expansion and yield quinoline derivatives. This method has been applied to the rearrangement of quinolyl glycine and cinchomeryl glycine esters. See also **Dieckmann** reaction and **Gabriel** synthesis.

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Houben – Weyl : **8**, 578; **E7a**, 590, 682

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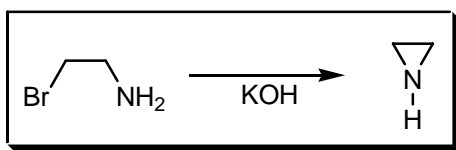
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## COMMENTS :

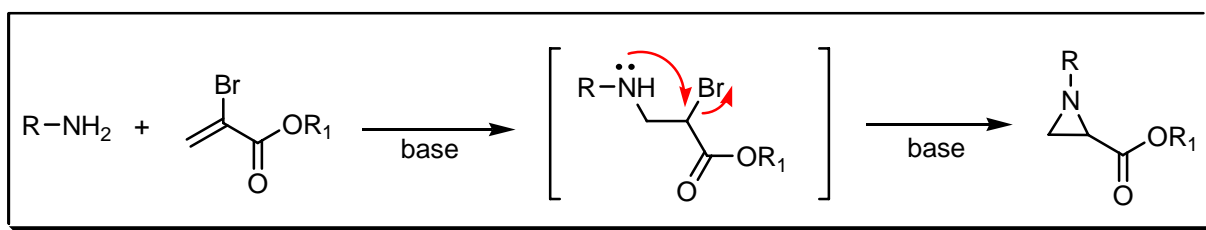
## GABRIEL – MARCKWALD – CROMWELL AZIRIDINE METHOD

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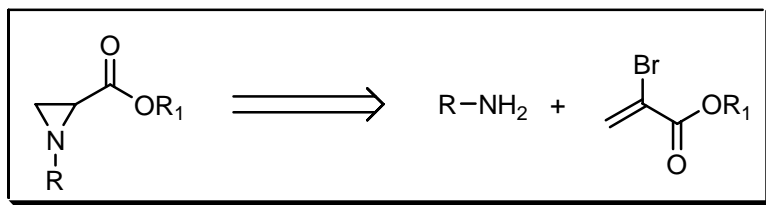
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

1,2-Halogenamines are treated with alkali to yield ethylenimines (aziridines). In addition, 5- and 6-membered rings can be formed. See also **Blum** aziridine, **Hassner** azide aziridine, **Hoch – Campbell**, **Mansuy – Evans**, **Scheiner** and **Wenker** ring-closure reactions.

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## REFERENCES :

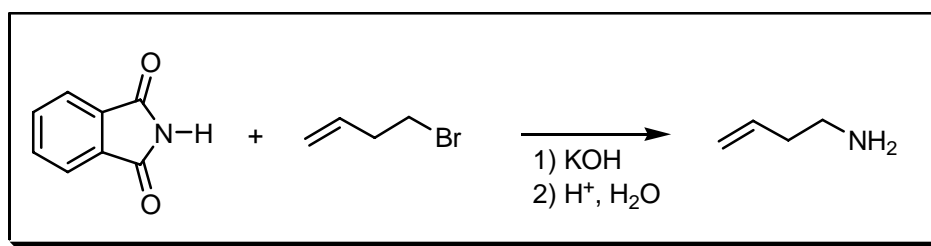
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## COMMENTS :

## GABRIEL SYNTHESIS

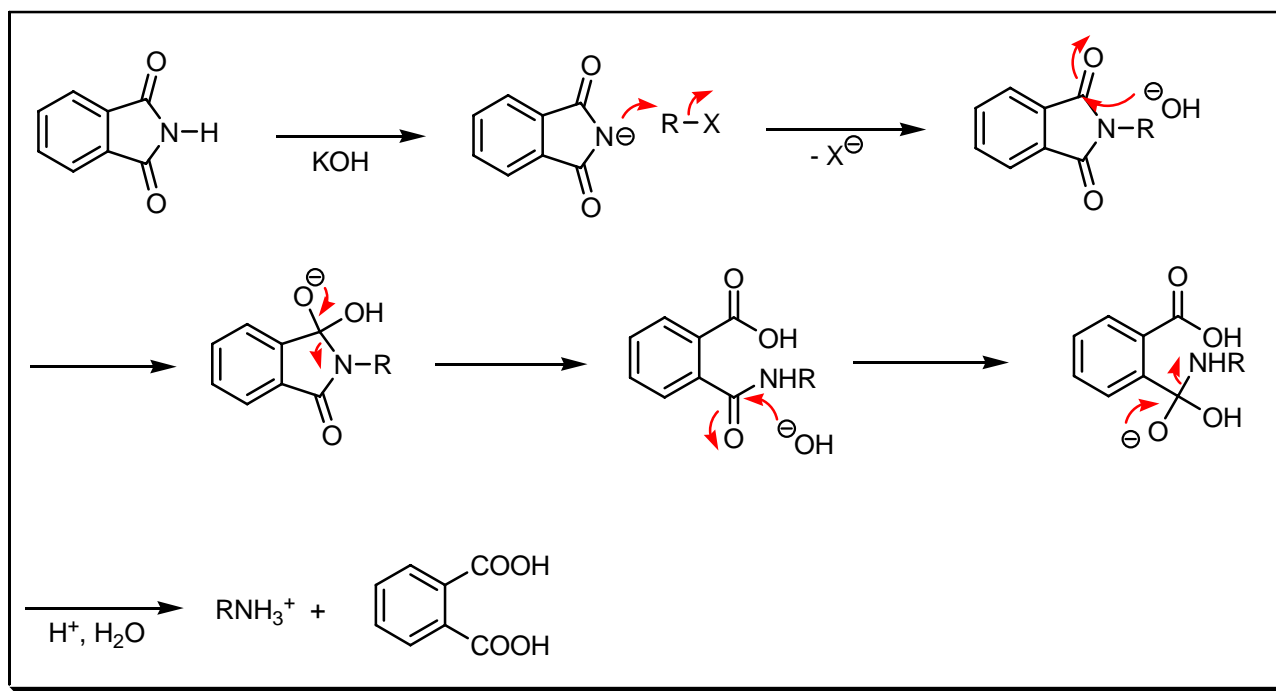
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### EXAMPLE :

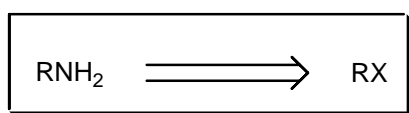




## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of primary amines by the hydrolysis of *N*-alkylphthalimides, which are obtained from potassium phthalimide and alkyl halides. See also **Delépine** amine, **Gabriel – Colman**, **Ing – Manske** and **Sheehan – Frank** reactions.

## REFERENCES :

**March** : 426, 657

**Smith – March** : 500, 513, 864

**Smith 2<sup>nd</sup>** : 111

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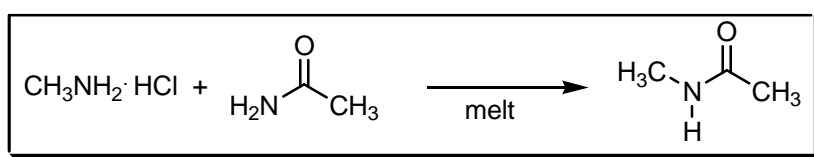
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COMMENTS :

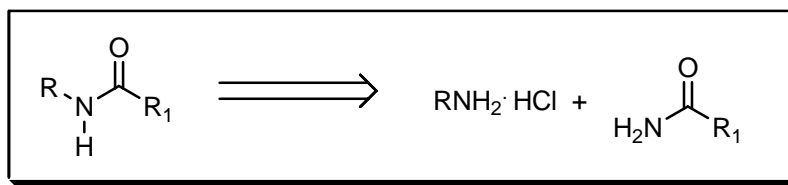
## GALAT – ELION ACYLATION

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EXAMPLE :



DISCONNECTION :



NOTES :

Amines are acylated quickly by heating the amine salt with a slight excess of anhydride. See also **Chattaway** acetylation, **Einhorn** acylation, **Lumière – Barbier**, **Schotten – Baumann** and **Weinreb** reactions.

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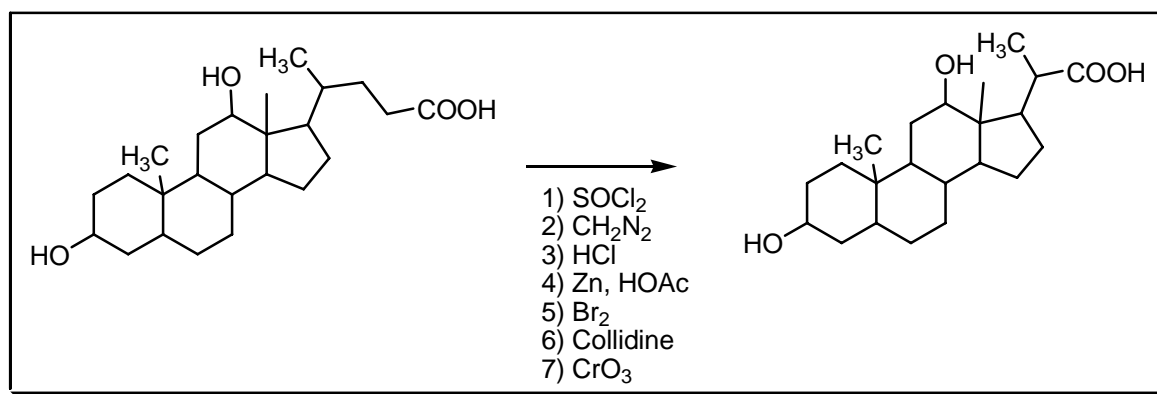
REFERENCES :

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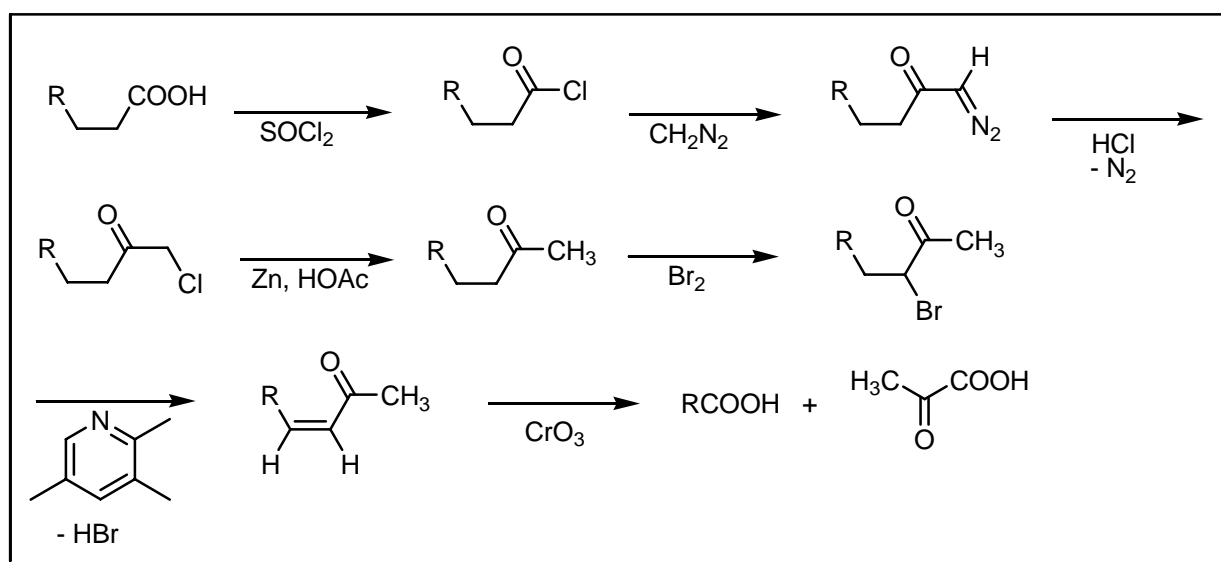
COMMENTS :

## GALLAGHER – HOLLANDER DEGRADATION

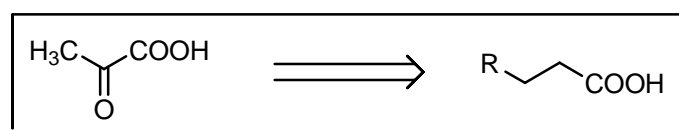
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

A method for the degradation of aliphatic acids, after an initial chain extension by one carbon atom, in which two carbon atoms are eliminated. See also **Barbier – Locquin – Wieland**, **Hoehn – Mason**, **Krafft**, **Miescher**, **Trost** oxidative decarboxylation and **Wieland – Dane** reactions.

## REFERENCES :

Smith : 304

Smith 2<sup>nd</sup> : 266

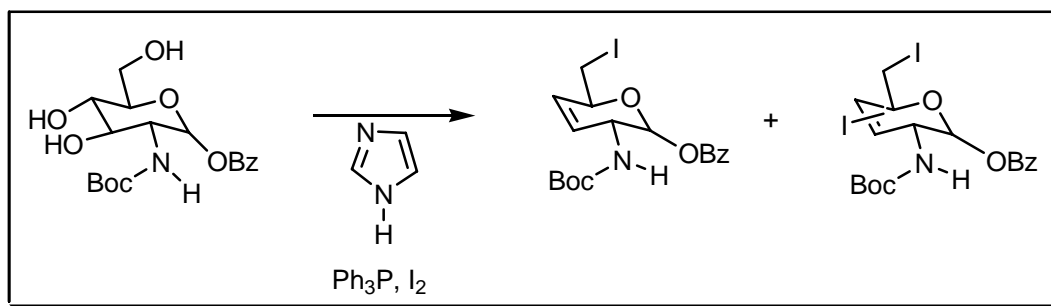
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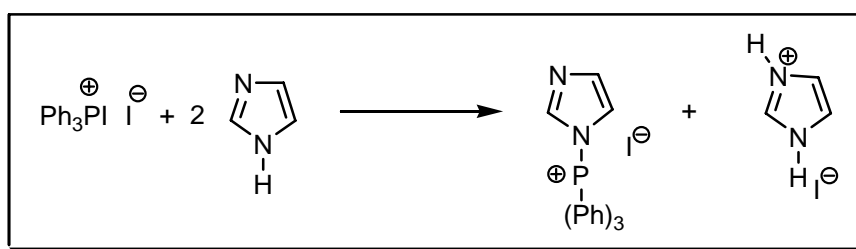
## COMMENTS :

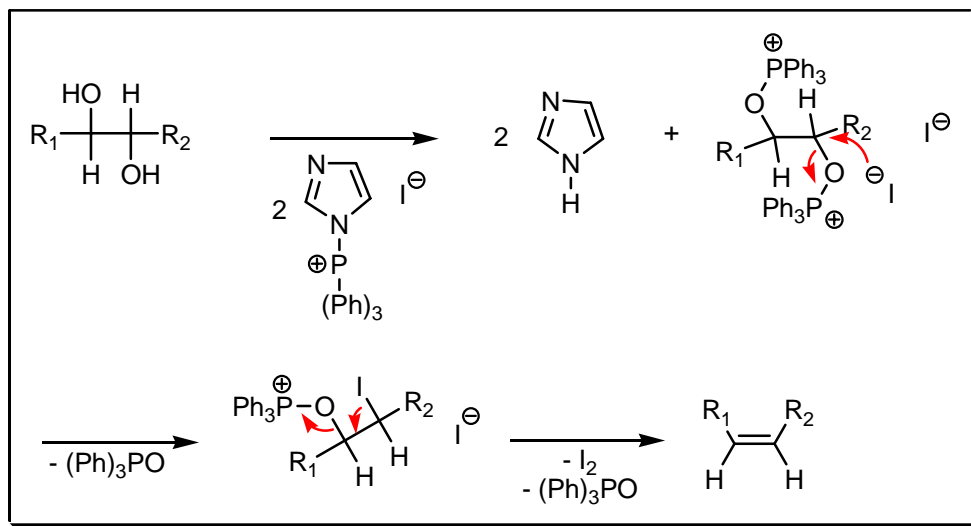
## GAREGG – SAMUELSSON OLEFIN SYNTHESIS

### EXAMPLE :

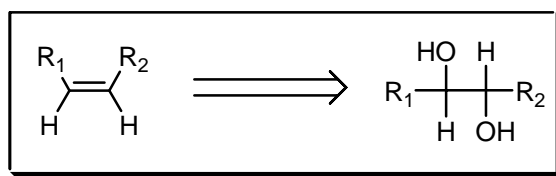


### MECHANISM :





#### DISCONNECTION :



#### NOTES :

The conversion of *vicinal trans*-diol groups into a double bond by an iodine-triphenylphosphine-imidazole reagent. See also **Corey – Kwiatkowski**, **Eastwood**, **Horner – Wadsworth – Emmons**, **Julia – Paris – Kocienski – Lythgoe**, **Krief – Reich – Chow**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Paquette**, **Petasis** reaction, **Peterson**, **Ramberg – Bäcklund**, **Still – Gennari**, **Takeda**, **Tebbe** and **Wittig** reactions.

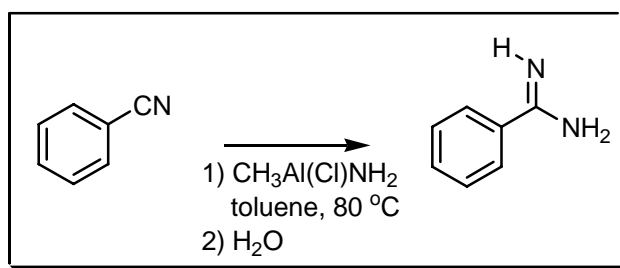
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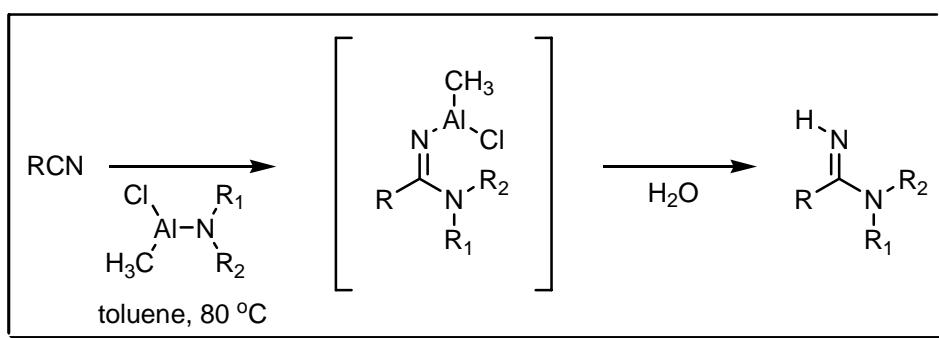
#### COMMENTS :

## GARIGIPATI SYNTHESIS

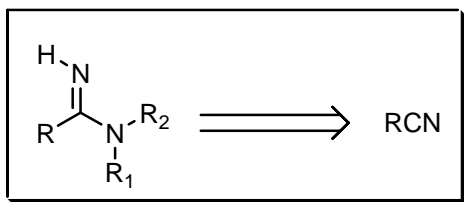
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The direct conversion of nitriles to amidines using an aluminium amide reagent. See also **Pinner** iminoether reaction.

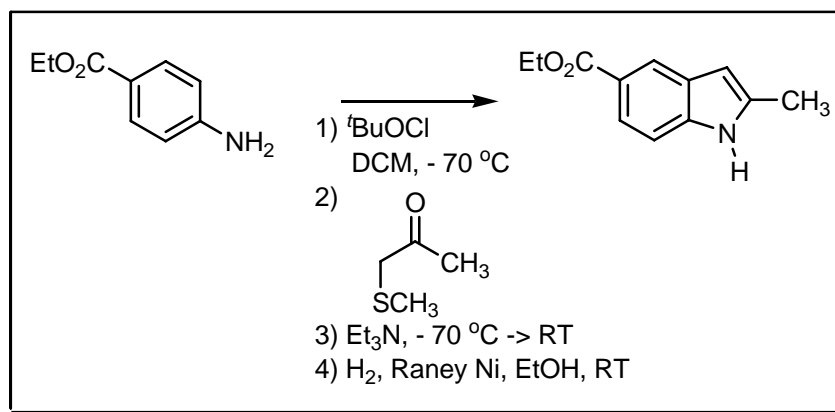
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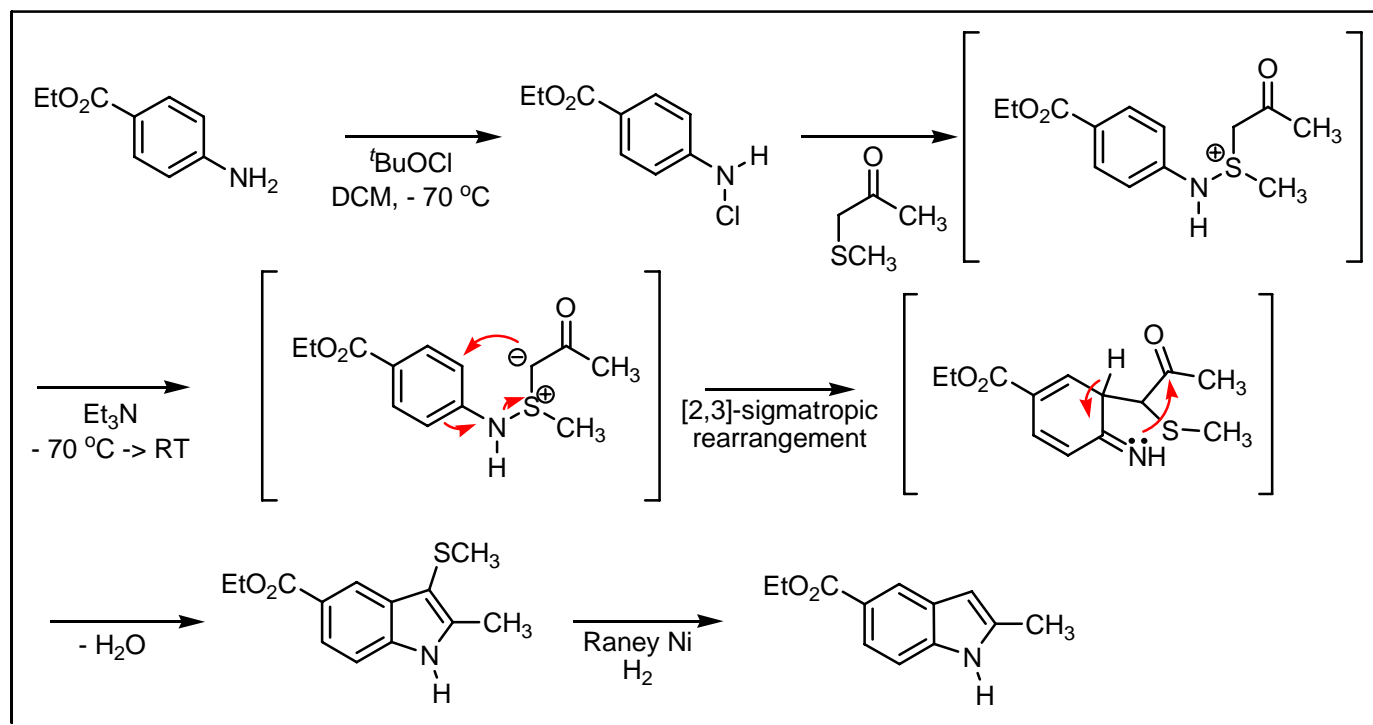
COMMENTS :

GASSMAN INDOLE SYNTHESIS

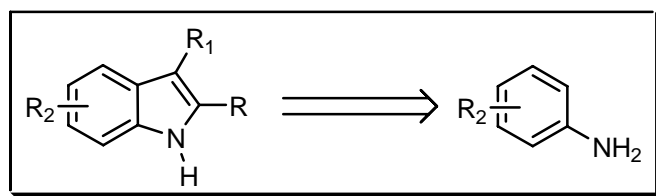
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

This procedure is an example of an indole synthesis, which can be utilised to prepare 1-, 2-, 4-, 5-, 6-, or 7-substituted indoles. Indoles substituted on the phenyl ring with nitro, ethoxycarbonyl, chloro, methyl, and acetoxycarbonyl groups have been prepared. Hydrogen, methyl, and phenyl groups have been placed in the 2-position and the method has been used to prepare 1-methylindoles. The main feature of this reaction is the [2,3]-sigmatropic rearrangement. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

## REFERENCES :

**Org. Synth.** : 56, 72

**Org. Synth. Coll. Vol.** : 6, 601

**Science of Synthesis** : 10, 387

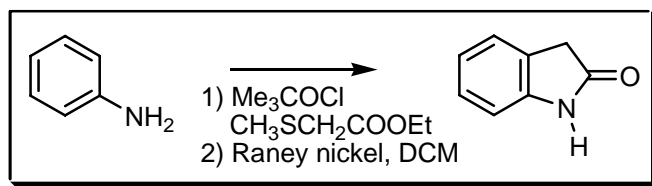
- 1) P.G. Gassman; T.J. van Bergen, *J. Am. Chem. Soc.*, 1973, **95**, 590.
- 2) P.G. Gassman; T.J. van Bergen; G.D. Gruetzmacher, *J. Am. Chem. Soc.*, 1973, **95**, 5608.
- 3) P.G. Gassman; D.P. Gilbert; T.-Y. Luh, *J. Org. Chem.*, 1977, **42**, 1340.
- 4) P.G. Gassman; J.J. Roos; S.J. Lee, *J. Org. Chem.*, 1984, **49**, 717.
- 5) B.M. Savall; W.W. McWhorter, *J. Org. Chem.*, 1996, **61**, 8696.

## COMMENTS :

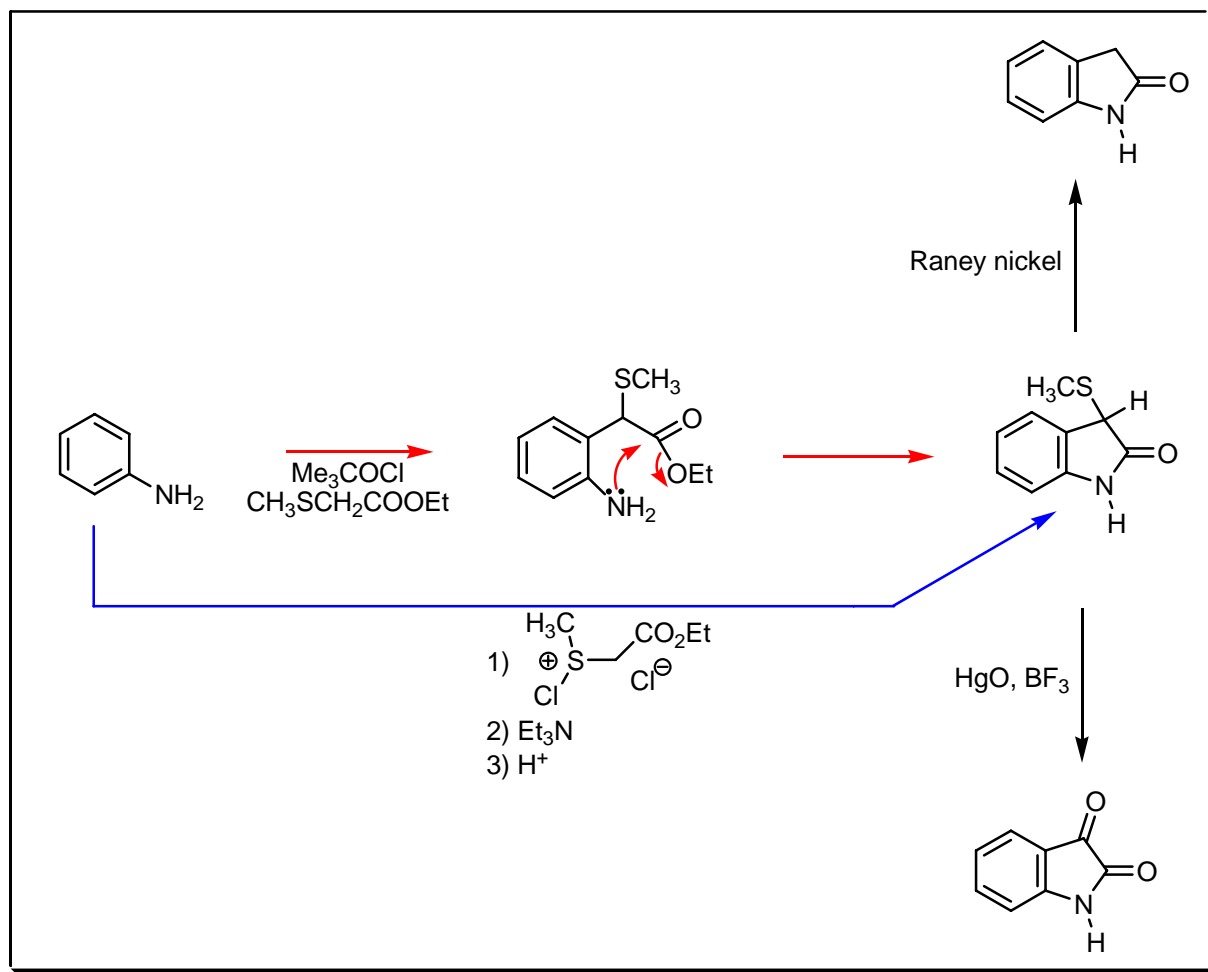


## GASSMAN OXINDOLE SYNTHESIS

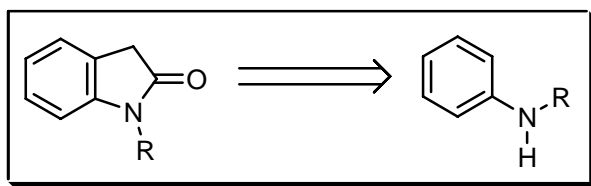
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

This is the synthesis of oxindoles from anilines. There are two possible reaction pathways. The use of sulfoxide instead of sulfonyl halide has been demonstrated by **Wright et al.** See also **von Baeyer** oxindole, **Brunner, Gassman** indole, **Hinsberg** oxindole, **Martinet, Neber – Bosset** and **Stollé** reactions.

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## REFERENCES :

**Science of Synthesis** : 10, 603

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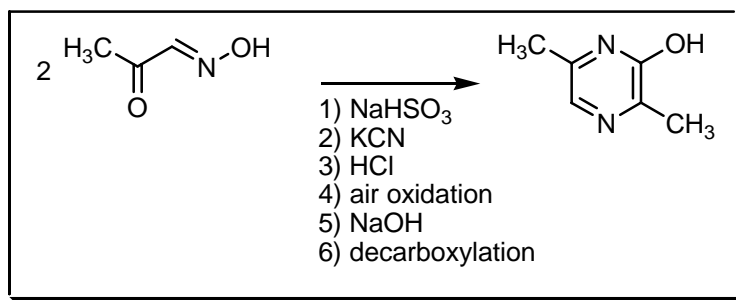
- 1) P.G. Gassman; T.J. van Bergen, *J. Am. Chem. Soc.*, 1973, **95**, 2718.
  - 2) P.G. Gassman; B.W. Cue, jr.; T.Y. Luh, *J. Org. Chem.*, 1977, **42**, 1344.
  - 3) P.D. Johnson; P.A. Aristoff, *J. Org. Chem.*, 1990, **55**, 1374.
  - 4) S.W. Wright; L.D. McClure; D.L. Hageman, *Tetrahedron Lett.*, 1996, **37**, 4631.
  - 6) J.F.M. da Silva; S.J. Garden; A.C. Pinto, *J. Braz. Chem. Soc.*, 2001, **12**, 273.
- 

## COMMENTS :

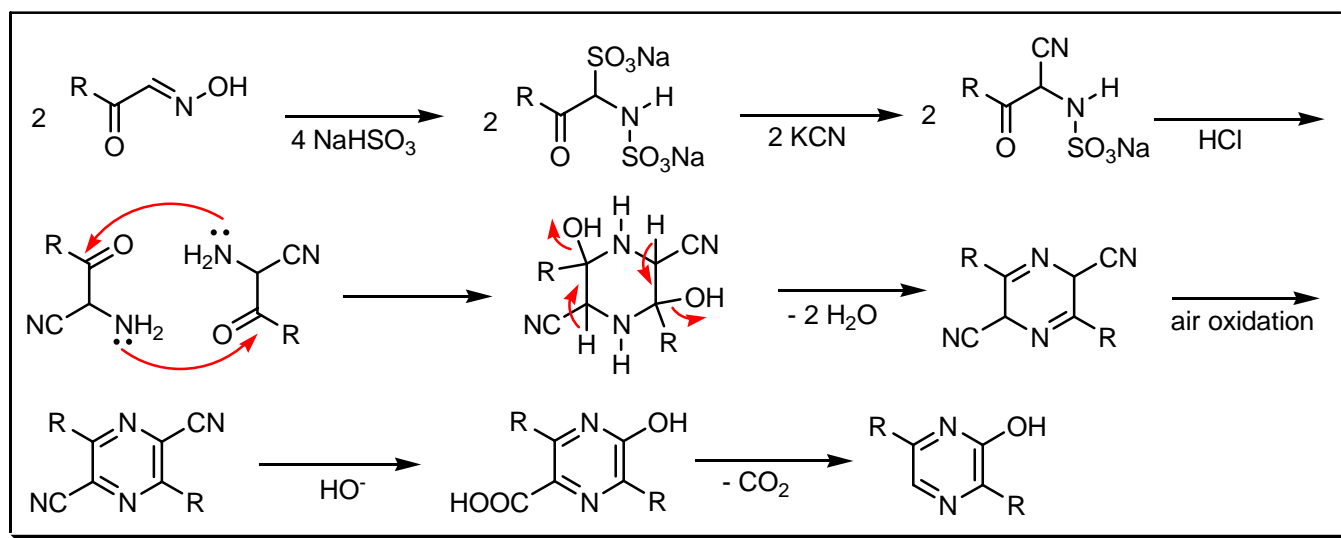
## GASTALDI PYRAZINE SYNTHESIS

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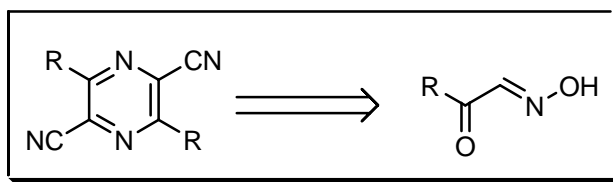
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

2,5-Dicyano-3,6-disubstituted pyrazines are obtained by treatment of an oximino ketone bisulfite with potassium cyanide, followed by heating the reaction product with hydrochloric acid and oxidation. When treated with alkali, the dicyano compound yields a 3,6-disubstituted 2-hydroxypyrazine-5-carboxylic acid, which is decarboxylated to give a 3,6-disubstituted-2-hydroxypyrazine. See also **Gutknecht** pyrazine and **Stadel – Rügheimer** reactions.

## REFERENCES :

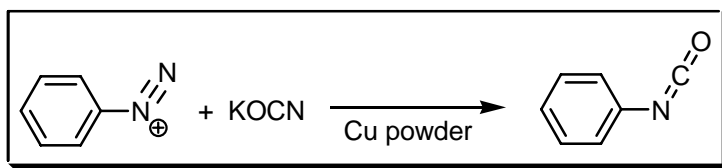
- 1) G. Gastaldi, *Gazz. Chim. Ital.*, 1921, **51**, 233.
- 2) I.J. Krems; P.E. Spoerri, *Chem. Rev.*, 1947, **40**, 279.
- 3) W.H. Sharp; F.S. Spring, *J. Chem. Soc.*, 1948, 1862.
- 4) E. Golombok; F.S. Spring, *J. Chem. Soc.*, 1949, 1364.
- 5) G. Karmas; P.E. Spoerri, *J. Am. Chem. Soc.*, 1957, **79**, 680.

## COMMENTS :

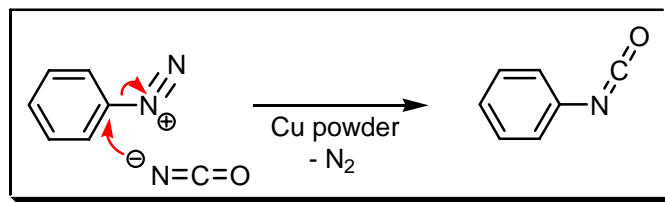
## GATTERMANN – CANTZLER SYNTHESIS

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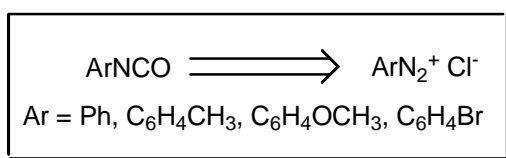
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This reaction involves the formation of aryl isocyanates by the treatment of aromatic diazonium salts with potassium cyanide in the presence of copper. It is a low yielding reaction and hardly used method. See also **Sandmeyer** diazonium reaction.

### REFERENCES :

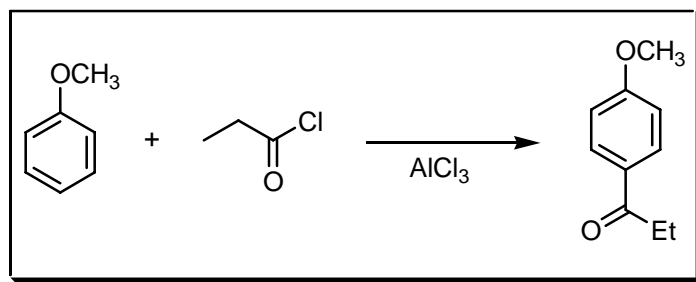
Houben – Weyl : 8, 127

- 1) L. Gattermann; A. Cantzler, *Ber. Dtsch. Chem. Ges.*, 1890, **23**, 1225.
- 2) L. Gattermann; A. Cantzler, *Ber. Dtsch. Chem. Ges.*, 1892, **25**, 1086.
- 3) W.A. Cowdry; D.S. Davies, *J. Chem. Soc., Quat. Rev.*, 1952, **6**, 358.

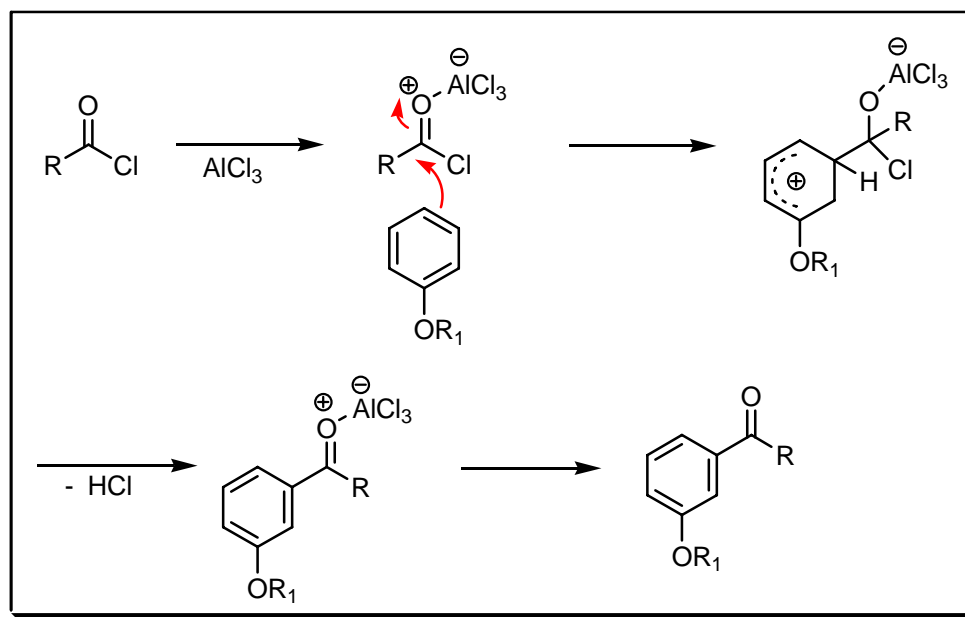
### COMMENTS :

## GATTERMANN – EHRHARDT ACYLATION

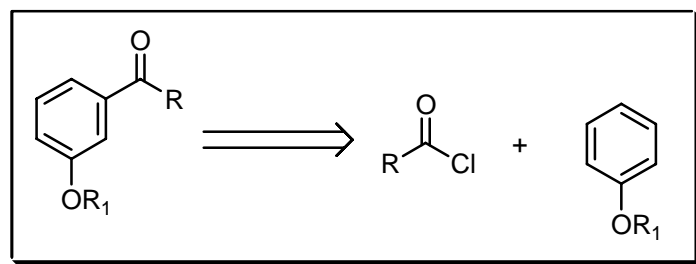
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Alkyl ethers of phenols react with acid chlorides in the presence of aluminium chloride to give *p*-acyl substitution. See also **Friedel – Crafts** reaction.

### REFERENCES :

March : 539

Smith – March : 718

Smith : 1324

Smith 2<sup>nd</sup> : 1090

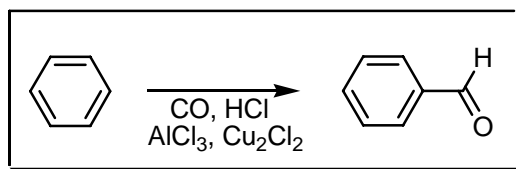
Org. React. : 2, 114; 3, 1; 5, 229

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- 1) L. Gattermann, *Ber. Dtsch. Chem. Ges.*, 1889, **22**, 1129.  
2) L. Gattermann; R. Ehrhardt; H. Maisch, *Ber. Dtsch. Chem. Ges.*, 1890, **23**, 1199.  
3) W.H. Hartung; J.C. Munch; E. Miller; F. Crossley, *J. Am. Chem. Soc.*, 1931, **53**, 4149.  
4) R. Frenette; M. Kakushima; R. Zamboni; R.N. Young; T.R. Verhoeven, *J. Org. Chem.*, 1987, **52**, 304.  
5) N. Tanaka; H. Yamazaki; H. Sakuragi; K. Tokumaru, *Bull. Chem. Soc. Jpn.*, 1994, **67**, 1434.  
6) S.R. Stauffer; C.J. Coletta; R. Tedesco; G. Nishiguchi; K. Carlson; J. Sun; B.S. Katzenellenbogen; J.A. Katzenellenbogen, *J. Med. Chem.*, 2000, **43**, 4934.
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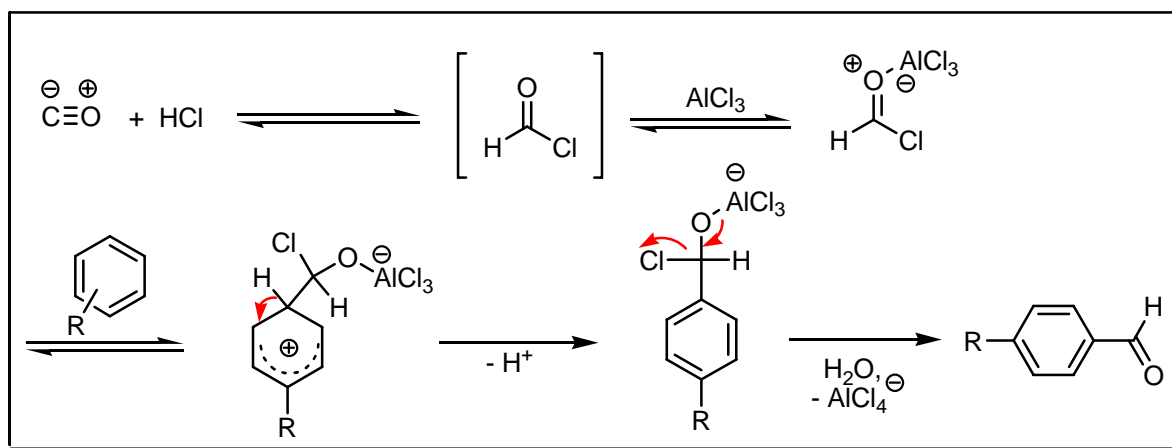
## COMMENTS :

## GATTERMANN – KOCH REACTION

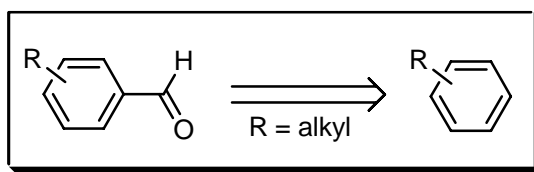
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

Aromatic aldehydes are obtained by the action of carbon monoxide and hydrogen chloride on aromatic hydrocarbons in the presence of aluminium chloride with or without a cuprous catalyst. A reverse reaction has been reported. See also **Gattermann** formylation, **Karrer**, **Reimer – Tiemann** and **Rieche** formylation reactions.

## REFERENCES :

**March** : 544, 563

**Smith – March** : 716, 732

**Houben – Weyl** : **7/1**, 16; **E3**, 32; **E6a**, 852; **E19c**, 362, 369

**Org. React.** : **5**, 290

**Org. Synth.** : **12**, 80

**Org. Synth. Coll. Vol.** : **2**, 583

1) L. Gattermann; J.A. Koch, *Ber. Dtsch. Chem. Ges.*, 1897, **30**, 1622.

2) P.H. Gore, *Chem. Rev.*, 1955, **55**, 235.

3) G.A. Olah; F. Pelizza; S. Kobayashi; J.A. Olah, *J. Am. Chem. Soc.*, 1976, **98**, 296.

4) M. Tanaka; M. Fujiwara; Q. Xiu; H. Ando; T.J. Raeker, *J. Org. Chem.*, 1998, **63**, 4408.

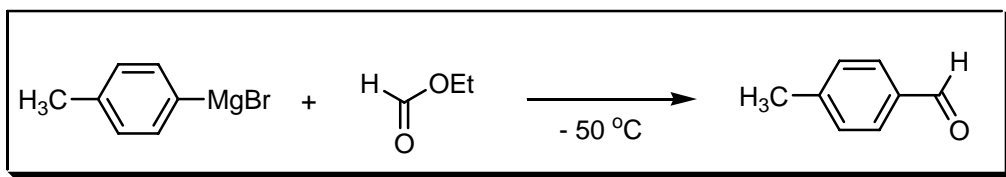
5) W. Kantlehner; M. Vettel; A. Gissel; E. Hang; G. Ziegler; M. Ciesielski; O. Scherr; R. Haas, *J. Prakt. Chem.*, 2000, **342**, 297.

6) I. Doanamona, *Rev. Roum. Chim.*, 2001, **46**, 345.

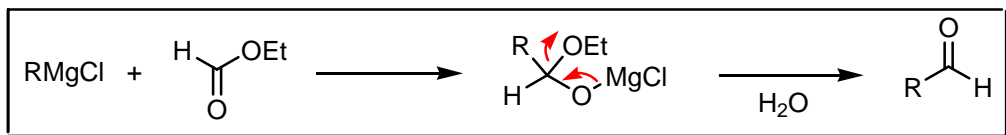
## COMMENTS :

## GATTERMANN – MAFFEZZOLI SYNTHESIS

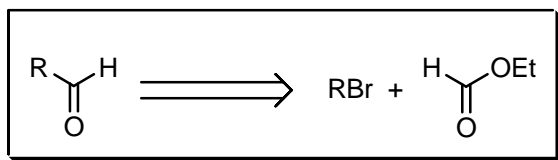
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Excess ethyl formate reacts with **Grignard** reagents at – 50 °C to yield aldehydes after hydrolysis. See also **Bodroux** – **Chichibabin** reaction.

### REFERENCES :

Houben – Weyl : 7/1, 65

1) L. Gattermann; F. Maffezzoli, *Ber. Dtsch. Chem. Ges.*, 1903, **36**, 4152.

2) L. Gattermann, *Liebigs Ann. Chem.*, 1912, **393**, 215.

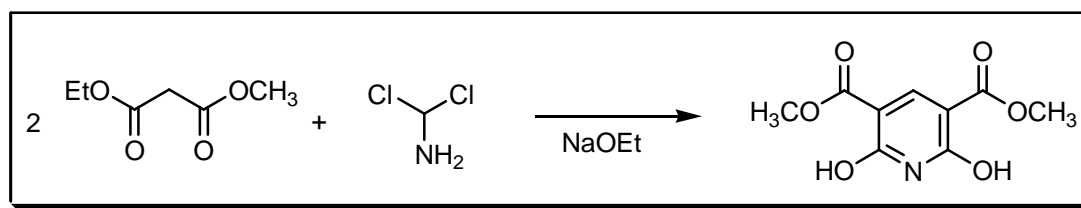
3) N. Boccara; P. Maitte, *Bull. Soc. Chim. Fr.*, 1972, 1448.

### COMMENTS :

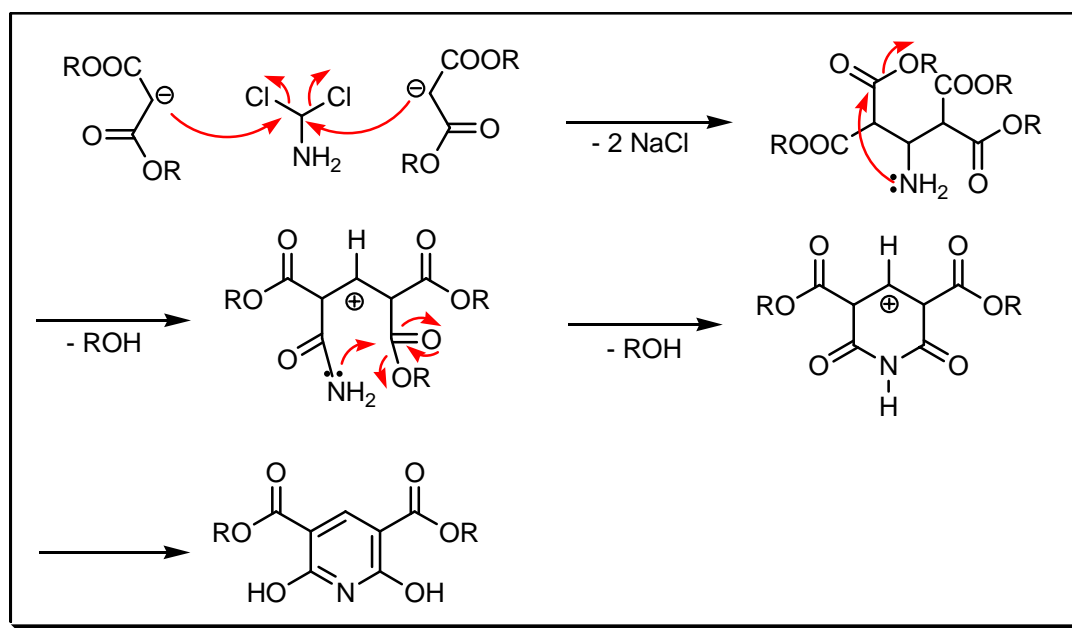


## GATTERMANN – SKITA SYNTHESIS

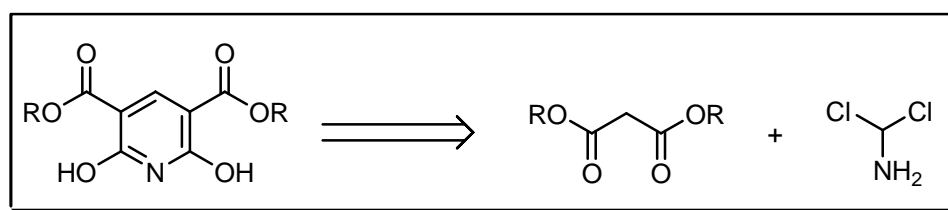
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Sodium diethyl malonate is condensed with dichloromethylamine to yield pyridine derivatives. See also **Bohlmann – Rahtz**, **Chichibabin** pyridine, **Guareschi – Thorpe**, **Hantzsch – Beyer**, **von Meyer – Mohr**, **Petrenko–Kritschenko**, **Riehm** pyridine and **Wakatsuki – Yamazaki – Bönnemann** reactions.

### REFERENCES :

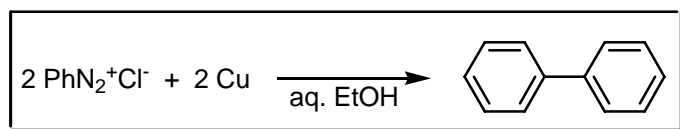
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- 2) V.P. Litvinov, *Russ. Chem. Rev.*, 2003, **72**, 69.

COMMENTS :

## GATTERMANN DIARYL SYNTHESIS

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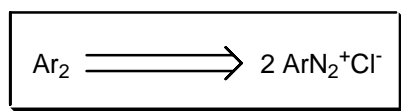
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

Aqueous ethanolic solutions of aryl diazonium salts, when treated with precipitated copper powder and other reducing agents (zinc), yields diaryls. See also **Gattermann**, **Gomberg – Bachmann – Hey**, **Graebe – Ullmann** and **Pschorr** reactions.

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REFERENCES :

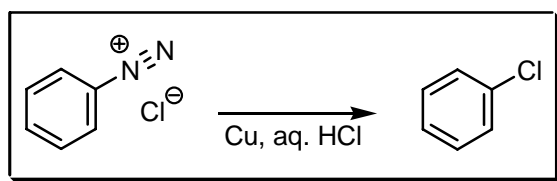
L. Gattermann, *Ber. Dtsch. Chem. Ges.*, 1890, **23**, 1218.

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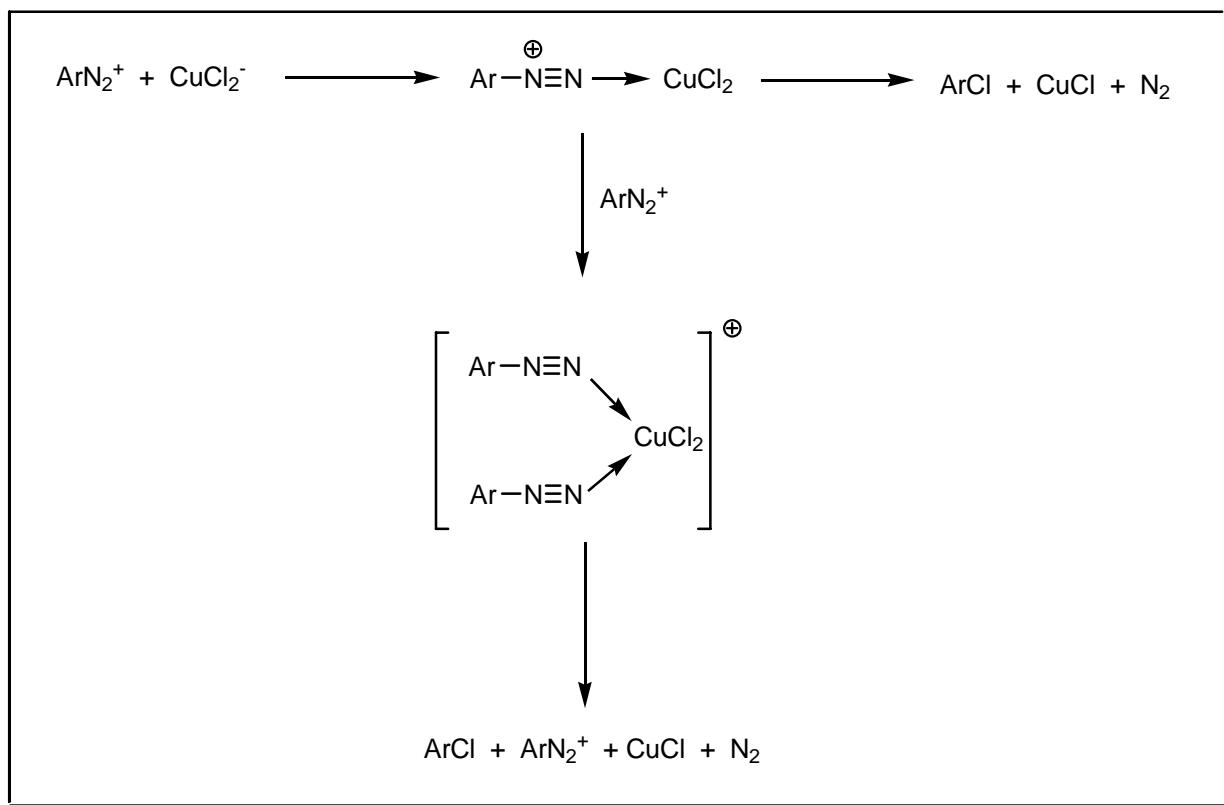
COMMENTS :

## GATTERMANN DIAZO REACTION

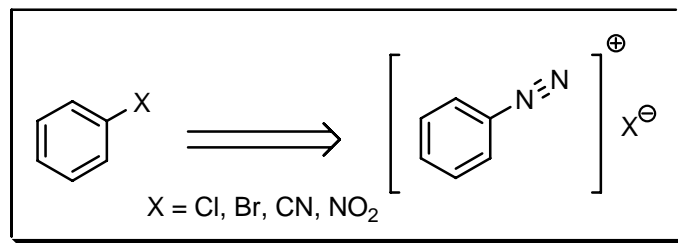
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This reaction is very similar to the **Gattermann** diaryl reaction. The synthesis of aromatic diazonium compounds of halogenated aromatic compounds and aromatic nitriles, using finely divided copper or copper bronze as a catalyst. See also **Balz – Schiemann**, **Cadogan** arylation, **Craig** exchange, **Demjanov** rearrangement, **Gattermann** sulfinic

acid, **Griess** deamination, **Knoevenagel** diazotation, **Körner – Contardi**, **Meerwein** arylation, **Sandmeyer** diazonium, **Schwechten** and **Witt** diazotation reactions.

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#### REFERENCES :

**Smith – March** : 936

**Smith 2<sup>nd</sup>** : 168

**Org. Synth.** : 3, 33; 13, 28

**Org. Synth. Coll. Vol.:** 1, 170; 2, 130

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1) L. Gattermann, *Ber. Dtsch. Chem. Ges.*, 1890, **23**, 1218.

2) H.H. Hodgson, *Chem. Rev.*, 1947, **40**, 251.

3) E. Pfeil, *Angew. Chem.*, 1953, **65**, 155.

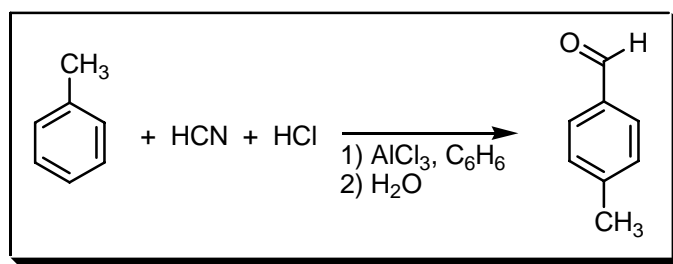
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#### COMMENTS :

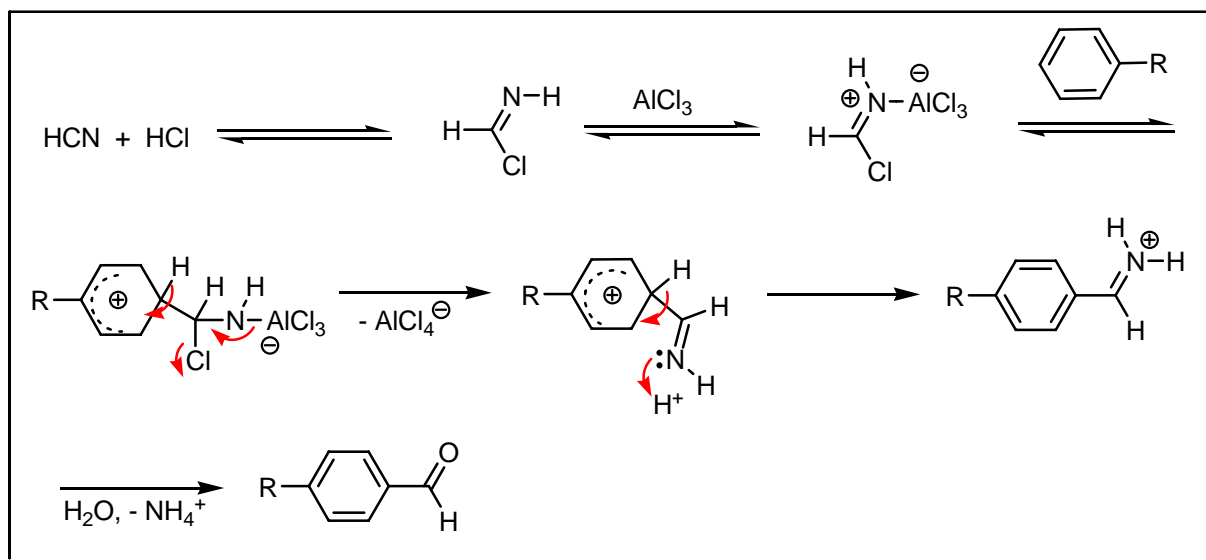
### GATTERMANN FORMYLATION

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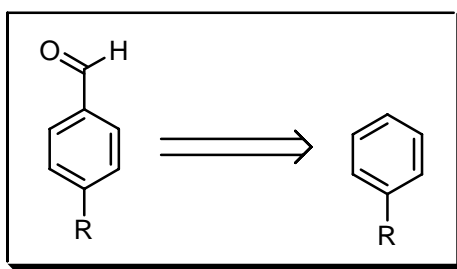
#### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The interaction of an aromatic compound, hydrogen cyanide and hydrogen chloride, usually in the presence of a metallic chloride, to give an aldimine hydrochloride, which is hydrolysed to the corresponding aldehyde. In the **Adams** modification, zinc cyanide replaces hydrogen cyanide. Sodium cyanide is also employed. In the **Hinkel** modification aluminium chloride and hydrogen cyanide in chlorobenzene or dichloroethane are used, a larger variety of compounds can be prepared under these conditions. In the **Shah – Laiwalla** modification rezorcine is synthesised using the **Adams** modification. See also **Duff**, **Fischer – Zerweck**, **Hoesch – Houben** and **Reimer – Tiemann** reactions.

## REFERENCES :

**March** : 543, 552

**Smith – March** : 715

**Houben – Weyl** : **7/1**, 20; **E3**, 19, 94; **E6a**, 95; **E6b**, 134; **E19c**, 366

**Org. React.** : **5**, 290, 387; **9**, 37

**Org. Synth.** : **23**, 57

**Org. Synth. Coll. Vol.** : **3**, 549

**Science of Synthesis** : **9**, 240

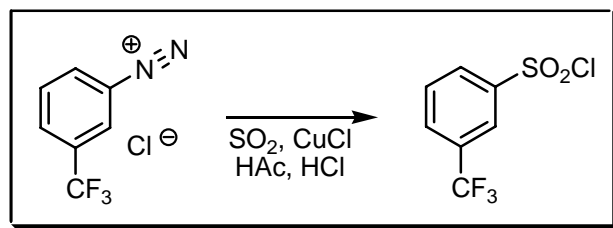
1) L. Gattermann, *Ber. Dtsch. Chem. Ges.*, 1898, **31**, 1149.

- 2) R. Adams; J. Levine, *J. Am. Chem. Soc.*, 1923, **45**, 2373.
- 3) L.E. Hinkel, *J. Chem. Soc.*, 1936, 339.
- 4) R.C. Shah; M.C. Laiwalla, *J. Chem. Soc.*, 1938, 1828.
- 5) E. Baltazzi; L.I. Krimen, *Chem. Rev.*, 1963, **63**, 526.
- 6) A. Kreutzberger, *Angew. Chem.*, 1967, **79**, 978.
- 7) Y. Sato; M. Yato; T. Ohwada; S. Saito; K. Shudo, *J. Am. Chem. Soc.*, 1995, **117**, 3037.

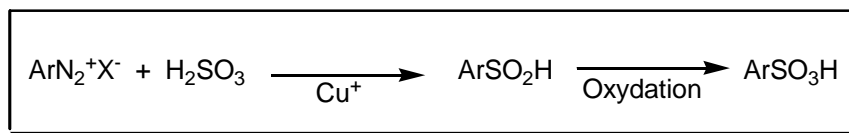
**COMMENTS :**

## GATTERMANN SULFINIC ACID SYNTHESIS

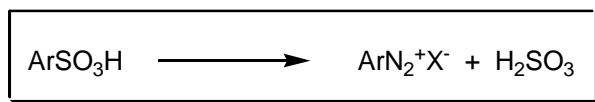
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

An aryl diazonium salt (sulfate) gives a sulfinic acid, which is readily oxidised to a sulfonic acid, on treatment with sulfurous acid with or without a copper catalyst. See also **Balz – Schiemann**, **Cadogan** arylation, **Craig** exchange, **Demjanov** rearrangement, **Gattermann** diazo, **Griess** deamination, **Knoevenagel** diazotation, **Körner – Contardi**, **Meerwein** arylation, **Sandmeyer** diazonium, **Schwechten** and **Witt** diazotation reactions.

## REFERENCES :

March : 724

Smith – March : 937

Houben – Weyl : 9, 534

Org. Synth. : 47, 4; 60, 121

Org. Synth. Coll. Vol. : 5, 60; 7, 508

1) L. Gattermann, *Ber. Dtsch. Chem. Ges.*, 1899, **32**, 1136.

2) J. Thomas, *J. Chem. Soc.*, 1909, **95**, 342.

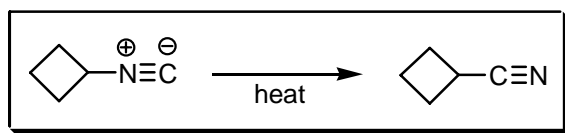
3) R.D. Haworth; A. Lapworth, *J. Chem. Soc.*, 1923, **123**, 2982.

4) W.E. Truce; J.F. Lyons, *J. Am. Chem. Soc.*, 1951, **73**, 126.

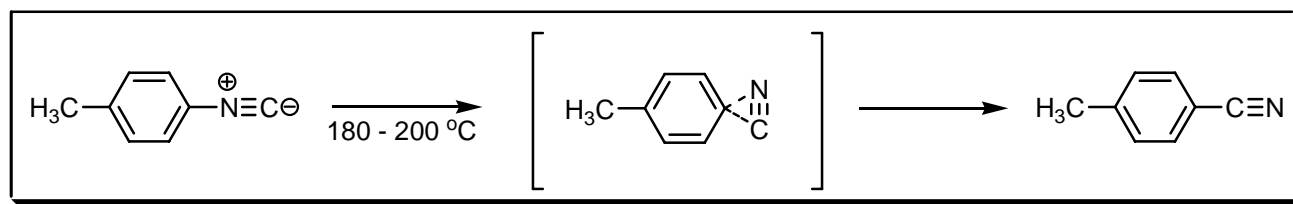
## COMMENTS :

## GAULTIER – GUILLEMARD REARRANGEMENT

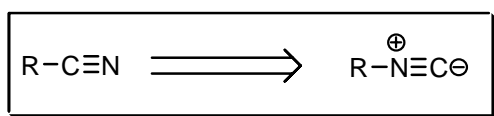
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

This is the thermal isonitrile rearrangement. The development of a new C-C bond is nearly synchronous with breaking of the N-C bond in non-polar solvents. In polar solvents, the mechanism is different, see **Rüchardt** *et al.*

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## REFERENCES :

**March** : 1102

**Smith – March** : 1421

**Smith 2<sup>nd</sup>** : 573

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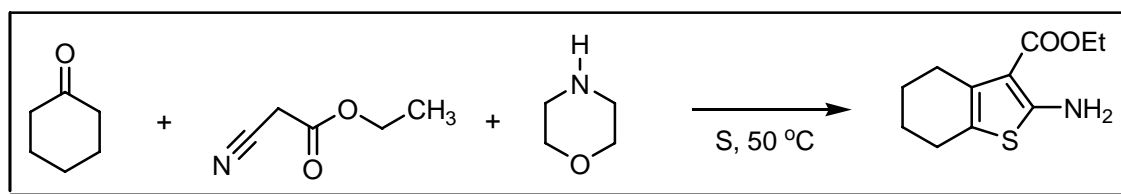
- 1) A. Gaultier, *Ann. Chim. (Paris)*, 1869, **17**, 215.
  - 2) A. Gaultier, *Ann. Chim. (Paris)*, 1869, **17**, 233.
  - 3) M.H. Guillemand, *C.R. Séances Acad. Sci.*, 1906, **143**, 1158.
  - 4) C. Grundmann, *Chem. Ber.*, 1958, **91**, 1380.
  - 5) G. Kohlmaier; B.S. Rabinovitch, *J. Phys. Chem.*, 1959, **63**, 1793.
  - 6) J. Casanova, jr.; N.D. Werner; R.E. Schuster, *J. Org. Chem.*, 1966, **31**, 3473.
  - 7) G.W. van Dine; R. Hoffmann, *J. Am. Chem. Soc.*, 1968, **90**, 3227.
  - 8) M. Meier; C. Rüchardt, *Chimia*, 1986, **40**, 238.
  - 9) J. Pakusch; C. Rüchardt, *Chem. Ber.*, 1991, **124**, 971.
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## COMMENTS :

## GEWALD HETEROCYCLE SYNTHESIS

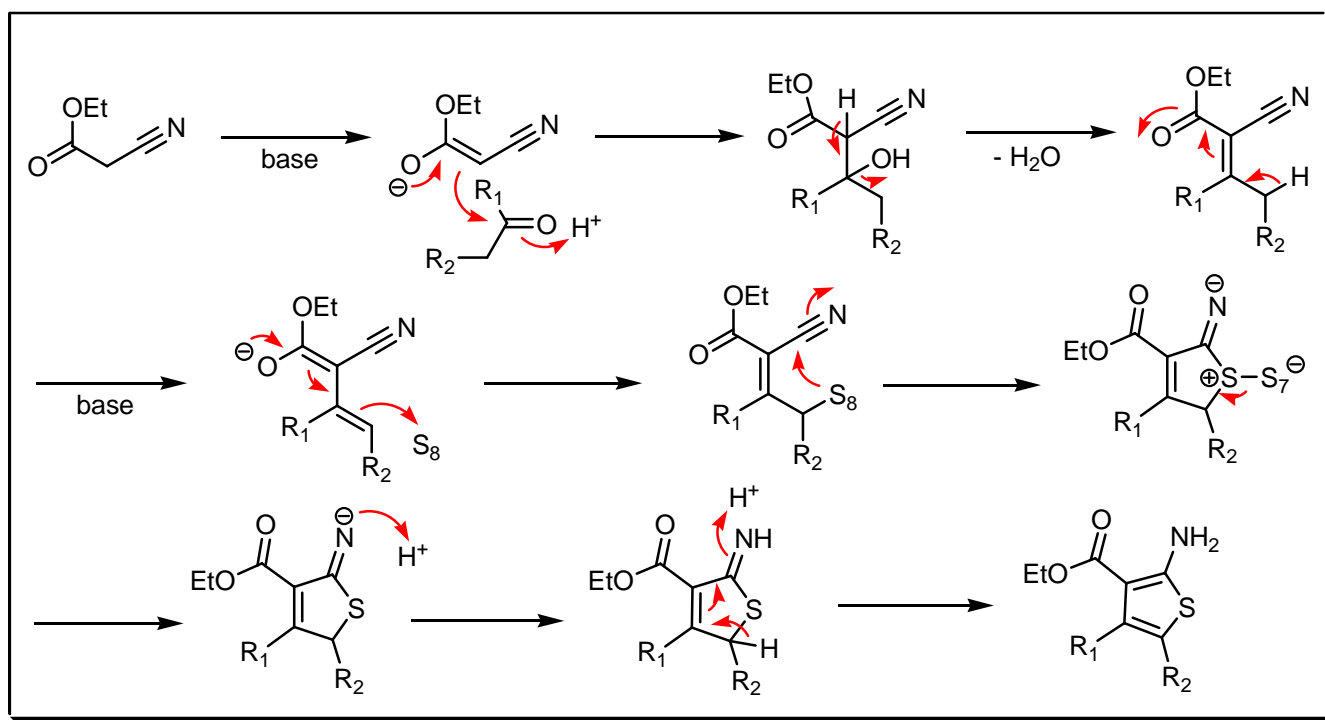
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### EXAMPLE :

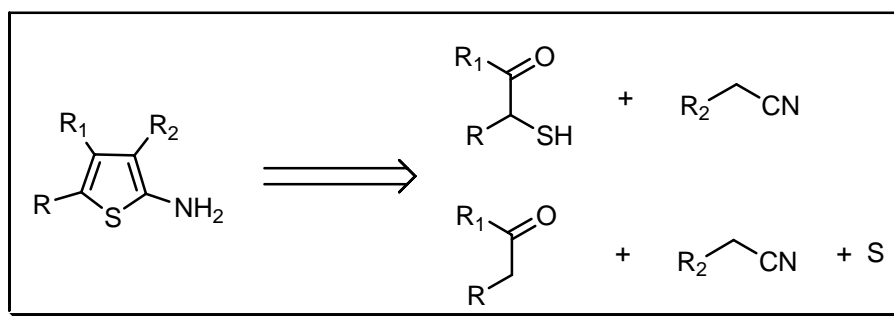




## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of 2-aminothiophenes by condensation of malononitriles with ketones. For more about the reaction mechanism see **Sabnis et al.**

## REFERENCES :

Houben – Weyl : E6a, 220, 241

Science of Synthesis : 9, 300, 307

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- 3) K. Gewald; E. Schinke; H. Boettcher, *Chem. Ber.*, 1966, **99**, 94.
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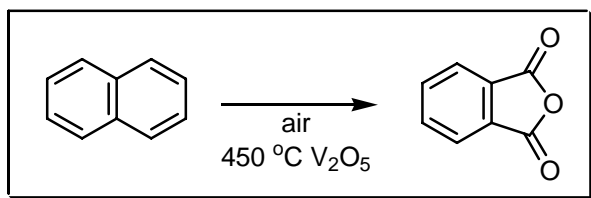
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7) S.M. Sherif, *Monatsh. Chem.*, 1996, **127**, 955.  
8) R.W. Sabnis; D.W. Rangnekar; N.D. Sonawane, *J. Heterocycl. Chem.*, 1999, **36**, 333.  
9) G.M. Castanedo; D.P. Sutherlin, *Tetrahedron Lett.*, 2001, **42**, 7181.  
10) A.P.F. Hoener; B. Henkel; J.-C. Gauvin, *Synlett*, 2003, 63.
- 

**COMMENTS :**

## GIBBS – WOHL PHTHALIC ANHYDRIDE PROCESS

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**EXAMPLE :**



**NOTES :**

Phthalic anhydride is obtained by the oxidation of naphthalene with air at 450 °C in the presence of a catalyst such as vanadium pentoxide.

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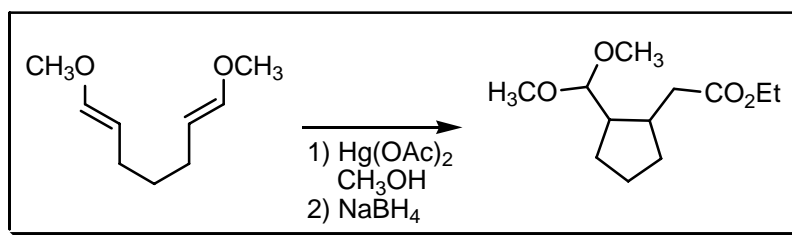
**REFERENCES :**

- 1) J. Walter, *J. Prakt. Chem.*, 1895, **51**, 107.  
2) H.D. Gibbs; C. Conover, *U.S. Patent*, 1918, 1285117.  
3) A. Wohl, *U.S. Patent*, 1930, 1787416.  
4) A. Wohl, *U.S. Patent*, 1930, 1787417.
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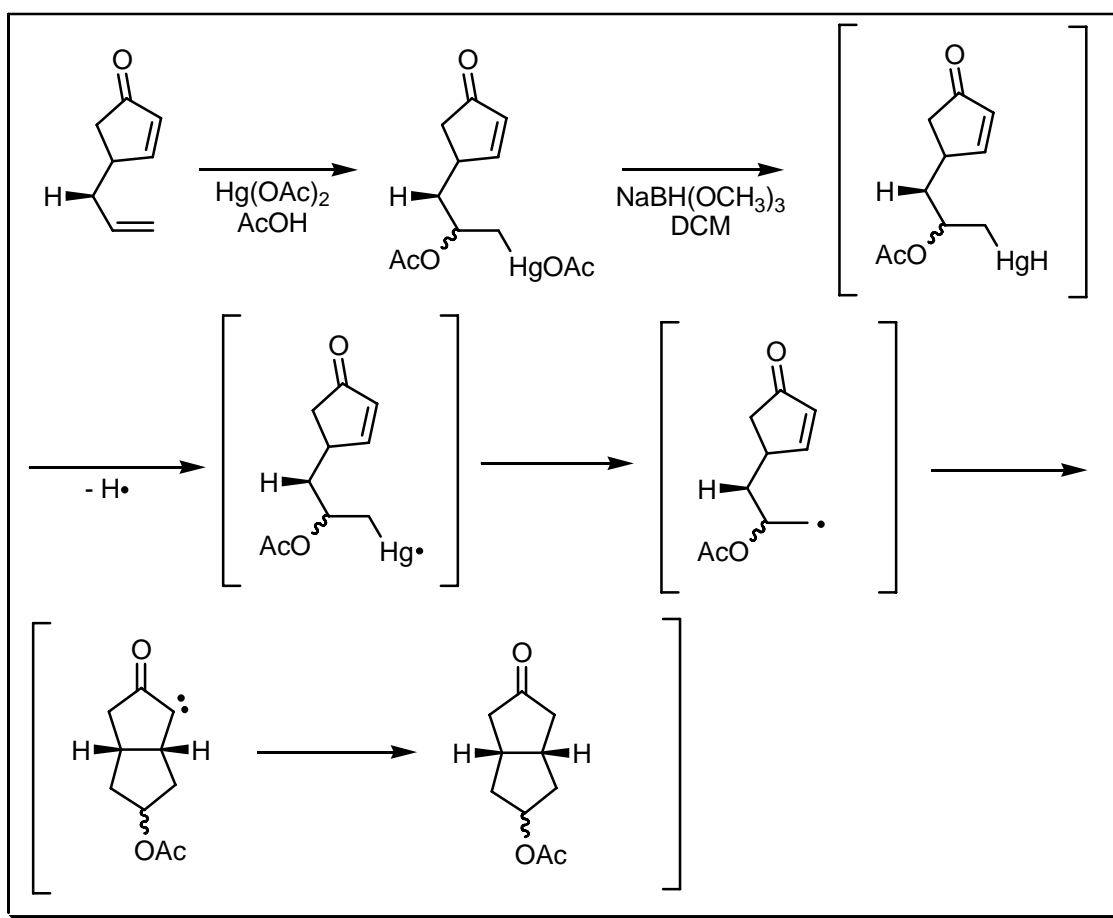
**COMMENTS :**

## GIESE REDUCTIVE MERCURY REACTION

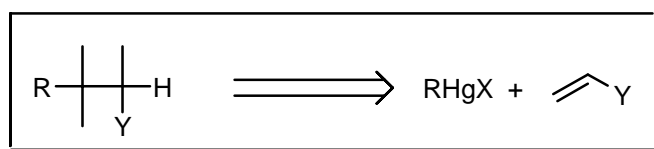
EXAMPLE :



MECHANISM :



DISCONNECTION :



**NOTES :**

The sodium trimethoxyborohydride or sodium borohydride or tributyltin hydride reduces the organomercuric acetate to give mercuric hydride. Homolytic cleavage of the mercury-hydrogen bond produces an organomercury-radical, which fragments to give a  $\beta$ -acetoxy radical. This reacts with the reactive enone double bond.

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**REFERENCES :**

**March** : 759

**Smith – March** : 993

**Smith** : 179

**Smith 2<sup>nd</sup>** : 150

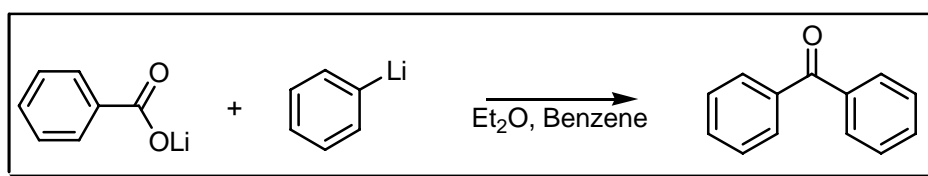
**Org. React.** : **48**, 301

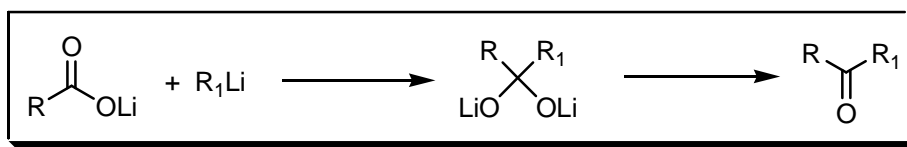
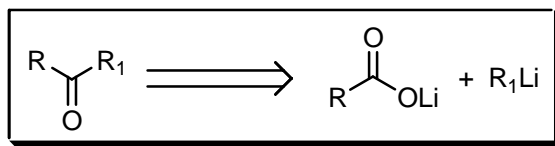
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  - 4) S.J. Danishefsky; S. Chackalamannil; B.-J. Uang, *J. Org. Chem.*, 1982, **47**, 2231.
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  - 6) J. Barluenga; M. Yus, *Chem. Rev.*, 1988, **88**, 487.
  - 7) D.P. Curran; J.Y. Xu, *J. Chem. Soc., Perkin Trans. 1*, 1995, 3061.
  - 8) S. Raghavan; K.A. Tony; S.R. Reddy, *Tetrahedron Lett.*, 2001, **42**, 8383.
- 

**COMMENTS :****GILMAN – van ESS SYNTHESIS**

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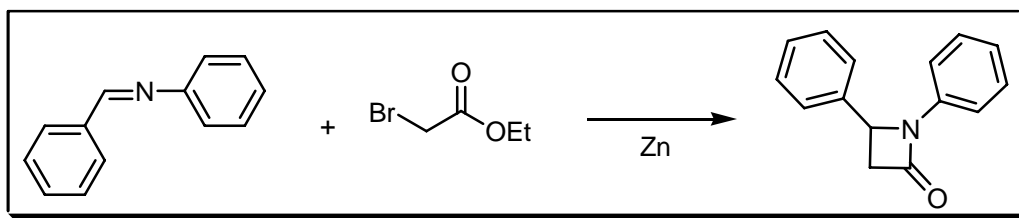
**EXAMPLE :**

**MECHANISM :****DISCONNECTION :****NOTES :**

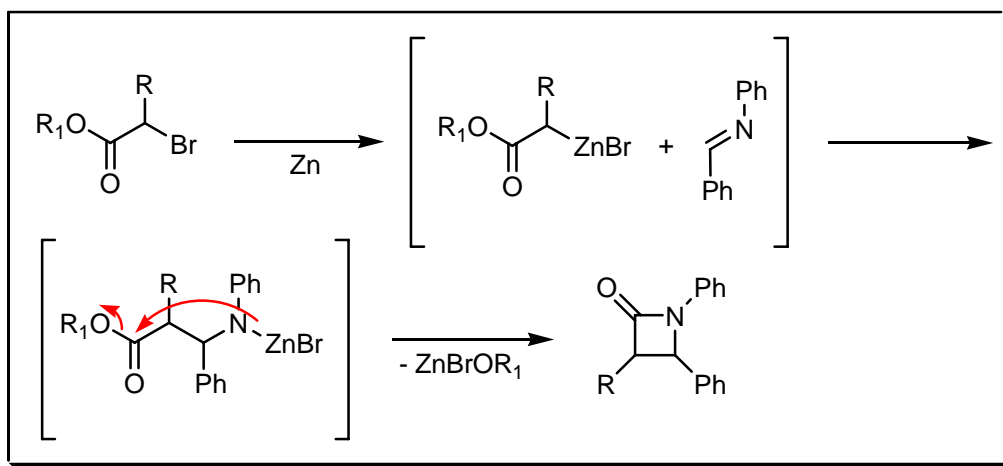
Phenyl alkyl ketones are prepared by the carbonation of organo lithium compounds.

**REFERENCES :**

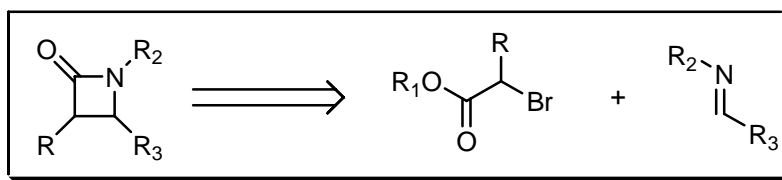
- 1) H. Gilman; P.R. van Ess, *J. Am. Chem. Soc.*, 1933, **55**, 1258.
- 2) C. Tegnér, *Acta. Chem. Scand.*, 1952, **6**, 782.
- 3) H.F. Bluhm; H.V. Donn; H.D. Zook, *J. Am. Chem. Soc.*, 1955, **77**, 4406.

**COMMENTS :****GILMAN – SPEETER REACTION****EXAMPLE :**

## MECHANISM :



## DISCONNECTION :



## NOTES :

The addition of zinc metal to a mixture of an  $\alpha$ -bromoester and an imine to afford a  $\beta$ -lactam (**Reformatsky** reaction). Catalytic and asymmetric versions of the reaction are known. See also **Dreiding – Schmidt** and **Reformatsky** reactions.

## REFERENCES :

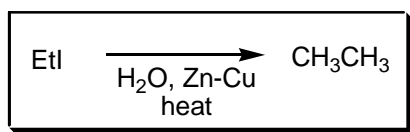
- 1) H. Gilman; M. Speeter, *J. Am. Chem. Soc.*, 1943, **65**, 2255.
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- 3) R. Brieva; J.Z. Crich; C.J. Sih, *J. Org. Chem.*, 1993, **58**, 1068.
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- 6) K. Tomioka; H. Fujieda; S. Hayashi; M.A. Hussein; T. Kambara; Y. Nomura; M. Kanai; K. Koga, *Chem. Commun.*, 1999, 715.
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## COMMENTS :

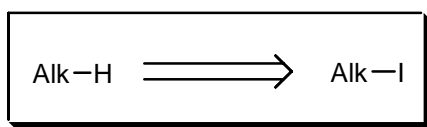
## GLADSTONE – TRIBE SYNTHESIS

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### EXAMPLE :



### DISCONNECTION :



### NOTES :

This reaction comprises the reduction of alkyl halides to the corresponding hydrocarbons using the zinc-copper couple in water or ethanol.

### REFERENCES :

**Org. Synth.** : **12**, 86

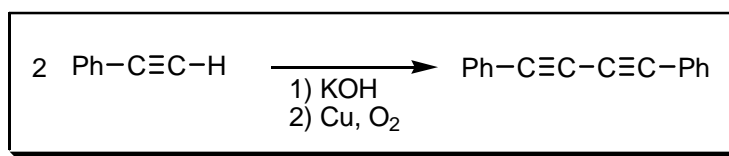
**Org. Synth. Coll. Vol.** : **2**, 184

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- 1) J.H. Gladstone; A. Tribe, *J. Chem. Soc.*, 1873, **26**, 445.
  - 2) J.H. Gladstone; A. Tribe, *J. Chem. Soc.*, 1873, **26**, 678.
  - 3) J.H. Gladstone; A. Tribe, *J. Chem. Soc.*, 1873, **26**, 961.
  - 4) J.H. Gladstone; A. Tribe, *J. Chem. Soc.*, 1884, **45**, 154.
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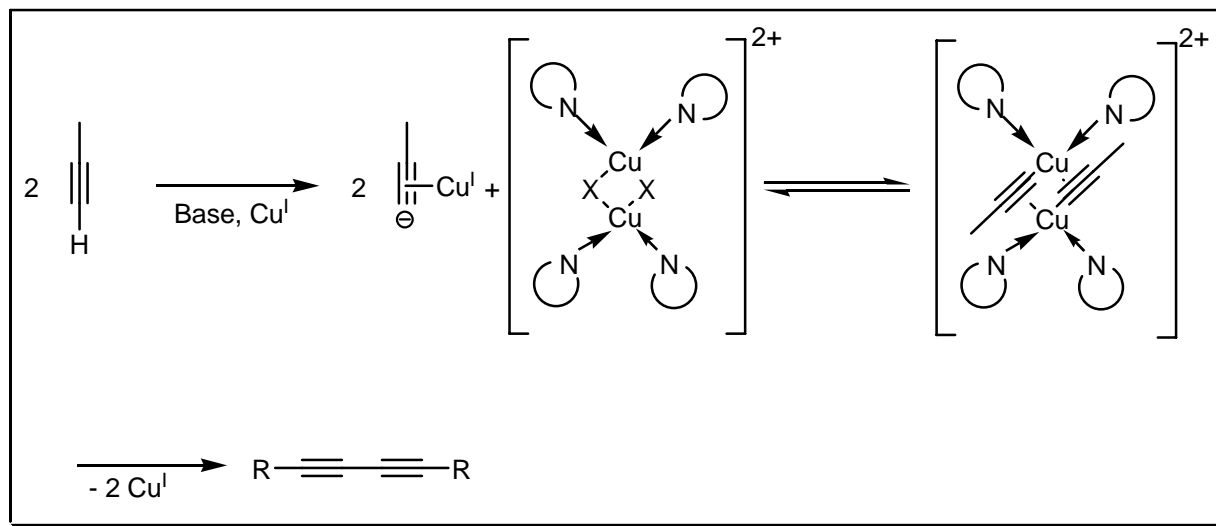
### COMMENTS :

## GLASER COUPLING (CADIOT – CHODKIEWICZ – EGLINGTON COUPLING)

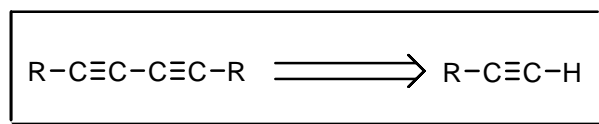
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Copper or silver acetylides containing acetylenic hydrogen on treatment with oxygen gas in the presence of ammonia or amines and ammonium chloride condense by oxidative coupling to form symmetrical di-yne compounds. When the reaction involves a terminal alkyne it is often called the **Cadiot – Chodkiewicz** reaction. A reaction of a terminal halogen-substituted alkyne is often called an **Eglinton – Galbraith** reaction. The **Hay** or **Glaser – Hay** coupling uses a triethylsilyl protecting group. A strictly pair selective synthesis has been published by **Negishi et al.** For a DFT study on the **Hay** modification see **Fomine et al.** A radical mechanism, although proposed, has been rejected. See also **Sonogashira – Hagihara** and **Ullmann** diaryl reactions.

### REFERENCES :

March : 714

Smith – March : 927

Smith : 680

Smith 2<sup>nd</sup> : 576, 1186



Houben – Weyl : **13/1**, 751; **E5**, 386, 393; **E15**, 3333

Org. Synth. : **45**, 39; **65**, 52, 61

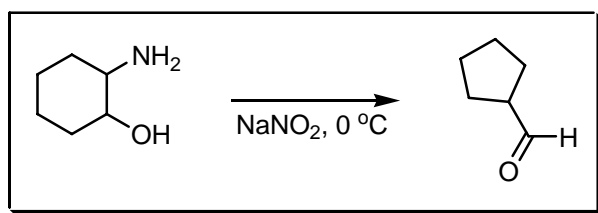
Org. Synth. Coll. Vol. : **5**, 517; **8**, 63, 606

- 1) C. Glaser, *Ber. Dtsch. Chem. Ges.*, 1869, **2**, 422.
- 2) C. Glaser, *Liebigs Ann. Chem.*, 1870, **154**, 159.
- 3) W. Chodkiewicz; P. Cadiot, *C.R. Séances Acad. Sci.*, 1955, **241**, 1055.
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- 8) A.S. Hay, *J. Org. Chem.*, 1962, **27**, 3320.
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- 13) L. Fomina; B. Vazquez; E. Tkatchouk; S. Fomine, *Tetrahedron*, 2002, **58**, 6741.

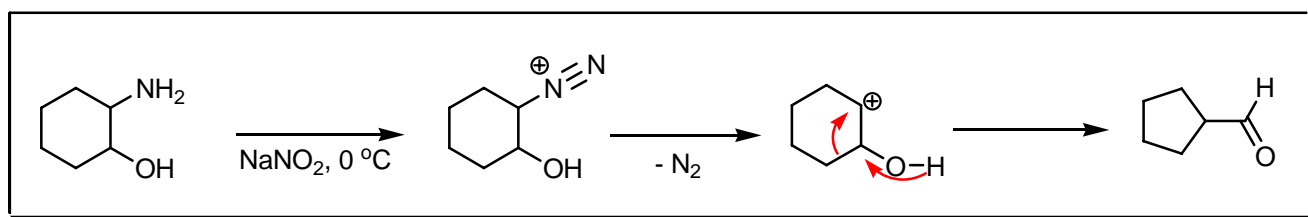
#### COMMENTS :

### GODCHOT – MOUSSERON RING CONTRACTION

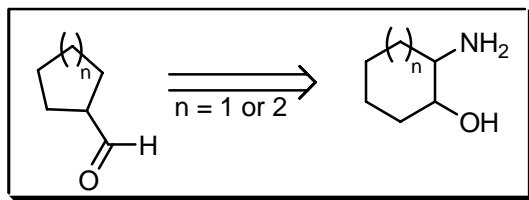
#### EXAMPLE :



#### MECHANISM :



## DISCONNECTION :



## NOTES :

A  $C_6$  or  $C_7$  2-amino-cycloalkanol yields on treatment with sodium nitrite at  $0^\circ\text{C}$  the cycloalkanoic aldehyde of the lower cycloalkane. See also **Demjanov** rearrangement, **Nametkin** rearrangement and **Tiffeneau – Demjanov** ring enlargement.

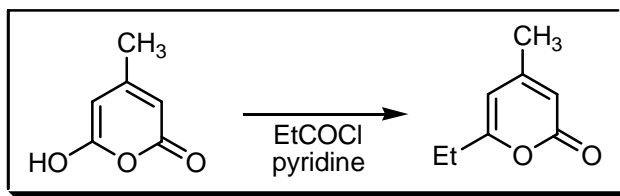
## REFERENCES :

M. Godchot; M. Mousseron, *C.R. Séances Acad. Sci.*, 1934, **198**, 2000.

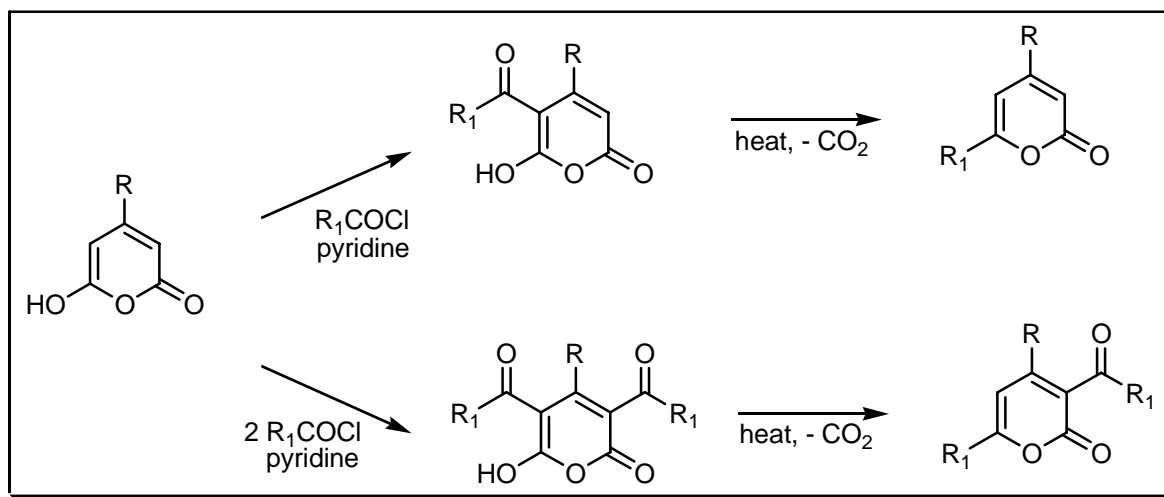
## COMMENTS :

## GOGTE SYNTHESIS

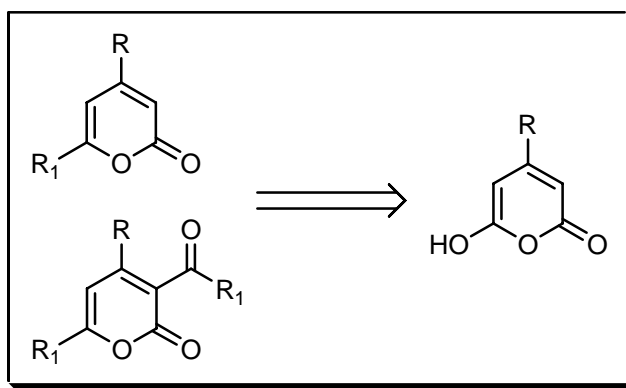
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

$\beta$ -Substituted glutaconic anhydrides react in the presence of pyridine with one or two molecules of an acyl chloride to form C-acylation products. These compounds afford  $\alpha$ -pyrone derivatives when heated.

### REFERENCES :

C.R. Gogte, *Proc. Indian Acad. Sci.*, 1938, **7A**, 214.

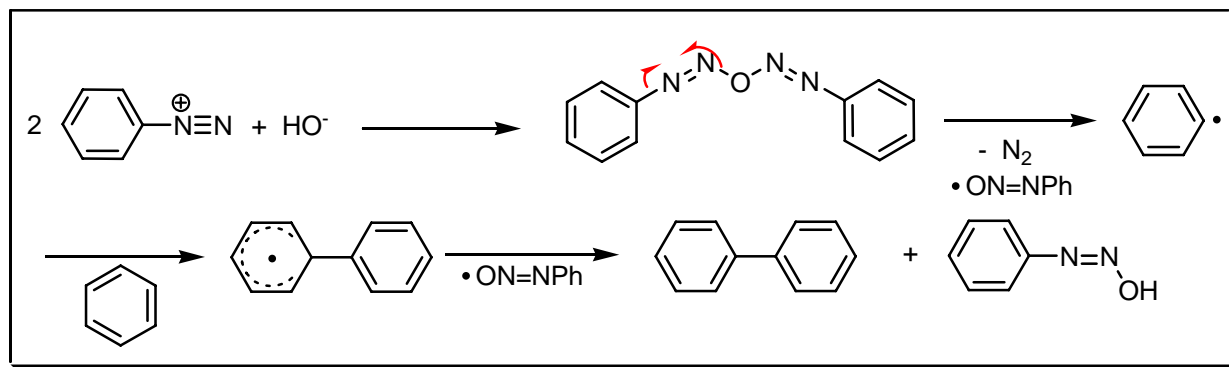
### COMMENTS :

## GOMBERG – BACHMANN – HEY REACTION

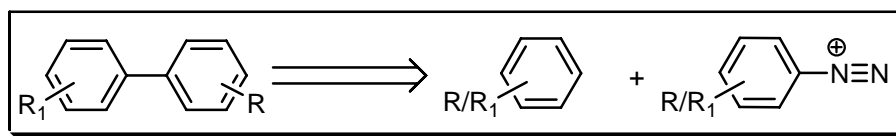
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Diaryls are produced by the addition of alkali to a mixture of a diazonium salt and a liquid aromatic hydrocarbon or its derivative. Heterocyclic compounds can also be employed and the method is of value for *intramolecular* cyclisations (**Pschorr** reaction). See also **Bamberger – Hey**, **Cadogan**, **Gattermann**, **Graebe – Ullmann**, **Pschorr**, **Ullmann** and **Vorländer – Meyer** reactions.

### REFERENCES :

March : 715, 1225

Smith – March : 928, 1560

Smith : 1436

Smith 2<sup>nd</sup> : 1184

Houben – Weyl : **E6a**, 928; **E7b**, 595; **E8d**, 568; **E16a**, 1129

Org. React. : **2**, 224; **9**, 409

Org. Synth. : **8**, 42; **33**, 56

Org. Synth. Coll. Vol. : **1**, 113; **4**, 718

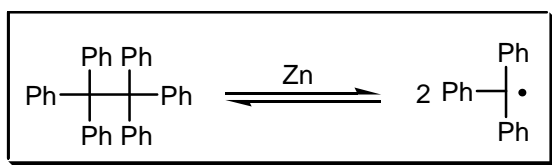
Science of Synthesis : **9**, 357

- 1) E. Bamberger, *Ber. Dtsch. Chem. Ges.*, 1895, **28**, 403.
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- 4) M. Sainsbury, *Tetrahedron*, 1980, **36**, 3329.
- 5) J.A. Beadle; S.H. Korzeniowski; D.E. Rosenberg; B.J. Garcia-Slanga; G.W. Gokel, *J. Org. Chem.*, 1984, **49**, 1594.
- 6) R. Bolton; G. Williams, *Chem. Soc. Rev.*, 1986, **15**, 261.
- 7) M. Gurczynski; P. Tomasik, *Org. Prep. Proced. Int.*, 1991, **23**, 438.
- 8) Y.H. Lai; J.P. Jiang, *J. Org. Chem.*, 1997, **62**, 4412.

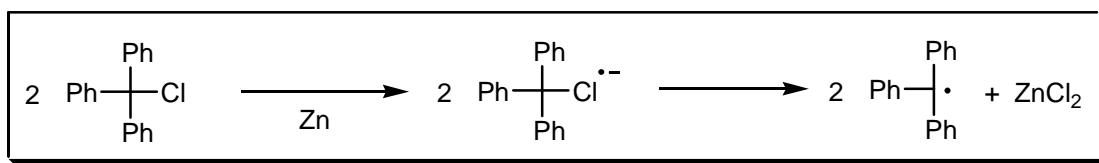
**COMMENTS :**

## GOMBERG FREE RADICAL REACTION

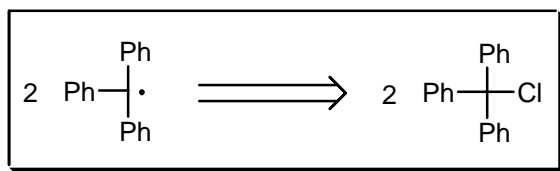
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

Free radicals are obtained by the reaction of triarylmethyl halides with metals.

## REFERENCES :

Houben – Weyl : E6a, 103

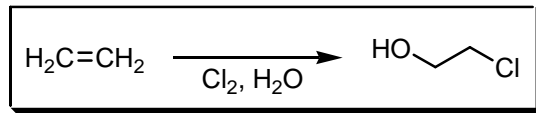
Science of Synthesis : 9, 246

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  - 3) J.M. McBride, *Tetrahedron*, 1974, **30**, 2009.
  - 4) B.E. Daikh; R.G. Finke, *J. Chem. Soc., Chem. Commun.*, 1991, 784.
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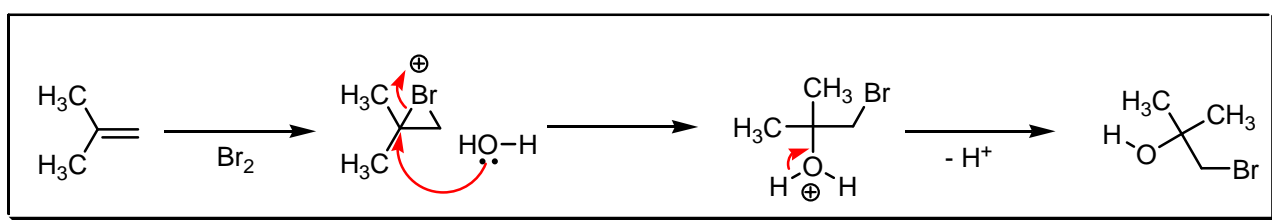
## COMMENTS :

## GOMBERG SYNTHESIS

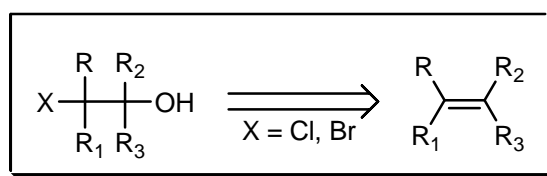
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



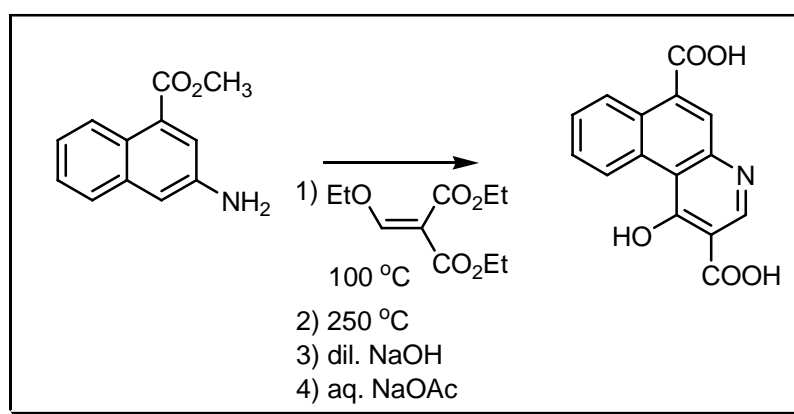
**NOTES :**

In the classic example ethylene chloro- or bromohydrin is obtained by treating ethylene with chlorine in the presence of water at temperatures from 0 – 20 °C. The active species can also be HOCl or HOBr. The reaction has been extended to other alkenes.

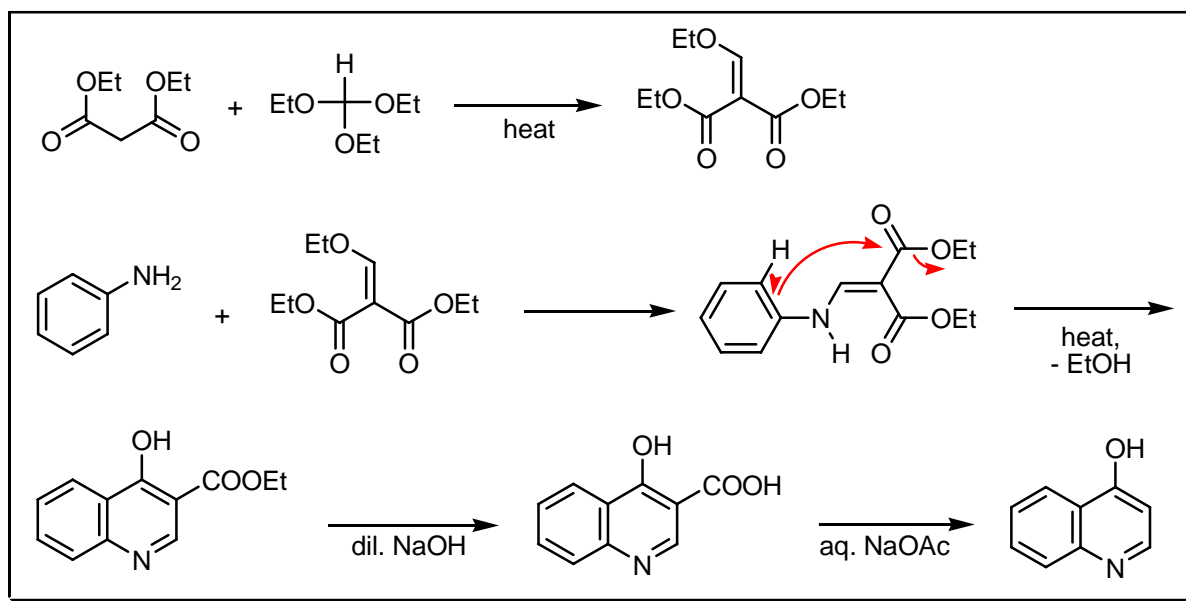
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**REFERENCES :**

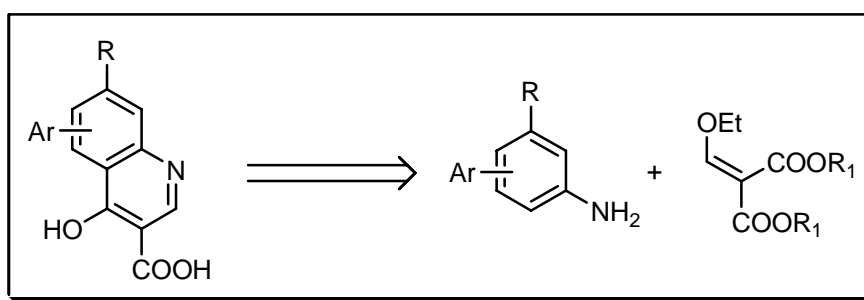
- 1) M. Gomberg, *J. Am. Chem. Soc.*, 1919, **41**, 1414.
  - 2) G. Braun, *J. Am. Chem. Soc.*, 1930, **52**, 3176.
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  - 5) S. Arai; T. Takeuchi; M. Ishikawa; T. Takeuchi; M. Yamazaki; M. Hida, *J. Chem. Soc., Perkin Trans. 1*, 1987, 481.
- 

**COMMENTS :****GOULD – JACOBS REACTION****EXAMPLE :**

## MECHANISM :



## DISCONNECTION :



## NOTES :

In this modification of the **Knorr** quinoline reaction the aromatic amine is heated with ethoxymethylene malonic ester and the resulting acrylate is subjected to high temperature cyclisation. Aminopyridines and aminoquinolines can be employed in this synthesis. See also **Conrad – Limpach**, **Combes**, **Doebner – Miller** and **Knorr** quinoline reactions.

## REFERENCES :

Smith : 1335

Smith 2<sup>nd</sup> : 1099

Org. Synth. : 28, 38

Org. Synth. Coll. Vol. : 3, 272



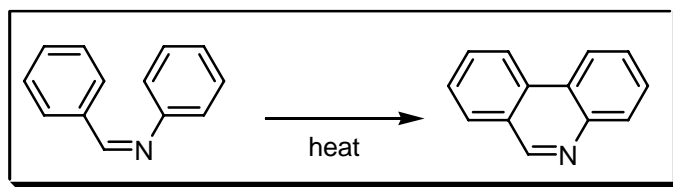
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  - 3) D.G. Markees; L.S. Schwab, *Helv. Chim. Acta*, 1972, **55**, 1379.
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- 

**COMMENTS :**

## GRAEBE – PICTET SYNTHESIS

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**EXAMPLE :**



**NOTES :**

The synthesis of phenanthridine by pyrolytic dehydrogenation of benzylideneaniline.

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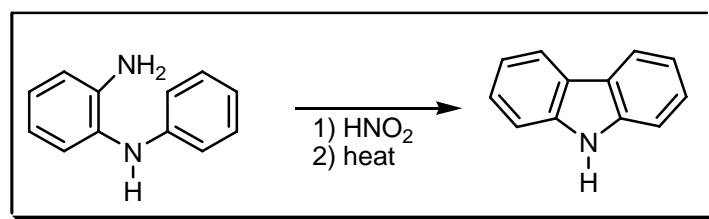
**REFERENCES :**

- 1) C. Graebe, *Ber. Dtsch. Chem. Ges.*, 1884, **17**, 1370.
  - 2) A. Pictet; H.J. Ankersmit, *Liebigs Ann. Chem.*, 1891, **266**, 138.
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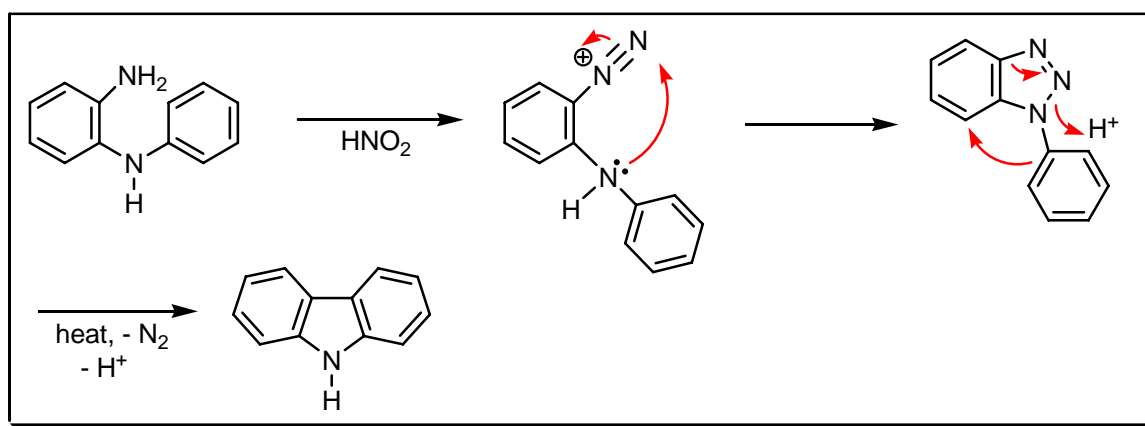
**COMMENTS :**

## GRAEBE – ULLMANN CARBAZOLE SYNTHESIS

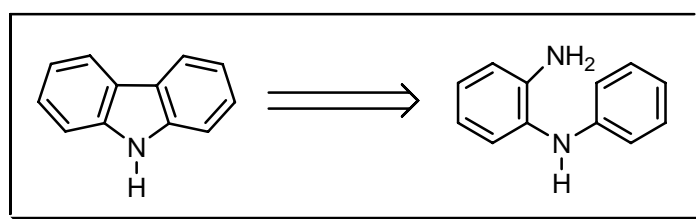
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

2-Aminodiphenylamine on treatment with nitrous acid yields a benzotriazole, which on heating loses nitrogen to give a carbazole. See also **Gomberg – Bachmann – Hey**, **Pschorr** and **Ullmann** fluorenone reactions.

### REFERENCES :

Houben – Weyl : E6a, 960

Science of Synthesis : 10, 717

1) C. Graebe; F. Ullmann, *Liebigs Ann. Chem.*, 1896, **291**, 16.

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3) P. Nantka-Namirski; J. Zieleniak, *Acta Pol. Pharm.*, 1977, **34**, 455.

4) D.J. Hagan; E. Giminez-Arnau; C.H. Schwalbe; M.F.G. Stevens, *J. Chem. Soc., Perkin Trans. 1*, 1997, 2739.

5) D.J. Hagan; D. Chan; C.H. Schwalbe; M.F.G. Stevens, *J. Chem. Soc., Perkin Trans. 1*, 1998, 915.

6) M.J. Ellis; M.F.G. Stevens, *J. Chem. Soc., Perkin Trans. 1*, 2001, 3174.

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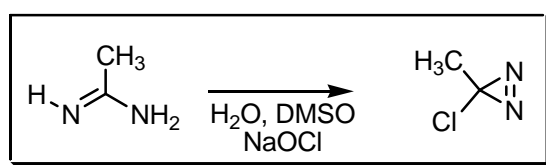
**COMMENTS :**

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**GRAHAM REACTION**

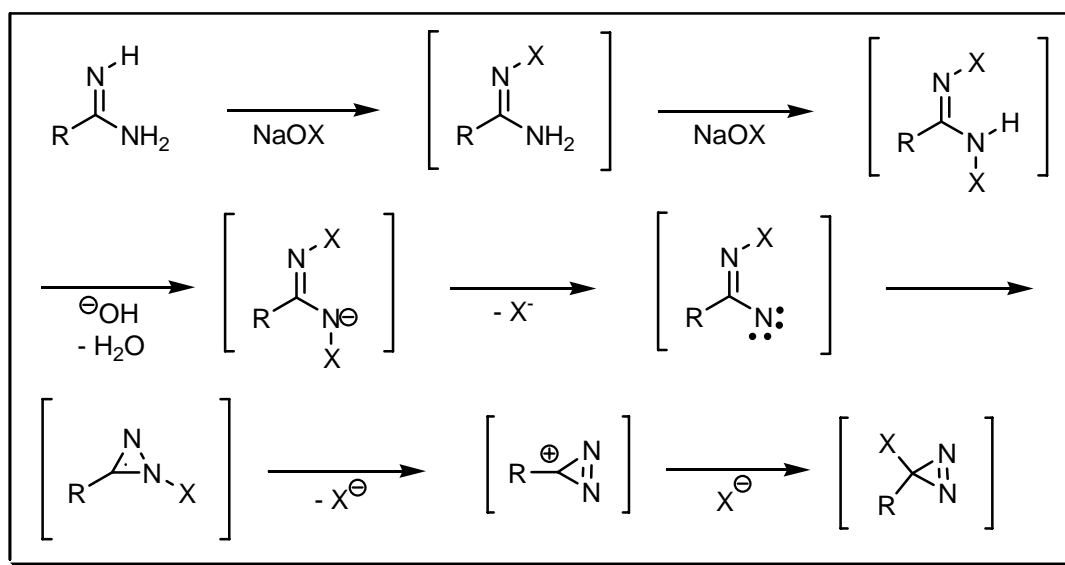
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**EXAMPLE :**



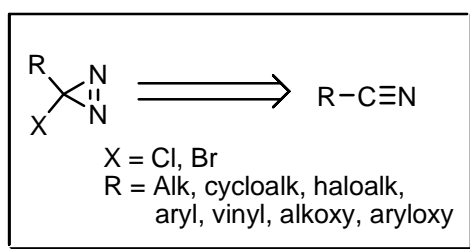
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**MECHANISM :**



---

**DISCONNECTION :**



## NOTES :

In general a nitrile is converted in a two-step process to an amidine. Oxidation of the latter with  $\text{^-\text{OCl}}$  or  $\text{^-\text{OBr}}$  will afford diazirines. See also **Pinner** and **Schmitz** diazirine reactions.

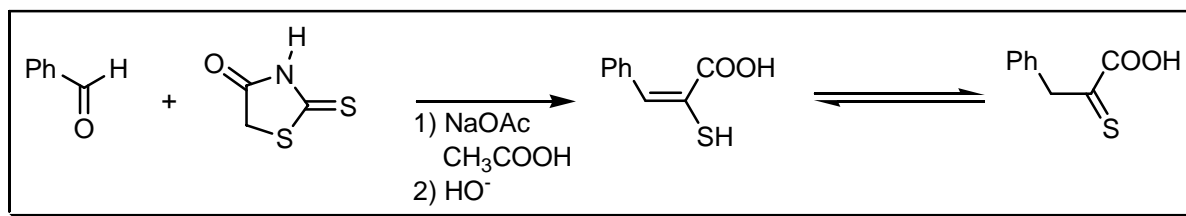
## REFERENCES :

- 1) W.H. Graham, *J. Am. Chem. Soc.*, 1965, **87**, 4396.
- 2) R.A. Moss; J. Włostowska; W. Guo; M. Fedorynski; J.P. Springer; J.M. Hirshfield, *J. Org. Chem.*, 1981, **46**, 5048.
- 3) J. Włostowska; R.A. Moss; W. Guo; M.J. Chang, *J. Chem. Soc., Chem. Commun.*, 1982, 432.
- 4) R.A. Moss, *Acc. Chem. Res.*, 1989, **22**, 15.
- 5) R.A. Moss; W. Ma; D.C. Merrer; S. Xue, *Tetrahedron Lett.*, 1995, **36**, 8761.

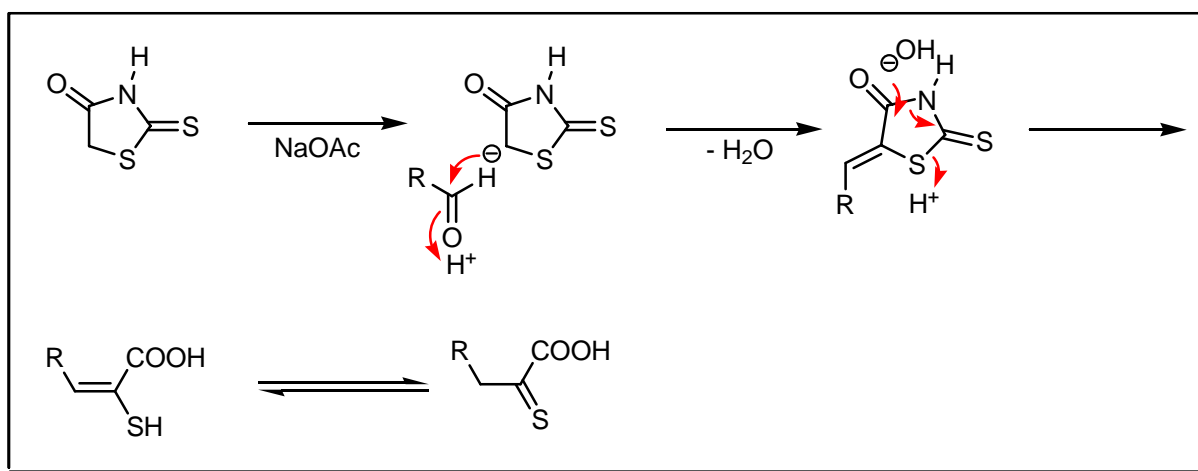
## COMMENTS :

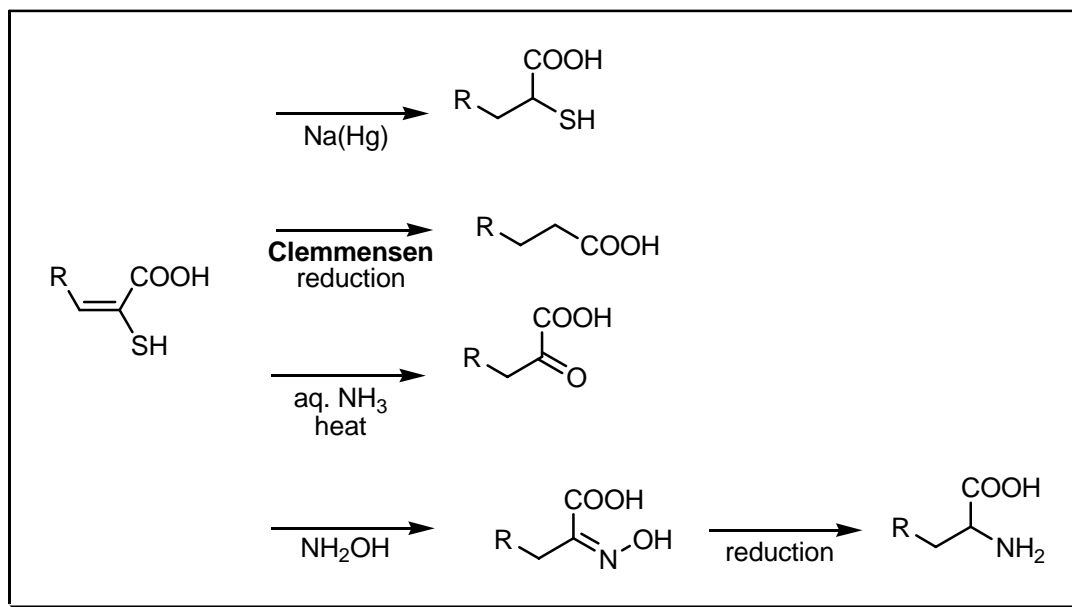
## GRÄNACHER CONDENSATION

### EXAMPLE :

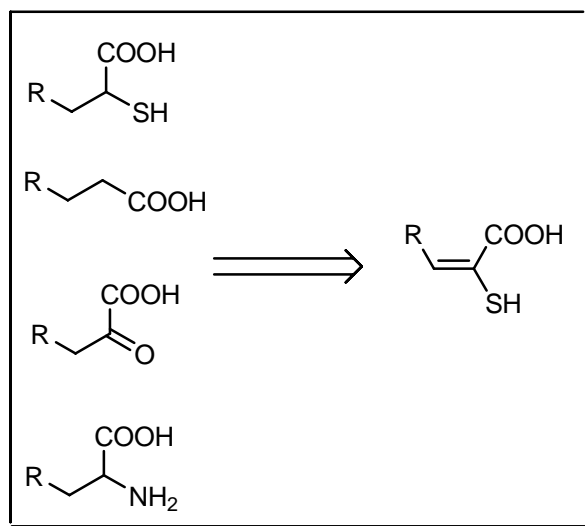


### MECHANISM :





#### DISCONNECTION :



#### NOTES :

An aromatic aldehyde condenses with rhodanine in the presence of sodium acetate and acetic acid to yield an aralrhodanine, which on hydrolysis with alkali gives a thioketo acid. This on treatment with hydroxylamine and sodium ethoxide gives an  $\alpha$ -oximino- $\beta$ -arylpropionic acid, which on heating with acetic anhydride is simultaneously decarboxylated and dehydrated to the nitrile. The oxime can be reduced to the corresponding amino acid. The nitrile can be converted into the amine or acid with one carbon atom more than the starting aldehyde.

#### REFERENCES :

Houben – Weyl : 9, 38

Org. Synth. : 27, 73

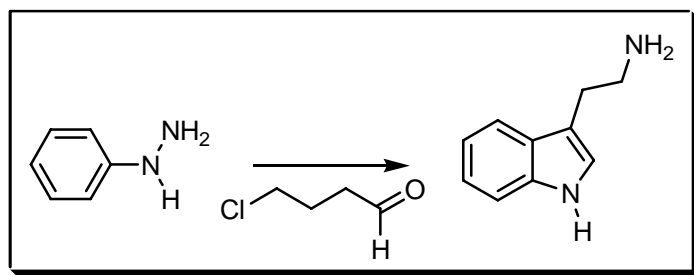
Org. Synth. Coll. Vol. : 3, 763

- 2) H.E. Fischer; H. Hibbert, *J. Am. Chem. Soc.*, 1947, **69**, 1208.  
3) F.J. Allan; G.G. Allan, *Recl. Trav. Chim. Pays-Bas*, 1959, **78**, 67.  
4) G. Buchbauer; M. Kern, *Arch. Pharm. (Weinheim, Ger.)*, 1980, **313**, 1043.

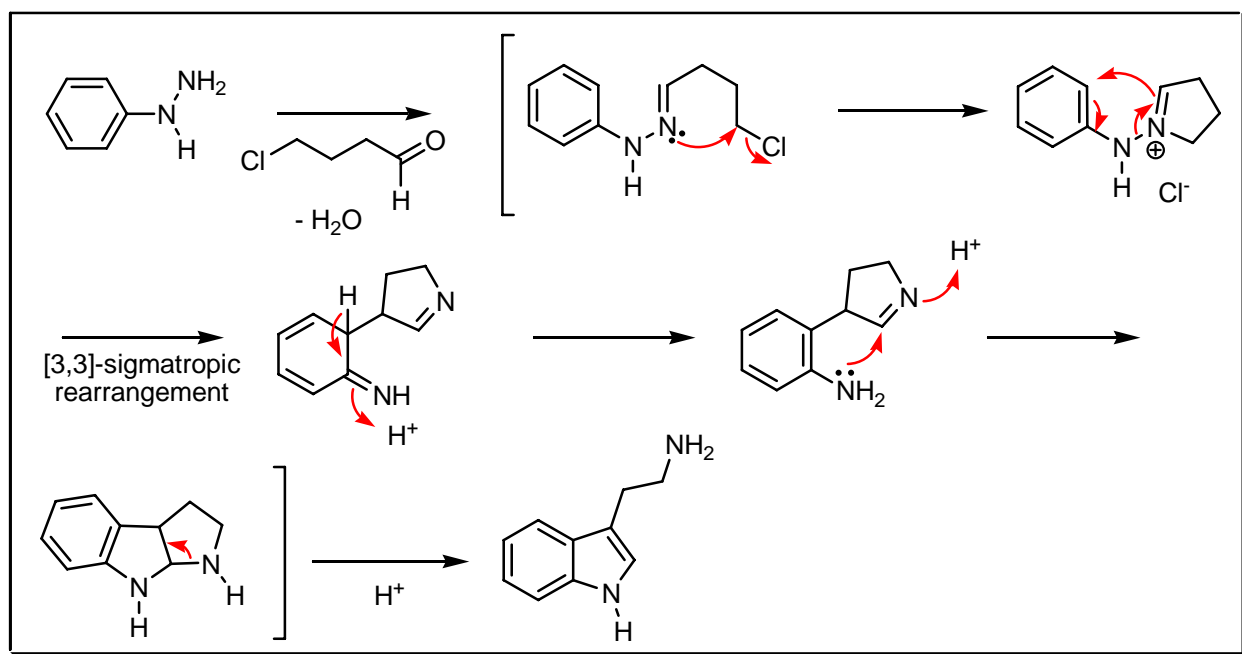
COMMENTS :

## GRANDBERG TRYPTAMINE SYNTHESIS

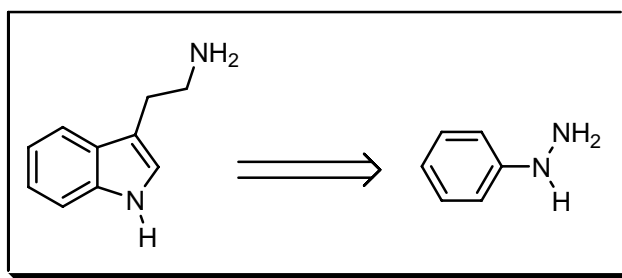
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The formation of tryptamine from 1-phenyl hydrazine. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

## REFERENCES :

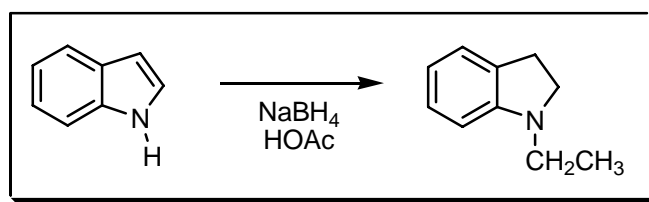
**Science of Synthesis : 10, 377**

I.I. Grandberg, *Chem. Heterocycl. Compd. (Engl. Transl.)*, 1974, **10**, 501.

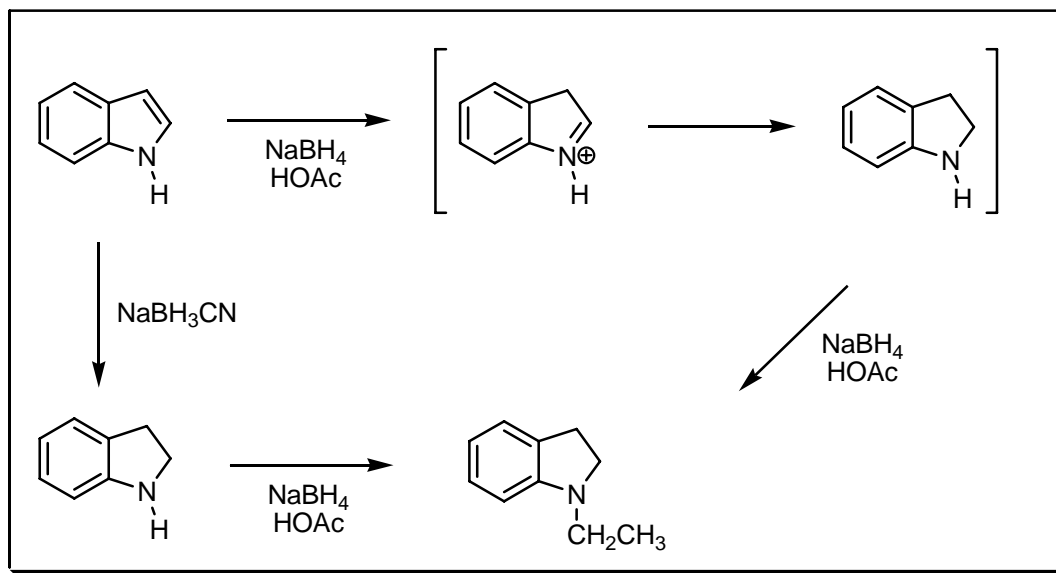
## COMMENTS :

## GRIBBLE INDOLE REDUCTION

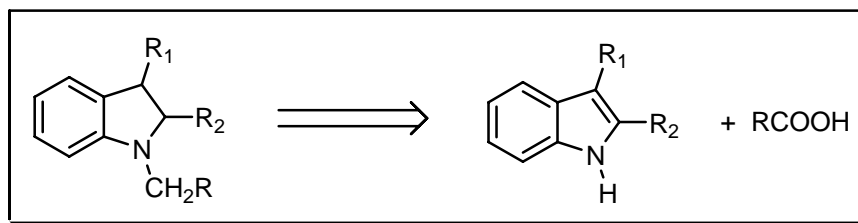
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Indole nitrogen atom is reduced and alkylated using sodium borohydride and acetic acid. The N-alkylation can be prevented by using sodium cyanoborohydride and acetic acid.

## REFERENCES :

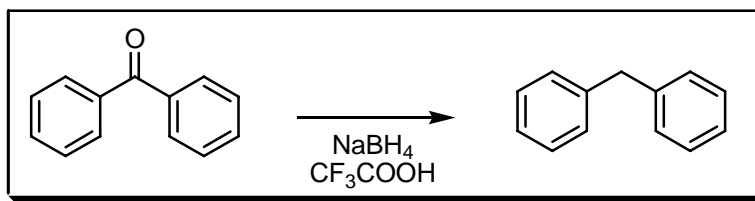
- 1) J.A. Marshall; W.S. Johnson, *J. Org. Chem.*, 1963, **28**, 421.
- 2) G.W. Gribble; P.D. Lord; J. Skotnicki; S.E. Dietz; J.T. Eaton; J.L. Johnson, *J. Am. Chem. Soc.*, 1974, **96**, 7812.
- 3) G.W. Gribble; J.H. Hoffman, *Synthesis*, 1977, 859.
- 4) G.W. Gribble; C.F. Nutaitis, *Org. Prep. Proced. Int.*, 1985, **17**, 317.
- 5) G.W. Gribble, *Chemtech*, 1996, **12**, 26.
- 6) M. Somei; F. Yamada; H. Morikawa, *Heterocycles*, 1997, **46**, 91.
- 7) G.W. Gribble, *Chem. Soc. Rev.*, 1998, **27**, 395.
- 8) F. He; B.M. Foxman; B.B. Snider, *J. Am. Chem. Soc.*, 1998, **120**, 6417.
- 9) K.C. Nicolaou; B.S. Safina; N. Winssinger, *Synlett*, 2001, 900.

## COMMENTS :

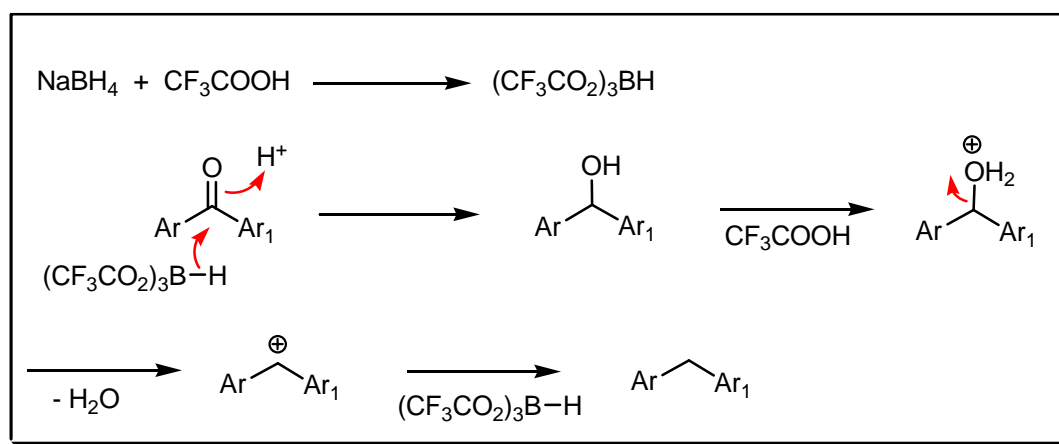


## GRIBBLE REDUCTION

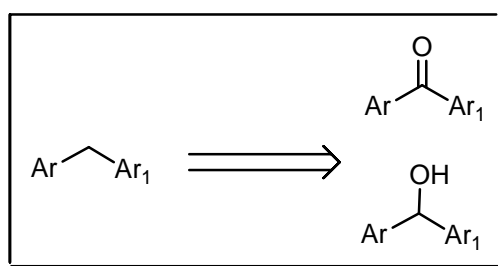
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Diarylketones and diarylmethanols are reduced using sodium borohydride in trifluoroacetic acid.

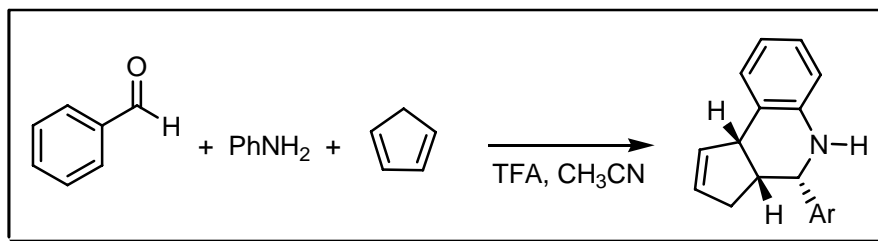
### REFERENCES :

- 1) G.W. Gribble; R.M. Leese; B.E. Evans, *Synthesis*, 1977, 172.
- 2) G.W. Gribble; C.F. Nutaitis, *Org. Prep. Proced. Int.*, 1985, **17**, 317.
- 3) A. Daich; B. Decroix, *J. Heterocycl. Chem.*, 1992, **29**, 1789.
- 4) T. Sattelkau; A.M. Qandil; D.E. Nichols, *Synthesis*, 2001, 262.

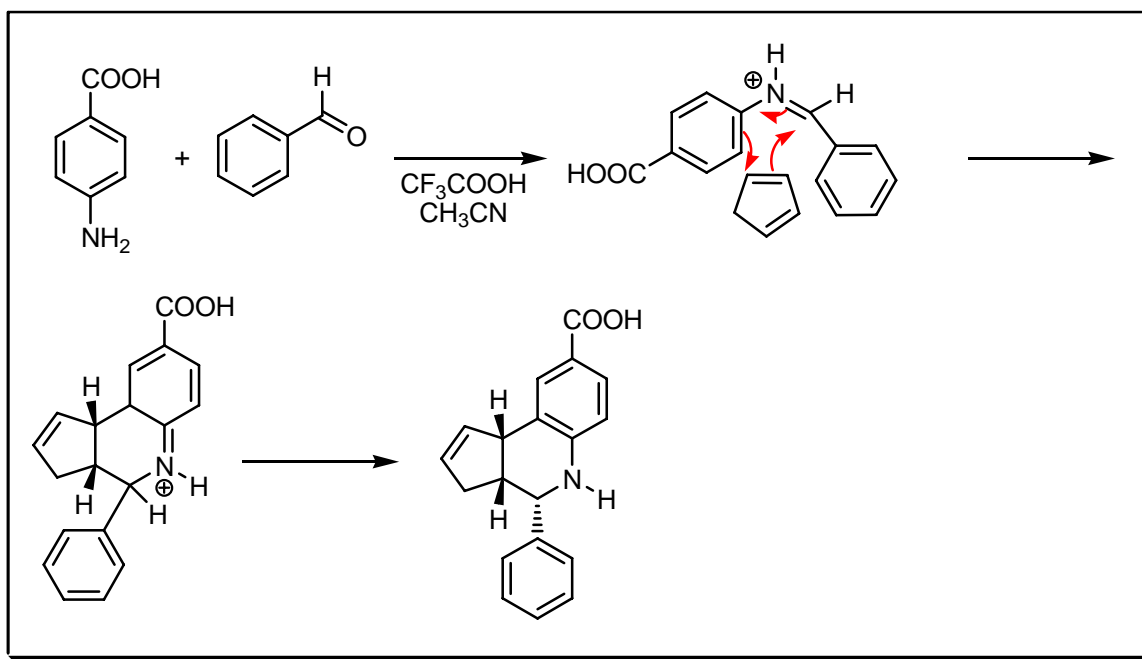
COMMENTS :

## GRIECO CONDENSATION

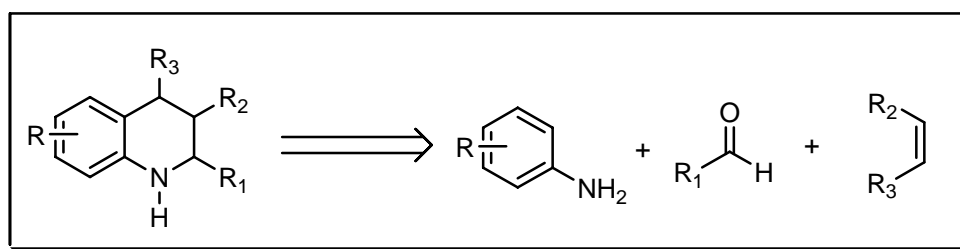
EXAMPLE :



MECHANISM :



DISCONNECTION :



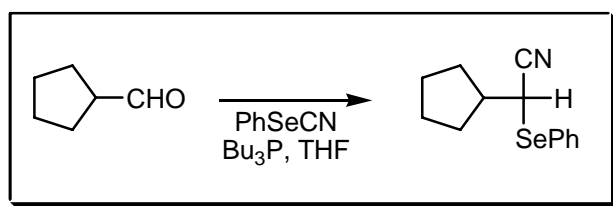
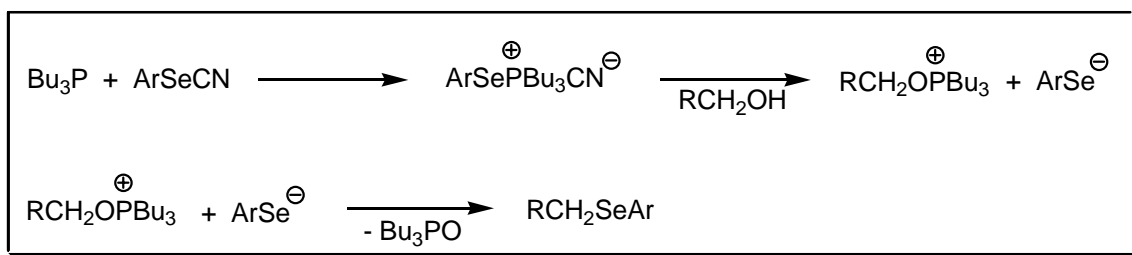
**NOTES :**

The three component condensation to afford tetrahydroquinolines. The immonium ions derived from the aryl amines and aldehydes function as heterodienes.

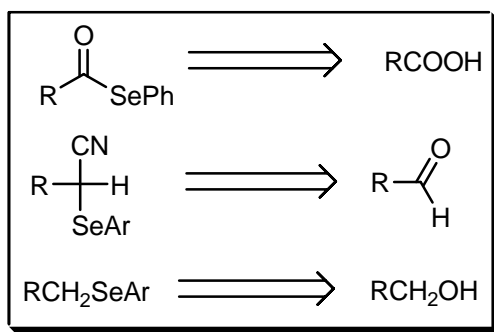
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**REFERENCES :**

- 1) S.D. Larsen; P.A. Grieco, *J. Am. Chem. Soc.*, 1985, **107**, 1768.
  - 2) P.A. Grieco; A. Bahsas, *Tetrahedron Lett.*, 1988, **29**, 5855.
- 

**COMMENTS :****GRIECO SELENIDE REACTION****EXAMPLE :****MECHANISM :**

## DISCONNECTION :



## NOTES :

The formation of selenides from aldehydes, alcohols and carboxylic acids in high yield.

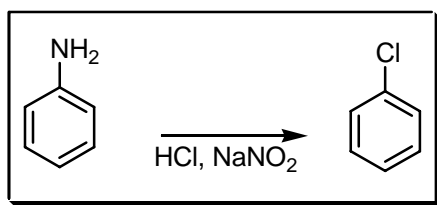
## REFERENCES :

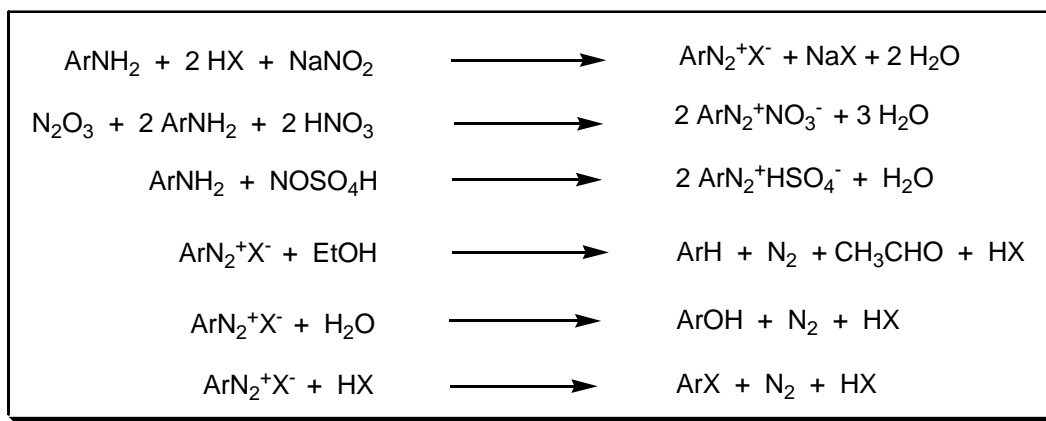
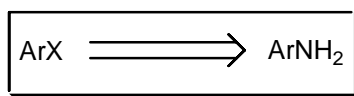
- 1) P.A. Grieco; S. Gilman; M. Nishizawa, *J. Org. Chem.*, 1976, **41**, 1485.
- 2) P.A. Grieco; Y. Yokoyama, *J. Am. Chem. Soc.*, 1977, **99**, 5210.
- 3) P.A. Grieco; Y. Yokoyama; E. Williams, *J. Org. Chem.*, 1978, **43**, 1283.
- 4) A. Krief; A.-M. Laval, *Bull. Soc. Chim. Fr.*, 1997, **134**, 869.
- 5) H. Abe, *Yakugaku Zasshi (J. Pharm. Soc. Jpn.)*, 2003, **123**, 423.

## COMMENTS :

## GRIESS DEAMINATION

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

The formation of aromatic diazo-compounds from primary amines and nitrous acid. The resulting diazo-compound has a high reactivity particularly in the presence of certain catalysts. See also **Balz – Schiemann**, **Cadogan** arylation, **Craig** exchange, **Demjanov** rearrangement, **Gattermann** diazo, **Gattermann** sulfinic acid, **Knoevenagel** diazotation, **Körner – Contardi**, **Meerwein** arylation, **Sandmeyer** diazonium, **Schwechten** and **Witt** diazotation reactions.

**REFERENCES :**

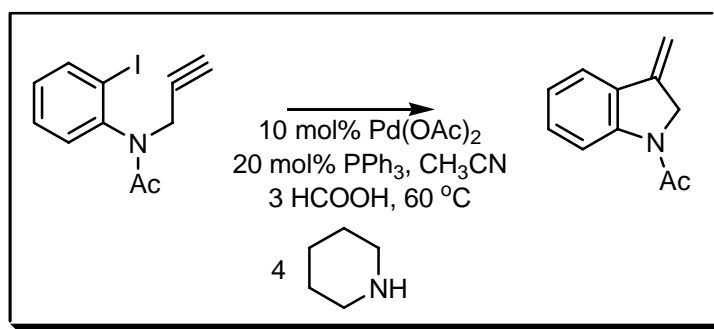
**Org. React.** : **2**, 264

- 1) P. Griess, *Liebigs Ann. Chem.*, 1858, **106**, 123.
- 2) W.A. Cowdrey; D.S. Davies, *J. Chem. Soc., Quat Rev.*, 1952, **6**, 358.
- 3) J.H. Ridd, *J. Chem. Soc., Quat. Rev.*, 1961, **15**, 418.
- 4) H.-L. Pan; T.L. Fletcher, *Synthesis*, 1973, 610.

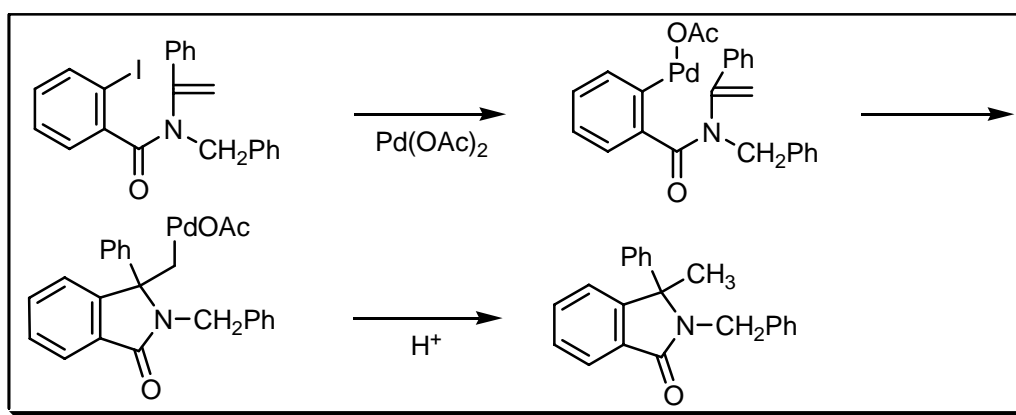
**COMMENTS :**

## GRIGG COUPLING

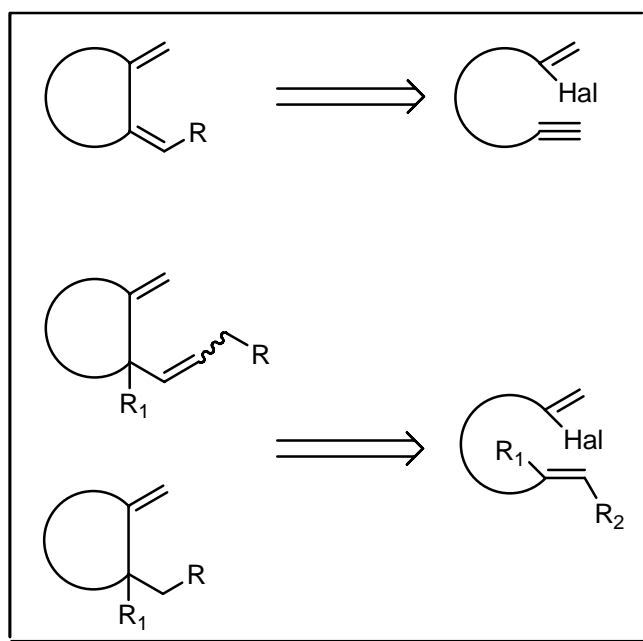
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

There is some confusion in the literature what exactly the **Grigg** reaction is. Some references name this reaction for the catalyst system  $\text{Pd}(0) / (\text{R}_3\text{Sn})_2$  ( $\text{R} = \text{CH}_3$  or  $^n\text{Bu}$ ) that effects *intra*- and *intermolecular* aryl-aryl, benzyl-aryl, benzyl-benzyl coupling of aryl and benzyl halides in a similar fashion as the **Stille – Migita – Kosugi** reaction. Other sources use the name in conjunction with the **Heck – Fujiwara – Mizoroki** reaction of compounds lacking  $\beta$ -hydrogen atoms. This author names this last reaction the **Grigg** reaction. The tandem cyclisation-anion capture process, which involves interception of the vinyl-palladium intermediate by transfer of a hydride ion from the formic acid. See also **Heck – Fujiwara – Mizoroki** reaction.

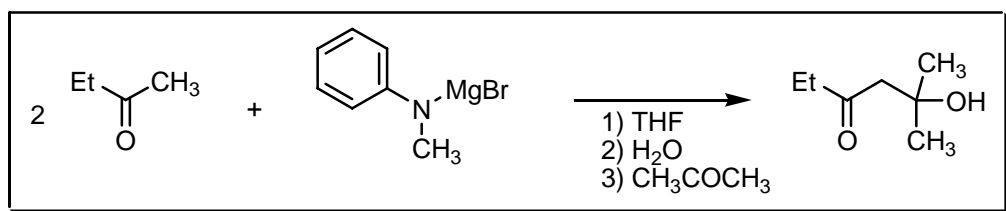
## REFERENCES :

- 1) B. Burns; R. Grigg; V. Sridharan; T. Worakun, *Tetrahedron Lett.*, 1988, **29**, 4325.
- 2) B. Burns; R. Grigg; P. Ratanakul; V. Sridharan; P. Stevenson; T. Worakun, *Tetrahedron Lett.*, 1988, **29**, 4329.

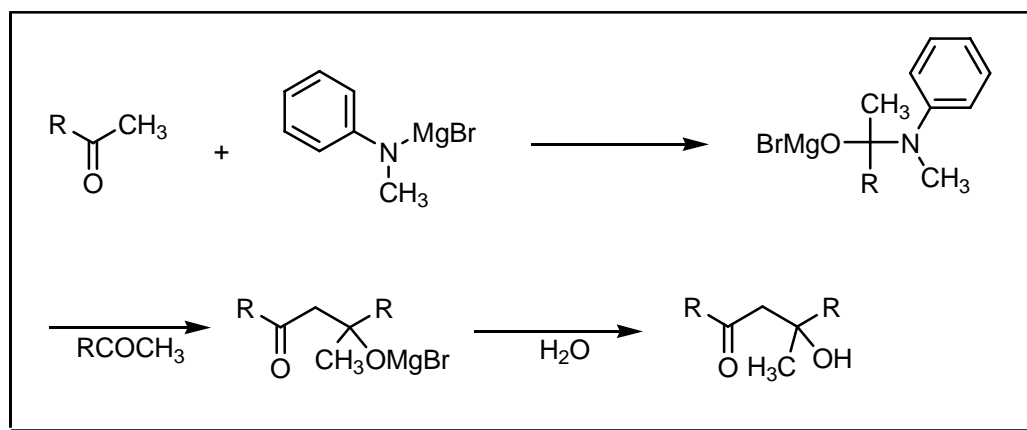
## COMMENTS :

## GRIGNARD – COLONGE SYNTHESIS

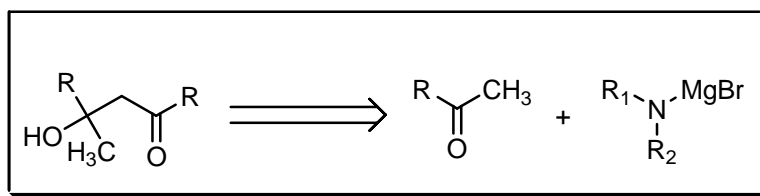
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of  $\beta$ -hydroxyketones by the action of a **Grignard** compound of the type  $R_1R_2NMgBr$  in ether or benzene on an excess of alkyl methyl ketone.

## REFERENCES :

Org. React. : 8, 44

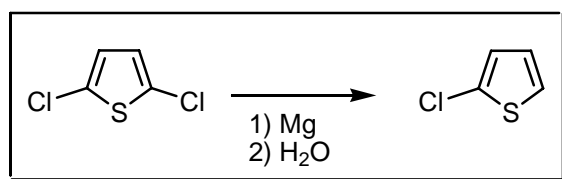
1) V. Grignard; J. Colonge, *C.R. Séances Acad. Sci.*, 1932, **194**, 929.

2) M. Stoll; A. Rouvé, *Helv. Chim. Acta*, 1947, **30**, 2019.

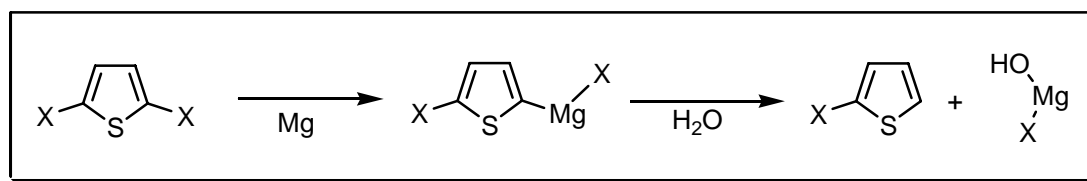
## COMMENTS :

## GRIGNARD DEHALOGENATION

### EXAMPLE :

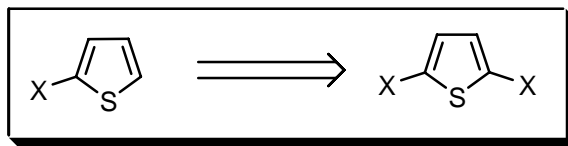


### MECHANISM :





## DISCONNECTION :



## NOTES :

The step-wise removal of halogen atoms from a polyhalo thiophene by formation of a **Grignard** reagent and subsequent decomposition with water. Halogen atoms in the  $\alpha$ -positions are easier to extract than halogen atoms in the  $\beta$ -position.

## REFERENCES :

Houben – Weyl : 13/2a, 125

- 1) V. Grignard, *C.R. Séances Acad. Sci.*, 1900, **130**, 1322.
- 2) L. Gattermann, *Liebigs Ann. Chem.*, 1912, **393**, 215.
- 3) W. Steinkopf; H. Jacob; H. Penz, *Liebigs Ann. Chem.*, 1934, **512**, 136.
- 4) W. Steinkopf, *Liebigs Ann. Chem.*, 1940, **543**, 128.

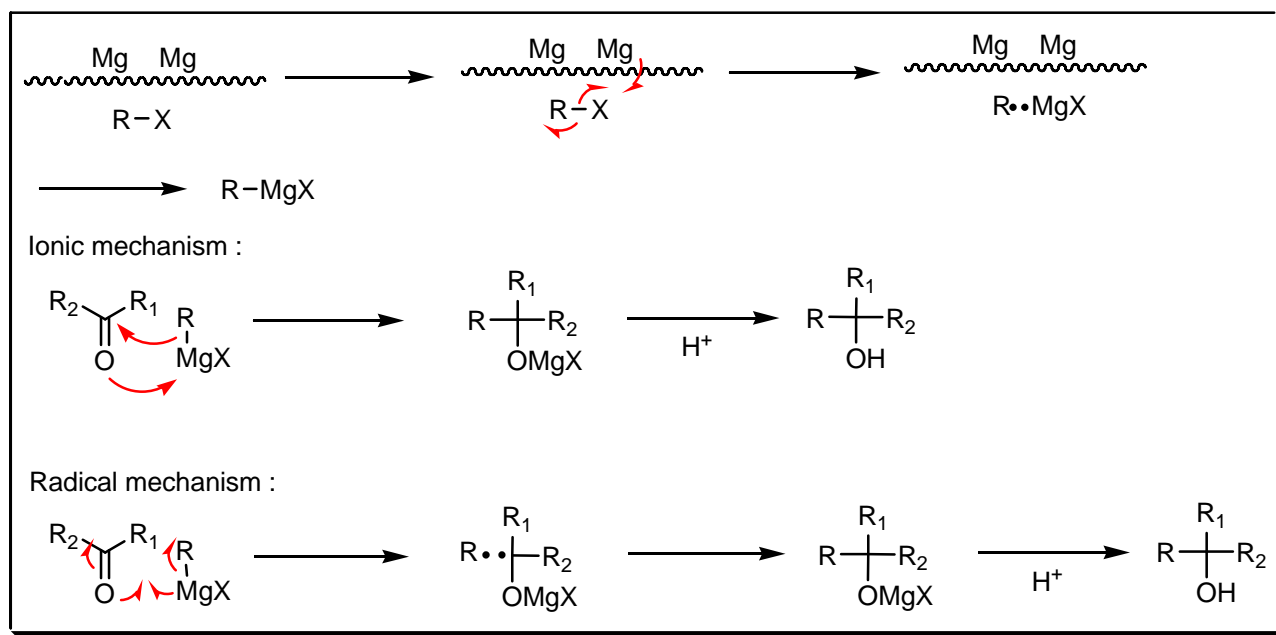
## COMMENTS :

## GRIGNARD REACTION

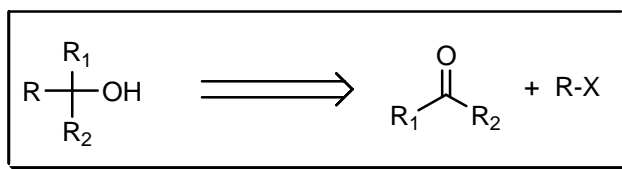
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Any addition of a **Grignard** reagent ( $\text{RMgX}$ ) to a carbonyl-containing compound is classified as a **Grignard** reaction. There are many named variations of the **Grignard** reaction. See also **Benary** reaction, **Blaise** ketoester, **Blaise – Maire**, **Bodroux – Chichibabin** aldehyde synthesis, **Boord** olefin synthesis and **Bouveault** aldehyde reactions.

## REFERENCES :

**March** : 799, 920, 924, 932

**Smith – March** : 1205

**Smith** : 685

**Smith 2<sup>nd</sup>** : 538, 560, 577, 580, 617, 622

**Houben – Weyl** : **8**, 237, 317, 371; **4/2**, 83, 643; **13/2a**, 54

**Org. React.** : **19**, 1; **41**, 135

**Org. Synth.** : numerous examples

**Science of Synthesis** : **10**, 381, 384, 394, 562

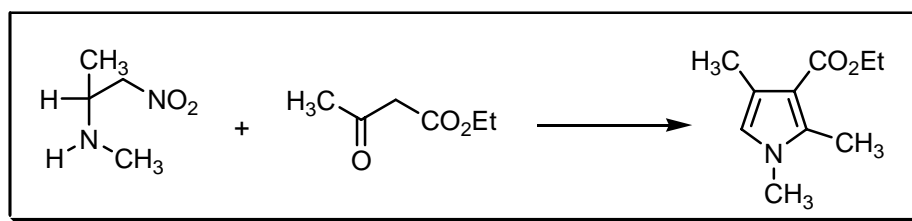
- 1) P. Barbier, *C.R. Séances Acad. Sci.*, 1899, **128**, 110.
- 2) V. Grignard, *C.R. Séances Acad. Sci.*, 1900, **130**, 1322.
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- 8) R.W. Hoffmann; O. Knopff; A. Kusche, *Angew. Chem., Int. Ed.*, 2000, **39**, 1462.
- 9) I. Fleming, *Chemtracts: Org. Chem.*, 2001, **14**, 505.
- 10) C. Jones; A.F. Richards; S. Fritsche; E. Hey-Hawkins, *Organometallics*, 2002, **21**, 438.

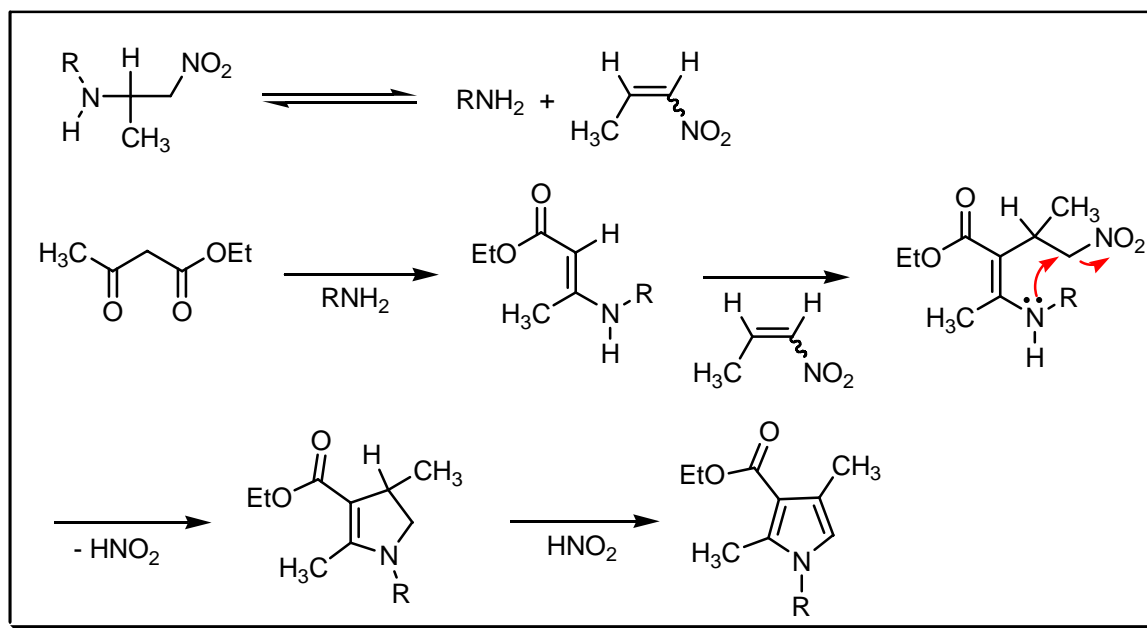
**COMMENTS :**

**GROB – CAMENISCH SYNTHESIS**

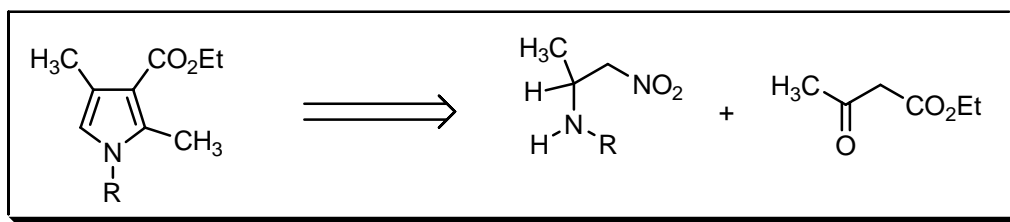
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

Pyrroles are synthesised from acetoacetic ester and 1-nitro-2-alkyliminopropanes. See also **Barton – Zard**, **Clauson–Kaas**, **Fischer – Fink**, **Hantzsch** pyrrole, **Harries** pyrrole, **Kenner**, **Knorr** pyrrole, **Miller – Plöchl**, **Paal – Knorr**, **Padwa**, **Piloty – Robinson**, **Schwanert**, **Trofimov** and **Zav'yalov** reactions.

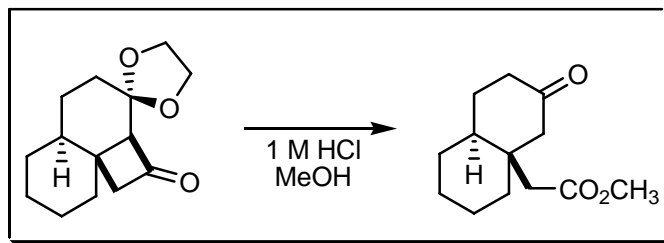
## REFERENCES :

- 1) C.A. Grob; K. Camenisch, *Helv. Chim. Acta*, 1953, **36**, 49.
- 2) H. Meyer, *Liebigs Ann. Chem.*, 1981, 1534.
- 3) A. Gómez–Sánchez; B. Marco Stiefel; R. Fernández–Fernández; C. Pascual; J. Bellanato, *J. Chem. Soc., Perkin Trans. 1*, 1982, 441.
- 4) F. Boberg; K.-H. Garburg; K.-J. Görlich; E. Pipereit; M. Ruhr, *Liebigs Ann. Chem.*, 1985, 239.

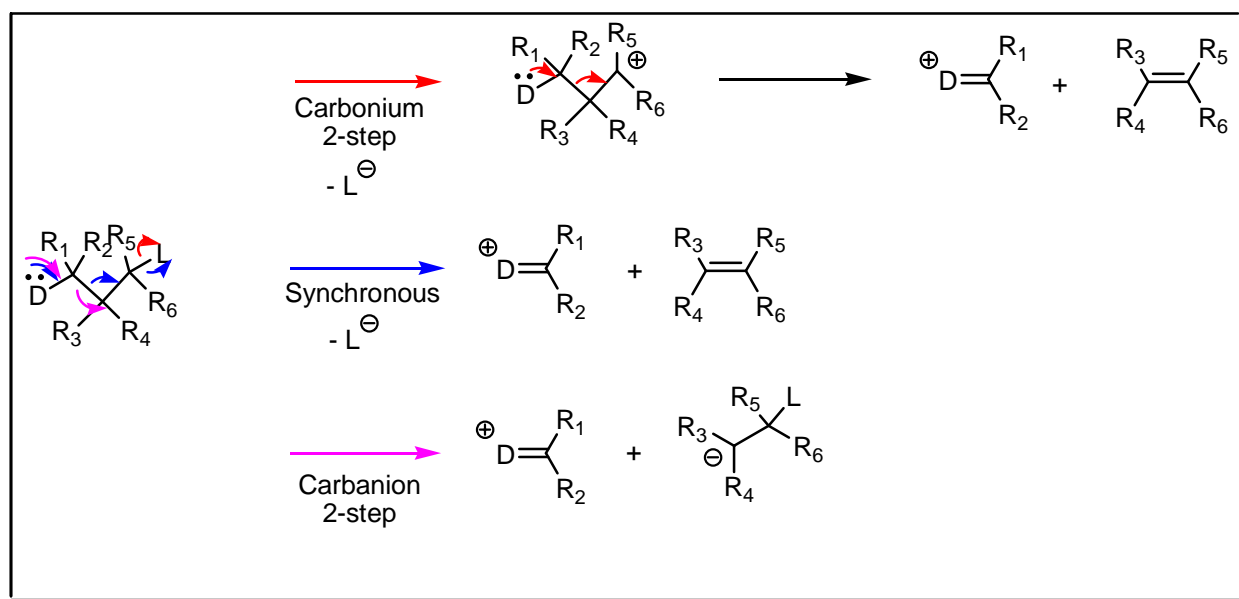
## COMMENTS :

## GROB FRAGMENTATION

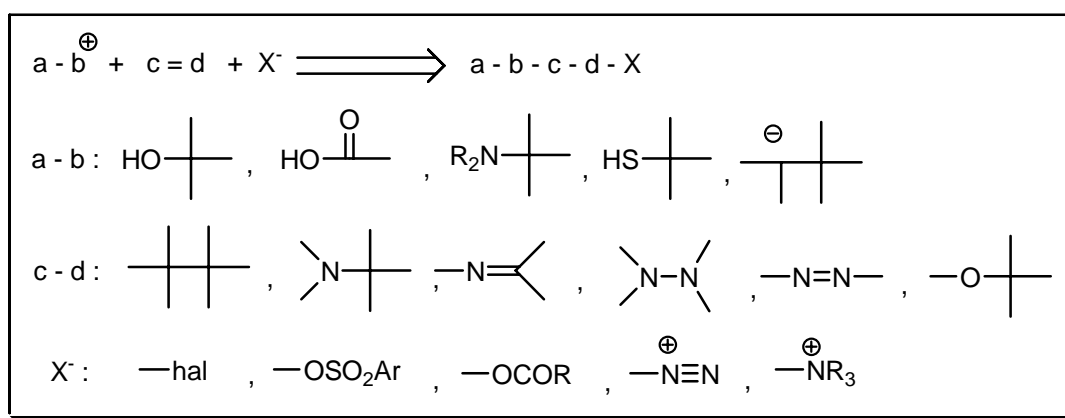
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The *intra*- or *intermolecular* concerted carbon-carbon bond cleavage involving a five atom system. The fragmentation is challenged by nucleophilic substitution, elimination or ring-closure. Carbonium : Good leaving groups (e.g. halogens) favour this pathway. Carbanion : Similar to a E1<sub>CB</sub> mechanism. Synchronous : The reaction is concerted and needs an *anti*-periplanar arrangement. See also **Eschenmoser – Tanabe** ring-cleavage, **Marshall – Minnaard** and **Wharton** reactions.

## REFERENCES :

Smith : 171

Smith 2<sup>nd</sup> : 143, 510, 850

Houben – Weyl : E6a, 647; E11,300; E19c, 72

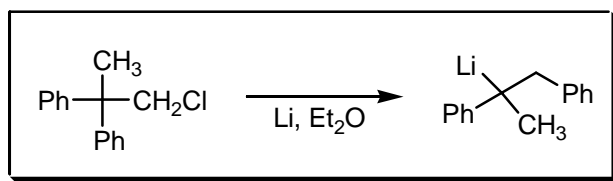
- 1) C.A. Grob; W. Baumann, *Helv. Chim. Acta*, 1955, **38**, 594.
- 2) C.A. Grob; P.W. Schiess, *Angew. Chem., Int. Ed. Engl.*, 1967, **6**, 1.

- 3) M. Shimizu; R. Ando; I. Kuwajama, *J. Org. Chem.*, 1981, **46**, 5246.
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- 5) S. Nagumo; A. Matsukuma; H. Suemune; K. Sakai, *Tetrahedron*, 1993, **49**, 10501.
- 6) D. Molm; N. Risch, *Liebigs Ann. Chem. / Recueil*, 1997, 1765.
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- 8) E.R. Alonso; K.A. Tehrani; M. Boelens; D.W. Knight; V. Yu; N. de Kimpe, *Tetrahedron Lett.*, 2001, **42**, 3921.
- 9) L.A. Paquette; J. Yang; Y.O. Long, *J. Am. Chem. Soc.*, 2002, **124**, 6542.
- 10) K. Vyakaranam; S. Körbe; H. Divišová; J. Michl, *J. Am. Chem. Soc.*, 2004, **126**, 15795.

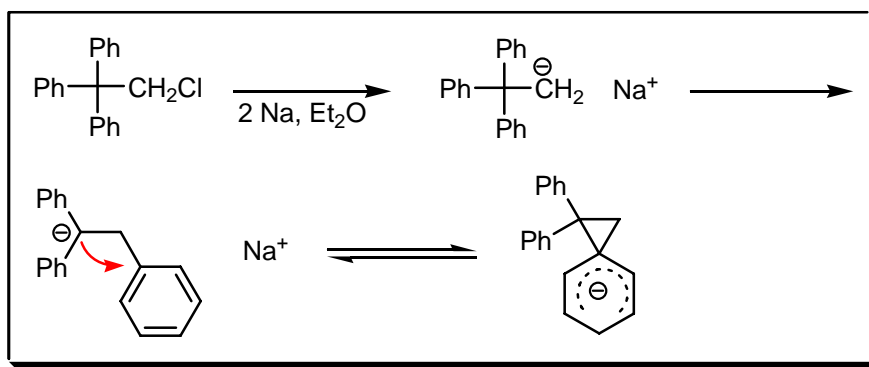
**COMMENTS :**

## GROVENSTEIN – ZIMMERMANN REARRANGEMENT

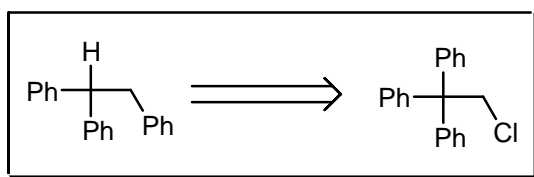
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

Phenyl or vinylic rearrangement of alkali metals of 1,1,1-triphenylethane or 2,2-diphenylpropanes. The phenyl ring migrates without an electron pair. See also **Fritsch – Buttenberg – Wiechell** reaction.

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## REFERENCES :

**March** : 1072

**Smith – March** : 1396

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3) E. Grovenstein, jr.; L.C. Rogers, *J. Am. Chem. Soc.*, 1964, **86**, 854.

4) E. Grovenstein, jr; K.W. Black; S.C. Goel; R.L. Hughes; J.H. Northrop; D.L. Streeter; D. VanDerveer, *J. Org. Chem.*, 1989, **51**, 1671.

5) A. Maercker; K. Reider; U. Girreser, *Eur. J. Org. Chem.*, 1998, 1455.

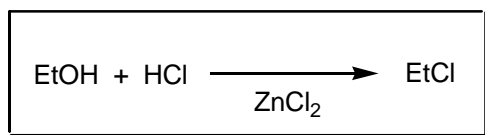
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## COMMENTS :

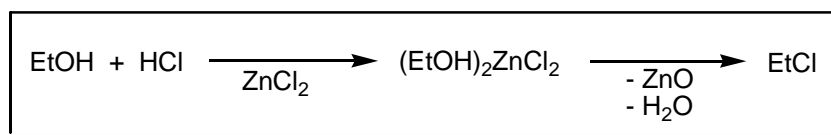
## GROVES SYNTHESIS

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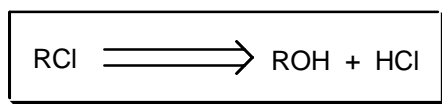
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



**NOTES :**

Alkyl halides are obtained by treatment of an alcohol with a hydrogen halide in the presence of zinc chloride. It is assumed that the zinc chloride reacts with the alcohol to form  $(\text{EtOH})_2\text{ZnCl}_2$ , this will decompose to zinc oxide, water and ethyl chloride.

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**REFERENCES :**

**March :** 431

**Smith – March :** 518

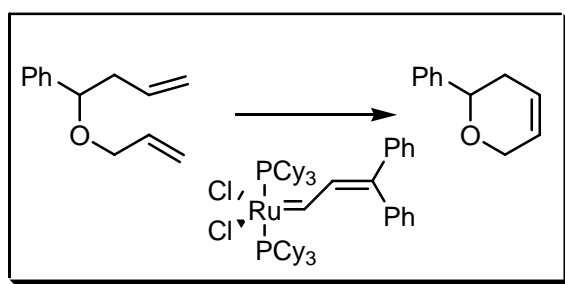
**Smith :** 150

**Smith 2<sup>nd</sup> :** 121

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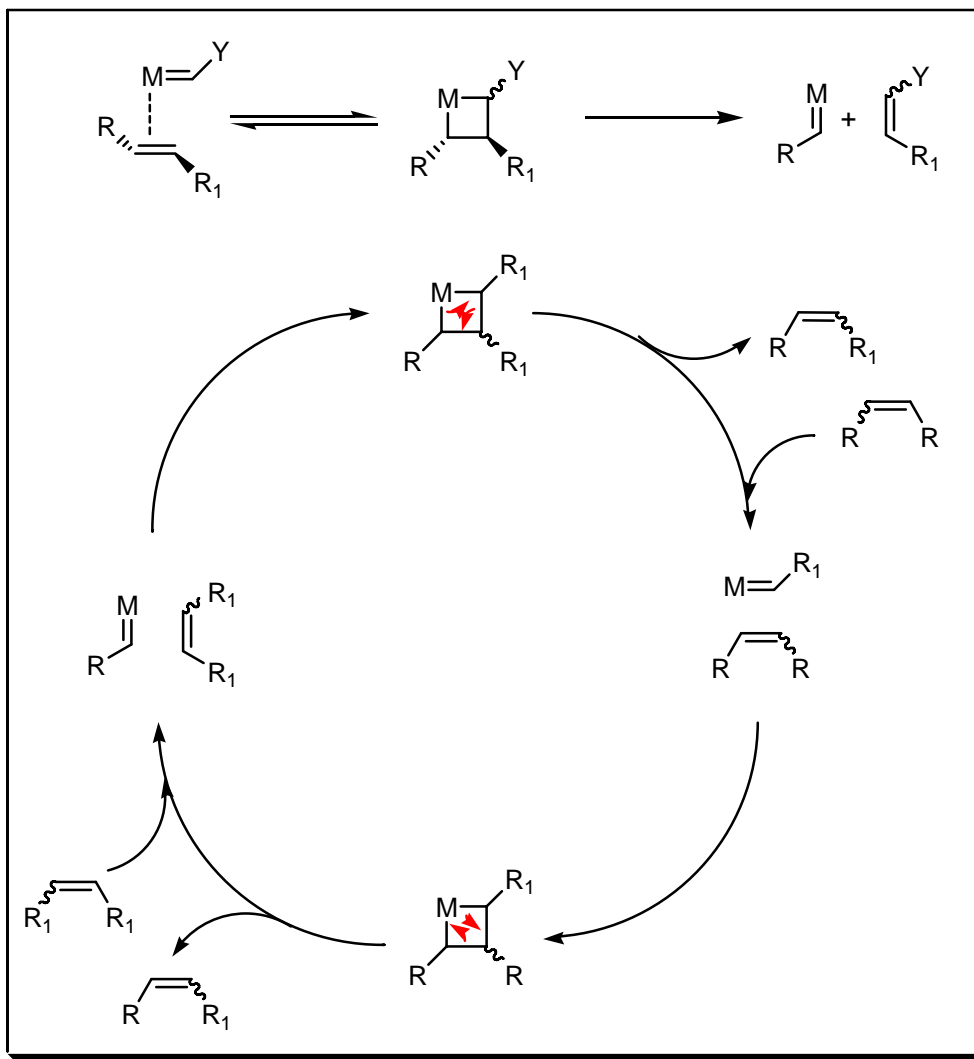
C.E. Groves, *J. Chem. Soc.*, 1874, **27**, 636.

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**COMMENTS :****GRUBBS REACTION****EXAMPLE :**



## MECHANISM :



## NOTES :

Olefin metathesis allows the exchange of substituents between different olefins – a transalkylidenation. The process was first used by Shell for the synthesis of higher olefins (SHOP). A large variety of first and second generation catalysts are commercially available.

## REFERENCES :

March : 1146

Smith – March : 1457

Smith 2<sup>nd</sup> : 1215

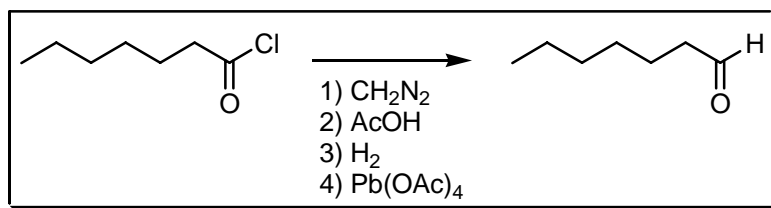
Org. Synth. : 81, 1

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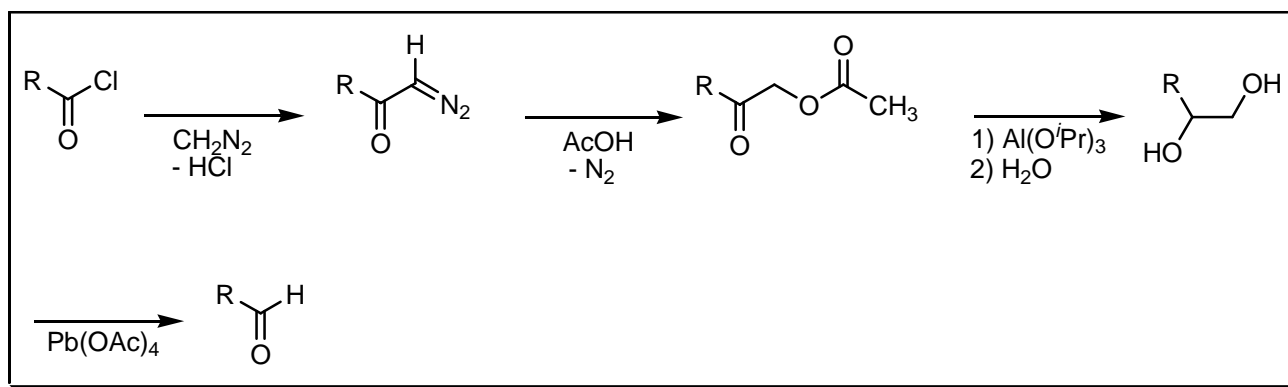
COMMENTS :

## GRUNDMANN ALDEHYDE SYNTHESIS

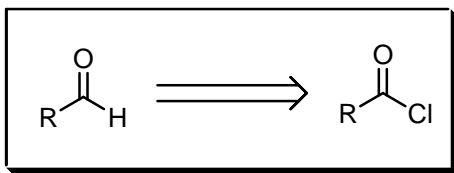
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

An acid chloride is converted into a diazo-ketone, which by treatment with glacial acetic acid gives an acetoxo-ketone. The reduction (**Meerwein – Ponndorf – Verley** reduction) of the keto group and simultaneous hydrolysis affords the corresponding glycol. Oxidative cleavage of the glycol (**Criegee**) yields an aldehyde containing the same number of carbon atoms as the starting material. See also **Arndt – Eistert**, **Brandt**, **Criegee**, **Hershberg**, **McFadyen – Stevens**, **Meerwein – Ponndorf – Verley**, **Reissert – Grosheintz – Fischer**, **Rosenmund – Saytzeff**, **Sonn – Müller** and **Stephen** reactions.

## REFERENCES :

**March** : 475

**Smith – March** : 532

**Houben – Weyl** : 7/1, 239; **E3**, 431

**Org. React.** : 8, 218

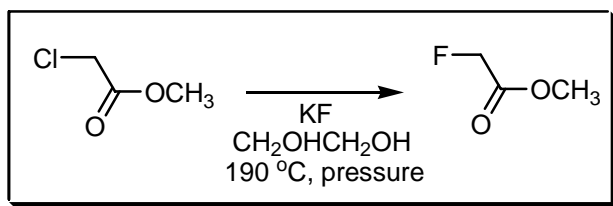
1) C. Grundmann, *Liebigs Ann. Chem.*, 1936, **524**, 31.

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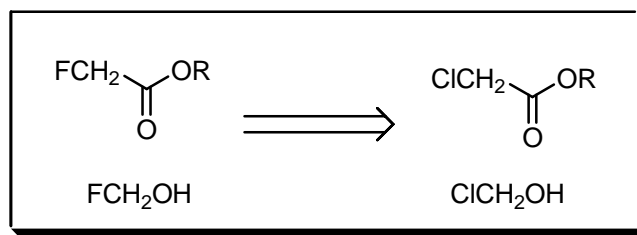
## COMMENTS :

## GRYSZKIEWICZ–TROCHIMOWSKI – McCOMBIE METHOD

## EXAMPLE :



## DISCONNECTION :



## NOTES :

Fluoro-esters and fluoro-alcohols are obtained by dry heating the corresponding chlorine compounds for some hours in an autoclave with large excess potassium fluoride. See also **Swarts** reaction.

## REFERENCES :

Houben – Weyl : 5/3, 151

Org. Synth. : 36, 40

Org. Synth. Coll. Vol. : 4, 525

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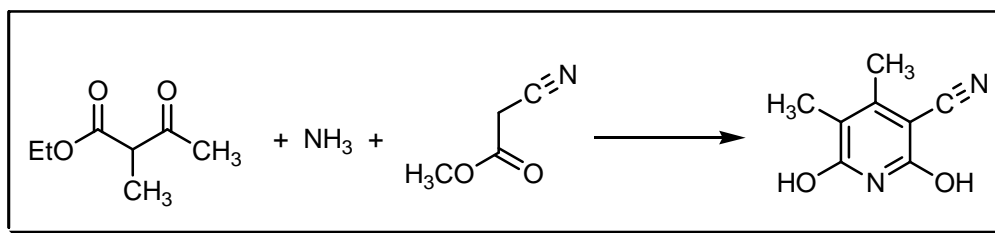
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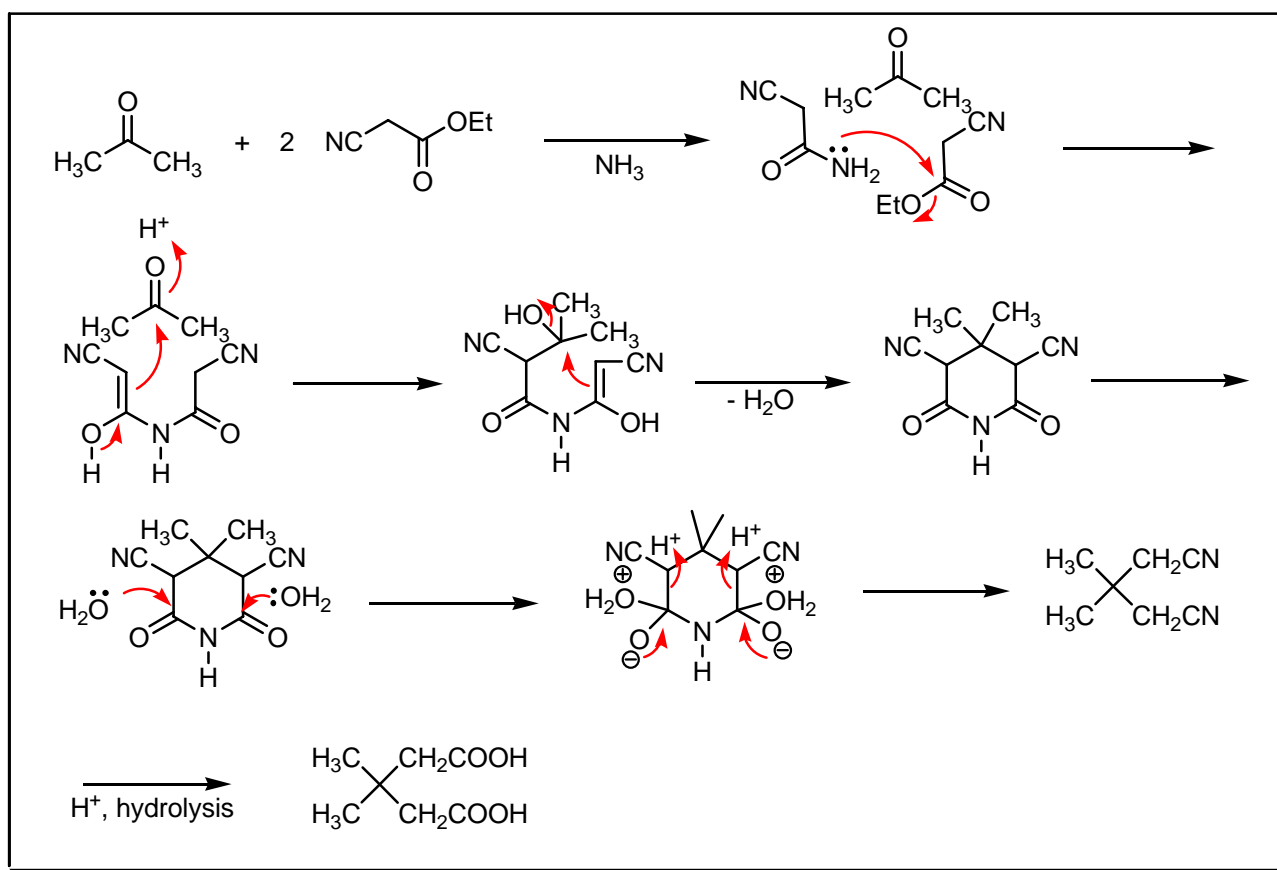
## COMMENTS :

## GUARESCHI – THORPE CONDENSATION

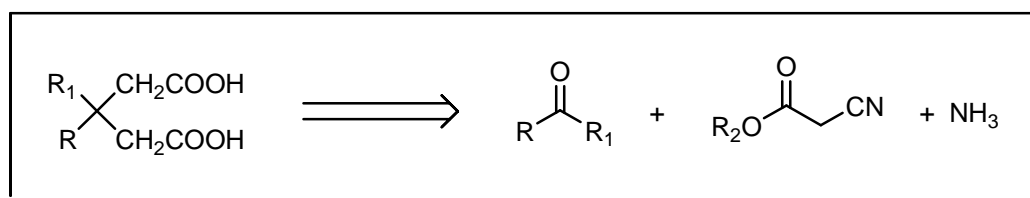
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Pyridine and piperidine derivatives can be obtained by the condensation of a cyano ester or cyanoacetamide or a primary amine or ammonia and either a ketone, aldehyde, ketonic- or cyanoester. The amides, which are intermediately formed, can also be used. The formed **Guareschi** imide can be hydrolysed and is sometimes called **Guareschi** hydrolysis. See also **Bohlmann – Rahtz**, **Chichibabin** pyridine, **Gattermann – Skita**, **Hantzsch – Beyer**, **von Meyer – Mohr**, **Petrenko–Kritschenko**, **Riehm** pyridine and **Wakatsuki – Yamazaki – Bönnemann** reactions.

## REFERENCES :

Org. Synth. : 36, 28

Org. Synth. Coll. Vol. : 4, 441

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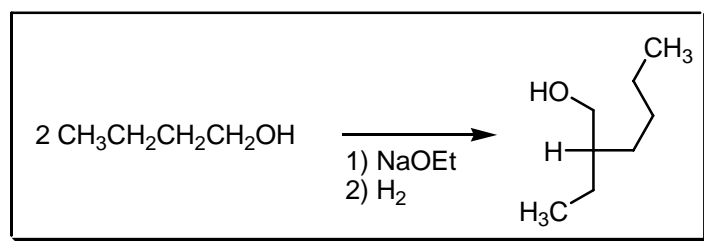
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- 10) D.J. Collins; A.M. Adams, *Aust. J. Chem.*, 1989, **42**, 215.
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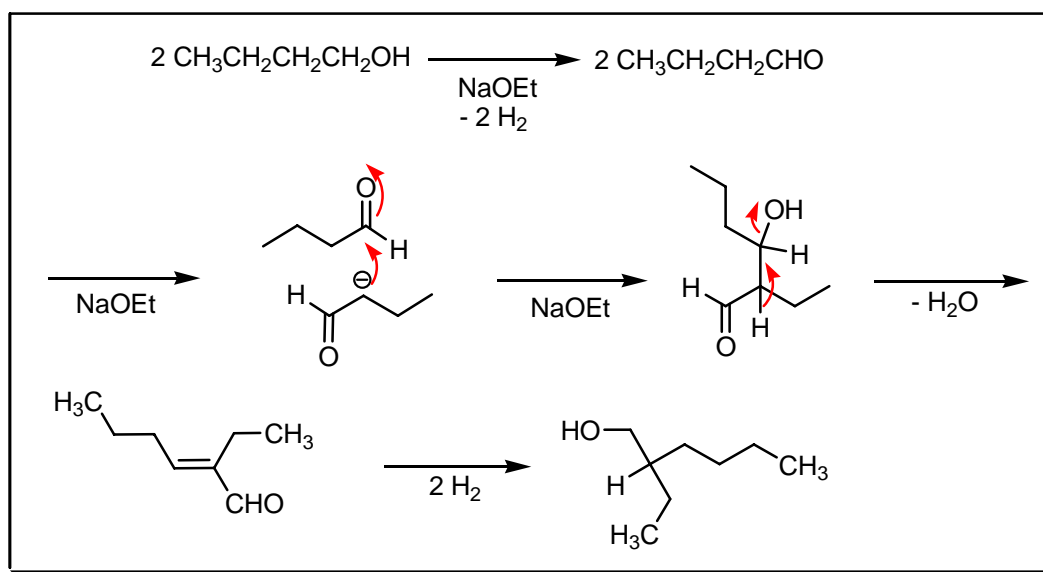
**COMMENTS :**

## GUERBET REACTION

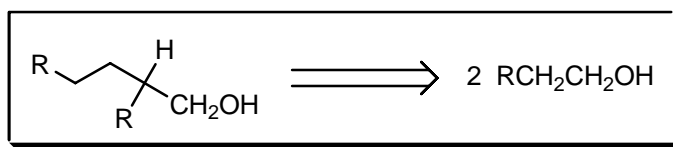
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

This is the condensation of primary and secondary alcohols at high temperatures under the influence of sodium alkoxides. A rhodium promoted reaction has been reported by **Burk *et al.*** See also **Lebedev** and **Ostromyslenskii** reactions.

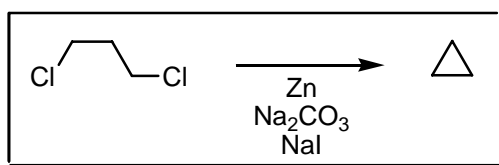
## REFERENCES :

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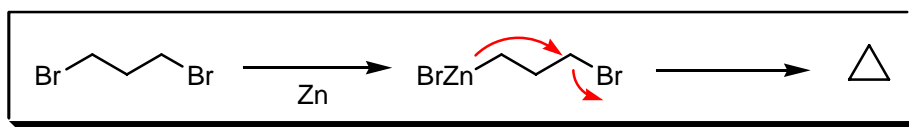
## COMMENTS :

## GUSTAVSON CYLISATION

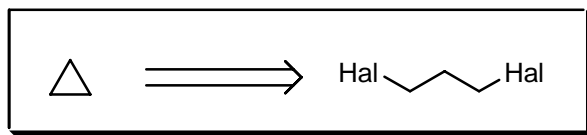
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

A variation of the **Freund** reaction in which an open chain dihalogen compound is cyclised by the action of zinc dust. See also **Charette**, **Freund**, **Hass** cyclopropane, **Ipatiew** cyclopropane, **Kishner**, **Mousseron – Fraisse – McCoy**, **Nerdel**, **Simmons – Smith** and **Wurtz** reactions.

## REFERENCES :

Houben – Weyl : 13/1, 492

Org. Synth. : 44, 30

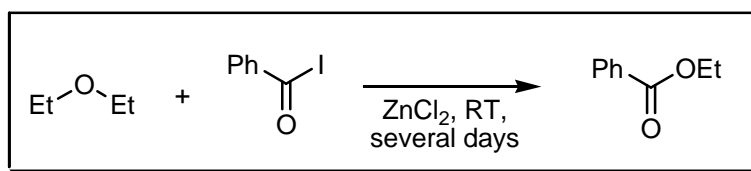
Org. Synth. Coll. Vol. : 5, 328

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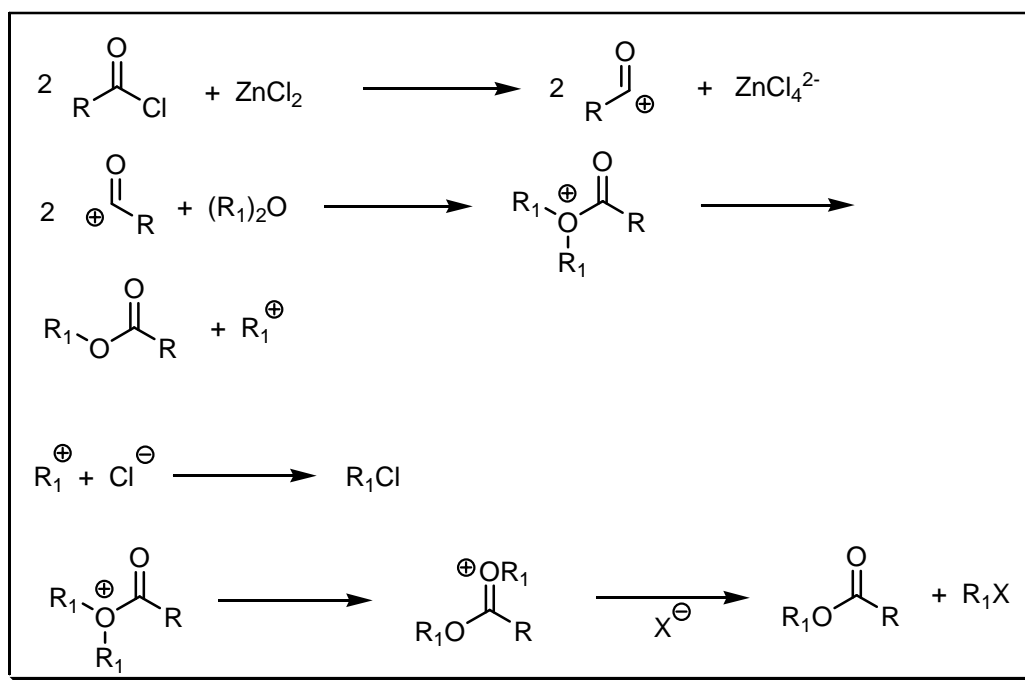
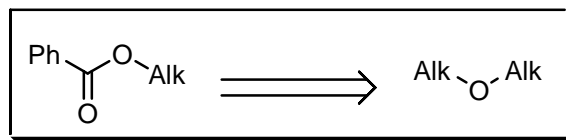
## COMMENTS :

## GUSTUS CLEAVAGE

### EXAMPLE :





**MECHANISM :****DISCONNECTION :****NOTES :**

Alkyl ethers are cleaved by acetyl iodide in the presence of zinc chloride at room temperature during several days. See also **Mann** dealkylation, **Prey** and **Stoermer** reactions.

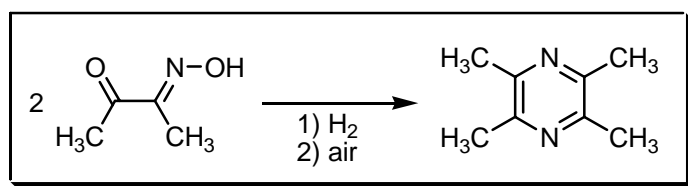
**REFERENCES :**

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- 2) E.L. Gustus; P.G. Stevens, *J. Am. Chem. Soc.*, 1933, **55**, 374.
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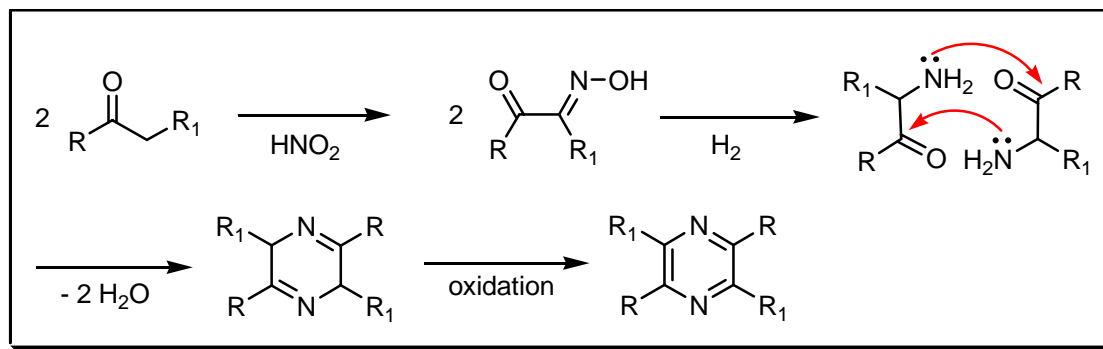
**COMMENTS :**

## GUTKNECHT PYRAZINE SYNTHESIS

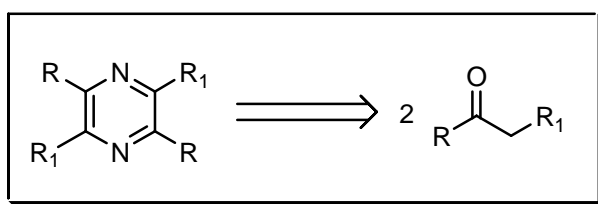
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Dihydropyrazines, which may be oxidised to pyrazines, are obtained by the reduction of oximino-ketones and subsequent treatment with alkali. The oxidation step can take place with mercury(I) oxide, copper(II) sulfate or atmospheric air. See also **Gastaldi** and **Stadel – Rugheimer** reactions.

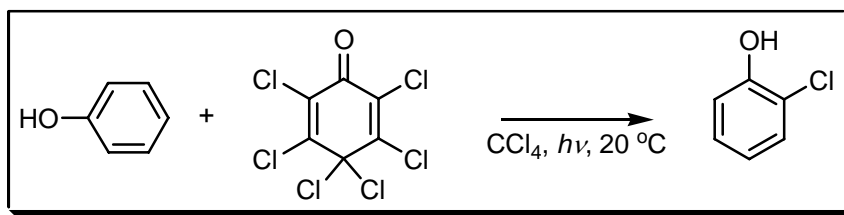
### REFERENCES :

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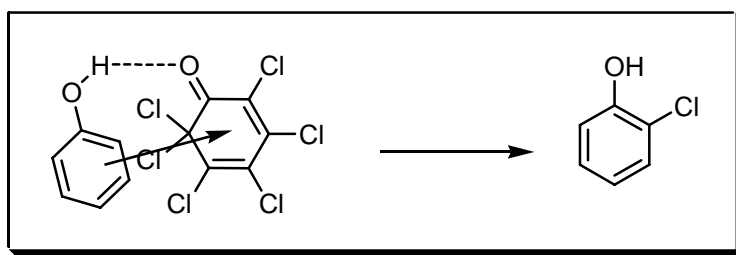
### COMMENTS :

## GUY – LEMAIRE – GUETTE REACTION

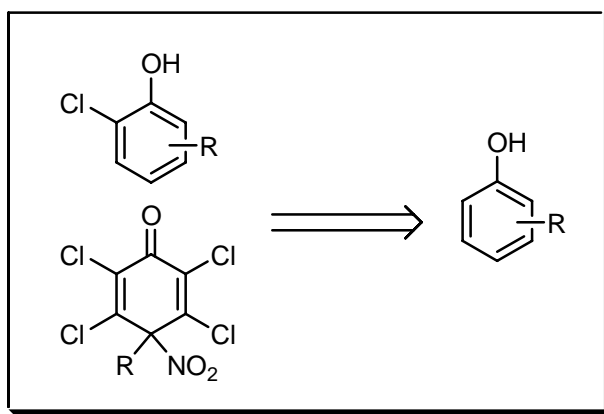
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The regioselective *ortho* or *para* halogenation or nitration of phenols or naphthols and the corresponding ethers (only *para*) by hexahalo cyclohexadiene or its nitro derivative. The *ortho* or *para* ratio depends on the solvent used.

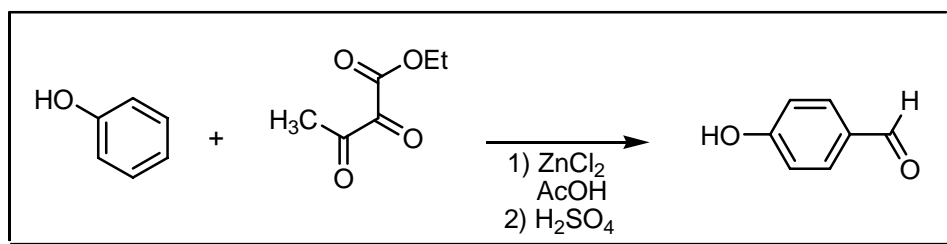
### REFERENCES :

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- 4) A. Guy; M. Lemaire; J. Roussel; J.-P. Guette, *Tetrahedron*, 1987, **43**, 835.

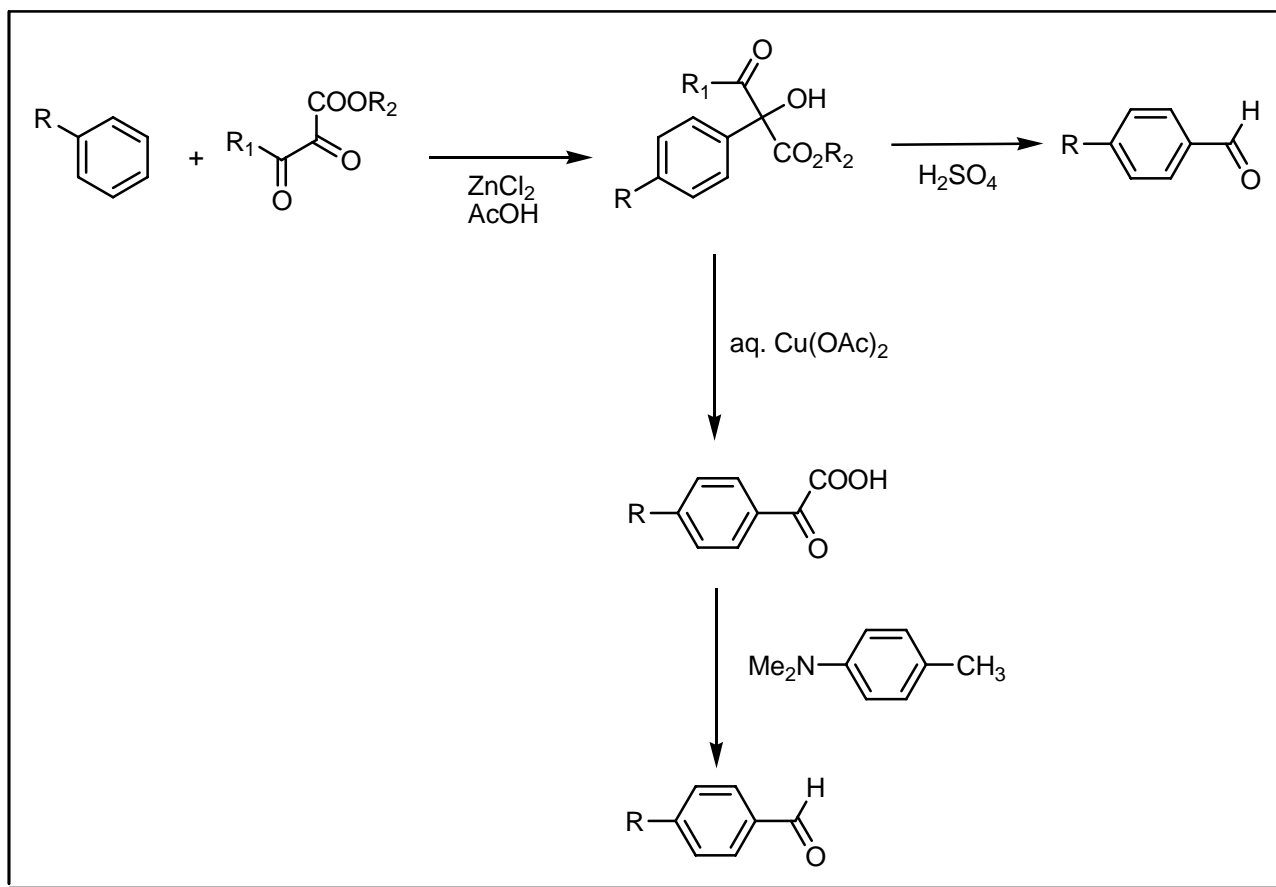
COMMENTS :

## GUYOT – GRY – BOUVEAULT SYNTHESIS

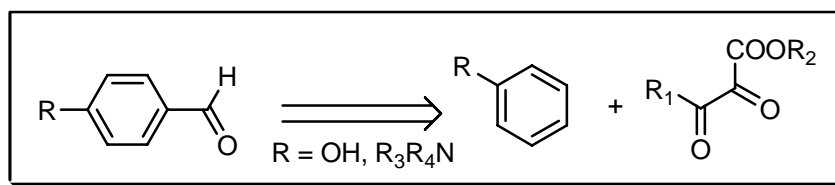
EXAMPLE :



MECHANISM :



## DISCONNECTION :



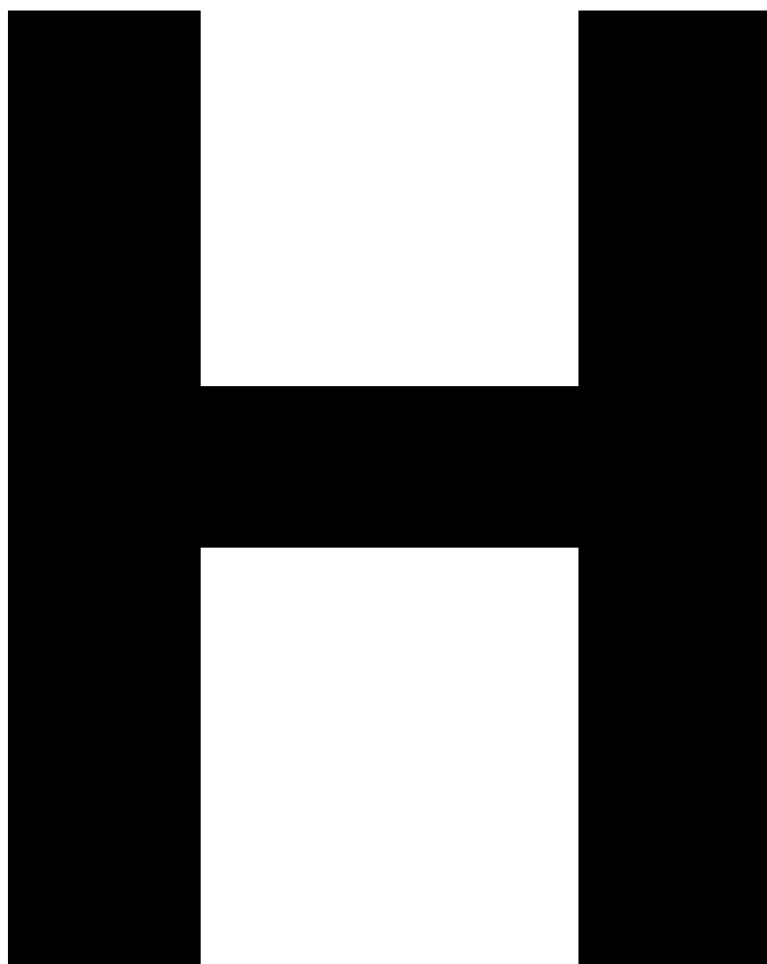
## NOTES :

The condensation of an  $\alpha,\beta$ -diketo ester with a compound containing replaceable hydrogen (a phenol or a *tert*-aromatic amine) to give an  $\alpha$ -hydroxy ester, which is decomposed to an aldehyde. A number of variations are possible. See also **Claisen – Mauthner – Bouveault** reaction.

## REFERENCES :

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## COMMENTS :



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ANDO MODIFICATION · 855

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**C**

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**F**

FISCHER – NOURI MODIFICATION · 830

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HORNING REACTION · 856

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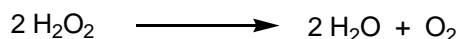
RÜHLMANN VARIATION · 757



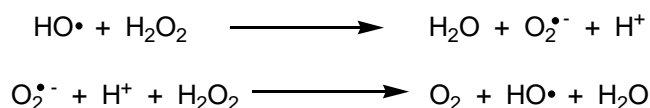
## HABER – WEISS REACTION (HABER – WILLSTÄTTER REACTION)

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### EXAMPLE :



### MECHANISM :



### NOTES :

This reaction is the reduction of hydrogen peroxide by the superoxide anion to produce the hydroxyl radical, which is a very reactive oxidant. This reaction is often invoked to explain aromatic hydroxylations in living organisms. Many people including Linus **Pauling** have claimed to be the discoverers of this reaction, but the real discoverers are **Haber** and **Willstätter**. See also **Fenton** reaction.

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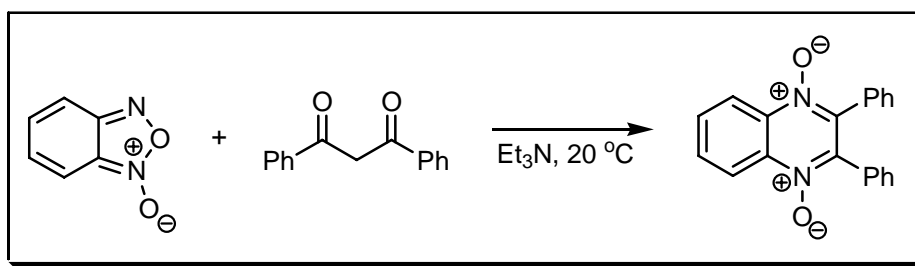
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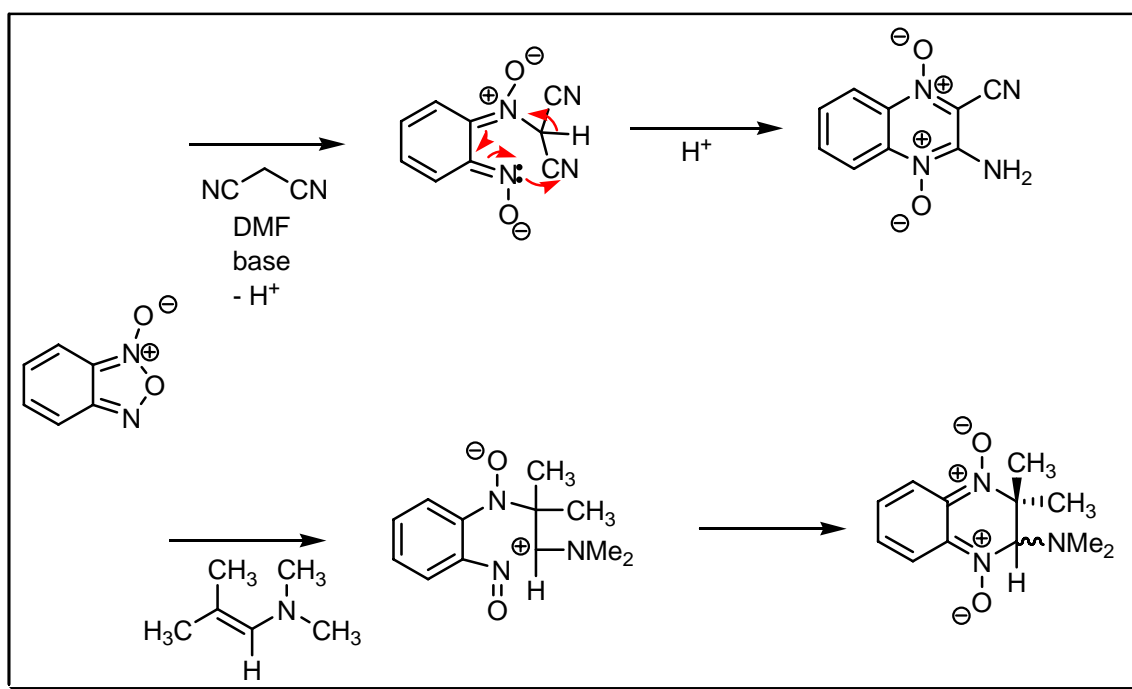
### COMMENTS :

## HADDADIN – ISSIDORIDES QUINOXALINE SYNTHESIS (BEIRUT REACTION)

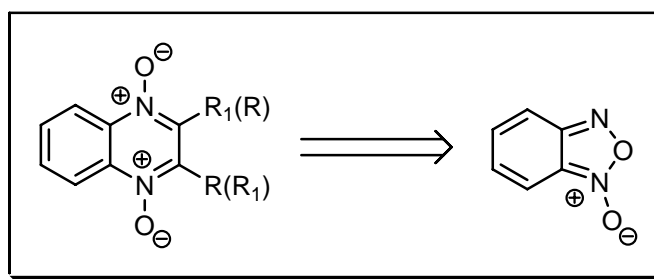
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Quinoxaline dioxide is prepared from benzofurazan oxide and ketone enolates or enamines. This reaction is also known as the **Beirut** reaction, named after the American university in Beirut Lebanon.

## REFERENCES :

Houben – Weyl : E8c, 799

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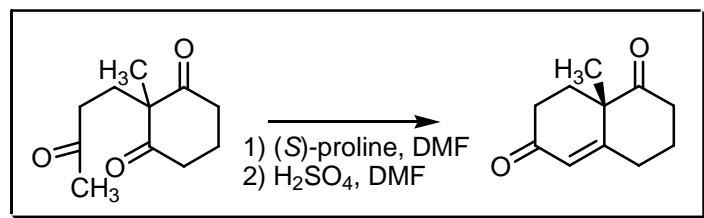
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## COMMENTS :

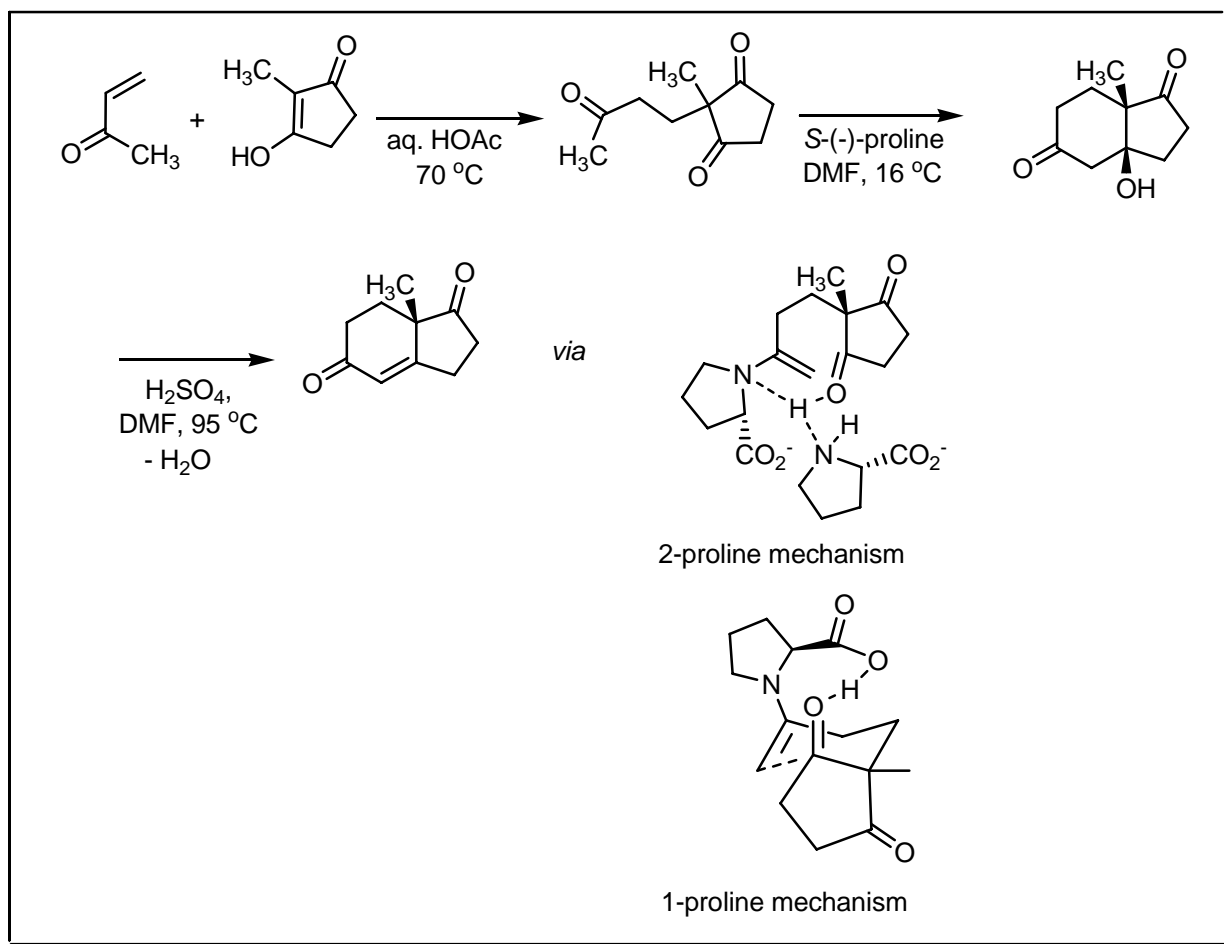
## HAJOS – PARRISH – EDER – SAUER – WIECHERT CYCLISATION

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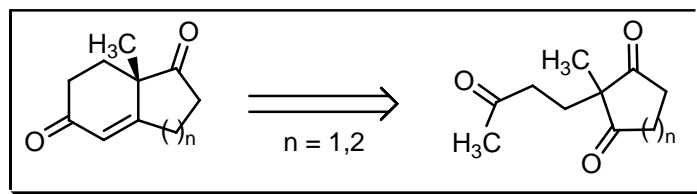
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The (S)-proline-catalysed *intramolecular* aldol reaction has high yields and high enantiomeric excess. A review about the possible mechanisms has been written by **Agami**. Recently, kinetic experiments and quantum mechanical calculations by **List** and **Houk** show evidence for a one-proline mechanism. See also **d'Angelo's** asymmetric **Michael** addition, **Mannich**, **Robinson – Mannich** annulation and **Stork** reductive cyclisation reactions.

## REFERENCES :

Smith – March : 1223

Smith 2<sup>nd</sup> : 798

Org. Synth. : 63, 26, 37

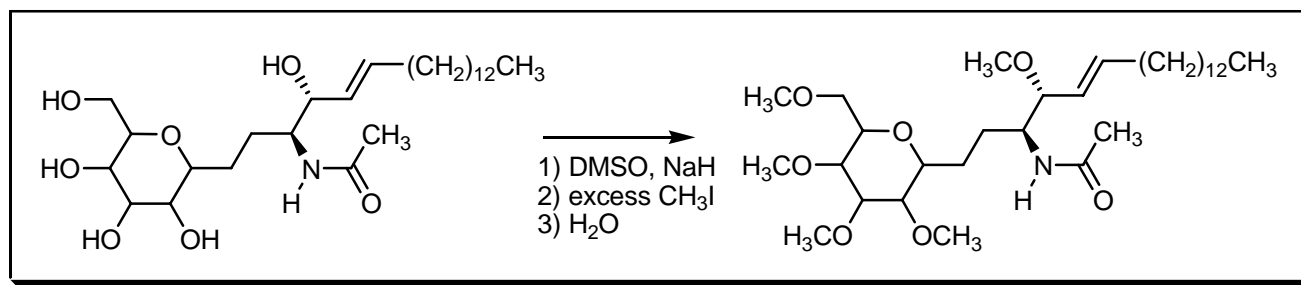
Org. Synth. Coll. Vol. : 7, 363, 368

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## COMMENTS :

## HAKOMORI REACTION

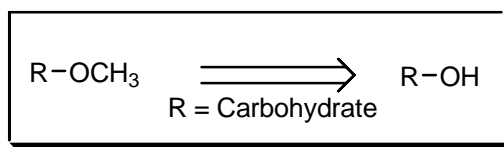
### EXAMPLE :



### MECHANISM :



**DISCONNECTION :**



**NOTES :**

This reaction is the formation of methyl ethers of sugars using the dimethylsulfinyl anion as base. Instead of methyl iodide, methyl triflate can be used in a protic solvent in the presence of a hindered base. See also **Haworth** methylation, **Irvine – Purdie**, **Meerwein** methylation and **Robertson – Robinson** reactions.

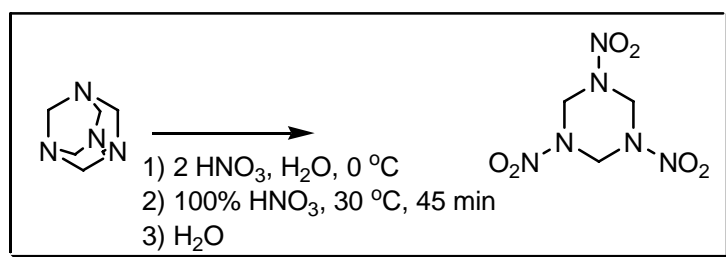
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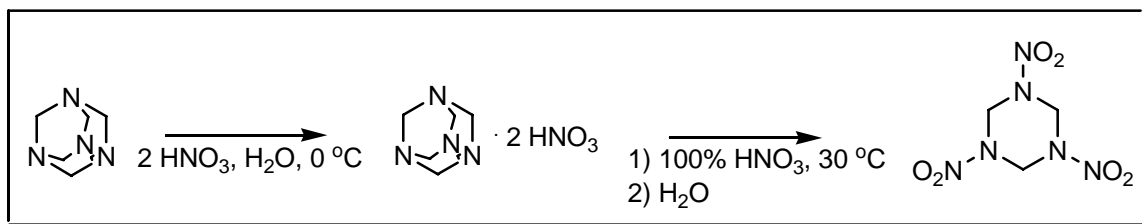
**COMMENTS :**

## HALE CYCLONITE SYNTHESIS

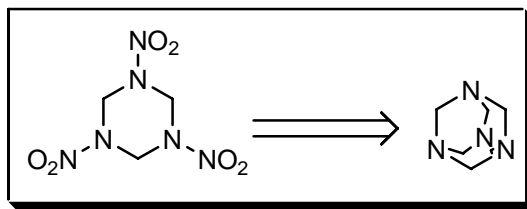
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

Cyclonite is formed by the treatment of hexamethylenetetramine with concentrated nitric acid at low temperatures. See also **Ebele – Schiessler – Ross**, **Knoffler – Bachmann** and **Wolfram** reactions.

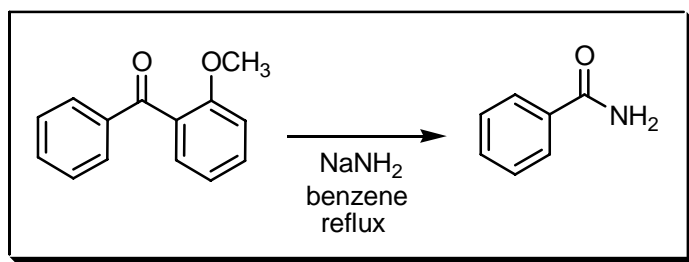
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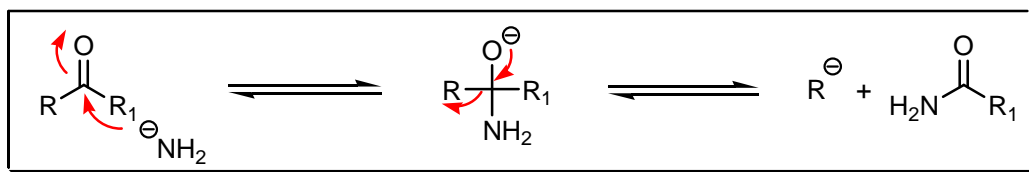
## COMMENTS :

## HALLER – BAUER REACTION

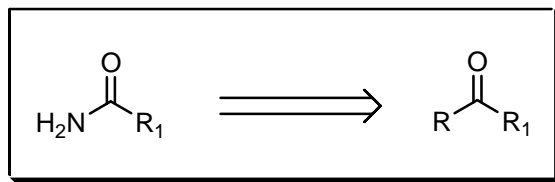
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



---

## NOTES :

The  $\alpha$ -position of an alkyl phenyl ketone is step-wise alkylated by an alkyl halide and sodamide, rupture of the alkylated product with sodamide, yields an amide which can be converted into a trisubstituted acetic acid. The reaction is normally applied only to non-enolisable ketones. See also **Ziegler** alkylation.

---

## REFERENCES :

**March** : 633

**Smith – March** : 512, 814

**Smith 2<sup>nd</sup>** : 730

**Houben – Weyl** : E5, 1104

**Org. React.** : 9, 1

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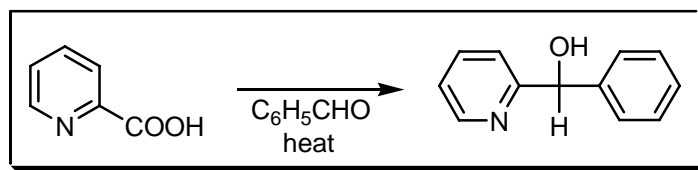
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## COMMENTS :

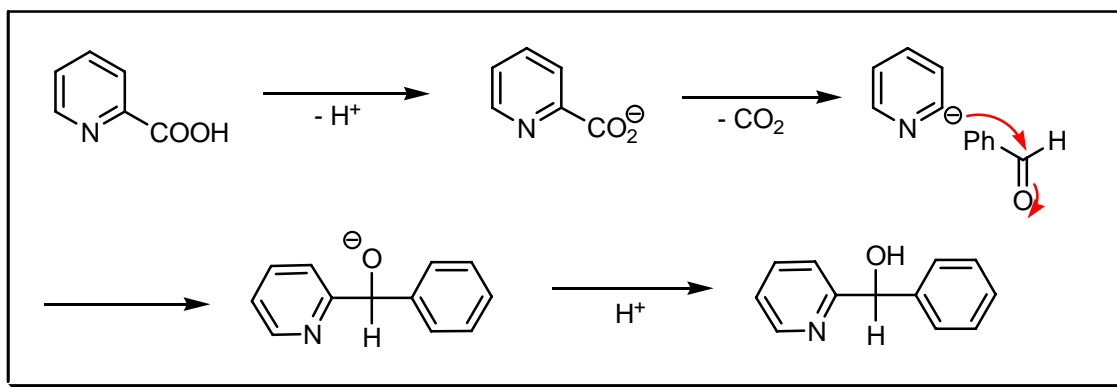


## HAMMICK PICOLINIC ACID DECARBOXYLATION

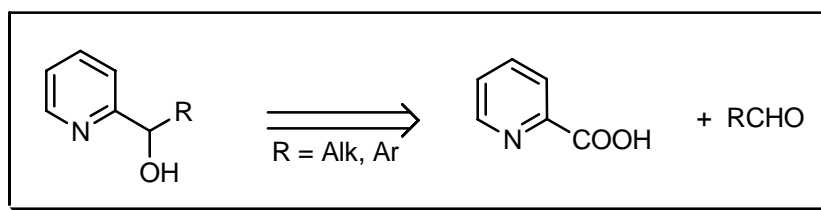
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The decarboxylation of  $\alpha$ -picolinic acid and related acids containing the carboxyl group  $\alpha$ - or  $\gamma$ - of the nitrogen atom by an excess of an aldehyde or ketone e.g. benzaldehyde, acetophenone or cyclohexanone yields an  $\alpha$ - or  $\gamma$ -pyridyl or related carbinol. See also **Zagoumenny** diphenyl carbinol reaction.

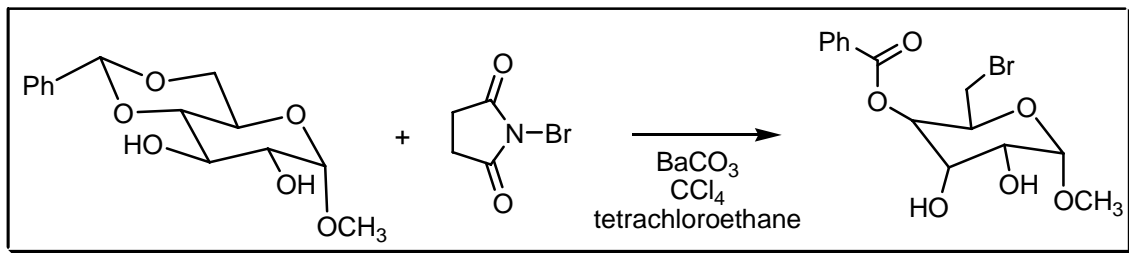
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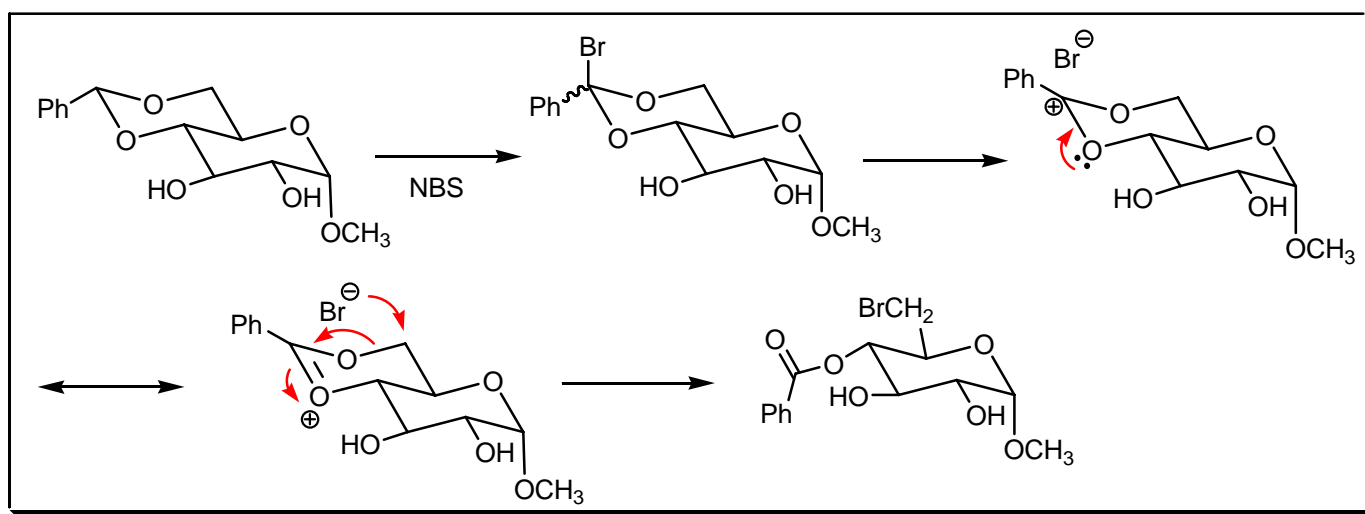
**COMMENTS :**

**HANESSION – HULLAR REACTION**

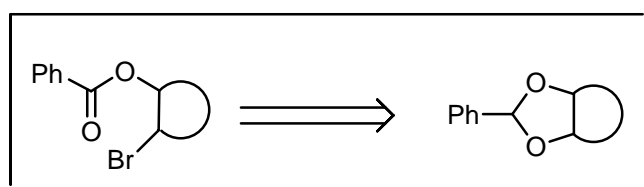
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

Benzylidene acetals of the 1,3-dioxane or 1,3-dioxolane type undergo a ring-opening reaction in the presence of NBS (*N*-bromosuccinimide) to afford in high yield the corresponding *O*-benzoylated bromohydrins. The reaction is

compatible with a variety of functional and protecting groups (ester, ether, amide, halide, epoxide). See also **Binkley** triflate displacement reaction.

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#### REFERENCES :

**Org. Synth.** : **65**, 243

**Org. Synth. Coll. Vol.** : **8**, 363

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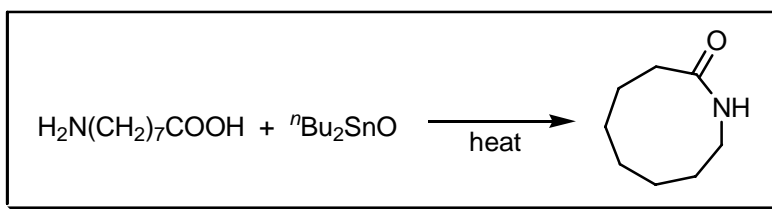
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#### COMMENTS :

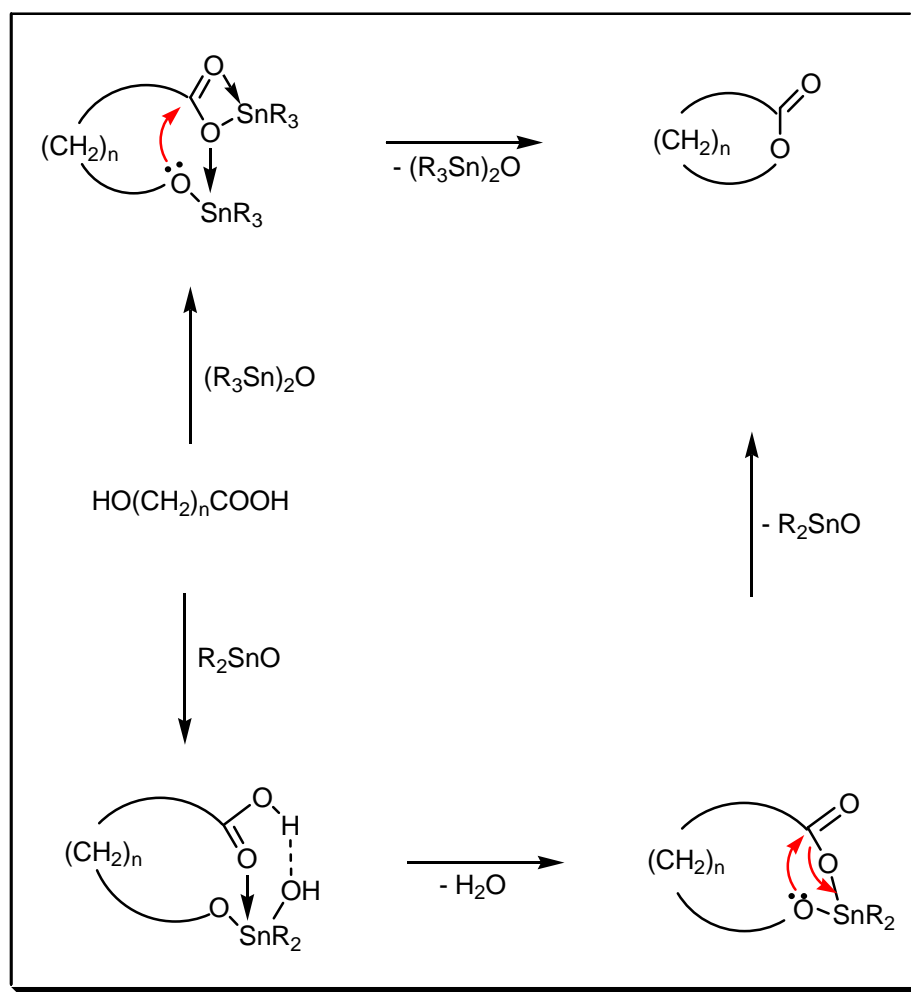
### HANESSION MACROLACTONISATION

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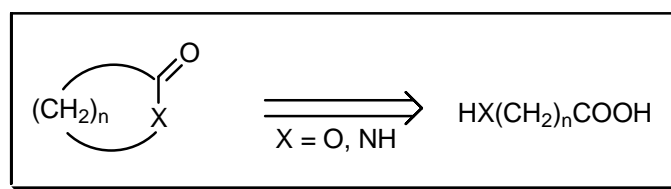
#### EXAMPLE :



## MECHANISM :



## DISCONNECTION :

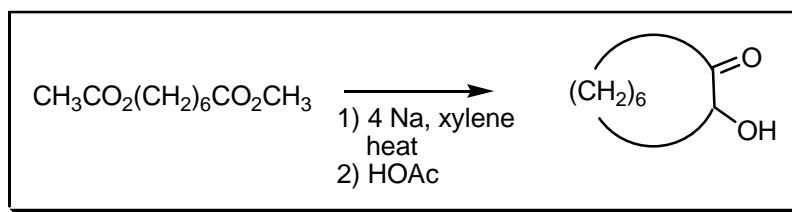


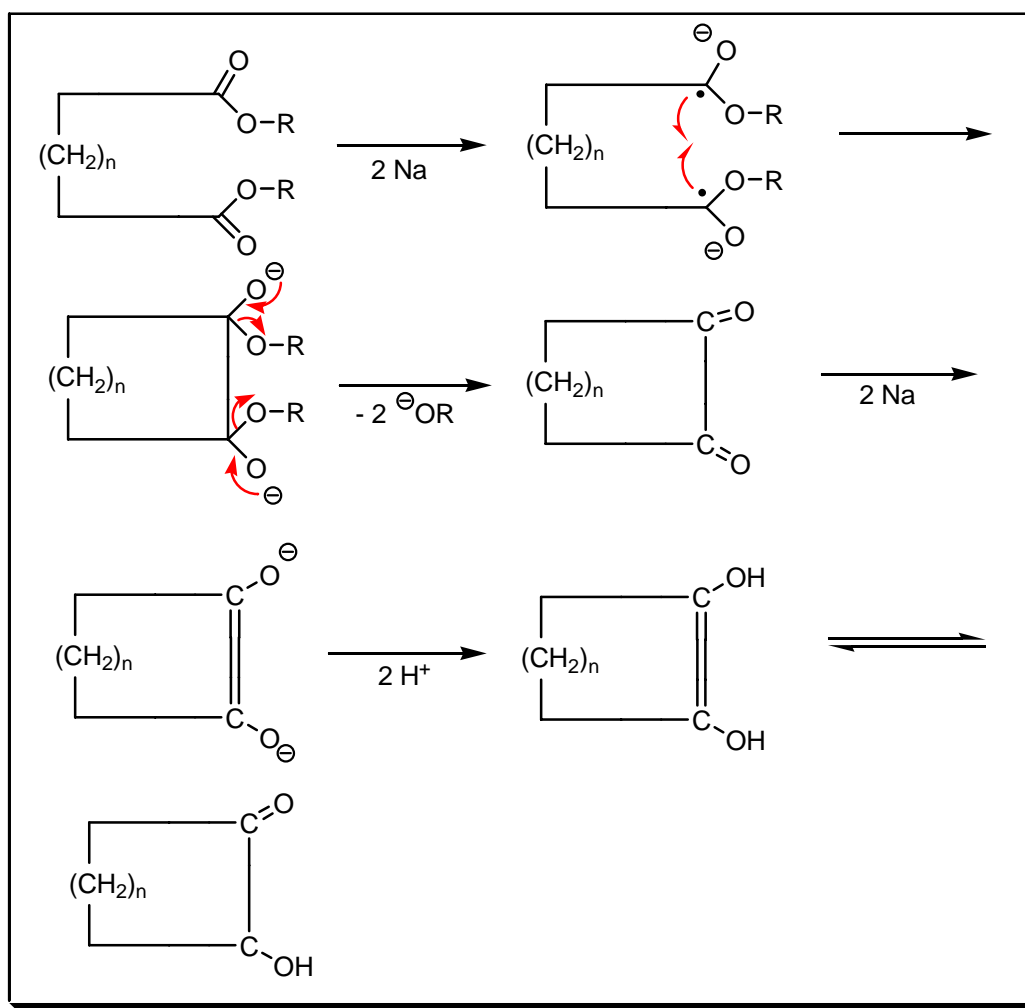
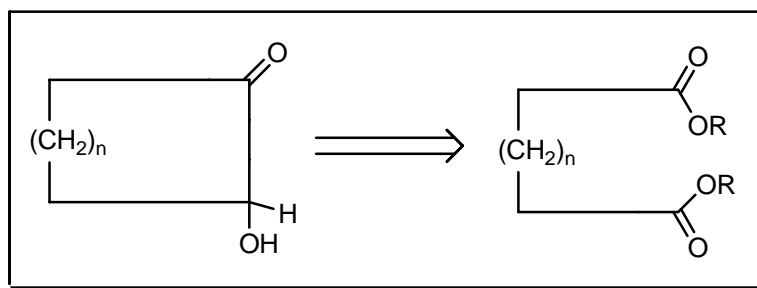
## NOTES :

The use of organostannyl oxides as catalytic neutral esterification agents in the preparation of macrolides. See also **Corey – Nicolaou**, **Diels – Alder**, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Kita**, **Masamune**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolikiewicz**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

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- 

**COMMENTS :****HANSLEY – PRELOG – STOLL SYNTHESIS****EXAMPLE :**

**MECHANISM :****DISCONNECTION :****NOTES :**

This reaction involves intensive heating of a well stirred mixture of an  $\alpha,\omega$ -dicarboxylic ester in boiling xylene in the absence of air with molten sodium. An *intramolecular* acyloin condensation takes place to yield a cyclic  $\alpha$ -hydroxy ketone (ring sizes 12-36). In the **Rühlmann** variation trimethylsilyl chloride is added and the released alcoholate is trapped. See also **Bouveault – Blanc**, **Bouveault – Locquin** acyloin, **Corey – Nicolaou**, **Diels – Alder**, **Hanessian** macrolactonisation, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Kita**, **Masamune**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Stille** –

Migita – Kosugi, Story, Suzuki – Miyaura, Thorpe – Ziegler, Venkataraman – Wagle, Vorbrüggen – Krolkiewicz, Wittig, Yamaguchi and Yamamoto macrolactonisation reactions.

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Houben – Weyl : **4/2**, 755

Org. React. : **4**, 256; **15**, 34; **23**, 259

Org. Synth. : **36**, 79

Org. Synth. Coll. Vol. : **4**, 840

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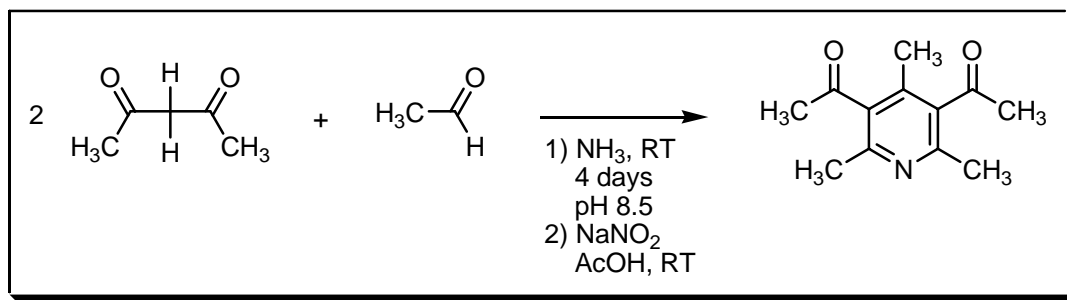
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#### COMMENTS :

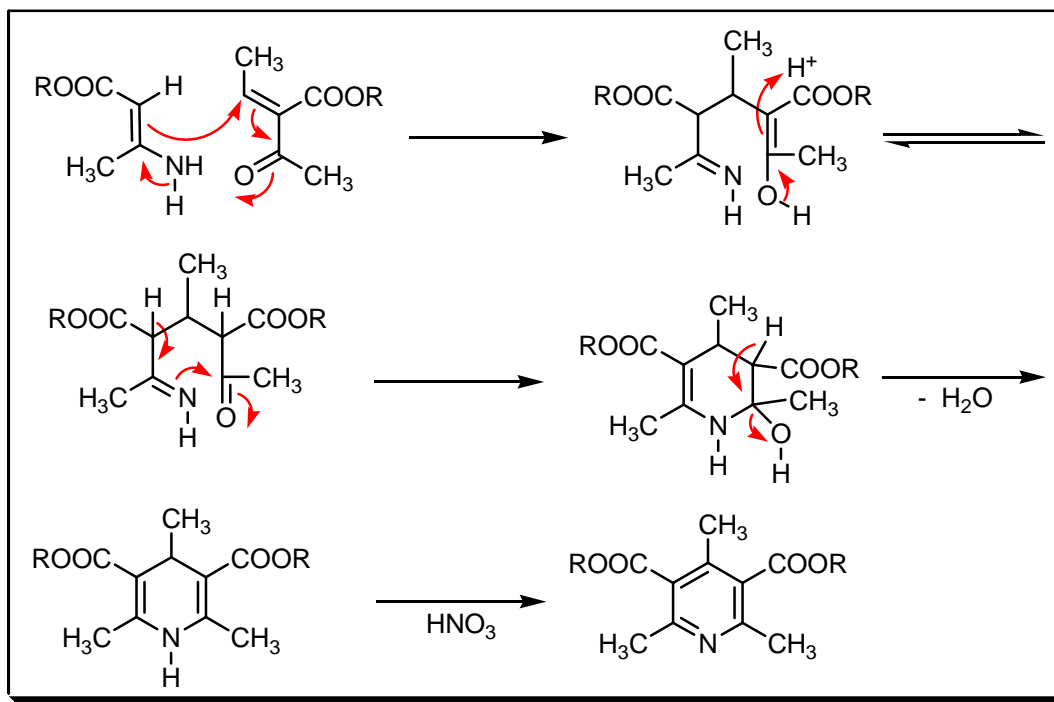
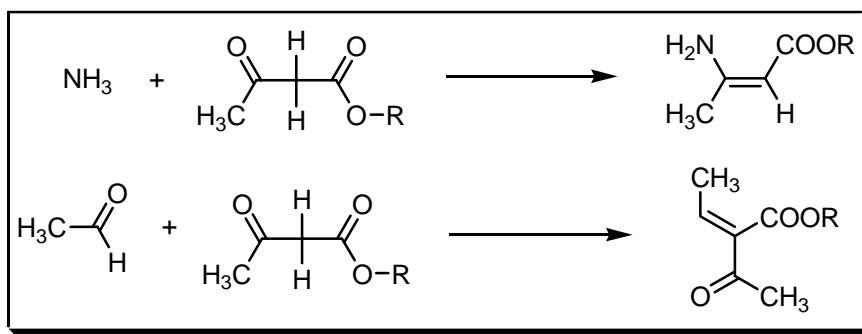
### HANTZSCH – BEYER PYRIDINE SYNTHESIS

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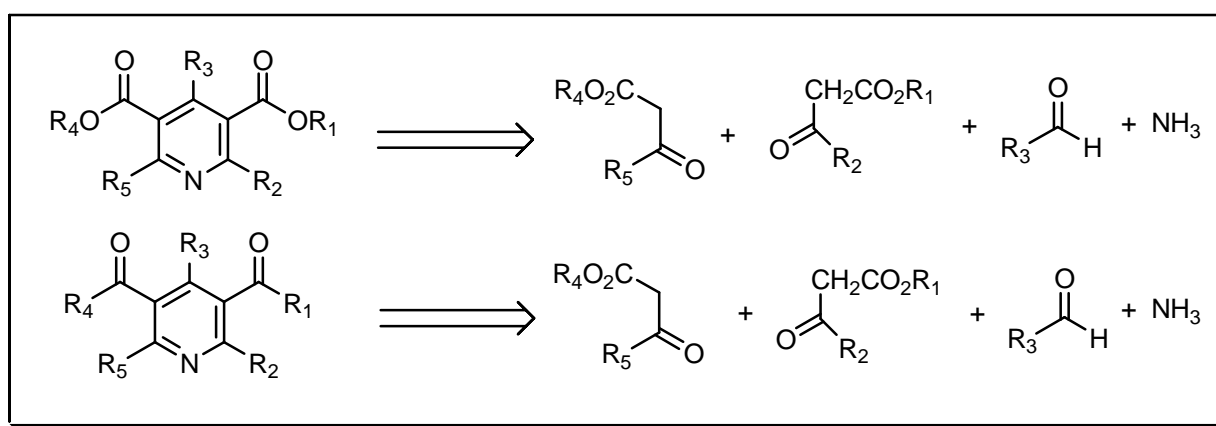
#### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The interaction of two moles of a  $\beta$ -keto ester or a 1,5-dicarbonyl compound with aldehyde and ammonia affords dihydropyridine derivatives which are readily oxidised to pyridines. Unsymmetrical 1,4-dihydropyridines can be synthesised by a 2-step synthesis. This reaction has been improved first by **Beyer** and later by **Knoevenagel**. See



also **Bohlmann – Rahtz**, **Chichibabin** pyridine, **Gattermann – Skita**, **Guareschi – Thorpe**, **von Meyer – Mohr**, **Petrenko–Kritschenko**, **Riehm** pyridine and **Wakatsuki – Yamazaki – Bönnemann** reactions.

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Houben – Weyl : **E7b**, 399

Org. Synth. : **14**, 30

Org. Synth. Coll. Vol. : **2**, 214

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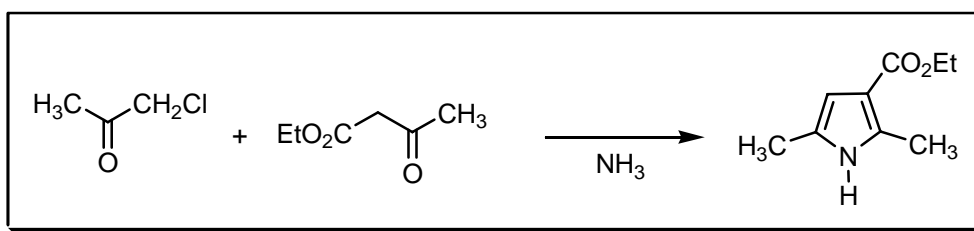
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  - 10) G.P. Shkil; D. Mutsenietse; L.V. Berdovich; V. Lasis, *Chem. Heterocycl. Compd. (Engl. Transl.)*, 1995, **31**, 76.
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  - 12) M. Kidwai; S. Saxena; R. Mohan; R. Venkataramanan, *J. Chem. Soc., Perkin Trans. 1*, 2002, 1845.
  - 13) N. Nakamichi; Y. Kawashita; M. Hayashi, *Synthesis*, 2004, 1015.
- 

#### COMMENTS :

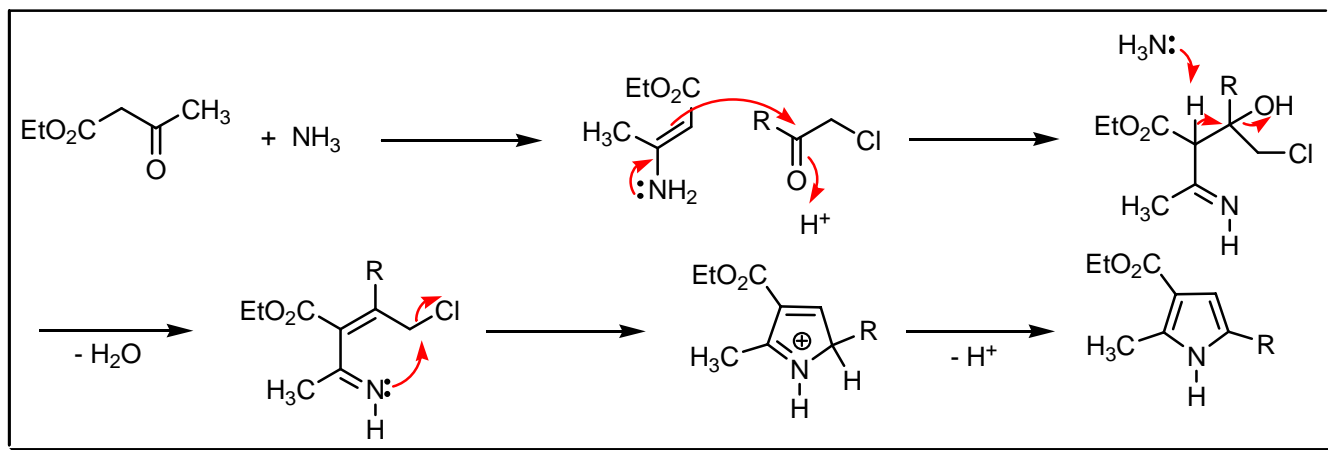
### HANTZSCH PYRROLE SYNTHESIS

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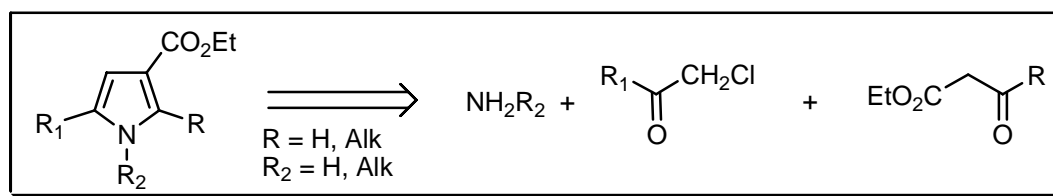
#### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The interaction of  $\alpha$ -chloro-aldehydes or ketones with  $\beta$ -ketoesters and ammonia or amines to give pyrroles. See also **Barton – Zard**, **Clauson–Kaas**, **Fischer – Fink**, **Grob – Camenisch**, **Harries** pyrrole, **Kenner**, **Knorr** pyrrole, **Miller – Plöchl**, **Paal – Knorr**, **Padwa**, **Piloty – Robinson**, **Schwanert**, **Trofimov** and **Zav'yalov** reactions.

## REFERENCES :

Houben – Weyl : E6a, 631, 648

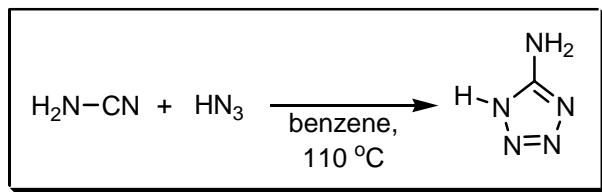
Science of Synthesis : 9, 444

- 1) A. Hantzsch, *Ber. Dtsch. Chem. Ges.*, 1890, **23**, 1474.
- 2) F. Feist, *Ber. Dtsch. Chem. Ges.*, 1902, **35**, 1538.
- 3) E. Baltazzi; L.I. Krimen, *Chem. Rev.*, 1963, **63**, 511.
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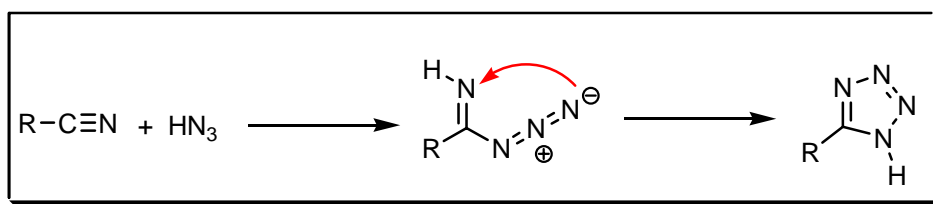
**COMMENTS :**

## HANTZSCH TETRAZOLE SYNTHESIS

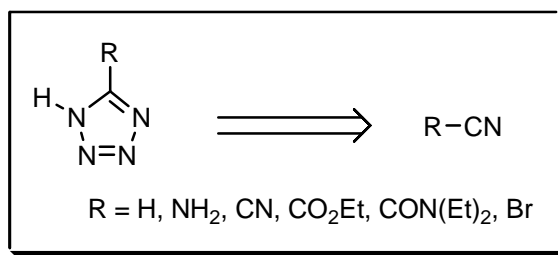
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

The addition of hydrazoic acid to the cyanides leads to the formation of 5-substituted tetrazoles.

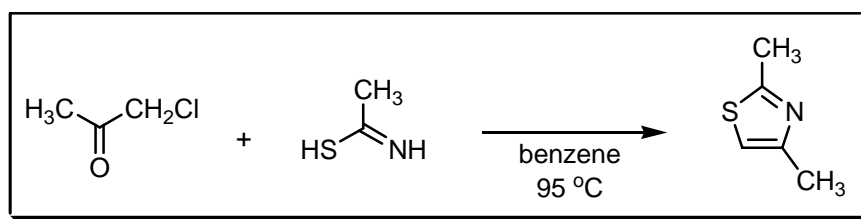
**REFERENCES :**

- 1) A. Hantzsch; A. Vagt, *Liebigs Ann. Chem.*, 1901, **314**, 339.
- 2) R. Stollé, *Ber. Dtsch. Chem. Ges.*, 1929, **62**, 1118.
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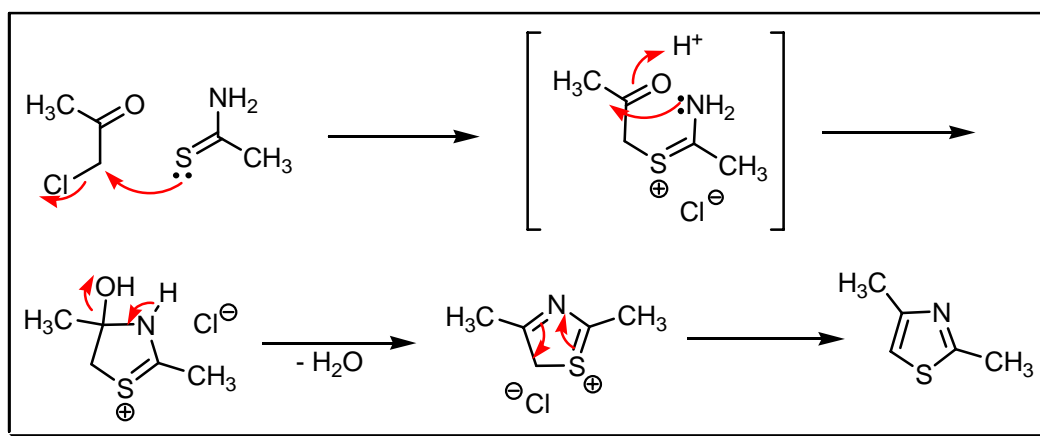
COMMENTS :

## HANTZSCH THIAZOLE SYNTHESIS

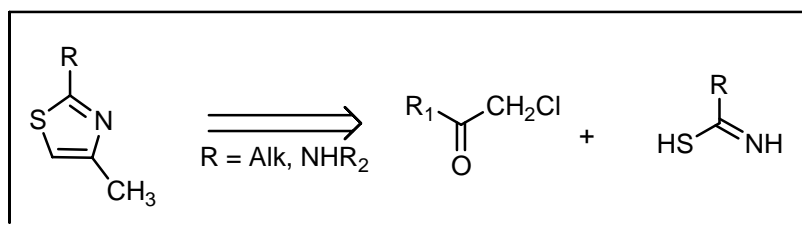
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

Thiazoles are formed by the condensation of  $\alpha$ -chloro-aldehydes or  $\alpha$ -ketones with thioamides. See also **Andreasch** and **Wohl – Marckwald** reactions.

## REFERENCES :

Org. Synth. : **19**, 10; **25**, 35

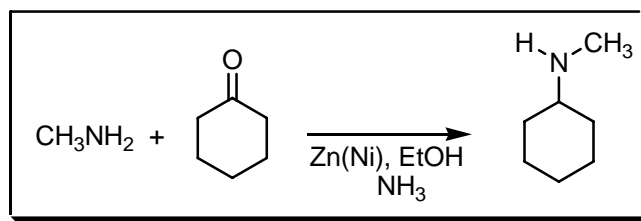
Org. Synth. Coll. Vol. : **2**, 31; **3**, 332

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- 1) A. Hantzsch, *Liebigs Ann. Chem.*, 1889, **250**, 257.
  - 2) R.H. Dodson; L.C. King, *J. Am. Chem. Soc.*, 1945, **67**, 2242.
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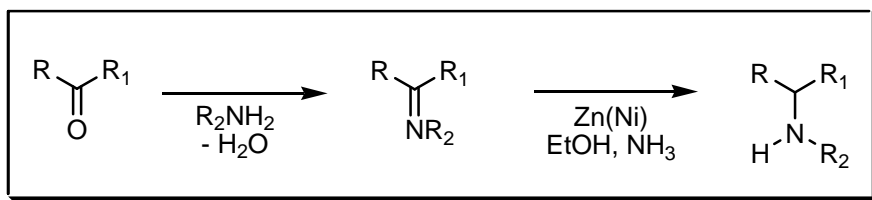
## COMMENTS :

## HARLAY AMINATION

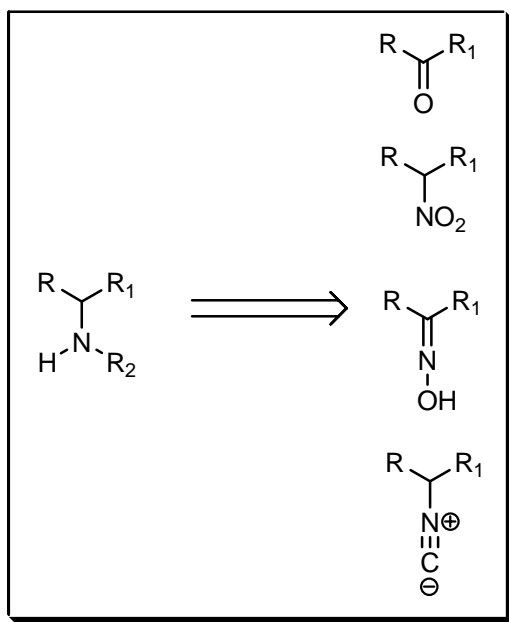
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

Ketones are converted directly into amines by treatment with zinc/nickel couple in ethanolic ammonia, ammonia can be replaced by primary amines. The same reaction conditions can be used for the reduction of nitro, nitriles, oximes and isonitriles to amines. See also **Eschweiler – Clark**, **Forster – Decker** and **Henze – Humphreys** reactions.

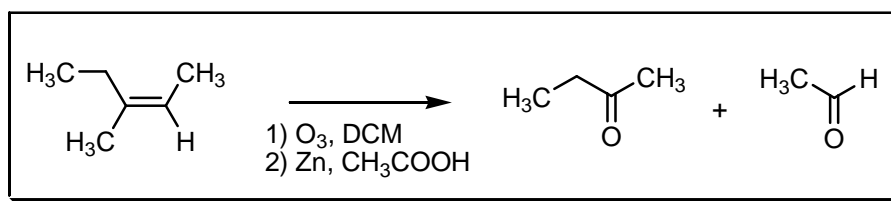
## REFERENCES :

- 1) V. Harlay; G. Bertrand, *C.R. Séances Acad. Sci.*, 1941, **213**, 304.
- 2) M. Mousseron; P. Froger, *Bull. Soc. Chim. Fr.*, 1947, 843.
- 3) J. Werner, *Ind. Eng. Chem.*, 1986, **40**, 1574.

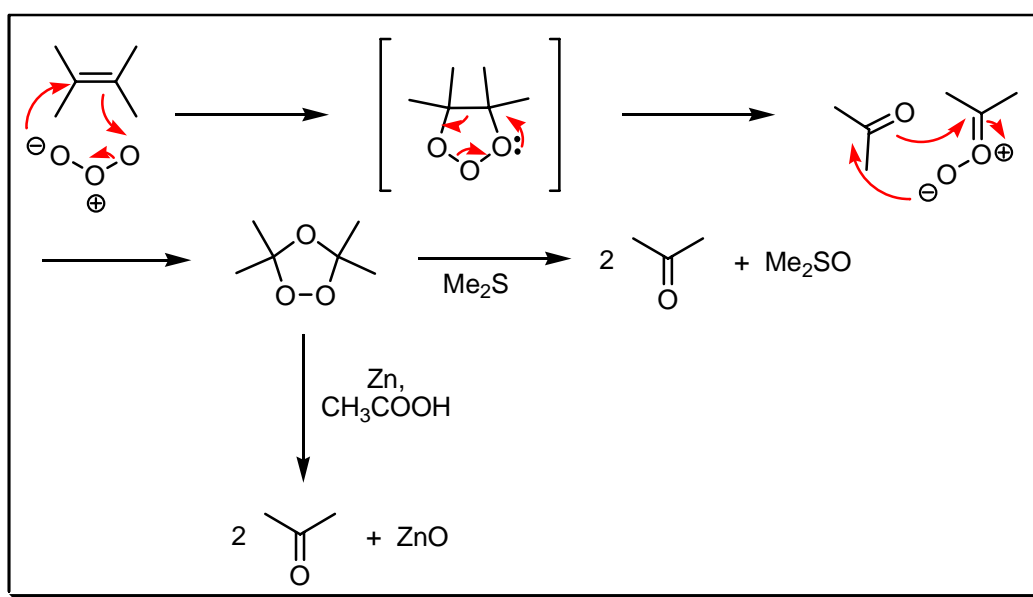
## COMMENTS :

## HARRIES OZONIDE REACTION

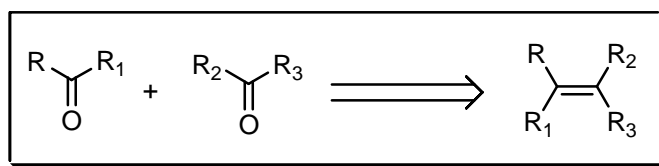
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Alkenes react with ozone to form initially a molozonide and rearranges *via* the carbonyl oxide to an ozonide which on decomposition gives two carbonyl compounds.

## REFERENCES :

March : 1177

Smith – March : 1522

Smith : 306

Smith 2<sup>nd</sup> : 267

Org. Synth. : 26, 63; 41, 41

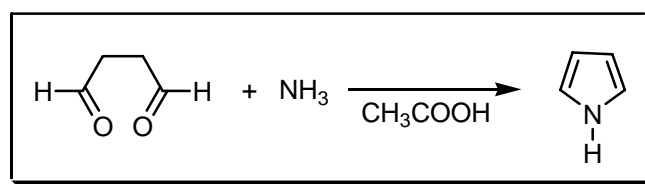
Org. Synth. Coll. Vol. : 3, 673; 5, 489

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  - 2) C. Harries, *Liebigs Ann. Chem.*, 1905, **343**, 311.
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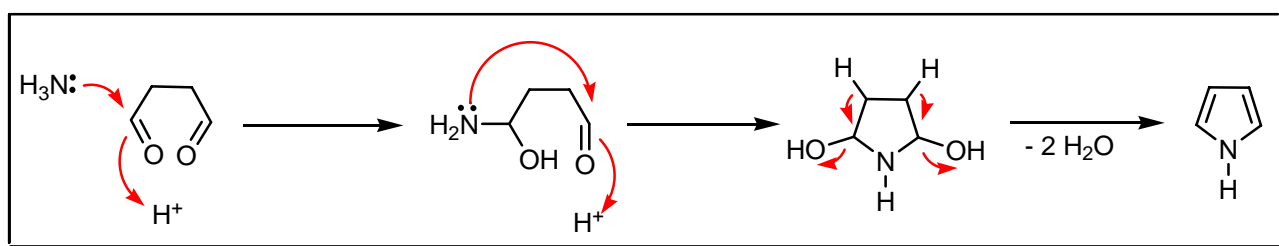
## COMMENTS :

## HARRIES PYRROLE SYNTHESIS

### EXAMPLE :

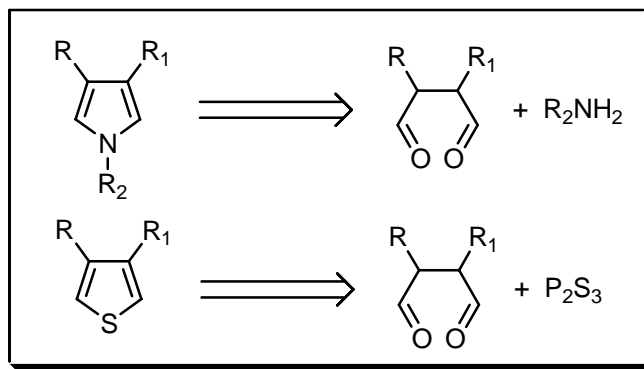


### MECHANISM :





## DISCONNECTION :



## NOTES :

Pyrrole is obtained by the interaction of ammonia and succinic dialdehyde in the presence of acetic acid. If diphosphorous trisulfide is used thiophene derivatives are obtained. See also **Barton – Zard**, **Clauson-Kaas**, **Fischer – Fink**, **Grob – Camenisch**, **Hantzsch** pyrrole, **Kenner**, **Knorr** pyrrole, **Miller – Plöchl**, **Paal – Knorr**, **Padwa**, **Piloty – Robinson**, **Schwanert**, **Trofimov** and **Zav'yalov** reactions.

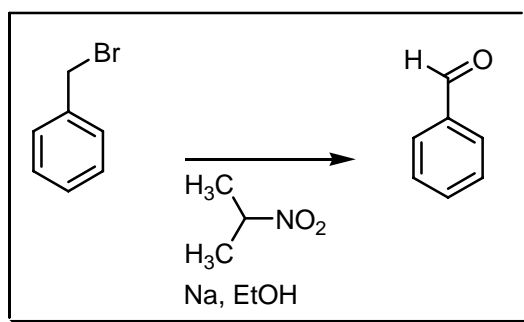
## REFERENCES :

- 1) C. Harries, *Ber. Dtsch. Chem. Ges.*, 1901, **34**, 1488.
- 2) C. Harries, *Ber. Dtsch. Chem. Ges.*, 1902, **35**, 1186.
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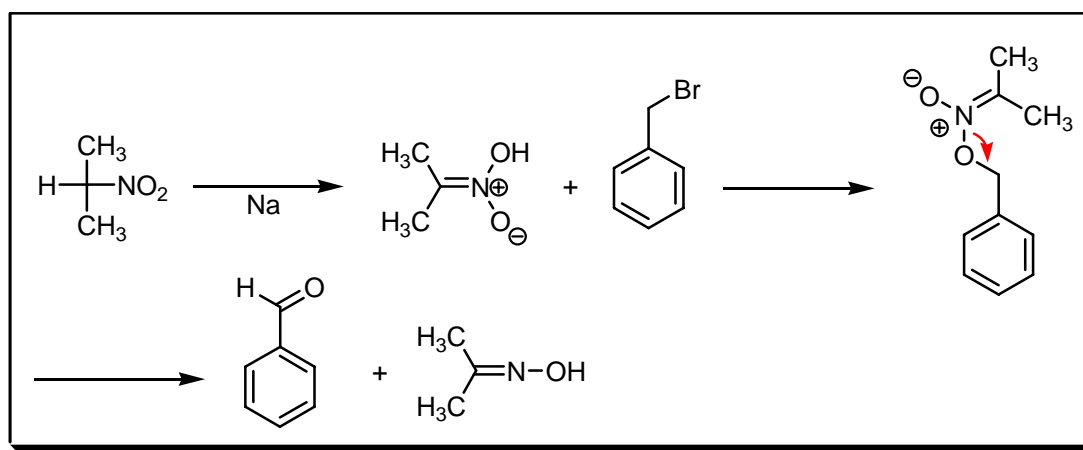
## COMMENTS :

## HASS – BENDER CARBONYL SYNTHESIS

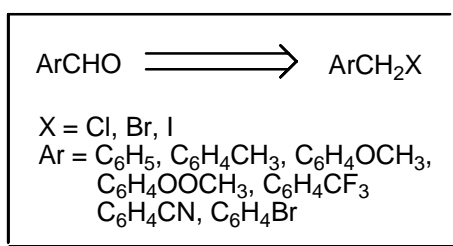
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

An aromatic aldehyde or ketone are synthesised by reaction of a benzyl halide or polycyclic compounds with the sodium salt of 2-nitroalkanes. See also **Kornblum** aldehyde and **Sommelet** aldehyde reactions.

## REFERENCES :

Houben – Weyl : E3, 251

Org. Synth. : 30, 99

Org. Synth. Coll. Vol. : 4, 932

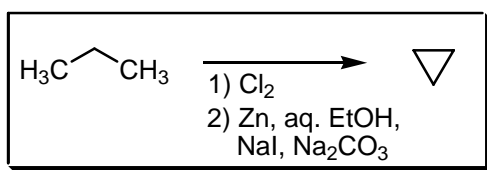
- 1) H.B. Hass; M.L. Bender, *J. Am. Chem. Soc.*, 1949, **71**, 1767.
- 2) D.B. Spoelstra; S.H. Weber; R.J.C. Kleipool, *Recl. Trav. Chim. Pays-Bas*, 1957, **76**, 205.
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## COMMENTS :

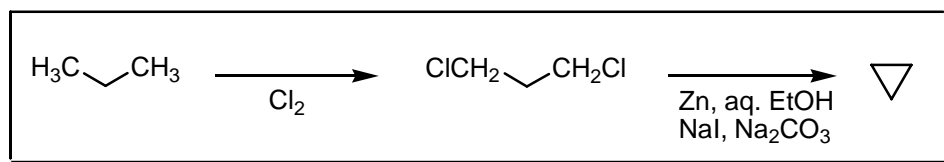
## HASS CYCLOPROPANE PROCESS

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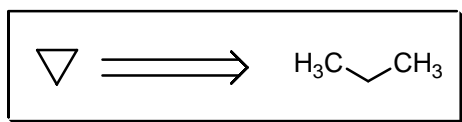
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Propane in natural gas is chlorinated and 1,3-dichloropropane is separated from the other products and converted to cyclopropane by treatment with zinc dust in aqueous ethanol in the presence of sodium carbonate and sodium iodide. See also **Charette**, **Freund**, **Gustavson**, **Ipatiew** cyclopropane, **Kishner**, **Mousseron – Fraisse – McCoy**, **Nerdel** and **Simmons – Smith** reactions.

### REFERENCES :

Houben – Weyl : 13/1, 492

1) H.B. Hass; G.E. Hinds, *Chemisches Zentralblatt*, 1938-I, 4237.

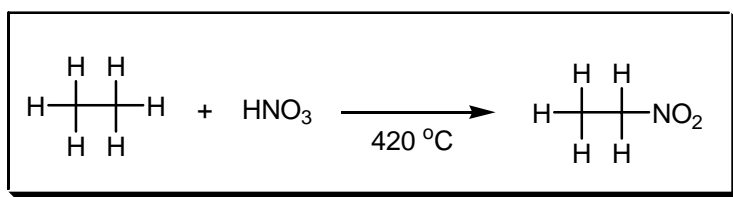
2) E. Vogel, *Angew. Chem.*, 1960, **72**, 4.

### COMMENTS :

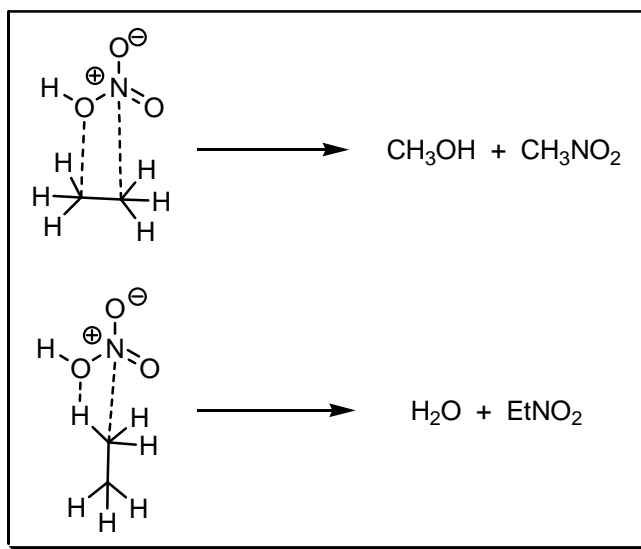
## HASS PROCESS

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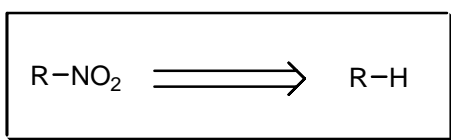
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Aliphatic hydrocarbons react with nitric acid vapour at 420 °C to afford aliphatic nitro compounds. Straight and branched hydrocarbons can be nitrated. Due to the high temperatures used oxidative cleavage will take place.

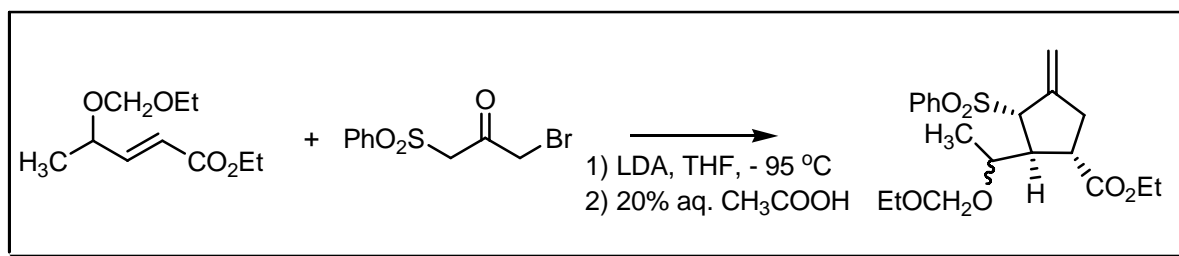
### REFERENCES :

- 1) H.B. Hass; E.B. Hodge; B.M. Vanderbilt, *U.S. Patent*, 1934, 1967667.
- 2) H.B. Hass; E.B. Hodge; B.M. Vanderbilt, *Ind. Eng. Chem.*, 1936, **28**, 339.
- 3) H.B. Hass; E.F. Riley, *Chem. Rev.*, 1943, **32**, 373.

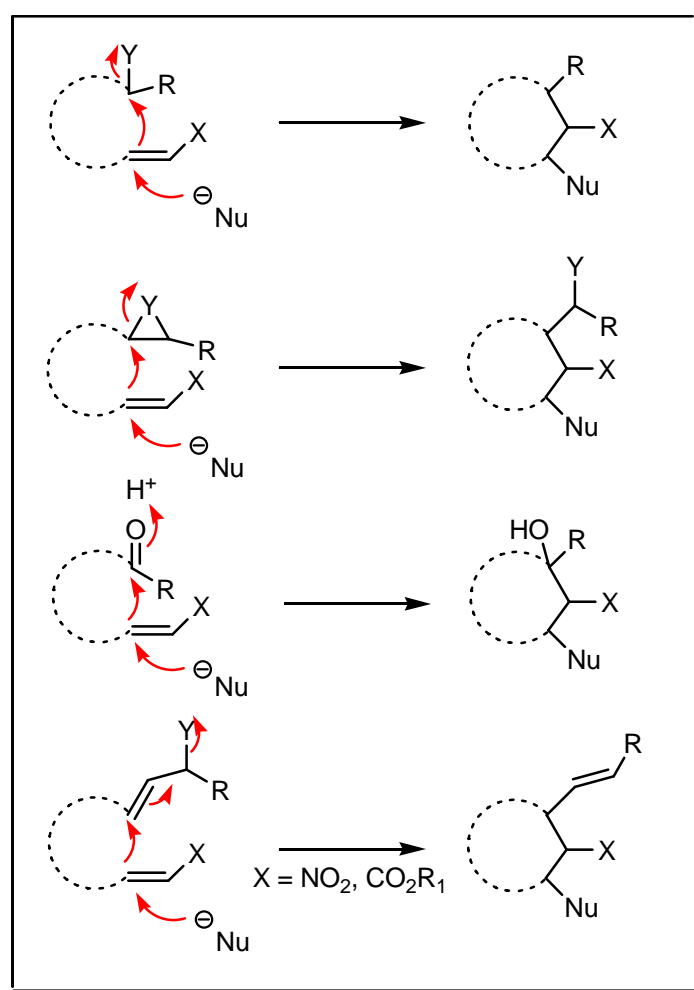
COMMENTS :

HASSNER – GHERA – LITTLE RING-CLOSURE

EXAMPLE :



MECHANISM :



## NOTES :

**Michael** initiated ring-closure (MIRC) of especially sulfones affords three, five, six and seven membered rings in the presence of lithium diisopropylamine. After the initial conjugate addition, the ring-closure can be *inter*- or *intramolecular*. The [3+2]-cycloadditions are stereoselective. See also **Michael** reaction.

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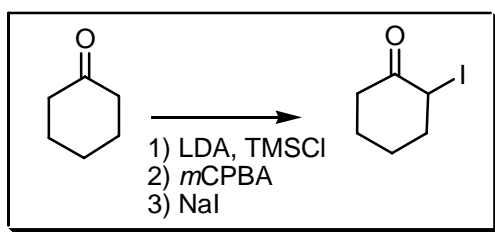
## REFERENCES :

- 1) R.D. Little; J.R. Dawson, *J. Am. Chem. Soc.*, 1978, **100**, 4607.
  - 2) E. Ghera; Y. Ben-David, *Tetrahedron Lett.*, 1979, **20**, 4603.
  - 3) R.D. Little; J.R. Dawson, *Tetrahedron Lett.*, 1980, **21**, 2609.
  - 4) E. Ghera; T. Yechezkel; A. Hassner, *Tetrahedron Lett.*, 1990, **31**, 3653.
  - 5) M.A. Amputch; R. Matamoros; R.D. Little, *Tetrahedron*, 1994, **50**, 5591.
  - 6) E. Ghera; T. Yechezkel; A. Hassner, *J. Org. Chem.*, 1996, **61**, 4959.
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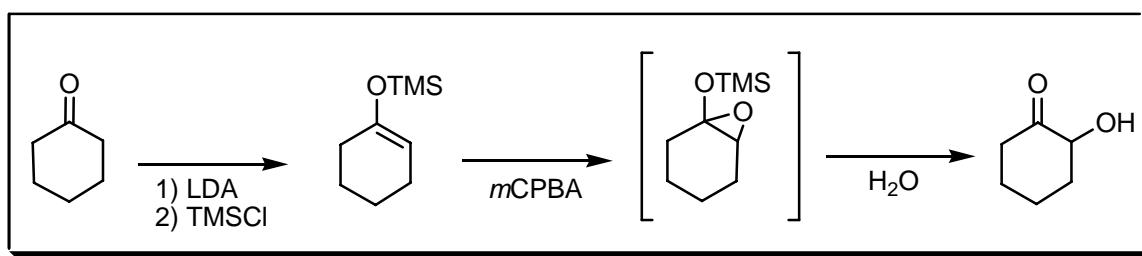
## COMMENTS :

## HASSNER – RUBOTTOM $\alpha$ -HYDROXYLATION

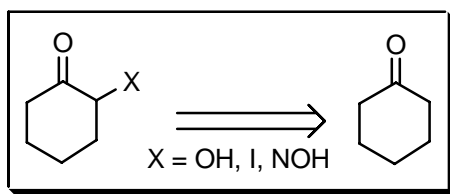
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

This is the  $\alpha$ -hydroxylation, iodination, or oximation of carbonyls *via* silyl enol ethers. See also **Vedejs** hydroxylation.

## REFERENCES :

**Org. Synth.** : **64**, 118; **73**, 123

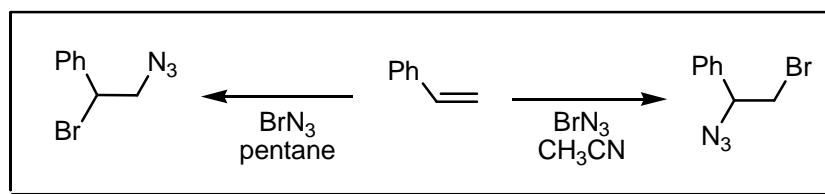
**Org. Synth. Coll. Vol.** : **7**, 282; **9**, 564

- 1) J. Rasmussen; A. Hassner, *Synthesis*, 1973, 682.
- 2) R.H. Reuss; A. Hassner, *J. Org. Chem.*, 1974, **39**, 1785.
- 3) G.M. Rubottom; R.C. Mott; H.D. Juve, jr., *J. Org. Chem.*, 1981, **46**, 2717.
- 4) G.M. Rubottom; H.D. Juve, jr., *J. Org. Chem.*, 1983, **48**, 422.
- 5) C.-K. Sha; J.-J. Young; T.-S. Jean, *J. Org. Chem.*, 1987, **52**, 3919.
- 6) R. Gleiter; R. Kraemer; H. Irngartinger; C. Bissinger, *J. Org. Chem.*, 1992, **57**, 252.

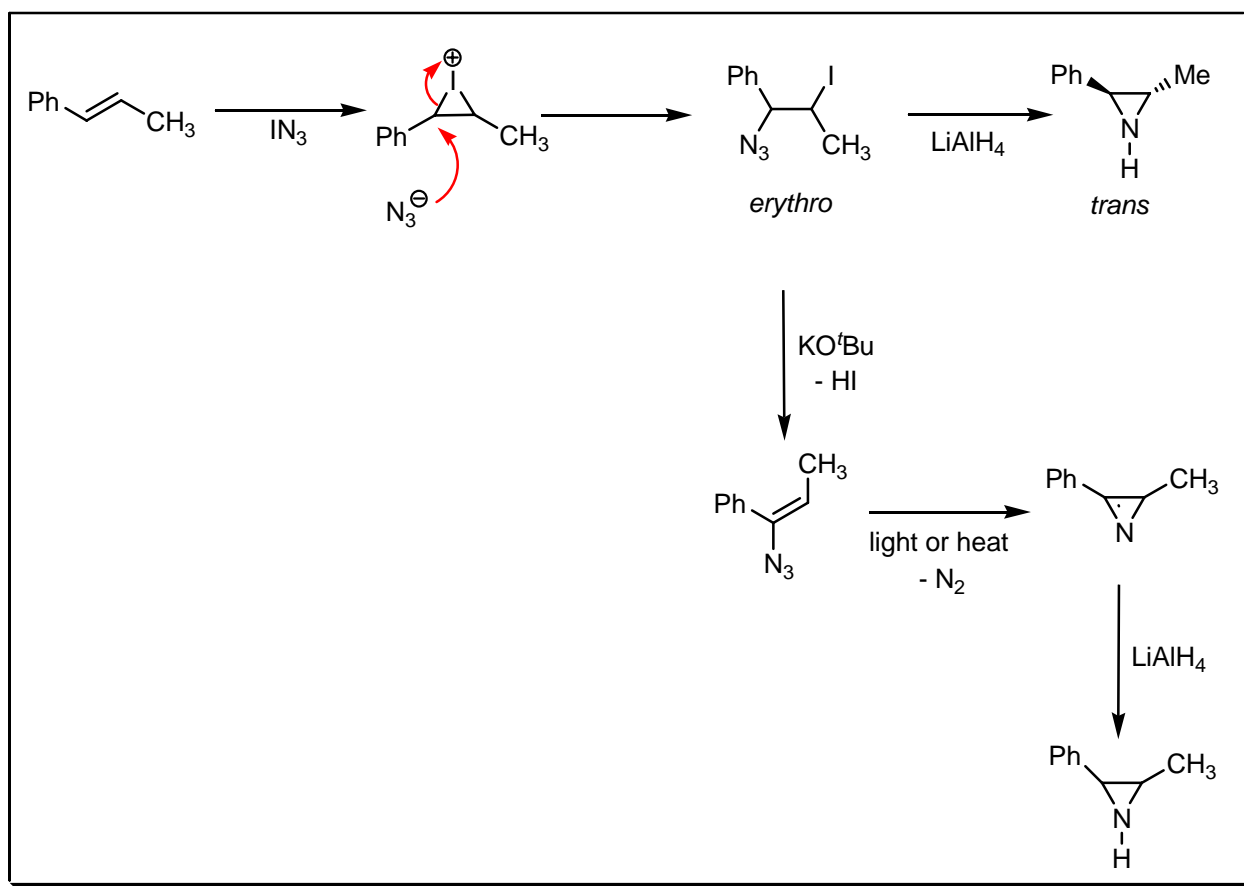
## COMMENTS :

## HASSNER AZIDE AZIRIDINE SYNTHESIS

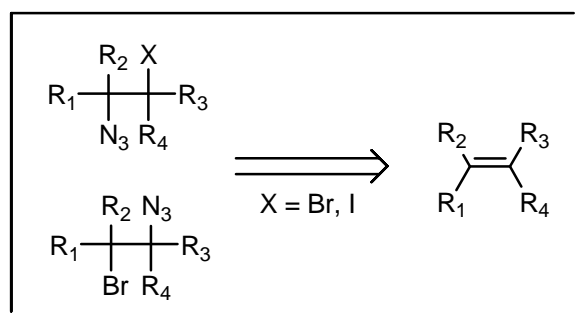
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The stereospecific and regioselective addition of  $\text{IN}_3$  (via iodonium ions) or of  $\text{BrN}_3$  (ionic or free radical) to olefins and conversion of the adducts to aziridines or azirines. This is a more convenient route than the **Wenker** synthesis. See also **Blum** aziridine, **Gabriel – Marckwald – Cromwell** ethylenimine method, **Hoch – Campbell**, **Mansuy – Evans**, **Scheiner** and **Wenker** ring-closure reactions.

## REFERENCES :

Org. Synth. : 51, 53, 112

Org. Synth. Coll. Vol. : 6, 795, 967



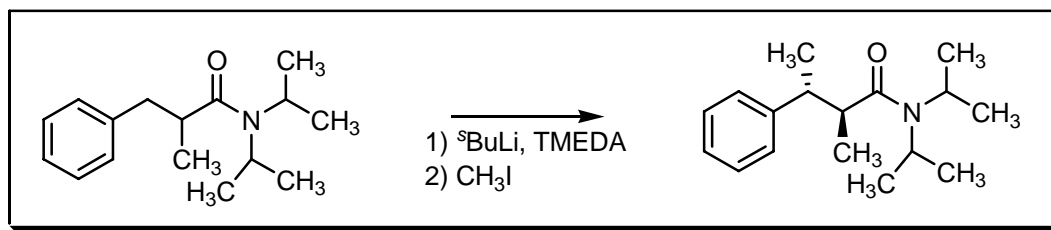
- 1) A. Hassner; C. Heathcock, *Tetrahedron*, 1964, **20**, 1037.
- 2) A. Hassner; C. Heathcock, *J. Org. Chem.*, 1965, **30**, 1748.
- 3) A. Hassner; J.E. Galle, *J. Am. Chem. Soc.*, 1970, **92**, 3733.
- 4) A. Hassner, *Acc. Chem. Res.*, 1971, **4**, 9.
- 5) R. Bushby; S. Mann, *J. Chem. Soc., Perkin Trans. 1*, 1987, 2497.
- 6) W. Chamchaang; A.R. Pinhas, *J. Org. Chem.*, 1990, **55**, 2943.
- 7) F.W. Eastwood; P. Perlmutter; Q. Yang, *J. Chem. Soc., Perkin Trans. 1*, 1997, 35.

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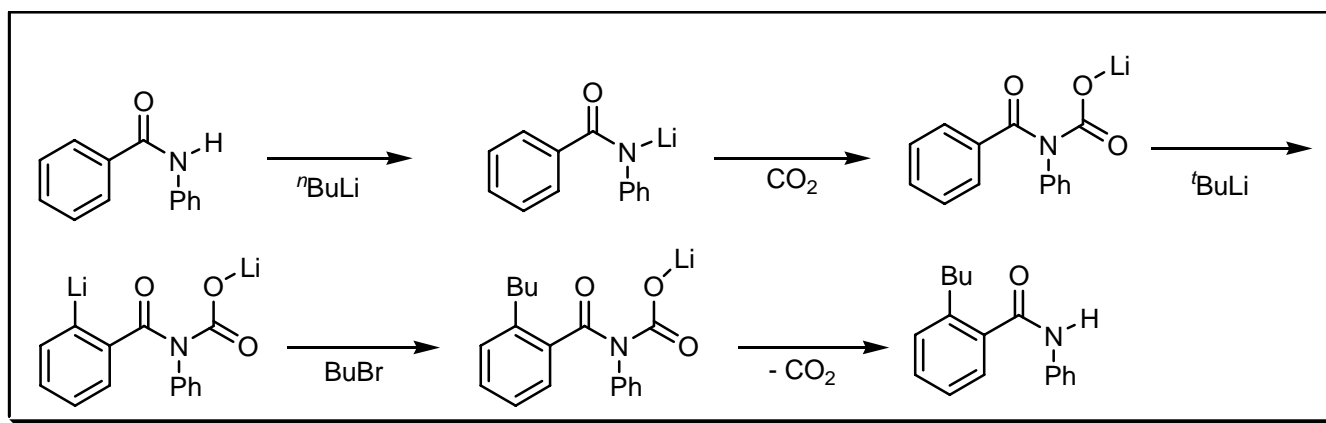
**COMMENTS :**

**HAUSER – BEAK ORTHO-LITHIATION**

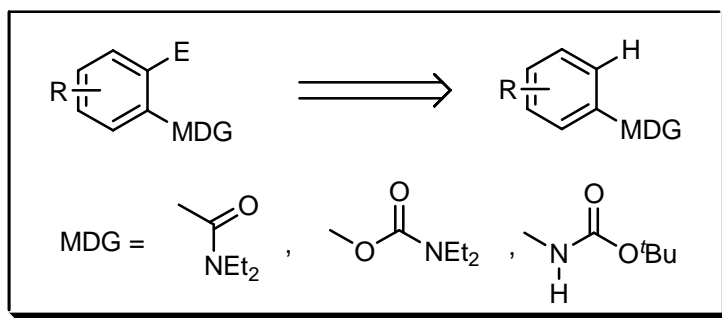
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

In general this is the *ortho*-selective electrophilic functionalisation of aromatic compounds *via* substituent-controlled lithiation. The **Hauser – Beak** *ortho*-lithiation deals with dipole-stabilised carbanions  $\alpha$  to nitrogen or a benzylic carbanion.

## REFERENCES :

**Org. React.** : **47**, 1

**Org. Synth.** : **74**, 23

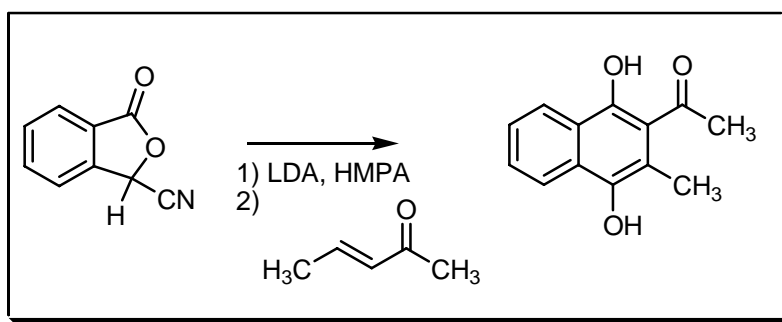
**Org. Synth. Coll. Vol.** : **9**, 391

- 1) C.-L. Mao; I.T. Barnish; C.R. Hauser, *J. Heterocycl. Chem.*, 1969, **6**, 475.
- 2) P. Beak; R.A. Brown, *J. Org. Chem.*, 1977, **42**, 1823.
- 3) P. Beak; V. Snieckus, *Acc. Chem. Res.*, 1982, **15**, 306.
- 4) P. Beak; A. Basu; D.J. Gallagher; Y.S. Park; S. Thayumanavan, *Acc. Chem. Res.*, 1996, **29**, 552.
- 5) H.J. Du; J.K. Cha, *J. Am. Chem. Soc.*, 1999, **121**, 10012.

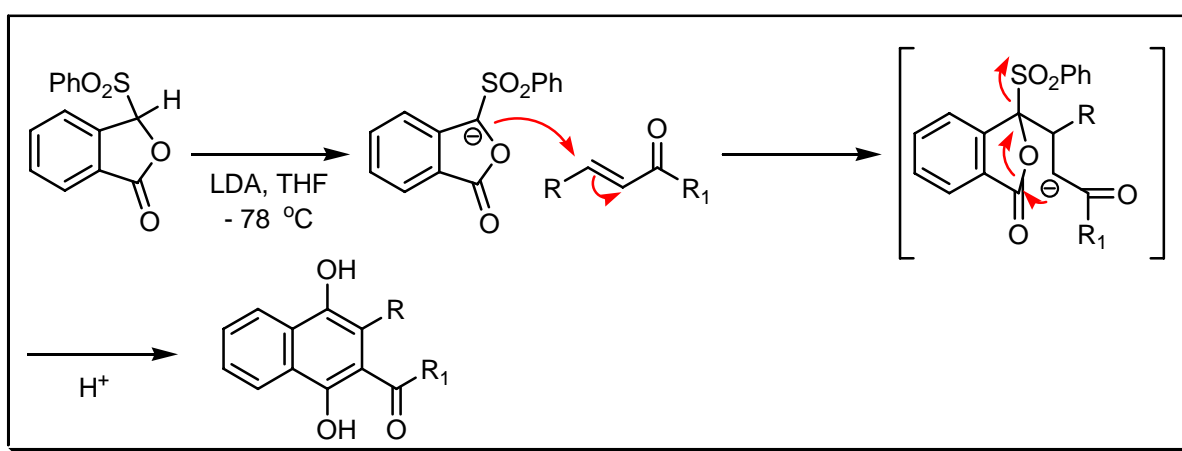
## COMMENTS :

## HAUSER – KRAUS ANNULATION

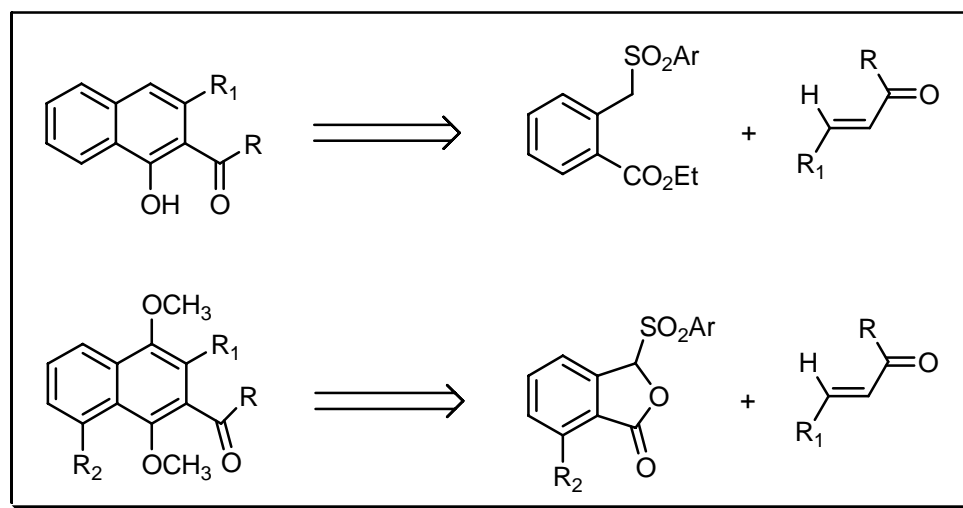
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



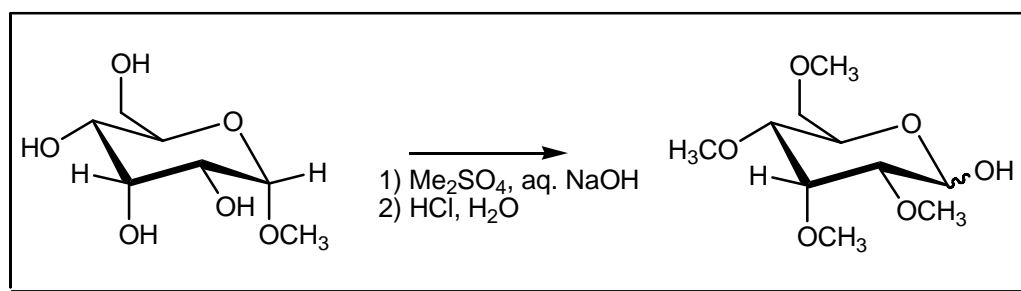
**NOTES :**

1-Hydroxy-2,3-disubstituted naphthalenes and 1,4-dihydroxy-2,3-disubstituted naphthalenes are prepared from ethyl 2-carboxybenzyl phenyl sulfoxides and 1*H*-2-benzofuran-1-one-3-phenyl sulfone with ketones and  $\alpha,\beta$ -unsaturated esters.

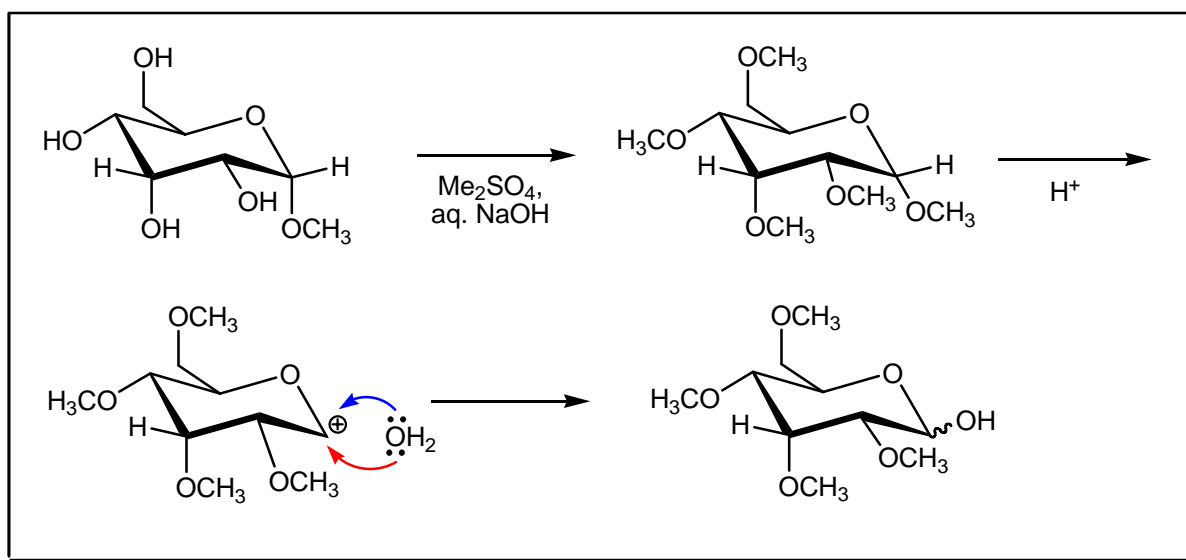
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**REFERENCES :**

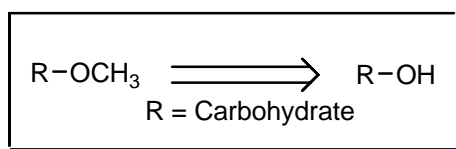
- 1) F.M. Hauser; R.P. Rhee, *J. Am. Chem. Soc.*, 1977, **99**, 4533.
  - 2) F.M. Hauser; R.P. Rhee, *J. Org. Chem.*, 1978, **43**, 178.
  - 3) G.A. Kraus; H. Sugimoto, *Tetrahedron Lett.*, 1978, **19**, 2263.
- 

**COMMENTS :****HAWORTH METHYLATION****EXAMPLE :**

## MECHANISM :



## DISCONNECTION :



## NOTES :

This is the O-alkylation of carbohydrates by alkyl sulfate and aqueous alkali. The glycosidic methyl group can be hydrolysed with acid. See also **Claisen** carbonate alkylation, **Fischer** glycosidation, **Hakomori**, **Irvine – Purdie**, **Meerwein** methylation, **Robertson – Robinson** and **Williamson** reactions.

## REFERENCES :

Houben – Weyl : 6/3, 35

Org. Synth. : 20, 97

Org. Synth. Coll. Vol. : 3, 800

1) W.S. Denham; H. Woodhouse, *J. Chem. Soc.*, 1913, **103**, 1735.

2) W.N. Haworth, *J. Chem. Soc.*, 1915, **107**, 13.

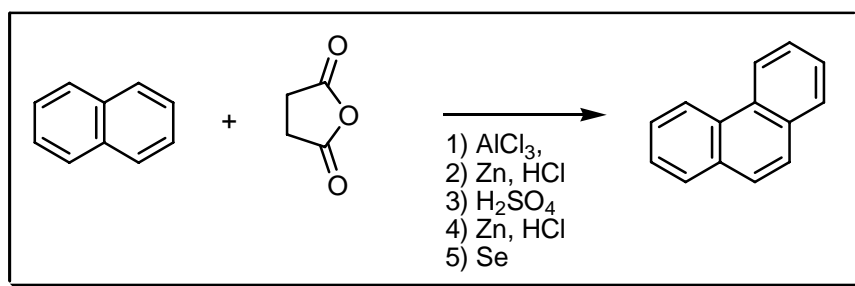
3) W.N. Haworth; H. Machemer, *J. Chem. Soc.*, 1932, 2270.

4) R. Kuhn; H. Trischmann, *Chem. Ber.*, 1963, **96**, 284.

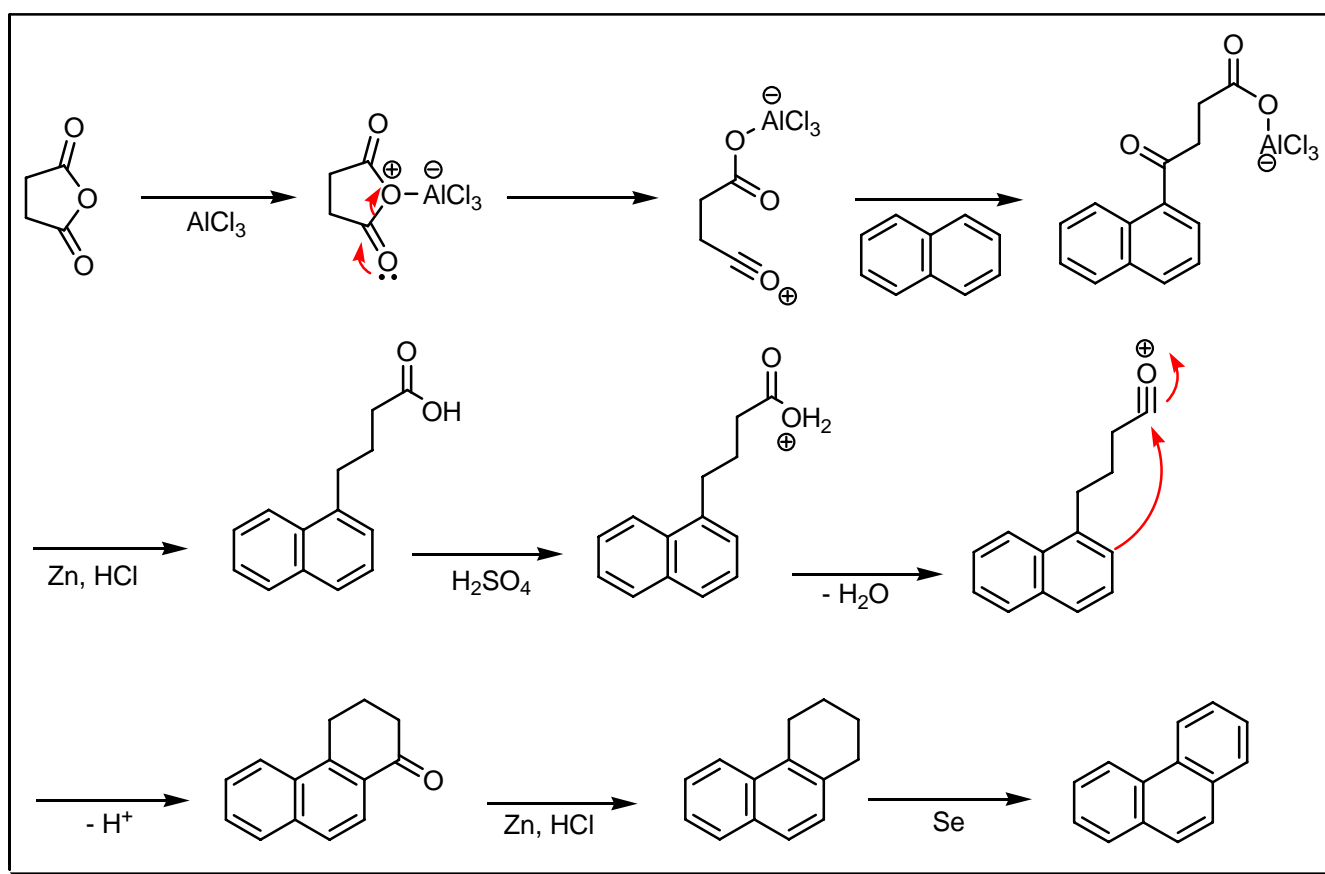
## COMMENTS :

## HAWORTH POLYNUCLEAR AROMATICS SYNTHESIS

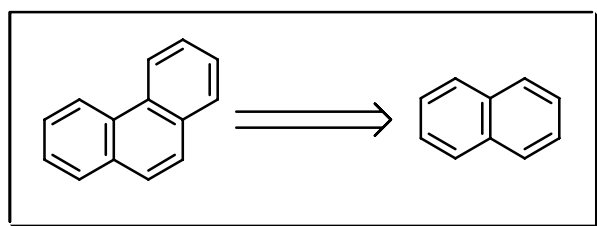
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The synthesis of polynuclear aromatic compounds by the **Friedel – Crafts** condensation of succinic anhydride with an aromatic compound to give a  $\beta$ -aroylpropionic acid. This acid is reduced and treated with moderately concentrated sulfuric acid to yield a cyclic ketone which is in turn reduced. Selenium dehydrogenation gives the polynuclear aromatic compound. See also **Friedel – Crafts**, **Stobbe** and **Wittig** phenanthrene reactions.

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## REFERENCES :

**March** : 541

**Smith – March** : 714

**Smith** : 1329

**Smith 2<sup>nd</sup>** : 1094

**Org. React.** : **5**, 229

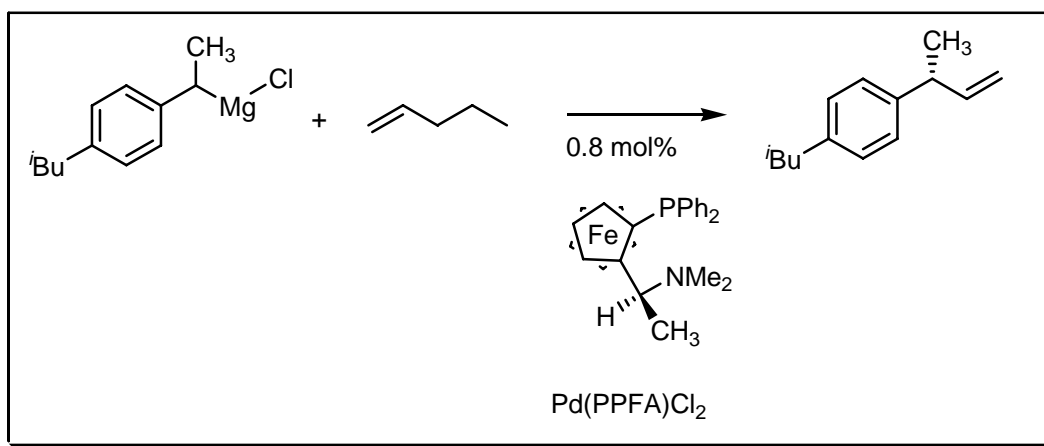
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- 1) F. Krollpfeiffer; W. Schäfer, *Ber. Dtsch. Chem. Ges.*, 1923, **56**, 620.
  - 2) R.D. Haworth, *J. Chem. Soc.*, 1932, 1125.
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  - 4) R.D. Haworth; C.R. Marvin; G. Sheldrick, *J. Chem. Soc.*, 1934, 454.
  - 5) D.D. Phillips; M.F. Bruno, *J. Org. Chem.*, 1963, **28**, 1627.
  - 6) R. Menicagli; O. Piccolo, *J. Org. Chem.*, 1980, **45**, 2581.
  - 7) I. Hashimoto; T. Kawaji; F.D. Badea; T. Sawada; S. Mataka; M. Tashiro; G. Fukata, *Res. Chem. Intermed.*, 1996, **22**, 855.
  - 8) P. Wipf; J.-K. Jung, *J. Org. Chem.*, 2000, **65**, 6319.
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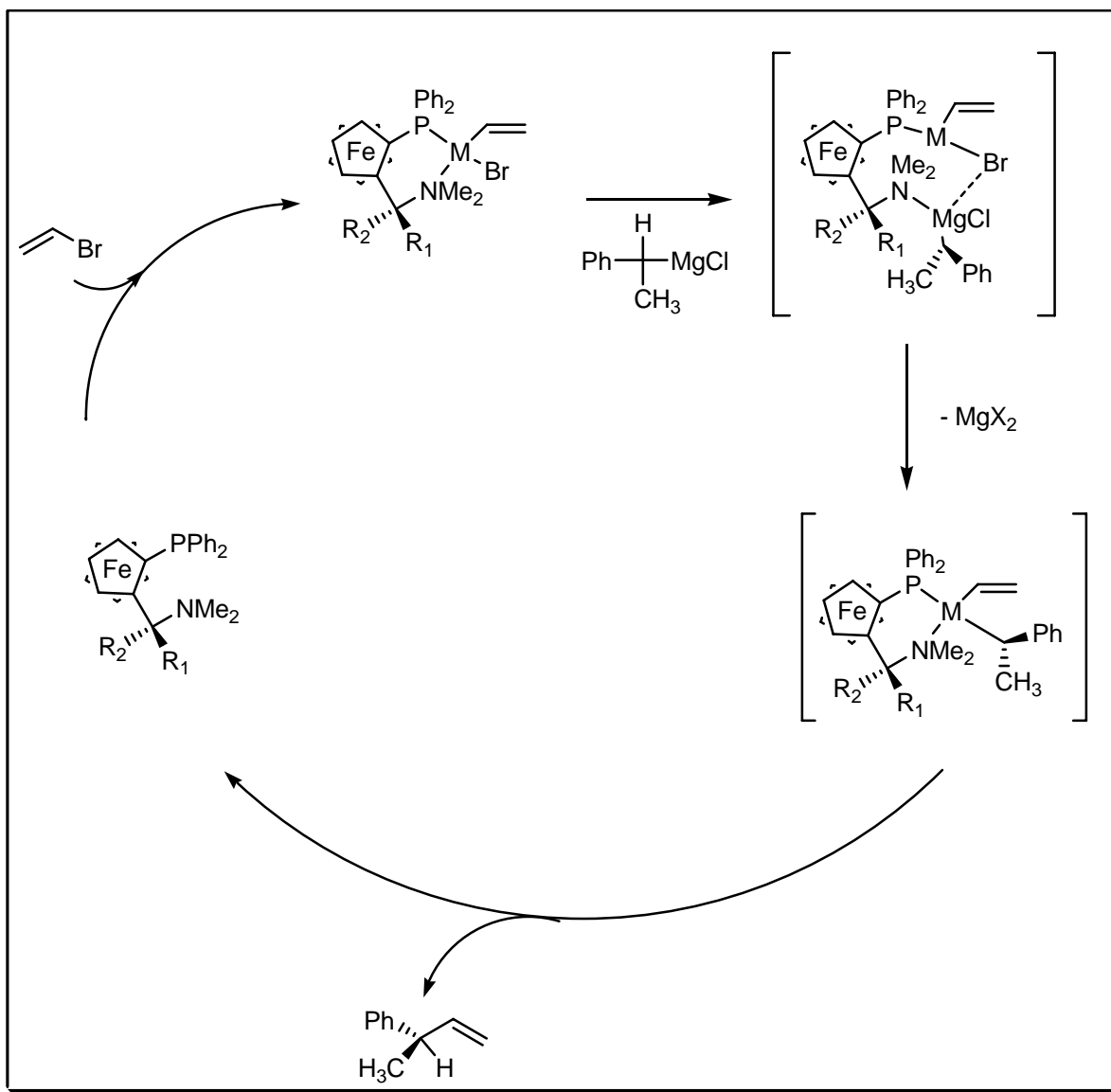
## COMMENTS :

## HAYASHI – ITO REACTION

### EXAMPLE :

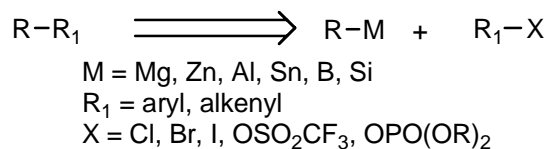


### MECHANISM :





## DISCONNECTION :



## NOTES :

The asymmetric carbon-carbon coupling of secondary alkyl magnesium and zinc reagents with aryl and alkenyl halide in the presence of nickel or palladium catalyst co-ordinated with a chiral phosphine ligand give optically active cross-coupling products. See also **Kumada – Tamao – Corriu** cross coupling.

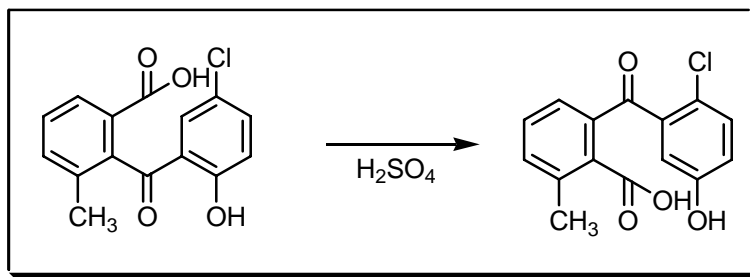
## REFERENCES :

- 1) C. Consiglio; C. Botteghi, *Helv. Chim. Acta*, 1973, **56**, 460.
- 2) T. Hayashi; M. Tajika; K. Tamao; M. Kumada, *J. Am. Chem. Soc.*, 1976, **98**, 3718.
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- 4) T. Hayashi; K. Hayashizaki; Y. Ito, *Tetrahedron Lett.*, 1989, **30**, 215.
- 5) M. Uemura; H. Nishimura; T. Hayashi, *J. Organomet. Chem.*, 1994, **473**, 129.
- 6) T. Kamikawa; Y. Uozumi; T. Hayashi, *Tetrahedron Lett.*, 1996, **37**, 3161.
- 7) T. Hayashi, *J. Organomet. Chem.*, 2002, **653**, 41.

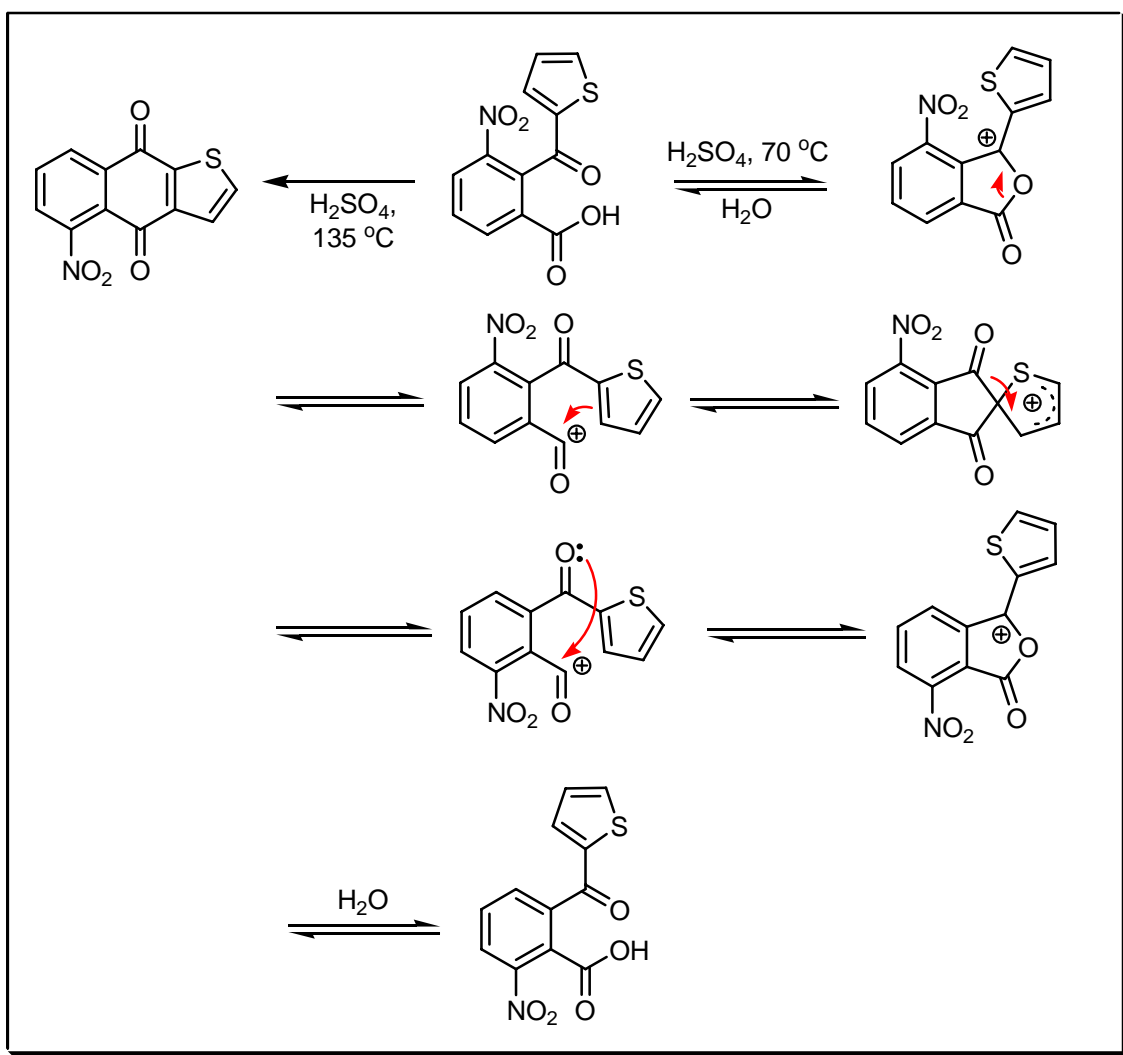
## COMMENTS :

## HAYASHI REARRANGEMENT

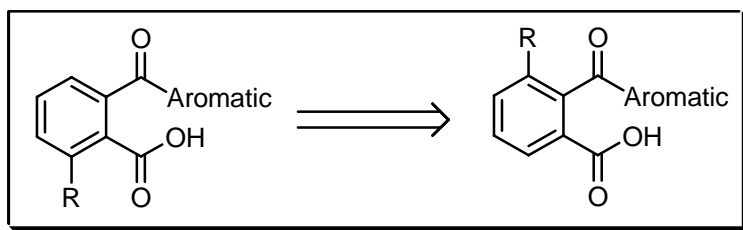
### EXAMPLE :



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

Certain substituted *o*-aromatic benzoic acids rearrange *via* a spirocyclic carbenium intermediate in concentrated sulfuric acid or phosphorous pentoxide to yield isomeric acids. See also **Beckmann** rearrangement, **Freudenberg – Schönberg**, **Newman – Karnes – Kwart** and **Smiles** reactions.

## REFERENCES :

**Houben – Weyl : E6a, 487**

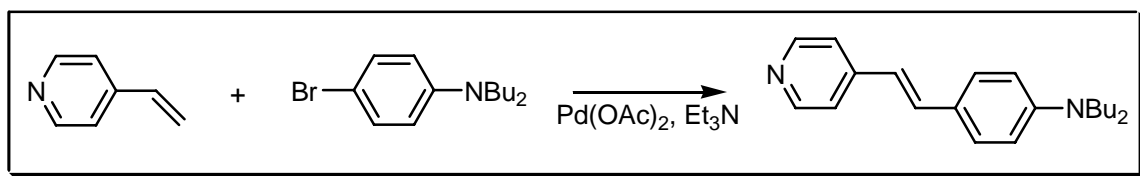
- 1) M. Hayashi, *J. Chem. Soc.*, 1927, 2516.
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  - 3) M.S. Newman; K.G. Ihrman, *J. Am. Chem. Soc.*, 1958, **80**, 3652.
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  - 5) M. Cushman; T.-C. Choong; J.T. Valko; M.P. Koleček, *J. Org. Chem.*, 1980, **45**, 5067.
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**COMMENTS :**

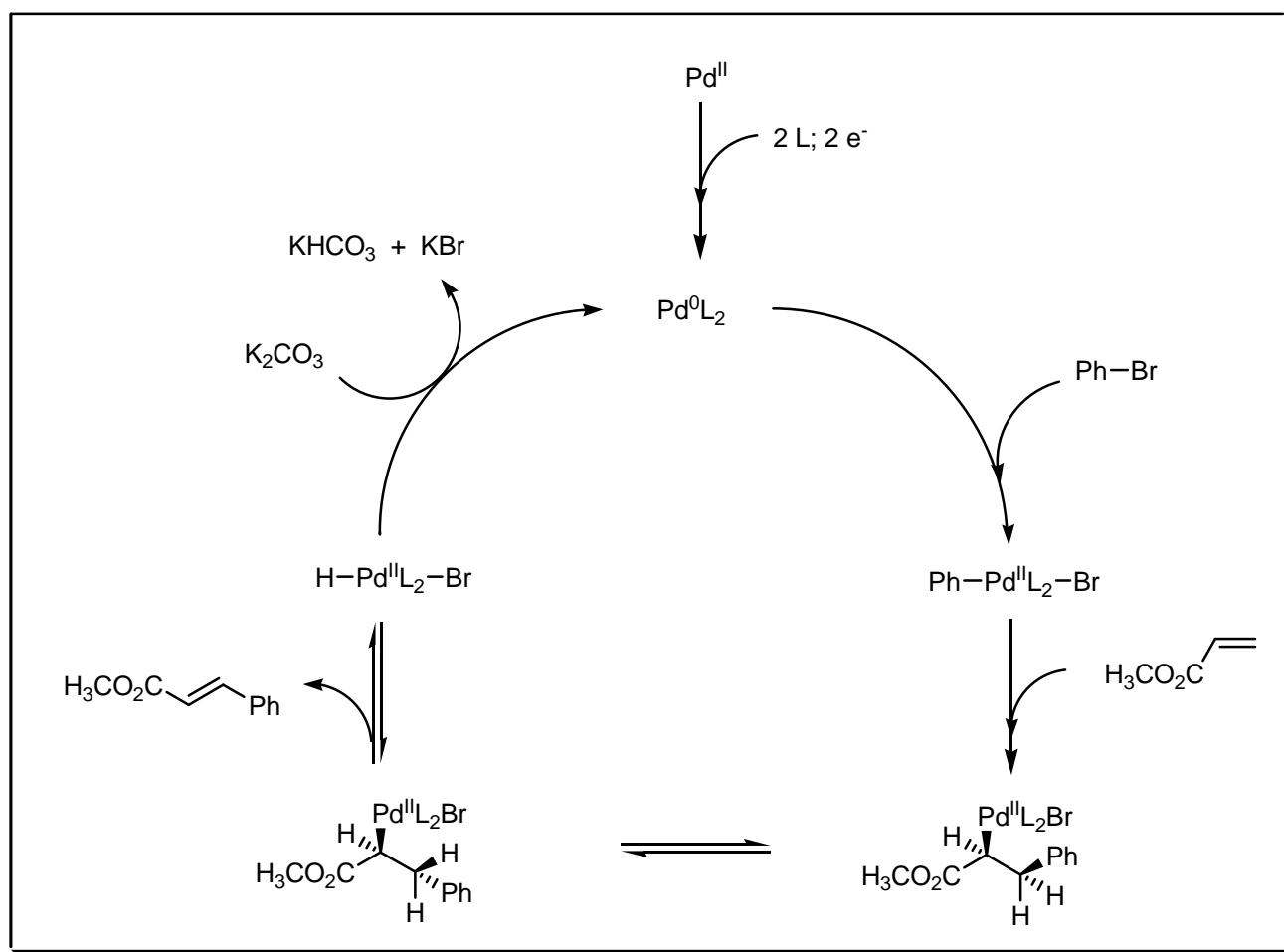
## HECK – FUJIWARA – MIZOROKI COUPLING

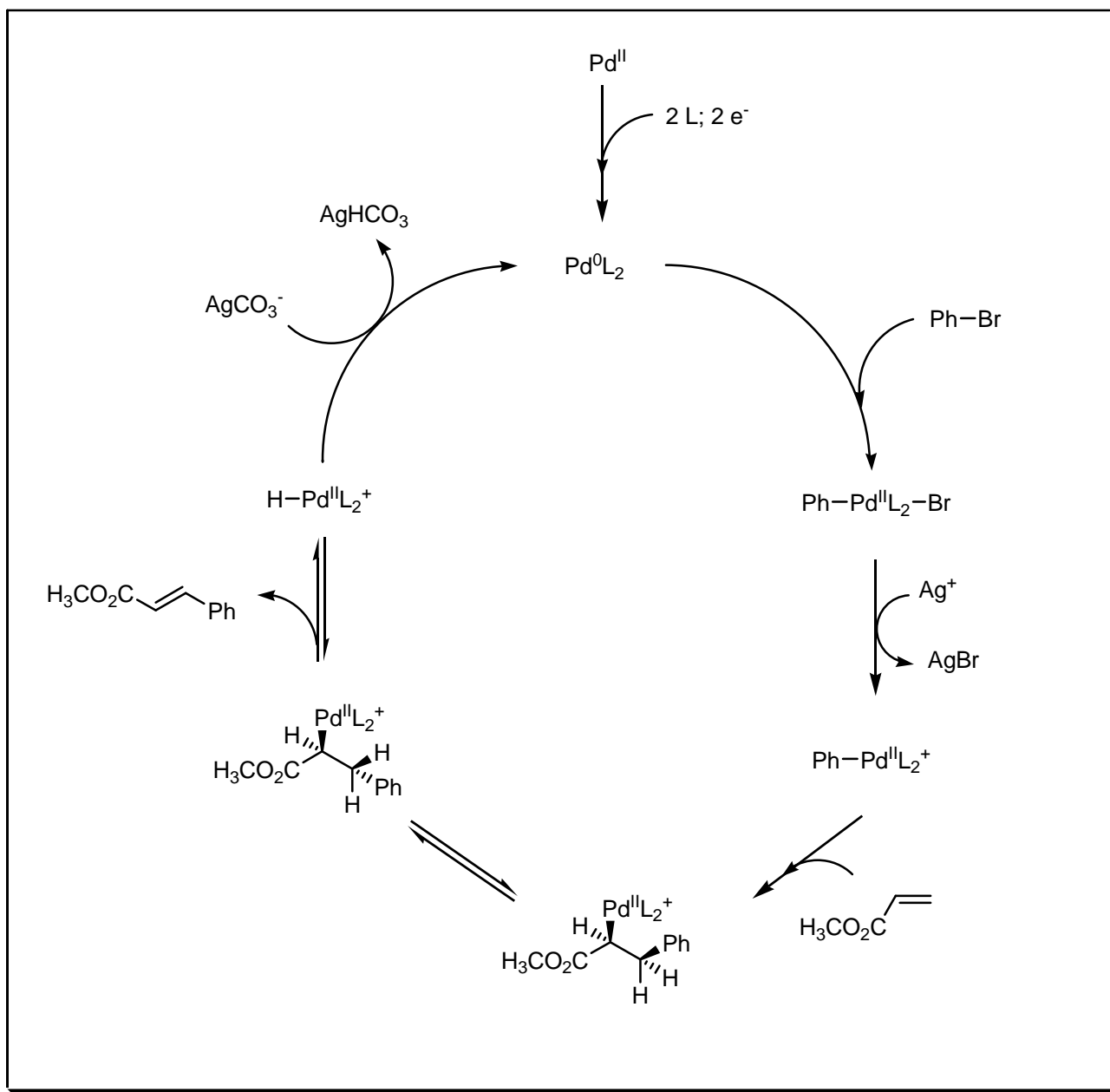
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**EXAMPLE :**

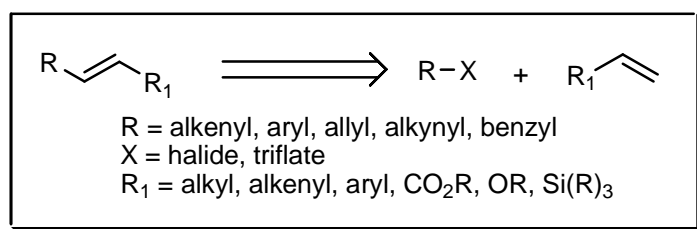


**MECHANISM :**





#### DISCONNECTION :



#### NOTES :

The oxidative cross-coupling reactions of aromatic or vinylic halides or tosylates lacking  $\text{sp}^3$ - $\beta$ -hydrogens and olefins catalysed by palladium. The catalytic cycle starts with palladium(0), which undergoes oxidative addition, *syn*-carbopalladation, internal rotation, *syn*- $\beta$ -H-elimination and finally reductive elimination. Excess silver(I) salts can be used to abstract the halide ion to produce a reactive cationic palladium species. There is a different mechanism for cationic palladium species. The first **asymmetric** version was reported by **Shibasaki** in 1989. The **Matsuda** variant is

used by Novartis to synthesis Prosulfuron<sup>tm</sup>, a highly active herbicide. See also **Grigg, Stille – Kelly, Stille** coupling and **Suzuki** reactions.

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## REFERENCES :

**March** : 717

**Smith – March** : 930

**Smith** : 1363

**Smith 2<sup>nd</sup>** : 1119, 1184

**Houben – Weyl** : **E6a**, 125; **E6b**, 138, 574; **E7b**, 613

**Org. React.** : **27**, 345

**Org. Synth.** : **61**, 82

**Org. Synth. Coll. Vol.** : **7**, 361

**Science of Synthesis** : **1**, 141; **9**, 265, 357, 388; **10**, 50, 101, 166, 400, 417, 420, 463, 467, 570, 573

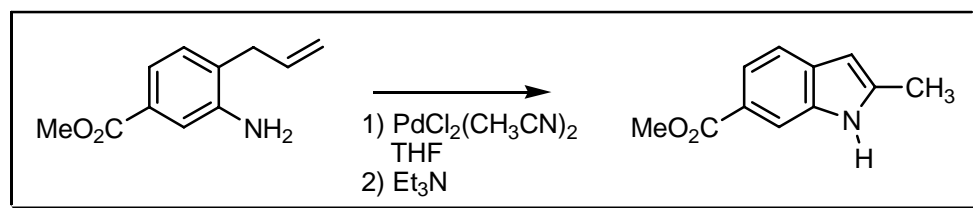
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  - 4) R.F. Heck; J.P. Nolley, jr., *J. Org. Chem.*, 1972, **37**, 2320.
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  - 6) N.A. Cortese; C.B. Ziegler; B.J. Hrncic; R.F. Heck, *J. Org. Chem.*, 1978, **43**, 2952.
  - 7) Y. Sato; M. Sodeoka; M. Shibasaki, *J. Org. Chem.*, 1989, **54**, 4738.
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  - 9) V. Farina; S. Kapadia; B. Krishnan; C. Wang; L.S. Liebeskind, *J. Org. Chem.*, 1994, **59**, 5905.
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  - 11) K. Hirabayashi; J. Ando; J. Kawashima; Y. Nishihara; A. Mori; T. Hiyama, *Bull. Soc. Chem. Jpn.*, 2000, **73**, 1409.
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  - 16) R. Imbos; A.J. Minnaard; B.L. Feringa, *J. Am. Chem. Soc.*, 2002, **124**, 184.
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  - 21) K. Hirabayashi; Y. Nara; T. Shimizu; N. Kamigata, *Chem. Lett.*, 2004, **33**, 1280.
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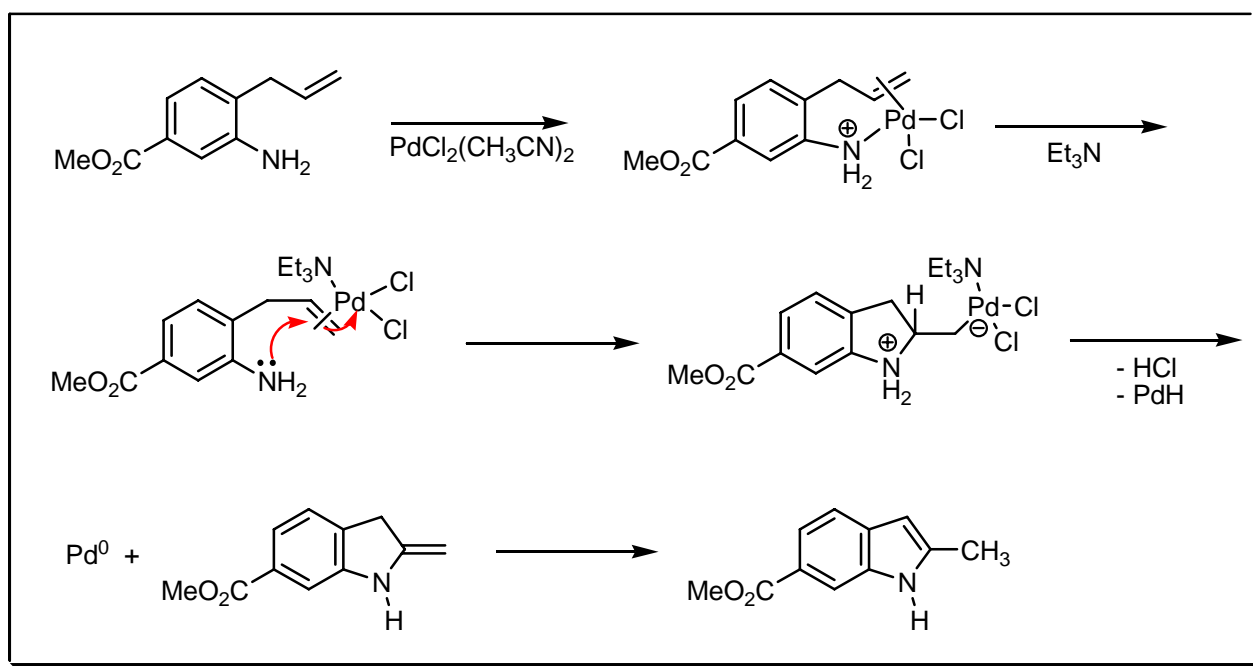
COMMENTS :

## HEGEDUS INDOLE SYNTHESIS

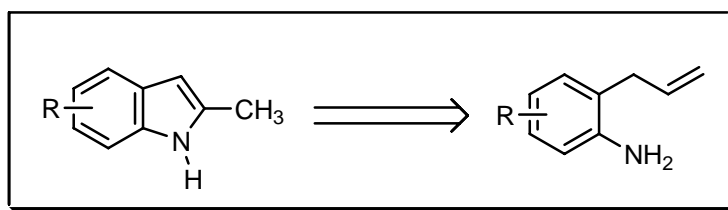
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

The indole ring is established *via* a palladium-catalysed amination (a **Tsuji – Wacker** type reaction). The reaction is sometimes called **Hegedus – Mori – Heck** indole synthesis. A ruthenium variant has also been published. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Nenitzescu** indole, **Piloty – Robinson**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe**, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

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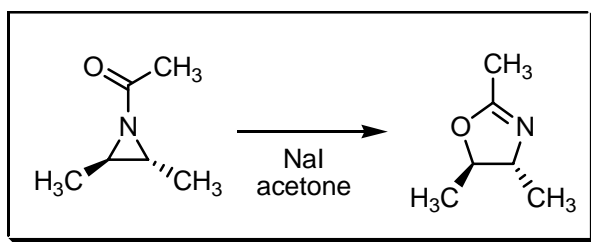
## REFERENCES :

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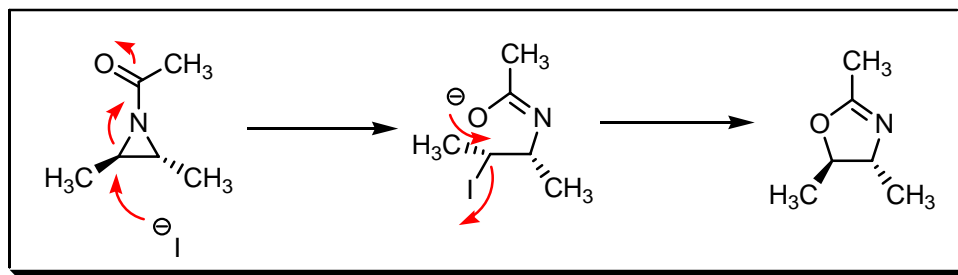
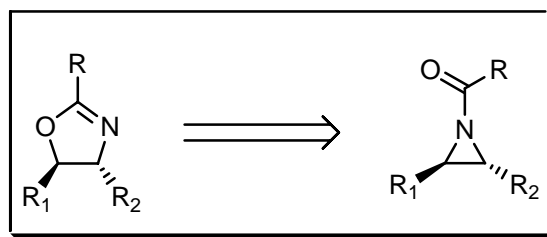
## COMMENTS :

## HEINE REACTION

### EXAMPLE :



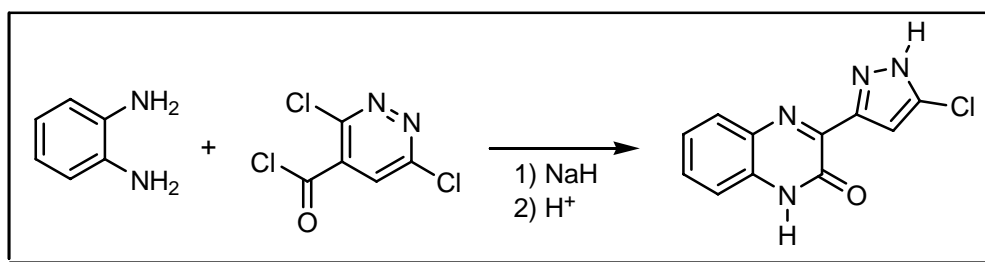


**MECHANISM :****DISCONNECTION :****NOTES :**

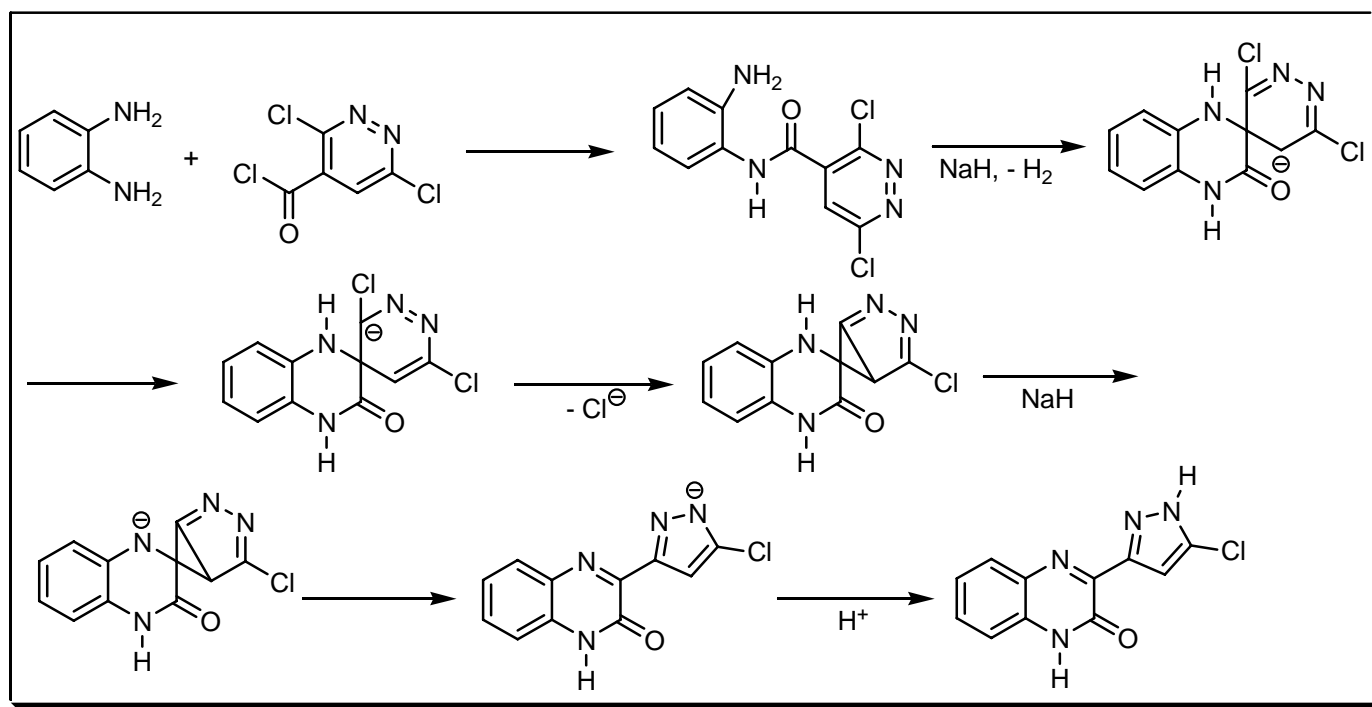
The ringexpansion of substituted *N*-acylaziridines by nucleophilic reagents to afford the corresponding oxazoline.

**REFERENCES :**

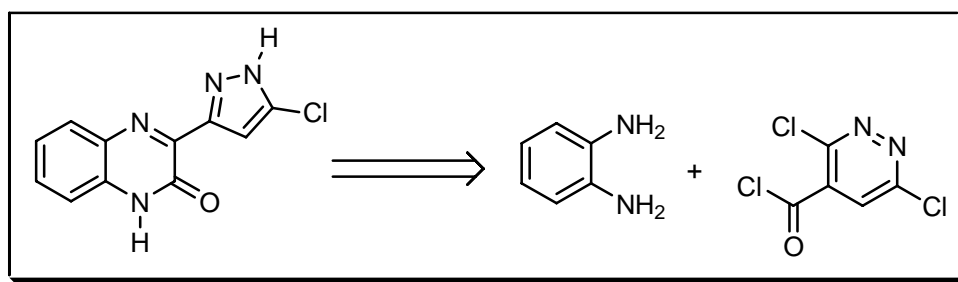
- 1) H.W. Heine; M.E. Fetter; E.M. Nicholson, *J. Am. Chem. Soc.*, 1959, **81**, 2202.
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**COMMENTS :****HEINISCH – MATUSZCZAZOV – MERETEIRA REACTION****EXAMPLE :**

## MECHANISM :



## DISCONNECTION :



## NOTES :

This is a very interesting synthesis of 1,2-dihydro-quinoxaline-2-ones derived from *ortho*-aminoanilide and 3,6-dichloropyridazine-4-acid chloride. The authors proposed the reaction mechanism shown but some of the intermediate structures do not appear to be probable.

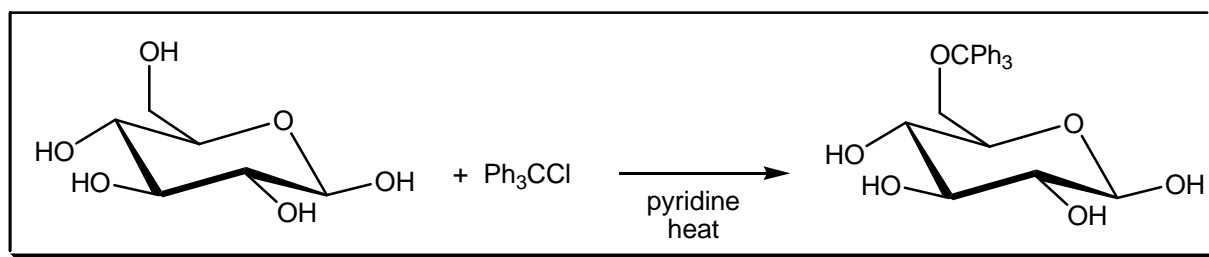
## REFERENCES :

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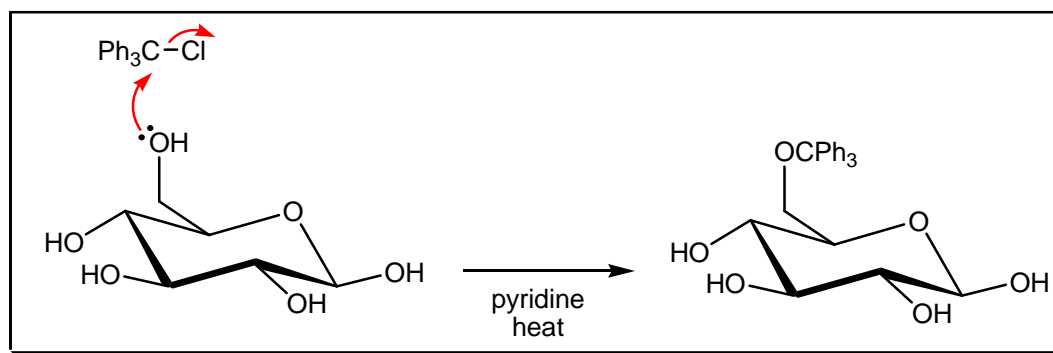
## COMMENTS :

# HELFERICH ETHERIFICATION

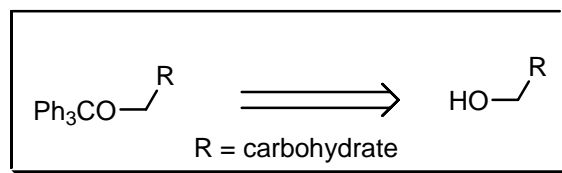
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Triphenylmethyl ethers of polyhydric alcohols and sugars are obtained by the use of triphenylmethyl chloride in pyridine. In this way the primary alcoholic group is preferentially etherified. It is generally used as a protecting group for alcohols.

## REFERENCES :

Org. Synth. : **22**, 56

Org. Synth. Coll. Vol. : **3**, 432

- 1) B. Helferich; L. Moog; A. Jünger, *Ber. Dtsch. Chem. Ges.*, 1925, **58**, 872.
- 2) B. Helferich; W. Klein, *Liebigs Ann. Chem.*, 1926, **450**, 219.
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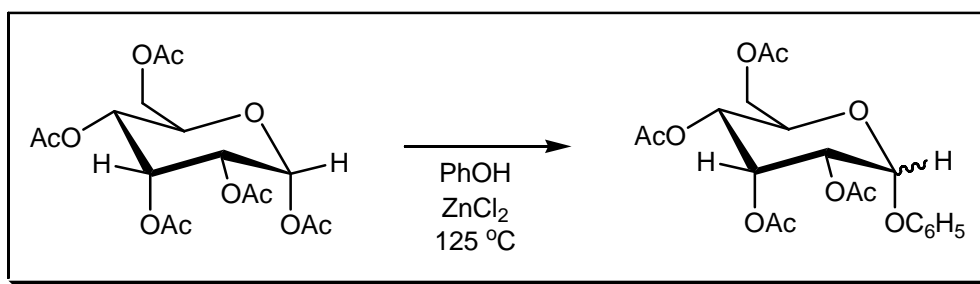
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**COMMENTS :**

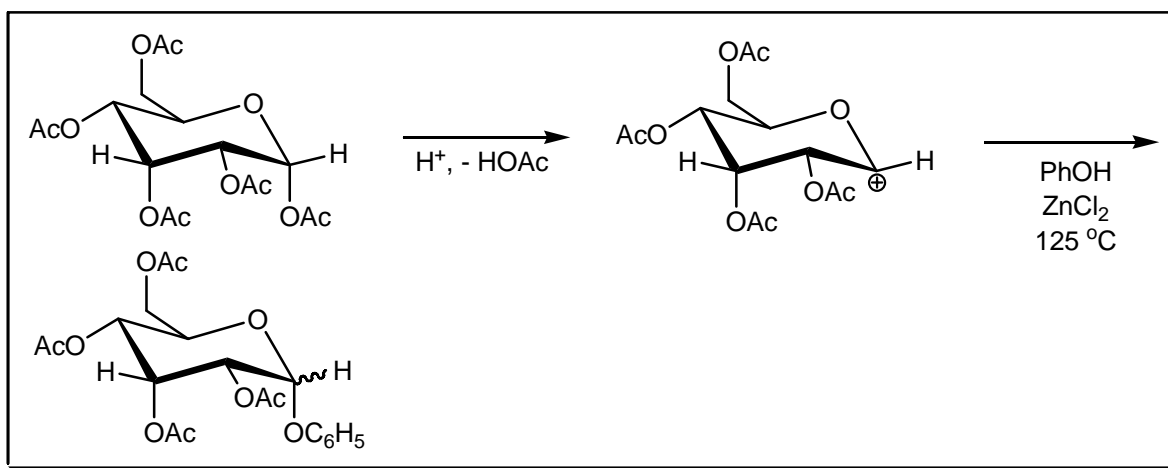
**HELFERICH METHOD**

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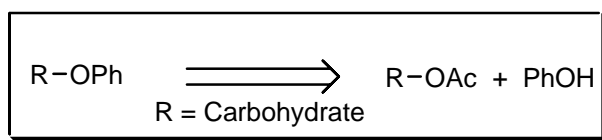
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

$\alpha$ - and  $\beta$ -Phenyl glycosides are prepared by heating acetates of reducing sugars with a phenol in the presence of acid or Lewis acid catalysts. The acetate group at C-1 is less strongly bound to the carbon atom than the other acetate groups. Normally only the  $\alpha$ -phenyl glycosides are formed.

## REFERENCES :

Org. Synth. : 6, 64

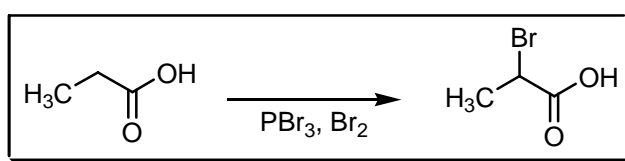
Org. Synth. Coll. Vol. : 1, 364

- 1) B. Helferich; E. Schmitz-Hillebrecht, *Ber. Dtsch. Chem. Ges.*, 1933, **66**, 378.
- 2) R.T. Williams, *J. Chem. Soc.*, 1940, 1402.
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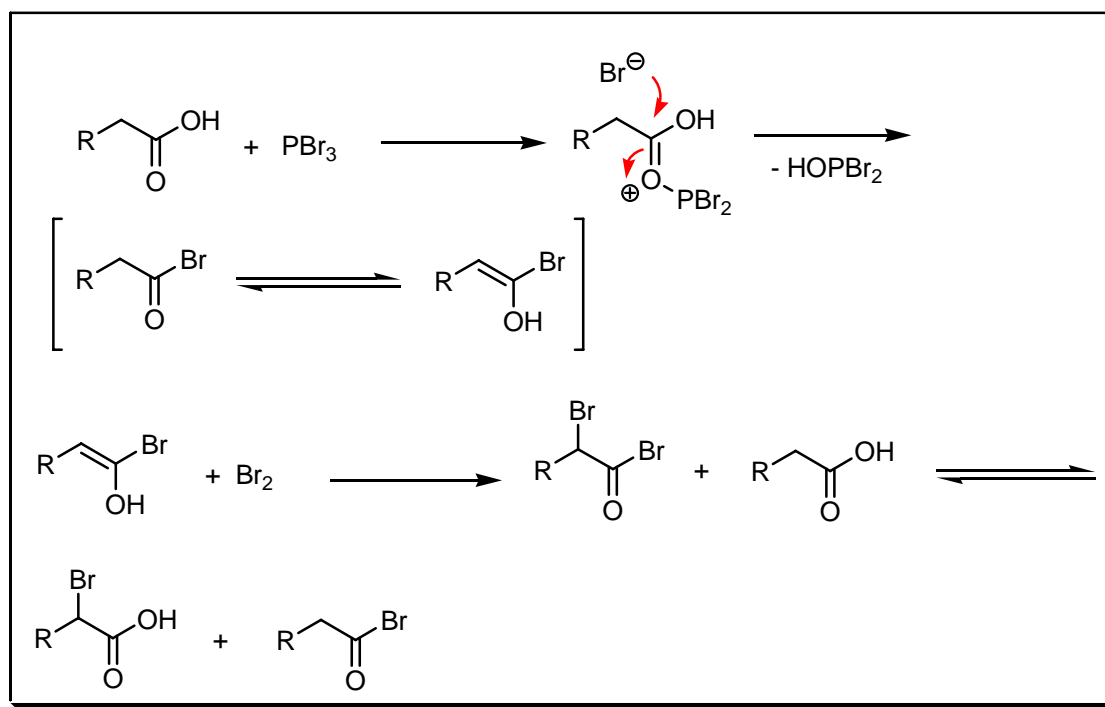
## COMMENTS :

## HELL – VOLLHARD – ZELINSKY HALOGENATION

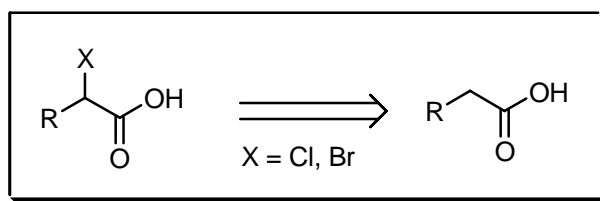
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

This reaction relates to the preparation of an  $\alpha$ -halo substituted acid or ester by the action of the halogen on the acid in the presence of phosphorous or a phosphorous halide, followed by hydrolysis or alcoholysis of the resulting haloacyl halide. Only catalytic amounts of  $PBr_3$  are required for this reaction. The reaction does not work with F or I. For  $\alpha$ -iodination see **Ogata *et al.*** See also **Bedoukian** reaction.

## REFERENCES :

**March** : 590

**Smith – March** : 777

**Smith** : 155

**Smith 2<sup>nd</sup>** : 125

**Houben – Weyl** : **E5**, 220, 465

**Org. Synth.** : **20**, 106; **21**, 74; **33**, 29; **55**, 27

**Org. Synth. Coll. Vol.** : **3**, 523, 848; **4**, 348; **6**, 190

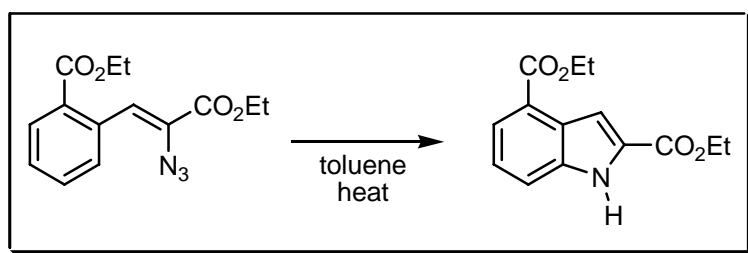
1) C. Hell, *Ber. Dtsch. Chem. Ges.*, 1881, **14**, 891.

- 2) J. Vollhard, *Liebigs Ann. Chem.*, 1887, **242**, 141.
- 3) N. Zelinsky, *Ber. Dtsch. Chem. Ges.*, 1887, **20**, 2026.
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- 5) H.J. Harwood, *Chem. Rev.*, 1962, **62**, 99.
- 6) Y. Ogata; S. Watanabe, *J. Org. Chem.*, 1980, **45**, 2831.
- 7) H.J. Liu; W.D. Luo, *Synth. Commun.*, 1991, **21**, 2097.
- 8) D.E. Stack; A.L. Hill; C.B. Differdaffer; N.M. Burns, *Org. Lett.*, 2002, **4**, 4487.

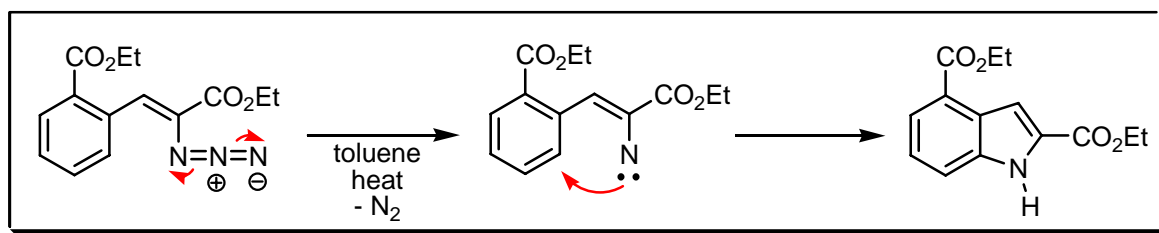
**COMMENTS :**

## HEMETSBERGER – KNITTEL INDOLE SYNTHESIS

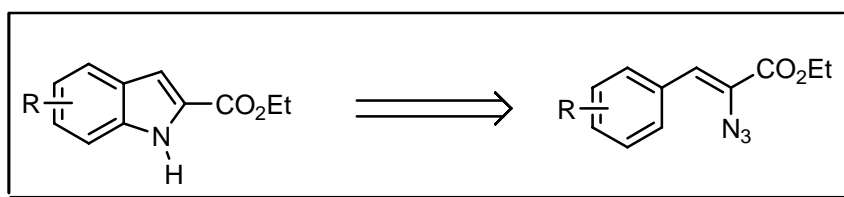
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

Indoles are obtained by heating araldehydes and  $\alpha$ -azidoacetate. The mechanism is not fully known, but the reaction proceeds most probably *via* the nitrene intermediate. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

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#### REFERENCES :

**Science of Synthesis : 10**, 439

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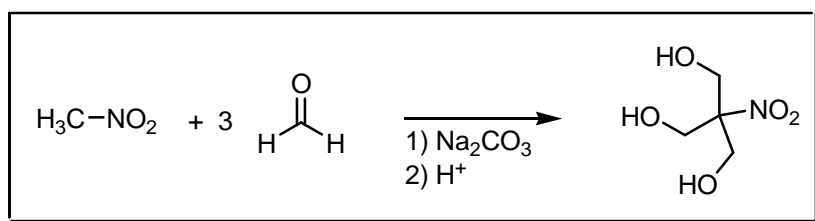
- 1) H. Hemetsberger; D. Knittel; H. Weidman, *Monatsh. Chem.*, 1969, **100**, 1599.
  - 2) D.M.B. Hickey; A.R. MacKenzie; C.J. Moody; C.W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1987, 921.
  - 3) R.E. Bolton; C.J. Moody; M. Pass; C.W. Rees; G. Tojo, *J. Chem. Soc., Perkin Trans. 1*, 1988, 2491.
  - 4) C.J. Moody; A.L. Beck; W.J. Coates, *Tetrahedron Lett.*, 1989, **30**, 4017.
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  - 6) P. Magnus; T.E. Mansley, *Tetrahedron Lett.*, 1999, **40**, 6909.
  - 7) F.A.F. da Rosa; R.A. Rebelo; M.G. Nascimento, *J. Braz. Chem. Soc.*, 2003, **14**, 11.
- 

#### COMMENTS :

### HENRY REACTION (KAMLET REACTION)

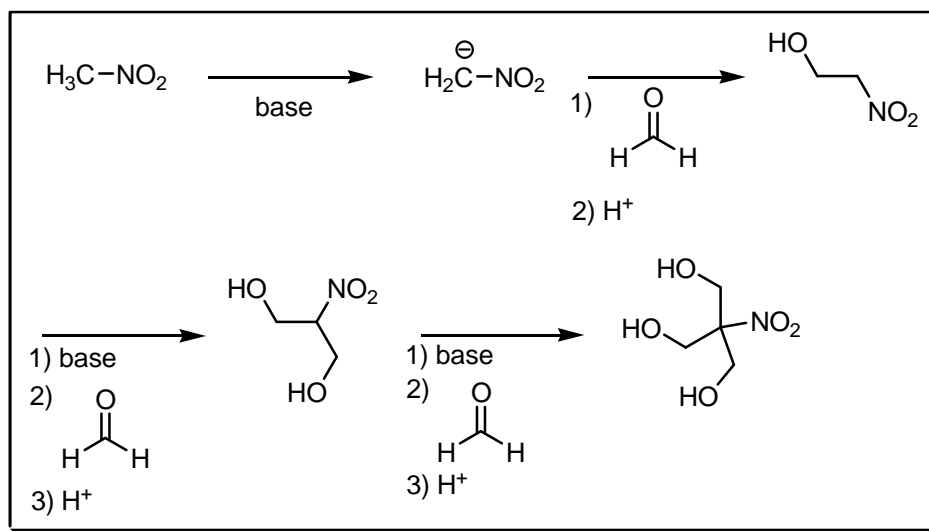
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#### EXAMPLE :

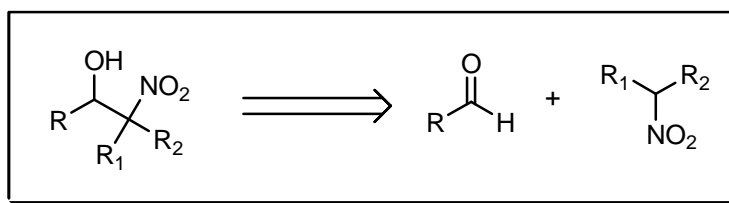




## MECHANISM :



## DISCONNECTION :



## NOTES :

The base-catalysed condensation of primary or secondary nitro alkanes with aldehydes to give nitro-alcohols. There are few examples of catalytic asymmetric **Henry** reactions with chiral heterobimetallic lanthanoid complexes as catalysts. **Kamlet** : These alcohols are formed by condensation of the alkali metal salt of an acid-nitro olefin with the bisulfite addition compound of an aromatic aldehyde in the presence of a trace of alkali or weak acid. See also **Bouveault – Wahl**, **Claisen – Geuther** and **Nef** reactions.

## REFERENCES :

March : 946

Smith : 898

Smith 2<sup>nd</sup> : 751

Houben – Weyl : E14b, 848, 941; E15, 1132

Org. Synth. : 74, 130

Org. Synth. Coll. Vol. : 9, 636

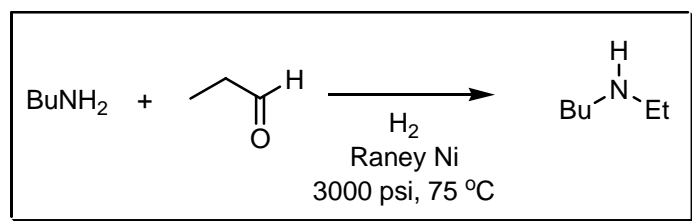
- 1) L. Henry, *C.R. Séances Acad. Sci.*, 1895, **120**, 1265.
- 2) J. Kamlet, *U.S. Patent*, 1939, 2151517.
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- 6) C. Christensen; K. Juhl; K.A. Jørgensen, *Chem. Commun.*, 2001, 2222.
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- 8) B. Westermann, *Angew. Chem., Int. Ed.*, 2003, **42**, 151.
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- 10) T. Risgaard; K.V. Gothelf; K.A. Jørgensen, *Org. Biomol. Chem.*, 2003, **1**, 153.
- 11) Y. Kogami; T. Nakajima; T. Ashizawa; S. Kezuka; T. Ikeno; T. Yamada, *Chem. Lett.*, 2004, **33**, 614.
- 12) Y.-W. Zhong; P. Tian; G.-Q. Lin, *Tetrahedron: Asymmetry*, 2004, **15**, 771.
- 13) J.C. Borah; S. Gogoi; J. Boruwa; B. Kilita; N.C. Barua, *Tetrahedron Lett.*, 2004, **45**, 3689.

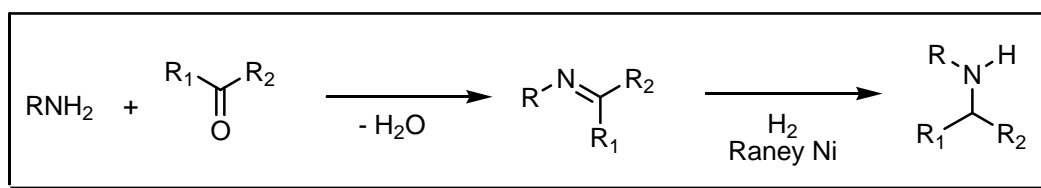
**COMMENTS :**

## HENZE – HUMPHREYS AMINE SYNTHESIS

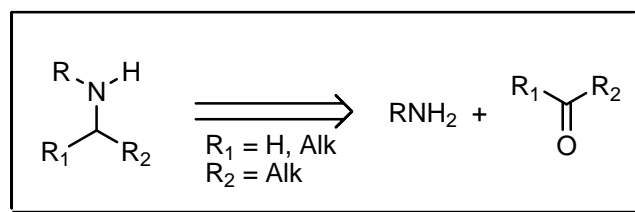
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



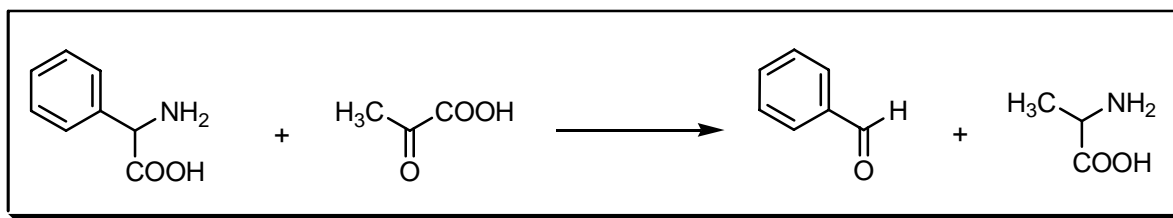
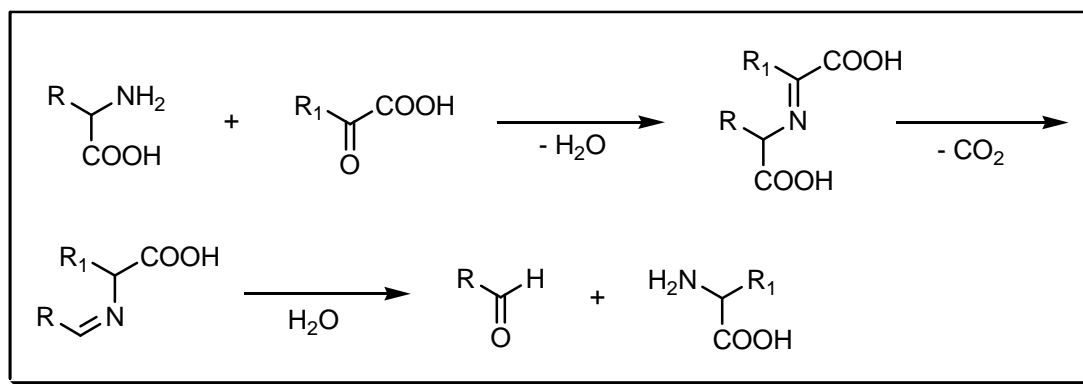
**NOTES :**

Secondary amines are obtained by the high pressure hydrogenation of aldimines or ketimines. See also **Eschweiler – Clarke**, **Forster – Decker** and **Harlay** reactions.

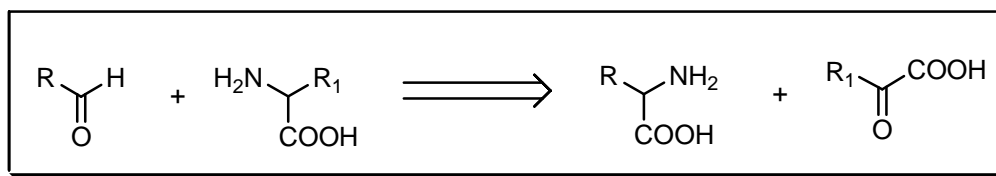
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- 

**COMMENTS :****HERBST – ENGEL AMINO ACID SYNTHESIS****EXAMPLE :****MECHANISM :**

## DISCONNECTION :



## NOTES :

The formation of amino acids from  $\alpha$ -amino acids and  $\alpha$ -ketocarboxylic acid by transfer of R-group. See also **Knoop – Oosterlin** reaction and **Strecker** amino acid synthesis.

## REFERENCES :

**Houben – Weyl** : 11/2, 325

1) R.M. Herbst; L.L. Engel, *J. Biol. Chem.*, 1934, **107**, 505.

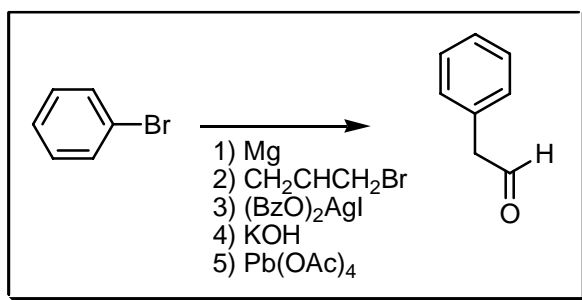
2) R.M. Herbst, *J. Am. Chem. Soc.*, 1936, **58**, 2239.

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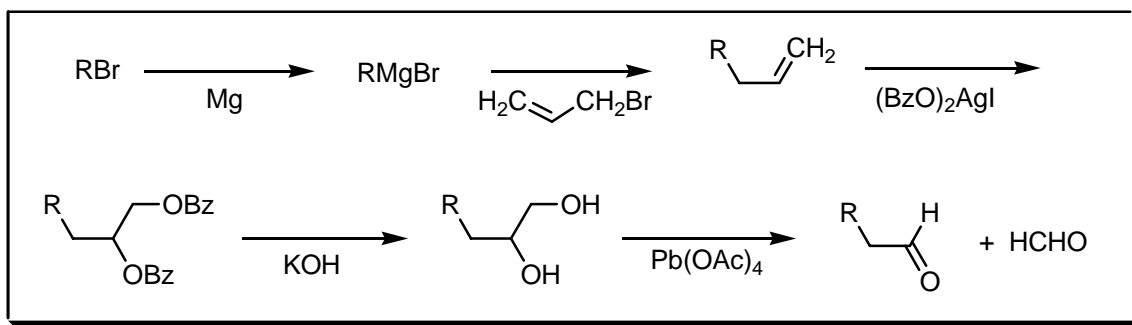
## COMMENTS :

## HERSHBERG SYNTHESIS

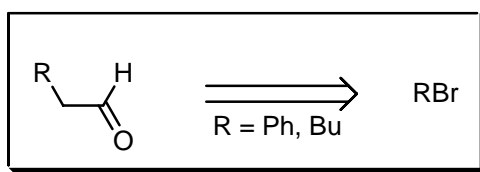
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The olefin obtained by the action of a **Grignard** reagent on an allyl halide is converted into an  $\alpha$ -glycol through the benzoate (**Prévost**). The glycol is oxidised with lead tetraacetate (**Criegee**) to the aldehyde. See also **Grundmann** and **Prévost** reactions.

### REFERENCES :

Houben – Weyl : 7/1, 106, 353

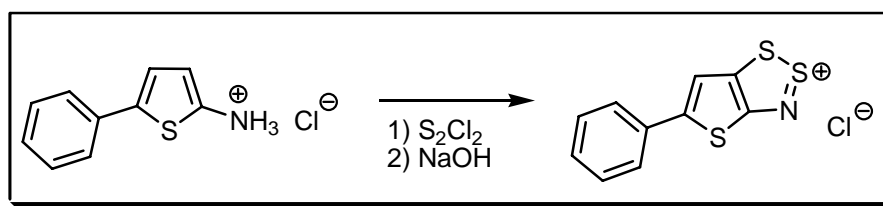
Org. React. : 8, 218

E.B. Hershberg, *Helv. Chim. Acta*, 1934, **17**, 351.

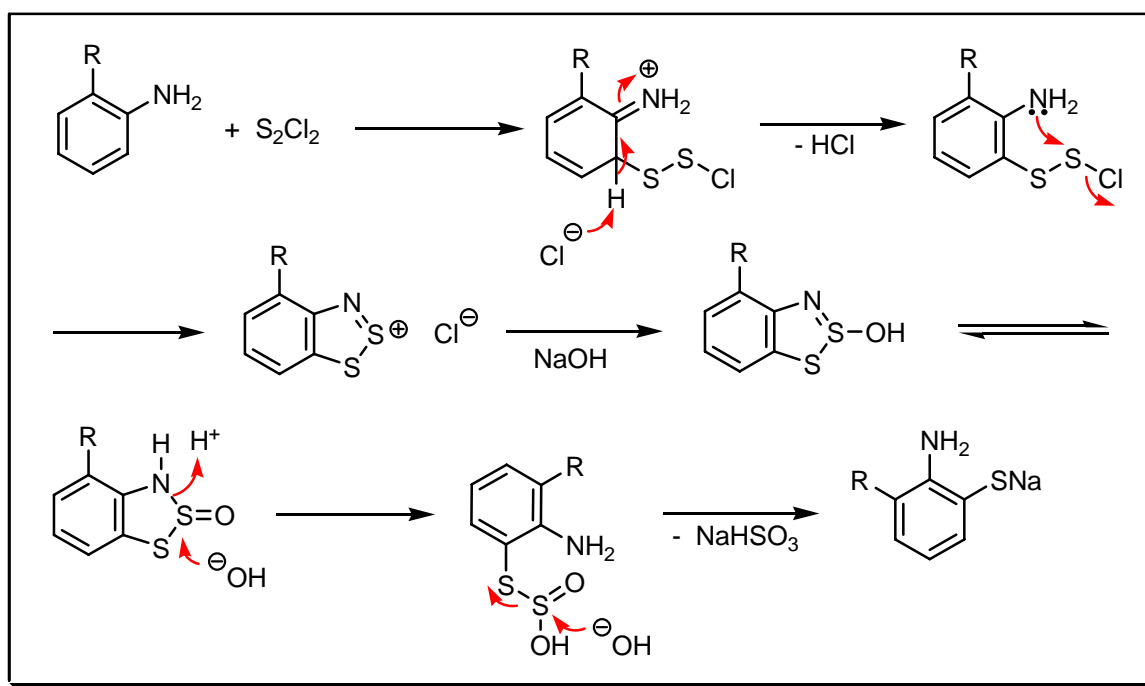
### COMMENTS :

## HERZ REACTION

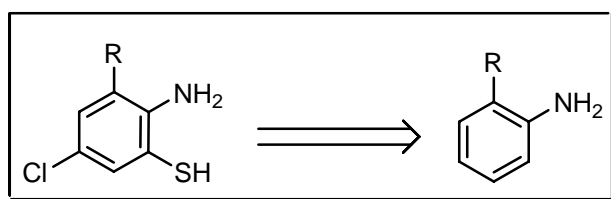
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Benzo-1,3-thiaza-2-thionium chlorides (**Herz** compounds) are formed from primary aromatic amines unsubstituted in the *ortho*-position to the amino group, or their salts and sulfur monochloride ( $S_2Cl_2$ ). These thionium salts can be converted into *o*-aminothiophenols by treatment with alkali. Other aromatic heterocycles can also be used.

### REFERENCES :

March : 530

Smith – March : 704

Houben – Weyl : 9, 40; E8d, 3; E11, 46

Org. Synth. : 22, 16

Org. Synth. Coll. Vol. : 3, 76

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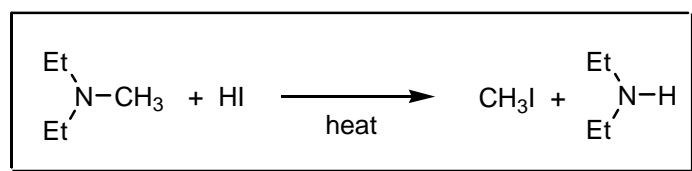
- 1) R. Herz, *U.S. Patent*, 1928, 1637023.
  - 2) W.K. Warburton, *Chem. Rev.*, 1957, **57**, 1011.
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COMMENTS :

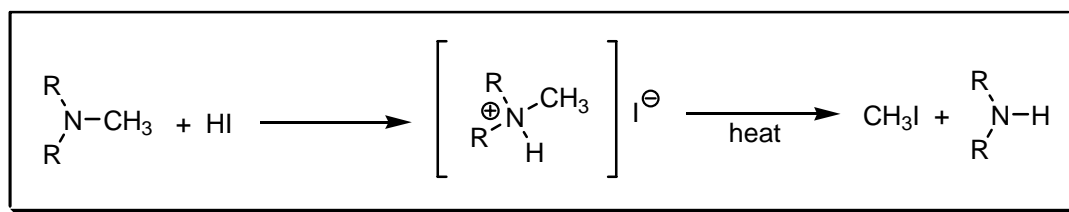
## HERZIG – MEYER N-ALKYL GROUP DETERMINATION

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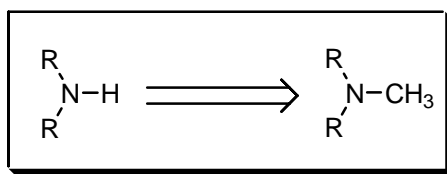
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

Compounds containing *N*-alkyl groups, when treated with hydrogen iodide form quaternary alkylammonium iodides, which on pyrolysis yield alkyl iodides. The latter may be determined by **Zeisel** determination.

## REFERENCES :

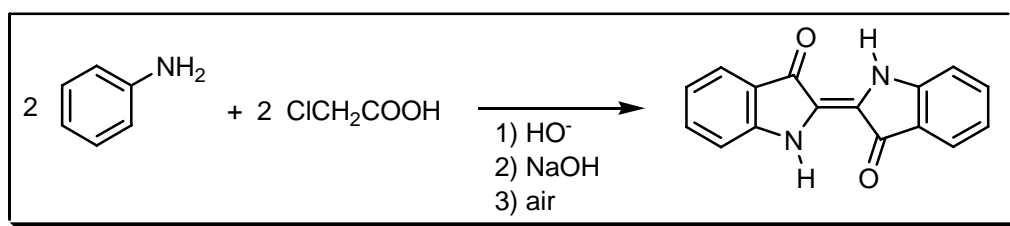
Houben – Weyl : **2**, 667

- 1) J. Herzig; H. Meyer, *Ber. Dtsch. Chem. Ges.*, 1894, **27**, 319.
- 2) J. Herzig; H. Meyer, *Monatsh. Chem.*, 1894, **15**, 613.
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## COMMENTS :

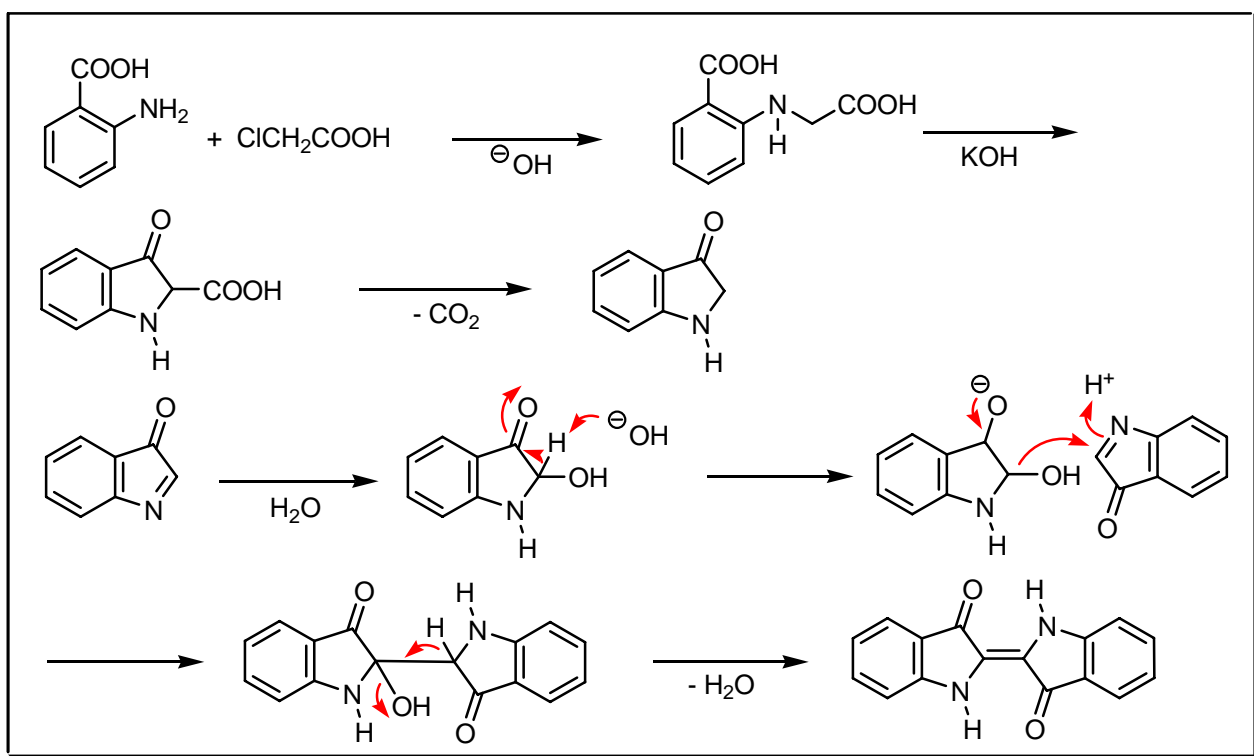
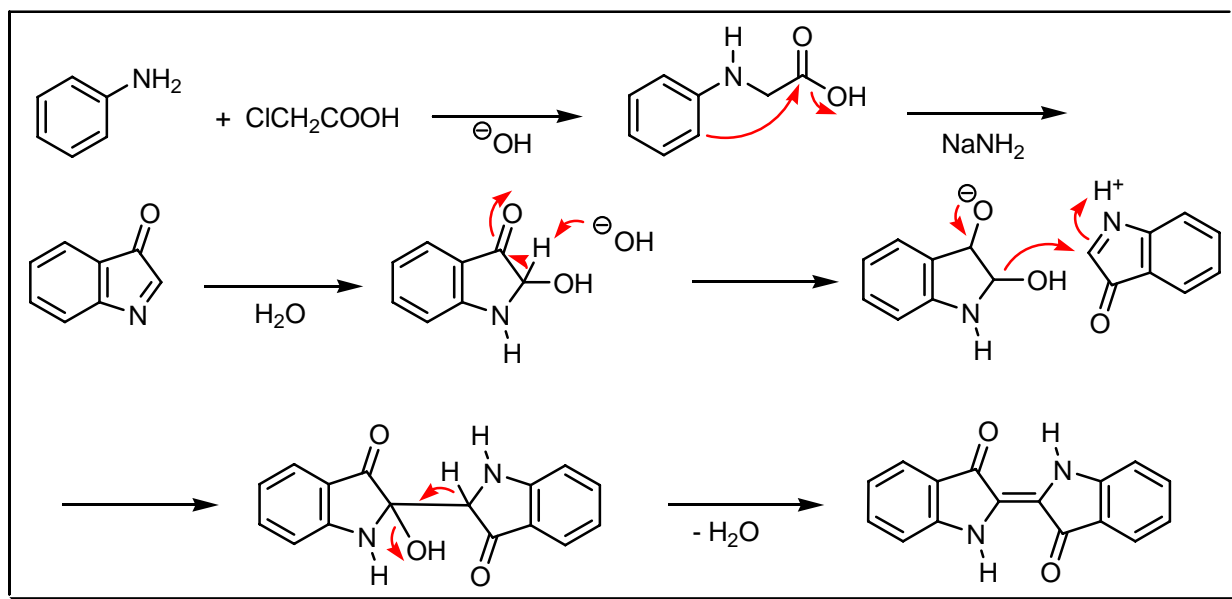
## HEUMANN INDIGO SYNTHESIS

### EXAMPLE :

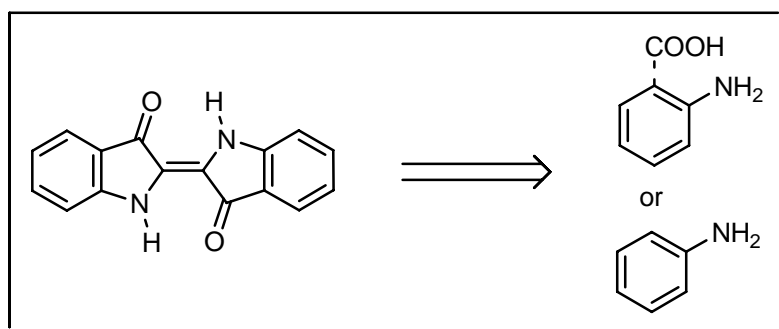




# MECHANISM :



# DISCONNECTION :



## NOTES :

There are two possible pathways for the synthesis of indigo : 1) Phenylglycine on fusion with alkali affords indoxyl which is converted into indigo by atmospheric oxidation. Cyanide moderators may be added. 2) Anthranilic acid is converted into *o*-carboxyphenylglycine, which on fusion with alkali yields indole. This reaction has been used by BASF to produce indigo since 1897. See also **von Baeyer – Drewson** indigo reaction.

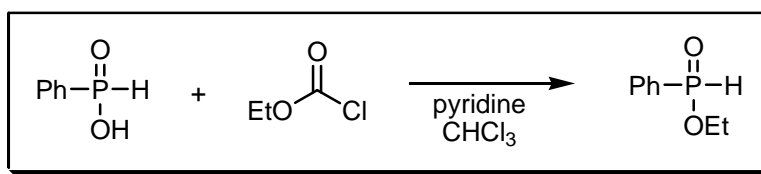
## REFERENCES :

- 1) K. Heumann, *Ber. Dtsch. Chem. Ges.*, 1890, **23**, 3043.
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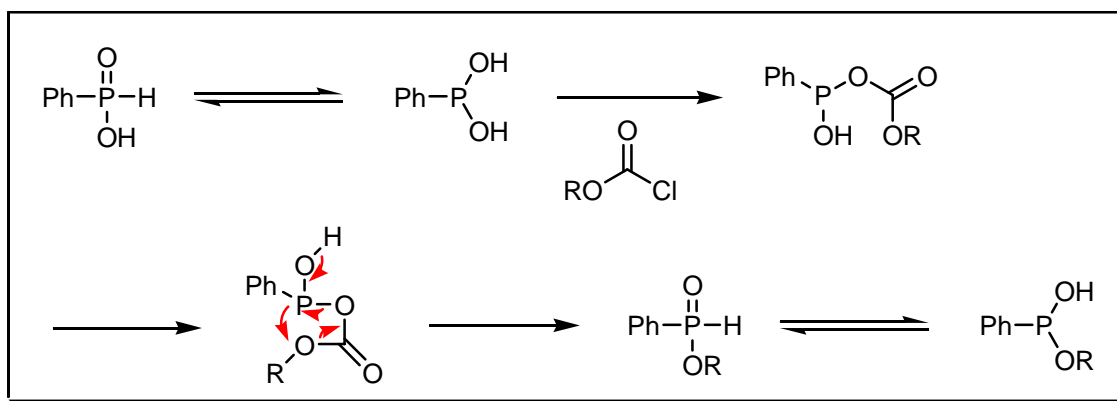
## COMMENTS :

## HEWITT REACTION

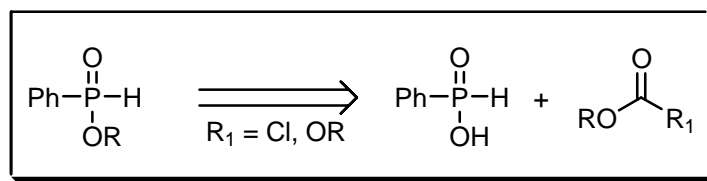
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

This is the transformation of phenylphosphinic acid to its monoalkyl ester in the presence of pyridine and commercial chloroform. A variety of phenylphosphinate esters can be prepared from the corresponding chloroformates in dichloromethane. Chloroform contains ethanol which gives rise to ethyl phenylphosphinate as impurity.

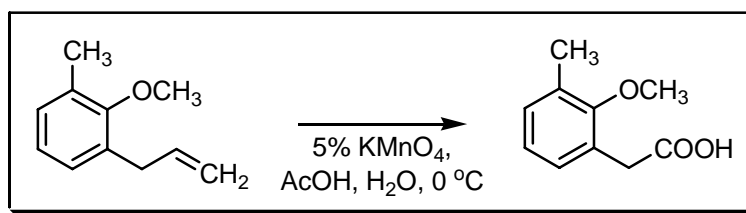
## REFERENCES :

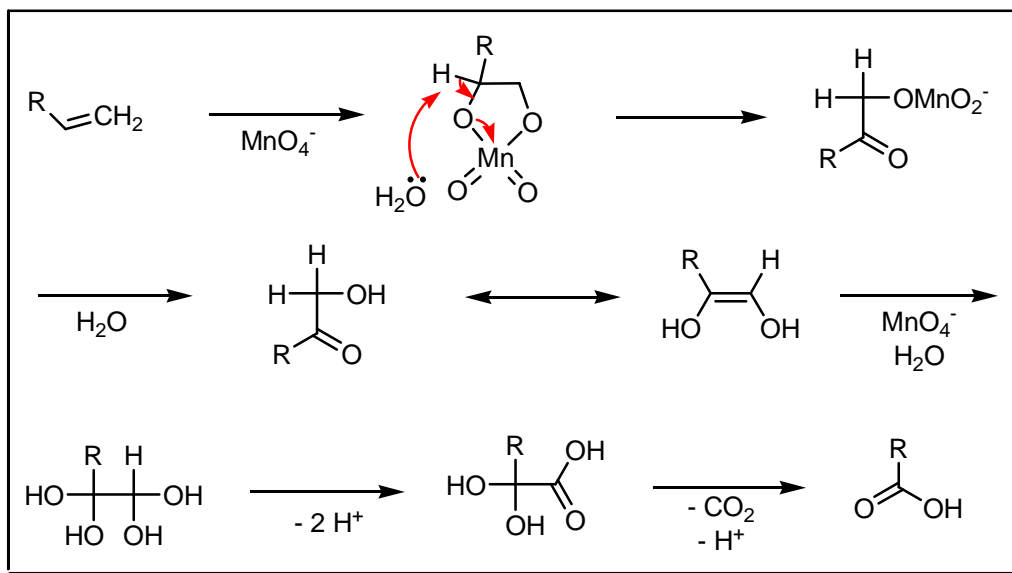
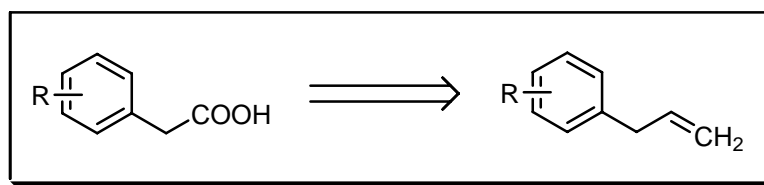
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- 5) K. Afarinkia; H-w. Yu, *Tetrahedron Lett.*, 2003, **44**, 781.

## COMMENTS :

## HILL REDUCTION

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

Substituted phenylacetic acids are obtained by the oxidation of the corresponding allylbenzene by potassium permanganate in the presence of acetic acid. The exact reaction mechanism is not known.

**REFERENCES :**

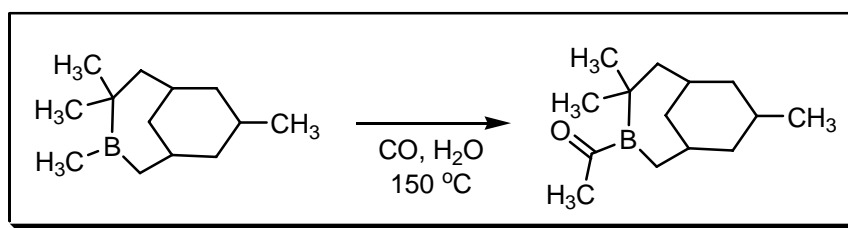
- 1) A. Higginbottom; W.F. Short, *Recl. Trav. Chim. Pays-Bas*, 1934, **53**, 1141.
- 2) P. Hill; W.F. Short, *J. Chem. Soc.*, 1937, 260.
- 3) A. Higginbottom; P. Hill; W.F. Short, *J. Chem. Soc.*, 1937, 263.

**COMMENTS :**

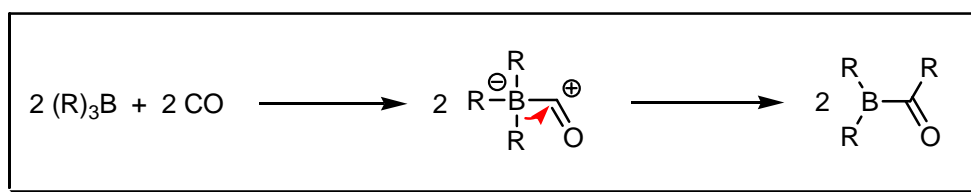
# HILLMAN REACTION

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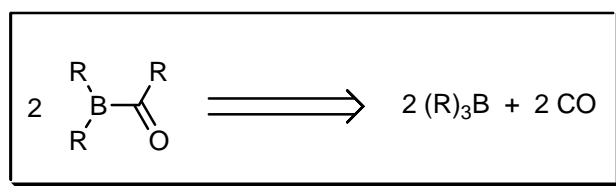
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The carbonylation of organoboranes.

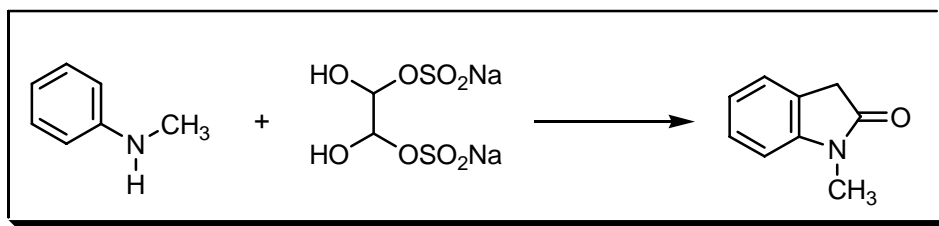
## REFERENCES :

- 1) M.E. Hillman, *J. Am. Chem. Soc.*, 1962, **84**, 4715.
- 2) M.E. Hillman, *J. Am. Chem. Soc.*, 1963, **85**, 982
- 3) L.S. Vasilyev; V.V. Veselovskii; M.I. Struchkova; B.M. Mikhailov, *J. Organomet. Chem.*, 1982, **226**, 115.
- 4) P.J. Persichini III, *Curr. Org. Chem.*, 2003, **7**, 1725.

## COMMENTS :

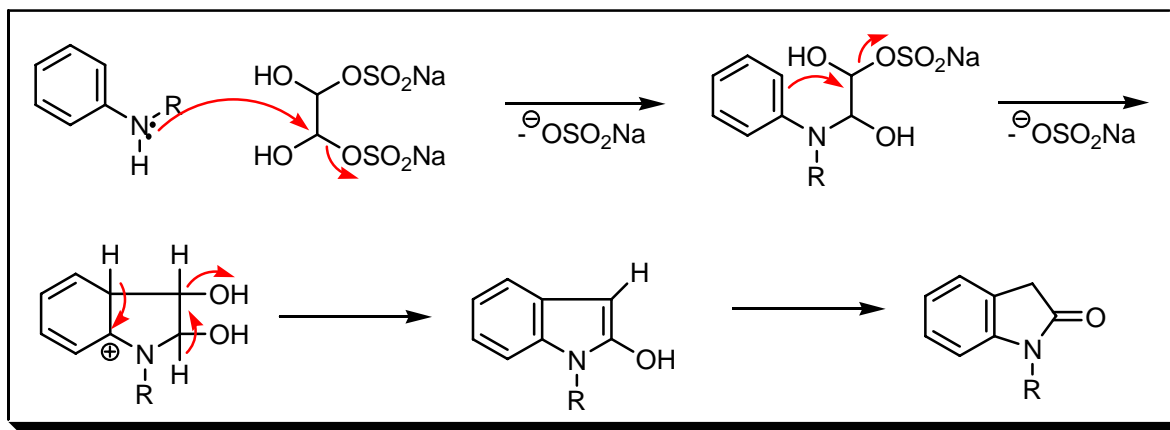
## HINSBERG OXINDOLE SYNTHESIS

EXAMPLE :

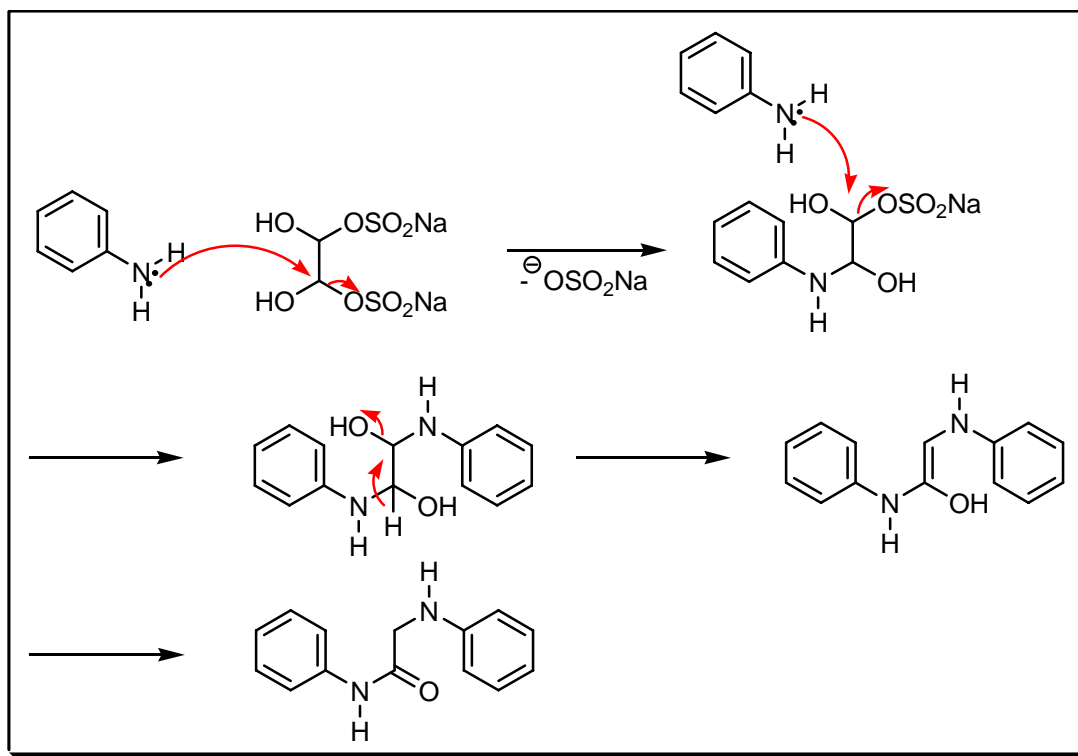


MECHANISM :

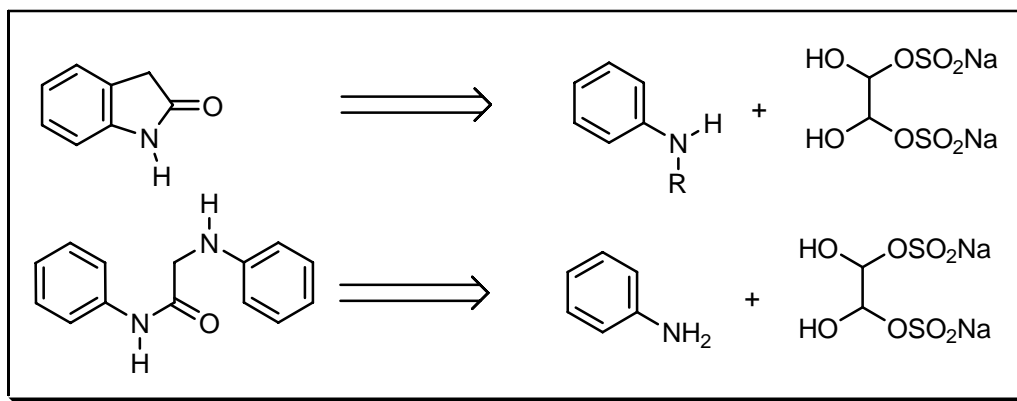
R  $\neq$  H :



R = H :



#### DISCONNECTION :



#### NOTES :

Oxindoles are obtained by condensing glyoxal bisulfite with a secondary aryl amine. See also **von Baeyer** oxindole, **Brunner**, **Gassman** oxindole, **Martinet**, **Neber – Bosset** and **Stollé** reactions.

#### REFERENCES :

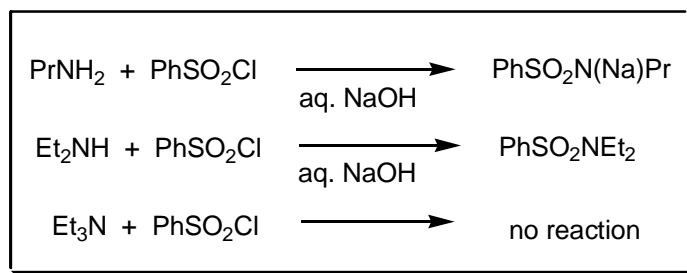
- 1) O. Hinsberg, *Ber. Dtsch. Chem. Ges.*, 1888, **21**, 110.
- 2) H. Burton, *J. Chem. Soc.*, 1932, 546.
- 3) W.C. Sumpter, *Chem. Rev.*, 1944, **34**, 393.
- 4) M.I. Abasolo; D. Bianchi; F. Atlasovich; C. Gaozza; B.M. Fernandez, *J. Heterocycl. Chem.*, 1990, **27**, 157.
- 5) M.I. Abasolo; B.M. Fernandez; E. Magrini, *J. Heterocycl. Chem.*, 1992, **29**, 1279.
- 6) G.A. Rodrigo; S.G. Renou; D.G. Bekerman; M.I. Abasolo; B.M. Fernandez, *J. Heterocycl. Chem.*, 1997, **34**, 505.

COMMENTS :

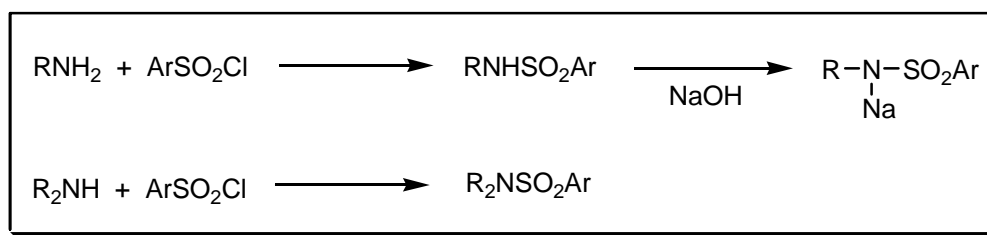
## HINSBERG REACTION

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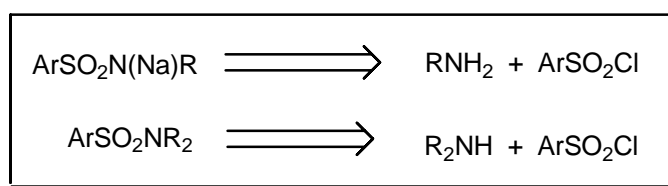
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

A mixture of primary, secondary, and tertiary amines is shaken with benzenesulfonyl chlorides in the presence of dilute alkali under **Schotten – Baumann** conditions. Primary amines form alkali soluble sulfonamides; while tertiary amines do not react and can usually be separated by distillation. See also **Schotten – Baumann** reaction.

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REFERENCES :

Houben – Weyl : 2, 640

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1) O. Hinsberg, *Ber. Dtsch. Chem. Ges.*, 1890, **23**, 2962.



- 2) R.S. Schreiber; R.L. Shriner, *J. Am. Chem. Soc.*, 1934, **56**, 114.  
3) W. Seamen; A.R. Norton; J.T. Woods; H.N. Bank, *J. Am. Chem. Soc.*, 1945, **67**, 1571.  
4) M. Wiechmann, *Hoppe-Seylers Zeit. Physiol. Chem.*, 1977, **358**, 967.  
5) B. Pfundstein; A.R. Tricker; R. Preussmann, *J. Chromatogr. A*, 1991, **539**, 141.

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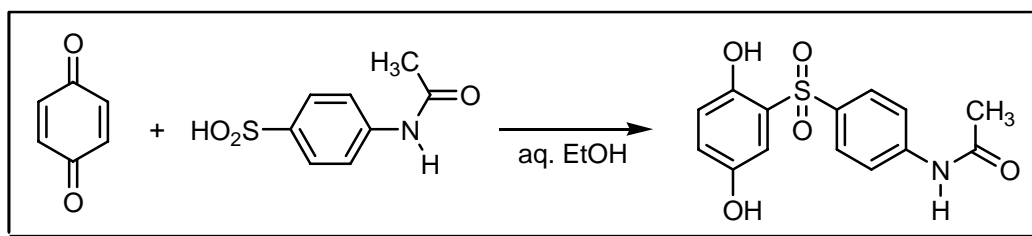
**COMMENTS :**

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## HINSBERG SULFONE SYNTHESIS

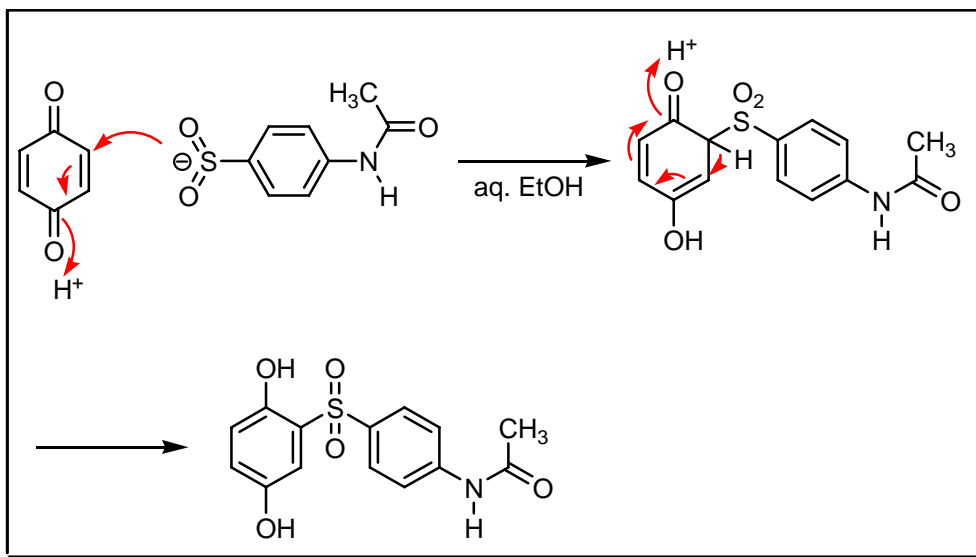
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**EXAMPLE :**

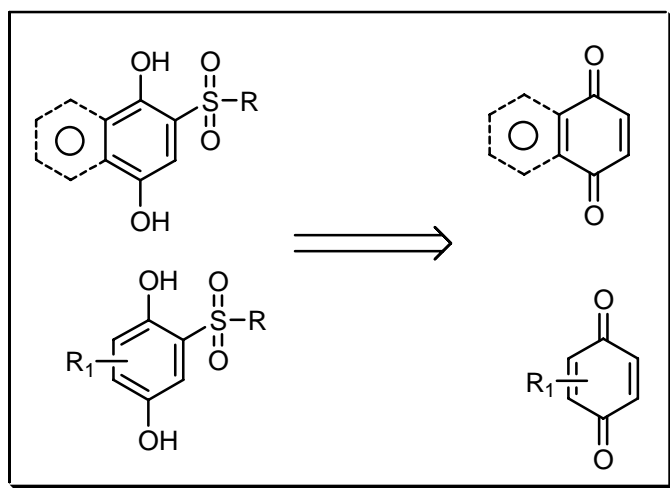


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**MECHANISM :**



## DISCONNECTION :



## NOTES :

Sulfinic acids condense with quinones to yield hydroquinone sulfones. See also **Thiele** reaction.

## REFERENCES :

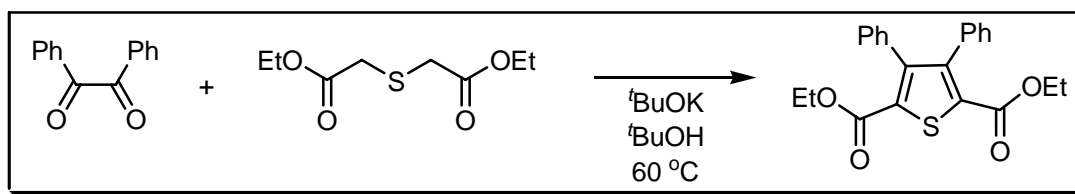
Houben – Weyl : 7/3a, 661

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- 6) M.P. Lockshin; M.P. Filosa; M.J. Zuraw; P.R. Carlier, *J. Org. Chem.*, 1996, **61**, 2556.

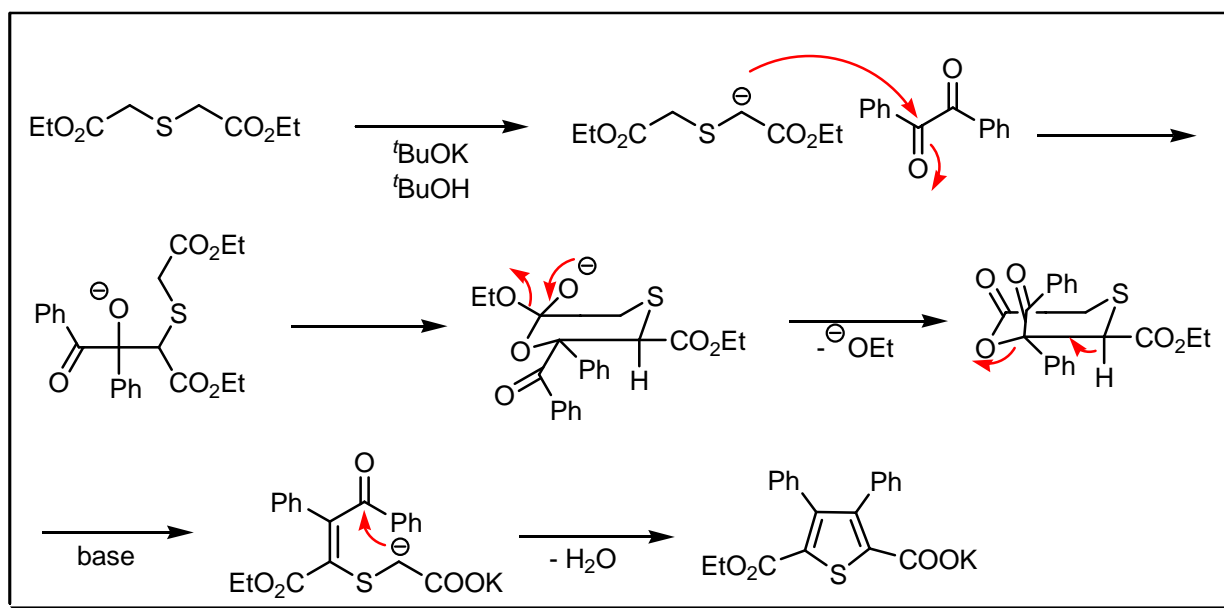
## COMMENTS :

## HINSBERG THIOPHENE SYNTHESIS

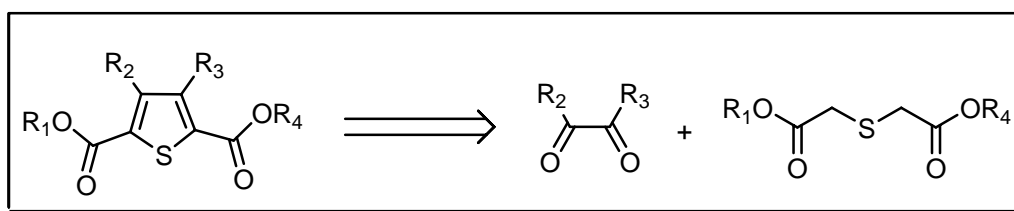
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Two aldol condensations between a 1,2-dicarbonyl compound and a thiodiester give thiophenes. The intermediate product is an ester-acid produced by a **Stobbe**-type condensation. See also **Baumann – Fromm**, **Bogert – Herrera**, **Fiesselmann**, **Harries** pyrrole, **Larock** fluorene-2, **Larock** indole, **Stobbe**, **Volhard – Erdmann** and **Willgerodt – Kindler** reactions.

### REFERENCES :

**Science of Synthesis** : 10, 190

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- 5) O. Meth-Cohn; H. Jiang, *J. Chem. Soc., Perkin Trans. 1*, 1998, 3737.

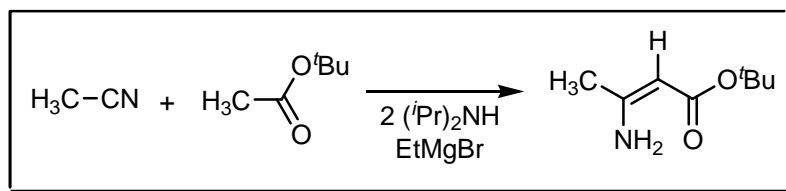
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**COMMENTS :**

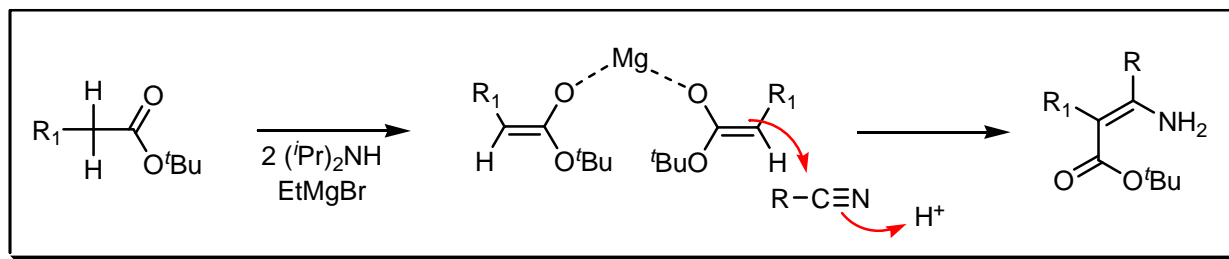
**HIYAMA AMINOACRYLATE SYNTHESIS**

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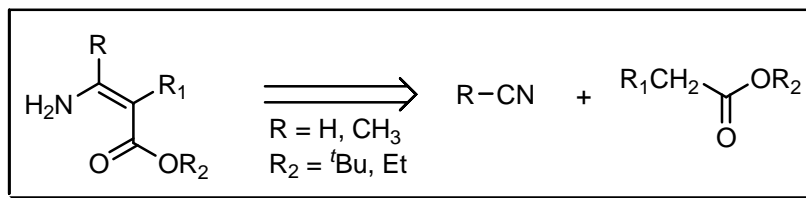
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

The synthesis of 3-aminoacrylic acids (Z-configuration) or derivatives from nitriles by aldol type condensation using magnesium enolates.

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## REFERENCES :

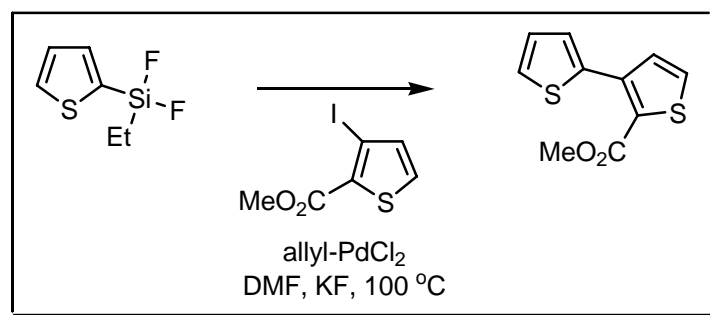
- 1) T. Hiyama; K. Kobayashi, *Tetrahedron Lett.*, 1982, **23**, 1597.
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  - 4) T. Hiyama; H. Oishi; Y. Suetsugu; K. Nishide; H. Saimoto, *Bull. Chem. Soc. Jpn.*, 1987, **60**, 2139.
- 

## COMMENTS :

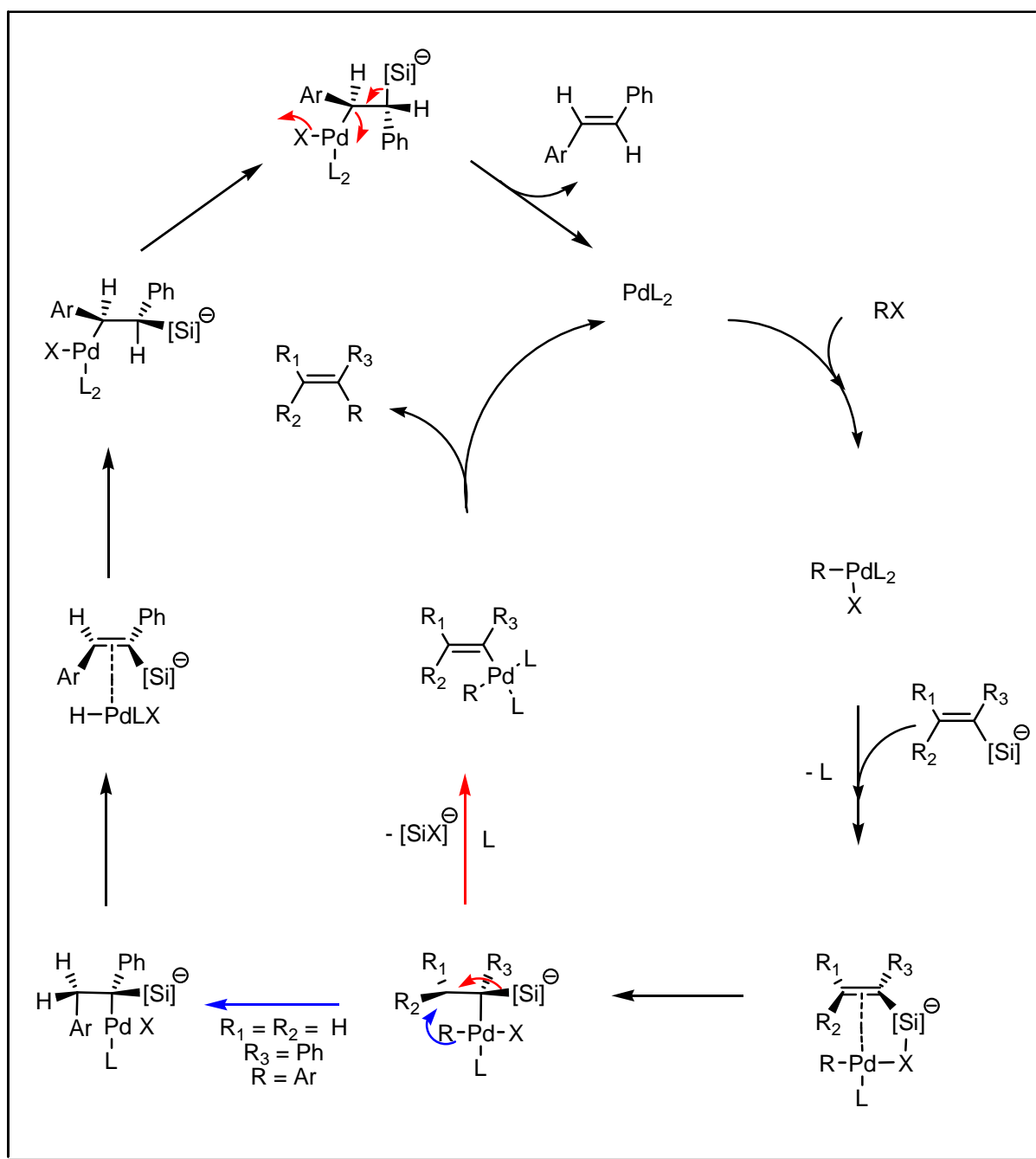
## HIYAMA COUPLING

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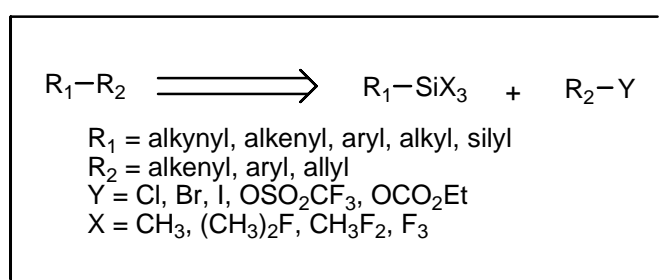
### EXAMPLE :



# MECHANISM :



# DISCONNECTION :



## NOTES :

In the presence of a palladium complex, a fluoride ion attacks the silicon atom and does not deactivate the catalyst. The formed anionic species is a penta-coordinated silicate, that transmetalates *via* a 4-centered transition state in which it becomes hexa-coordinated. The fluorine atom can be replaced by a hydroxyl, alkoxy or other heteroatom. The stereochemical transmetalation in THF at low temperatures proceeds with retention of the configuration while at higher temperatures or in polar solvents inversion dominates. An activator (KF, TBAF, TASF, NaOH) for this reaction is necessary. The **Hiyama** coupling has better tolerances of functional groups in comparison to other strong nucleophilic organometallic reagents. This reaction has been expanded by the **DeShong** group to work with hypervalent siloxanes. See also **Yamamoto** allylation.

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## REFERENCES :

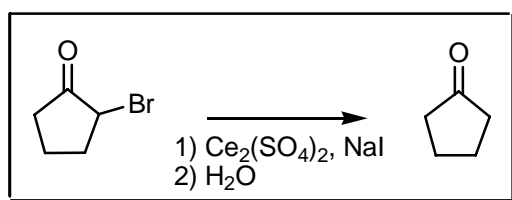
- 1) Y. Hatanaka; T. Hiyama, *J. Org. Chem.*, 1988, **53**, 918.
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- 8) M.E. Hoke; M.-R. Brescia; S. Bogaczyk; P. DeShong; B.W. King; M.T. Crimmins, *J. Org. Chem.*, 2002, **67**, 327.

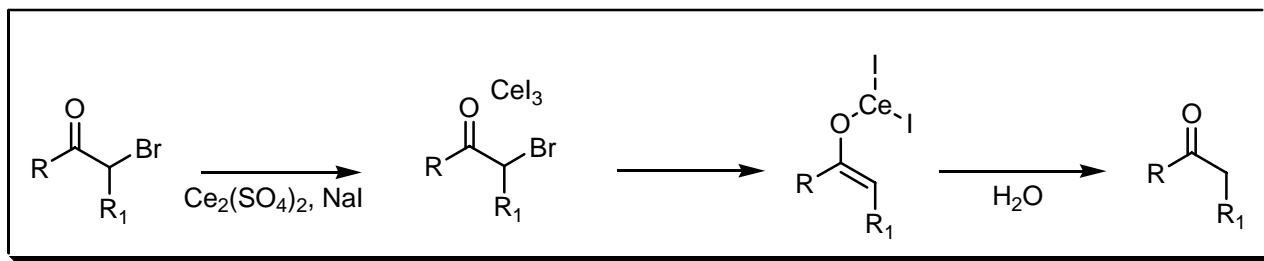
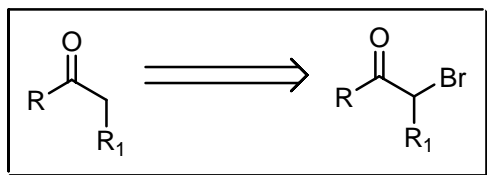
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## COMMENTS :

## HO DEHALOGENATION

### EXAMPLE :

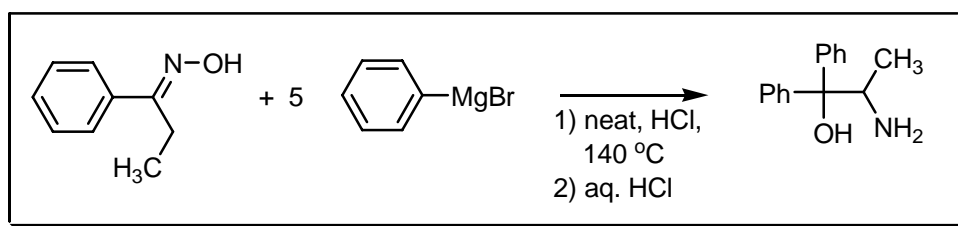


**MECHANISM :****DISCONNECTION :****NOTES :**

This reaction is the dehalogenation of  $\alpha$ -halo ketones with an aqueous mixture of cerium(III) sulphate and sodium iodide to produce cerium iodide intermediate to afford ketones.

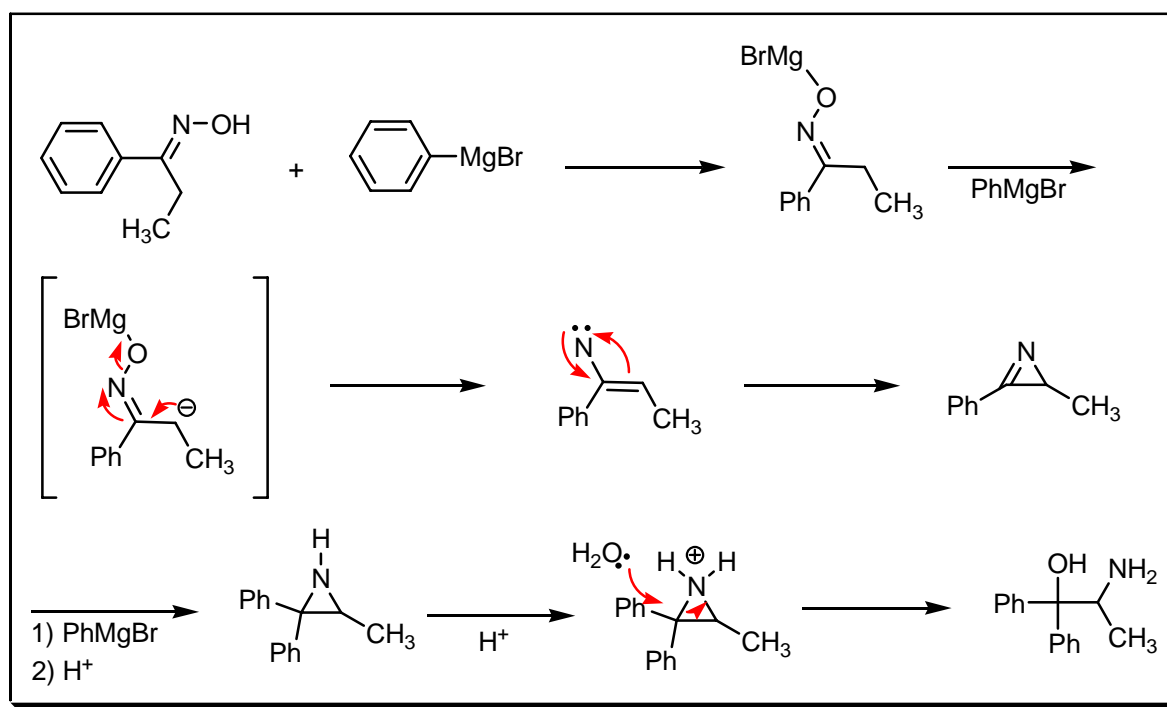
**REFERENCES :**

- 1) T.-L. Ho, *J. Chem. Educ.*, 1978, **55**, 355.
- 2) T.-L. Ho, *Synth. Commun.*, 1979, **9**, 241.
- 3) J.R. Long, *Aldrichimica Acta*, 1985, **18**, 87.

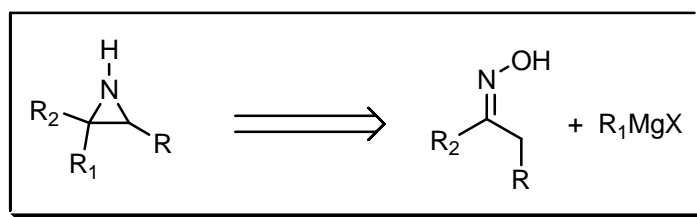
**COMMENTS :****HOCH – CAMPBELL AMINO ALCOHOL SYNTHESIS****EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

Ethylenimines are obtained by the interaction of ketoximes and **Grignard** compounds, followed by controlled hydrolysis of the complex formed to give an amino alcohol. See also **Blum** aziridine, **Hassner** azide aziridine, **Gabriel – Marckwald – Cromwell**, **Mansuy – Evans**, **Neber** rearrangement, **Scheiner** and **Wenker** ring-closure reactions.

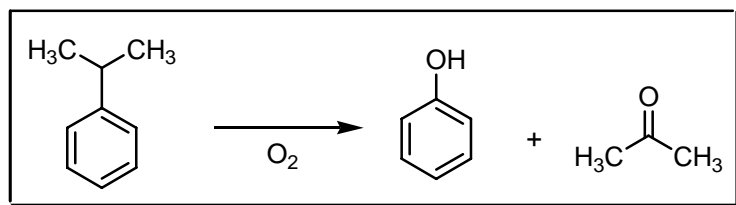
## REFERENCES :

- 1) J. Hoch, *C.R. Séances Acad. Sci.*, 1934, **198**, 1865.
- 2) K.N. Campbell; J.F. McKenna, *J. Org. Chem.*, 1939, **4**, 198.
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- 6) J.P. Freeman, *Chem. Rev.*, 1973, **73**, 283.
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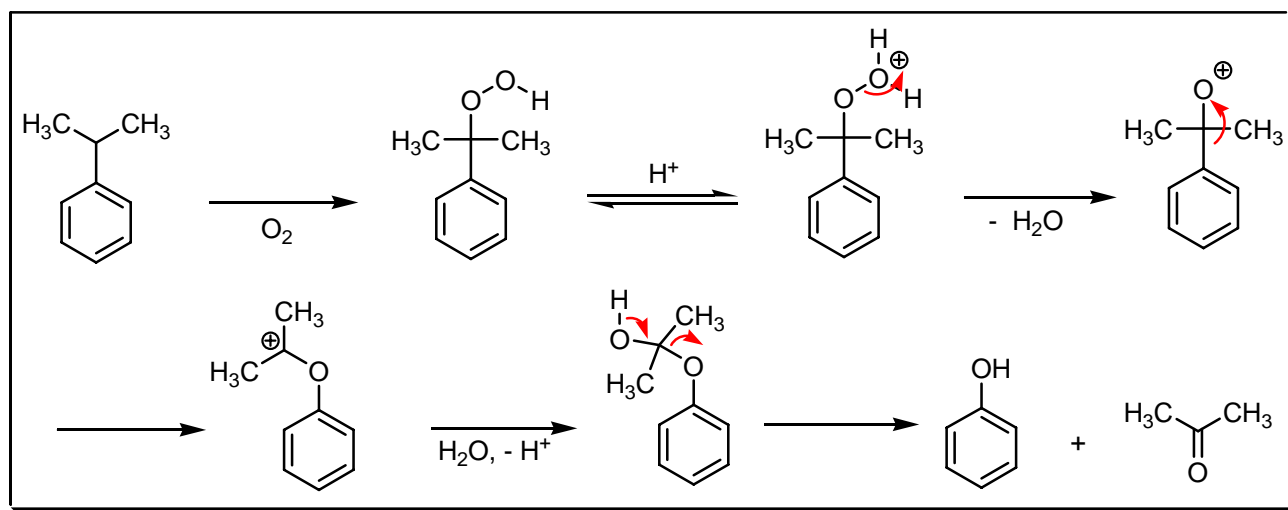
COMMENTS :

## HOCK – LANG OXIDATION

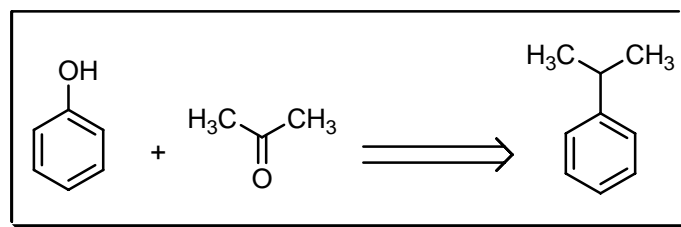
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

This reaction involves the autoxidation of certain aromatic hydrocarbons to give hydro-peroxides, e.g. isopropylbenzene yields a peroxide which decomposes with acid to phenol and acetone. Since 1990, a new process

utilising the oxidation of toluene (via benzoic acid) has gradually replaced the **Hock – Lang** process. See also **Friedel – Crafts** reaction.

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#### REFERENCES :

Houben – Weyl : **4/2**, 352; **7/2a**, 712; **E19c**, 407, 429

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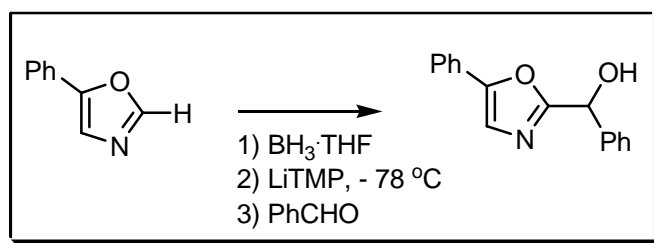
- 1) H. Hock; S. Lang, *Ber. Dtsch. Chem. Ges.*, 1944, **77**, 257.
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  - 3) H. Hock; H. Kropf, *Chem. Ber.*, 1955, **88**, 1544.
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#### COMMENTS :

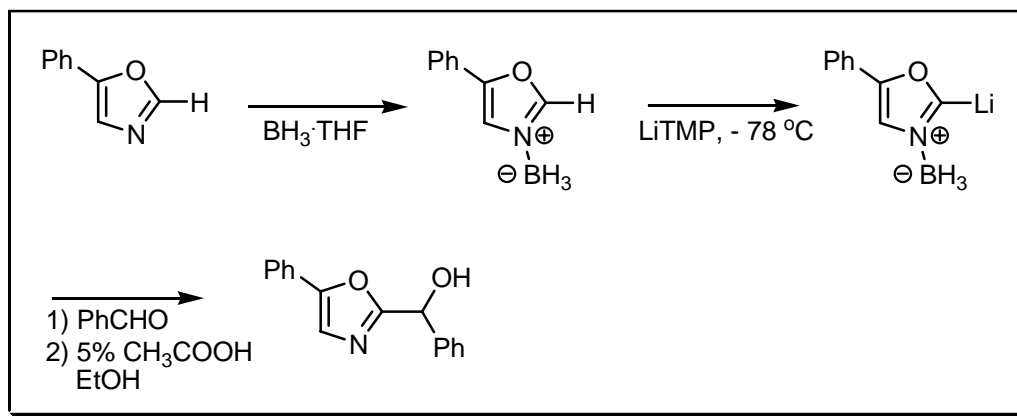
### HODGES – VEDEJS REACTION

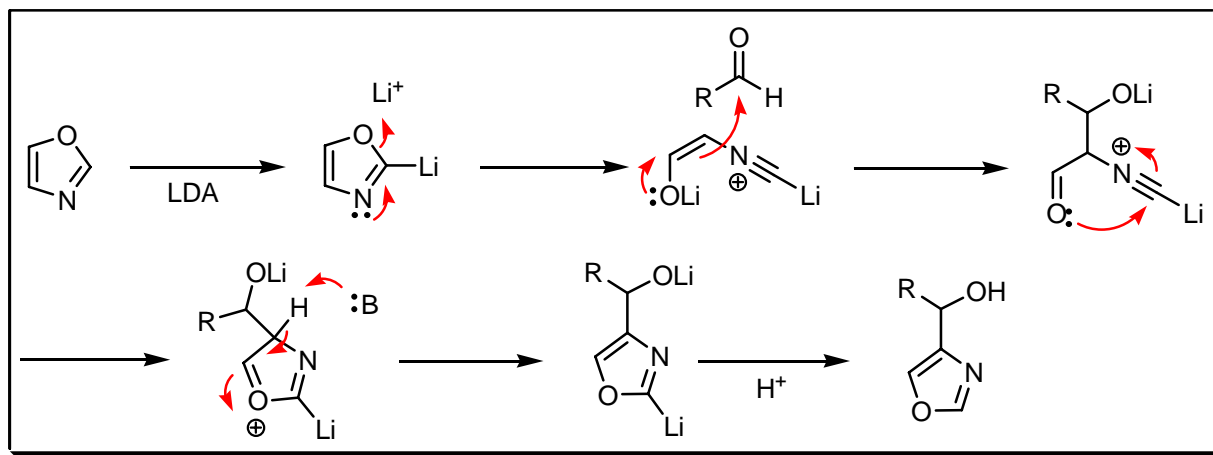
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#### EXAMPLE :

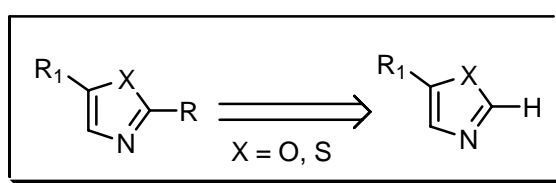


#### MECHANISM :





#### DISCONNECTION :



#### NOTES :

The metallation of oxazoles and thiazoles using borane THF complex and lithium 2,2,6,6-tetramethylpiperidine. This borane complex prevents the ring-opening process. The lithium derivative can be trapped with electrophiles. The intermediate borane complex can be isolated. See also **Dondoni** reaction.

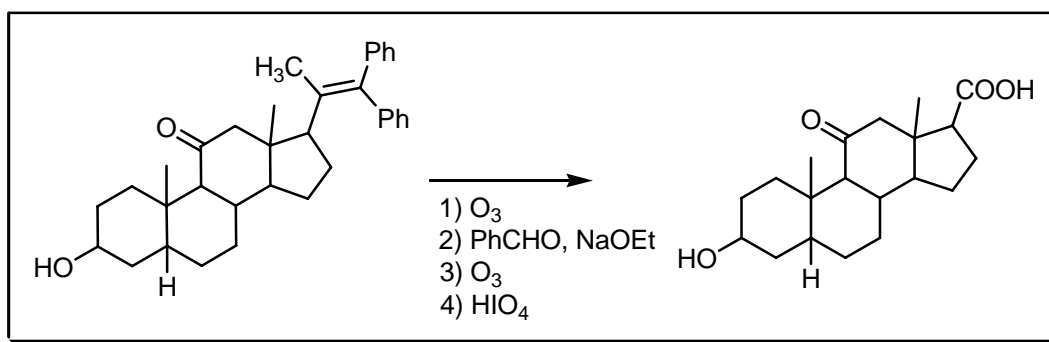
#### REFERENCES :

- 1) J.C. Hodges; W.C. Pratt; C.J. Connolly, *J. Org. Chem.*, 1991, **56**, 449.
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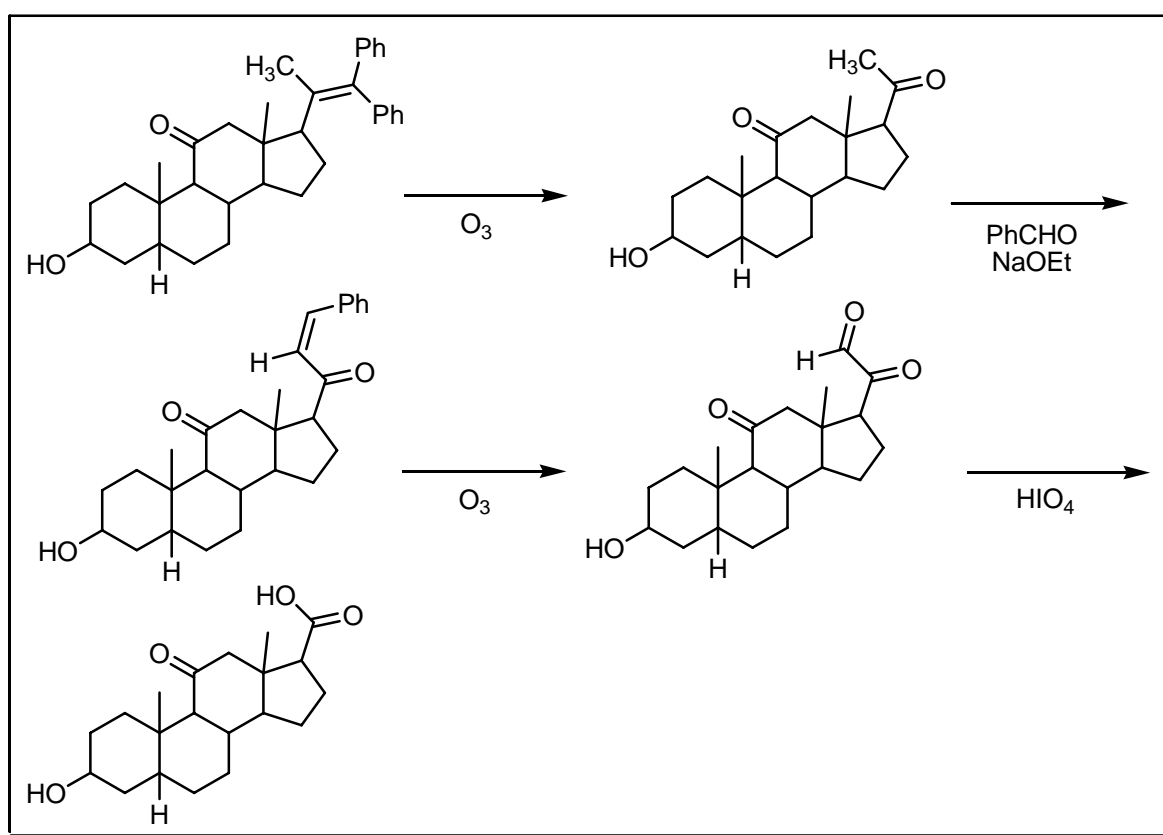
#### COMMENTS :

## HOEHN – MASON DEGRADATION

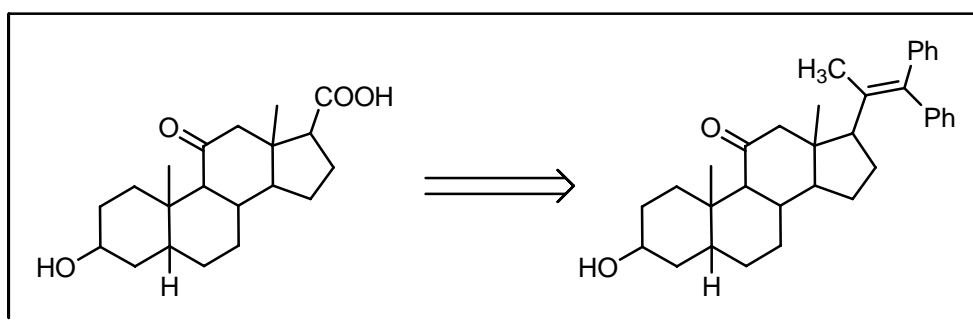
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :

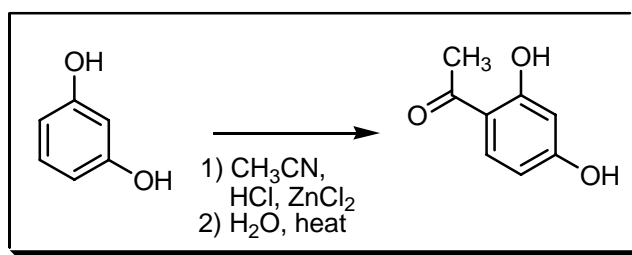
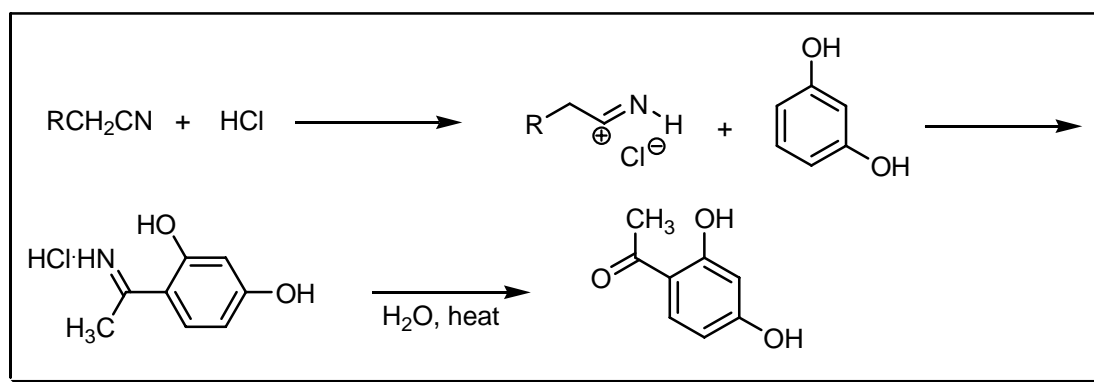


**NOTES :**

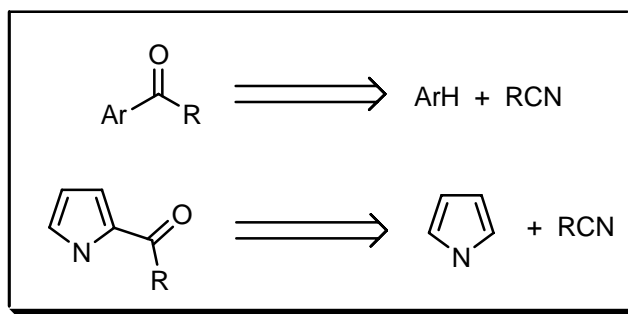
An improvement in the **Barbier – Locquin – Wieland** degradation in which the elimination of carbons 21 and 22 of the steroid side chain is effected. See also **Barbier – Locquin – Wieland** degradation, **Gallagher – Hollander**, **Miescher** degradation, **Trost** oxidative decarboxylation and **Wieland – Dane** degradation reactions.

**REFERENCES :**

- 1) W.M. Hoehn; H.L. Mason, *J. Am. Chem. Soc.*, 1938, **60**, 1493.
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**COMMENTS :****HOESCH – HOUBEN SYNTHESIS****EXAMPLE :****MECHANISM :**

## DISCONNECTION :



## NOTES :

This synthesis of phenolic ketones involves the condensation in diethyl ether of phenols or their ethers with nitriles. Pyrroles can be used instead of phenols. The reaction is carried out in the presence of anhydrous zinc chloride or aluminium chloride and hydrogen chloride. The resulting ketimine is hydrolysed. In the abnormal **Hoesch** reaction an  $\alpha,\beta$ -unsaturated nitrile reacts with a phenol. The phenol adds on to the olefinic double bond. The **Fischer – Nouri** modification involves the **Hoesch – Houben** condensation of  $\beta$ -(4-acetoxyphenyl)-propionitrile with phloroglucinol. See also **Fischer – Zerweck**, **Friedel – Crafts**, **Gattermann – Ehrhardt**, **Houben – Fischer**, **Karrer** and **Nencki** reactions.

## REFERENCES :

**March** : 552

**Smith – March** : 723

**Houben – Weyl** : **E5**, 819; **E6a**, 977; **E6b**, 73; **E19c**, 366

**Org. React.** : **5**, 387

**Org. Synth.** : **15**, 70

**Org. Synth. Coll. Vol.** : **2**, 522

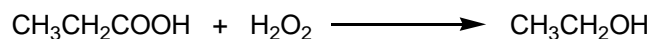
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- 8) S. Repichet; C. Le Roux; J. Dubac; J.R. Desmurs, *Eur. J. Org. Chem.*, 1998, 2743.
- 9) D. Basavaiah; T. Satyanarayana, *Chem. Commun.*, 2004, 32.

## COMMENTS :

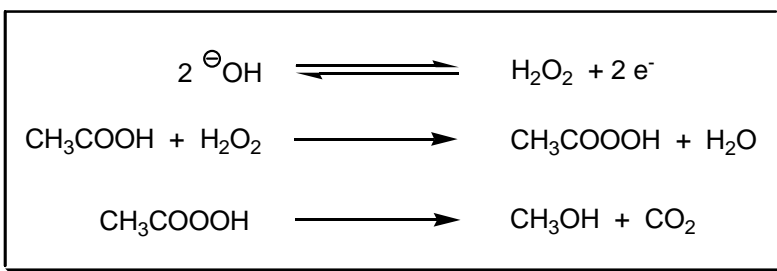
## HOFER – MOEST REACTION

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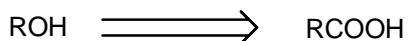
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This reaction relates to the electrolysis of aqueous solution of a salt of an aliphatic acid to yield an alcohol, e.g., in the electrolysis of an aqueous solution of acetic acid a high efficiency of ethane formation is observed, but if an inorganic acid or potassium salt of an inorganic acid is added, the efficiency is greatly decreased and methyl alcohol is formed instead of ethane. See also **Crum Brown – Walker** and **Kolbe** reactions.

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### REFERENCES :

Houben – Weyl : 8, 501

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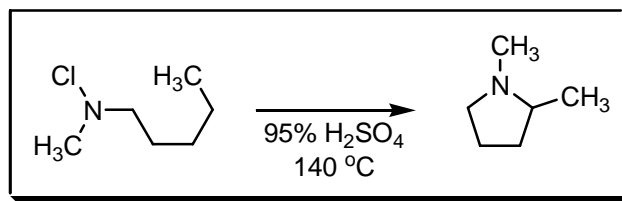
- 1) H. Kolbe, *Liebigs Ann. Chem.*, 1849, **69**, 257.
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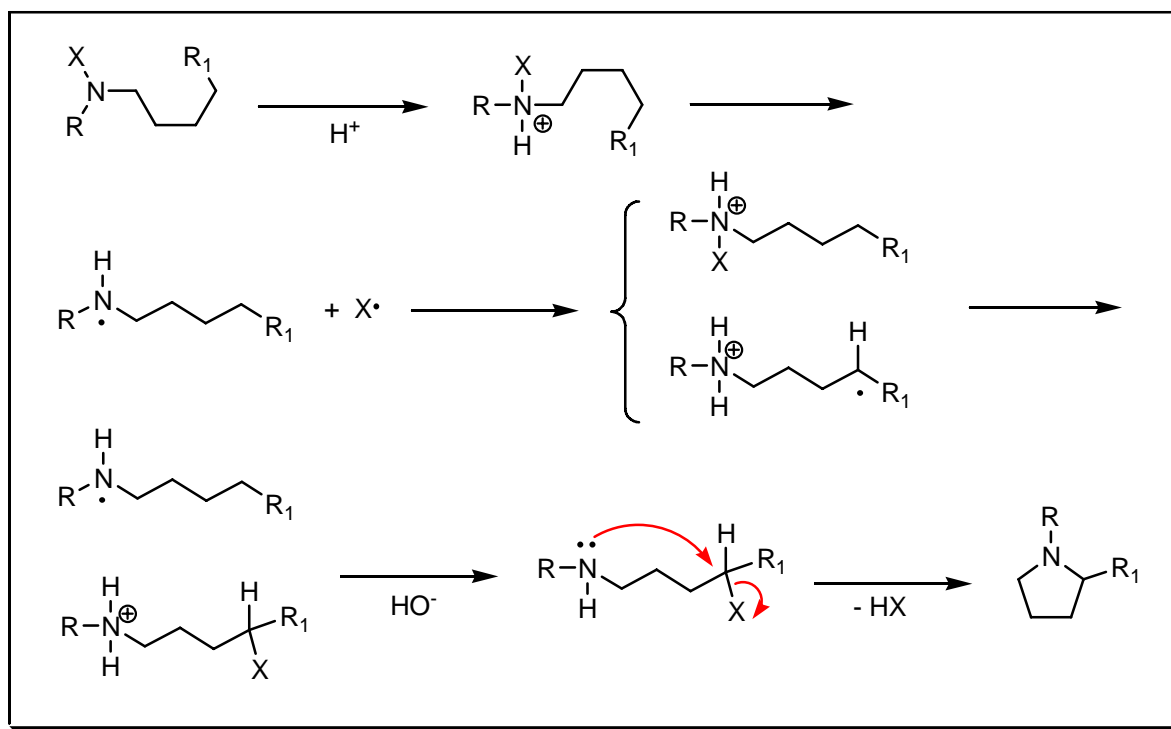
COMMENTS :

## HOFMANN – LÖFFLER – FREYTAG REACTION

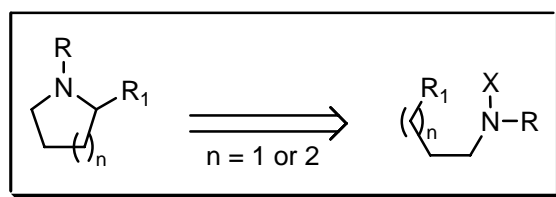
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

*N*-Haloamines in which one alkyl group has a hydrogen in the 4- or 5-position are heated with sulfuric acid. Pyrrolidines and piperidines are formed by a free-radical mechanism. *N*-Haloamides will give  $\gamma$ -lactones. See also **Miller – Plöchl** reaction.

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## REFERENCES :

**March** : 1153

**Smith – March** : 909, 1462

**Smith** : 1430

**Smith 2<sup>nd</sup>** : 1180

**Houben – Weyl** : **E16a**, 856; **E16d**, 649, 655; **E19a**, 8, 70, 305

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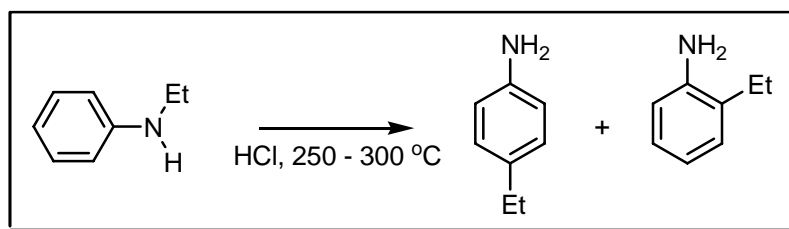
- 1) A.W. Hofmann, *Ber. Dtsch. Chem. Ges.*, 1883, **16**, 558.
  - 2) K. Löffler; C. Freytag, *Ber. Dtsch. Chem. Ges.*, 1909, **42**, 3427.
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## COMMENTS :

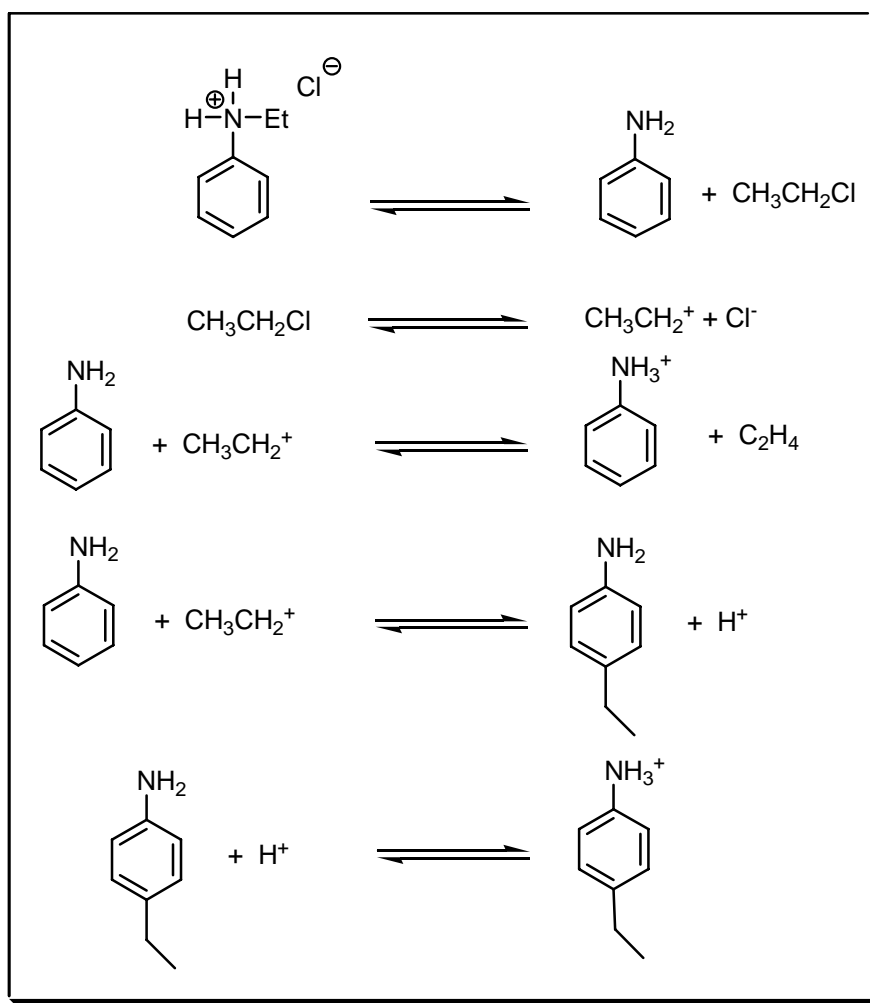
## HOFMANN – MARTIUS REARRANGEMENT (REILLY – HICKINBOTTOM)

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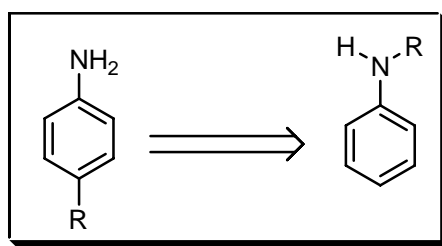
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The hydrohalide of *N*-alkylaniline rearranges *intermolecularly* on heating to give amino-alkylbenzenes. When *N*-alkylanilines are heated with certain metal halides, e.g. cobaltous and zinc chlorides, the **Reilly – Hickinbottom** rearrangement occurs with migration of the alkyl group into the ring. See also **Claisen** rearrangement, **Fischer – Hepp** rearrangement, **Fries** rearrangement, **Ladenburg** rearrangement and **Orton** rearrangement.

## REFERENCES :

March : 560

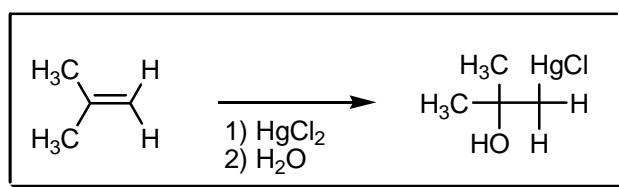
Smith – March : 729

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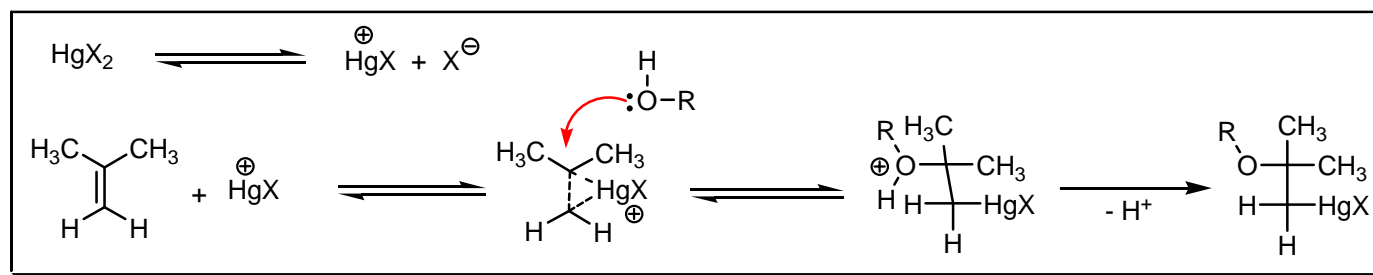
## COMMENTS :

## HOFMANN – SAND OXYMERCURATION

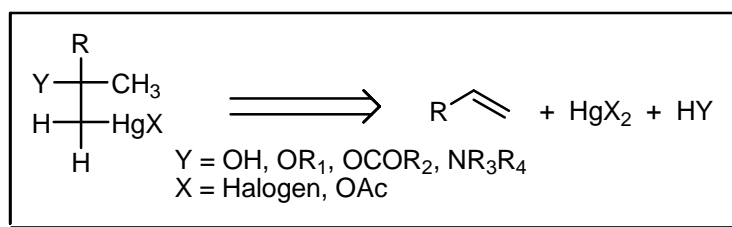
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Olefins react with mercuric salts in aqueous solution to give addition compounds. See also **Giese** and **Kutscheroff – Denigès** reaction.

## REFERENCES :

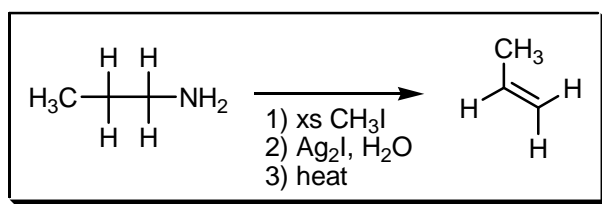
Houben – Weyl : 13/2b, 130

- 1) G. Denigès, *C.R. Séances Acad. Sci.*, 1898, **126**, 1043.
- 2) K.A. Hofmann; J. Sand, *Ber. Dtsch. Chem. Ges.*, 1900, **33**, 1340.
- 3) J. Chatt, *Chem. Rev.*, 1951, **48**, 7.
- 4) W. Kitching, *Organomet. Chem. Rev.*, 1968, **3**, 35.

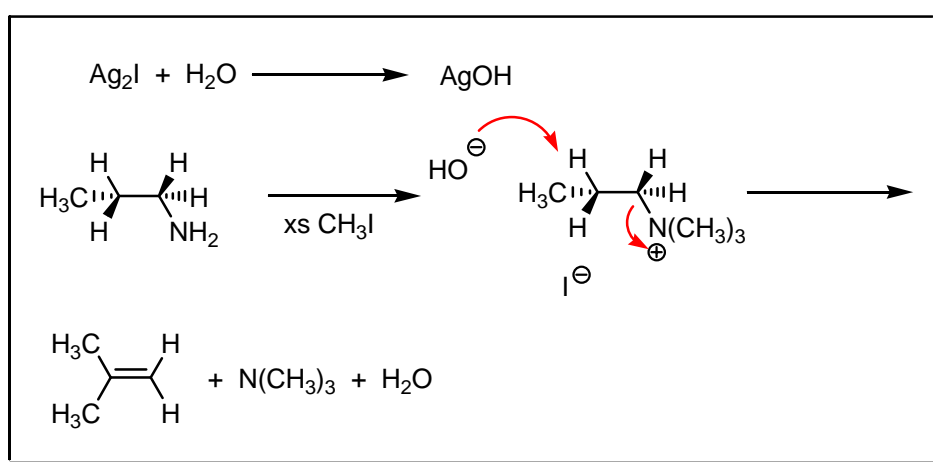
## COMMENTS :

## HOFMANN DEGRADATION

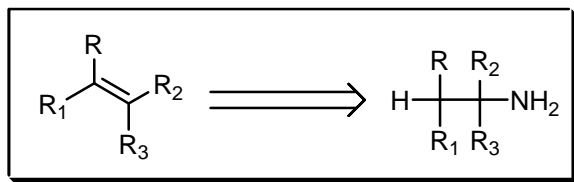
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

**Hofmann** elimination products are generally the least-substituted alkenes. Where **Hofmann** degradation does not work, **Emde** degradation is often used. See also **von Braun** amide, **Curtius**, **Emde** and **Menschutkin** reactions.

## REFERENCES :

**March** : 1016

**Smith – March** : 1331

**Smith** : 163

**Smith 2<sup>nd</sup>** : 109, 135, 679

**Houben – Weyl** : **11/1**, 963; **E3**, 527; **E5**, 554; **E8c**, 677

**Org. React.** : **11**, 317; **18**, 403

**Org. Synth.** : **55**, 3

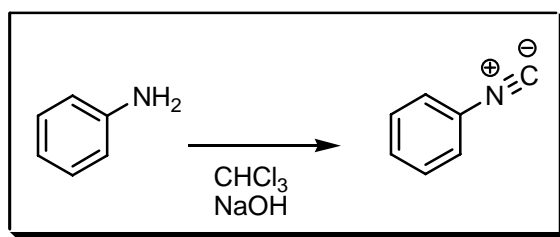
**Org. Synth. Coll. Vol.** : **6**, 552

- 1) A.W. Hofmann, *Liebigs Ann. Chem.*, 1851, **78**, 253.
- 2) A.W. Hofmann, *Ber. Dtsch. Chem. Ges.*, 1881, **14**, 494.
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- 4) A.R. Katritzky; A.M.E. El-Mowafy, *Chem. Commun.*, 1981, 96.
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- 6) Y. Yamamoto; M.V. Sefton, *J. Appl. Polym. Sci.*, 1996, **61**, 351.
- 7) B.M. Novak; J.T. Cafmeyer, *J. Am. Chem. Soc.*, 2001, **123**, 11083.

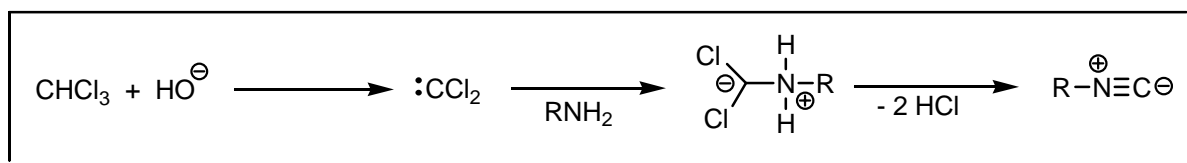
## COMMENTS :

# HOFMANN ISONITRILE SYNTHESIS

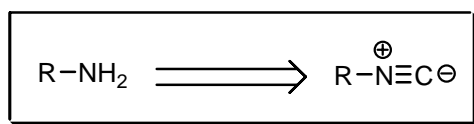
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The formation of isocyanides involves the reaction between chloroform and primary amines under alkaline conditions. Secondary amines hydrolyse with water to *N,N*-disubstituted formamides.

## REFERENCES :

March : 417

Smith – March : 506

Houben – Weyl : 2, 643

Org. Synth. : 55, 96

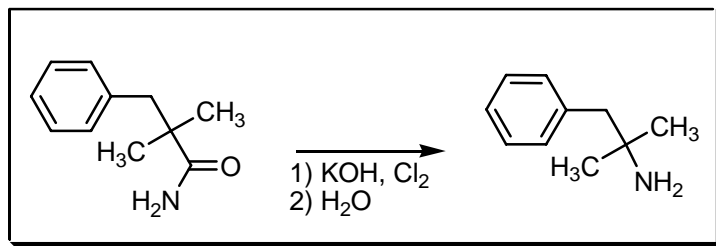
Org. Synth. Coll. Vol. : 6, 232

- 1) A.W. Hofmann, *Liebigs Ann. Chem.*, 1868, **146**, 107.
- 2) P.A.S. Smith; N.W. Kalenda, *J. Org. Chem.*, 1958, **23**, 1599.
- 3) W.P. Weber; G.W. Gokel, *Tetrahedron Lett.*, 1972, **13**, 1637.
- 4) M.P. Periasamy; H.M. Walborsky, *Org. Prep. Proced. Int.*, 1979, **11**, 293.

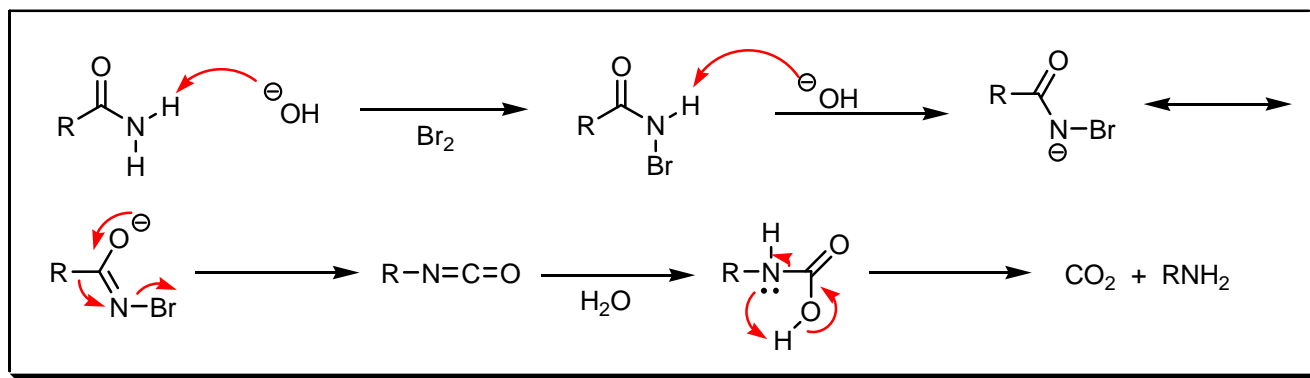
COMMENTS :

## HOFMANN REARRANGEMENT

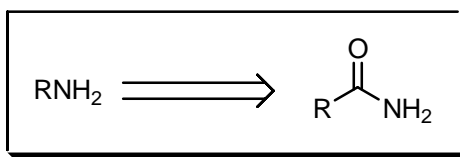
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

An amide is converted with intermediate formation of an isocyanate into a primary amine with one less carbon atom by treatment with bromine and alkali or with a hypohalite solution. See also **Curtius** rearrangement, **Lossen** rearrangement, **Schmidt** rearrangement, **Tiemann** rearrangement and **Weerman** degradation reactions.

REFERENCES :

March : 1090

Smith – March : 1380, 1384



Houben – Weyl : 11/1, 854; E8a, 273; E15, 3446; E16a, 888

Org. React. : 3, 267

Org. Synth. : 66, 132; 78, 234

Org. Synth. Coll. Vol. : 8, 132

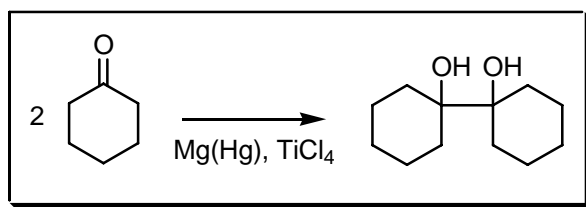
- 
- 1) A.W. Hofmann, *Ber. Dtsch. Chem. Ges.*, 1881, **14**, 2725.
  - 2) A.O. Sy; J.A. Raksis, *Tetrahedron Lett.*, 1980, **21**, 2223.
  - 3) C.J. Kowalski; K.W. Fields, *J. Am. Chem. Soc.*, 1982, **104**, 321.
  - 4) M.S. Park; C.-U. Choi, *Arch. Pharm. Res.*, 1993, **16**, 152.
  - 5) L.-H. Zhang; G.S. Kauffman; J.A. Pesti; J. Yin, *J. Org. Chem.*, 1997, **62**, 6918.
  - 6) Y.H. Jung; J.D. Kim, *Arch. Pharm. Res.*, 2001, **24**, 371.
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COMMENTS :

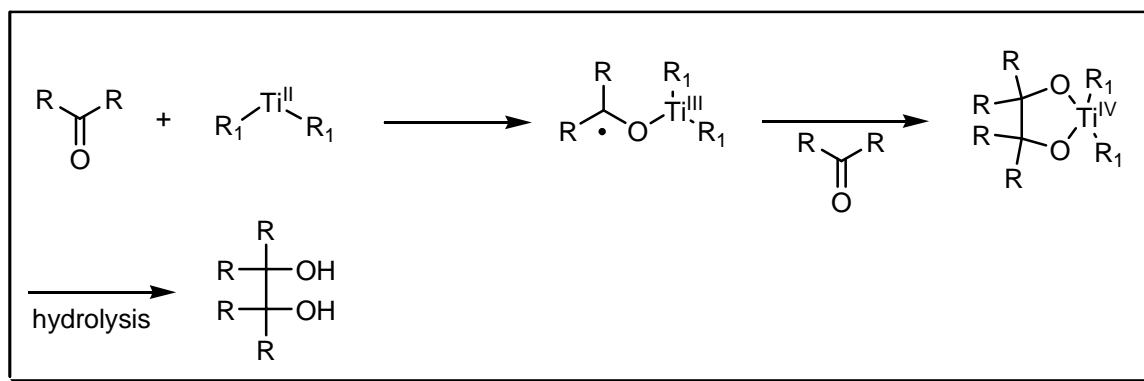
## HOLLEMANN PINACOL SYNTHESIS

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EXAMPLE :



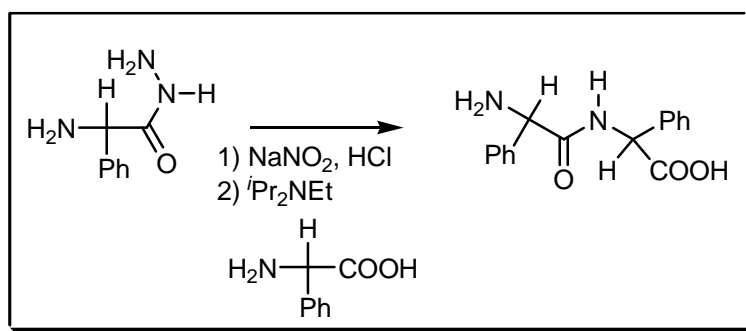
MECHANISM :



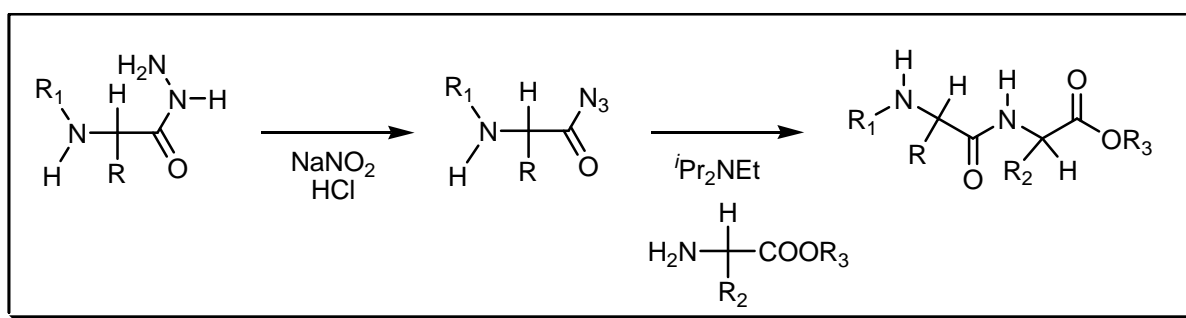


# HONZL – RUDINGER PEPTIDE SYNTHESIS

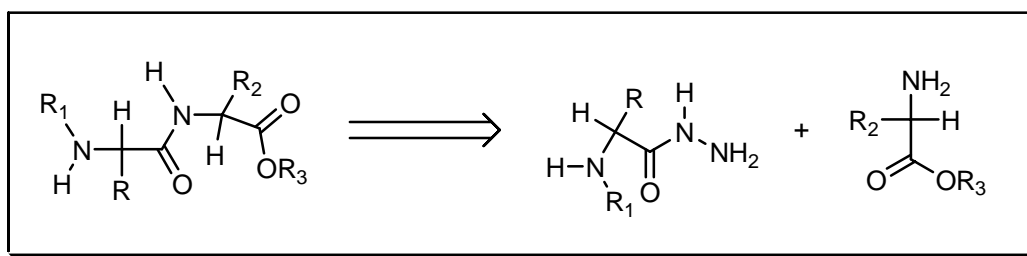
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

In this peptide synthesis acyl azides couple with amino esters. The preparation of the azide has to be done at low temperature, in homogenous solution, at high acidity, and with an organic nitrate or nitrosyl chloride to give the best results. In the **Medzihradsky** method the hydrazide is converted to the azide in DMF, with aqueous hydrochloric acid and sodium nitrite. See also **Bergmann**, **Fischer** peptide synthesis, **Leuchs – Bergmann** and **Sheehan – Frank** reactions.

## REFERENCES :

- 1) I. Honzl; I. Rudinger, *Coll. Czech. Chem. Commun.*, 1961, **26**, 2333.
- 2) K. Medzihradsky; V. Bruckner; M. Kajtár; L. Kisfaludy; S. Bajusz; M. Löw, *Acta Chim. Acad. Sci. Hung.*, 1962, **30**, 105.
- 3) M. Zaoral; F. Šorm, *Coll. Czech. Chem. Commun.*, 1965, **30**, 1853.

- 4) M.A. Ondetti; V.L. Narayanan; M. von Saltza; J.T. Sheehan; E.F. Sabo; M. Bodanszky, *J. Am. Chem. Soc.*, 1968, **90**, 4711.
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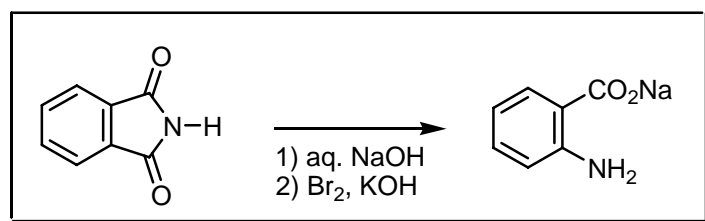
**COMMENTS :**

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**HOOGEWERFF – VAN DORP SYNTHESIS**

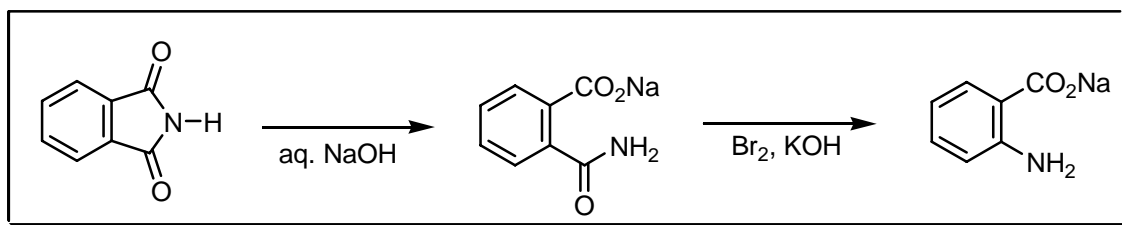
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**EXAMPLE :**



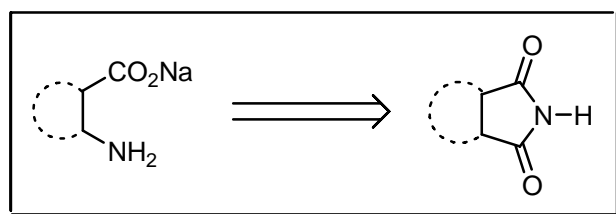
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**MECHANISM :**



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**DISCONNECTION :**



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**NOTES :**

Phthalimide is hydrolysed to o-amidobenzoic acid which is submitted to a **Hofmann** rearrangement. See also **Hofmann** rearrangement.

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**REFERENCES :**

Org. Synth. : 16, 1

Org. Synth. Coll. Vol. : 2, 19

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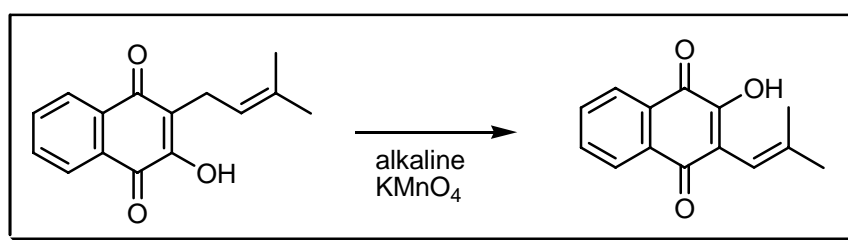
S. Hoogewerff; W.A. van Dorp, *Recl. Trav. Chim. Pays-Bas*, 1891, **10**, 5.

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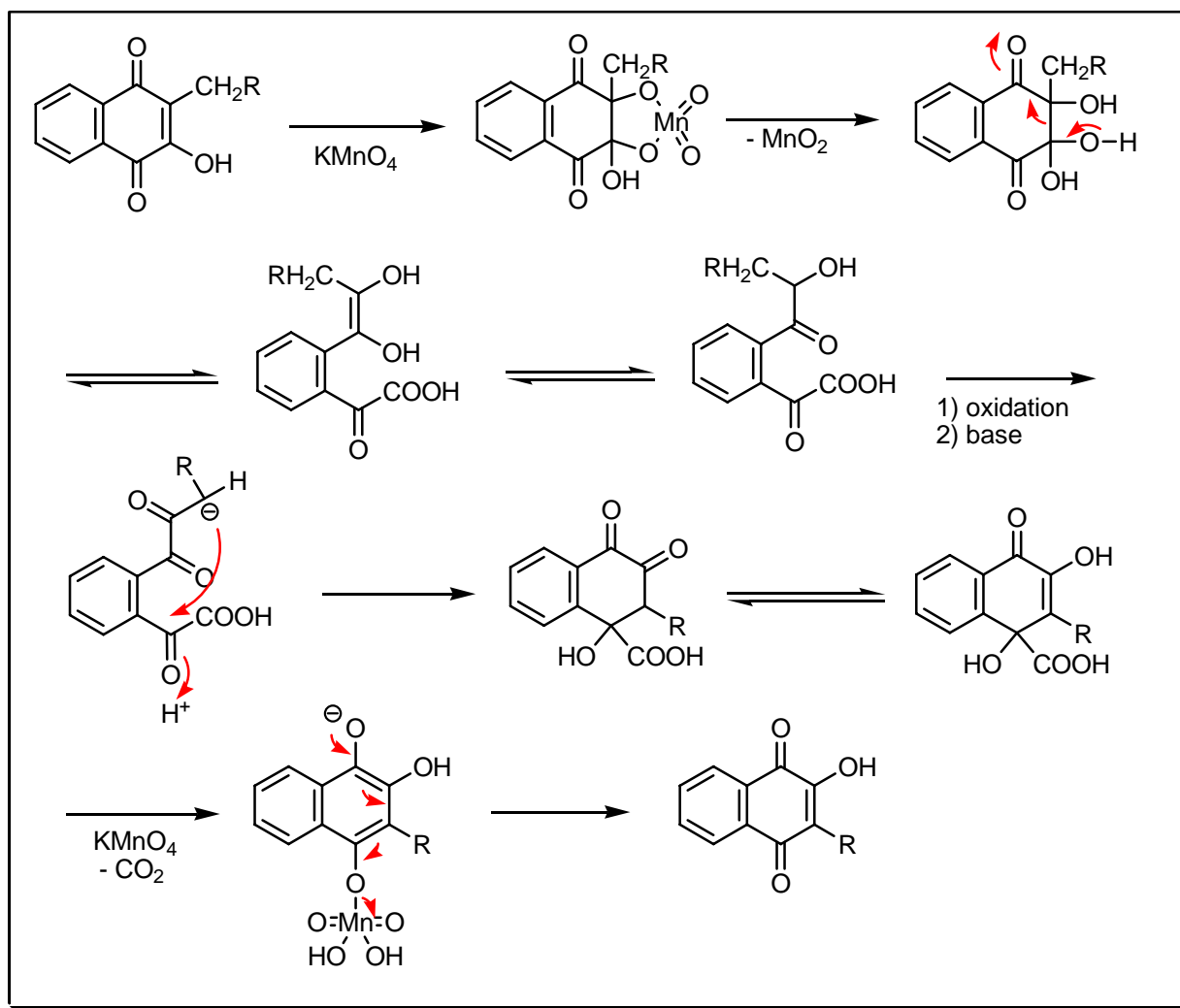
**COMMENTS :**

## HOOKER REACTION

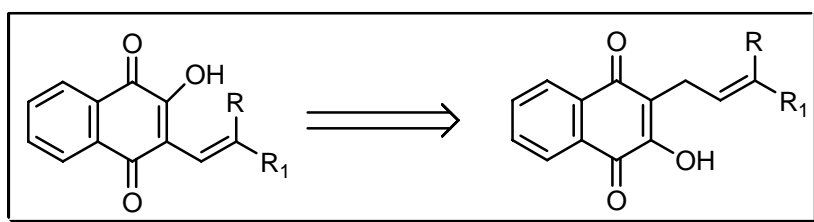
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**EXAMPLE :**

## MECHANISM :



## DISCONNECTION :



## NOTES :

Alkaline potassium permanganate oxidation of certain hydroxynaphthaquinone derivatives (Lapachol) eliminates  $-\text{CH}_2-$  adjoining the quinone ring with the simultaneous interchange of the alkyl and hydroxyl groups. The quinone ring seems to open and to close in a different manner.

## REFERENCES :

- 1) S.C. Hooker, *J. Am. Chem. Soc.*, 1936, **58**, 1168.
- 2) S.C. Hooker, *J. Am. Chem. Soc.*, 1936, **58**, 1174.
- 3) S.C. Hooker; A. Steyermark, *J. Am. Chem. Soc.*, 1936, **58**, 1179.
- 4) L.F. Fieser; M. Fieser, *J. Am. Chem. Soc.*, 1948, **70**, 3215.

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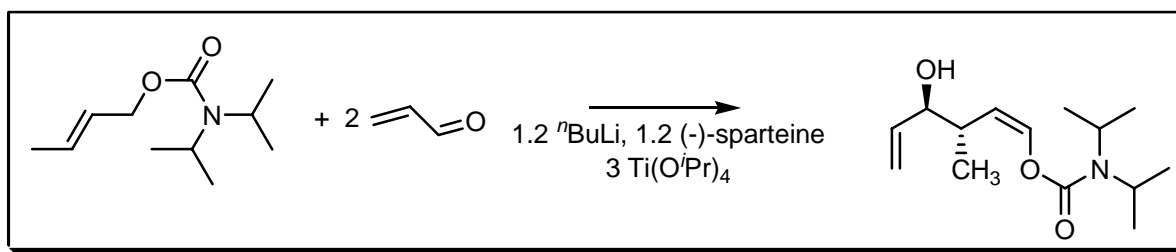
**COMMENTS :**

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**HOPPE HOMOALDOL REACTION**

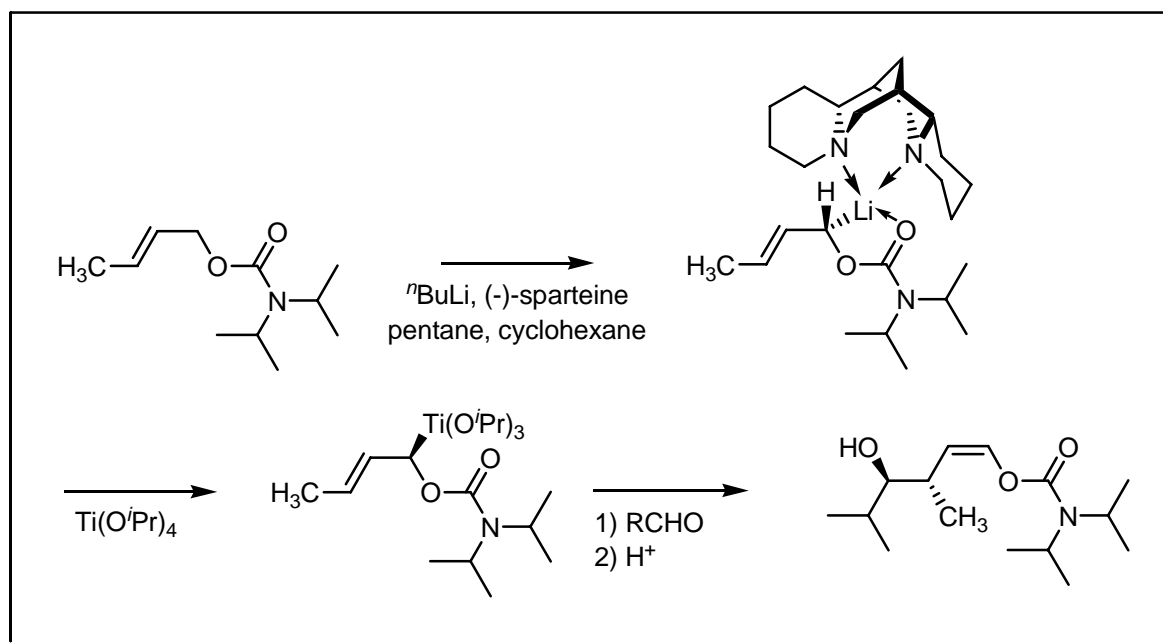
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**EXAMPLE :**

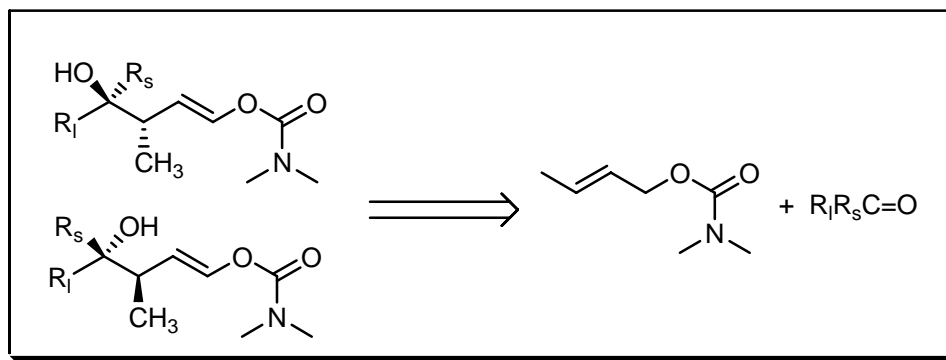


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**MECHANISM :**



## DISCONNECTION :



## NOTES :

Enantioselective homoaldolisation process Lewis acid catalysed with high e.e.'s and yields induced by (-)-sparteine.

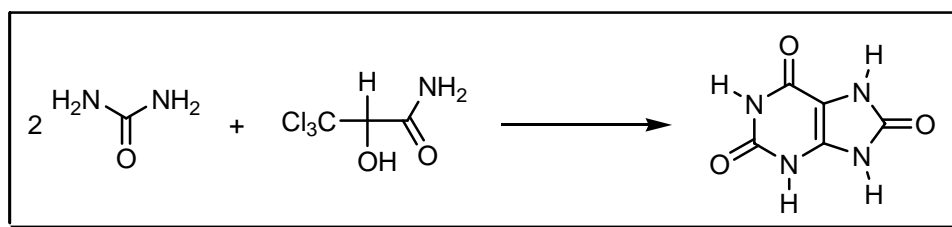
## REFERENCES :

- 1) D. Hoppe; O. Zschage, *Angew. Chem., Int. Ed. Engl.*, 1989, **28**, 67.
- 2) H. Paulsen; D. Hoppe, *Tetrahedron*, 1992, **48**, 5657.
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- 4) D. Hoppe; T. Hense, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 2282.
- 5) K.R.K. Prasad; D. Hoppe, *Synlett*, 2000, 1067.
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## COMMENTS :

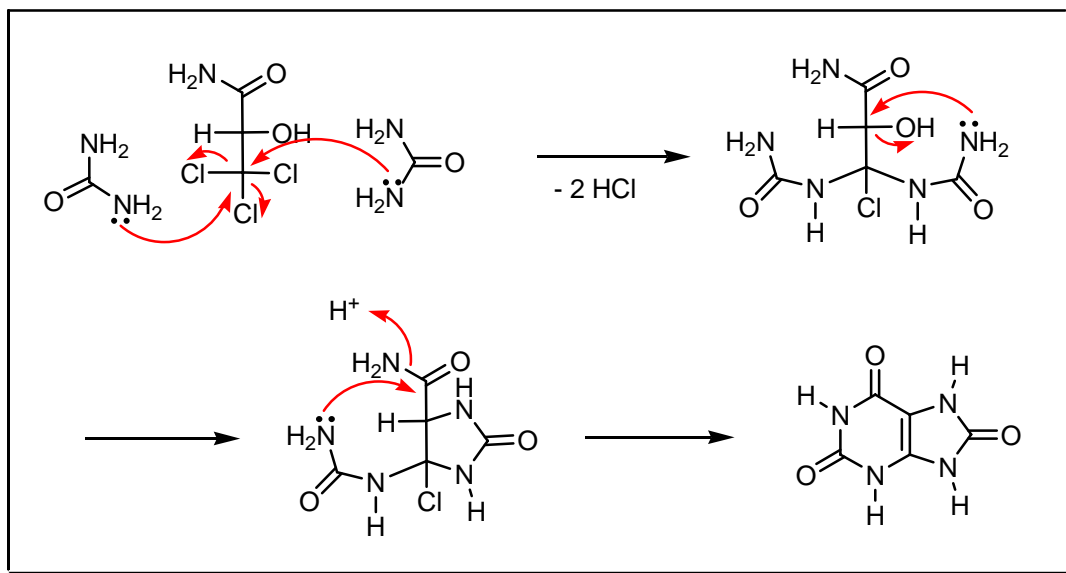
## HORBACZEWSKI SYNTHESIS

### EXAMPLE :

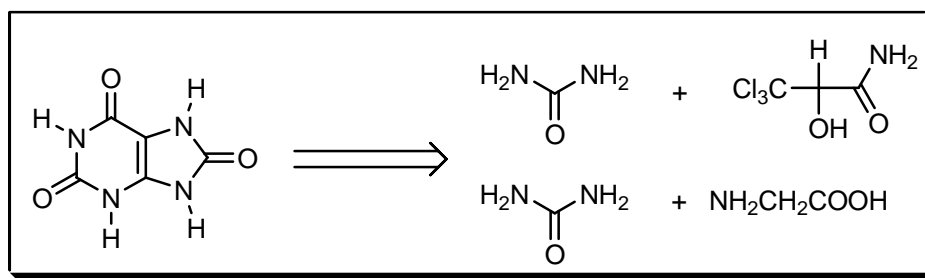




### MECHANISM :



### DISCONNECTION :



### NOTES :

The condensation of glycine or trichlorolactamide with urea yields uric acid. See also **Behrend – Roosen**, **Fischer – Ach** and **Traube** reactions.

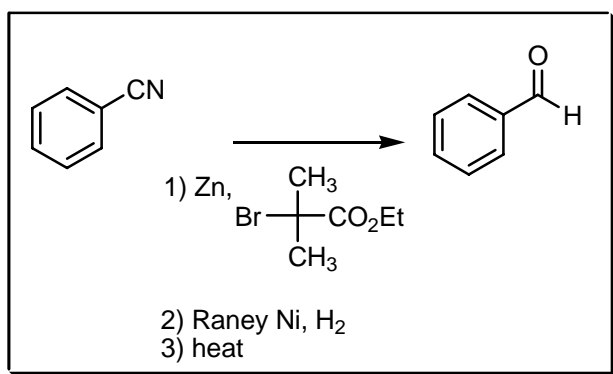
### REFERENCES :

- 1) J. Horbaczewski, *Monatsh. Chem.*, 1882, **3**, 796.
- 2) R. Behrend, *Liebigs Ann. Chem.*, 1925, **441**, 215.

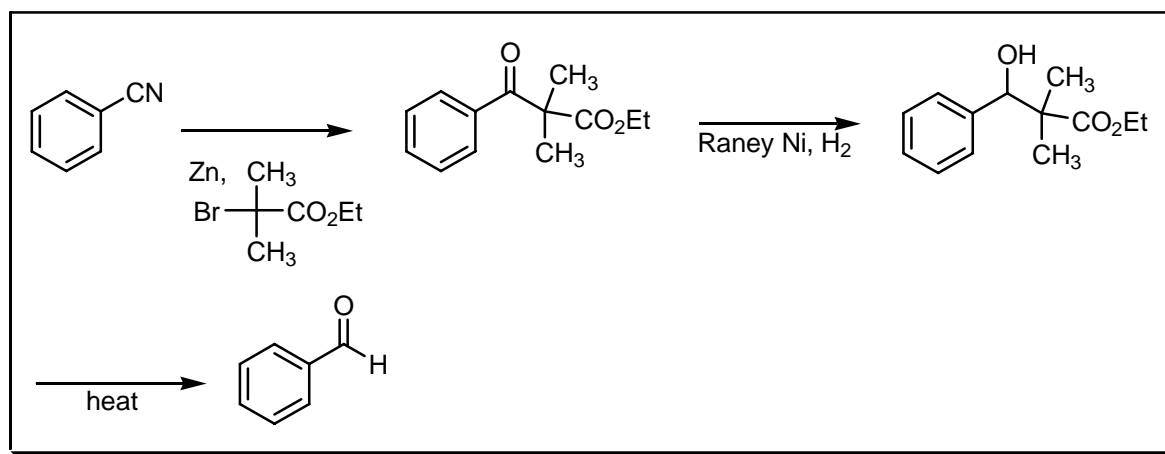
### COMMENTS :

## HOREAU – ORMANCEY SYNTHESIS

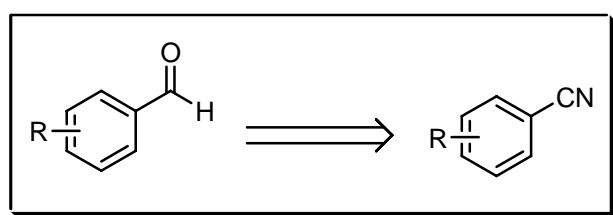
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The interaction of an aromatic nitrile with ethyl 2-bromoisobutyrate (**Blaise** ketoester) in the presence of zinc gives the corresponding  $\beta$ -keto ester. This ester is reduced to the hydroxy-ester, which on heating yields the aldehyde. See also **Blaise** ketoester and **Reformatsky** reactions.

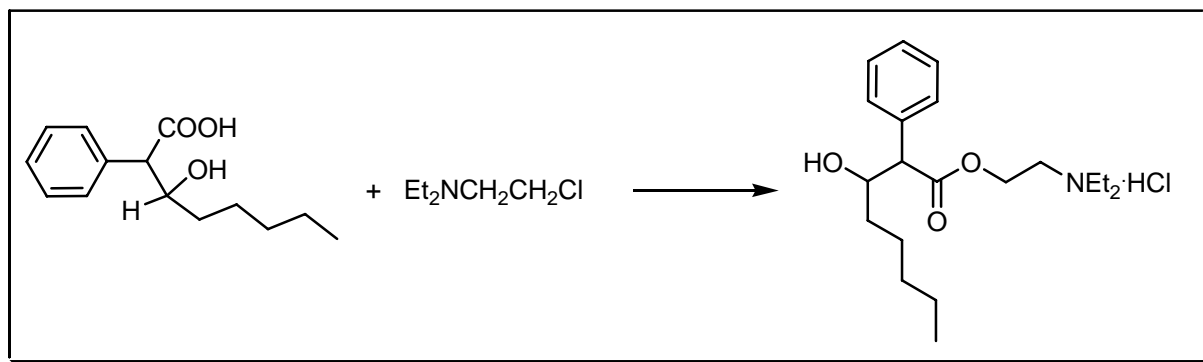
### REFERENCES :

A. Horeau; A. Ormancey, *C.R. Séances Acad. Sci.*, 1953, **236**, 826.

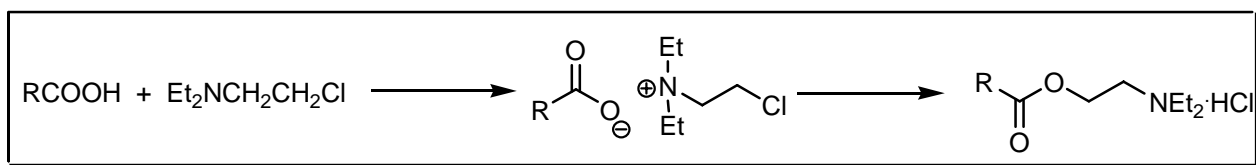
COMMENTS :

## HORENSTEIN – PÄHLICKE ESTERIFICATION

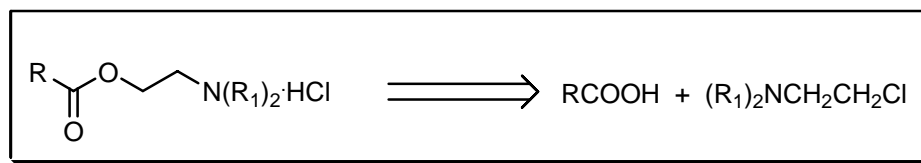
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

This method involves the treatment of acid with a β-dialkylaminoalkyl halide. The resulting salt readily isomerises to the ester.

REFERENCES :

- 1) H. Horenstein; H. Pählicke, *Ber. Dtsch. Chem. Ges.*, 1938, **71**, 1644.
- 2) F.F. Blicke; C. Otsuki, *J. Am. Chem. Soc.*, 1941, **63**, 1945.
- 3) L. Ružička; P.A. Plattner; B.G. Engel, *Helv. Chim. Acta*, 1944, **27**, 1553.
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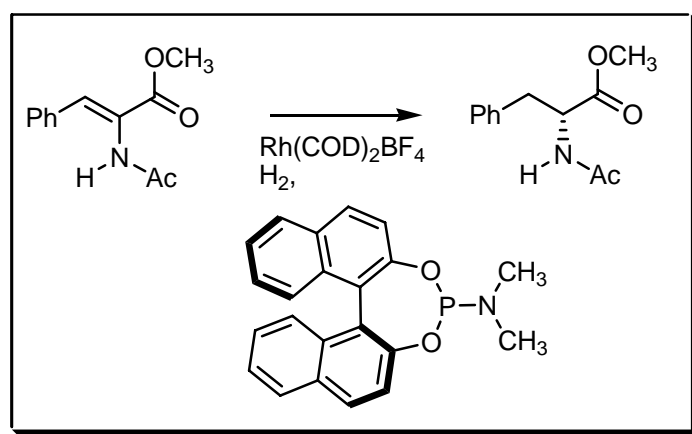
- 5) F.F. Blicke; H. Zinnes, *J. Am. Chem. Soc.*, 1955, **77**, 6247.  
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**COMMENTS :**

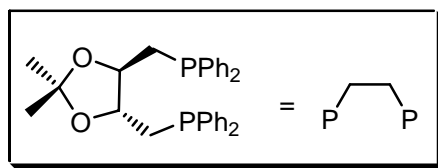
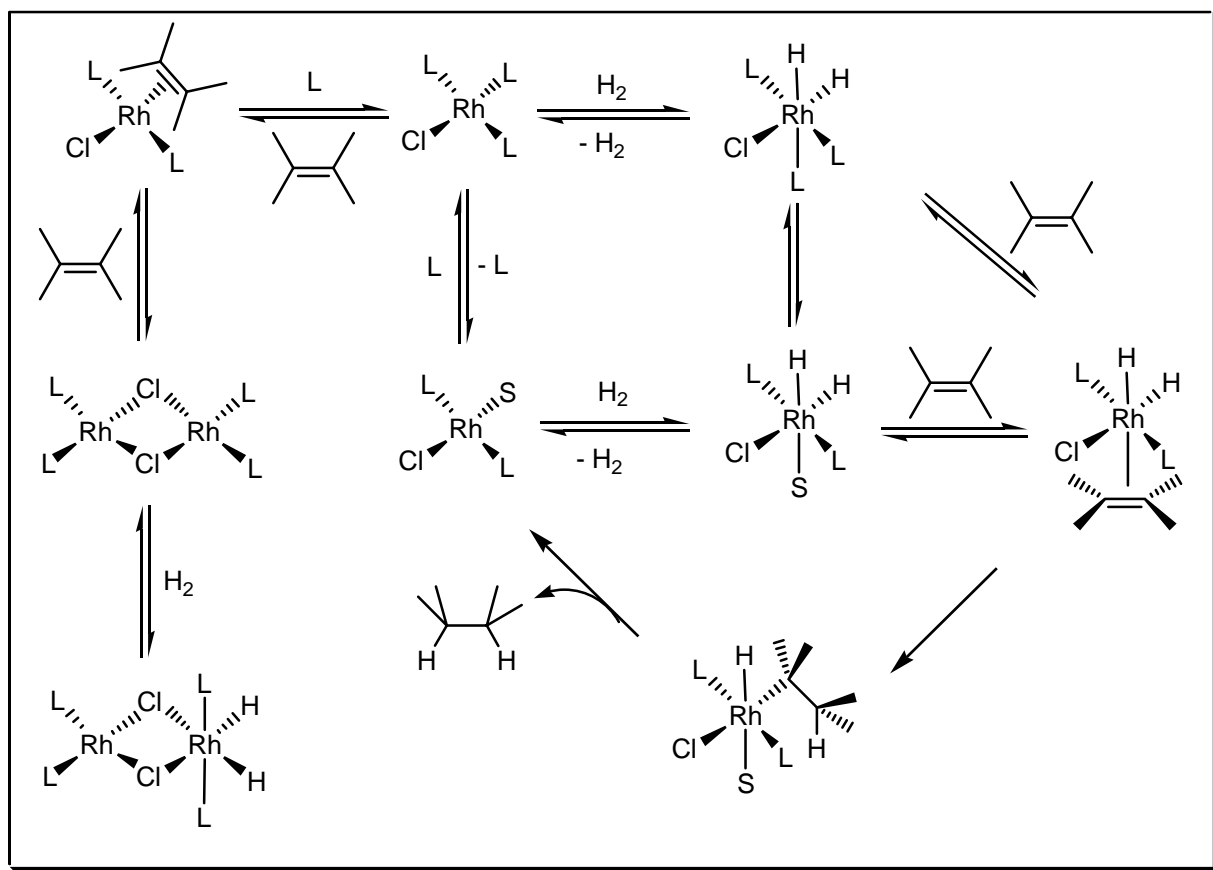
## HORNER – KNOWLES – KAGAN ASYMMETRIC HYDROGENATION

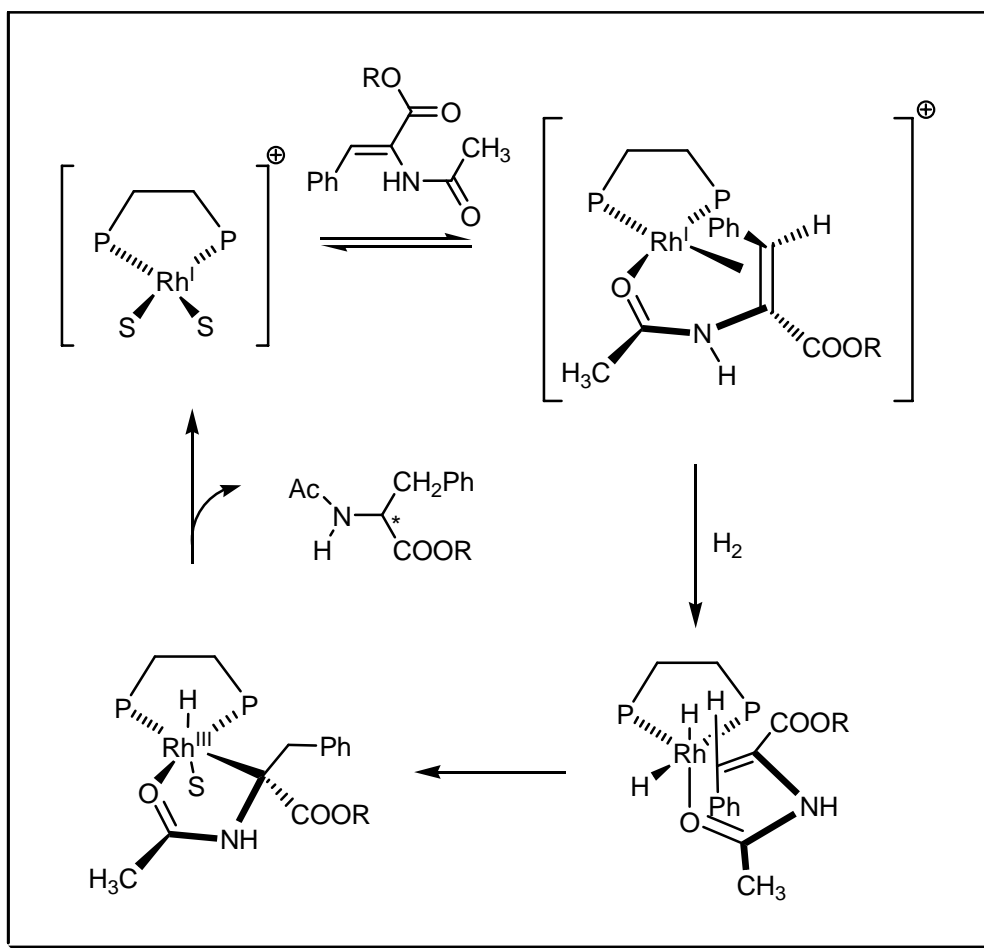
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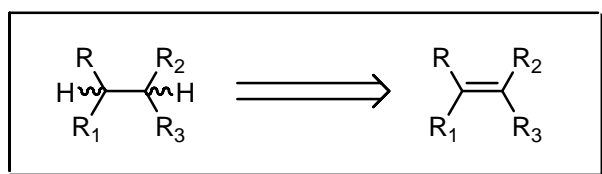


**MECHANISM :**





#### DISCONNECTION :



#### NOTES :

The enantioselective hydrogenation of prochiral olefins with chiral rhodium catalysts and ligands like DIPAMP (**Knowles**), Chiraphos (**Bosnich**), Duphos (**Burk**), DIOP (**Kagan**), Josiphos (**Togni**, **Spindler**), Norphos (**Blaser**, **Spindler**), BINAP (**Noyori**) BICP (**Zhang**), and Ferrophos (**Kang**). In the early years chiral Wilkinson type catalysts were used and monodentate phosphines as ligands (DIOP). In later years bidentate ligands are used affording highly enantioselective hydrogenations.

#### REFERENCES :

Houben – Weyl : 4/1c, 60; E21, 4334

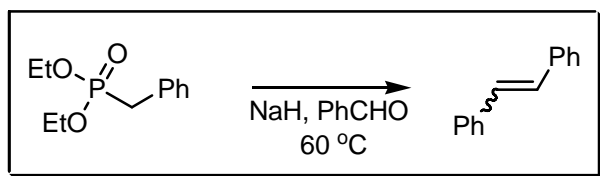
- 1) L. Horner; H. Siegel; H. Buthe, *Angew. Chem., Int. Ed. Engl.*, 1968, **7**, 941.
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- 12) W.S. Knowles, *Adv. Synth. Catal.*, 2003, **345**, 3.
- 13) M. Diéguez; O. Pàmies; C. Claver, *Chem. Rev.*, 2004, **104**, 3189.

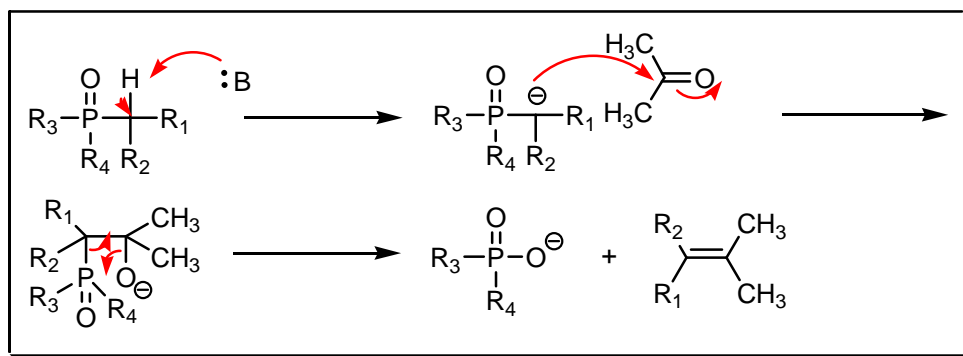
**COMMENTS :**

## HORNER – WADSWORTH – EMMONS REACTION

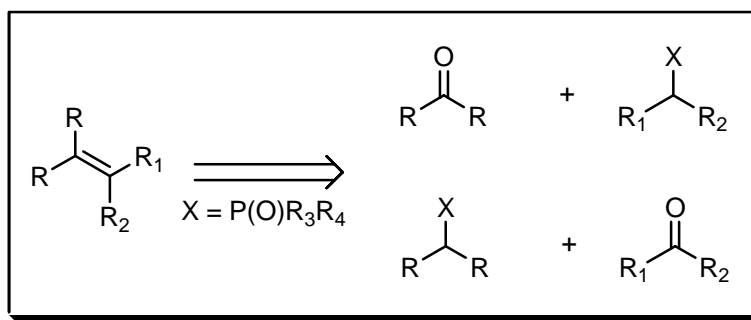
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

This procedure is useful for the transfer of electron-withdrawing groups to the alkene. The asymmetric version has been reported by **Shioiri** *et al.* An unusual alternative to this reaction using a diazoacetate and a rhenium catalyst has been reported by **Ledford** and **Carreira**. Lithium chloride and an amine can be used for base-sensitive compounds. In the **Ando** modification ethyl(diarylphosphono)acetates are used. See also **Corey – Kwiatkowski**, **Corey – Nicolaou**, **Diels – Alder**, **Eastwood**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Hunsdiecker** ring-closure, **Julia – Paris – Kocienski – Lythgoe**, **Keck** macrolactonisation, **Kita**, **Krief – Reich – Chow**, **Masamune**, **McMurry**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Nysted**, **Paquette**, **Petasis** reaction, **Peterson**, **Ramberg – Bäcklund**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Still – Gennari**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Takeda**, **Tebbe**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolakiewicz**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

## REFERENCES :

**March** : 959

**Smith – March** : 1233

**Smith** : 792

**Smith 2<sup>nd</sup>** : 665

**Houben – Weyl** : **E3**, 647; **E7b**, 156; **E8a**, 1001; **E15**, 644, 2632

**Org. Synth.** : **45**, 44; **78**, 177

**Org. Synth. Coll. Vol.** : **5**, 547

**Science of Synthesis** : **9**, 306; **10**, 338

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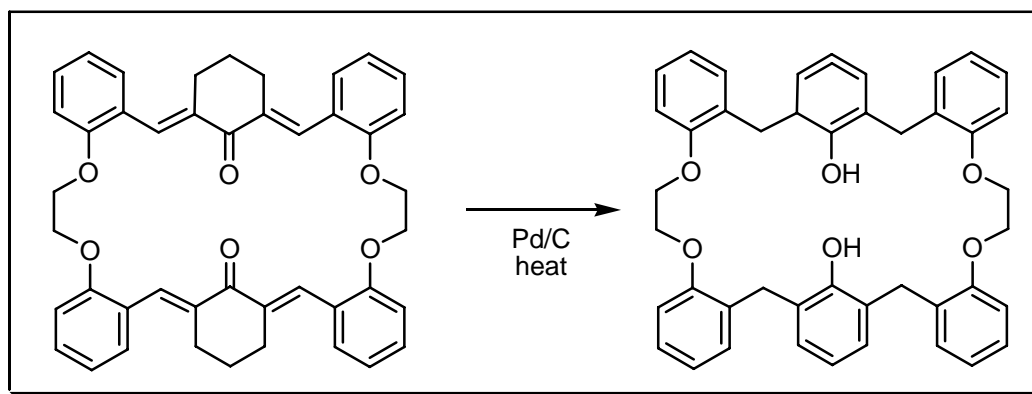
**COMMENTS :**

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**HORNING REACTION**

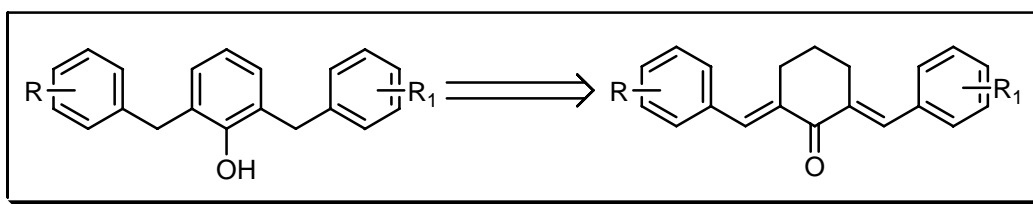
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**EXAMPLE :**



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**DISCONNECTION :**



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**NOTES :**

The thermolysis of a dibenzylidenephthalone to a dibenzylphenol in the presence of a palladium catalyst. The reaction is nowadays used to make crown macrocycles.

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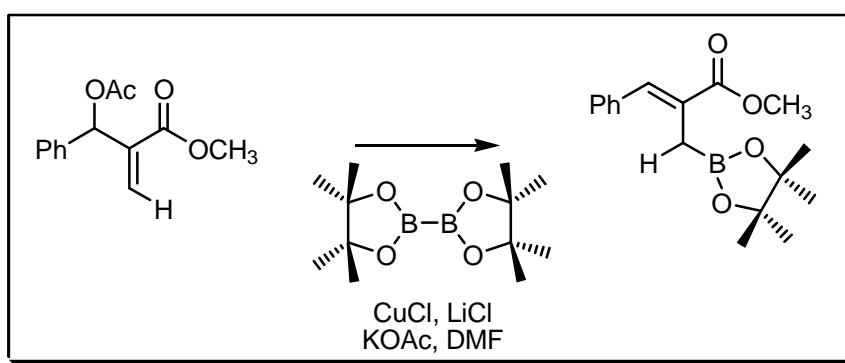
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- 

**COMMENTS :**

## HOSOMI – MIYAURA BORYLATION

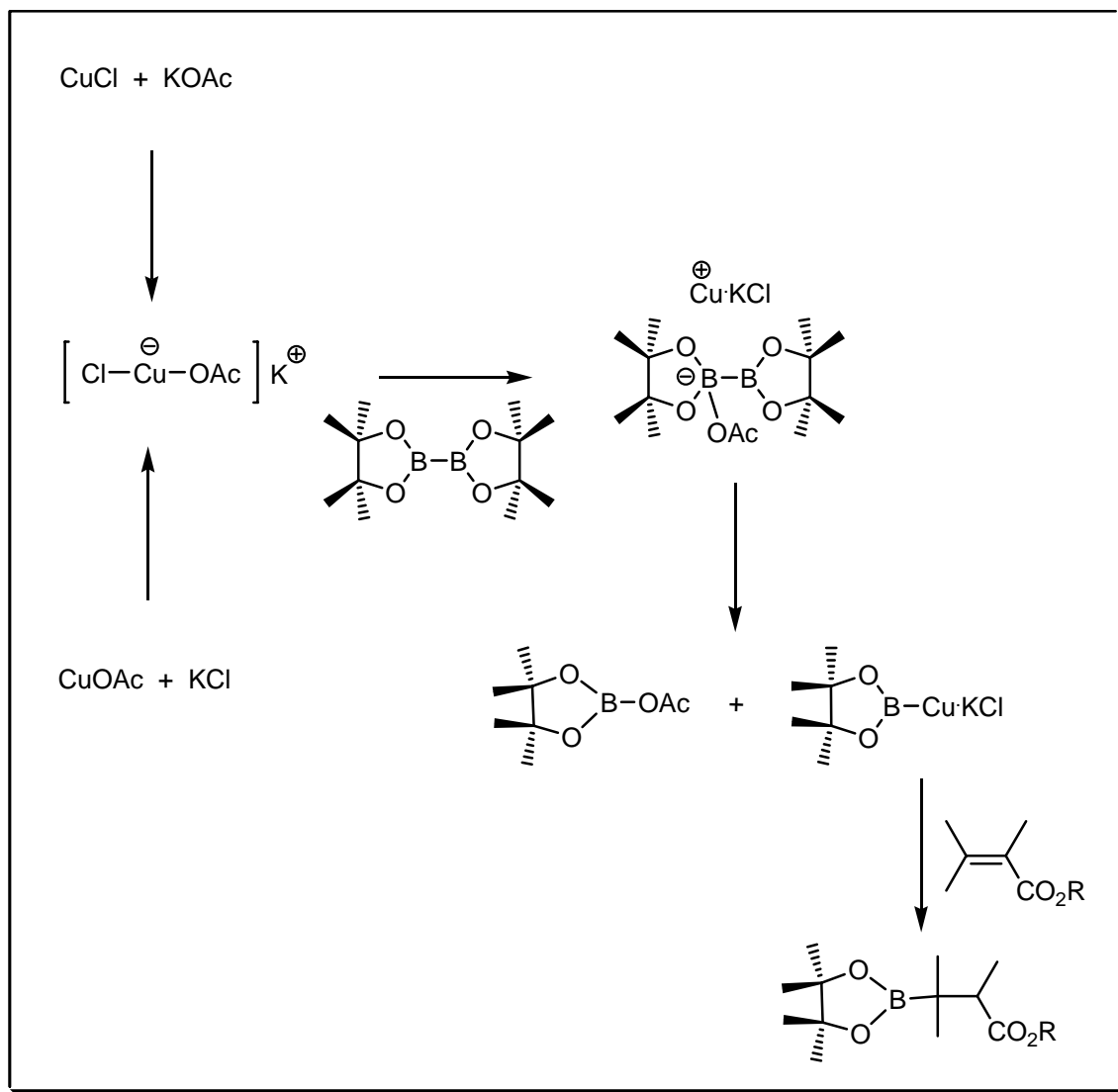
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**EXAMPLE :**

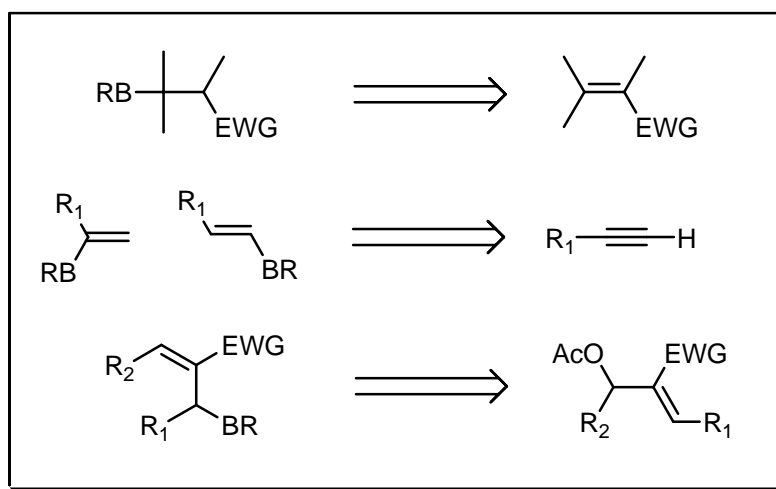


**MECHANISM :**

**Miyaura :**



**DISCONNECTION :**



## NOTES :

The 1,4-addition of nucleophilic boryl copper species generated *in situ* from diboronates to simple  $\alpha,\beta$ -unsaturated compounds. This reaction was later expanded to allyl acetates and terminal alkynes. The mechanism under the **Hosomi** conditions is not fully understood. **Miyaura**-conditions : CuCl, LiCl, KOAc and DMF. **Hosomi**-conditions : CuCl or  $(\text{CuOTf})_2\text{C}_6\text{H}_6$ ,  $\text{Bu}_3\text{P}$  and DMF.

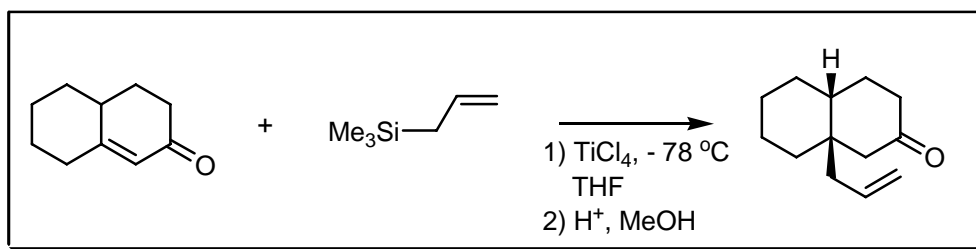
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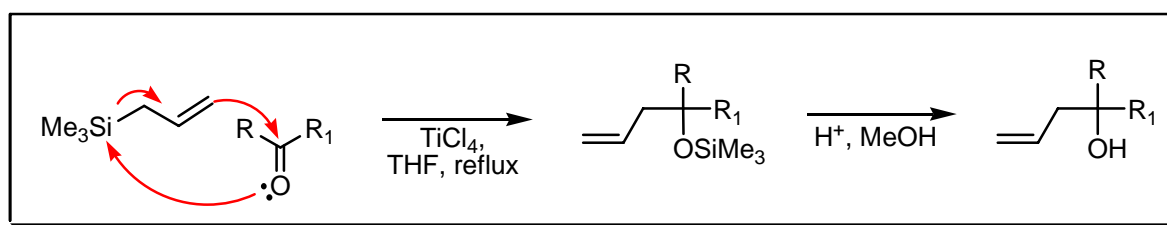
## COMMENTS :

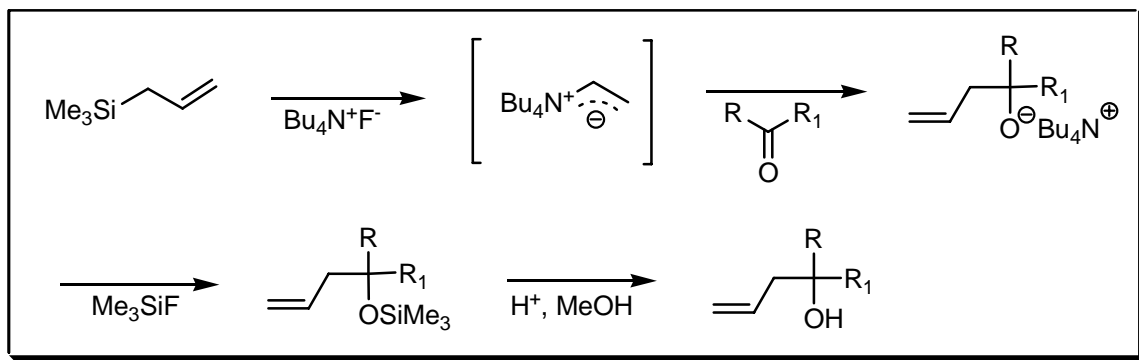
## HOSOMI – SAKURAI ALLYLATION

### EXAMPLE :

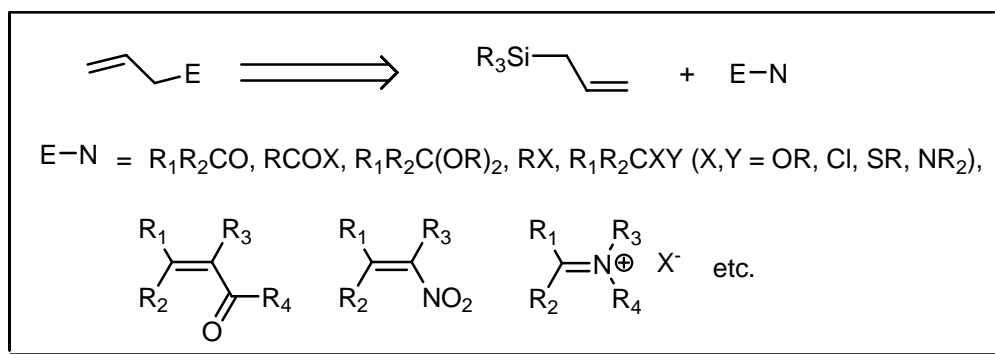


### MECHANISM :





## DISCONNECTION :



## NOTES :

The Lewis acid mediated *inter*- or *intramolecular* addition of allylic silanes to  $\alpha,\beta$ -unsaturated ketones or to ketones, aldehydes and many other compounds, see **Hosomi** review. **Hou et al.** reported on a fluoride-triggered reaction, while **Baba et al.** reported an indium(III) chlorotrimethylsilane catalyst system.

## REFERENCES :

**March** : 797

**Smith – March** : 1024

**Smith** : 1375

**Smith 2<sup>nd</sup>** : 1130

**Org. React.** : **37**, 57

**Org. Synth.** : **62**, 86

**Org. Synth. Coll. Vol.** : **7**, 443

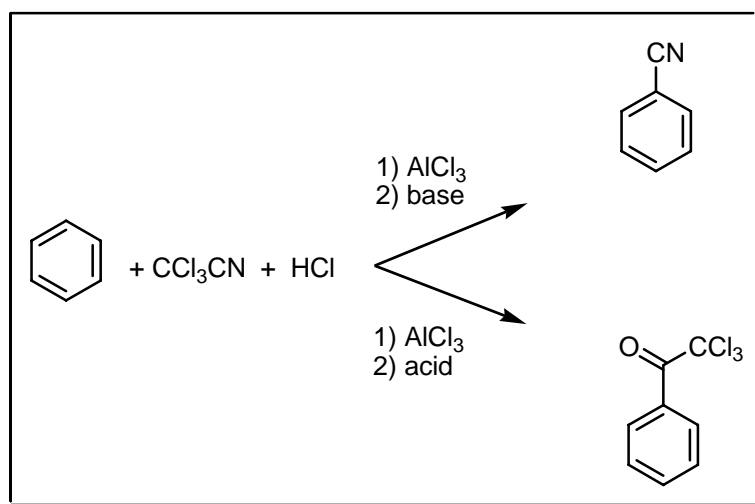
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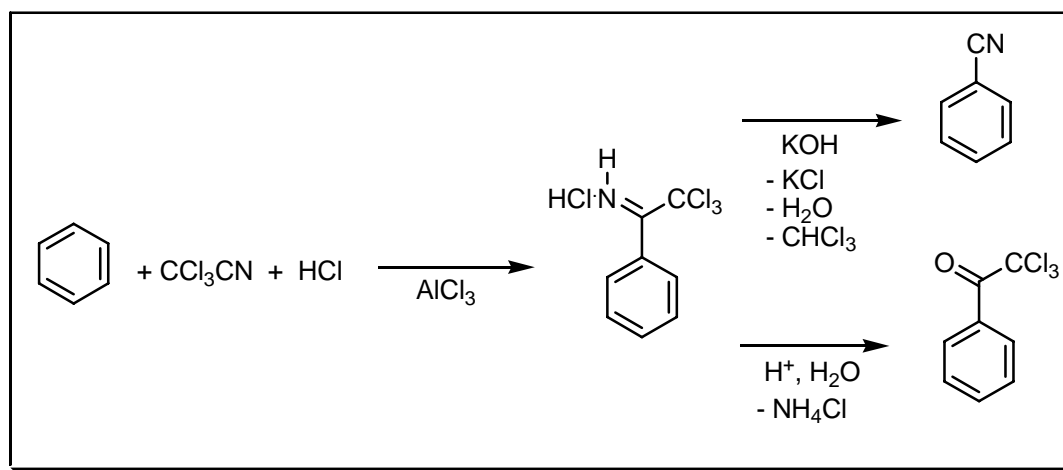
**COMMENTS :**

## HOUBEN – FISCHER SYNTHESIS

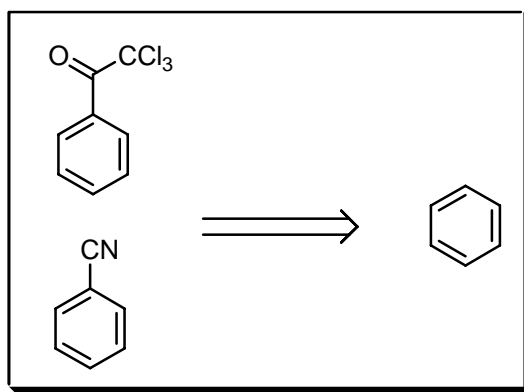
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

The ketimine hydrochloride obtained from aromatic hydrocarbons or phenols, when trichloroacetonitrile is used in the **Hoesch – Houben** synthesis of aryl ketones gives with alkali the corresponding aromatic nitrile in excellent yield. With acid the trichloromethyl aryl ketones are obtained. See also **Friedel – Crafts – Karrer**, **Houben – Hoesch** and **Rosenmund – von Braun** reactions.

## REFERENCES :

**Houben – Weyl** : 4/2, 103; **E6a**, 976

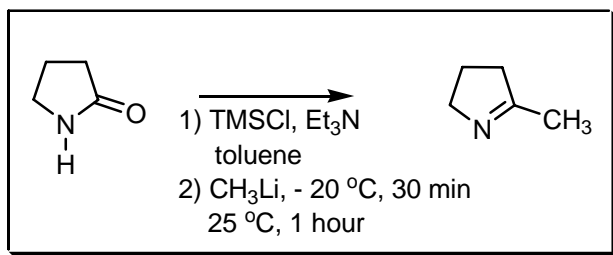
**Org. React.** : 5, 390

- 1) J. Houben; W. Fischer, *J. Prakt. Chem.*, 1929, **123**, 313.
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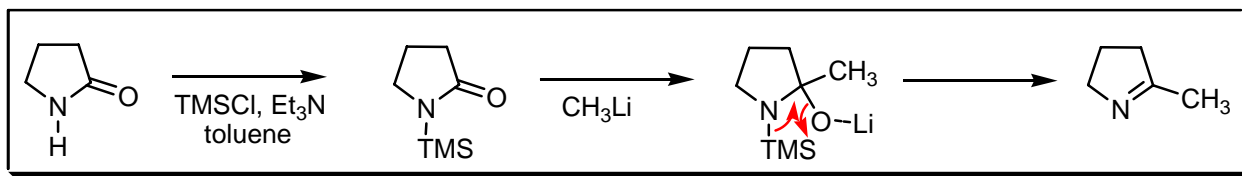
## COMMENTS :

## HUA REACTION

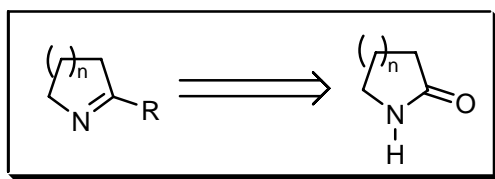
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The nucleophilic addition of alkyl lithium reagents to *N*-(trimethylsilyl)lactams to give cyclic ketimines in high yields.

### REFERENCES :

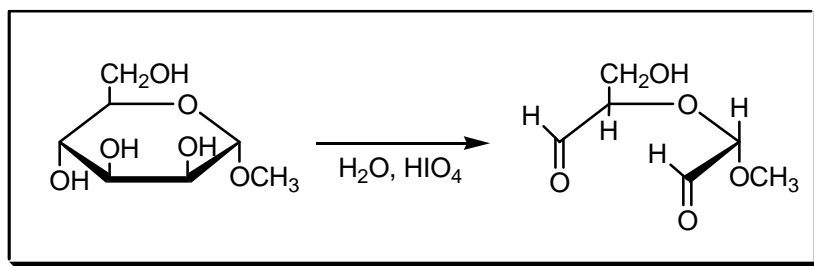
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### COMMENTS :

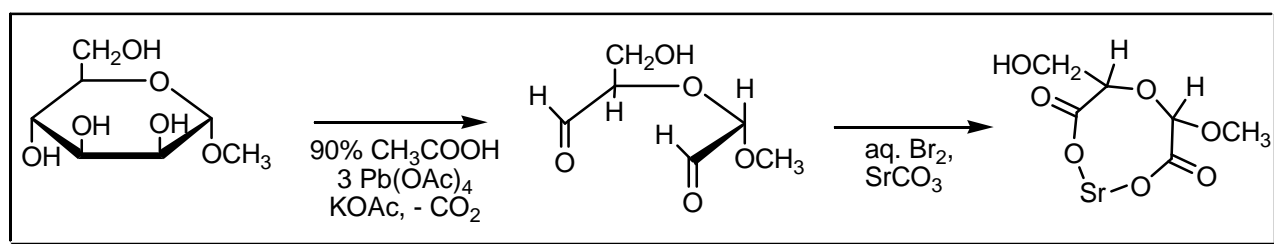


## HUDSON – JACKSON OXIDATION

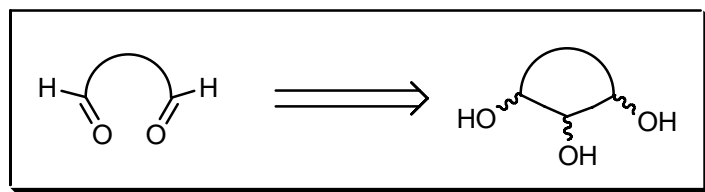
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Glycosides are oxidised by periodic acid to yield a dialdehyde by cleavage of the 2,3,4-triol group. The dialdehyde can be further oxidised by bromine water in the presence of strontium carbonate to the strontium salt of the diacid (Barium salts can also be used.). This cleavage type of oxidation, provides a method for the determination of ring structure and for the correlation of the configuration of carbon atom 1 of glycosides. It also affords a direct way of correlating the configuration of sugars with glyceric acid. See also **Criegee** glycol cleavage, **Djerassi – Rylander** and **Lemieux – Johnson** reactions.

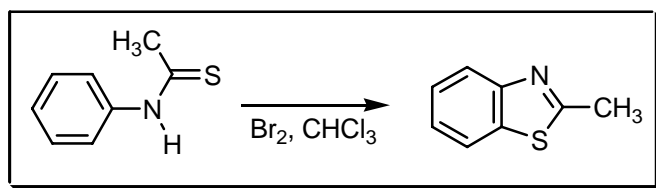
### REFERENCES :

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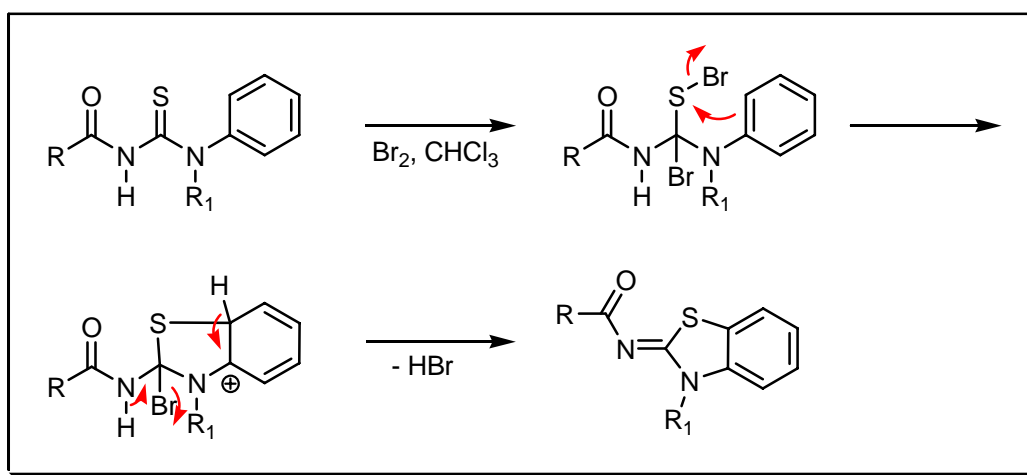
COMMENTS :

## HUGERSHOFF REACTION

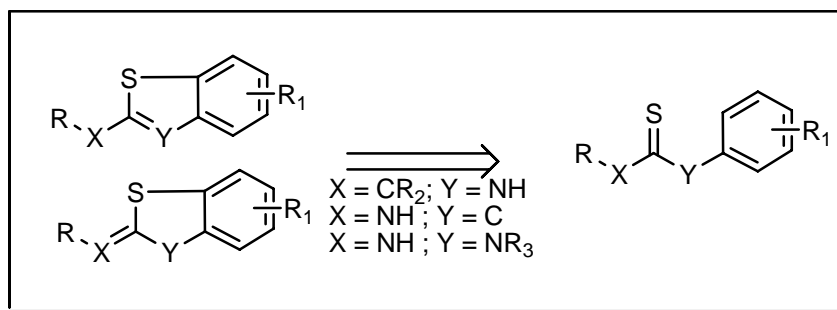
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The oxidative C-S bond formation with iodine, bromine or thionyl chloride. See also **Werner** reaction.

## REFERENCES :

Houben – Weyl : E8a, 692

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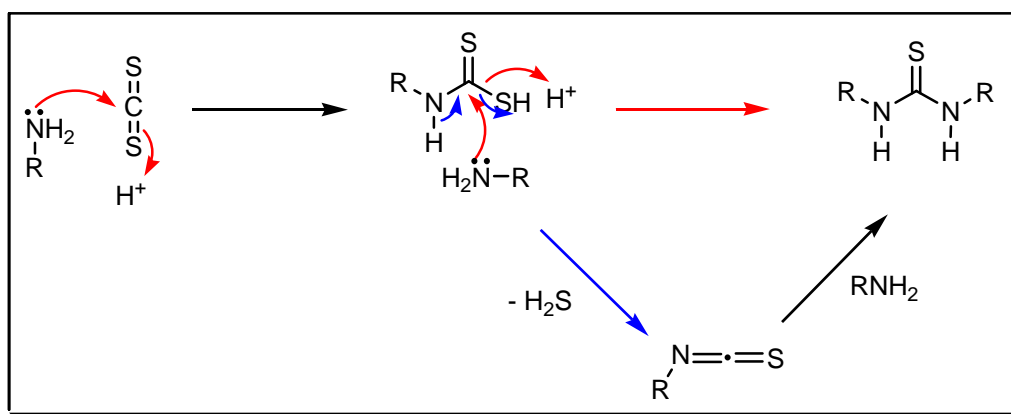
## COMMENTS :

## HUGERSHOFF SYNTHESIS

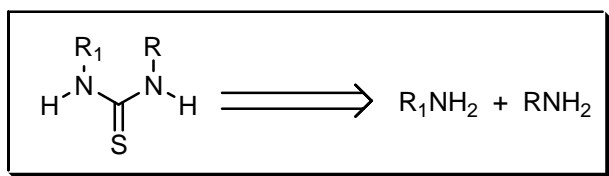
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

Symmetrical *N,N'*-diarylthioureas are obtained by heating a primary aryl amine with carbon disulfide and sulfur in ethanol.

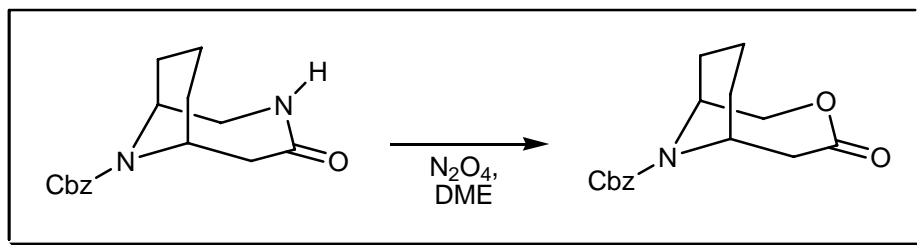
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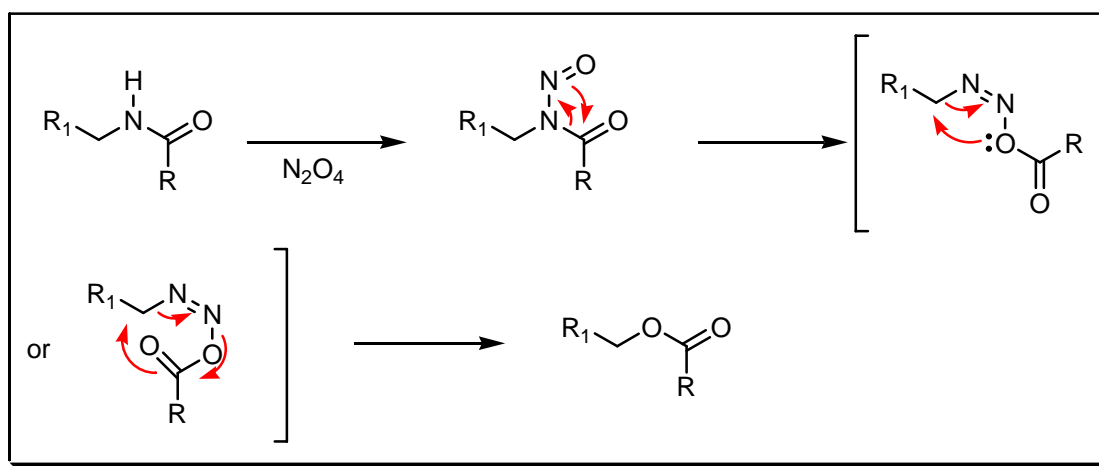
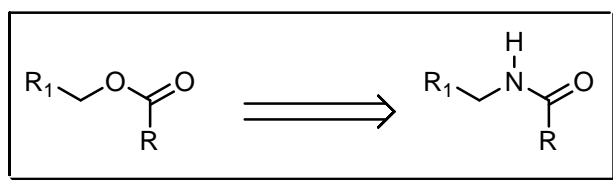
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## COMMENTS :

## HUISGEN – WHITE REACTION

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

The rearrangement of amides into esters by thermolysis of the corresponding *N*-nitroso intermediates.

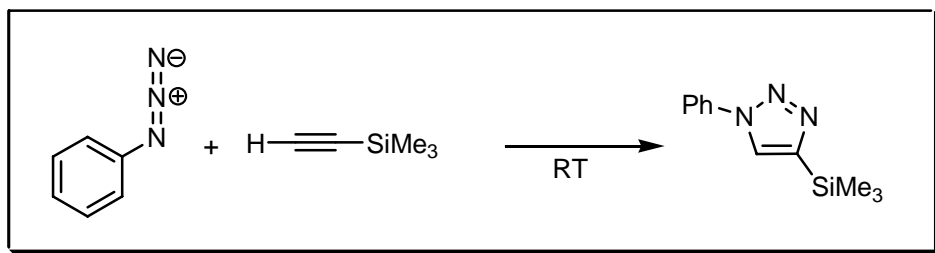
**REFERENCES :**

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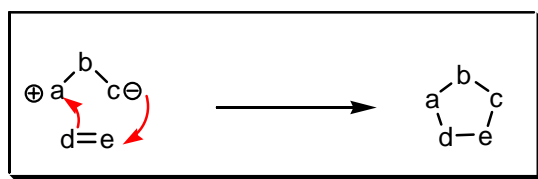
**COMMENTS :**

# HUISGEN REACTION

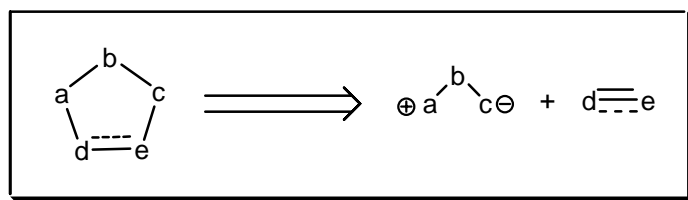
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The cycloaddition of 1,3-dipoles e.g. azides, nitrones, nitrile oxides, diazoalkenes, azomethine ylides with olefins or acetylenes. See also **Alder** ene, **Banert** Cascade, **Diels – Alder**, **Finegan** and **Harries** ozonide reactions.

## REFERENCES :

March : 836

Smith – March : 1059

Smith : 1208

Smith 2<sup>nd</sup> : 999

Org. React. : 36,1 ; 51, 3

Org. Synth. : 46, 96, 127; 49, 70; 53, 59; 58, 106; 67, 133

Org. Synth. Coll. Vol. : 5, 504, 957, 1124; 6, 670, 592; 8, 231

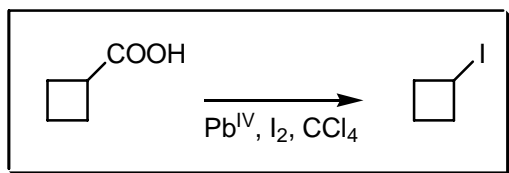
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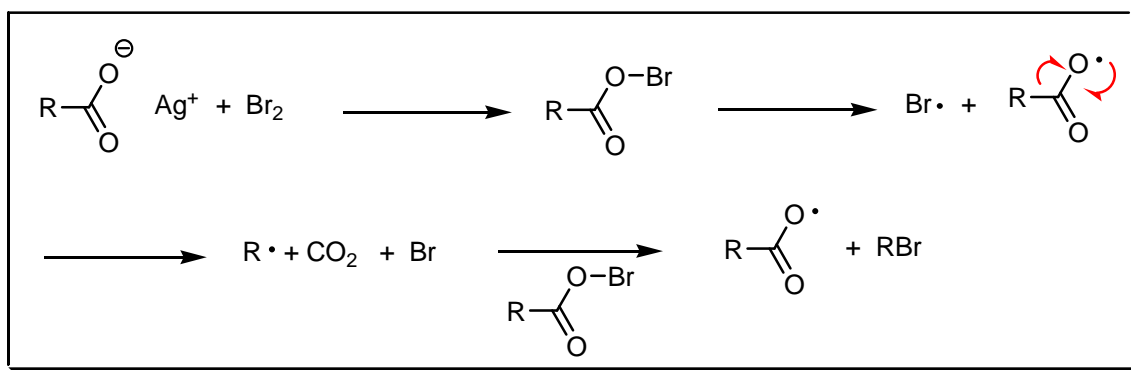
**COMMENTS :**

## HUNSDIECKER – BORODINE REACTION

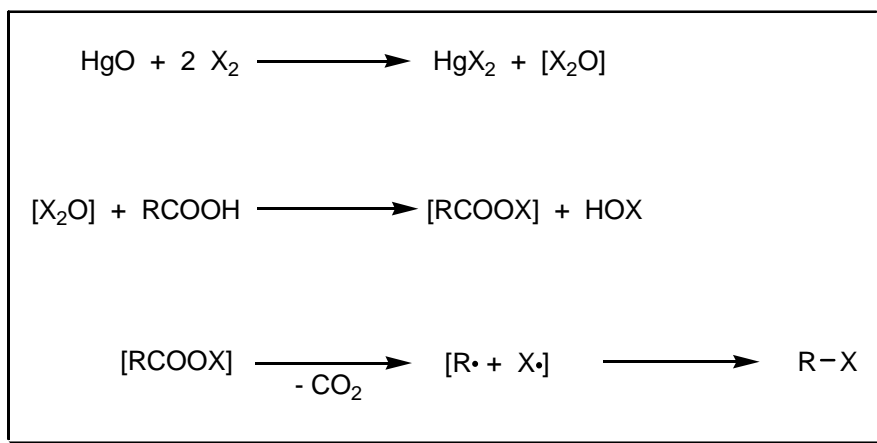
**EXAMPLE :**



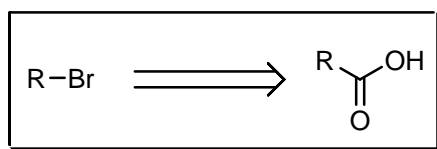
**MECHANISM :**



### Cristol – Firth :



### DISCONNECTION :



### NOTES :

This reaction can be summarised as a decarboxylative bromination or iodination. The **Cristol – Firth** modification of this reaction uses a mixture of the acid and mercuric oxide. When iodine is used with a two-fold excess of the acid salt, the reaction is known as the **Birnbaum – Simoni** reaction, and the product is an ester. There is also a thallium modification. See also **Birnbaum – Simoni**, **Kochi** decarboxylation and **Prévost** reactions.

### REFERENCES :

**March** : 730

**Smith – March** : 899, 942

**Smith** : 155

**Smith 2<sup>nd</sup>** : 125, 254

**Houben – Weyl** : **E5**, 367; **E7b**, 630; **E19a**, 365

**Org. React.** : **9**, 332; **19**, 279

**Org. Synth.** : **26**, 52; **43**, 9; **51**, 106

**Org. Synth. Coll. Vol.** : **3**, 578; **5**, 126; **6**, 179

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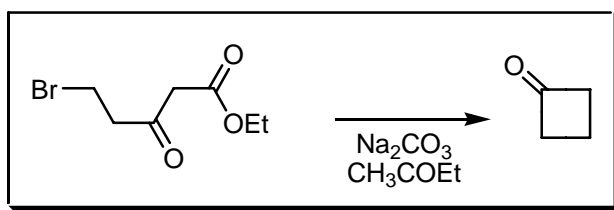
**COMMENTS :**

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**HUNSDIECKER RING-CLOSURE**

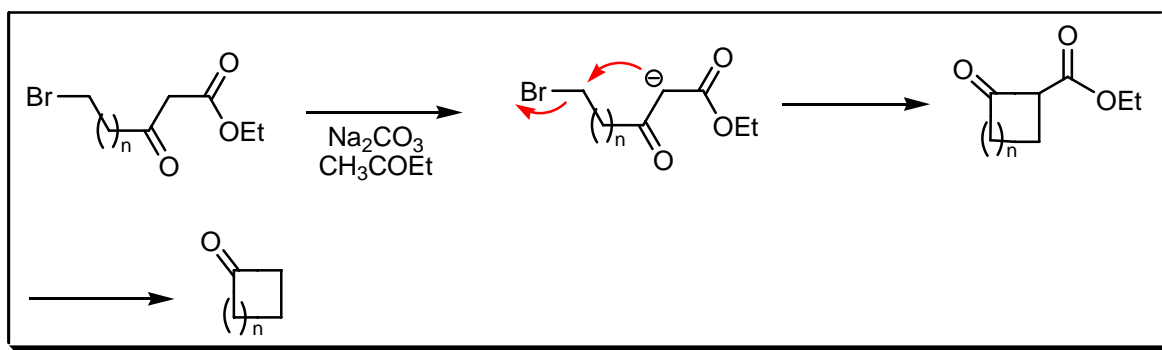
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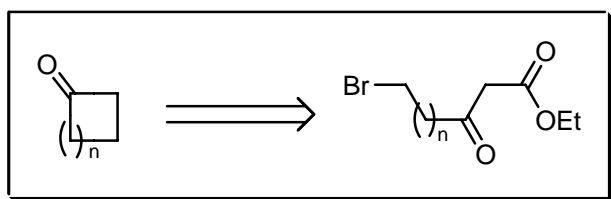
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**MECHANISM :**



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**DISCONNECTION :**



## NOTES :

This preparation involves the *intramolecular* condensation of an  $\omega$ -halogenacylacetic ester to yield a cyclic  $\beta$ -ketoester which on hydrolysis and decarboxylation furnishes the corresponding cyclic ketone. This reaction is carried out in high dilution in methyl ethyl ketone and alkali carbonate is employed as a condensing agent. See also **Corey – Nicolaou**, **Diels – Alder**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Keck** macrolactonisation, **Kita**, **Masamune**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolikiewicz**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

## REFERENCES :

Houben – Weyl : 4/2, 754

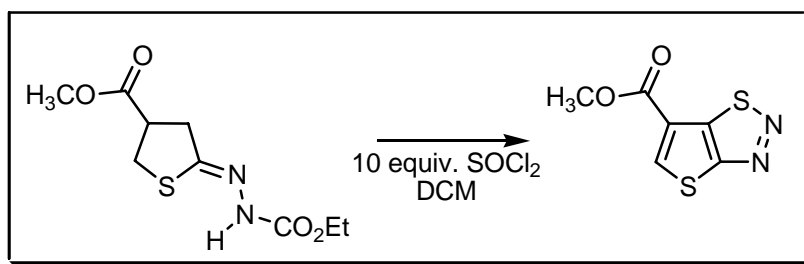
1) H. Hundiecker, *Ber. Dtsch. Chem. Ges.*, 1942, **75**, 1190.

2) M. Stoll, *Helv. Chim. Acta*, 1947, **30**, 1401.

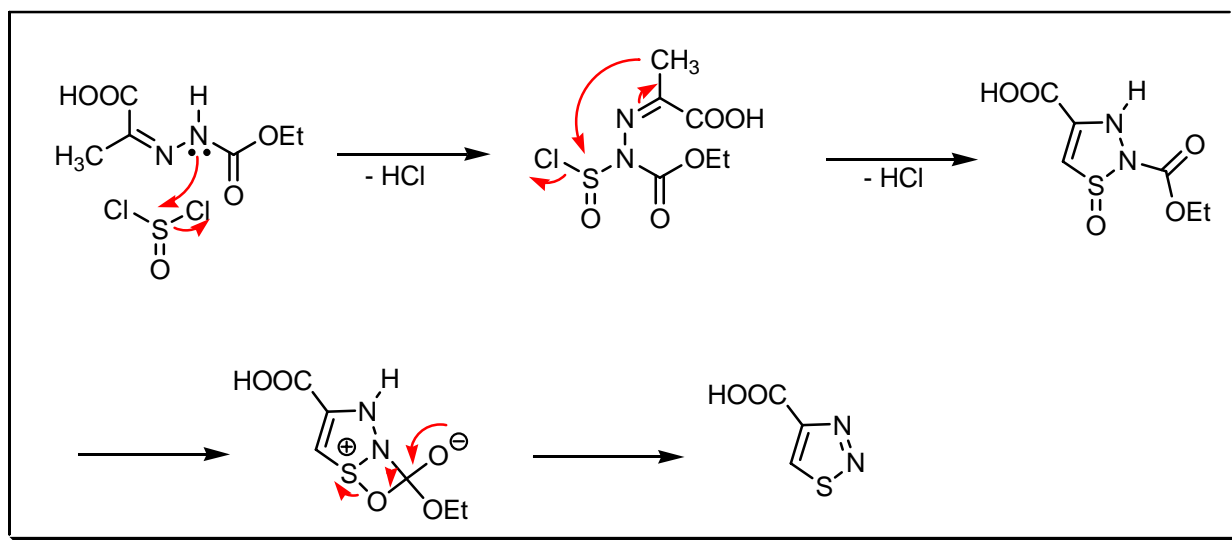
## COMMENTS :

## HURD – MORI REACTION

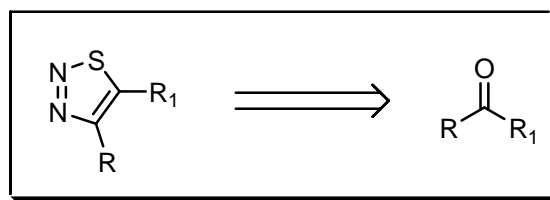
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The formation of 1,2,3-thiadiazoles from hydrazones by cyclisation using thionyl chloride.

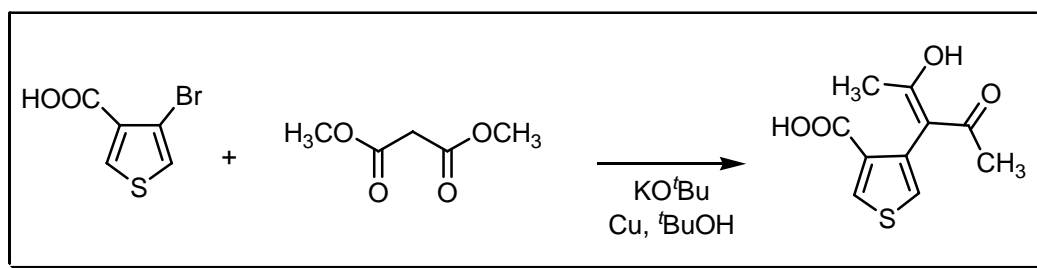
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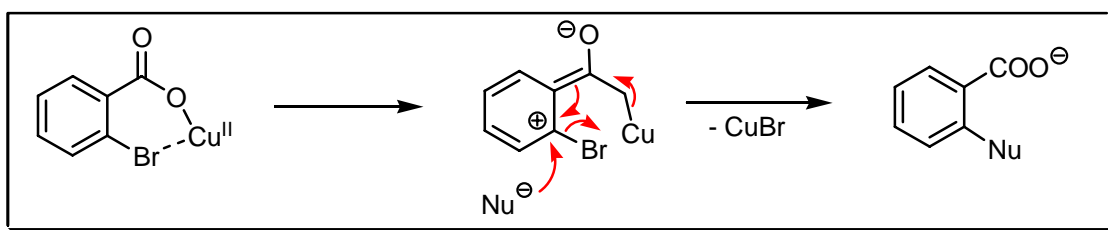
## COMMENTS :

## HURTLEY REACTION

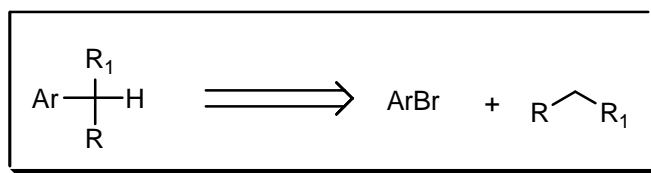
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The arylation of compounds with active methylene groups of the form  $\text{RCH}_2\text{R}_1$ . Activated aryl halides give good results. The **Hurtley** reaction uses copper halide catalysts (or palladium complexes) to react unactivated halides.

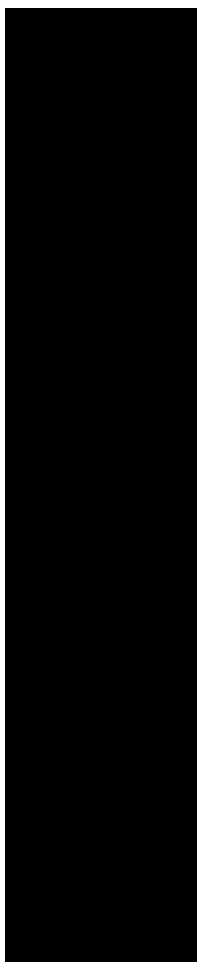
### REFERENCES :

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**Smith – March** : 869

- 1) W.R.H. Hurtley, *J. Chem. Soc.*, 1929, 1870.
- 2) J.A. Lowe; M.E. Newman, *Synth. Commun.*, 1987, **17**, 803.
- 3) H.L. Aalten; G. van Koten; K. Goubitz; C.H. Stam, *Organometallics*, 1989, **8**, 2293.
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**COMMENTS :**



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**G**

GABRIEL – ISAY REACTION · 889

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**I**

IBUKA – YAMAMOTO 1,3-CHIRALITY TRANSFER · 879

IMAMOTO ALKYLATION · 880

INANAGA INDOLE SYNTHESIS · 881

ING – MANSKE PROCEDURE · 883

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IRVINE – PURDIE SUGAR METHYLATION · 887

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ISLER SYNTHESIS · 890

IVANOV REACTION · 893

IWAO INDOLE SYNTHESIS · 894

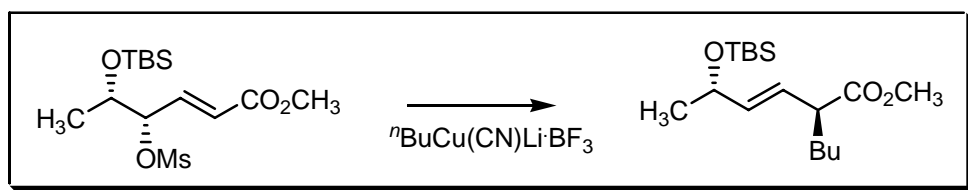
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**K**

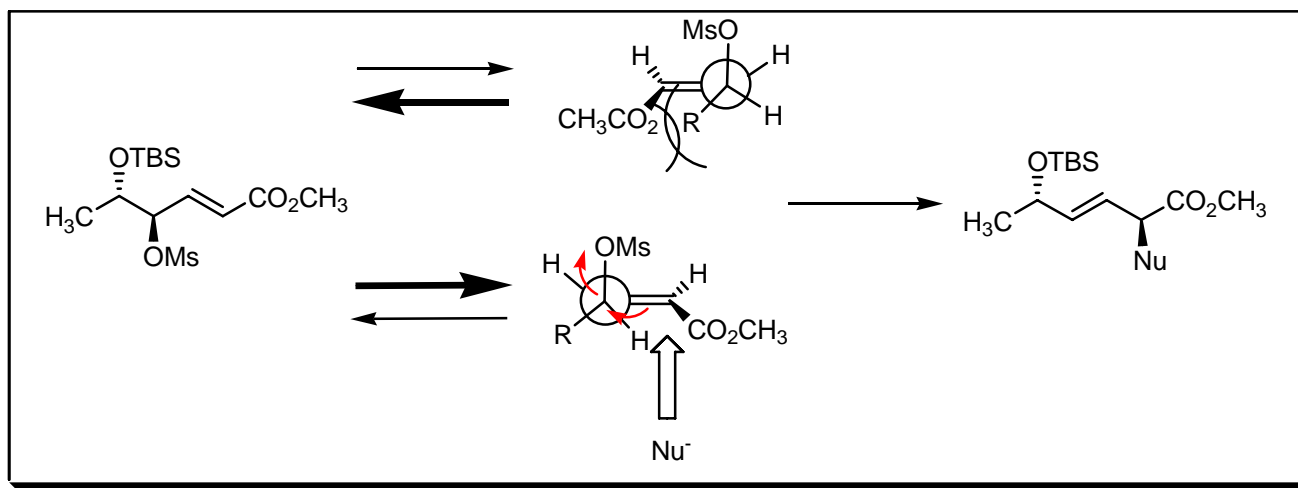
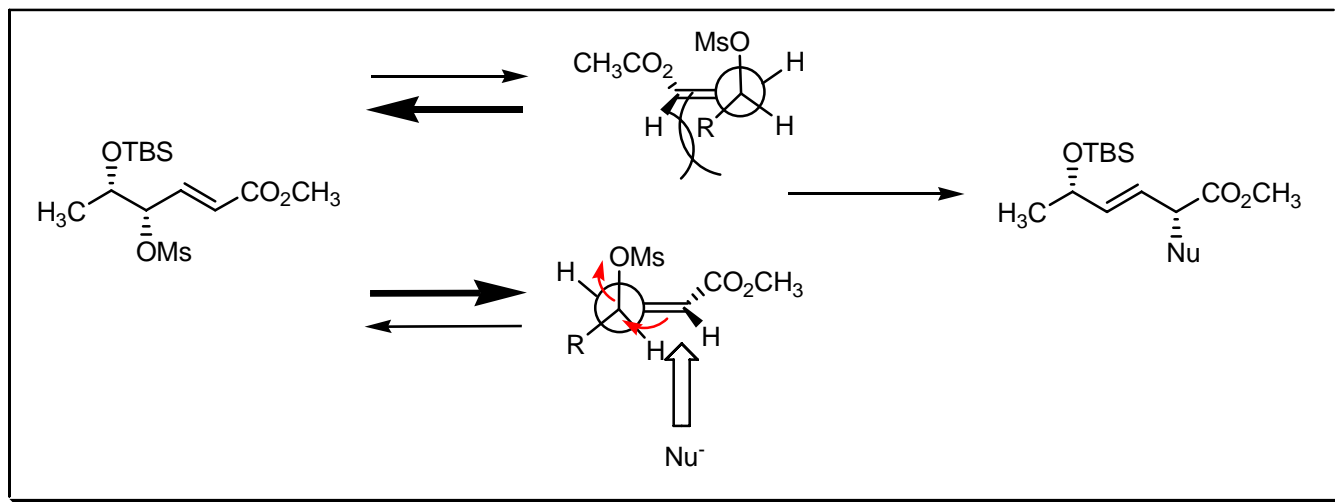
KUHN MODIFICATION · 888

## IBUKA – YAMAMOTO 1,3-CHIRALITY TRANSFER

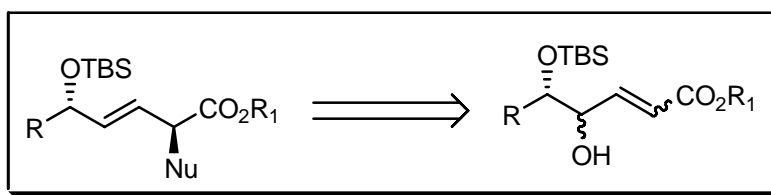
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :





## NOTES :

Both (*E*) and (*Z*)- $\alpha,\beta$ -enolates are transformed into (*E*)-alkenes. This diastereoselectivity is due to unfavourable interactions between the bulky R-group and the hydrogen or between the R-group and the methoxycarbonyl. As a result the nucleophile attacks *anti* to the mesyloxy group. See also **Duthaler – Hafner**, **Matteson**, **Roush – Hoffmann – Yamamoto** and **Thomas** reactions.

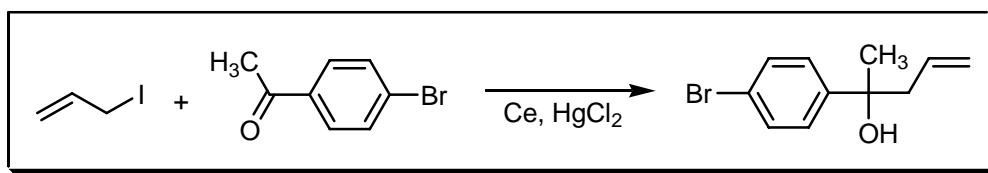
## REFERENCES :

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- 2) T. Ibuka; N. Akimoto; M. Tanaka; S. Nishii; Y. Yamamoto, *J. Org. Chem.*, 1989, **54**, 4055.
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- 4) T. Ibuka; K. Nakai; H. Habashita; K. Bessho; N. Fujii; Y. Chounan; Y. Yamamoto, *Tetrahedron*, 1993, **49**, 9479.

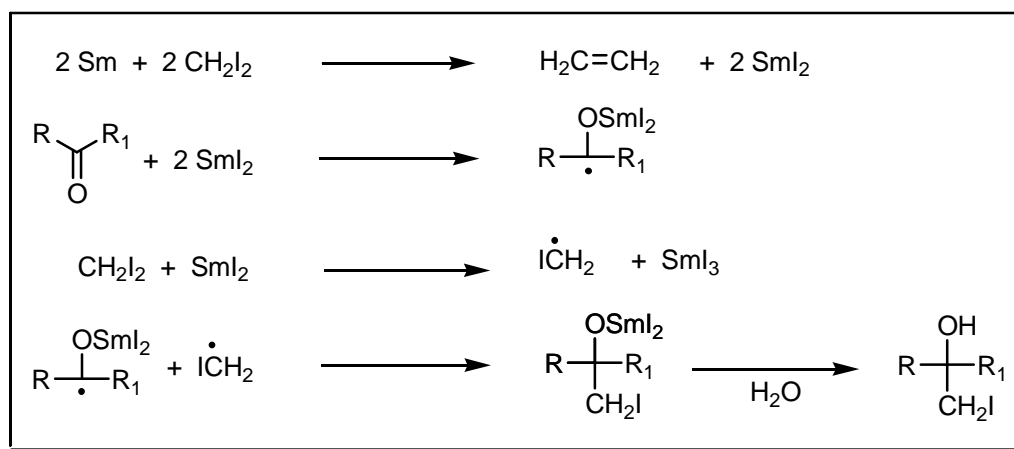
## COMMENTS :

## IMAMOTO ALKYLATION

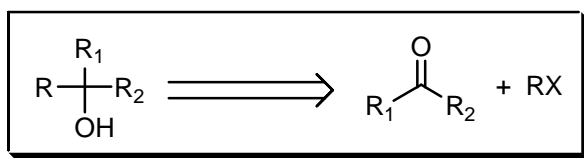
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The cerium or samarium mediated **Barbier**-type and **Reformatsky**-type alkylation of ketones and aldehydes in the presence of esters, nitrile and aryl bromides. See also **Barbier**, **Kagan – Molander** and **Reformatsky** reactions.

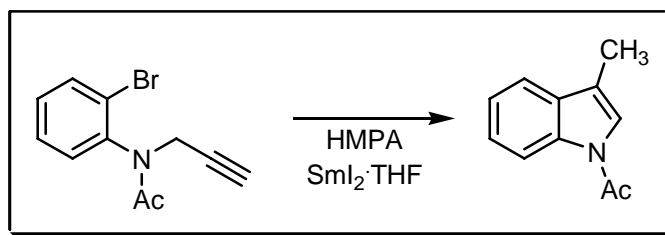
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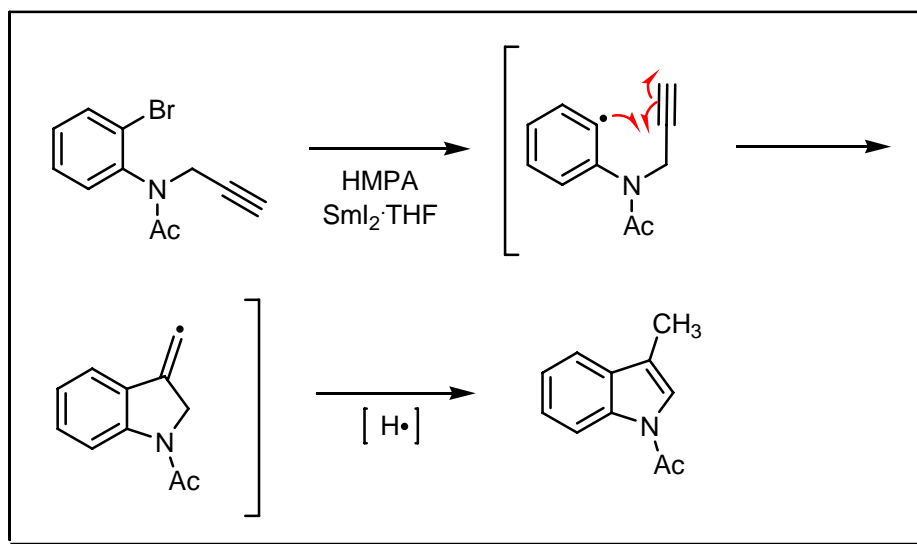
## COMMENTS :

## INANAGA INDOLE SYNTHESIS

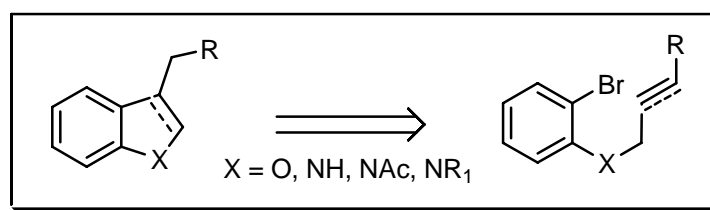
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The samarium iodide mediated electron transfer to synthesise 3-substituted indoles or benzofurans. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

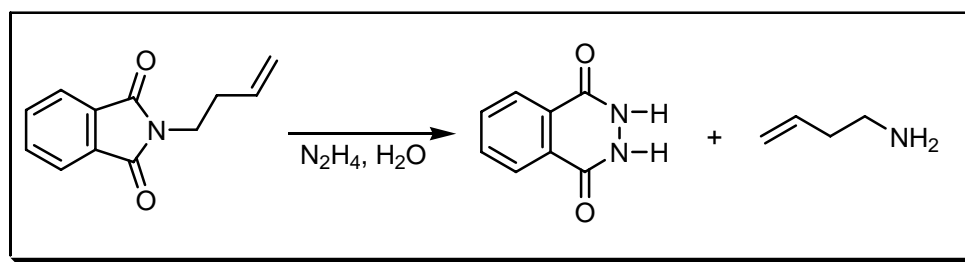
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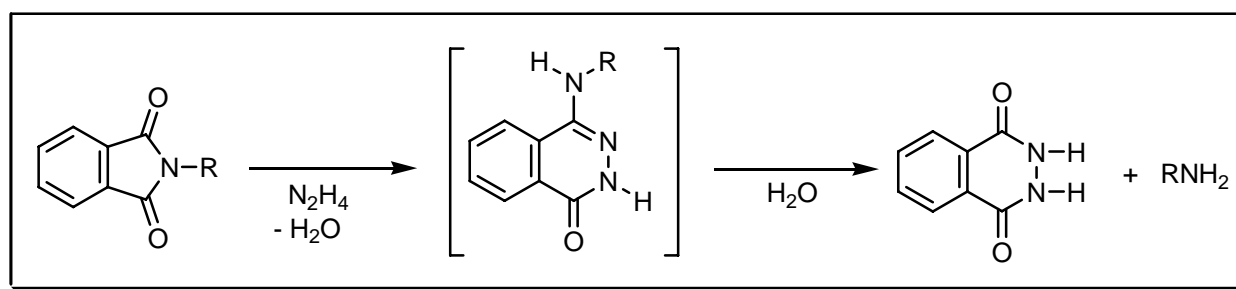
## COMMENTS :

## ING – MANSKE PROCEDURE

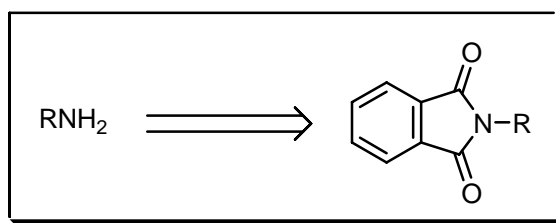
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The *N*-alkylphthalimide formed in the **Gabriel** synthesis reacts with ethanolic hydrazine hydrate to form an intermediate product, which is readily decomposed by acids to yield primary amines and phthalylhydrazine. See also **Gabriel** synthesis and **Sheehan – Frank** reactions.

### REFERENCES :

March : 426

Smith – March : 513

Smith : 473

Smith 2<sup>nd</sup> : 112, 411

Org. Synth. : 12, 10; 27, 12

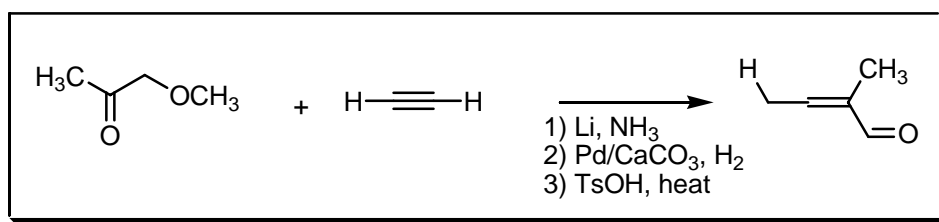
Org. Synth. Coll. Vol. : 2, 83; 3, 148

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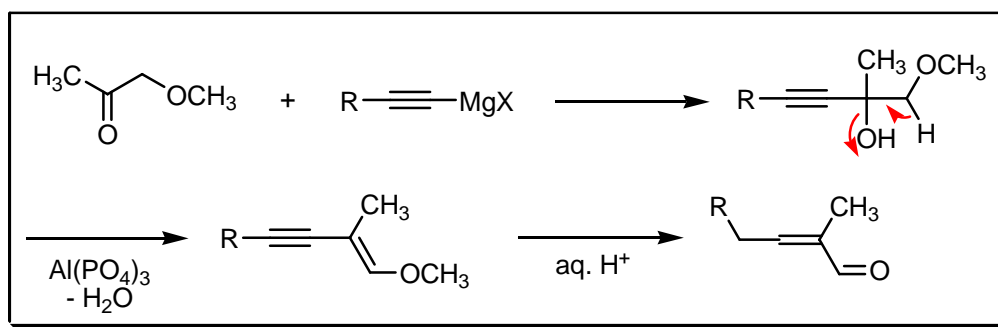
**COMMENTS :**

## INHOFFEN ALDEHYDE SYNTHESIS

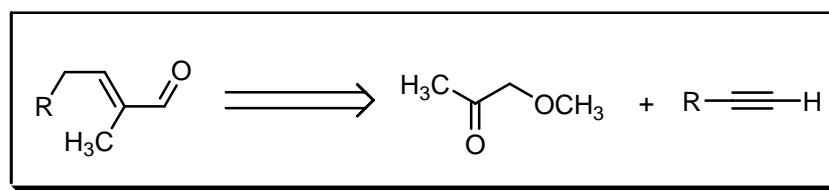
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

This reaction is one of the key steps in the synthesis of  $\beta$ -carotene. 1-Methoxyacetone reacts with an acetylenic **Grignard** reagent (or with an acetylenic lithium reagent) to yield an acetylenic hydroxy-ether. This ether on partial reduction, either catalytically or by lithium aluminium hydride reduction, furnishes the corresponding ethylenic compound, which on dehydration and subsequent hydrolysis of the enol ether gives the required ethylenic aldehyde. Several modifications appeared shortly after the first publication. See also **Arens – van Dorp** and **Isler** reactions.

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## REFERENCES :

Houben – Weyl : 7/1, 113

- 
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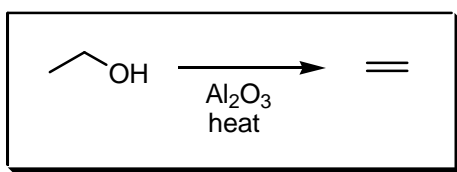
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## COMMENTS :

## IPATIEW – SENDERENS OLEFIN SYNTHESIS

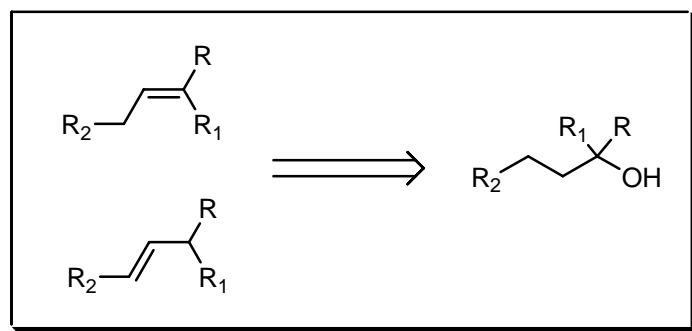
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### EXAMPLE :



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### DISCONNECTION :



## NOTES :

This reaction relates to the preparation of olefins by dehydration of the corresponding alcohol (even 1-dodecanol) by passage of the vapour over heated alumina. See also **Senderens** diethyl ether synthesis.

## REFERENCES :

**March** : 1011

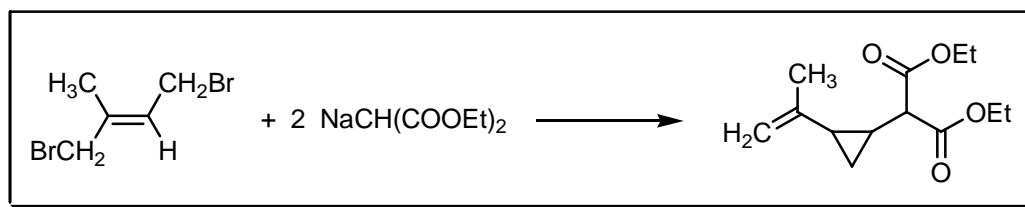
**Smith – March** : 1326

- 1) W. Ipatiew, *Ber. Dtsch. Chem. Ges.*, 1903, **36**, 1990.
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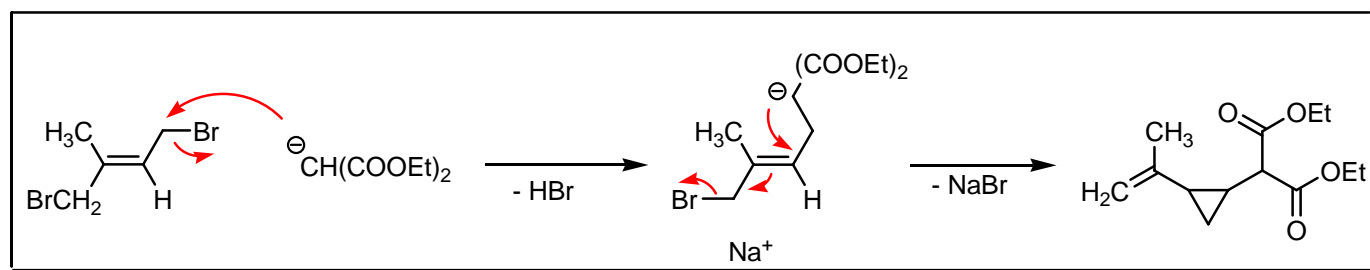
## COMMENTS :

## IPATIEW CYCLOPROPANE SYNTHESIS

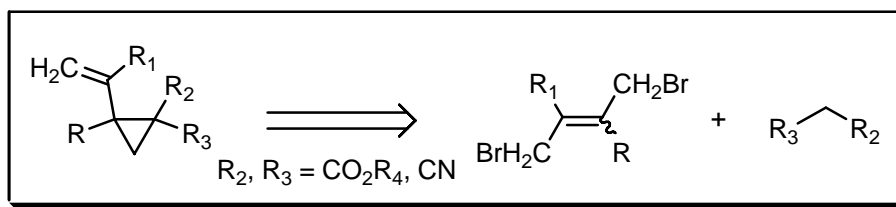
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The cyclopropane ring is formed from 1,4-dibromo-olefines and alkali salts of acidic methylene compounds. See also **Charette**, **Freund**, **Gustavson**, **Hass** cyclopropane, **Kishner**, **Mousseron – Fraisse** – **McCoy**, **Nerdel** and **Simmons – Smith** reactions.

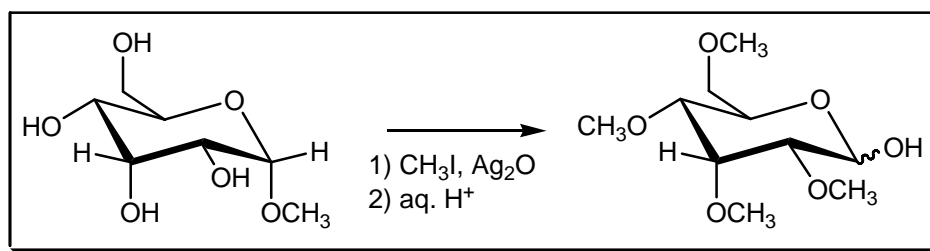
## REFERENCES :

- 1) W. Ipatiew, *J. Russ. Physik. Chem. Ges.*, 1901, **33**, 540.
- 2) J. Nickel, *Chem. Ber.*, 1958, **91**, 553.

## COMMENTS :

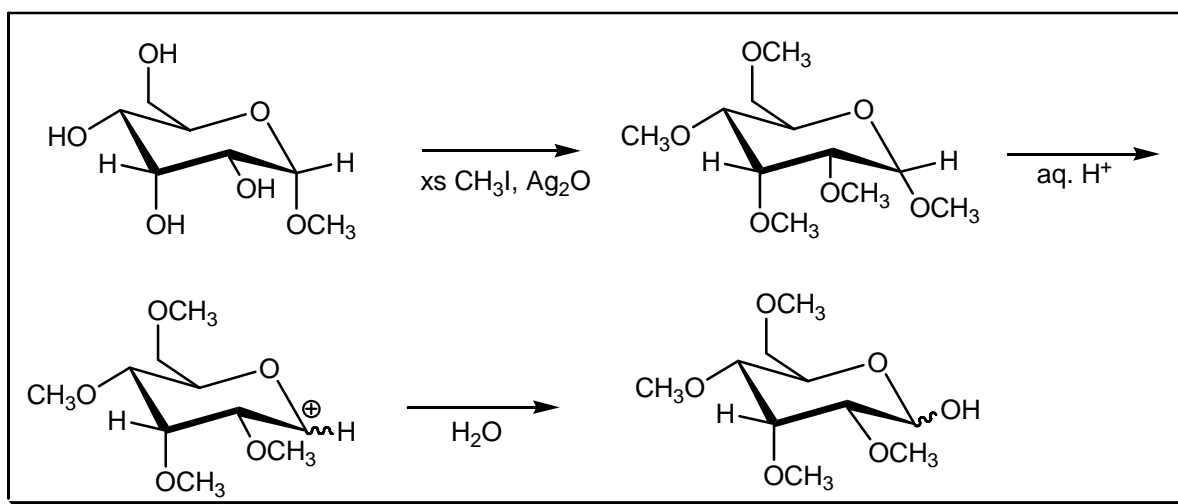
## IRVINE – PURDIE SUGAR METHYLATION

### EXAMPLE :

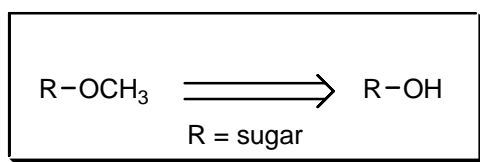




## MECHANISM :



## DISCONNECTION :



## NOTES :

The exhaustive methylation of a methyl glycoside by repeated treatment with methyl iodide and silver oxide, followed by hydrolysis of the pentamethyl ether with dilute acid to yield the anomeric hydroxyl group. There is a **Kuhn** modification, which uses barium or strontium oxides or hydroxides in DMF. See also **Fischer** glycosidation, **Hakomori**, **Haworth** methylation, **Meerwein** methylation, **Robertson – Robinson** and **Williamson** reactions.

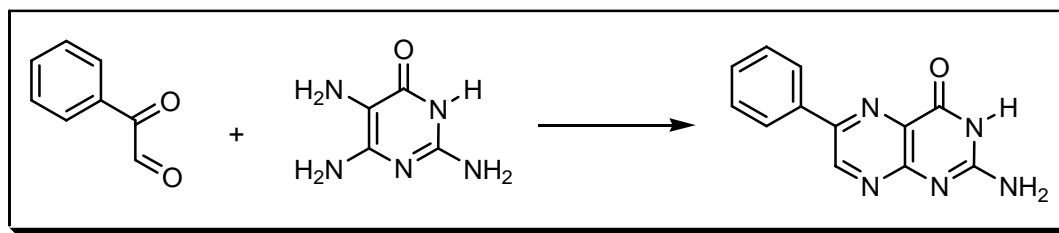
## REFERENCES :

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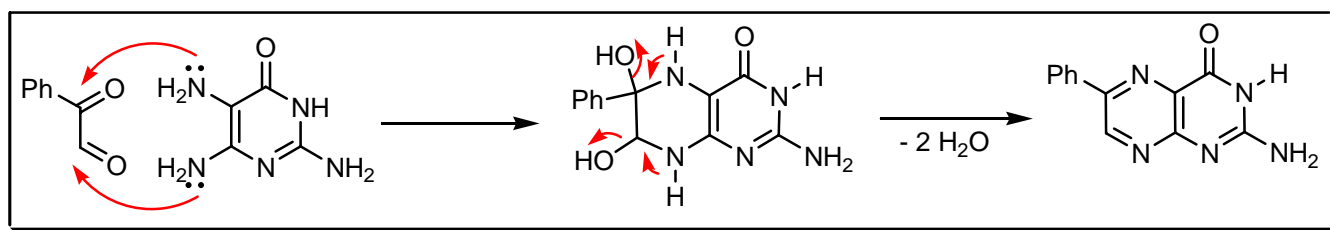
## COMMENTS :

## ISAY PTERIDINE REACTION

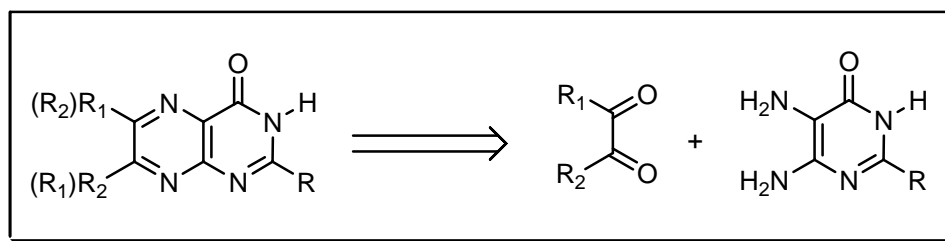
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The synthesis of pteridines from diaminopyrimidines and  $\alpha$ -diketones or  $\alpha$ -ketoaldehydes. The disadvantage of this synthesis is that the condensation of the heterocyclic 1,2-diamine with an unsymmetrical 1,2-dicarbonyl compound will lead to both 5- and 6-substituted isomers. The **Taylor** synthesis avoids these problems. This reaction is also known under the name **Gabriel – Isay** reaction. See also **Blicke – Pachter**, **Boon – Polonovski**, **Taylor** and **Timmis** reactions.

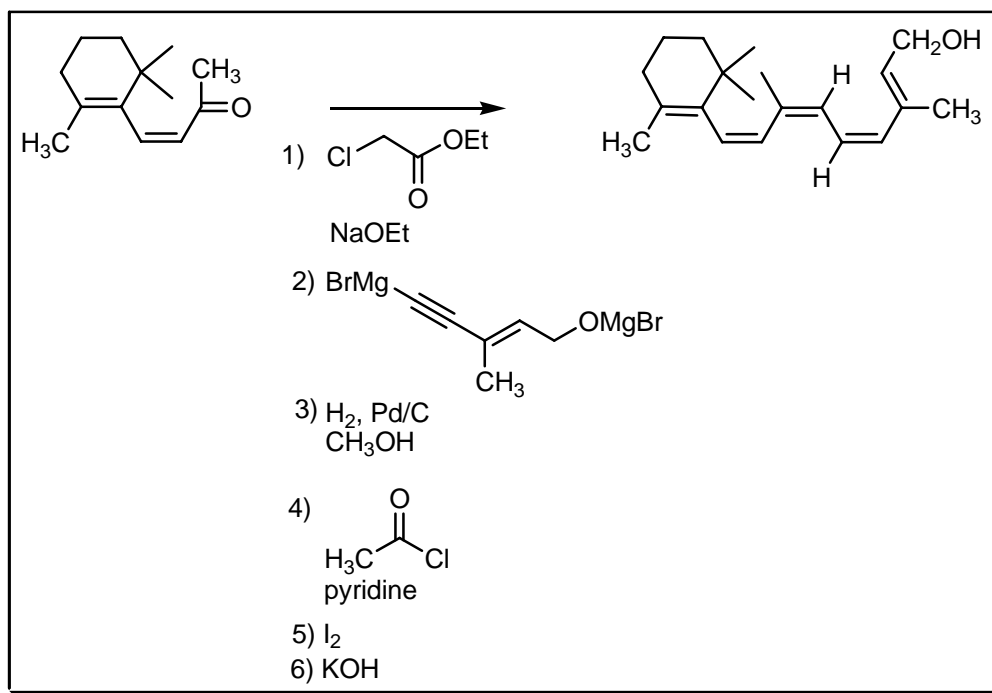
### REFERENCES :

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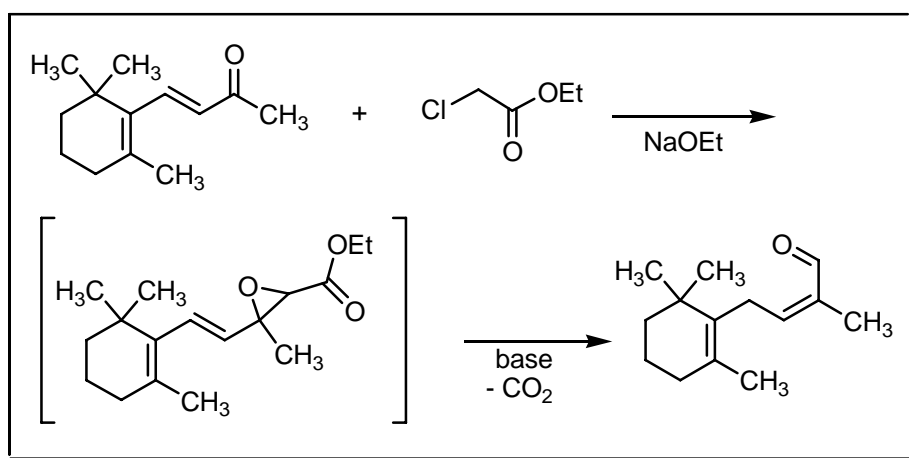
COMMENTS :

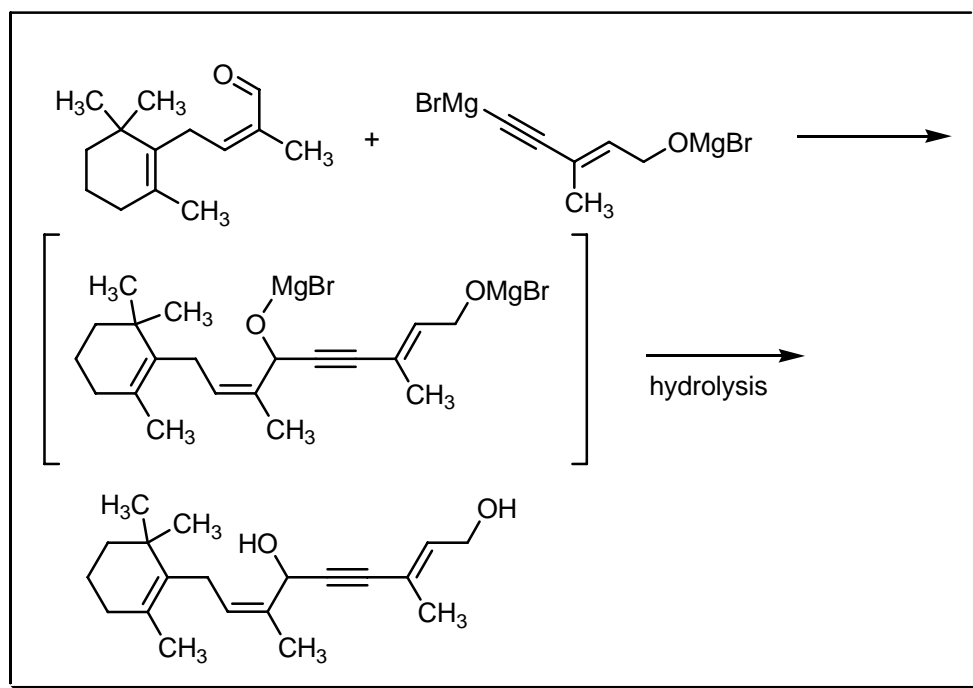
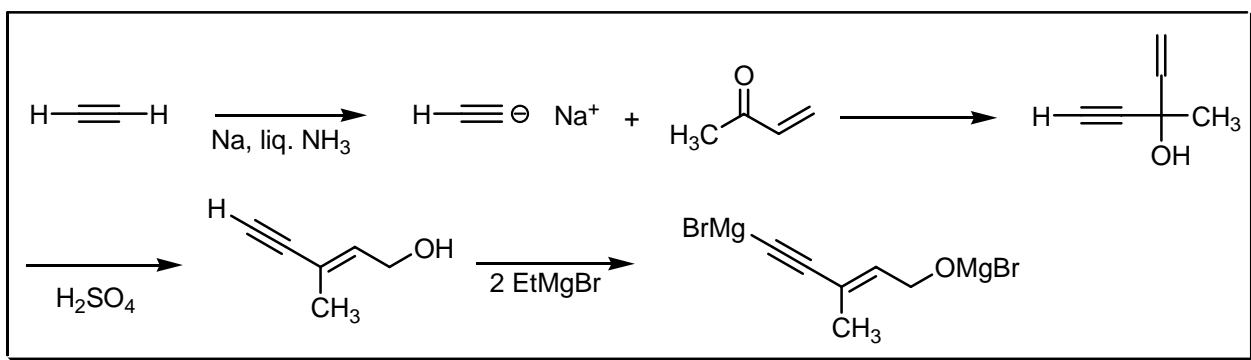
## ISLER SYNTHESIS

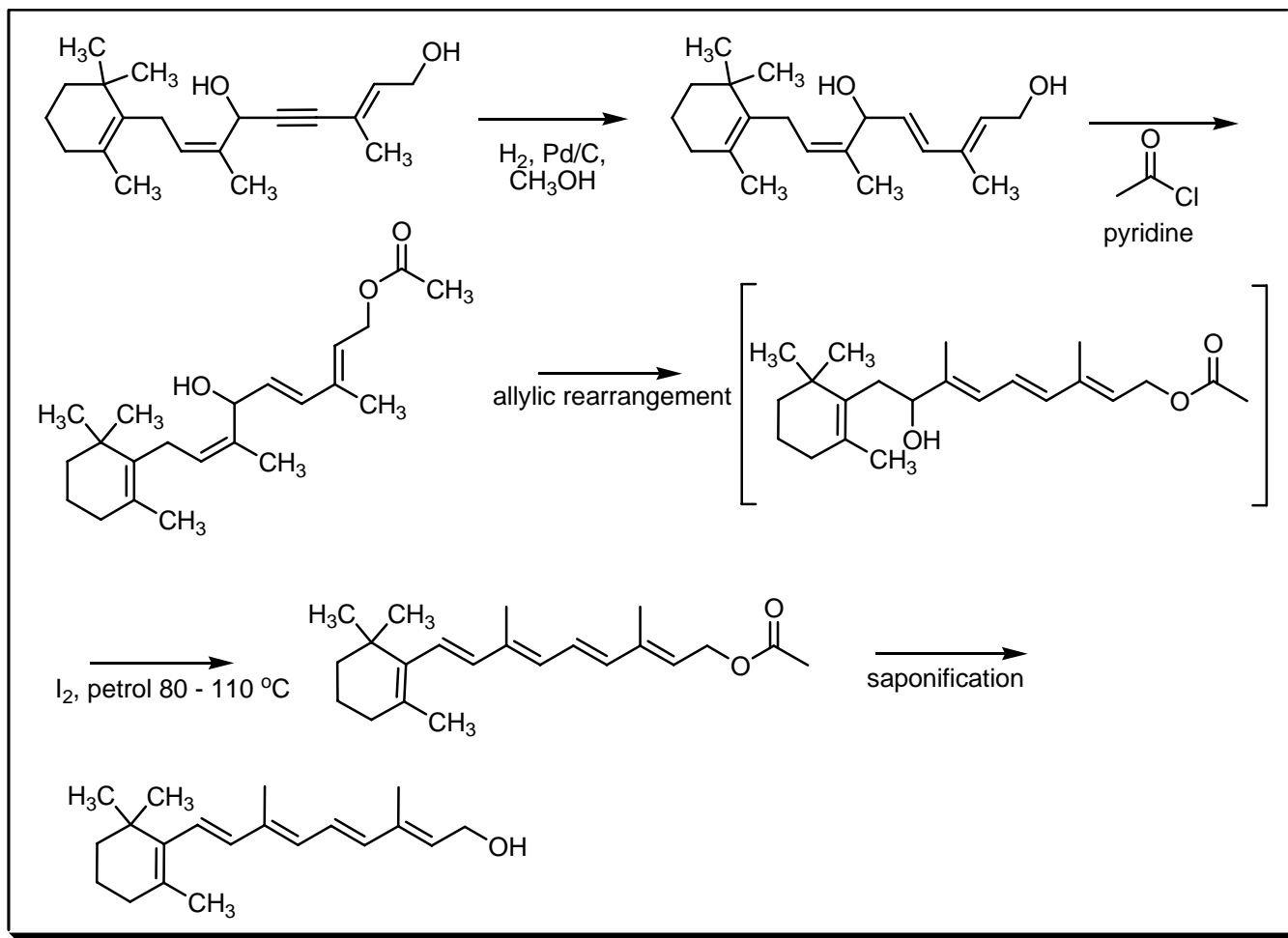
EXAMPLE :



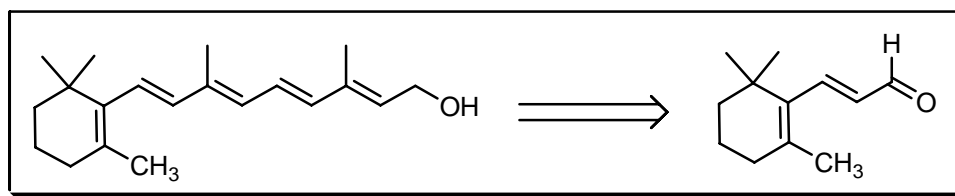
MECHANISM :







#### DISCONNECTION :



#### NOTES :

The synthesis of retinol starting with  $\beta$ -Jonon. See also **Arens – van Dorp**, **Darzens – Claisen**, **Darzens** dichloroacetate synthesis, **Favorskii – Babayan**, **Inhoffen**, **Nef** synthesis and **Reppe** acetylene reactions.

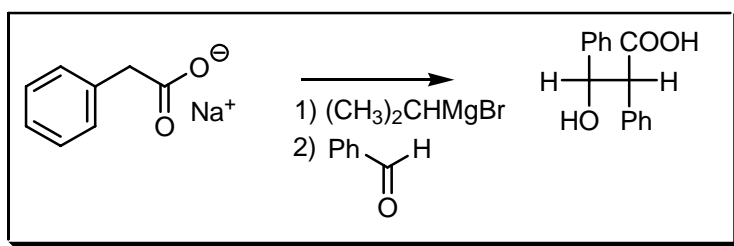
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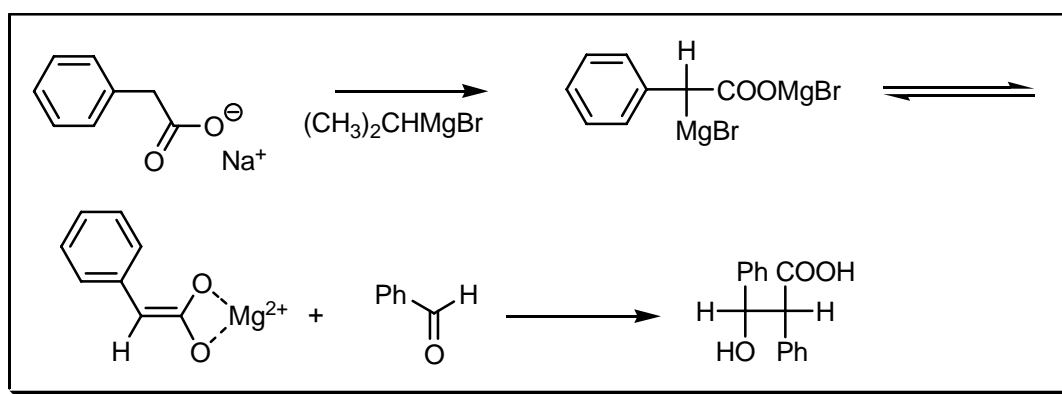
#### COMMENTS :

## IVANOV REACTION

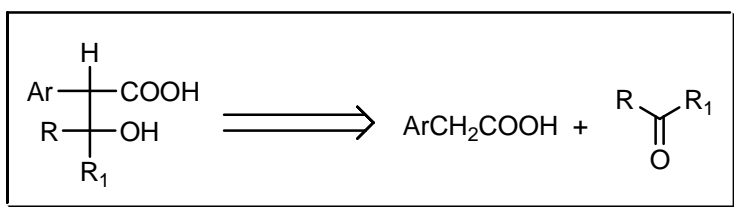
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

An arylacetic acid or its sodium salt reacts with isopropyl magnesium halide to form a **Grignard** complex which with an aldehyde yields a  $\beta$ -substituted  $\alpha$ -aryl- $\beta$ -hydroxypropionic acid or gives with a ketone the corresponding  $\beta,\beta$ -disubstituted compound. The **Ivanov** reaction yields a mixture of *threo* and *erythro* diastereoisomers. For a mechanistic study see **Toullec et al.** See also **Reformatsky** reaction.

### REFERENCES :

March : 946

Smith – March : 791

Smith : 923

Smith 2<sup>nd</sup> : 770

Houben – Weyl : E5, 377

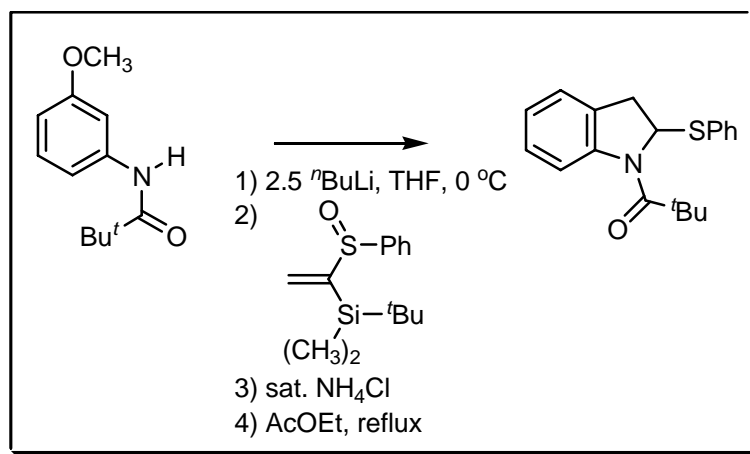
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**COMMENTS :**

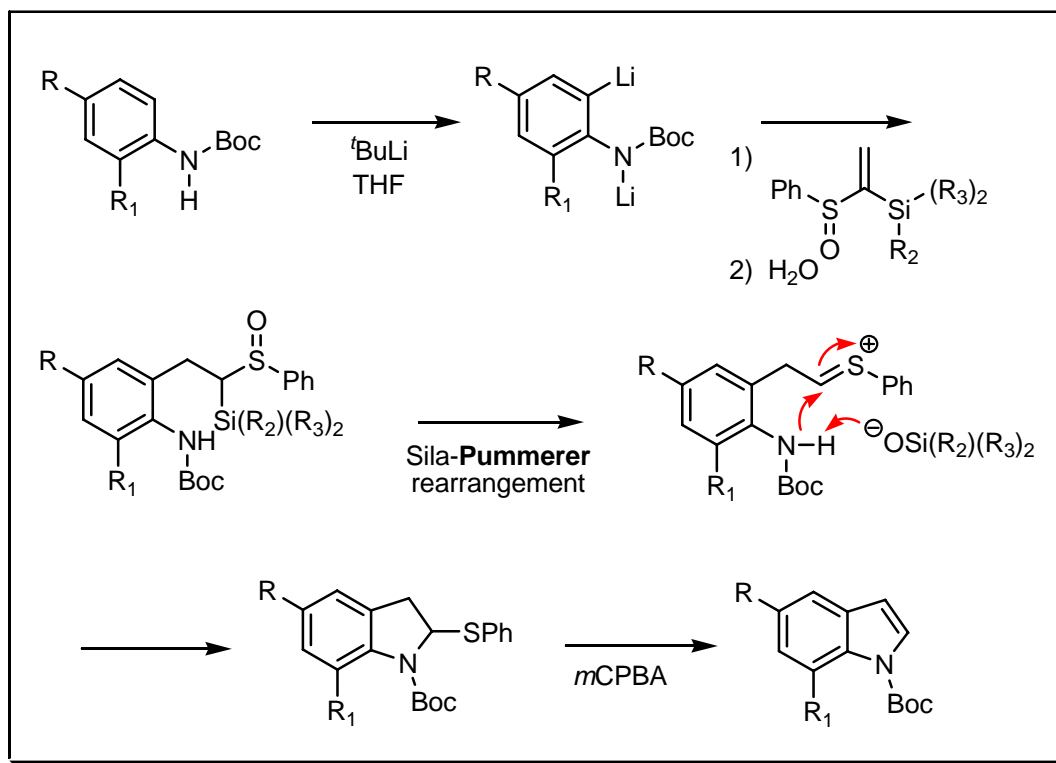
## IWAO INDOLE SYNTHESIS

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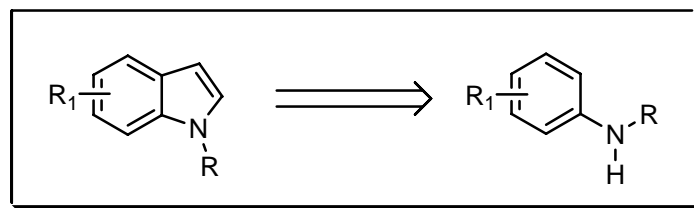
**EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

*N*-*tert*-butoxycarbonylaniline is lithiated with *t*BuLi and subsequently reacted with 1-*tert*-butyldimethylsilyl-1-phenylsulfine to give the conjugate addition product. These compounds are without isolation cyclised to the corresponding phenylthioindolines under thermal **sila-Pummerer** rearrangement. Treatment of these compounds with *m*CPBA gives the *N*-protected indoles. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Neenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Pummerer**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

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**COMMENTS :**

J

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**J**

JACOBSEN – KATSUKI EPOXIDATION · 899

JACOBSEN REARRANGEMENT · 901

JACOBSON INDAZOLE SYNTHESIS · 903

JAPP – KLINGEMANN REACTION · 904

JAPP – MURRAY INDOLE SYNTHESIS · 906

JAPP OXAZOLE SYNTHESIS · 907

JÉGER THF SYNTHESIS · 908

JOHNSON – CLAISEN REARRANGEMENT · 910

JOHNSON – McINTOSH – Mc NELIS  $\alpha$ -IODINATION · 911

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JOHNSON ALKYNYLATION · 914

JOHNSON ANGULAR METHYLATION · 915

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JULIÁ – COLONNA REACTION · 925

JULIA – JOHNSON CYCLOPROPYL CARBINOL

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JULIA – PARIS – KOCIENSKI – LYTHGOE SYNTHESIS · 927

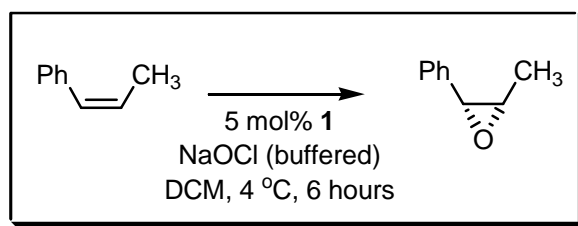
JULIA INDOLE SYNTHESIS · 930

JUNG – OLAH – VORONKOV ETHER CLEAVAGE · 931

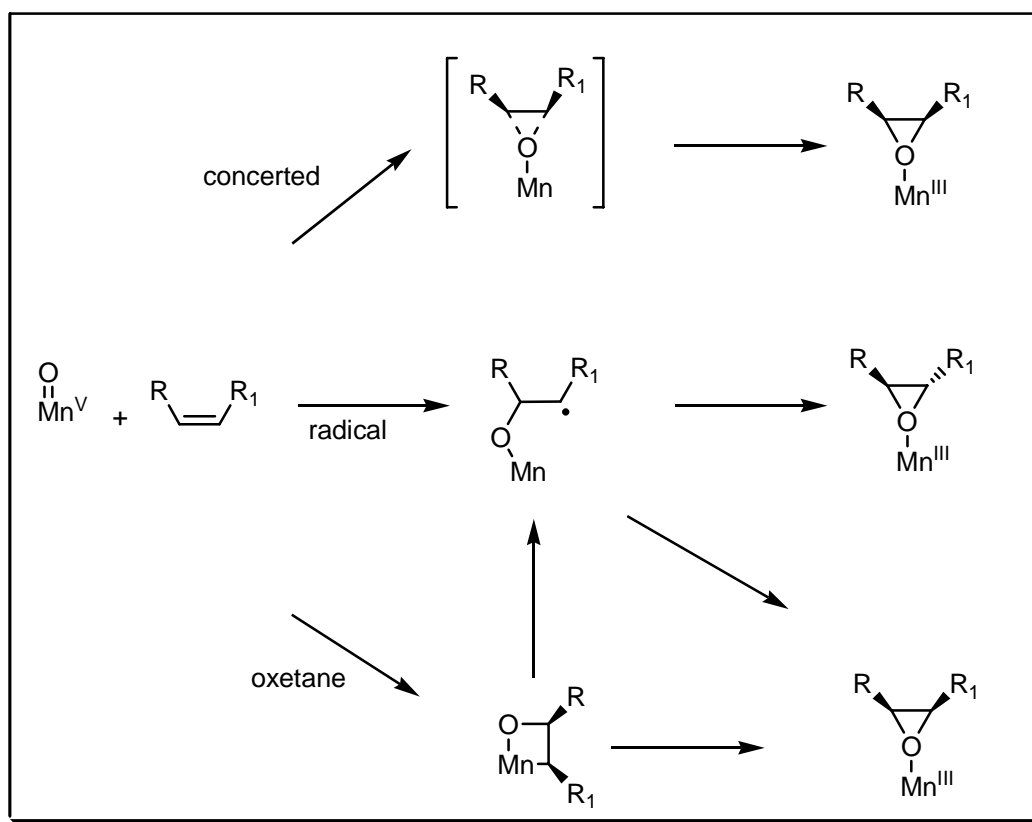
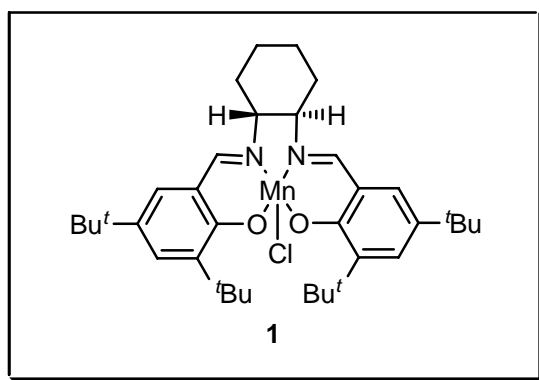
JUST SYNTHESIS · 932

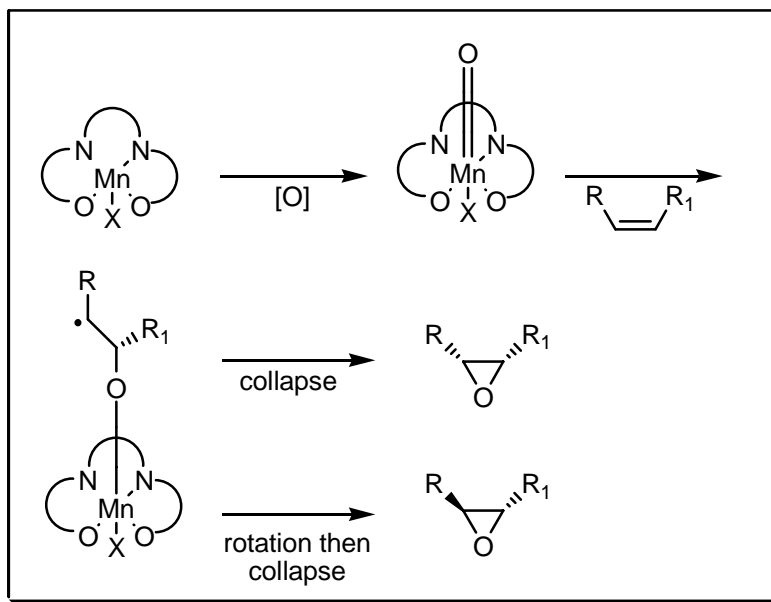
## JACOBSEN – KATSUKI EPOXIDATION

### EXAMPLE :

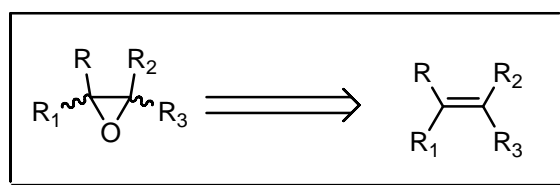


### MECHANISM :





#### DISCONNECTION :



#### NOTES :

The asymmetric epoxidation of simple olefins has been performed using chiral derivatives of [Mn(salen)] complexes with oxidants as PhIO (**Katsuki**) and aqueous NaOCl (**Jacobsen**). In some cases extra oxidants like Bu<sub>4</sub>NHSO<sub>5</sub> and *N*-methylmorpholine-*N*-oxide are used. The mechanism is still controversial. It can either be in a concerted manner, *via* a radical intermediate or *via* a manganooxetane (**Åkermark et al.**) (although disputed by **Jacobsen**). See also **Buchner – Curtius – Schlotterbeck**, **Corey – Chaykovsky**, **Juliá – Colonna**, **Katsuki – Sharpless**, **Mukaiyama – Yamada**, **Prileschajew**, **Shi** and **Weitz – Scheffer** reactions.

#### REFERENCES :

**Smith – March** : 1053

**Smith 2<sup>nd</sup>** : 244

**Org. React.** : **48**, 1

**Org. Synth.** : **75**, 1; **76**, 46

**Org. Synth. Coll. Vol.** : **10**, 29, 96

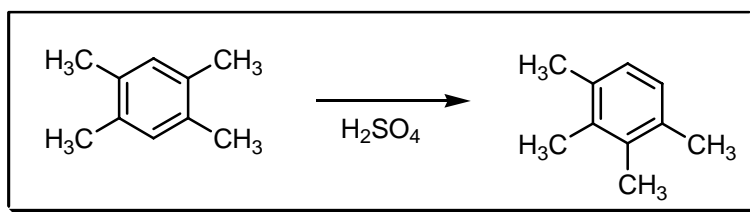
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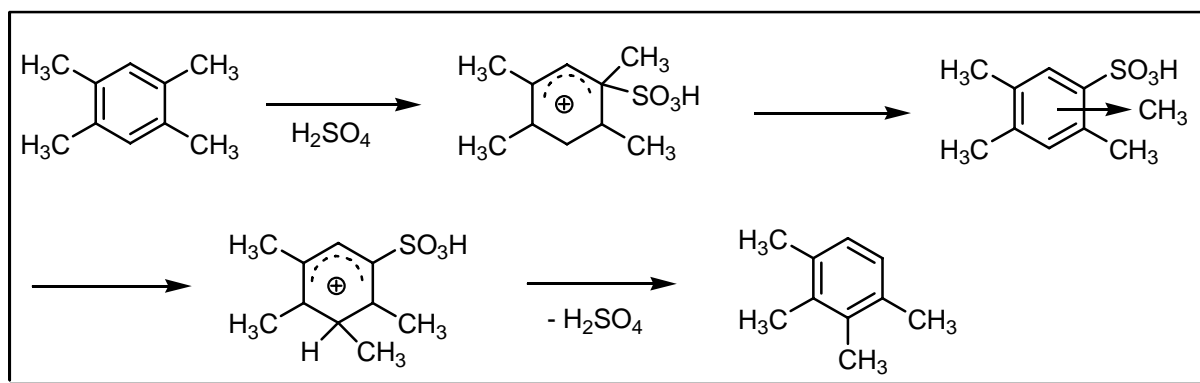
**COMMENTS :**

**JACOBSEN REARRANGEMENT**

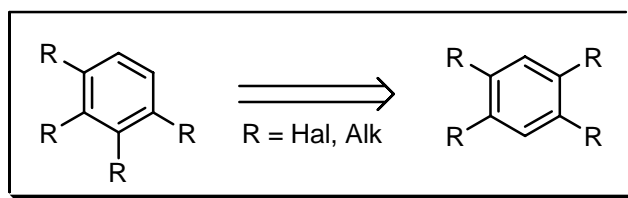
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

This reaction involves the migration of an alkyl group or halogen atom in the presence of sulfuric acid in a sulfonic acid derived polyalkylbenzene, a halogenated polyalkylbenzene or a polyhalogenated benzene with at least four substituents. See also **Baddeley** rearrangement.

## REFERENCES :

**March** : 565

**Smith – March** : 734

**Smith** : 1318

**Smith 2<sup>nd</sup>** : 1086

**Houben – Weyl** : **5/4**, 246; **9**, 530; **E19c**, 404

**Org. React.** : **1**, 370

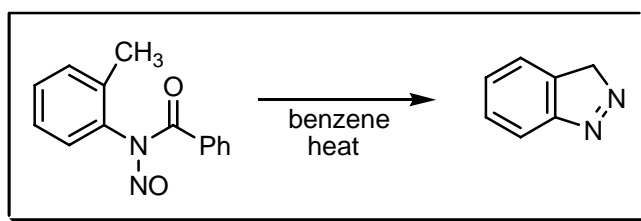
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## COMMENTS :

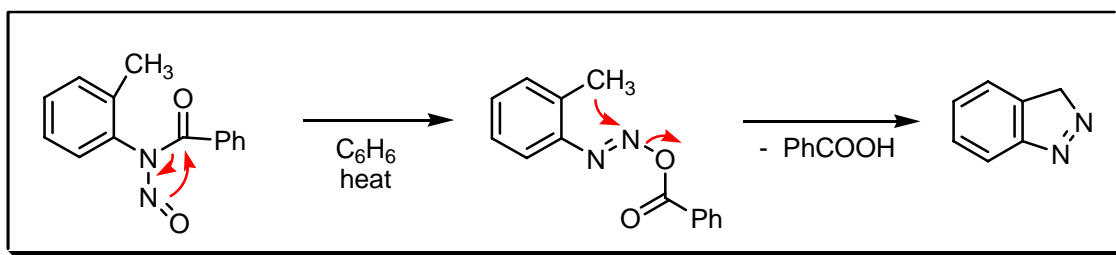
## JACOBSON INDAZOLE SYNTHESIS

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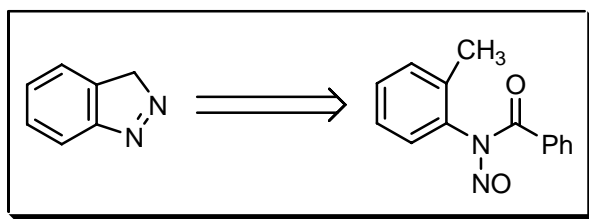
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Indazoles are obtained by warming a benzene solution of a *N*-nitrosoacyl-*o*-toluidide. The product is formed *via* an isomerisation of the diazobenzoate.

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### REFERENCES :

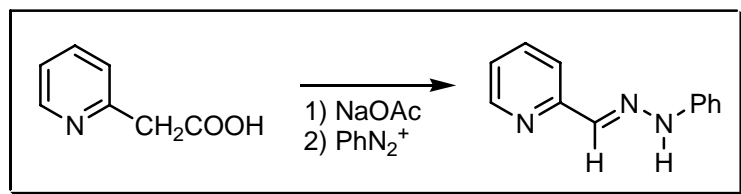
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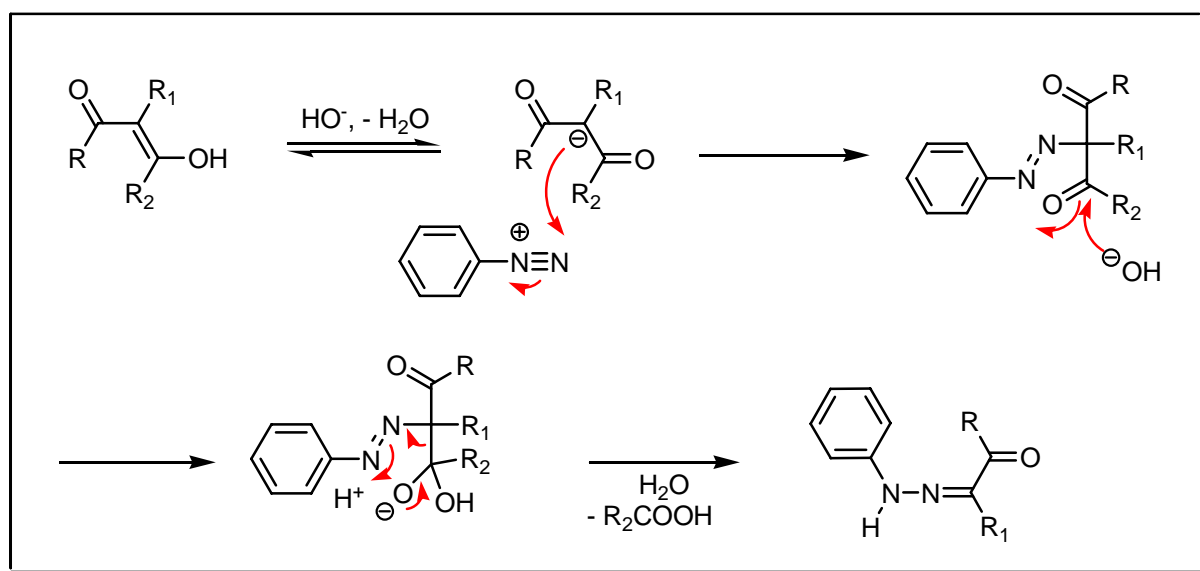
COMMENTS :

## JAPP – KLINGEMANN REACTION

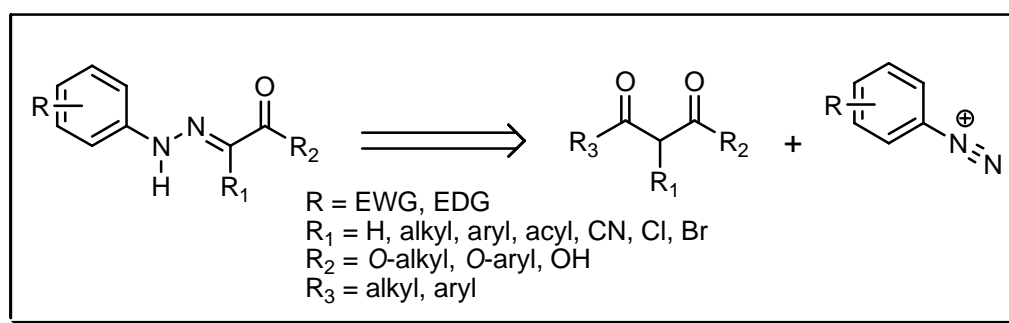
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

Diazonium compounds couple with the enolic forms of  $\beta$ -diketones or  $\beta$ -ketonic esters to form O-azo compound, which rearranges to a C-azo compound and hence to a hydrazone. The elimination of e.g. carbon dioxide or acetyl may occur and the name is restricted by some to such elimination reactions. Other systems containing acidic methylene groups behave in a similar fashion.

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## REFERENCES :

**March** : 592

**Smith – March** : 779

**Houben – Weyl** : **10/3**, 523; **11/2**, 312; **E6b**, 710, 756; **E14b**, 451; **E16d**, 99, 614, 1093

**Org. React.** : **10**, 143

**Org. Synth.** : **32**, 84

**Org. Synth. Coll. Vol.** : **4**, 633

**Science of Synthesis** : **10**, 378

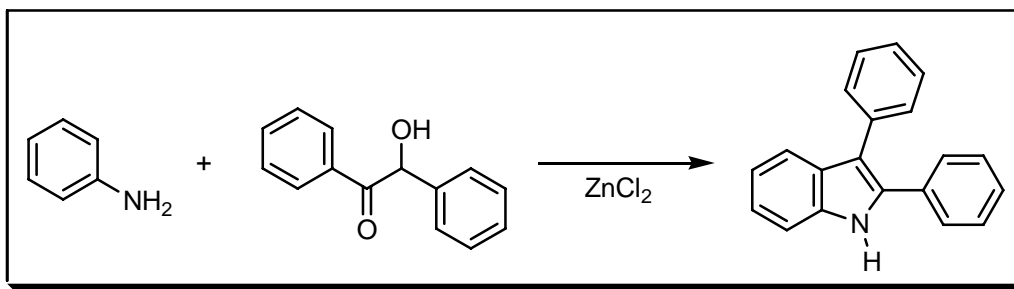
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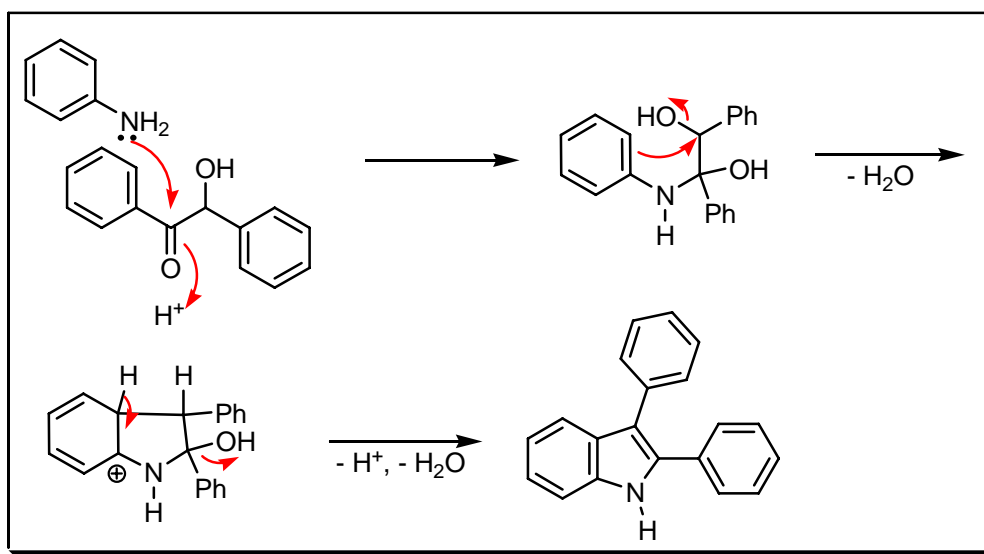
## COMMENTS :

## JAPP – MURRAY INDOLE SYNTHESIS

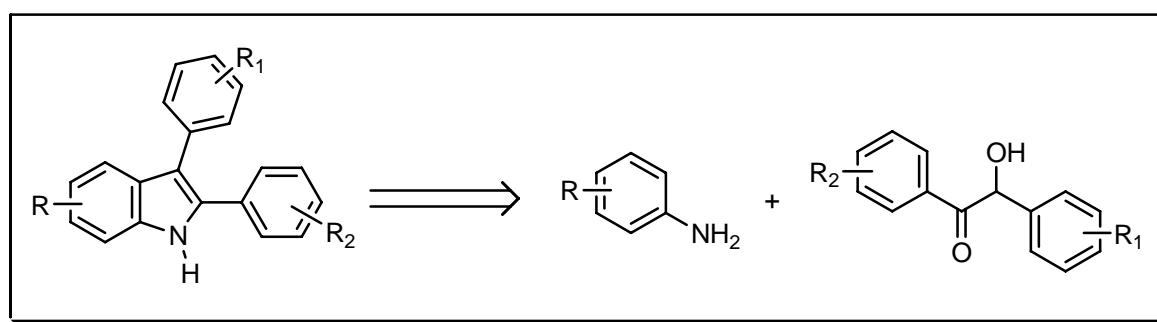
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The synthesis of an indole by the condensation of a primary aromatic amine with a benzoin in the presence of zinc chloride. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa**

indole, Schmid, Smith, Sugasawa indole, Sundberg, Thiele – Dimroth, Thyagarajan, Watanabe heterocyclisation, Watanabe indole, Weerman indole, Wender, Widman, Yamamoto indole-1, Yamamoto indole-2 and Yurovskaya reactions.

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#### REFERENCES :

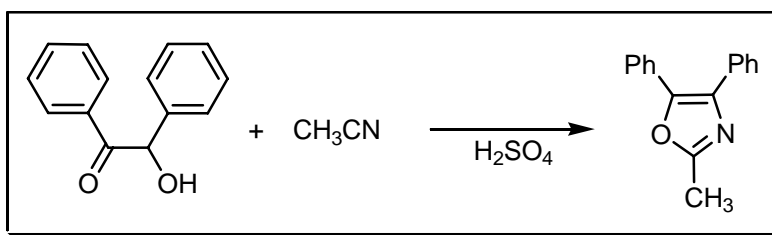
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#### COMMENTS :

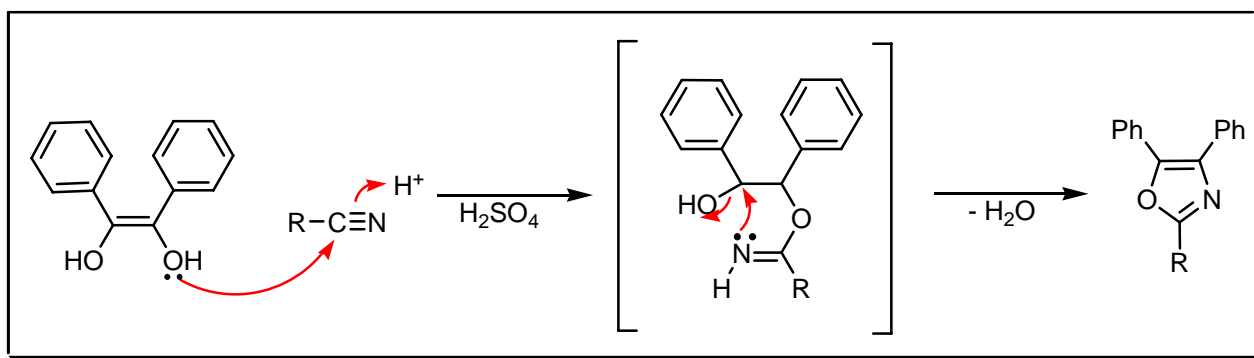
### JAPP OXAZOLE SYNTHESIS

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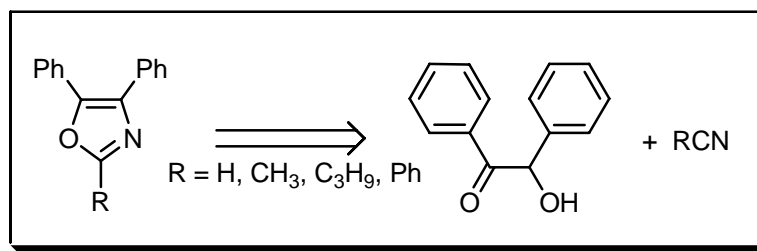
#### EXAMPLE :



#### MECHANISM :



## DISCONNECTION :



## NOTES :

The addition of a mixture of benzoin and a nitrile (containing hydrogen cyanide) to concentrated sulfuric acid yields a 4,5-diphenyloxazole. See also **Davidson**, **Fischer** oxazole, **Japp – Murray** indole and **Robinson – Gabriel** reactions.

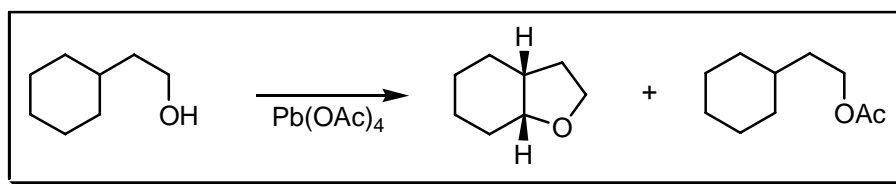
## REFERENCES :

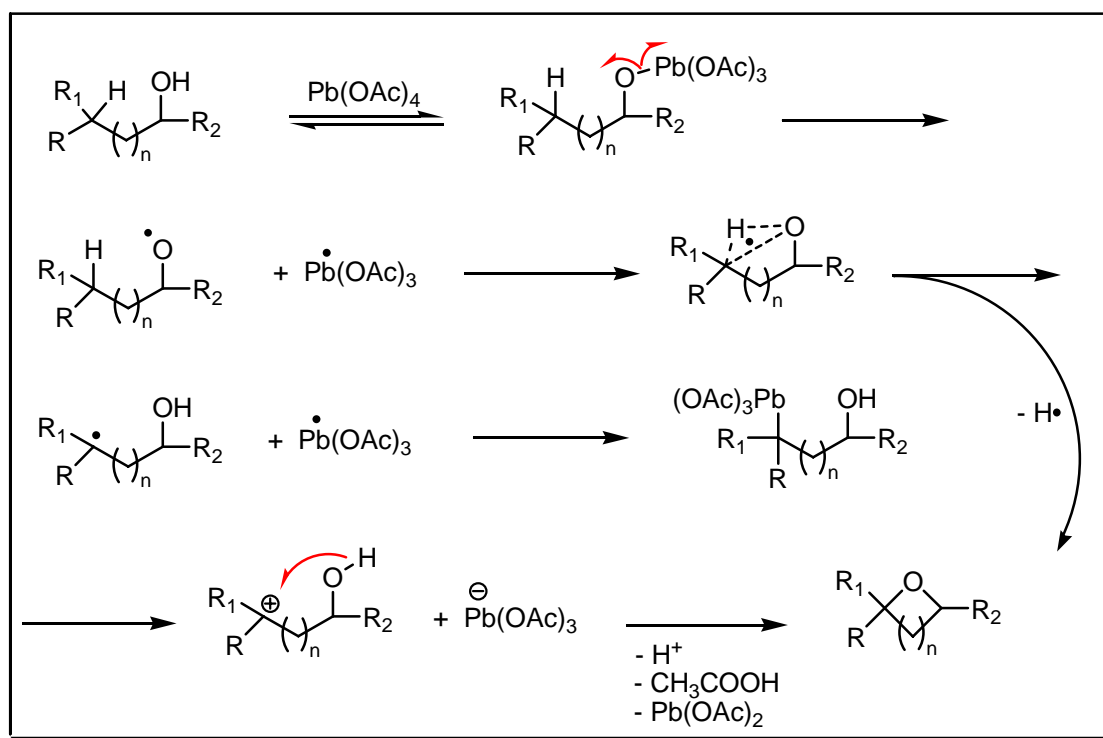
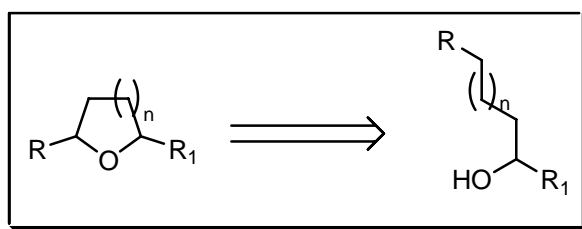
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## COMMENTS :

## JÉGER THF SYNTHESIS

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

The free radical ring-closure of alcohols with  $\text{Pb}(\text{OAc})_4$  to tetrahydrofurans. 1-Heptanol will afford 2-alkyltetrahydrofuran, while secondary aliphatic alcohols will afford a mixture of *cis* and *trans* dialkyltetrahydrofurans.

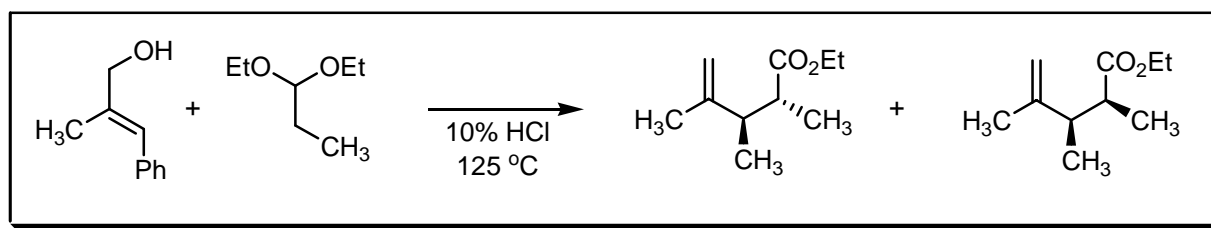
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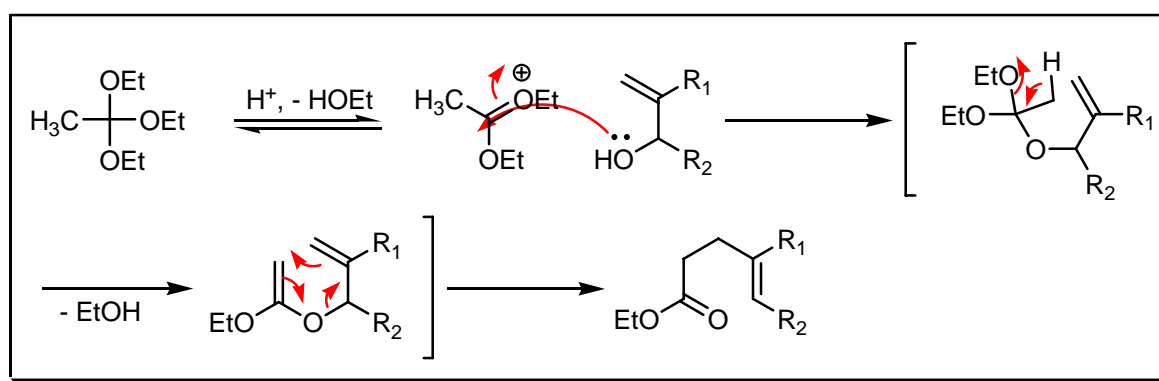
**COMMENTS :**

## JOHNSON – CLAISEN REARRANGEMENT

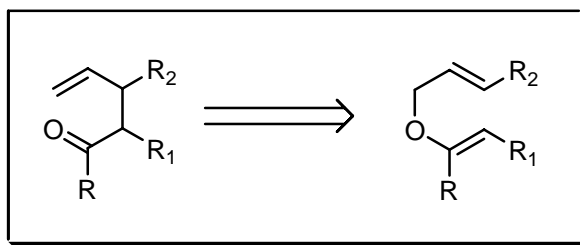
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This is another variation of the **Claisen** rearrangement. It involves ketene acetals which are synthesised from allylic alcohols with orthoesters. The rearrangement of secondary allylic alcohols proceed with high *E*-selectivity due to the destabilising 1,3-diaxial interactions in the transition state, which would give *Z*-selectivity. The reaction temperature can be lowered by use clay-catalysed microwave conditions. See also **Belluš – Claisen** rearrangement, **Carroll (Kimel – Cope)**, **Claisen** rearrangement (**Claisen – Ireland** rearrangement), **Eschenmoser – Meerwein – Claisen** rearrangement, **Ficini – Claisen**, **Marbet – Saucy** and **Overman** rearrangement reactions.

### REFERENCES :

March : 1139

Smith – March : 1451

Smith : 1242

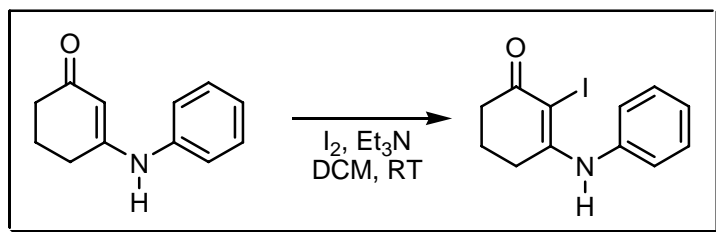
Smith 2<sup>nd</sup> : 1024

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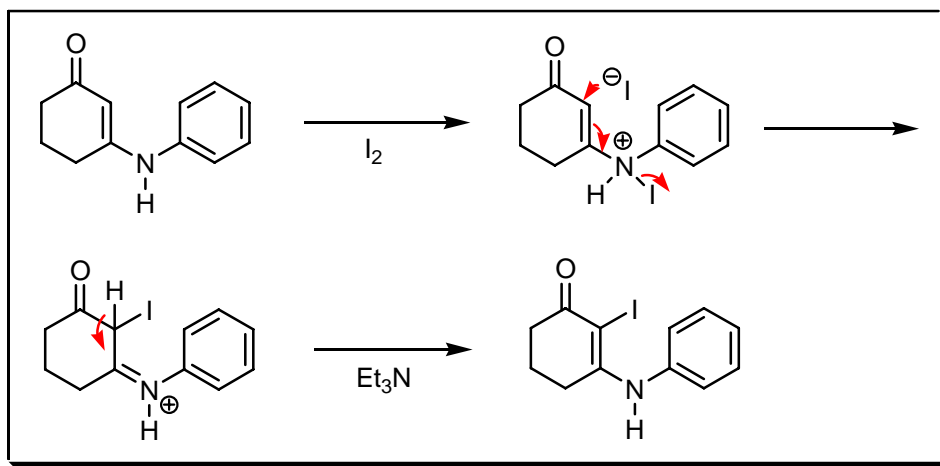
**COMMENTS :**

**JOHNSON – McINTOSH – Mc NELIS  $\alpha$ -IODINATION**

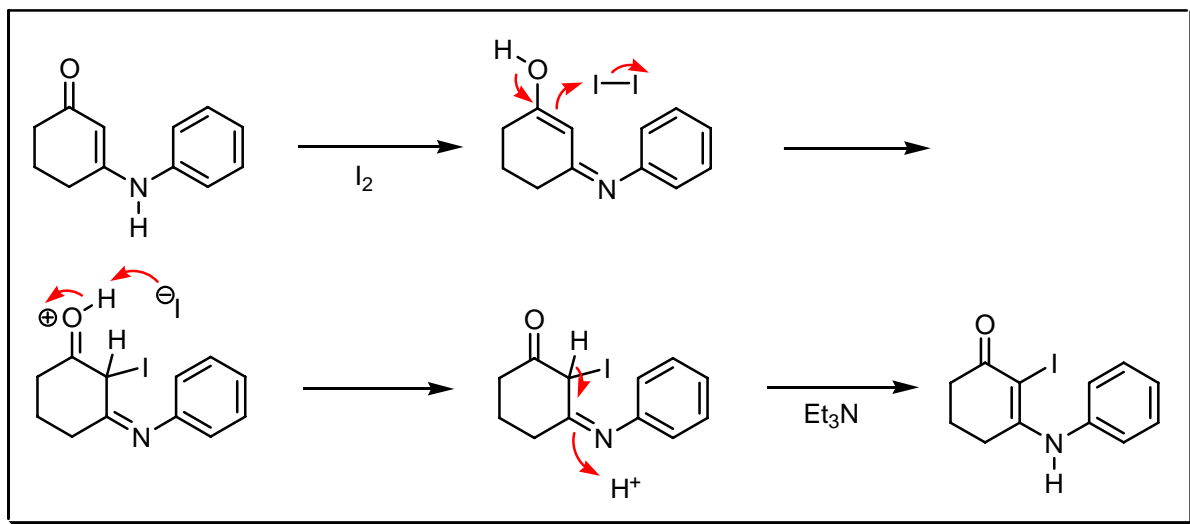
**EXAMPLE :**



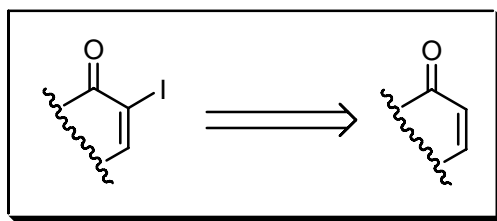
**MECHANISM :**







#### DISCONNECTION :



#### NOTES :

$\alpha$ -Iodination of  $\alpha,\beta$ -unsaturated carbonyl compounds (also enaminones) is carried out using iodine in  $\text{CCl}_4$  and pyridine solvent. In the modifications of this procedure DMAP, triethylamine or trimethylsilyl azide are used. The reaction can be made catalytic. There are two possible reaction mechanisms proposed for the reaction with enaminones.

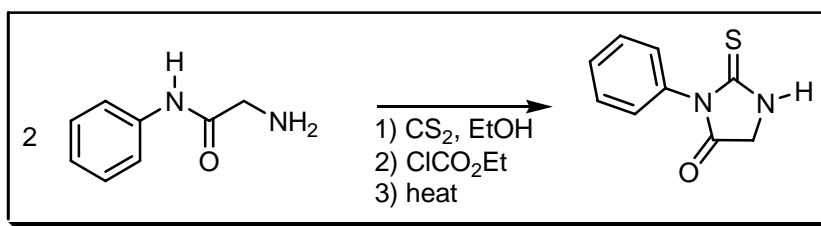
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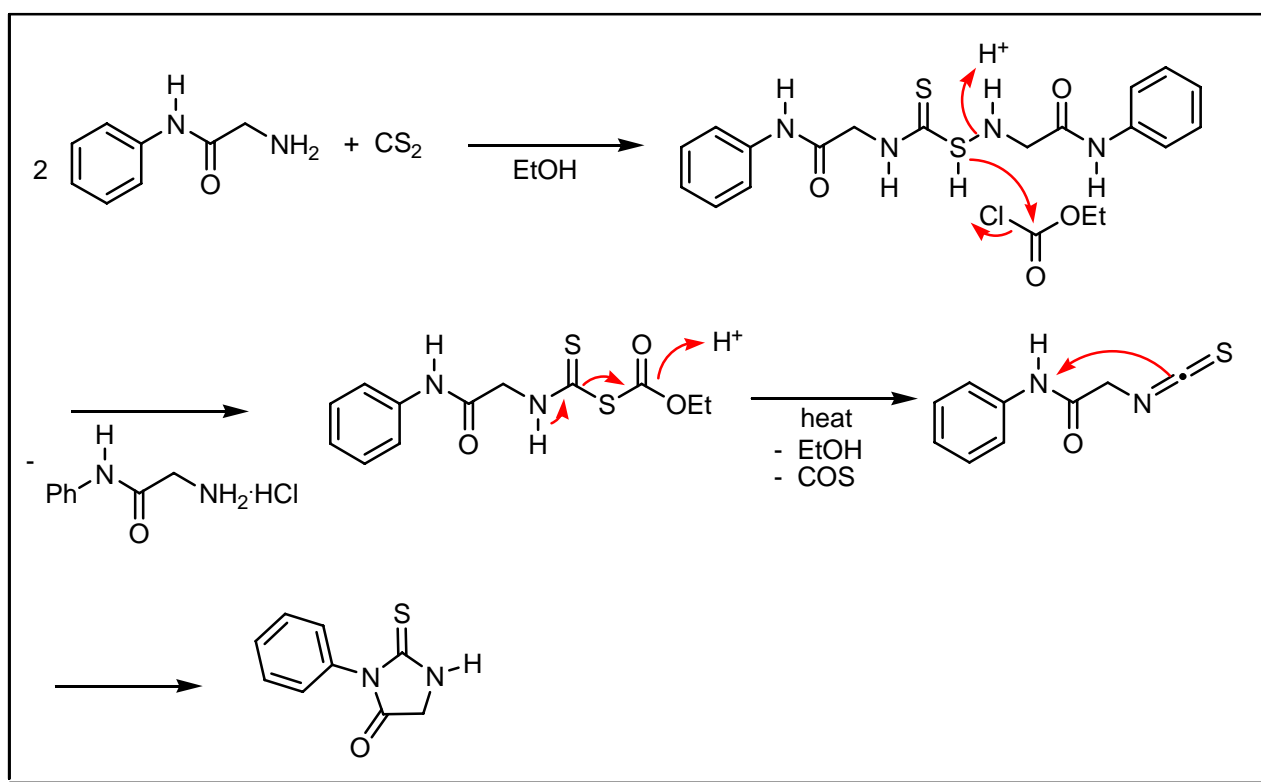
#### COMMENTS :

## JOHNSON 2-THIOHYDANTOIN SYNTHESIS

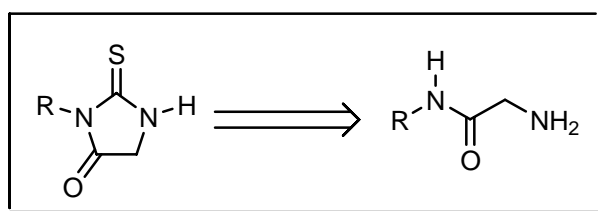
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

An anilide of glycine reacts with carbon disulfide. The formed compound reacts with ethyl chloroformate which on distillation decomposes and rearranges to form the 3-aryl-2-thiohydantoin. See also **Hugershoff** synthesis.

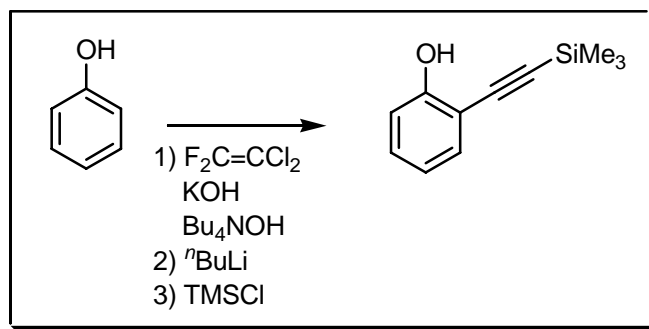
## REFERENCES :

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- 2) T.B. Johnson; A.J. Hill; E.B. Kelsey, *J. Am. Chem. Soc.*, 1920, **42**, 1711.
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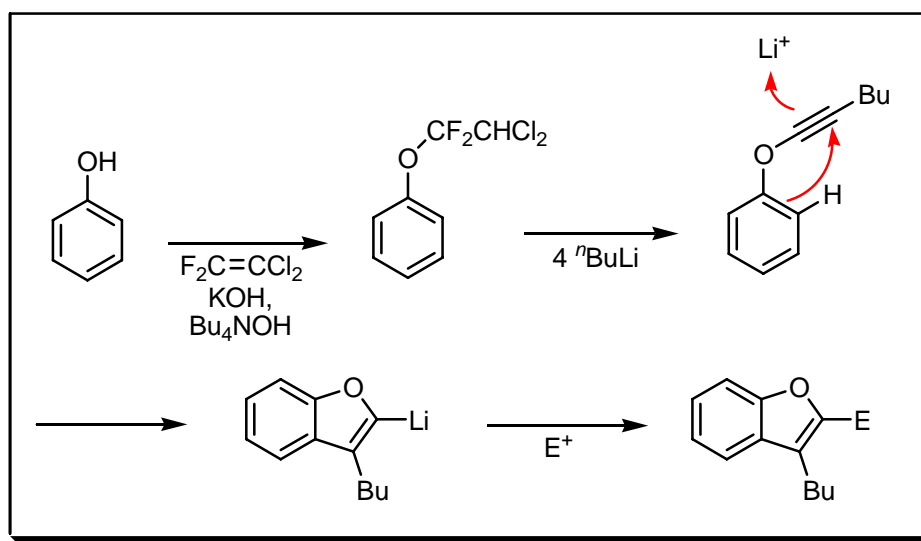
## COMMENTS :

## JOHNSON ALKYNYLATION

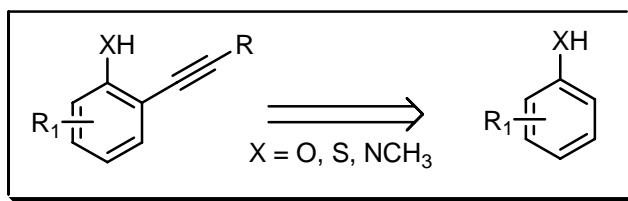
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

A base-induced oxygen to carbon rearrangement by conversion of aryl tri- or tetra-haloether into o-hydroxyphenylalkynes which under basic conditions can be converted to benzofurans and under acid conditions to 2-hydroxyacetophenones.

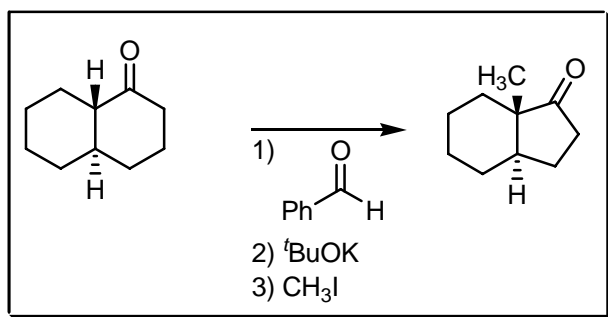
## REFERENCES :

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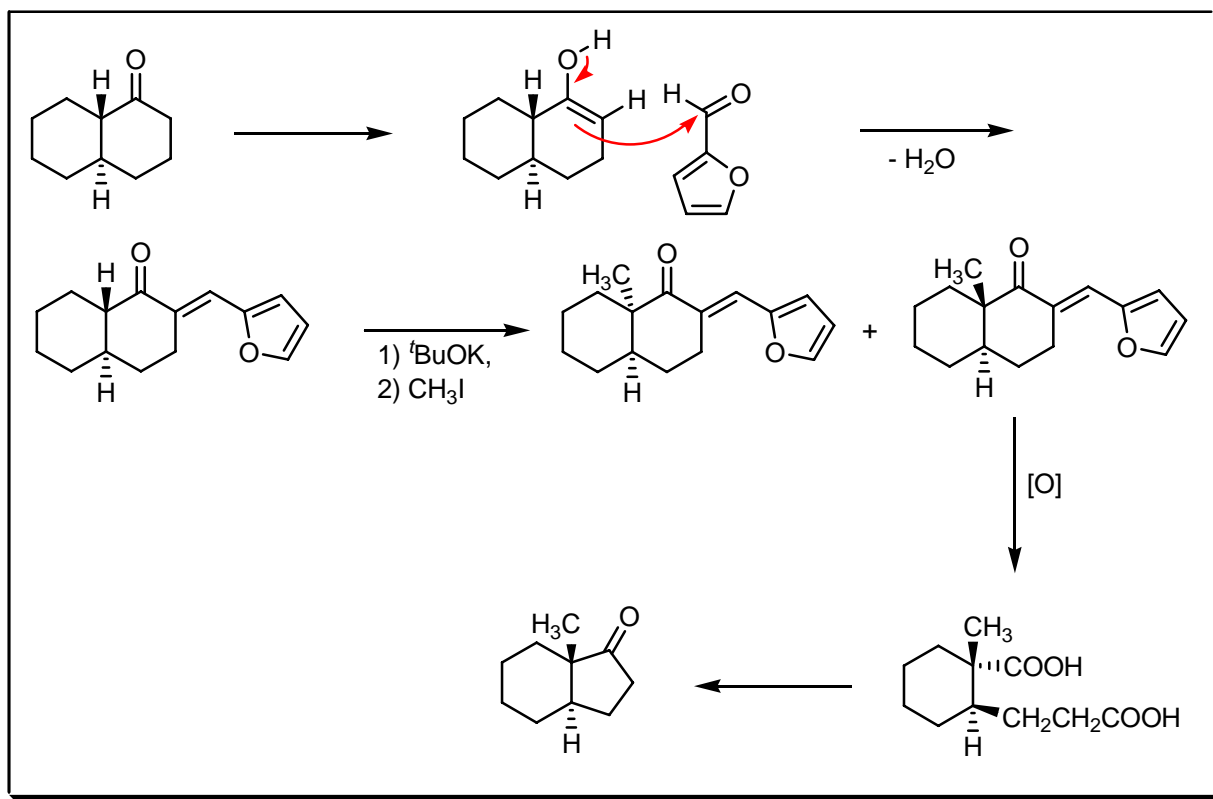
## COMMENTS :

## JOHNSON ANGULAR METHYLATION

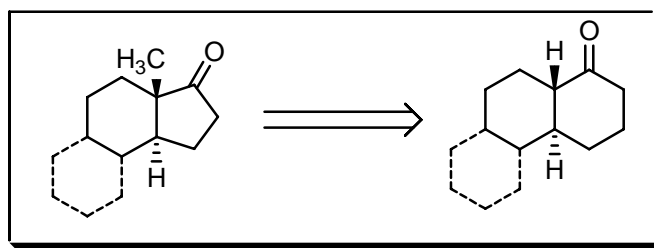
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The angular methylation of fused ring ketones using base and methyl iodide. This method has been developed for the elaboration of the D-ring of steroids.

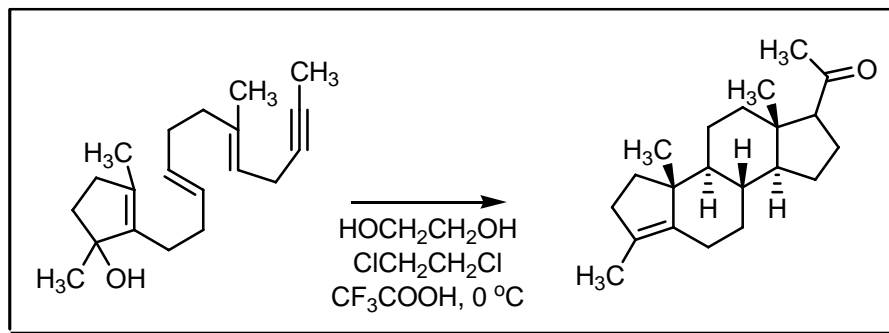
## REFERENCES :

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- 2) W.S. Johnson; H. Posvic, *J. Am. Chem. Soc.*, 1945, **67**, 504.
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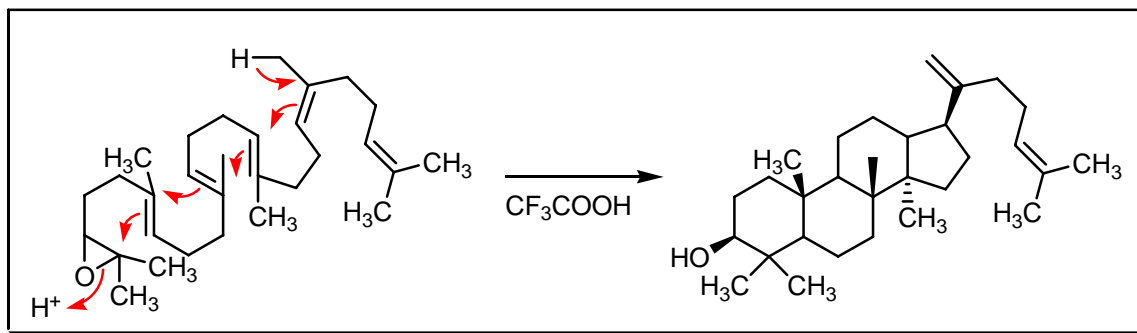
COMMENTS :

## JOHNSON POLYENE CYCLISATION

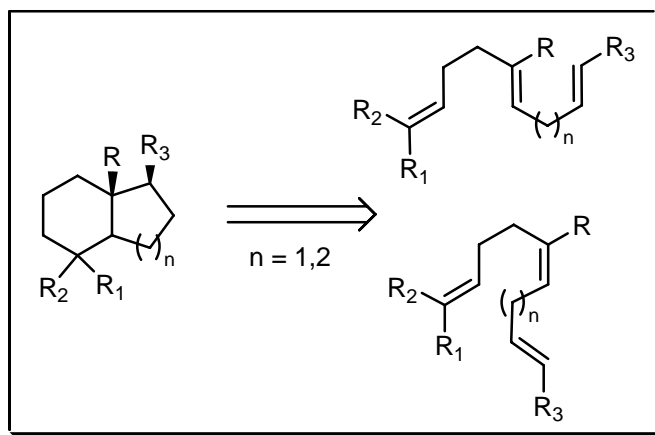
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

This is a non-enzymic biogenetic-like olefinic cyclisation promoted by a cation-stabilising group. See also **Nazarov** reaction.

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## REFERENCES :

**Smith – March** : 1019

**Smith** : 1058

**Smith 2<sup>nd</sup>** : 864, 1072

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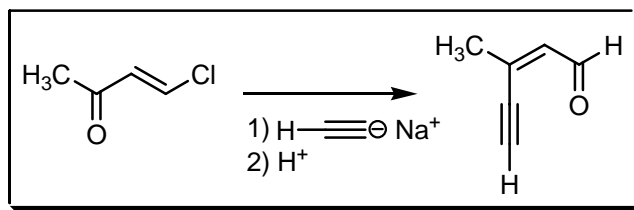
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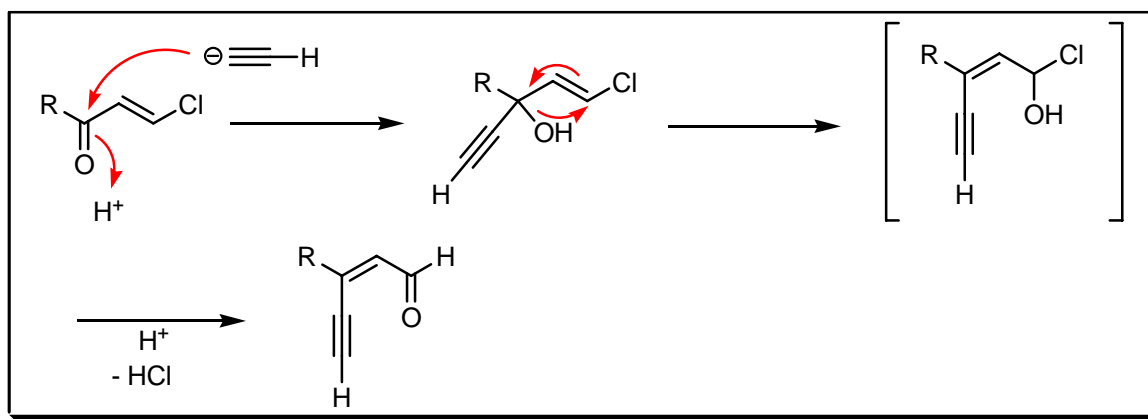
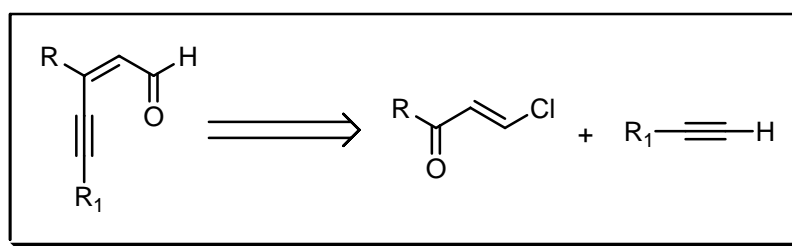
## COMMENTS :

## JONES – WEEDON SYNTHESIS

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### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

$\beta$ -Chlorovinyl methyl ketone reacts with sodium acetylide in liquid ammonia or with acetylenic **Grignard** complexes to yield acetylenic-chloro-ethylenic carbinols. These carbinols on treatment with dilute acids undergo anionotropic rearrangement followed by elimination of hydrogen chloride to yield conjugated acetylenic-ethylenic aldehydes. See also **Arens – van Dorp**, **Favorskii – Babayan**, **Inhoffen**, **Isler**, **Nef** synthesis and **Reppe** acetylene reactions.

**REFERENCES :**

Houben – Weyl : 7/1, 230

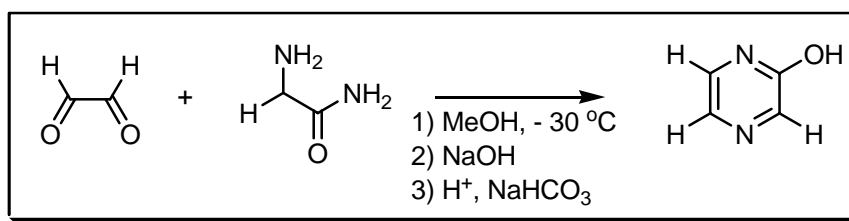
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**COMMENTS :**

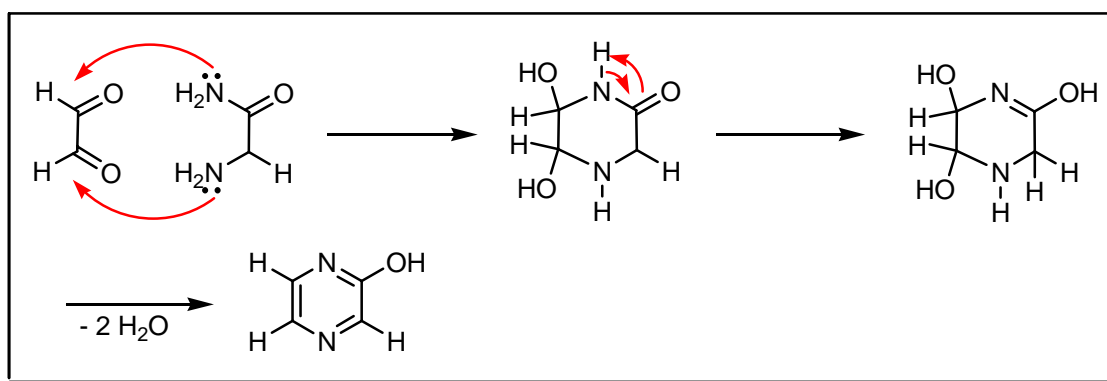


## JONES HYDROXYPYRAZINE SYNTHESIS

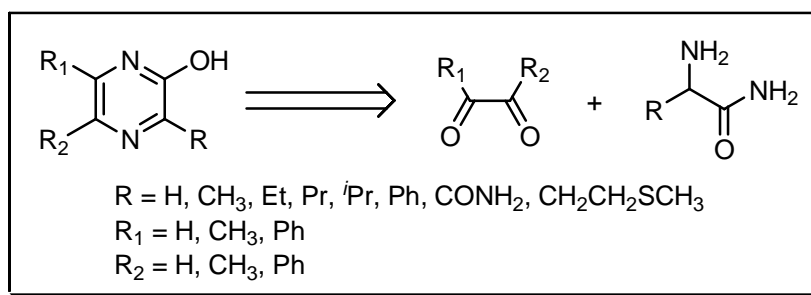
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Hydroxypyrazines are obtained by the base-catalysed condensation of an  $\alpha$ -amino acid amide with a 1,2-dicarbonyl compound.

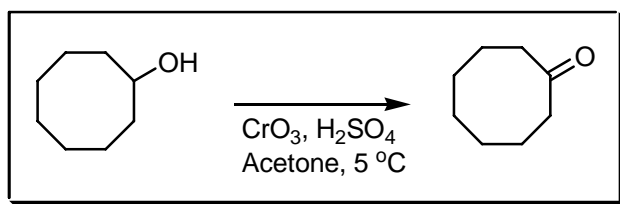
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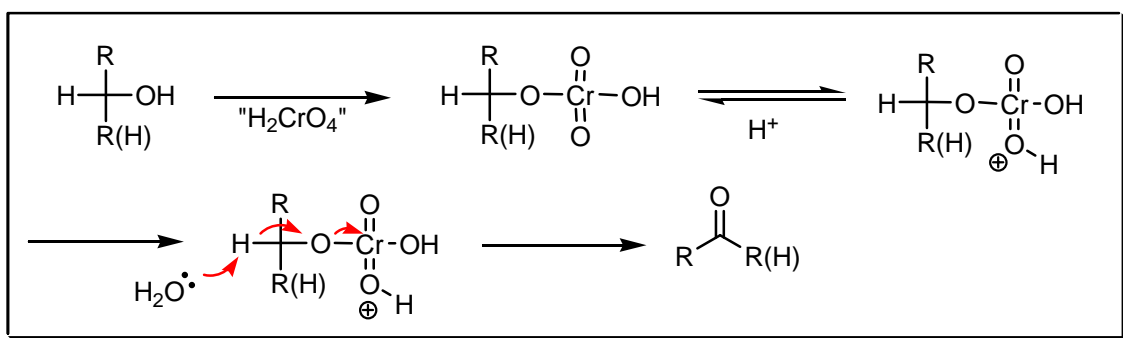
COMMENTS :

## JONES OXIDATION

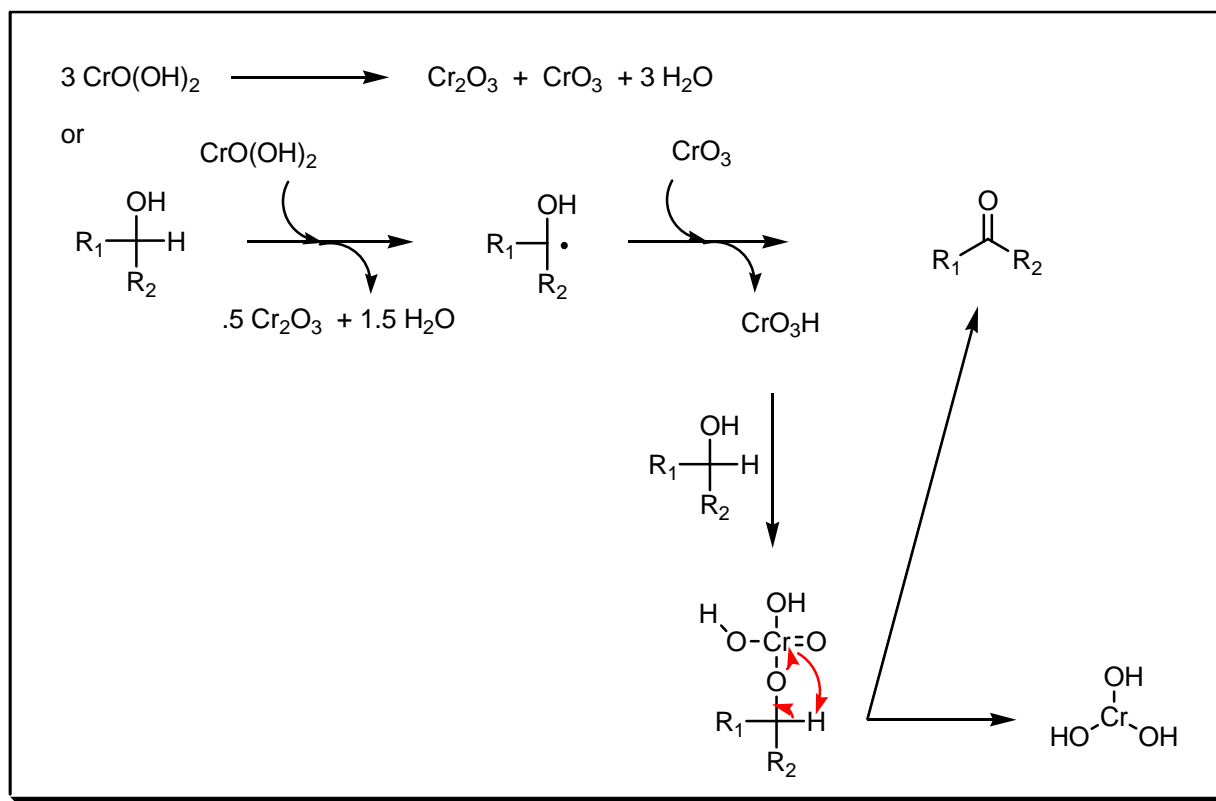
EXAMPLE :



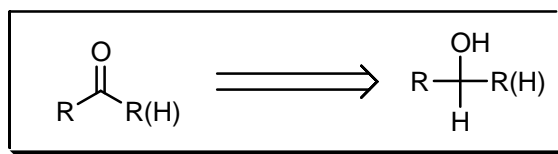
MECHANISM :



### Follow-up chemistry of Cr(IV) :



**DISCONNECTION :**



**NOTES :**

The **Jones** reagent is generally prepared from  $\text{CrO}_3$  and  $\text{H}_2\text{SO}_4$  and is used in acetone or water. During the reaction  $\text{Cr}^{6+}$  is reduced to  $\text{Cr}^{3+}$ . Double and triple bonds and also chiral centres are not disturbed by this reagent. Silyl ethers however will be cleaved under **Jones** conditions. Chromium-mediated oxidations have a competing pathway involving free-radical intermediates. See also **Anelli**, **Ball – Goodwin – Morton**, **Collins**, **Corey – Kim**, **Corey – Schmidt**, **Corey – Suggs**, **David – Thieffry**, **Delépine**, **Dess – Martin**, **Einhorn** oxidation, **Fétizon**, **Ley**, **Maurer – Drefahl**, **Mukaiyama** oxidation, **Nicolaou**, **Oppenauer**, **Parikh – von Doering**, **Pfitzner – Moffatt**, **Pinnick**, **Sarett**, **Swern** and **Uemura** reactions.

## REFERENCES :

**March : 1167**

**Smith – March : 1514, 1531**

**Smith : 228**

**Smith 2<sup>nd</sup> : 198, 563, 1260**

**Houben – Weyl : E16d, 357**

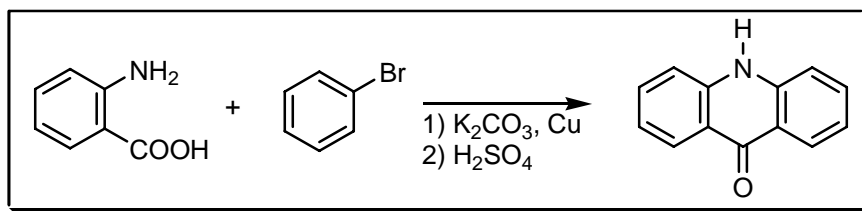
**Org. React. : 53, 1**

- 
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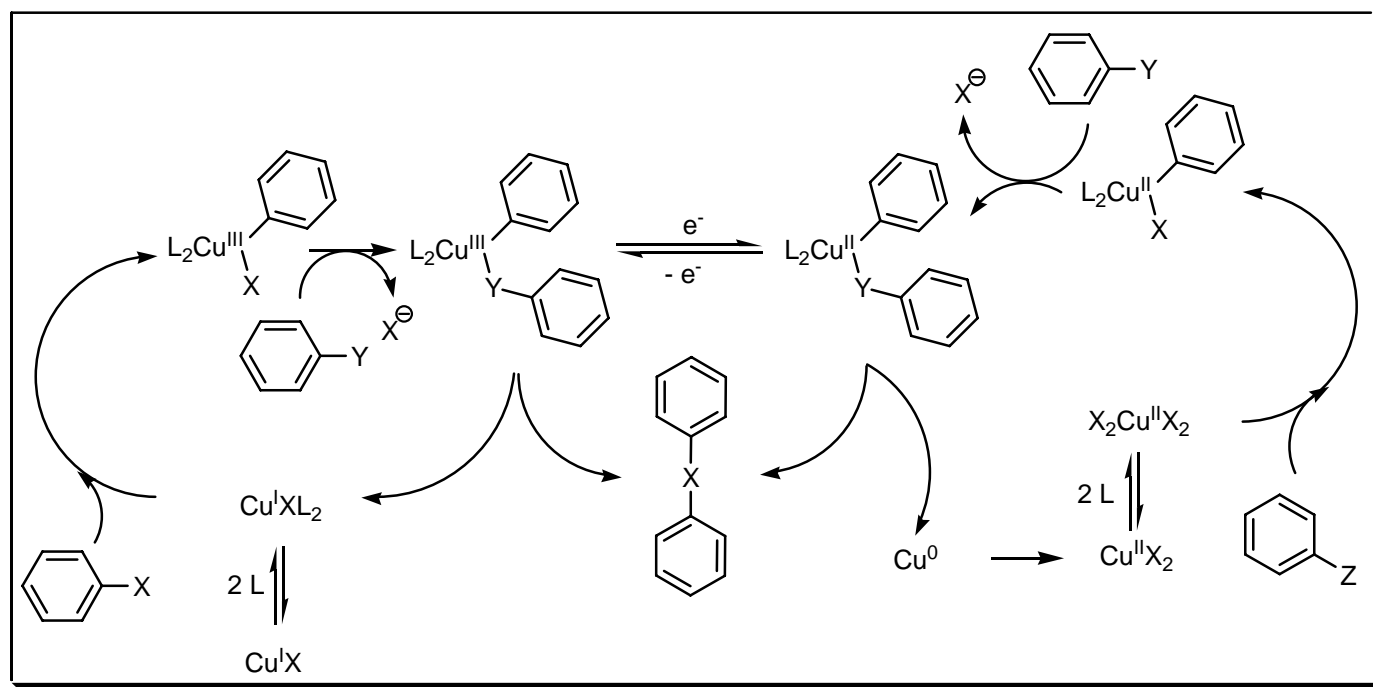
**COMMENTS :**

**JOURDAN – ULLMANN – GOLDBERG SYNTHESIS**

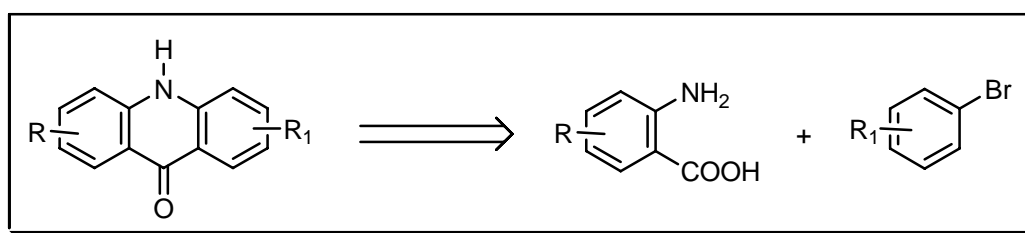
**EXAMPLE :**



**MECHANISM :**



### DISCONNECTION :



**NOTES :**

The condensation of anthranilic acid or derivatives with bromobenzene in the presence of copper and base to give a diphenylamino-*o*-carboxylic acid, which on treatment with sulfuric acid cyclises to an acridone. In general this reaction is between a halogeno benzene and an *N*-acylarylamine in the presence of a copper catalyst under drastic reaction conditions. The reaction is reported under ultrasound and microwave irradiation. See also **Lehmstedt – Tanasescu**, **Rosenmund – von Braun** and **Ullmann diaryl ether synthesis** reactions.

## REFERENCES :

**March : 657**

**Smith – March : 864, 928**

**Org. React. : 14, 19**

**Org. Synth. : 19, 6**

**Org. Synth. Coll. Vol. : 2, 15**

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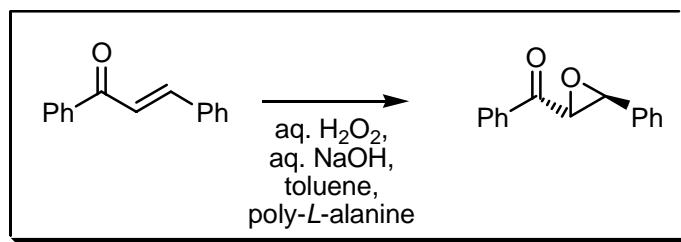
- 4) N. Tuttle, *J. Am. Chem. Soc.*, 1923, **45**, 1906.  
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#### COMMENTS :

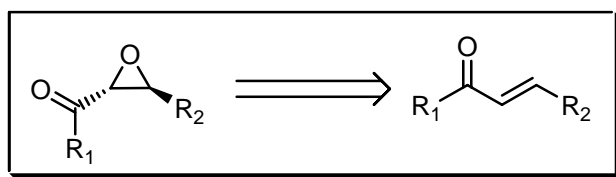
### JULIÁ – COLONNA REACTION

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#### EXAMPLE :



#### DISCONNECTION :



#### NOTES :

Initially, the oxidation of (*E*)-chalcone in a stereoselective manner using a triphasic reaction medium, consisting of aqueous H<sub>2</sub>O<sub>2</sub>, a water-immiscible organic solvent and an insoluble polyamino acid. Later it was shown that a range

of (*E*)-disubstituted enones including alkyl, aryl and extended conjugated systems could be converted to the oxiranes. Other electrophilic olefins possessing other substitution patterns have been tried without success. New two phase reaction mediums have been introduced. Not all polyamino acids can be used (poly *L*-phenylalanine, poly *L*-valine). It has been established that the chiral matrix adjacent to the amino terminus is responsible for the stereochemistry of the product. An industrially viable process has been patented by Bayer chemicals. See also **Buchner – Curtius – Schlotterbeck**, **Corey – Chaykovsky**, **Jacobsen – Katsuki**, **Katsuki – Sharpless**, **Mukaiyama – Yamada**, **Prileschajew**, **Shi** and **Weitz – Scheffer** reactions.

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#### REFERENCES :

Smith 2<sup>nd</sup> : 233

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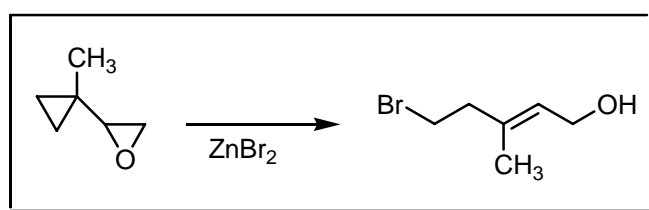
#### COMMENTS :

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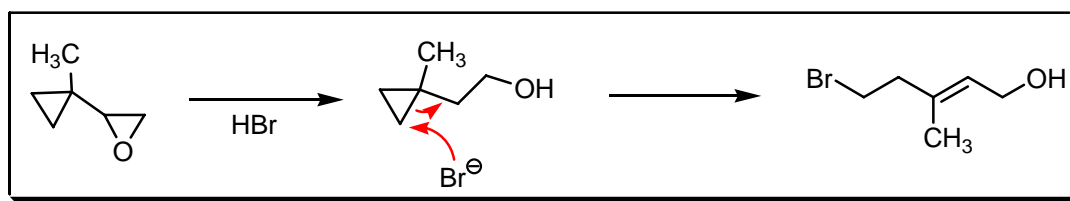
### JULIA – JOHNSON CYCLOPROPYL CARBINOL REARRANGEMENT

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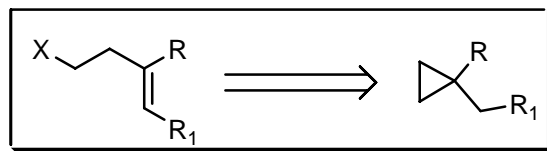
#### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The synthesis of allyl halides (usually *E*) by rearrangement of cyclopropyl carbinols (acid-catalysed). This reaction is also known under **Julia – Bruylants** cyclopropyl carbinol rearrangement.

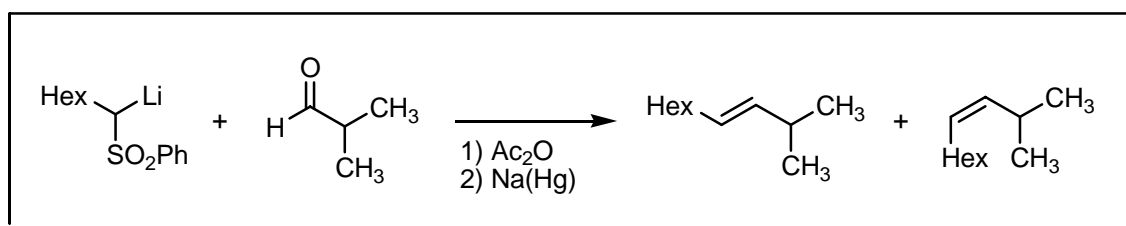
### REFERENCES :

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### COMMENTS :

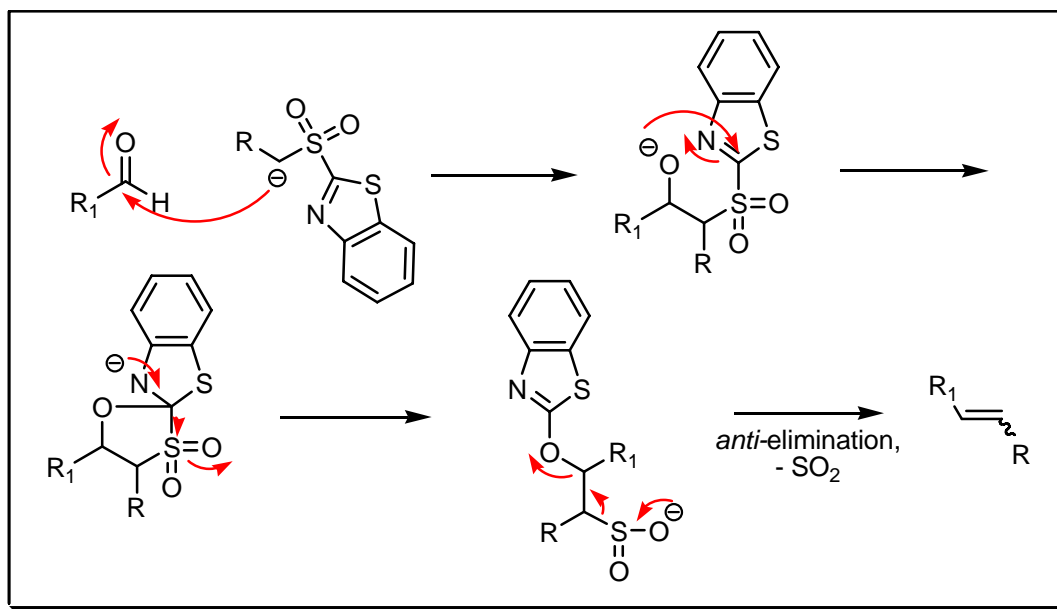
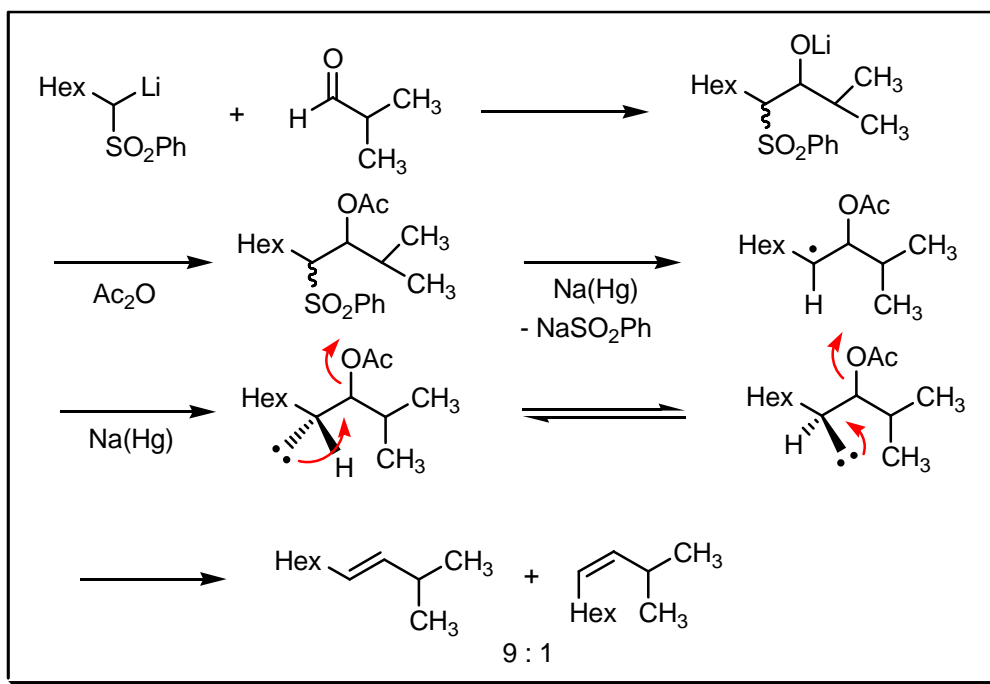
## JULIA – PARIS – KOCIENSKI – LYTHGOE SYNTHESIS

### EXAMPLE :

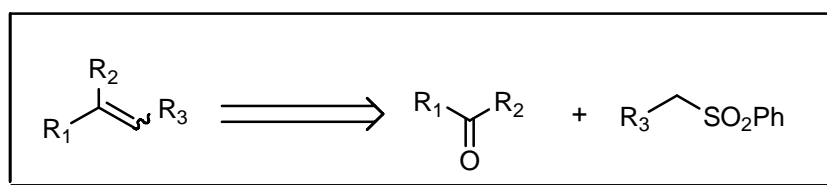




## MECHANISM :



## DISCONNECTION :



## NOTES :

The formation of a mixture of *E/Z* isomers substituted olefins by the combination of a sulfone with a carbonyl derivative followed by reductive elimination. Instead of sodium amalgam samarium diiodide can also be used. The use of samarium diiodide can give different results compared to the sodium amalgam method. Several modifications

of this reaction have been published by **Kocienski, Charette** (*E, Z*-dienes) and **Julia**. For more on the mechanism see **Keck et al.** See also **Corey – Kwiatkowski, Horner – Wadsworth – Emmons, Krief – Reich – Chow, Nozaki – Hiayama – Kishi (Takai – Utimoto), Nysted, Paquette, Petasis** reaction, **Peterson, Ramberg – Bäcklund, Smiles** rearrangement, **Still – Gennari, Takeda, Tebbe** and **Wittig** olefination reactions.

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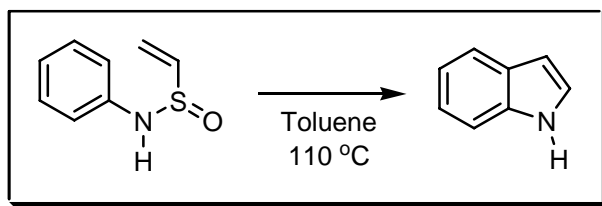
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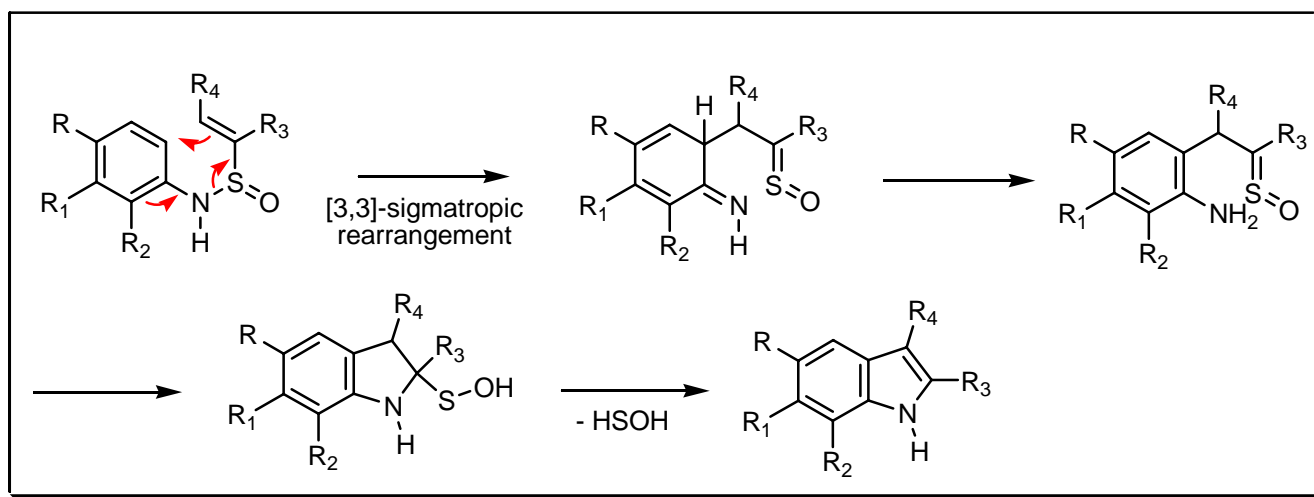
#### COMMENTS :

## JULIA INDOLE SYNTHESIS

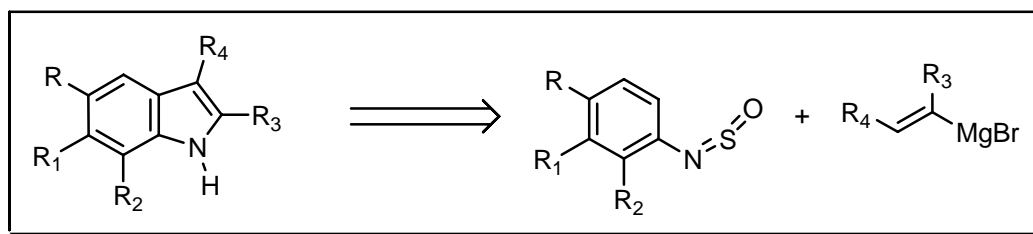
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

A clever synthesis of the indole ring system from sulfonamides involving a 1-aza-1'-oxa-[3,3]-sigmatropic rearrangement. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

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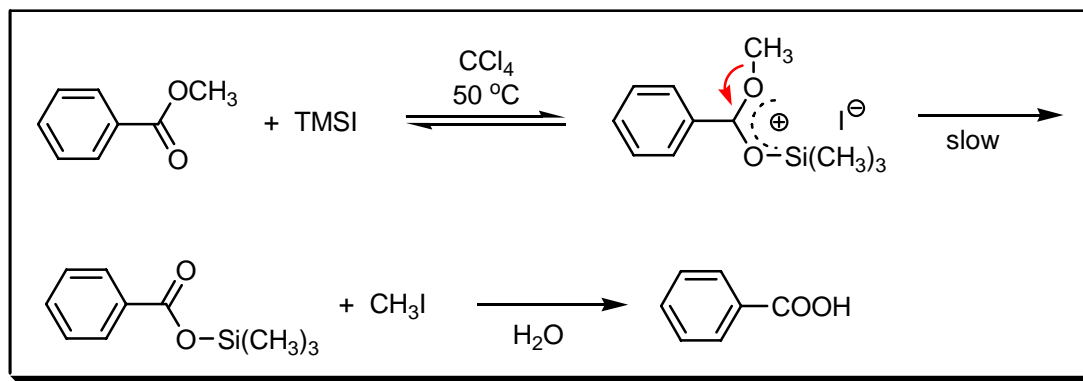
## COMMENTS :

## JUNG – OLAH – VORONKOV ETHER CLEAVAGE

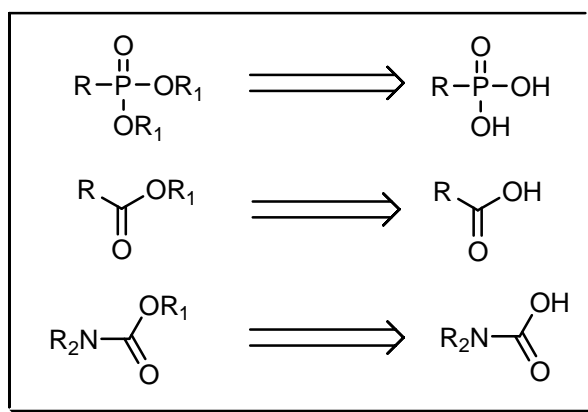
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The cleavage of ethers of esters, carbamates, phosphonates with trimethylsilyl bromides or iodides. See also **Appel – Robinson**, **Gustus** cleavage, **Herzig – Meyer**, **Mann** dealkylation, **Prey**, **Stoermer** dealkylation and **Zeisel** reactions.

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Smith – March : 520

Smith : 137, 638

Org. Synth. : 59, 35

Org. Synth. Coll. Vol. : 6, 353

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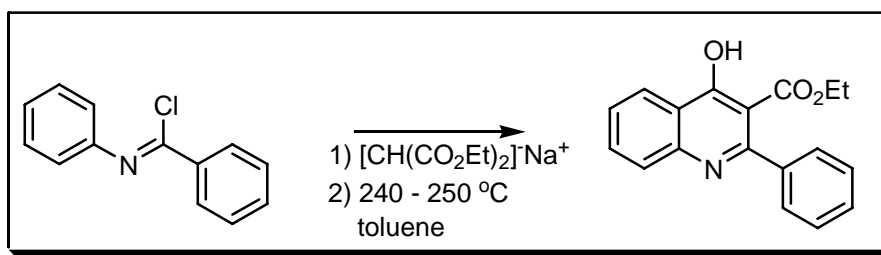
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## COMMENTS :

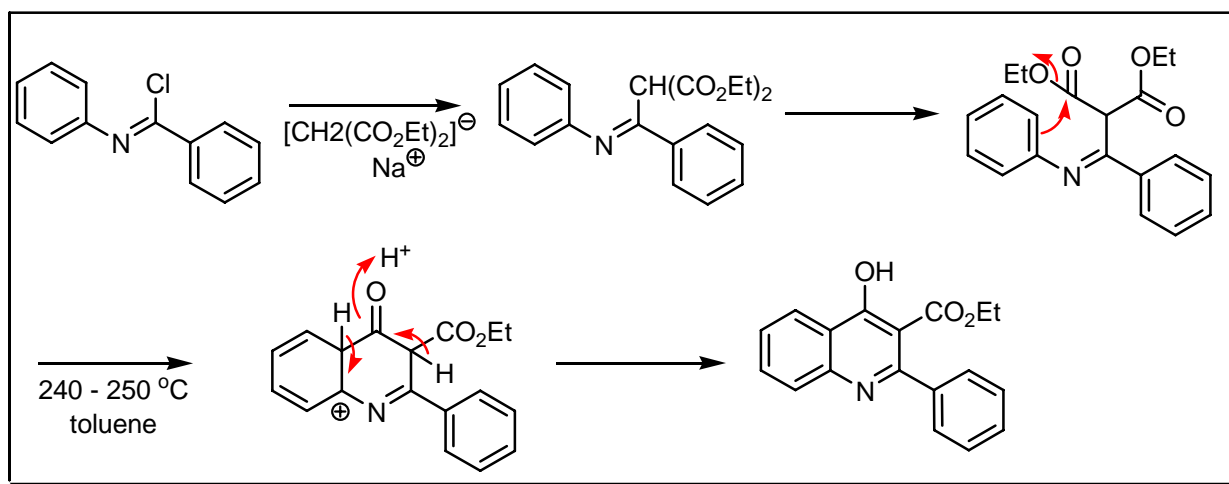
## JUST SYNTHESIS

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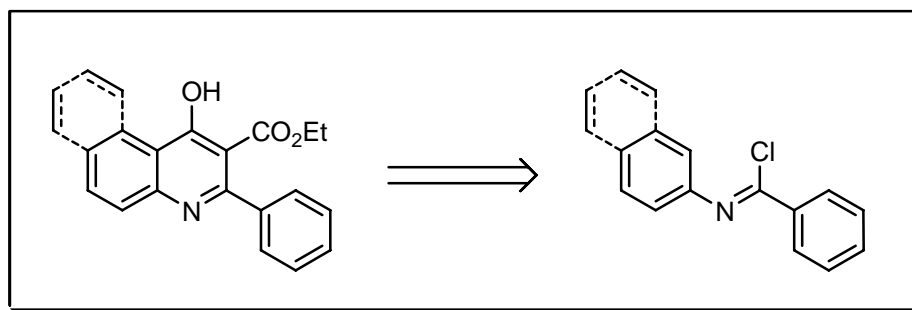
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



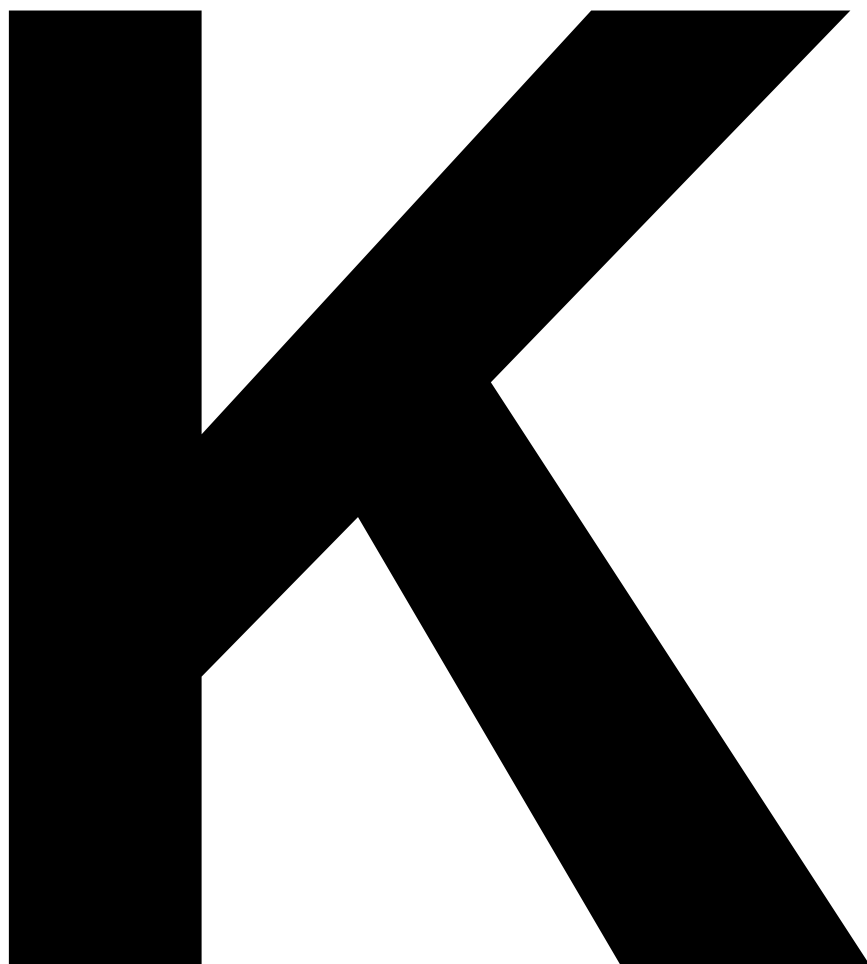
### NOTES :

Quinolines are obtained by the condensation of benzanilide imidochlorides with sodium diethyl malonate followed by the thermal cyclisation of the propionic acid derivatives. Analogous compounds are formed when sodium diethyl malonate is replaced by sodium diethyl acetoacetate. The method is also applicable to naphthylbenzyl iminochlorides. See also **Conrad – Limpach** and **Pfitzinger** reactions.

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### COMMENTS :



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**G**

GANEM OXIDATION · 1027

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*Z*

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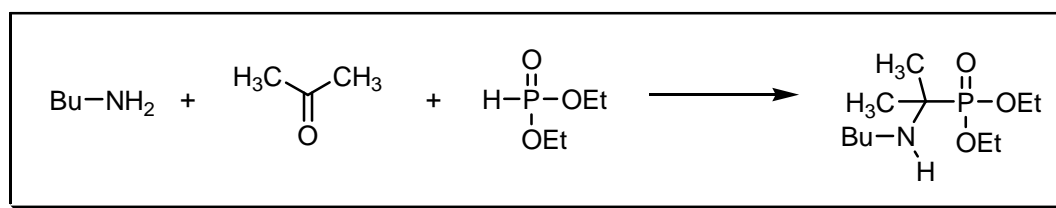
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*S*

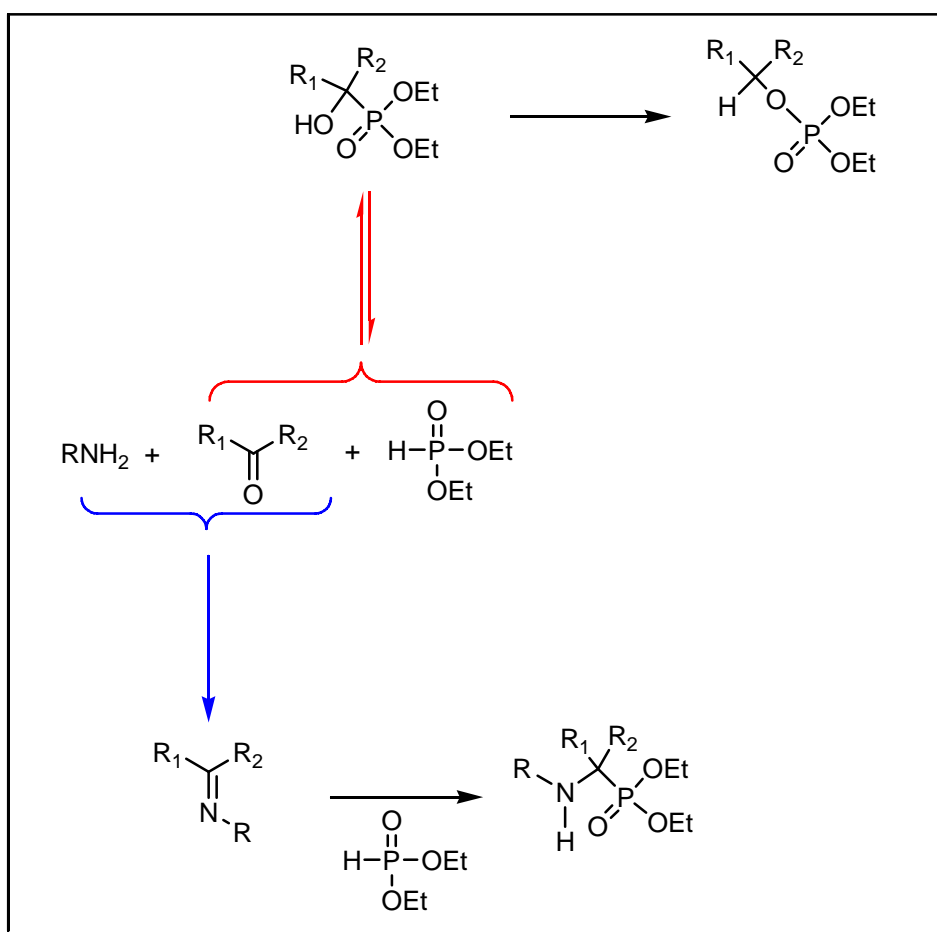
SCHROEDER MODIFICATION · 1013

## KABACHNIK – FIELDS REACTION

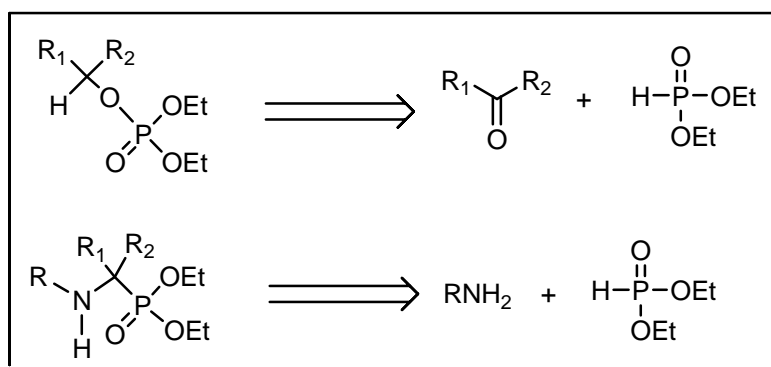
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The key step in the **Kabachnik – Fields** reaction is the nucleophilic addition of a nucleophilic amine to a carbonyl compound followed by the addition of a dialkyl or diaryl phosphite. Besides the formation of the aminophosphate, the hydroxyphosphate is observed. The carbonyl compound can be attacked by two nucleophiles, the amine and the phosphite. Both may compete for the electrophile. **Gancarz** has explained the different ratio of products obtained, in terms of the softer the carbonyl compound, the faster it will react with the softer phosphorus nucleophile and the slower it reacts with the harder amine nucleophile. See also **Moedritzer – Irani**, **Oleksyszyn** and **Pudovik** reactions.

---

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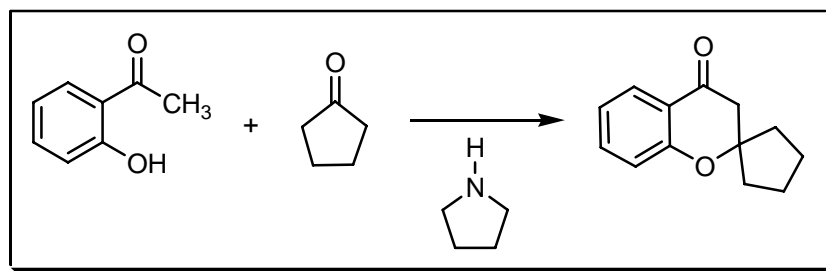
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## COMMENTS :

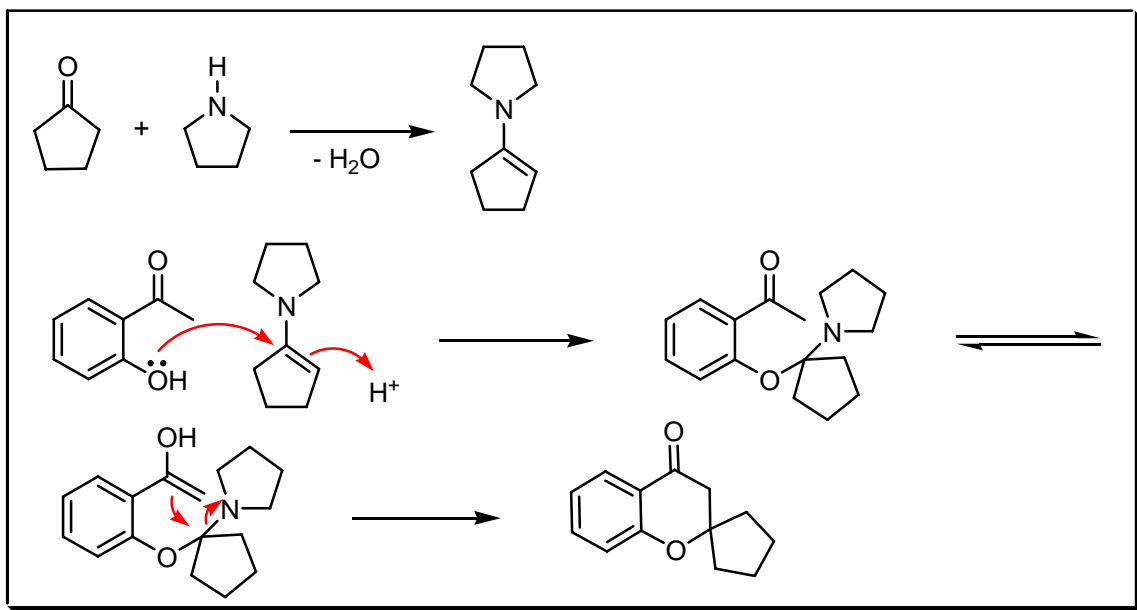
## KABBE CHROMANONE SYNTHESIS

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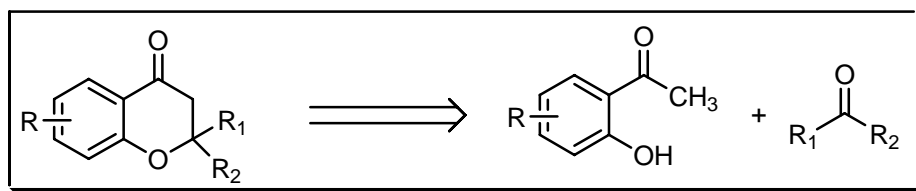
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of 4-chromanones by condensation of salicylaldehydes or  $\alpha$ -hydroxyaryl ketones with enamines or ketones. This is a **Mukaiyama** aldol reaction followed by acidic ring-closure of the  $\beta$ -hydroxy ketone.

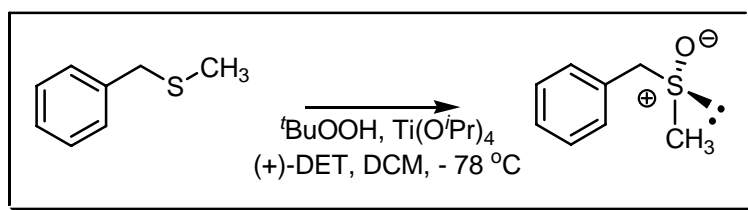
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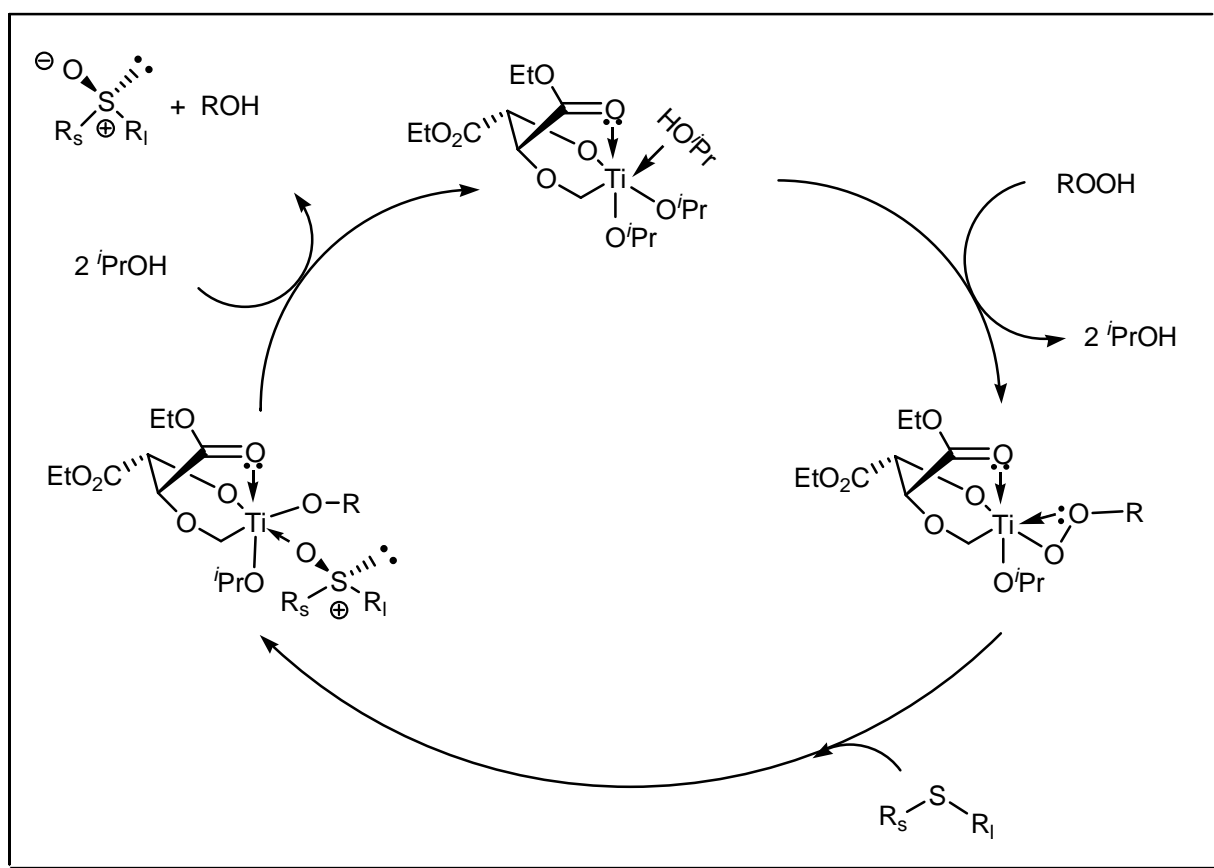
## COMMENTS :

## KAGAN – MODENA REACTION

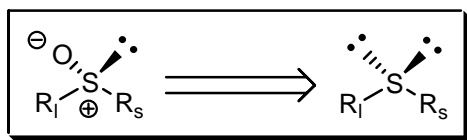
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The use of diethyltartrate and titanium isopropoxide and hydroperoxides as oxidant in the oxidation of aromatic thioethers. The use of the **Sharpless** reagent only afforded racemic sulfoxides. By adding one equivalent of water (later 2-propanol) and by adding molecular sieves the reaction was not only made enantioselective but also catalytic. For more details about the active species see **Potvin et al.** See also **Katsuki – Sharpless** epoxidation reaction.

## REFERENCES :

March : 1201

Smith – March : 1541

Smith : 320

Smith 2<sup>nd</sup> : 280

Org. Syn : 68, 49

Org. Syn. Coll. Vol. : 8, 464

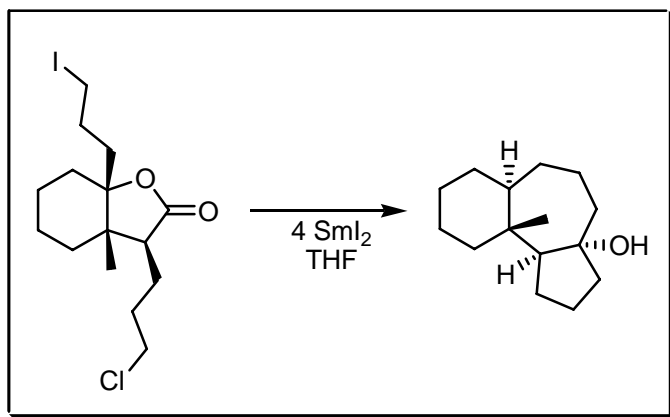
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## COMMENTS :

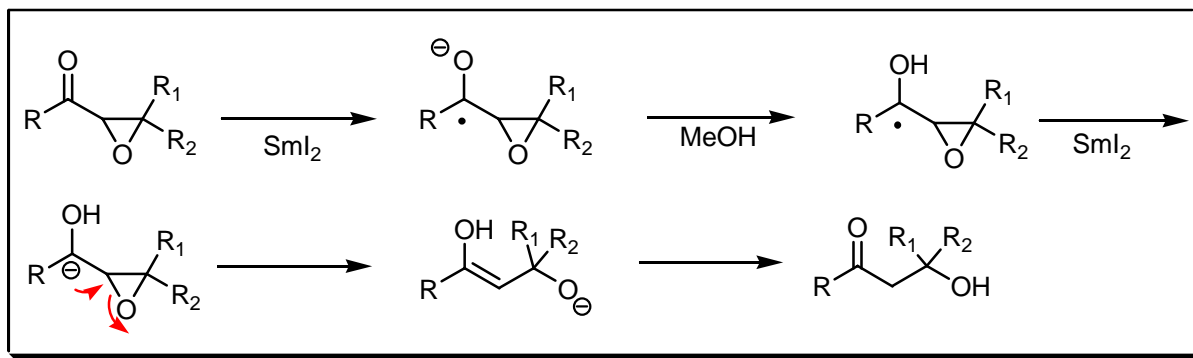
## KAGAN – MOLANDER REACTION

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### EXAMPLE :



## MECHANISM :



## NOTES :

Samarium and ytterbium reagents are used for the generation of free radicals, useful in **Barbier**-type reactions, reductions and cyclisations.

## REFERENCES :

**March** : 443, 1029, 1225

**Smith – March** : 528, 568

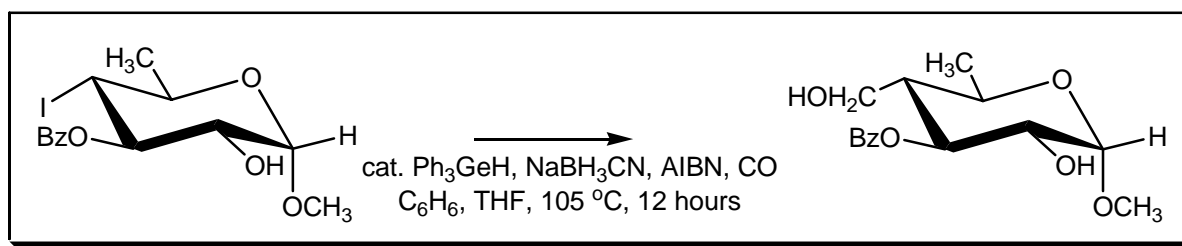
**Org. React.** : **46**, 211

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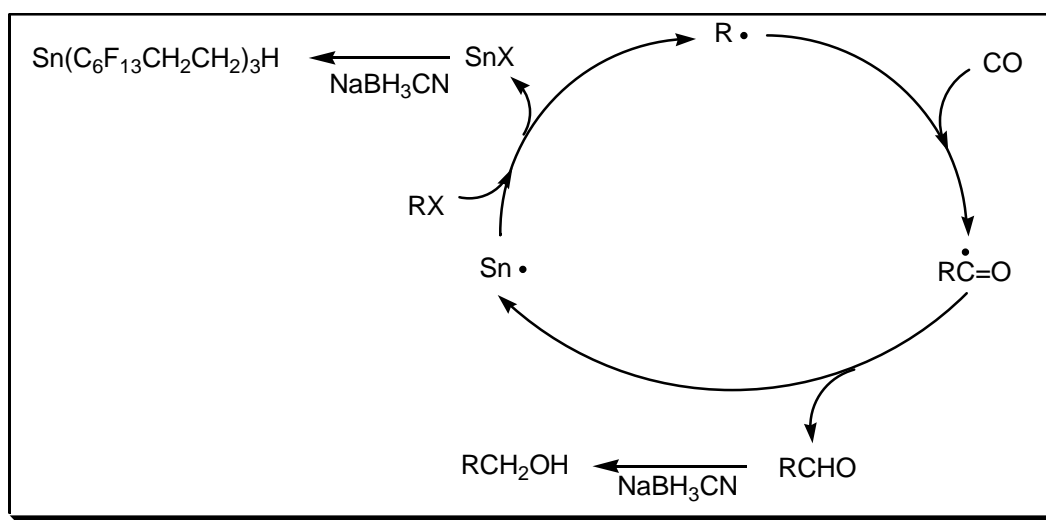
## COMMENTS :

## KAHNE – RYU – CURRAN HYDROXYMETHYLATION

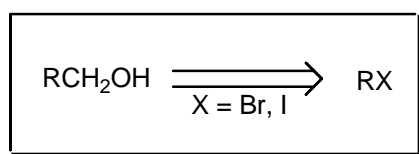
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Alkyl or aryl bromides or iodides are converted to the corresponding hydroxymethyl compounds by treatment with a catalytic amount of triphenylgermane or fluoros tin hydrides,  $\text{NaBH}_3\text{CN}$ , AIBN in benzene and THF or in the case of the tin compounds benzotrifluoride and *tert*-butyl alcohol.

### REFERENCES :

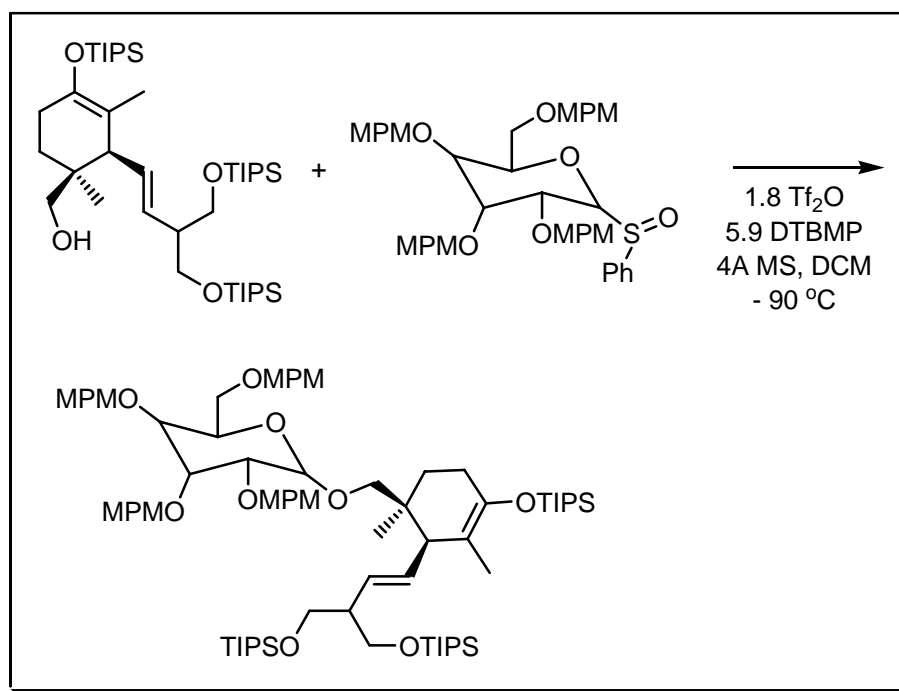
- 1) V. Gupta; D. Kahne, *Tetrahedron Lett.*, 1993, **34**, 591.
- 2) I. Ryu; T. Niguma; S. Minakata; M. Komatsu; S. Hadida; D.P. Curran, *Tetrahedron Lett.*, 1997, **38**, 7883.
- 3) T. Nakamura; H. Yorimitsu; H. Shinokubo; K. Oshima, *Synlett*, 1999, 1415.



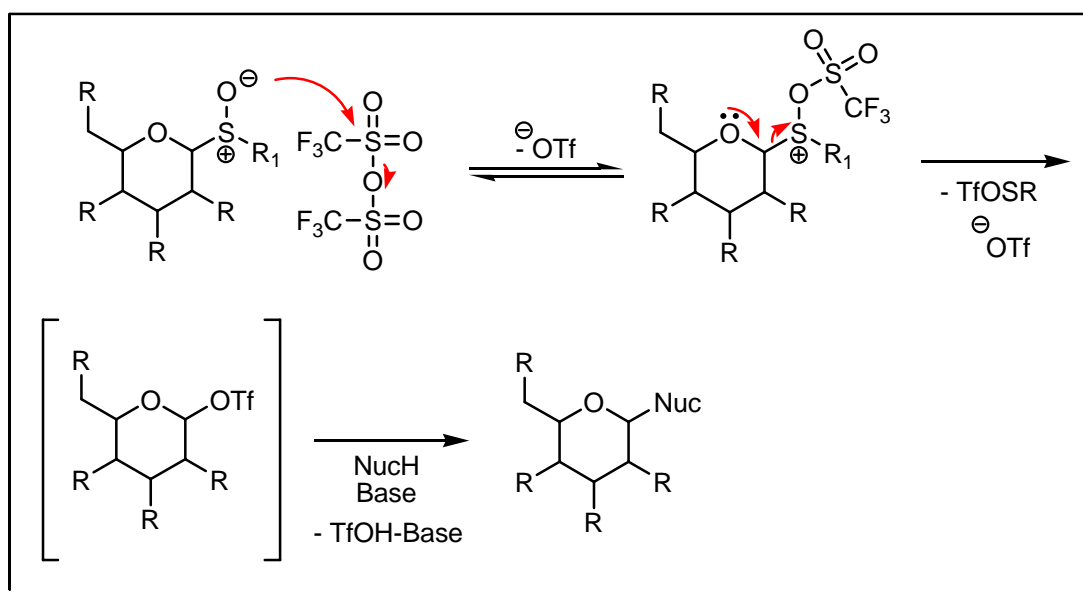
COMMENTS :

## KAHNE GLYCOSIDATION

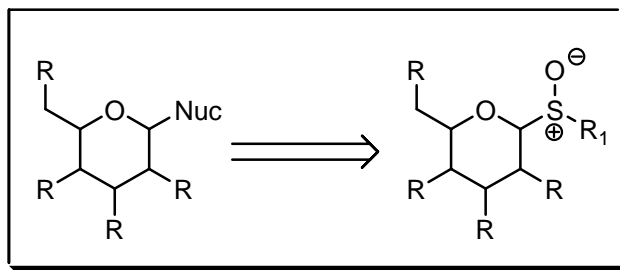
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The diastereoselective glycosidation at the anomeric centre of glycosyl sulfoxides with trifluoromethanesulfonic acid. See also **Fischer** glycosidation, **Koenigs – Knorr** glycosidation, **Michael** glycosidation and **Schmidt** glycosidation reactions.

## REFERENCES :

**Org. React.** : **64**, 115

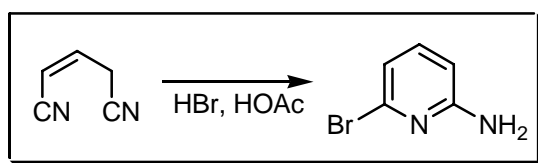
## REFERENCES :

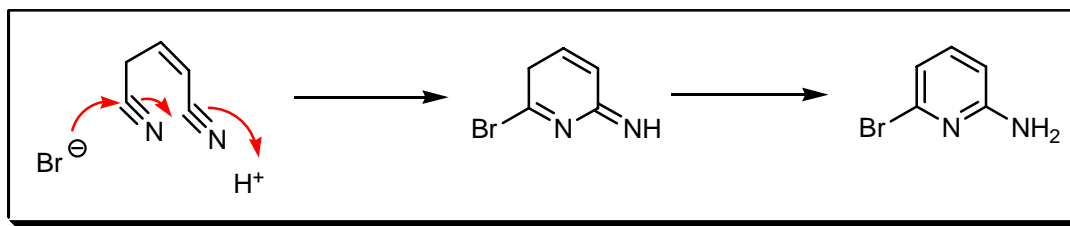
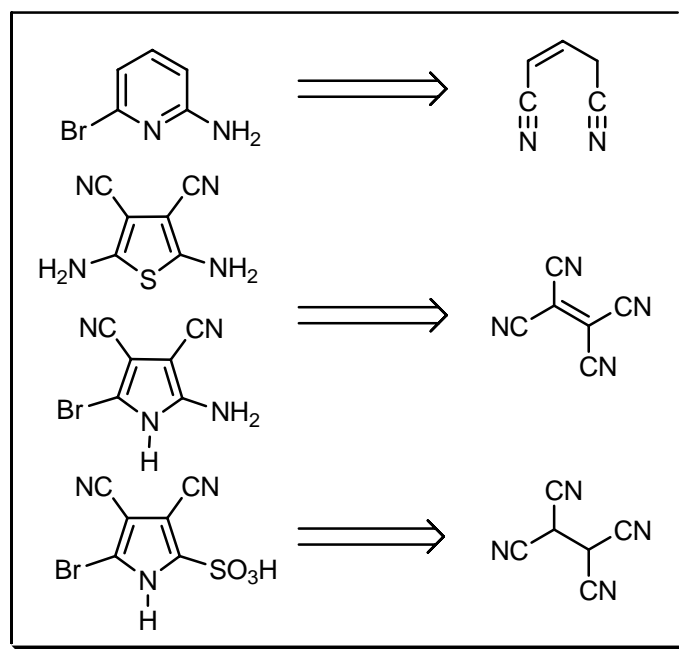
- 1) D. Kahne; S. Walker; Y. Cheng; D. van Engen, *J. Am. Chem. Soc.*, 1989, **111**, 6881.
- 2) L. Yan; C.M. Taylor; R. Goodnow, jr.; D. Kahne, *J. Am. Chem. Soc.*, 1994, **116**, 6953.
- 3) D. Crich; H. Li, *J. Org. Chem.*, 2000, **65**, 801.
- 4) H. Pellissier, *Tetrahedron*, 2004, **60**, 5123.

## COMMENTS :

## KAISER – JOHNSON – MIDDLETON DINITRILE CYCLISATION

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

The synthesis of heterocycles by cyclisation of dinitriles with HBr to afford pyridines, imidazoles, thiophenes and pyrroles.

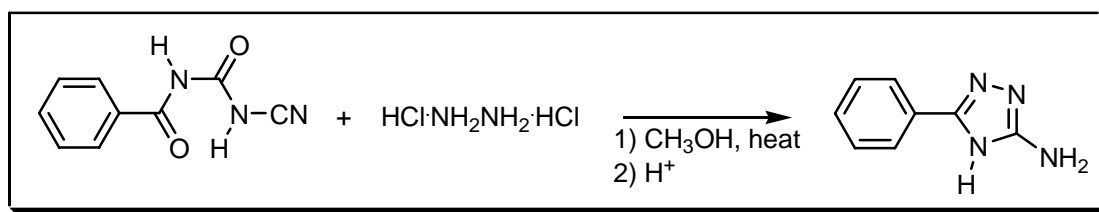
**REFERENCES :**

- 1) A.M. Kaiser; J.J. Roemer, *U.S. Patent*, 1953, 2630433.
- 2) W.J. Middleton; V.A. Engelhardt; B.S. Fisher, *J. Am. Chem. Soc.*, 1958, **80**, 2822.
- 3) F. Johnson; W.A. Nasutuavicus, *J. Org. Chem.*, 1964, **29**, 153.

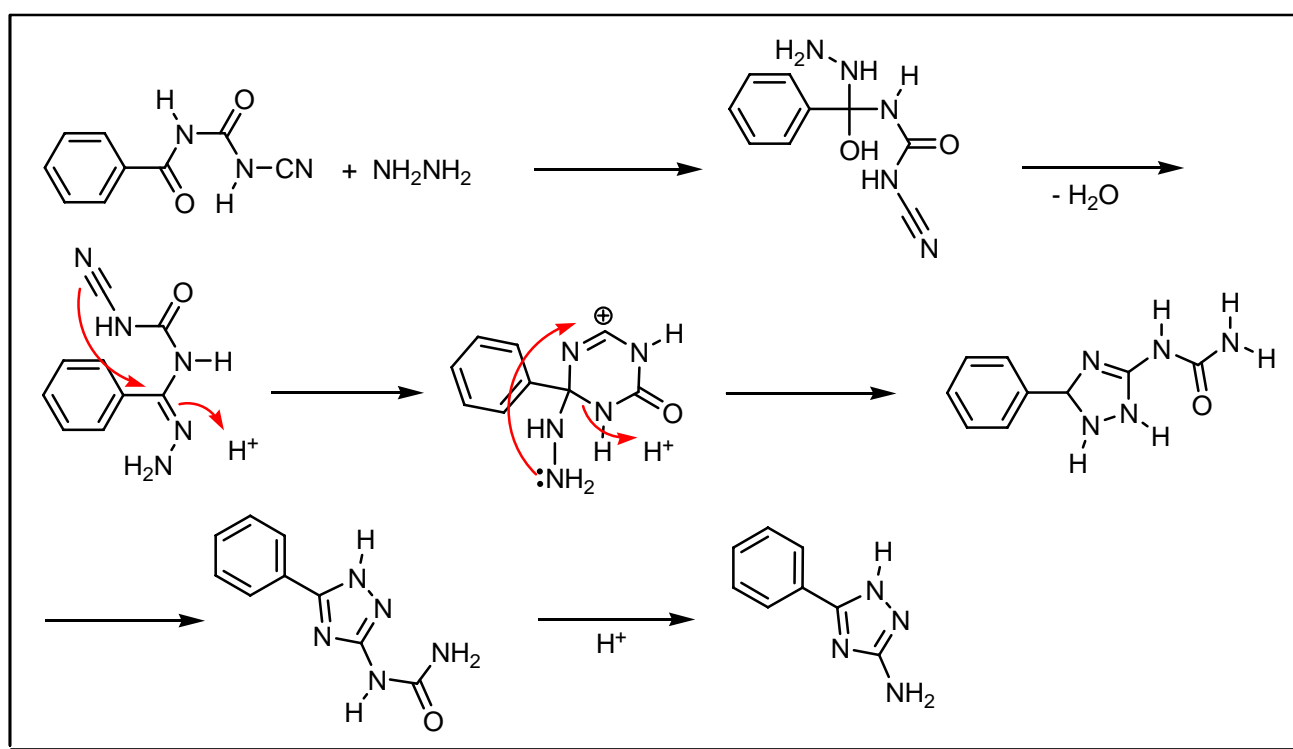
**COMMENTS :**

## KAISER TRIAZOLE SYNTHESIS

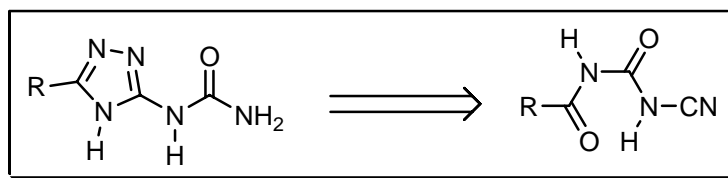
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

The synthesis of 3-amino- and 3-ureido-1,2,4-triazoles by condensation of acyl-3-cyanoureas with hydrazines. See also **Einhorn – Brunner** and **Pellizzari** reactions.

## REFERENCES :

- 1) D.W. Kaiser, *U.S. Patent*, 1945, 2382156. (*Chem. Abs.*, 1946, **40**, 368)

2) D.W. Kaiser, *U.S. Patent*, 1946, 2399598. (*Chem. Abs.*, 1946, **40**, 4227)

3) A.A. Komzak; J.B. Polya, *J. Appl. Chem.*, 1952, **2**, 666.

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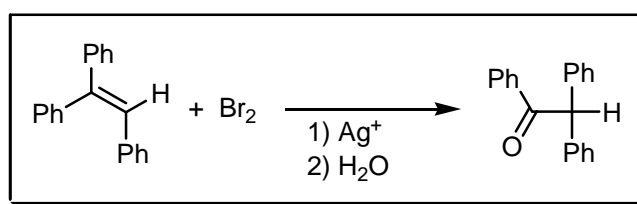
**COMMENTS :**

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**KAKIS – KIKUCHI REARRANGEMENT**

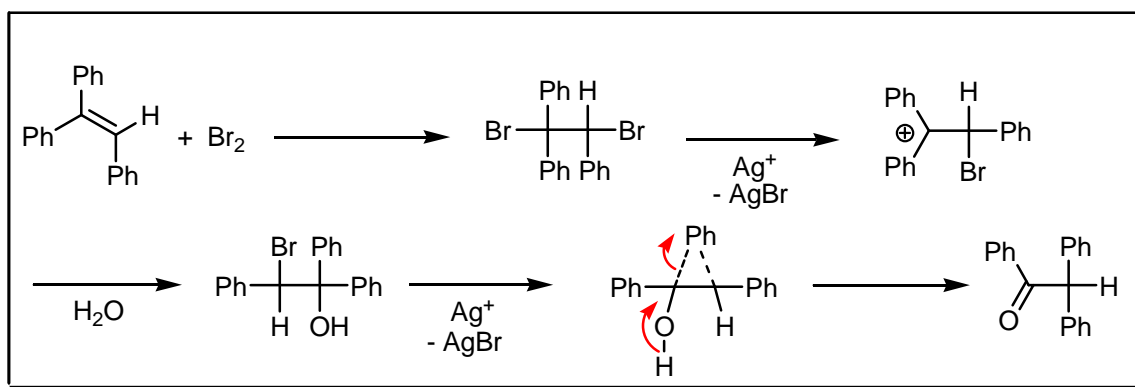
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**EXAMPLE :**



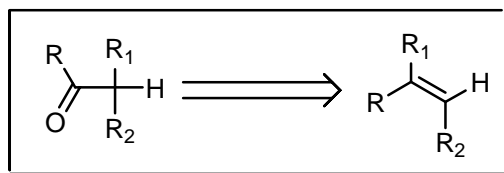
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**MECHANISM :**



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**DISCONNECTION :**



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**NOTES :**

The formation of ketones by bromination followed by rearrangement of substituted ethylenes using silver(I) salts.

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## REFERENCES :

March : 1197

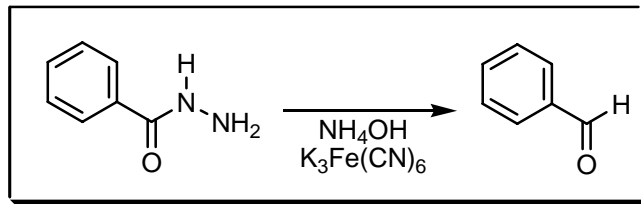
Smith – March : 1538

- 
- 1) F.J. Kakis; D. Brase; A. Oshima, *J. Org. Chem.*, 1971, **36**, 4117.
  - 2) M. Fétizon; F.J. Kakis; V. Ignatiadou–Ragoussis, *J. Org. Chem.*, 1973, **38**, 1732.
  - 3) H. Kikuchi; K. Kogure; M. Toyoda, *Chem. Lett.*, 1984, 341.
  - 4) M. Koreeda; L.A. Dixon; J.D. Hsi, *Synlett*, 1993, 555.
  - 5) K.W. Field; J.S. Moroz, *Abstr. Pap. Am. Chem. Soc.*, 2001, **222**, 426.
- 

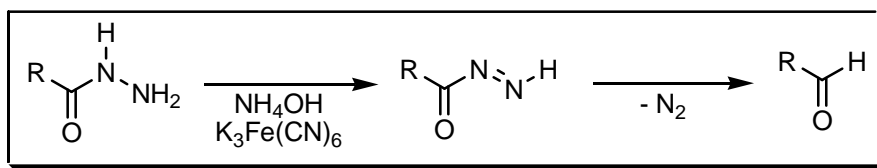
## COMMENTS :

## KALB – GROSS SYNTHESIS

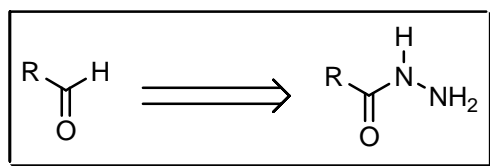
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

Aldehydes are obtained by the alkaline oxidation of acylhydrazines (potassium ferricyanide in an excess ammonia solution). Also other oxidation reagents have been used. See also **McFadyen – Stevens** reaction.

## REFERENCES :

Houben – Weyl : 7/1, 297

Org. React. : 8, 218

1) L. Kalb; O. Gross, *Ber. Dtsch. Chem. Ges.*, 1926, **59**, 727.

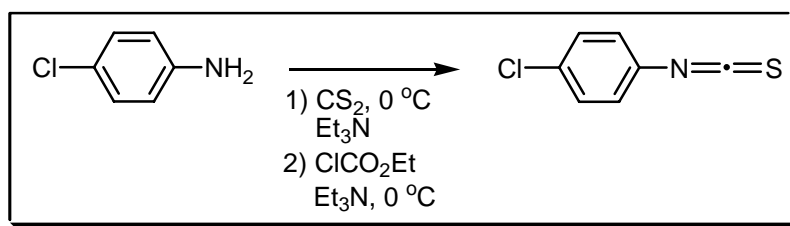
2) L.N. Ferguson, *Chem. Rev.*, 1946, **38**, 227.

3) H.N. Wingfield; W.R. Harlan; H.R. Hanmer, *J. Am. Chem. Soc.*, 1952, **74**, 5796.

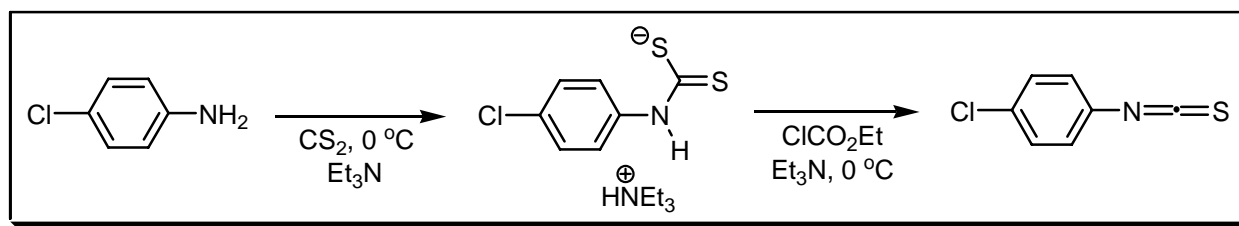
## COMMENTS :

## KALUZA ISOTHIOCYANATE SYNTHESIS

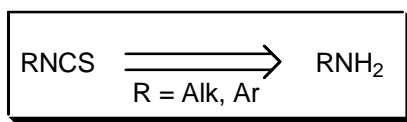
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The formation of thioisocyanates from amines. The second step can also be done with lead nitrate. The original **Kaluza** reaction is not applicable to aryl amines, see **Hodgkins** *et al.* See also **Böttiger – Michaelis** reaction and **Hugershoff** synthesis.

## REFERENCES :

Org. Synth. : 6, 72

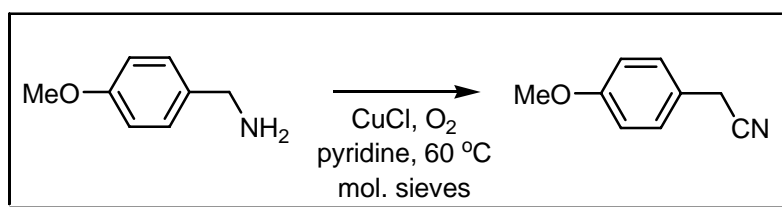
Org. Synth. Coll. Vol. : 1, 447

- 1) H. Kaluza, *Monatsh. Chem.*, 1912, **33**, 363.
- 2) E. Schmidt; E. Kammerl; D. Ross, *Liebigs Ann. Chem.*, 1955, **594**, 233.
- 3) J.E. Hodgkins; M.G. Ettlinger, *J. Org. Chem.*, 1956, **21**, 404.
- 4) J.E. Hodgkins; W.P. Reeves; Y.T. Liu, *J. Am. Chem. Soc.*, 1961, **83**, 2532.
- 5) J.E. Hodgkins; W.P. Reeves, *J. Org. Chem.*, 1964, **29**, 3098.
- 6) S. Rádl, *Coll. Czech. Chem. Commun.*, 1992, **57**, 656.

## COMMENTS :

## KAMETANI – TSUJI AMINE OXIDATION

### EXAMPLE :





### Oxidation in pyridine :



952

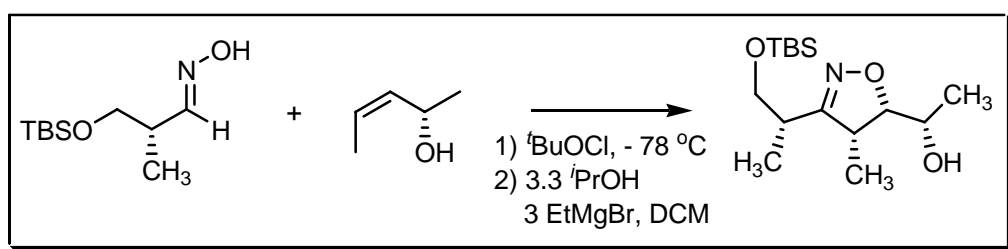
## REFERENCES :

- 1) T. Kajimoto; H. Takahashi; J. Tsuji, *J. Org. Chem.*, 1976, **41**, 1389.
- 2) T. Kametani; K. Takahashi; T. Ohsawa; M. Ihara, *Synthesis*, 1977, 245.
- 3) P. Capdevielle; A. Lavigne; M. Maumy, *Synthesis*, 1989, 453.
- 4) P. Capdevielle; A. Lavigne; M. Maumy, *Tetrahedron*, 1990, **46**, 2835.
- 5) P. Capdevielle; A. Lavigne; D. Sparfel; J. Baranne-Lafont; N.K. Cuong; M. Maumy, *Tetrahedron Lett.*, 1991, **31**, 3305.
- 6) Y. Maeda; T. Nishimura; S. Uemura, *Bull. Chem. Soc. Jpn.*, 2003, **76**, 2399.

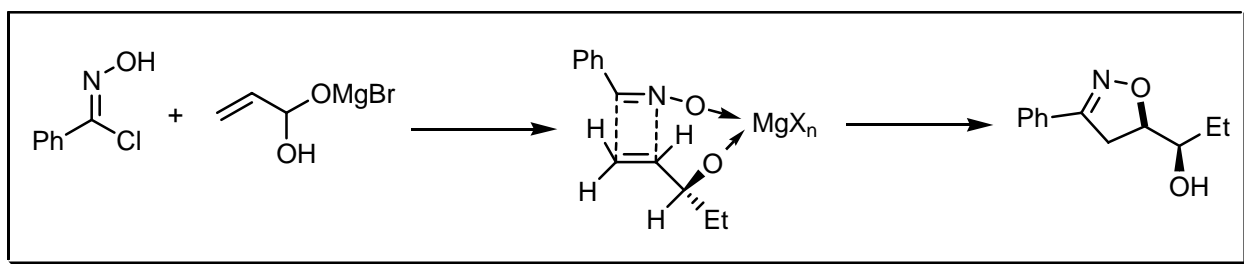
## COMMENTS :

## KANEMASA REACTION

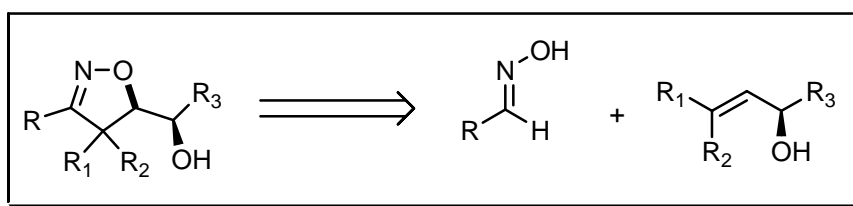
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



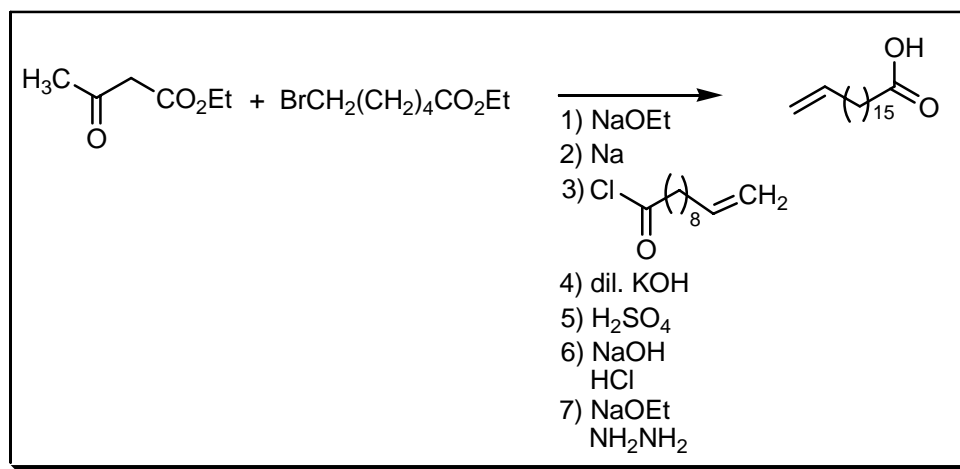
**NOTES :**

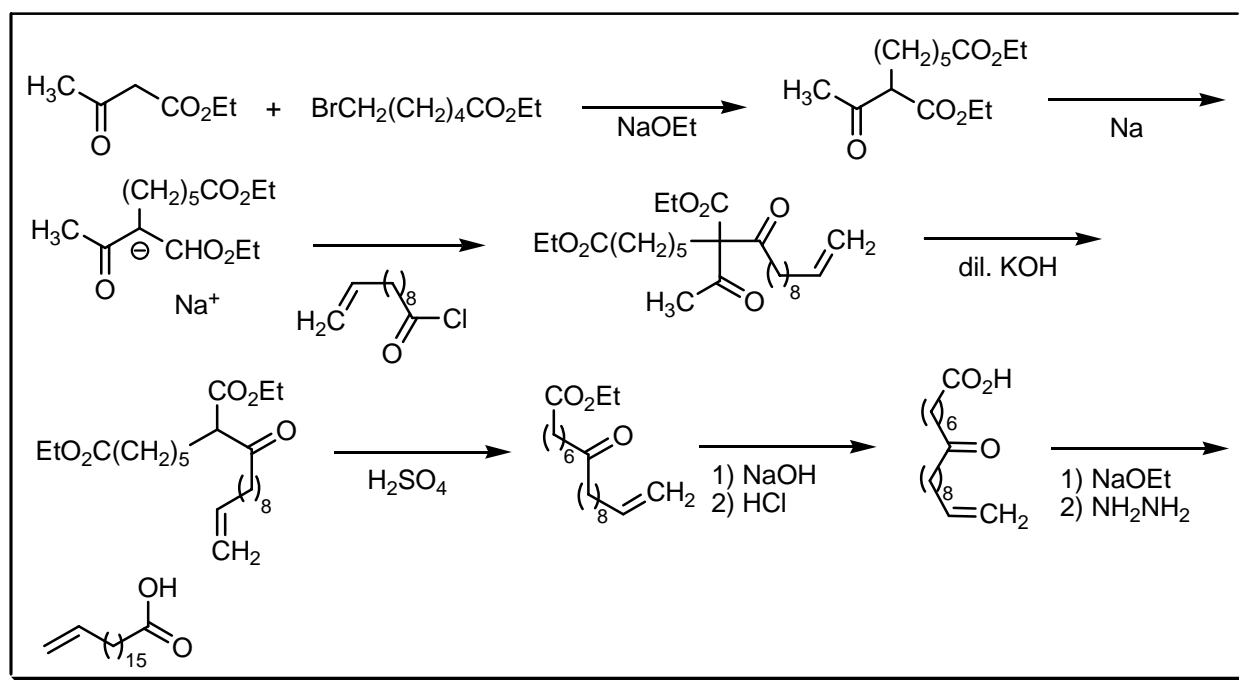
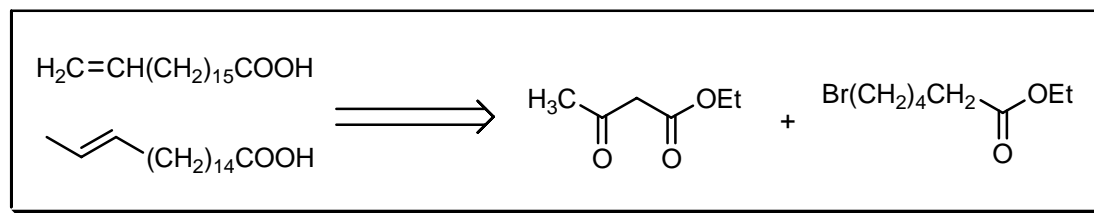
This reaction is a magnesium(II) directed nitrile oxide cycloaddition with allylic alcohols.

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**REFERENCES :**

- 1) S. Kanemassa; M. Nishiuchi; A. Kamimure; K. Hori, *J. Am. Chem. Soc.*, 1994, **116**, 2324.
  - 2) S. Kanemassa; K. Okuda; H. Yamamoto; S. Kaga, *Tetrahedron Lett.*, 1997, **38**, 4095.
  - 3) K.V. Gothelf; K.A. Jørgensen, *Chem. Rev.*, 1998, **98**, 863.
  - 4) J.W. Bode; N. Fraefel; D. Muri; E.M. Carreira, *Angew. Chem., Int. Ed.*, 2001, **40**, 2082.
- 

**COMMENTS :****KAPP – KNOLL SYNTHESIS****EXAMPLE :**

**MECHANISM :****DISCONNECTION :****NOTES :**

This synthesis of these acids (16, 17- or 17,18-octadecenoic acid) involves the preparation of the unsaturated keto-acids from acetoacetic ester, followed by the reduction of these acids by the **Wolff – Kishner – Staudinger** method. This method is an example of the **Robinson – Robinson** synthesis. See also **Baudart**, **Bowman**, **Noller** and **Robinson – Robinson** reactions.

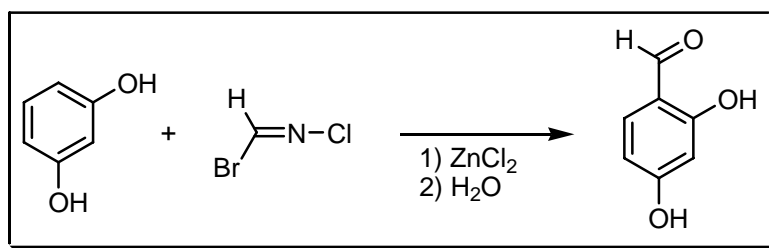
**REFERENCES :**

R. Kapp; A. Knoll, *J. Am. Chem. Soc.*, 1943, **65**, 2062.

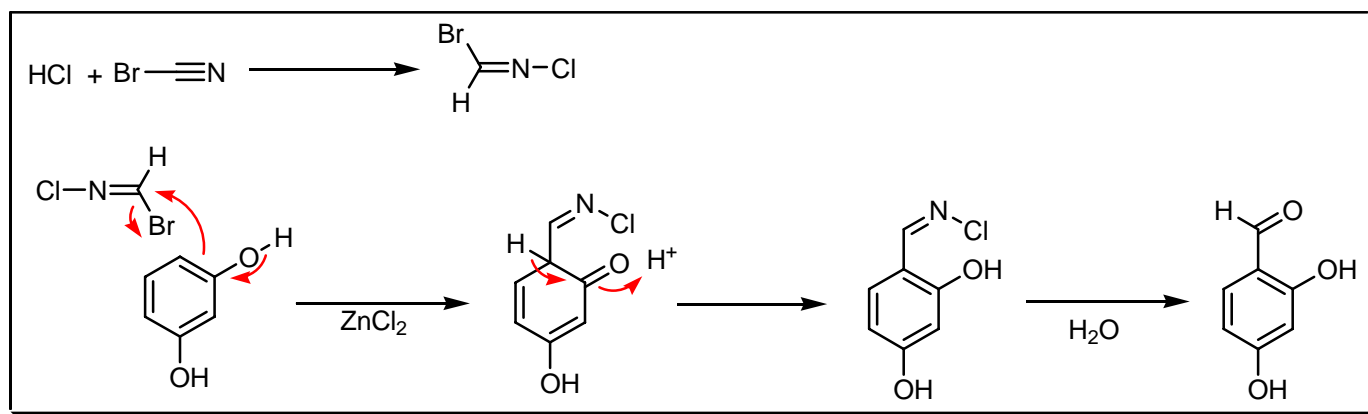
**COMMENTS :**

## KARRER SYNTHESIS

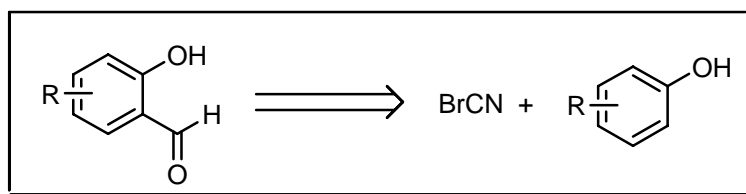
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

A phenolic aldehyde is obtained by treating a phenol with cyanogen bromide, hydrogen chloride and zinc chloride. See also **Gattermann – Koch**, **Houben – Fischer** and **Houben – Hoesch** reactions.

### REFERENCES :

**Houben – Weyl** : E5, 1444

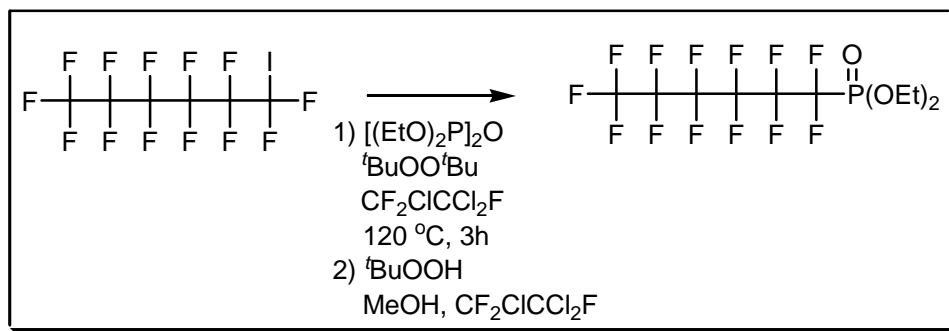
1) P. Karrer, *Helv. Chim. Acta*, 1919, **2**, 89.

2) J. Renz, *Helv. Chim. Acta*, 1947, **30**, 124.

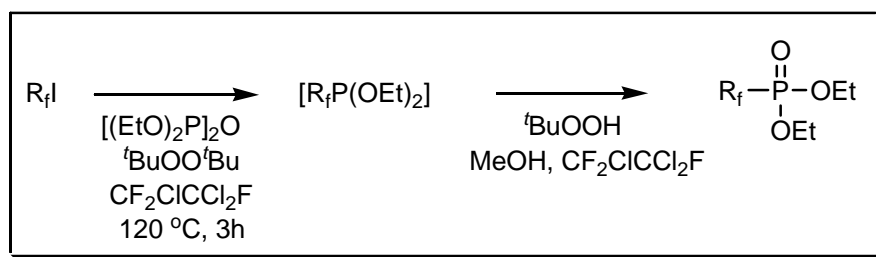
COMMENTS :

## KATO – YAMABE REACTION

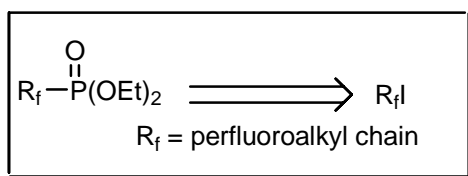
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

A synthetic route to perfluoroalkyl phosphonates *via* phosphates. See also **Burton – Wiemers** reaction.

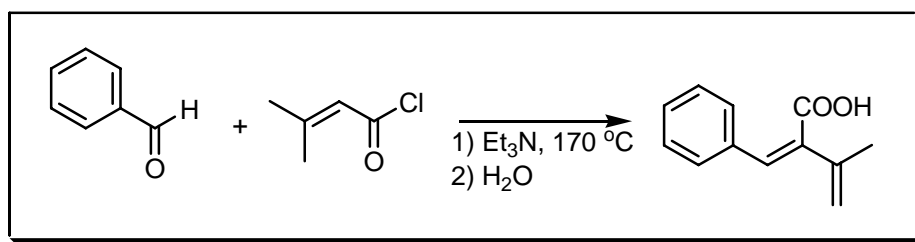
REFERENCES :

- 1) M. Kato; M. Yamabe, *J. Chem. Soc., Chem. Commun.*, 1981, 1173.
- 2) H.K. Nair; D.J. Burton, *J. Am. Chem. Soc.*, 1997, **119**, 9137.

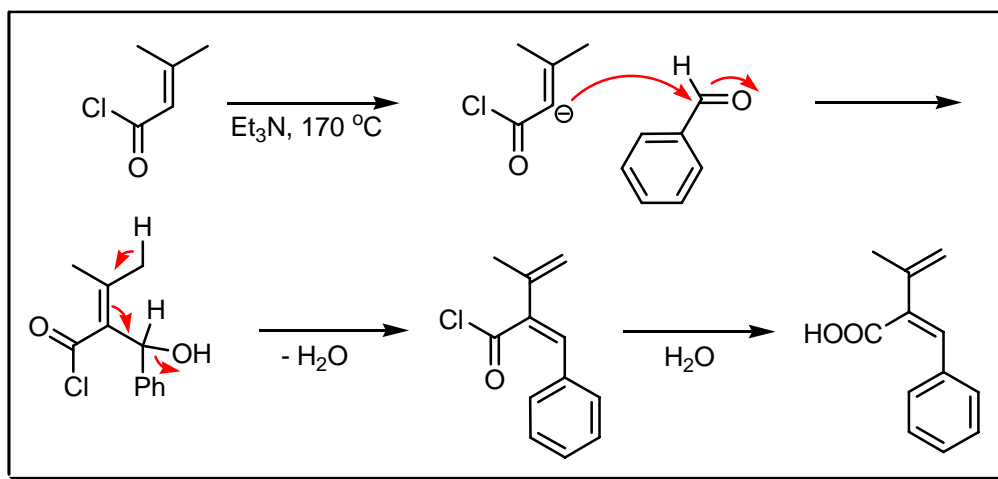
COMMENTS :

## KATOH SYNTHESIS

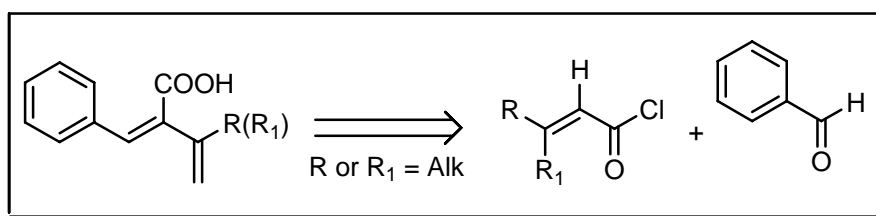
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

Acid chlorides of the type RCH<sub>2</sub>COCl condense with benzaldehydes in the presence of triethylamine to yield substituted cinnamic acids.

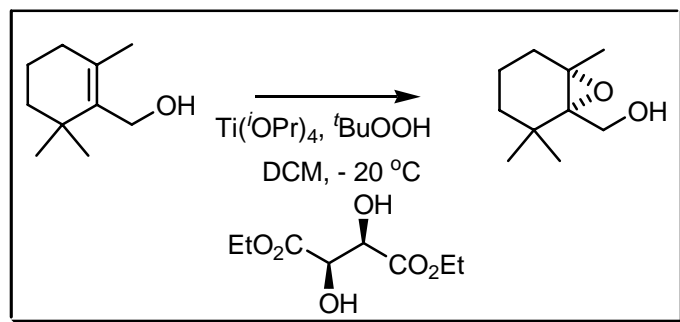
## REFERENCES :

- 1) Katoh, *Sci. Rep. Tokyo Bunrika Daigaku*, 1935, 257. (*Chem. Zentralbl.* 1936, **107**, 2324)
- 2) C.A. VanderWerf, *Trans. Kansas Acad. Sci.*, 1947, **50**, 363. (*Chem. Abs.*, 1948, **42**, 2571.)

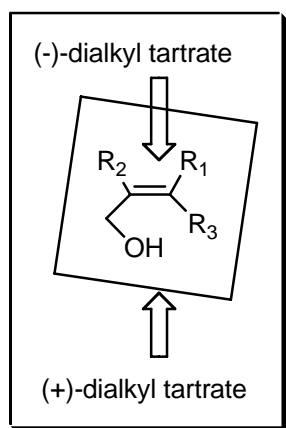
## COMMENTS :

## KATSUKI – SHARPLESS EPOXIDATION

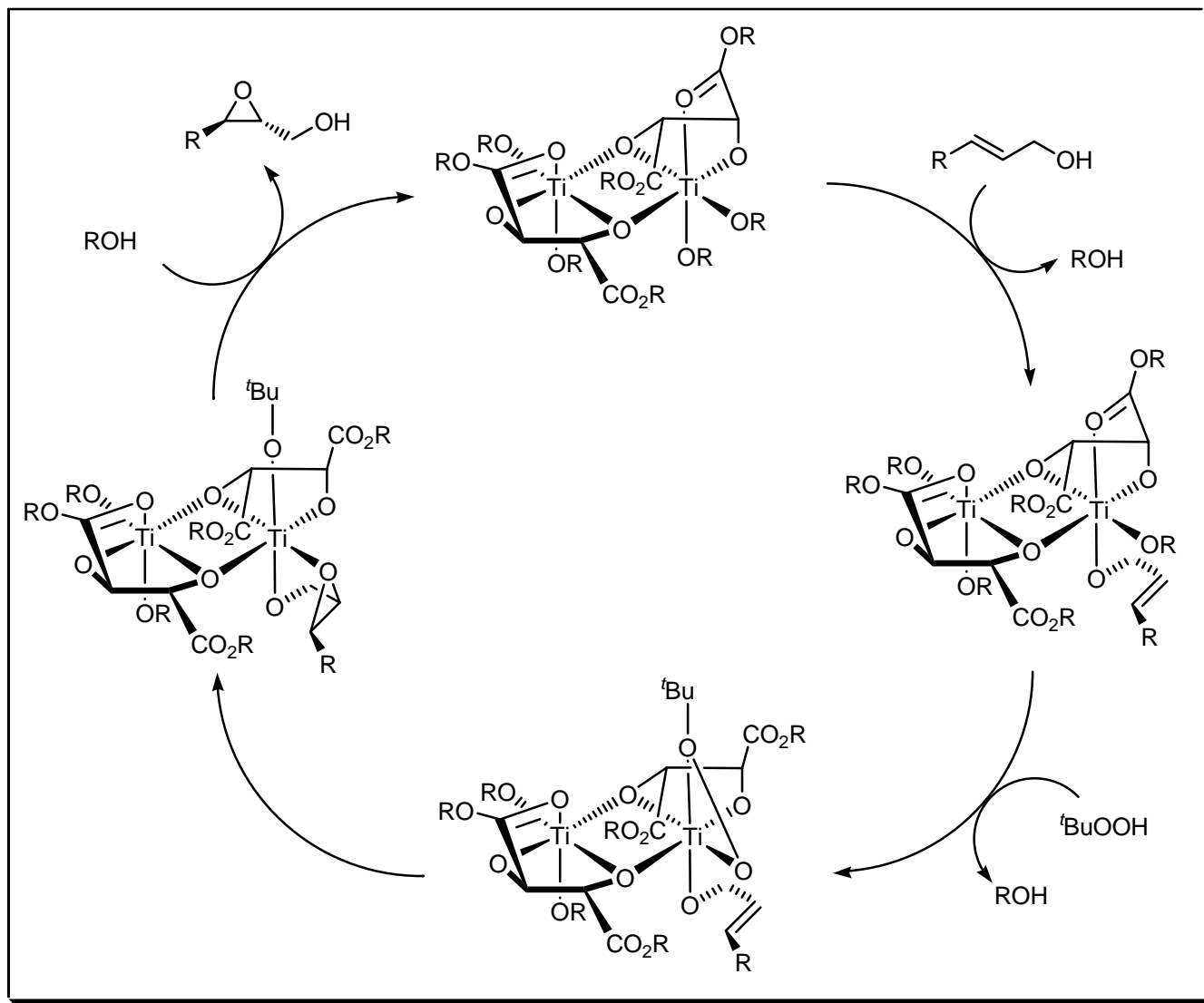
### EXAMPLE :



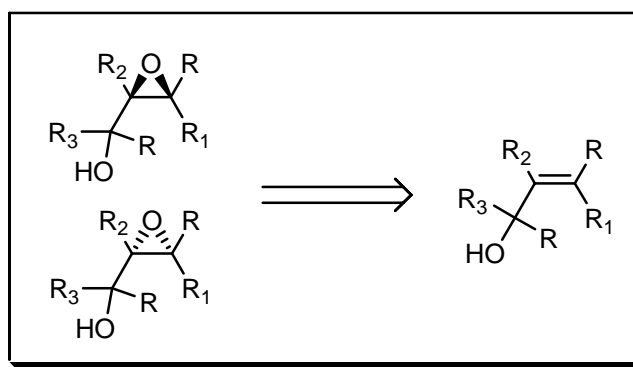
### MECHANISM :







#### DISCONNECTION :



#### NOTES :

This is the enantioselective epoxidation of a wide range of allyl alcohols using titanium alkoxide, (+) or (-) diethyltartarate (DET) and *t*-butyl hydroperoxide (TBHP). It is compatible with a various amount of functional groups. The use of tartrate esters results in enantioselective epoxidation of the alkene. The reaction was later fine-tuned to a catalytic version by the addition of molecular sieves. The reaction is almost insensitive to the identity of R and R<sub>1</sub>. R<sub>2</sub> has to be small for the reaction to be fast and highly enantioselective. R<sub>3</sub> has to be hydrogen otherwise the reaction rate will decrease. Titanium has also been replaced by zirconium. See also **Buchner – Curtius – Schlotterbeck**,

**REFERENCES :**

Smith – March : 1053

Smith : 275

Smith 2<sup>nd</sup> : 239

Org. React. : 48, 1

Org. Synth. : 63, 66

Org. Synth. Coll. Vol. : 7, 461

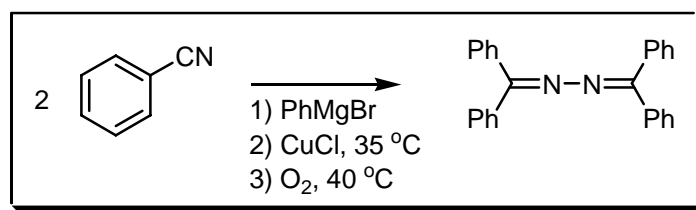
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- 1) T. Nakata; G. Schmid; B. Vranessis; M. Okigawa; T. Smith–Palmer; Y. Kishi, *J. Am. Chem. Soc.*, 1978, **100**, 2933.
  - 2) E.J. Corey; A. Marfat; J.R. Falck; J.O. Albright, *J. Am. Chem. Soc.*, 1980, **102**, 1433.
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  - 5) S. Danishefsky; R. Zamboni; M. Kahn; S.J. Etheredge, *J. Am. Chem. Soc.*, 1981, **103**, 3460.
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  - 8) M.G. Finn; K.B. Sharpless, *J. Am. Chem. Soc.*, 1991, **113**, 113.
  - 9) S. Takano; Y. Iwabuchi; K. Ogasawara, *Tetrahedron Lett.*, 1991, **32**, 3527.
  - 10) A.H. Hoveyda; D.A. Evans; G.C. Fu, *Chem. Rev.*, 1993, **93**, 1307.
  - 11) T. Yoshimitsu; K. Ogasawara, *Chem. Commun.*, 1994, 2197.
  - 12) A.C. Spivey; S.J. Woodhead; M. Weston; B.I. Andrews, *Angew. Chem., Int. Ed.*, 2001, **40**, 769.
  - 13) J. Huang; E.J. Corey, *Org. Lett.*, 2003, **5**, 3455.
  - 14) N.N. Reed; T.J. Dickerson; G.E. Boldt; K.D. Janda, *J. Org. Chem.*, 2005, **70**, 1728.
- 

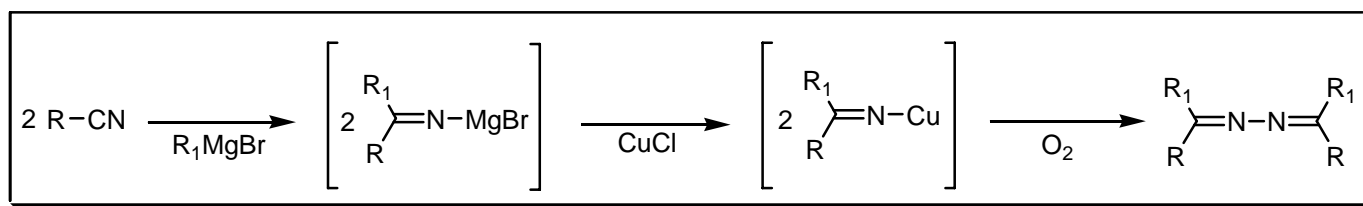
**COMMENTS :**

## KAUFFMANN DIMERISATION

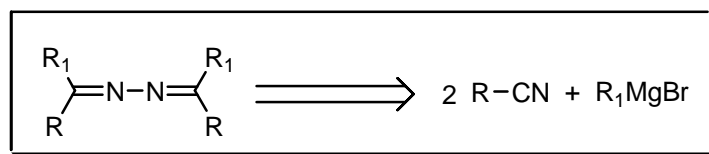
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Substituted methyleneamidomagnesium halides, which are readily obtainable by the action of **Grignard** compounds on nitriles, are converted by copper(I) chloride in THF, diethyl ether mixtures into thermally fairly stable copper(I) amides, which react rapidly with oxygen to form ketazines.

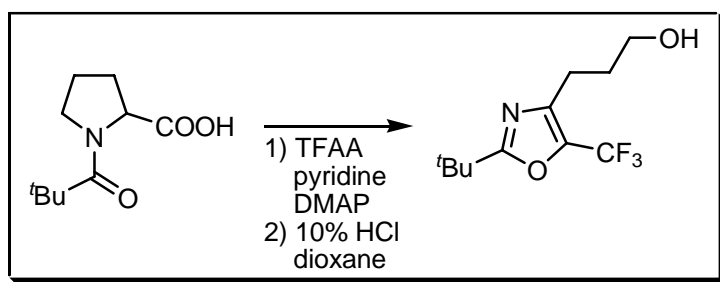
### REFERENCES :

- 1) Th. Kauffmann; J. Albrecht; D. Berger; J. Legler, *Angew. Chem., Int. Ed. Engl.*, 1967, **6**, 633.
- 2) Th. Kauffmann; D. Berger, *Chem. Ber.*, 1968, **101**, 3022.
- 3) Th. Kauffmann, *Angew. Chem., Int. Ed. Engl.*, 1974, **13**, 291.

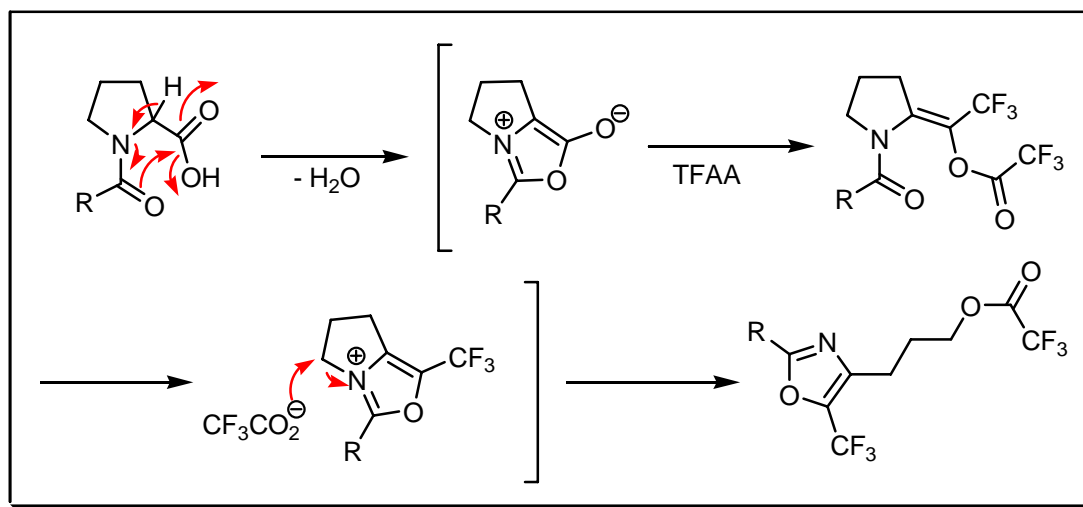
### COMMENTS :

# KAWASE REARRANGEMENT

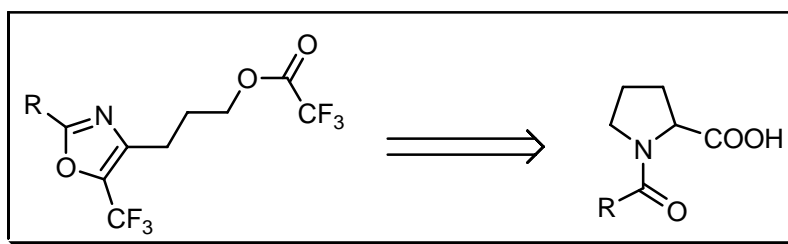
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The base-catalysed reaction of *N*-acyl prolines with trifluoroacetic anhydride proceeds through mesoionic 1,3-oxazolium-5-olates, followed by ring-closure of the pyrrolidine ring. See also **Dakin – West** reaction.

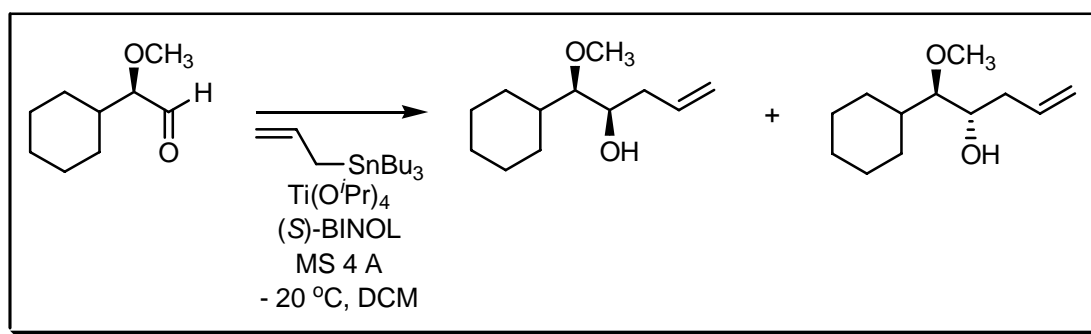
## REFERENCES :

- 1) M. Kawase, *Chem. Commun.*, 1992, 1076.
- 2) M. Kawase; H. Miyamae; M. Narita; T. Kurihara, *Tetrahedron Lett.*, 1993, **34**, 859.
- 3) M. Kawase, *Tetrahedron Lett.*, 1994, **35**, 149.
- 4) M. Kawase; S. Saito; H. Kikuchi; H. Miyamae, *Heterocycles*, 1997, **45**, 2185.

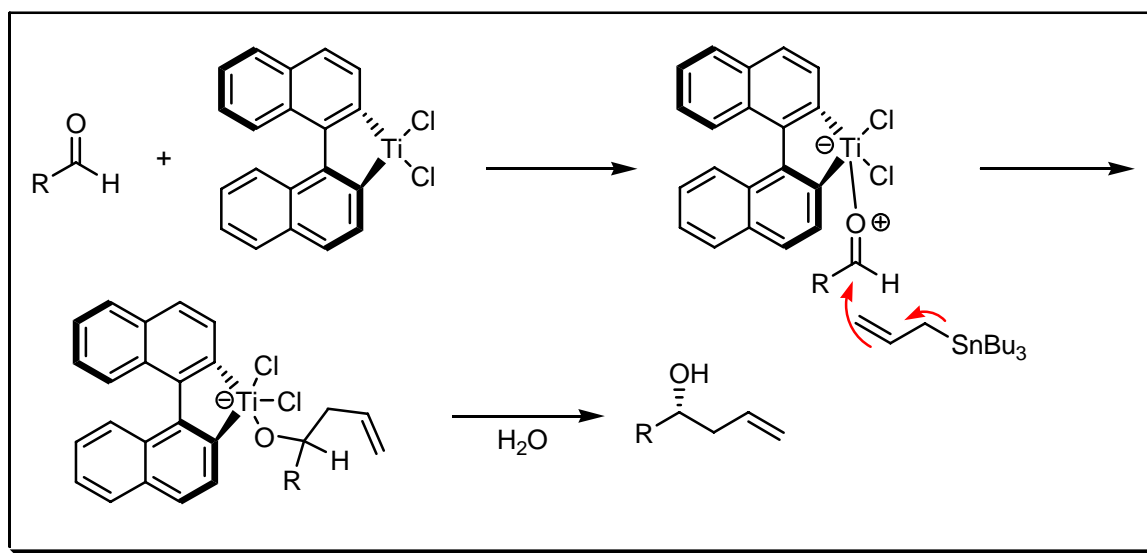
COMMENTS :

KECK ALLYLATION

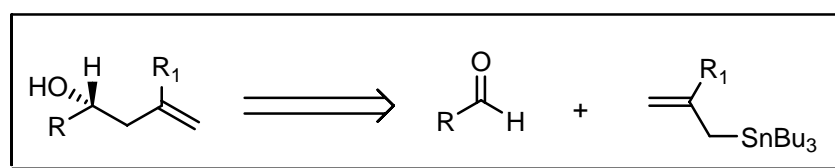
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

This is the efficient catalytic and enantioselective addition of allyl tin reagents to aldehydes. The diastereoselectivity can be controlled by the mode of addition of the Lewis acid and allyl tin reagent. See also **Duthaler – Haffner**, **Hoffmann – Yamamoto**, **Ibuka – Yamamoto**, **Matteson** and **Thomas** reactions.

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## REFERENCES :

**Org. Synth.** : **68**, 104; **75**, 12

**Org. Synth. Coll. Vol.** : **8**, 23; **10**, 2305

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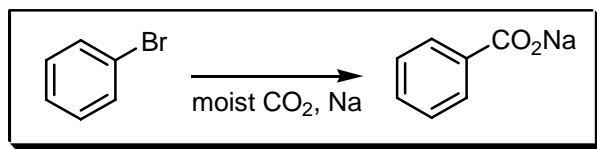
- 1) G.E. Keck; E.P. Boden, *Tetrahedron Lett.*, 1984, **25**, 265.
  - 2) G.E. Keck; D. Krishnamurthy; M.C. Grier, *J. Am. Chem. Soc.*, 1993, **115**, 6543.
  - 3) G.E. Keck; K.H. Tarbet; L.S. Geraci, *J. Am. Chem. Soc.*, 1993, **115**, 8467.
  - 4) B.A. Roe; C.G. Boojamra; J.L. Griggs; C.R. Bertozzi, *J. Org. Chem.*, 1996, **61**, 6442.
  - 5) A. Fürstner; K. Langemann, *J. Am. Chem. Soc.*, 1997, **119**, 9130.
  - 6) S. Knapp; Y. Dong, *Tetrahedron Lett.*, 1997, **38**, 3813.
  - 7) M.J. Mitton-Fry; T. Sammakia; G. Kim, *Abstr. Pap. Am. Chem. Soc.*, 2000, **220**, 565.
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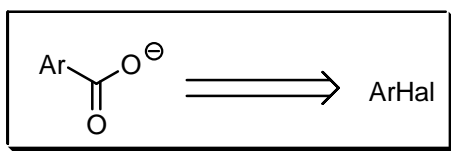
## COMMENTS :

## KEKULÉ SYNTHESIS

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### EXAMPLE :

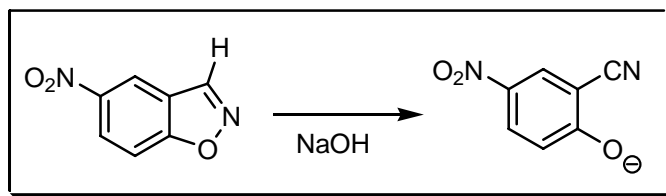
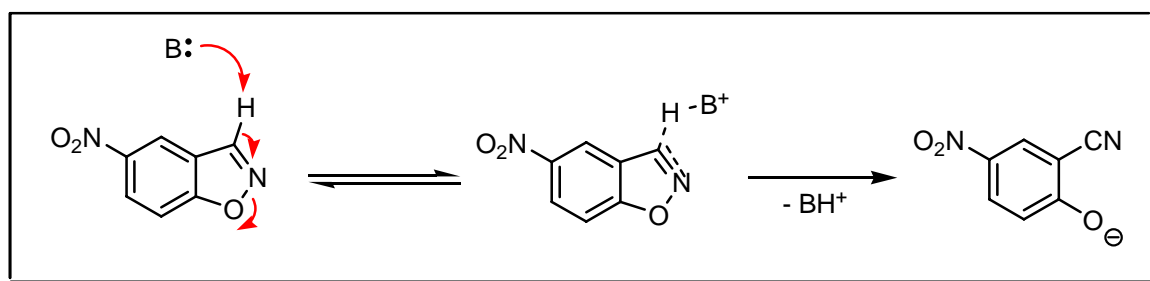


**DISCONNECTION :****NOTES :**

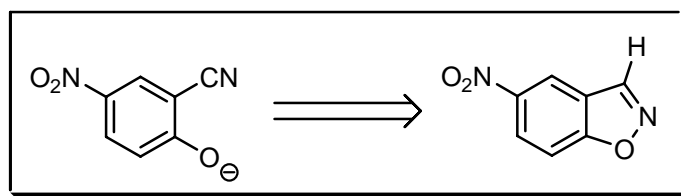
Aromatic halides react with carbon dioxide in the presence of sodium in an inert solvent to yield salts of acids. Modern variants use transition metals as catalysts.

**REFERENCES :**

A. Kekulé, *Liebigs Ann. Chem.*, 1866, **137**, 129.

**COMMENTS :****KEMP ELIMINATION****EXAMPLE :****MECHANISM :**

## DISCONNECTION :



## NOTES :

The **Kemp** elimination involves the general base-catalysed removal of a proton from carbon and is known to be highly sensitive to medium effects. Serum albumins and vesicles catalyse the elimination. The important proton transfer from carbon has been a prime target for enzyme mimics.

## REFERENCES :

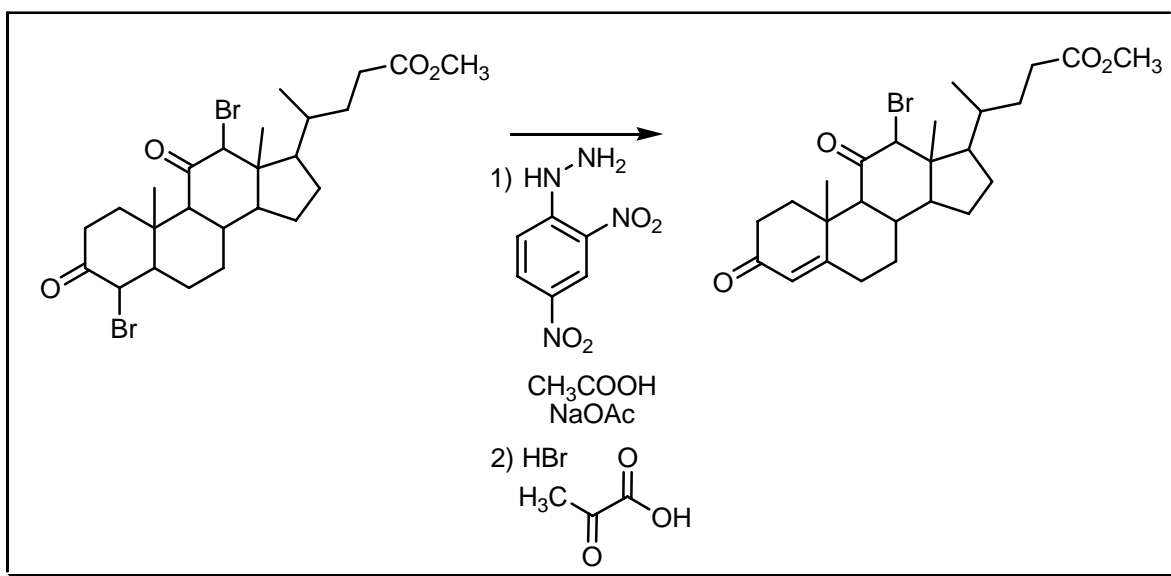
- 1) D.S. Kemp; M.L. Casey, *J. Am. Chem. Soc.*, 1973, **95**, 6670.
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- 10) J.E. Klijn; J.B.F.N. Engberts, *Org. Biomol. Chem.*, 2004, **2**, 1789.

## COMMENTS :

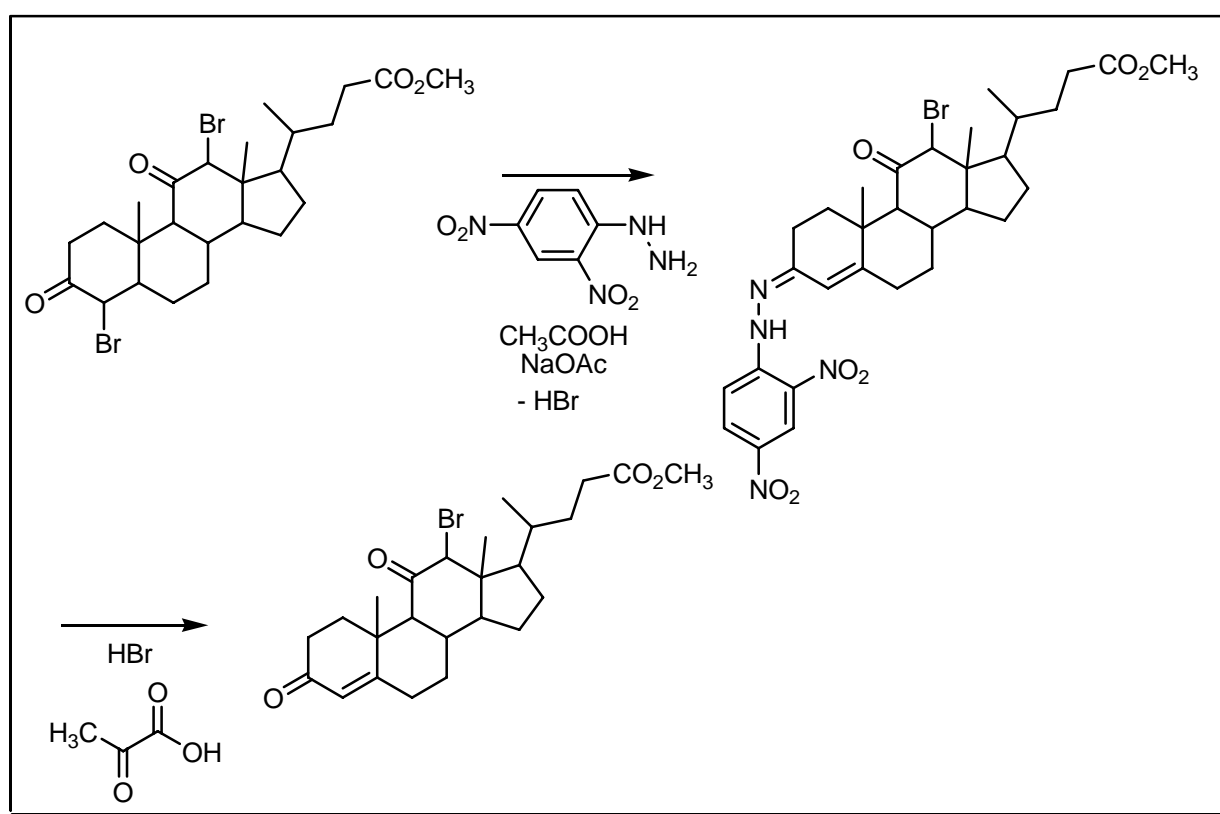


## KENDALL – MATTOX REACTION

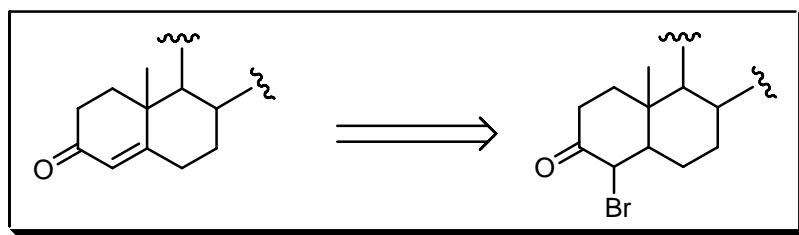
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The method for the introduction of a double bond at the C4 – C5 position in 3-keto-steroids involves the treatment of the 4-bromo-derivative with 2,4-dinitrophenylhydrazine (2,4-DNPH), acetic acid and sodium acetate to yield a hydrazone with elimination of hydrogen bromide. The product reacts with pyruvic acid and hydrogen bromide in chloroform and acetic acid to form the 3-keto- $\Delta^4$ -steroid. Instead of 2,4-DNPH lithium chloride in dimethylformamide can also be used.

## REFERENCES :

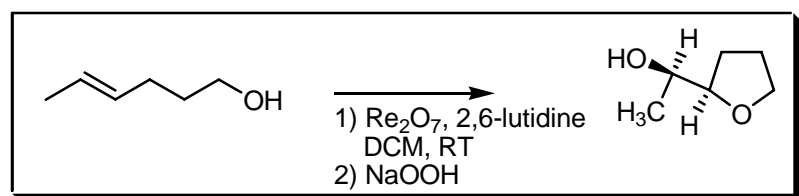
Houben – Weyl : E14b, 509; E15, 941

- 1) V.R. Mattox; E.C. Kendall, *J. Am. Chem. Soc.*, 1948, **70**, 882.
- 2) C. Djerassi, *J. Am. Chem. Soc.*, 1949, **71**, 1003.
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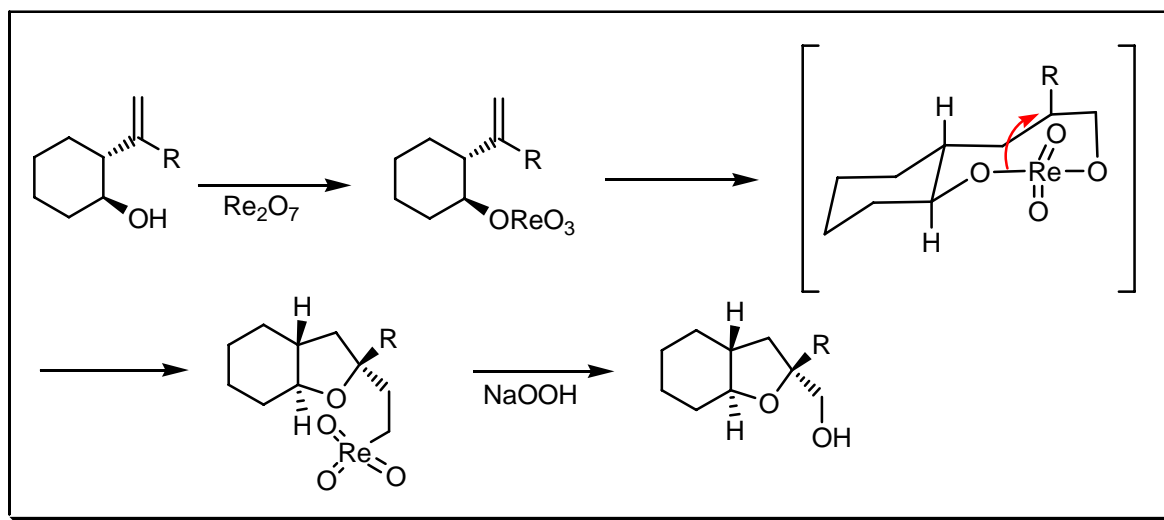
## COMMENTS :

## KENNEDY OXIDATIVE CYCLISATION

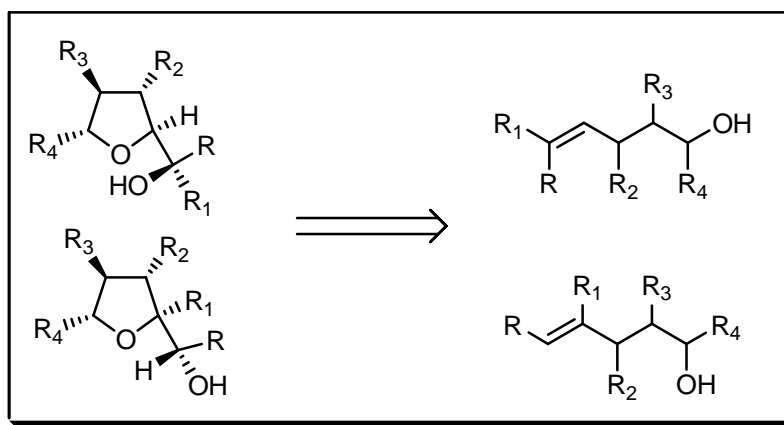
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The oxidative cyclisation of 5-hydroxyalkenes with rhenium oxide to provide 2-hydroxymethyltetrahydrofurans.

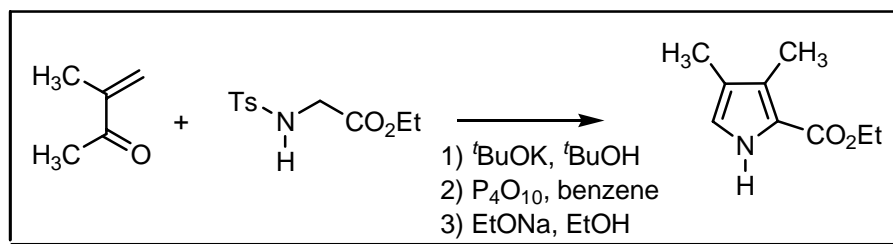
## REFERENCES :

- 1) R.M. Kennedy; S. Tang, *Tetrahedron Lett.*, 1992, **33**, 3729.
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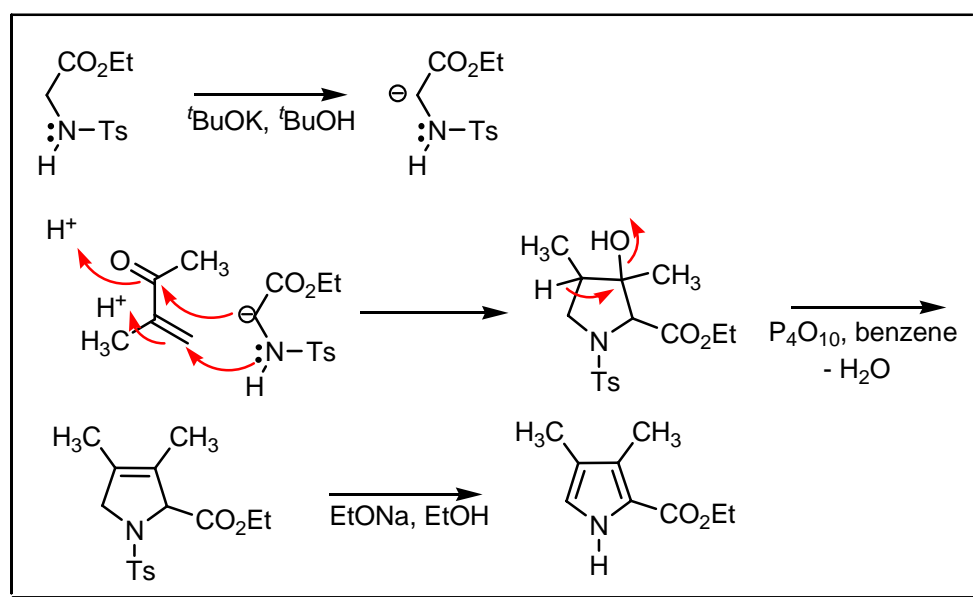
COMMENTS :

## KENNER SYNTHESIS

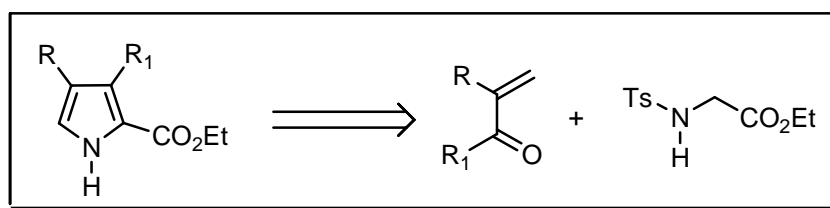
EXAMPLE :



MECHANISM :



DISCONNECTION :



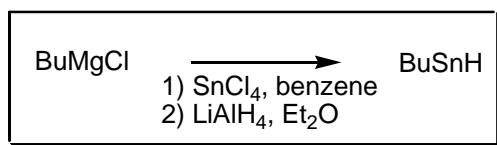
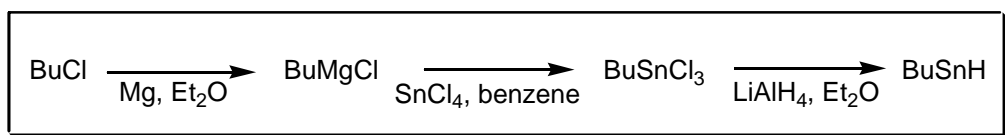
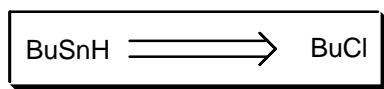
**NOTES :**

An  $\alpha,\beta$ -unsaturated ketone and *N*-tosyl glycine are reacted to afford a pyrrole. See also **Barton – Zard**, **Clauson–Kaas**, **Fischer – Fink**, **Grob – Camenisch**, **Hantzsch** pyrrole, **Harries** pyrrole, **Knorr** pyrrole, **Miller – Plöchl**, **Paal – Knorr**, **Padwa**, **Piloty – Robinson**, **Schwanert**, **Trofimov** and **Zav'yalov** reactions.

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**REFERENCES :**

- 1) W.G. Terry; A.H. Jackson; G.W. Kenner; G. Kornis, *J. Chem. Soc.*, 1965, 4389.
  - 2) T.D. Lash; M.C. Hoehner, *J. Heterocycl. Chem.*, 1991, **28**, 1671.
- 

**COMMENTS :**van der KERK – SCHLESINGER REACTION**EXAMPLE :****MECHANISM :****DISCONNECTION :****NOTES :**

This is the synthesis of butyltin hydride. Instead of tin, silicon or germanium can be used to afford butylsilicon or butylgermanium hydride.

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## REFERENCES :

- 1) A.E. Finholt; A.C. Bond; K.E. Wilzbach; H.I. Schlesinger, *J. Am. Chem. Soc.*, 1947, **69**, 2692.
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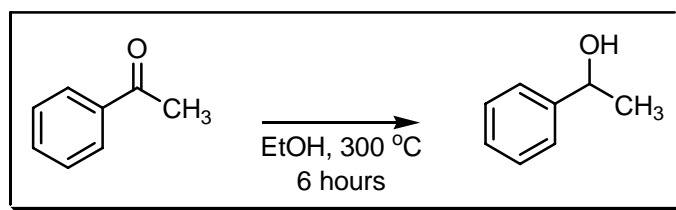
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## COMMENTS :

## KERP REDUCTION

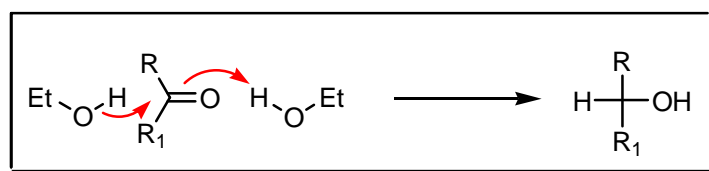
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### EXAMPLE :



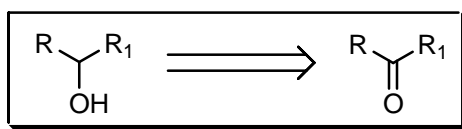
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### MECHANISM :



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### DISCONNECTION :



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### NOTES :

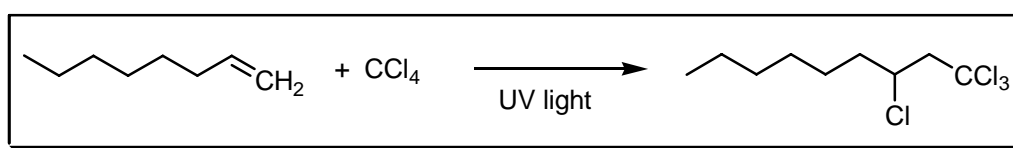
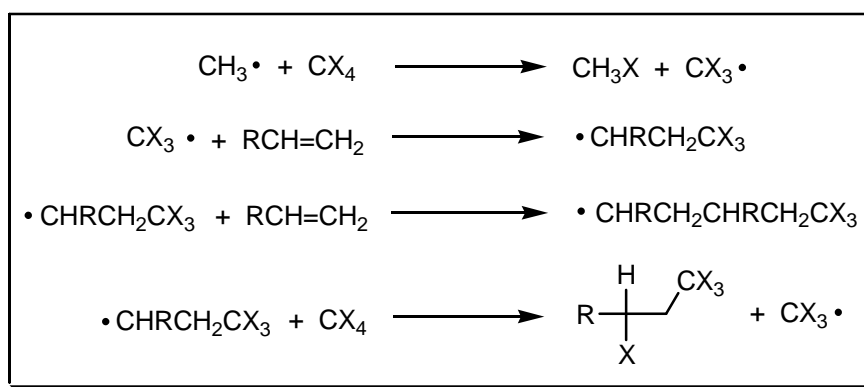
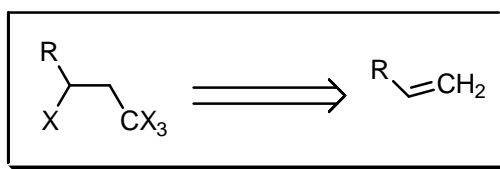
Ketones such as benzophenone and anthraquinone are reduced to the corresponding secondary alcohol when heated with ethanol in a sealed tube at 300 – 320 °C. See also **Meerwein – Ponndorf – Verley** and **Noyori** hydrogenation reactions.

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**REFERENCES :**

W. Kerp, *Ber. Dtsch. Chem. Ges.*, 1895, **28**, 1476.

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**COMMENTS :****KHARASCH – CURRAN REACTION****EXAMPLE :****MECHANISM :****DISCONNECTION :**

## NOTES :

Olefins or acetylenes add in an *anti*-Markovnikov manner on carbon tetrachloride, carbon tetrabromide, chloroform, bromoform or derivatives of chlorinated acetic acids in the presence of peroxides, or photochemically, to yield addition or polymerisation addition products. The polymers arise from free radicals produced in the reaction. The addition can be transition-metal catalysed. Sometimes this reaction is called the **Prins** reaction but this causes confusion with the **Kriewitz – Prins** reaction between formaldehyde and olefins.

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## REFERENCES :

Smith : 689

Smith 2<sup>nd</sup> : 583, 613

Org. Synth. : 45, 104

Org. Synth. Coll. Vol. : 5, 1076

Science of Synthesis : 1, 969

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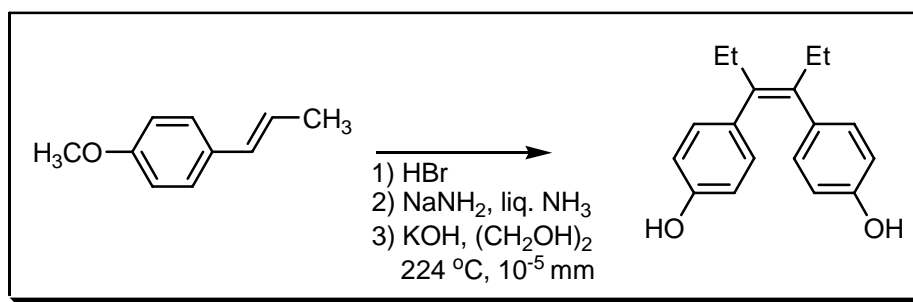
- 1) M.S. Kharasch; E.V. Jensen; W.H. Urry, *Science*, 1945, **102**, 128.
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## COMMENTS :

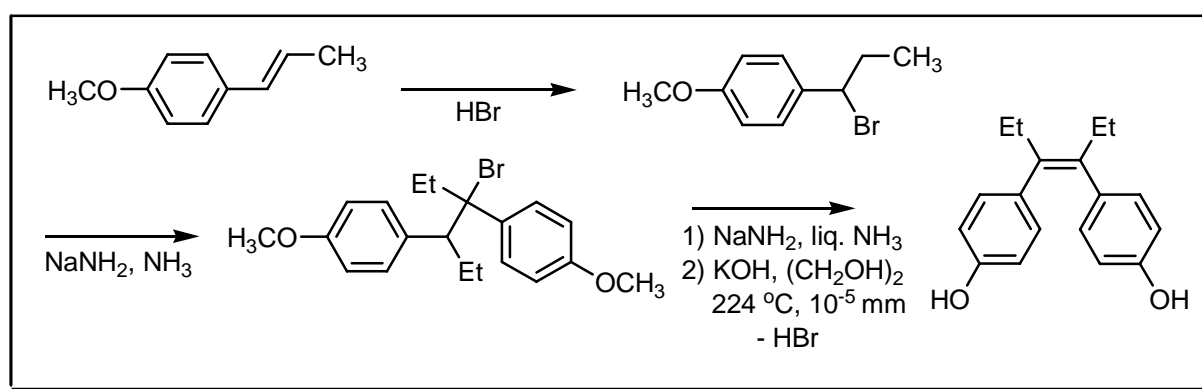


## KHARASCH – KLEIMANN SYNTHESIS

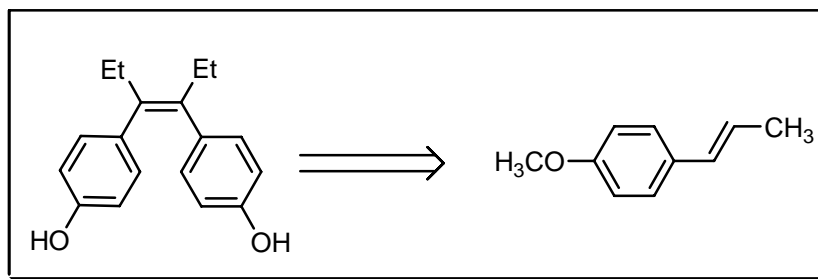
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The synthesis of diethylstilbestrol (*trans*-4,4'-dihydroxy- $\alpha,\alpha'$ -diethylstilbene). See also **Dodds – Robinson** reaction.

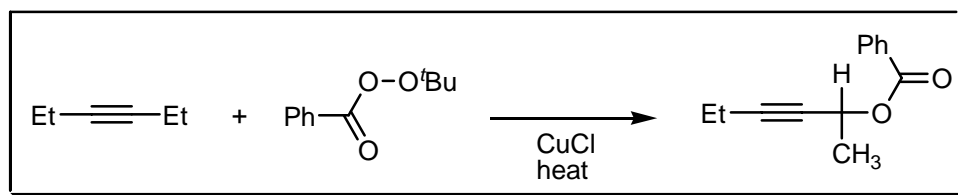
### REFERENCES :

- 1) M.S. Kharasch; M. Kleimann, *J. Am. Chem. Soc.*, 1943, **65**, 11.
- 2) J. Grundy, *Chem. Rev.*, 1957, **57**, 281.

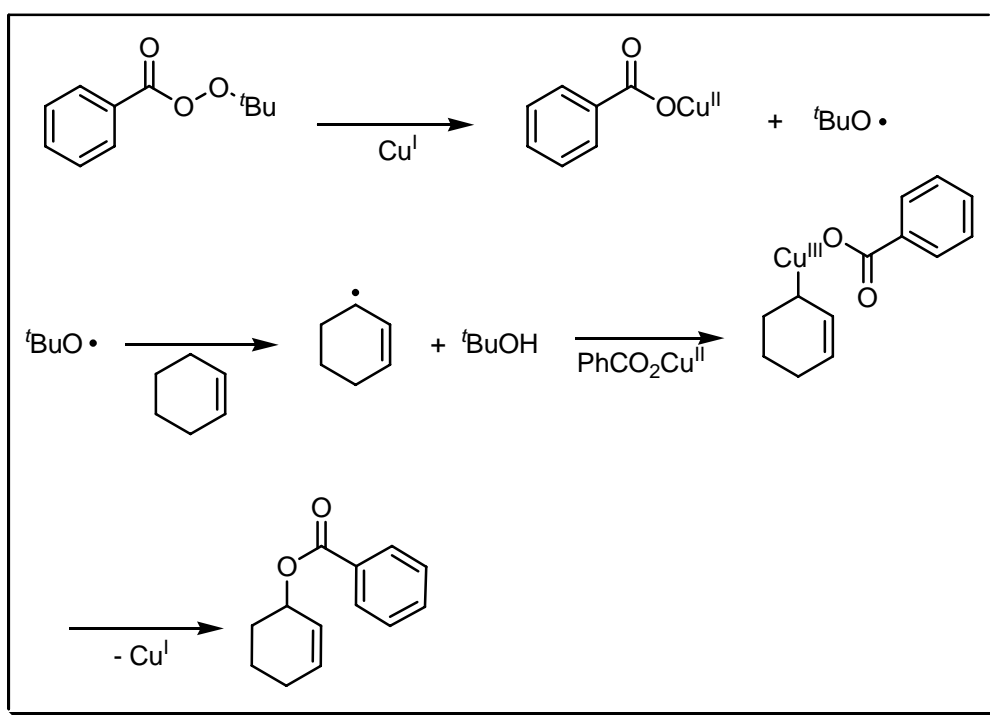
COMMENTS :

## KHARASCH – SOSNOVSKY REACTION

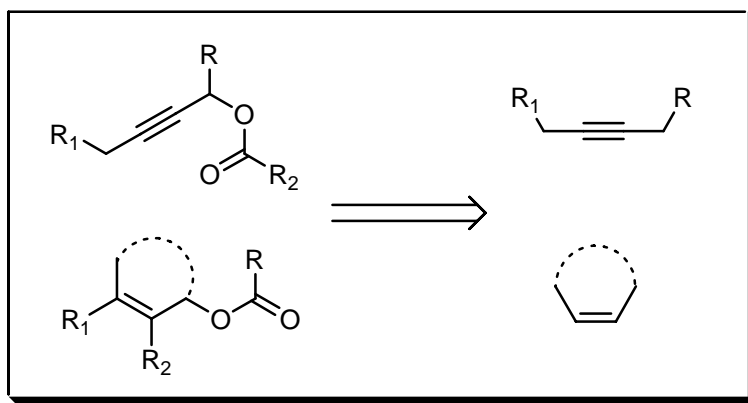
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The allylic or propargylic oxidation using *tert*-butyl peresters as the oxidant in the presence of copper or cobalt salts. The reaction can also be done enantioselective with copper complexes of nitrogen-containing ligands, e.g. C<sub>2</sub>-symmetric bis oxazolines. Oxazolines and thiazolines can be oxidised by this method to the corresponding oxazoles and thiazoles.

## REFERENCES :

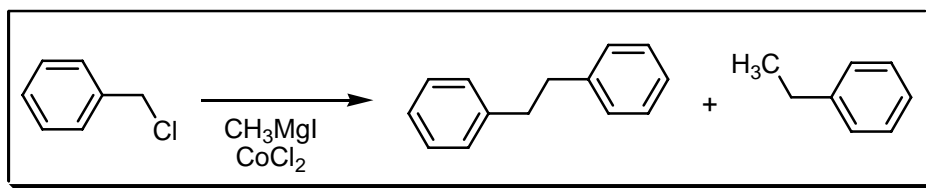
Houben – Weyl : E5, 695

- 1) M. Kharasch; G. Sosnovsky, *J. Am. Chem. Soc.*, 1958, **80**, 756.
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- 6) Y. Kohmura; T. Katsuki, *Synlett*, 1999, 1231.
- 7) P. Brandt; P.G. Andersson, *Synlett*, 2000, 1092.
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- 9) J. Eames; M. Watkinson, *Angew. Chem., Int. Ed.*, 2001, **40**, 3567.

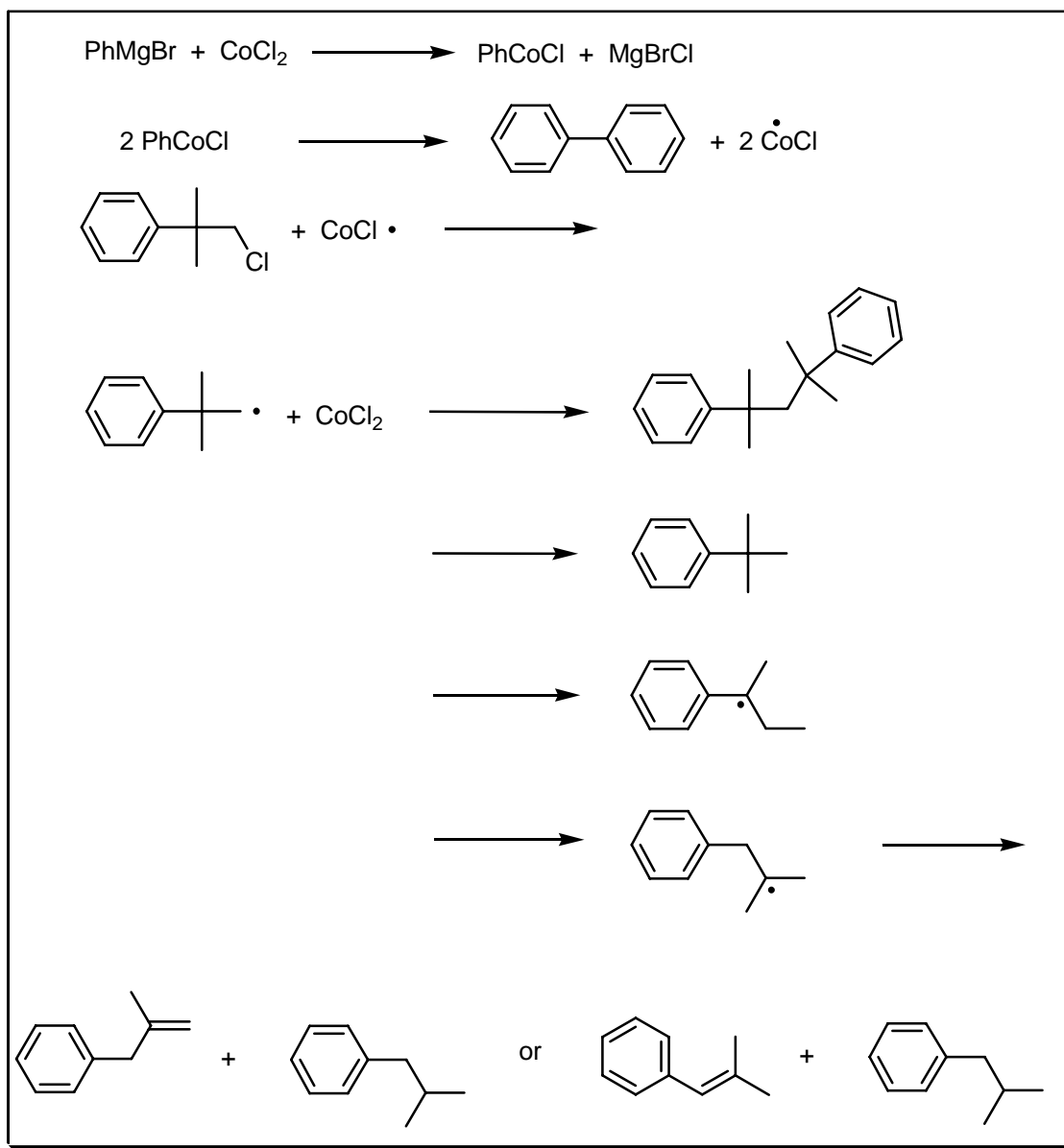
## COMMENTS :

## KHARASCH – URRY REARRANGEMENT

**EXAMPLE :**



**MECHANISM :**



**NOTES :**

Many coupling reactions involving **Grignard** reagents and organo halides in the presence of cobaltous salts involve the formation of free radicals by the abstraction of a halogen atom from the organo halide. Interchange reactions or rearrangement products are very competing reactions.

## REFERENCES :

Smith : 689

Smith 2<sup>nd</sup> : 583, 613

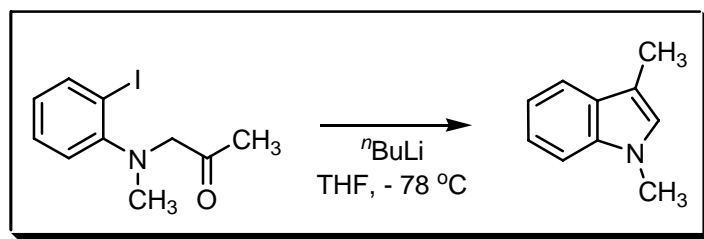
- 
- 1) M.S. Kharasch; D.W. Lewis; W.B. Reynolds, *J. Am. Chem. Soc.*, 1943, **65**, 493.
  - 2) W.H. Urry; M.S. Kharasch, *J. Am. Chem. Soc.*, 1944, **66**, 1438.
  - 3) M.S. Kharasch; W.H. Urry, *J. Org. Chem.*, 1948, **13**, 101.
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  - 9) R.G. Gough; J.A. Dixon, *J. Org. Chem.*, 1968, **33**, 2148.
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## COMMENTS :

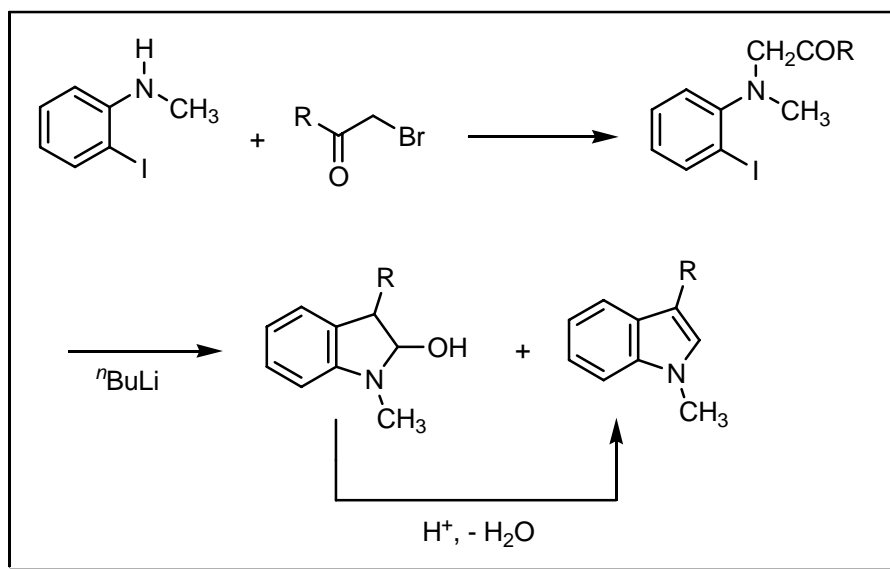
## KIHARA INDOLE SYNTHESIS

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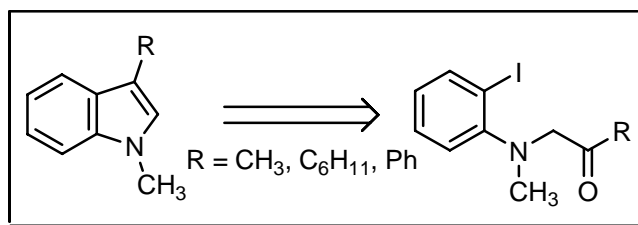
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The formation of the indole ring *via* an *intramolecular Barbier* reaction of phenyl or alkyl *N*-(2-iodophenyl)-*N*-methylaminomethyl ketones. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Barbier**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

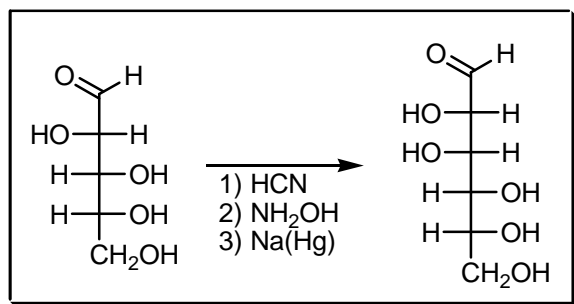
## REFERENCES :

M. Kihara; Y. Iwai; Y. Nagao, *Heterocycles*, 1995, **41**, 2279.

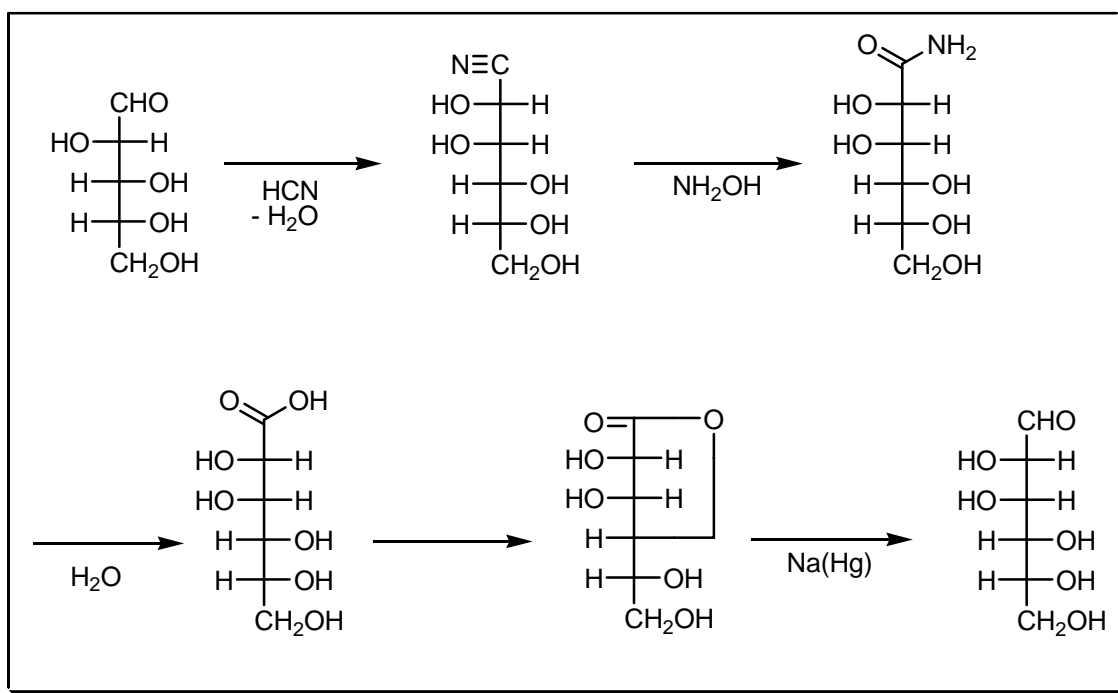
COMMENTS :

## KILIANI – FISCHER SYNTHESIS

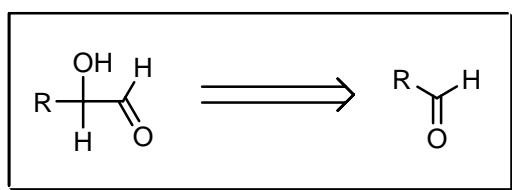
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

A method for passing from an aldose to the next higher homologue by the formation of the epimeric cyanohydrins, which are hydrolysed to a mixture of the corresponding acids. These may be separated by fractional crystallisation and subsequent decomposition of the phenylhydrazides. Each acid is converted to the  $\gamma$ -lactone by heating and the latter is reduced by sodium amalgam (pH 3) to the higher aldose. See also **Kiliani**, **Ultee**, **Urech** and **Wohl** reactions.

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## REFERENCES :

**March** : 965

**Smith – March** : 1240

**Org. Syn.** : 36, 38

**Org. Synth. Coll. Vol.** : 4, 506

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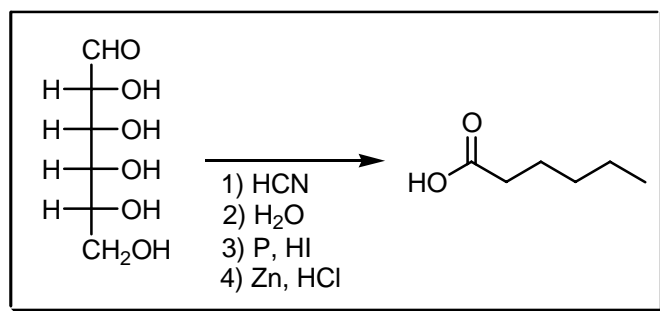
- 1) F. Winkler, *Liebigs Ann. Chem.*, 1832, **4**, 246.
  - 2) H. Kiliani, *Ber. Dtsch. Chem. Ges.*, 1885, **18**, 3066.
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  - 9) J. Roos; F. Effenberger, *Tetrahedron: Asymmetry*, 1999, **10**, 2817.
- 

## COMMENTS :

## KILIANI REDUCTION

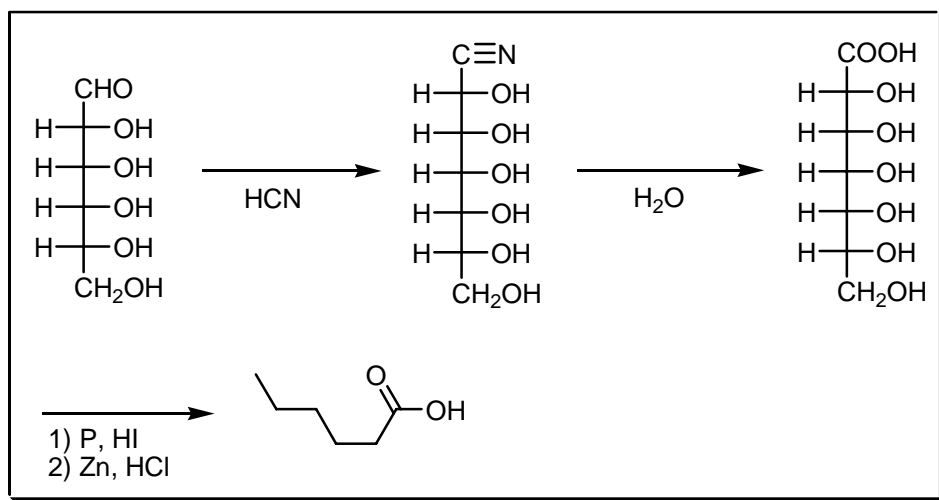
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### EXAMPLE :

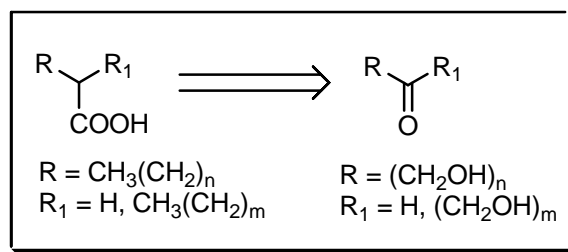




## MECHANISM :



## DISCONNECTION :



## NOTES :

These acids or their corresponding lactone are transformed to the cyanohydrin. Hydrolysis with water affords the polyhydroxylated carboxylic acid when this is reduced by hydrogen iodide in the presence of red phosphorous yields the corresponding aliphatic carboxylic acid. This reaction has been used by **Kiliani** to proof that D-glucose is an *aldo*-hexose. See also **Kiliani – Fischer** reaction.

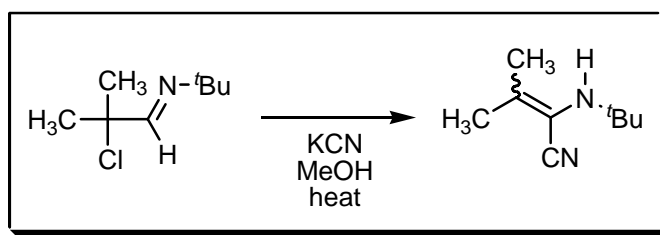
## REFERENCES :

- 1) H. Kiliani, *Ber. Dtsch. Chem. Ges.*, 1885, **18**, 3066.
- 2) H. Kiliani, *Ber. Dtsch. Chem. Ges.*, 1888, **21**, 915.
- 3) A.S. Perlin; C.B. Purves, *Can. J. Chem.*, 1953, **31**, 227.
- 4) W.H. Kruizinga; R.M. Kellogg, *J. Am. Chem. Soc.*, 1981, **103**, 5183.
- 5) Z.C. Liu; A. Granata; X.H. Shen; A.S. Perlin, *Can. J. Chem.*, 1992, **70**, 2081.

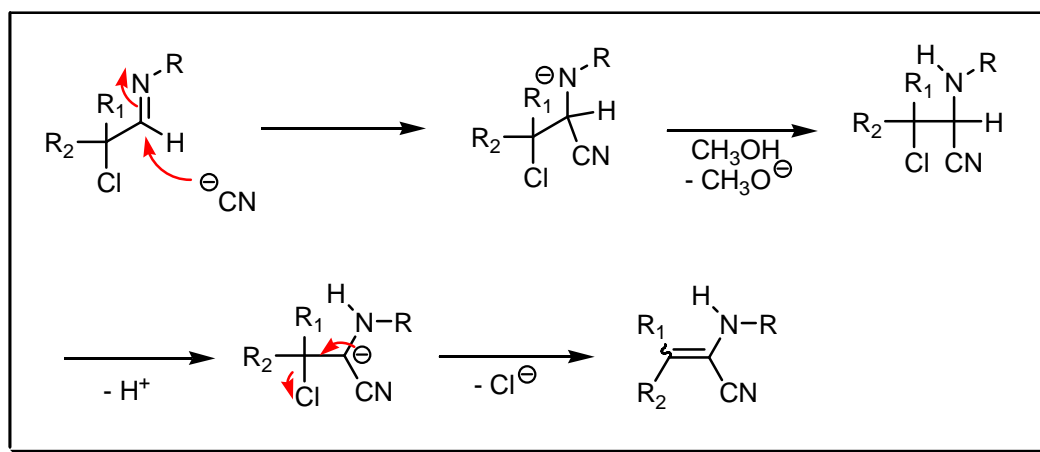
## COMMENTS :

## de KIMPE SYNTHESIS

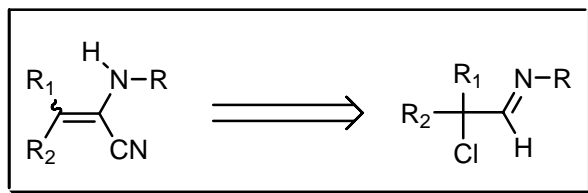
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

$\alpha$ -Cyanoenamines have been prepared from  $\alpha$ -chloroaldehydes and potassium cyanide in methanol.

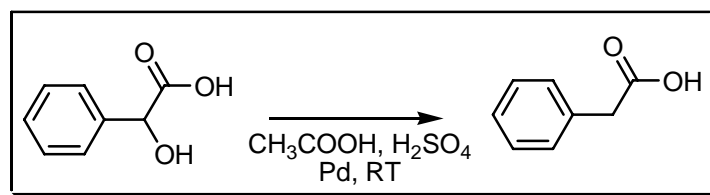
### REFERENCES :

- 1) N. de Kimpe; R. Verhé; L. De Buyck; H. Hasma; N. Schamp, *Tetrahedron*, 1976, **32**, 3063.
- 2) N. de Kimpe; R. Verhé; L. De Buyck; J. Chys; N. Schamp, *J. Org. Chem.*, 1978, **43**, 2670.
- 3) N. de Kimpe; R. Verhé; L. De Buyck; J. Chys; N. Schamp, *Synth. Commun.*, 1979, **9**, 901.
- 4) N. de Kimpe; R. Verhé; L. De Buyck; N. Schamp, *Chem. Ber.*, 1983, **116**, 3846.
- 5) N. de Kimpe; R. Verhé; L. De Buyck; N. Schamp, *Can. J. Chem.*, 1984, **62**, 1812.

COMMENTS :

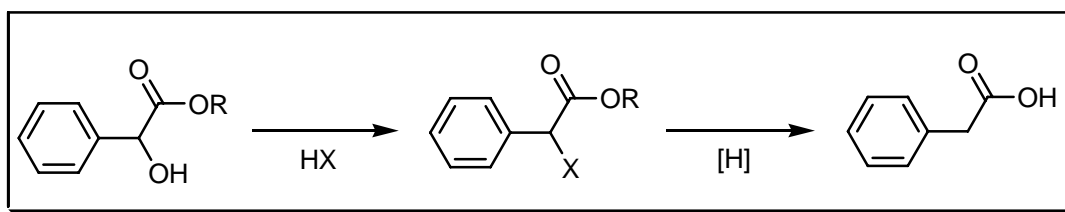
## KINDLER SYNTHESIS

EXAMPLE :

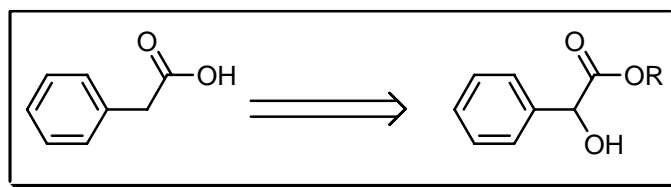


MECHANISM :

In the presence of  $\text{HClO}_4$  :



DISCONNECTION :



NOTES :

Mandelic acids and their esters are hydrogenated to the corresponding derivatives of phenylacetic acid at room temperature in acetic acid containing sulfuric acid. In the presence of perchloric acid the hydrogenation is catalytic. At higher temperatures the phenyl ring can be hydrogenated to a cyclohexyl ring.

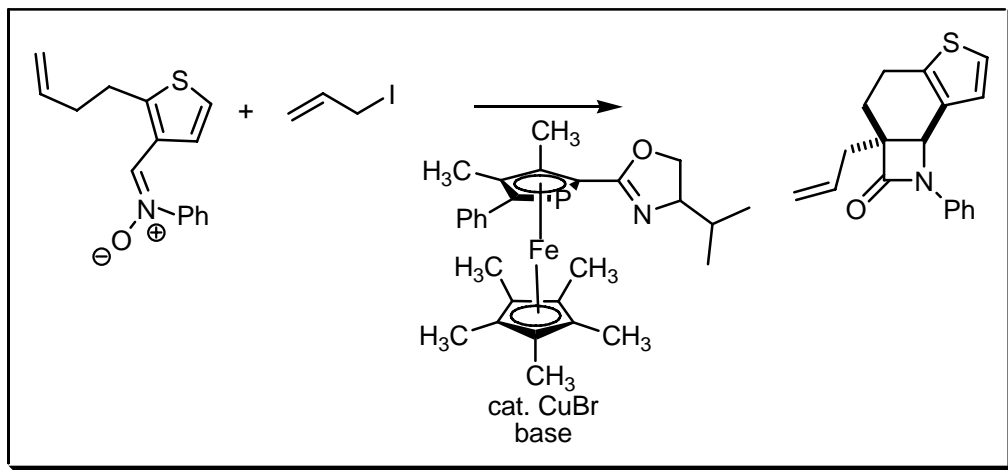
REFERENCES :

- 1) K. Kindler; W. Metzendorf; D-y. Kwok, *Ber. Dtsch. Chem. Ges.*, 1943, **76B**, 308.
- 2) K. Kindler; D-y. Kwok, *Liebigs Ann. Chem.*, 1943, **554**, 9.

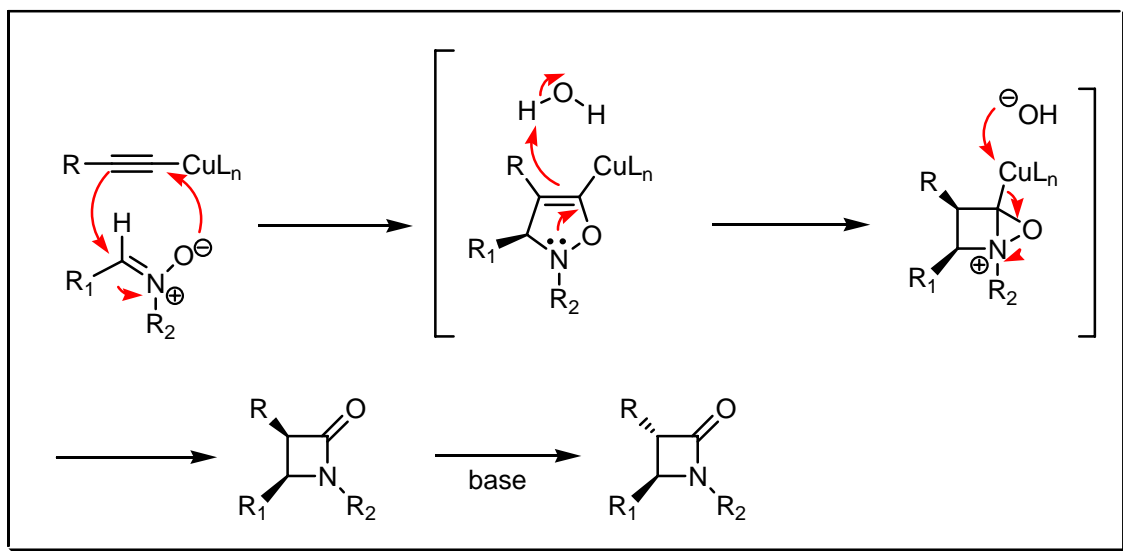
COMMENTS :

## KINUGASA REACTION

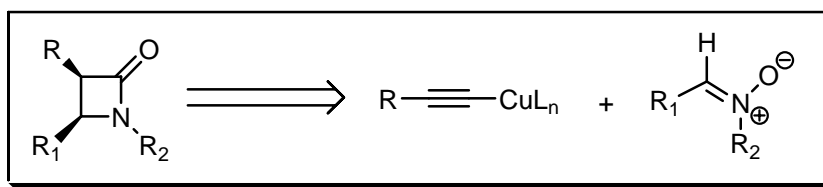
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

*cis*- $\beta$ -Lactams are afforded by the reaction between copper acetylides and nitrones. The carbonyl oxygen is derived from the oxygen of the nitron. The reaction has been made asymmetric and catalytic in copper. The use of base inverts the stereochemistry of the  $\beta$ -lactams.

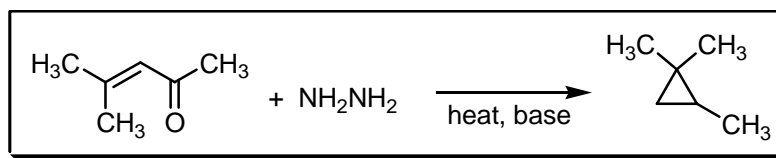
## REFERENCES :

- 1) M. Kinugasa; S. Hashimoto, *J. Chem. Soc., Chem. Commun.*, 1972, 466.
- 2) L.K. Ding; W.J. Irwin, *J. Chem. Soc., Perkin Trans. 1*, 1976, 2382.
- 3) M. Miura; M. Enna; K. Okuro; M. Nomura, *J. Org. Chem.*, 1995, **60**, 4999.
- 4) M.M.-C. Lo; G.C. Fu, *J. Am. Chem. Soc.*, 2002, **124**, 4572.
- 5) R. Shintani; G.C. Fu, *Angew. Chem., Int. Ed.*, 2003, **42**, 4082.
- 6) J. Marco-Contelles, *Angew. Chem., Int. Ed.*, 2004, **43**, 2198.
- 7) A. Basak; S.C. Ghosh, *Synlett*, 2004, 1637.

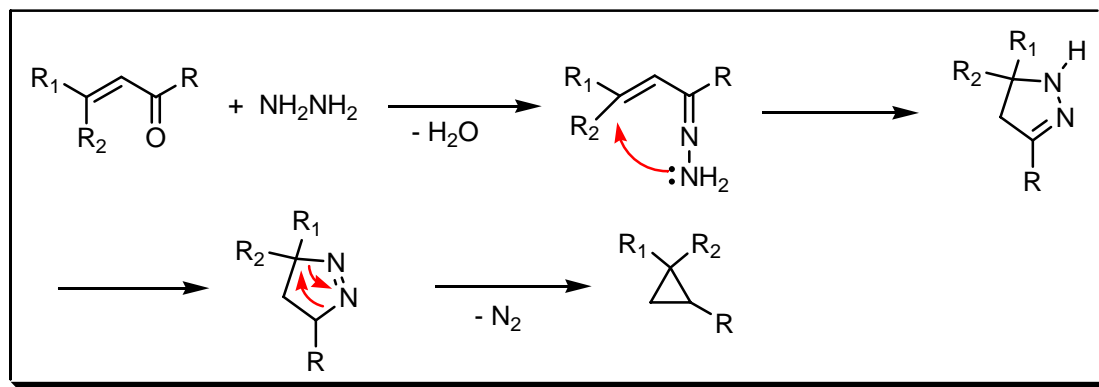
## COMMENTS :

## KISHNER CYCLOPROPANE SYNTHESIS

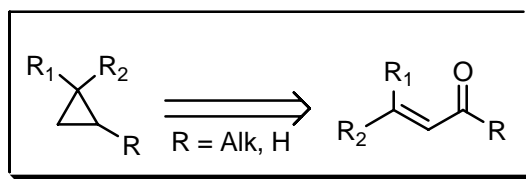
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Pyrazolines which are obtained by the action of hydrazine on compounds containing the group  $-CH=CHCO-$  eliminate nitrogen when treated with alkali to form cyclopropane derivatives. See also **Charette**, **Freund**, **Hass** cyclopropane, **Ipatiew** cyclopropane, **Mousseron – Fraisse – McCoy**, **Nerdel** and **Simmons – Smith** reactions.

## REFERENCES :

**Org. Synth.** : **47**, 98

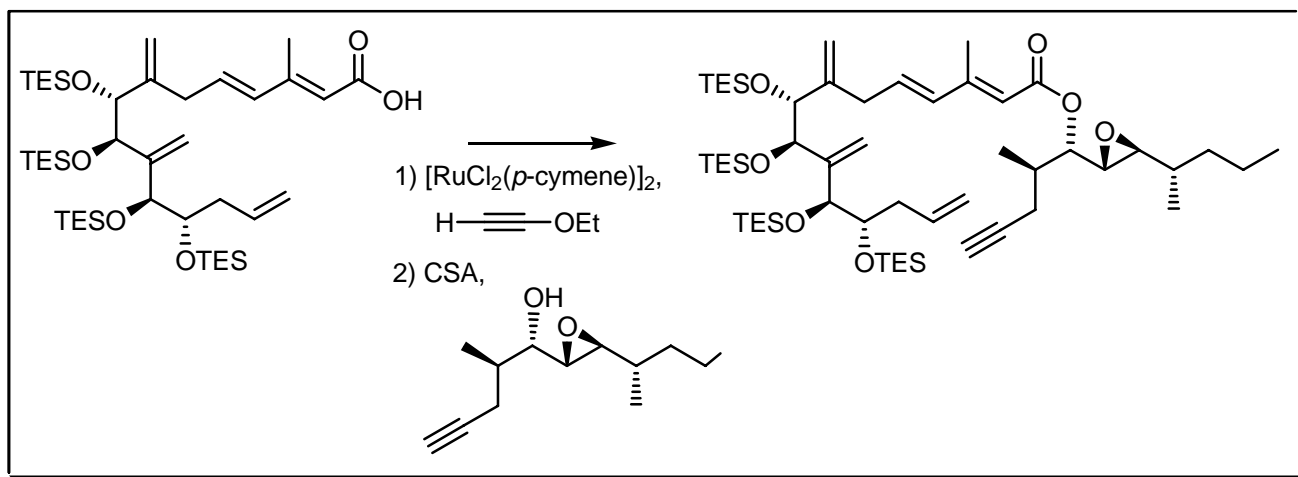
**Org. Synth. Coll. Vol.** : **5**, 929

- 1) N. Kishner; A. Zavadovskii, *J. Russ. Physik. Chem. Ges.*, 1911, **43**, 1132.
- 2) L.I. Smith; E.R. Rogier, *J. Am. Chem. Soc.*, 1951, **73**, 3840.
- 3) G.S. Hammond; R.W. Todd, *J. Am. Chem. Soc.*, 1954, **76**, 4081.
- 4) R.J. Crawford; M. Ohno, *Can. J. Chem.*, 1974, **54**, 3134.
- 5) R.J. Crawford; H. Tokunaga, *Can. J. Chem.*, 1974, **54**, 4033.

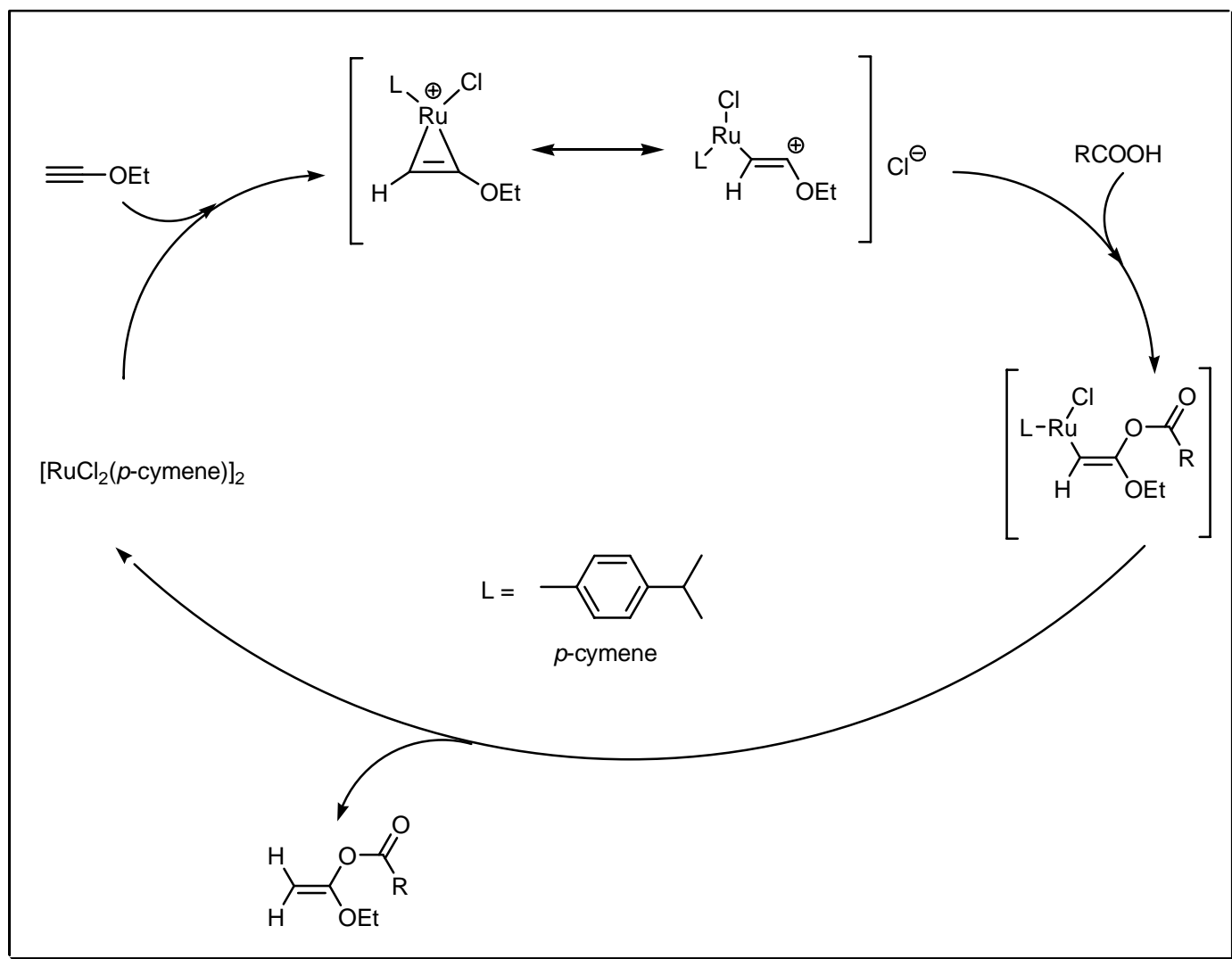
## COMMENTS :

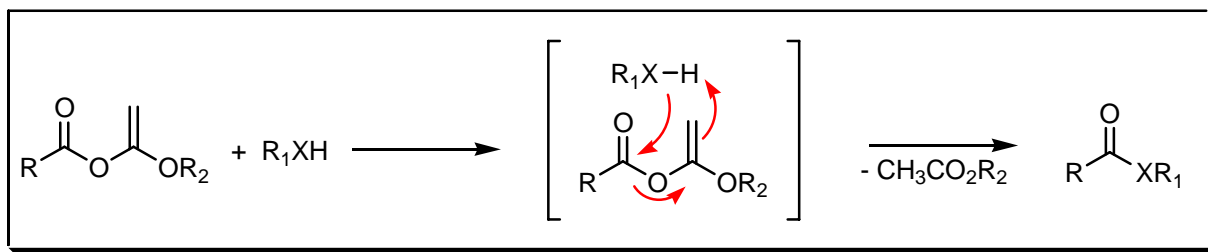
## KITA ESTERIFICATION

### EXAMPLE :

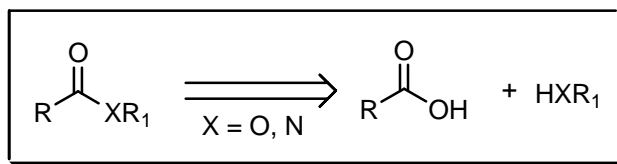


### MECHANISM :





#### DISCONNECTION :



#### NOTES :

1-Ethoxyvinyl esters, prepared from carboxylic acids and ethoxyacetylene in the presence of a catalytic amount of  $[\text{RuCl}_2(p\text{-cymene})]_2$  (in the past mercury(II) compounds were used.), react with alcohols and amines to afford the corresponding *O*- and *N*-acylated compounds. See also **Corey – Nicolaou**, **Diels – Alder**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Masamune**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolakiewicz**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

#### REFERENCES :

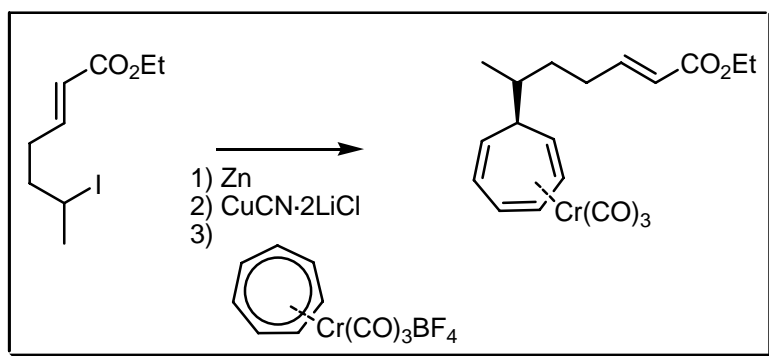
- 1) H.H. Wasserman; P.S. Wharton, *J. Am. Chem. Soc.*, 1960, **82**, 661.
- 2) B. Zwanenburg, *Recl. Trav. Chim. Pays-Bas*, 1963, **82**, 593.
- 3) Y. Kita; S. Akai; N. Ajimura; M. Yoshigi; T. Tsugoshi; H. Yasuda; Y. Tamura, *J. Org. Chem.*, 1986, **51**, 4150.
- 4) Y. Kita; H. Maeda; K. Omori; T. Okuno; Y. Tamura, *Synlett*, 1993, 273.
- 5) B.M. Trost; P.E. Harrington, *J. Am. Chem. Soc.*, 2004, **126**, 5028.

#### COMMENTS :

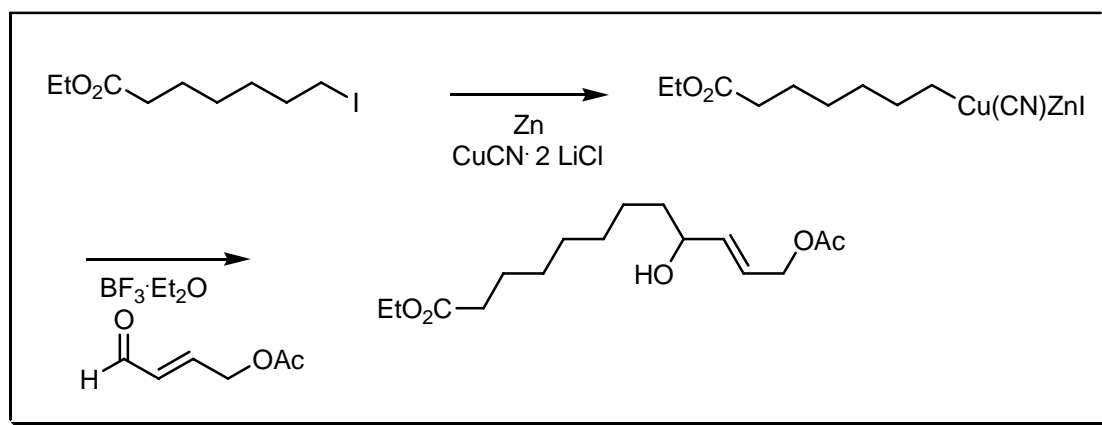


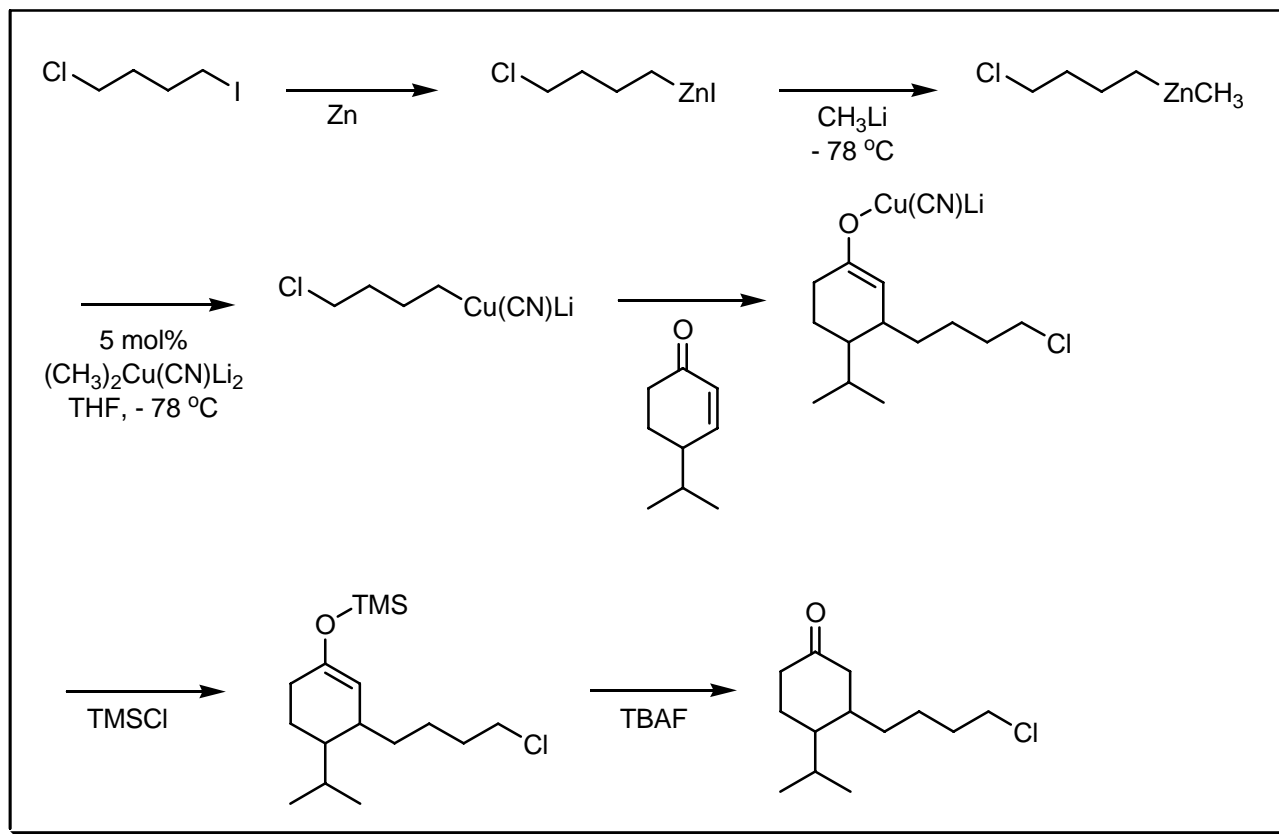
## KNOCHEL REACTION

### EXAMPLE :

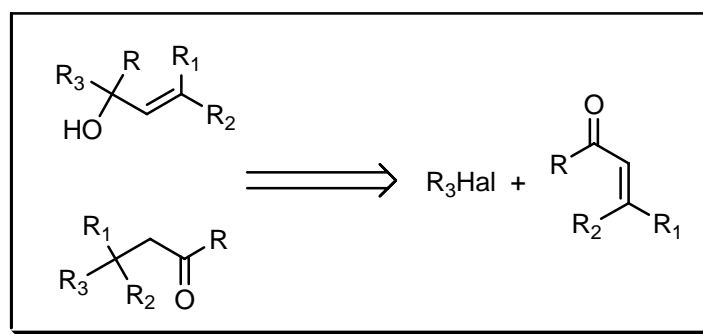


### MECHANISM :





#### DISCONNECTION :



#### NOTES :

Alkyl zinc iodides are poor nucleophiles. However, they are turned into good nucleophiles when they are converted into so-called **Knochel** cuprates  $R-Cu(CN)ZnHal$  with solubilised  $CuCN$ . These compounds add to  $\alpha,\beta$ -unsaturated aldehydes in the presence of Lewis acids (1,2-addition), but can also undergo 1,4-additions or give other **Michael** adducts.

#### REFERENCES :

Org. React. : **58**, 417

Org. Synth. : **70**, 195; **76**, 252

Org. Synth. Coll. Vol. : **9**, 502

- 1) M.J. Dunn; R.F.W. Jackson, *J. Chem. Soc., Chem. Commun.*, 1992, 319.
- 2) P. Knochel; M.J. Rozema; C.E. Tucker; C. Retherford; M. Furlong; S.A. Rao, *Pure Appl. Chem.*, 1992, **64**, 361.
- 3) P. Knochel; R.D. Singer, *Chem. Rev.*, 1993, **93**, 2117.
- 4) I. Gridnev; G. Kanai; N. Miyaura; A. Suzuki, *J. Organomet. Chem.*, 1994, **481**, C4.
- 5) P. Knochel, *Chemtracts: Org. Chem.*, 1995, **8**, 205.
- 6) A.M. Caporusso; S. Filippi; F. Barontini; P. Salvadori, *Tetrahedron Lett.*, 2000, **41**, 1227.

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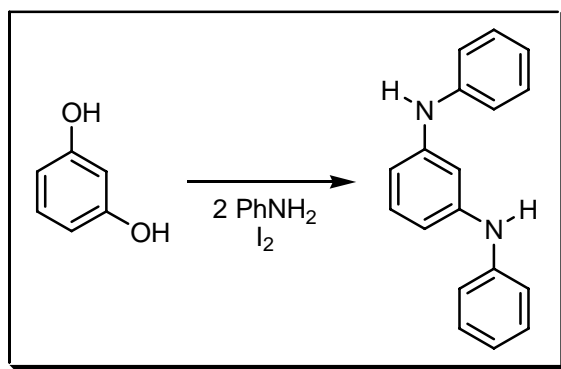
**COMMENTS :**

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**KNOEVENAGEL AMINE SYNTHESIS**

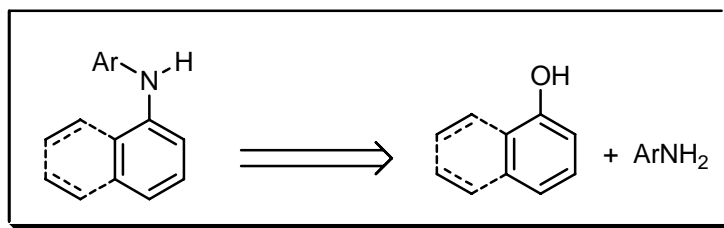
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**EXAMPLE :**



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**DISCONNECTION :**



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**NOTES :**

Certain phenols and naphthols react with aromatic amines in the presence of small amounts of iodine to yield secondary amines on dehydration.

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**REFERENCES :**

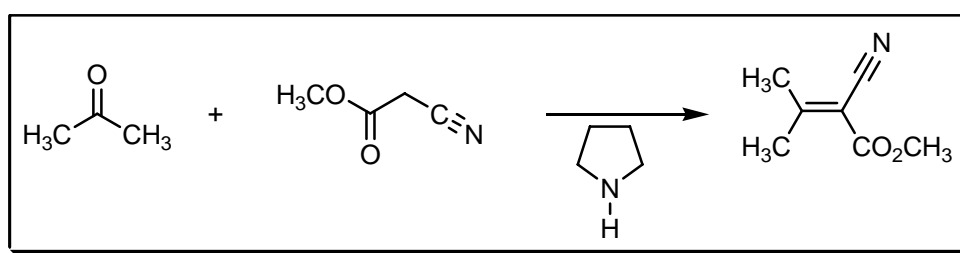
- 1) E. Knoevenagel, *J. Prakt. Chem.*, 1914, **89**, 1.
- 2) Ng.Ph. Buu-Hoi, *J. Chem. Soc.*, 1954, 4346.

3) M. Kozaki; S. Nakamura; K. Sato; T. Takui; T. Kametani; M. Oda; K. Tokumaru; K. Okada, *Tetrahedron Lett.*, 1998, **39**, 5979.

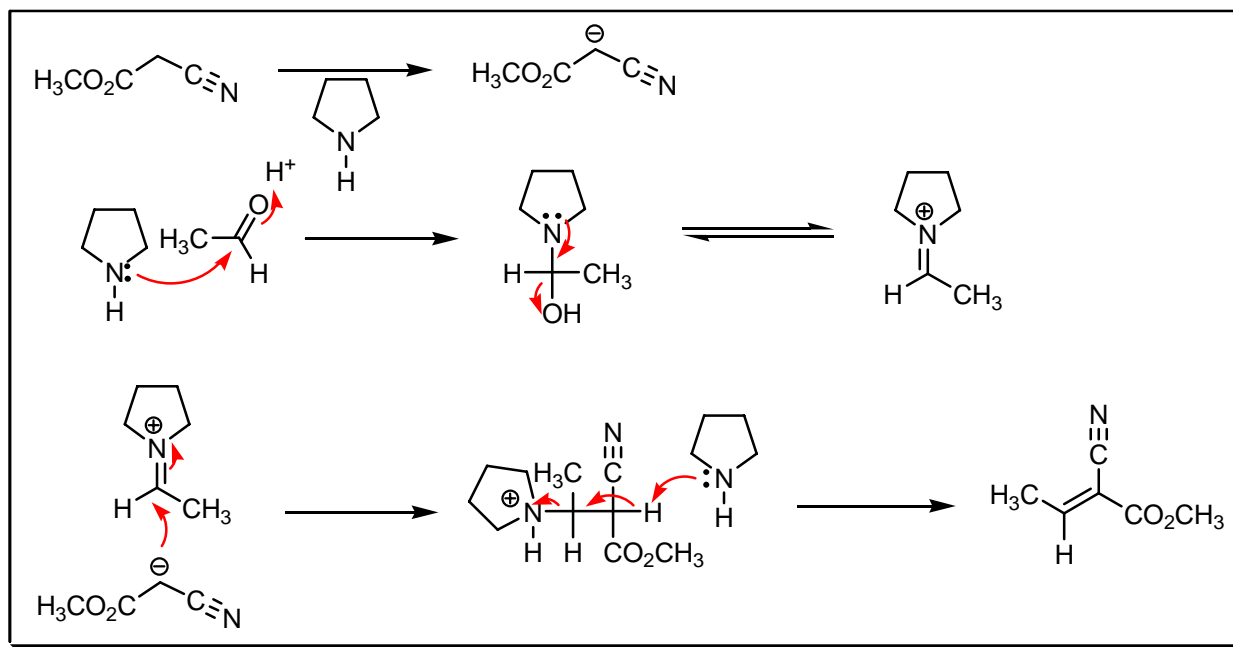
COMMENTS :

## KNOEVENAGEL CONDENSATION

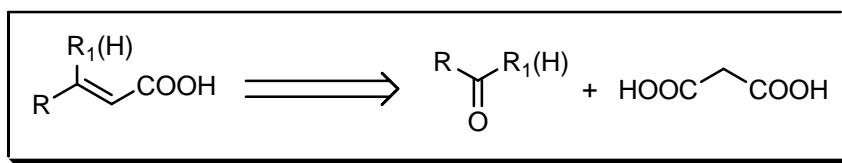
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The condensation of certain types of compounds containing a highly reactive methylene group with a variety of carbonyl compounds in the presence of a weak base, a primary or secondary amine or an ion-exchange resin. It is possible to condense one or two molecules of the carbonyl compound with the aldehyde. See **Claisen** cinnamic, **Doebner** modification and **Perkin** reactions.

## REFERENCES :

**March** : 945

**Smith – March** : 1219, 1225

**Smith** : 897

**Smith 2<sup>nd</sup>** : 750

**Org. React.** : 1, 1; 15, 204

**Houben – Weyl** : 4/2, 25; 6/2, 640; **E3**, 646; **E7a**, 195; **E7b**, 412; **E8a**, 316

**Org. Synth.** : 25, 42; 27, 24; 29, 83; 32, 63; 71, 167

**Org. Synth. Coll. Vol.** : 3, 317, 377, 715; 4, 392; 9, 310

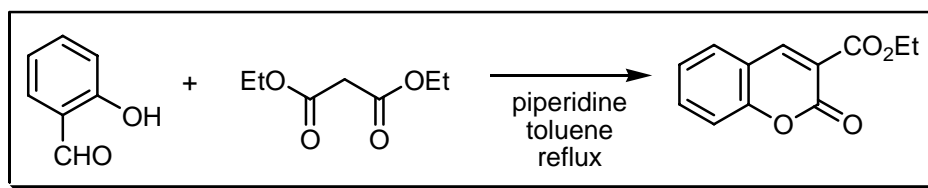
**Science of Synthesis** : 9, 194, 317

- 1) F.R. Japp; F.W. Streatfield, *J. Chem. Soc.*, 1883, **43**, 27.
- 2) E. Knoevenagel, *Ber. Dtsch. Chem. Ges.*, 1896, **29**, 172.
- 3) E. Knoevenagel, *Ber. Dtsch. Chem. Ges.*, 1898, **31**, 735.
- 4) G. Charles, *Bull. Soc. Chim. Fr.*, 1963, 1576.
- 5) J.L. van der Baan; F. Bickelhaupt, *Tetrahedron*, 1974, **30**, 2088.
- 6) L.F. Tietze; U. Beifuß, *Comp. Org. Syn.*, 1991, **2**, 341.
- 7) L.F. Tietze; P. Saling, *Chirality*, 1993, **5**, 329.
- 8) M.L. Kantam; B. Bharathi, *Catal. Lett.*, 1998, **55**, 235.
- 9) G. Alcerreca; R. Sanabria; R. Miranda; G. Arroyo; J. Tamiriz; F. Delgado, *Synth. Commun.*, 2000, **30**, 1295.
- 10) S. Balalaie; N. Nemati, *Heterocycl. Commun.*, 2001, **7**, 67.
- 11) A. Loupy; S.J. Song; S.M. Sohn; Y.M. Lee; T.W. Kwon, *J. Chem. Soc., Perkin Trans. 1*, 2001, 1220.
- 12) A. McCluskey; P.J. Robinson; T. Hill; J.L. Scott; J.K. Edwards, *Tetrahedron Lett.*, 2002, **43**, 3117.
- 13) W.-X. Zuo; R. Hua; X. Qiu, *Synth. Commun.*, 2004, **34**, 3219.
- 14) M. Hayashi; N. Nakamura; K. Yamashita, *Tetrahedron*, 2004, **60**, 6777.

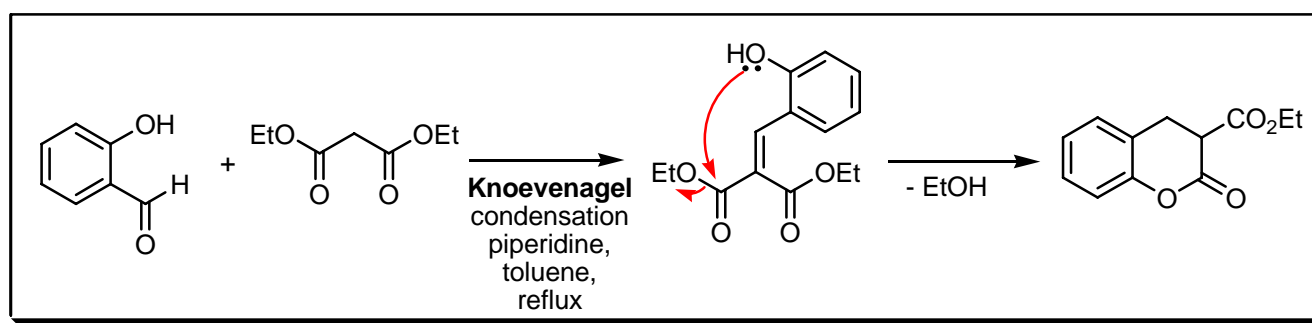
## COMMENTS :

## KNOEVENAGEL COUMARIN SYNTHESIS

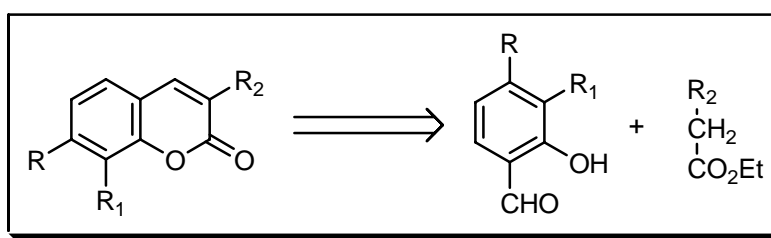
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Coumarin derivatives are obtained by the condensation of *o*-hydroxyaldehydes with highly reactive methylene compounds, in the presence of piperidine, pyridine and other organic bases. The synthesis can be done also under microwave irradiation. See also **Anschütz** hydroxyl coumarin, **Boyd – Robinson**, **Dieckmann – Meiser**, **Knoevenagel** condensation, **Mentzer**, **Pauly – Lockemann**, **von Pechmann – Duisberg**, **Perkin** coumarin and **Simonis** reactions.

### REFERENCES :

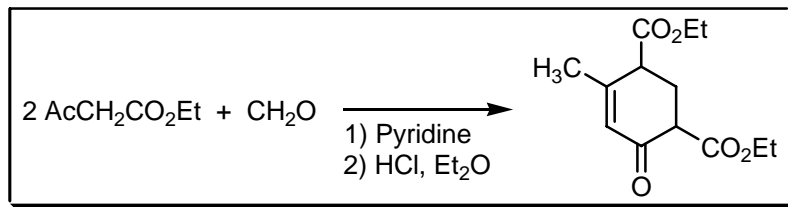
Org. Synth. : 28, 24

- 1) E. Knoevenagel, *Ber. Dtsch. Chem. Ges.*, 1898, **31**, 2585.
- 2) S.M. Setha; N.M. Shah, *Chem. Rev.*, 1945, **36**, 1.
- 3) A.K. Bose; M.S. Manhas; M. Ghosh; V.S. Raju; K. Tabei; Z. Urbanczyk-Lipkowska, *Heterocycles*, 1990, **30**, 741.
- 4) S. Padmanabhan; R. Peri; D.J. Trigg, *Synth. Commun.*, 1996, **26**, 827.
- 5) B.T. Watson; G.E. Christiansen, *Tetrahedron Lett.*, 1998, **39**, 6087.
- 6) T. Sugino; K. Tanaka, *Chem. Lett.*, 2001, 110.
- 7) A. Kakehi; S. Ito; H. Suga; K. Yasuraoka, *Heterocycles*, 2001, **54**, 185.

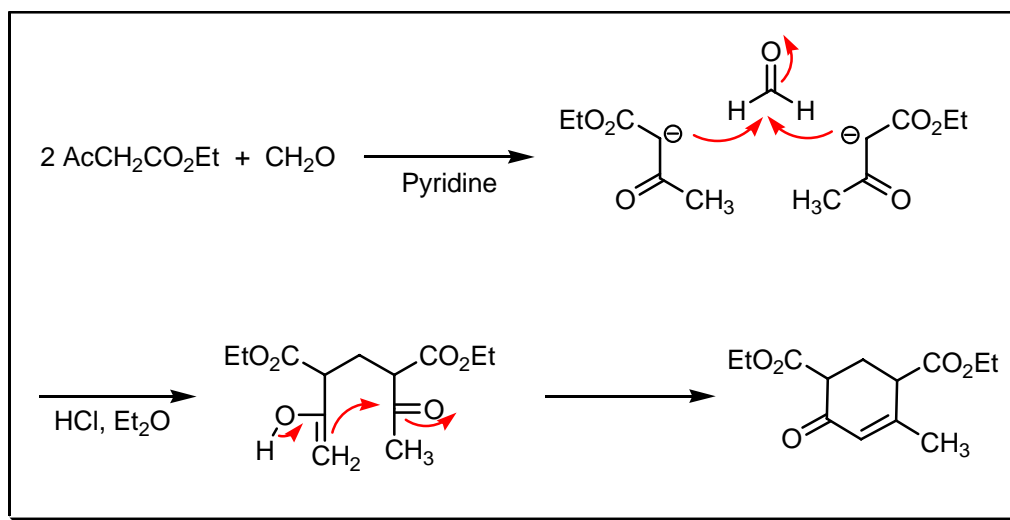
**COMMENTS :**

**KNOEVENAGEL CYCLOHEXENONE SYNTHESIS**

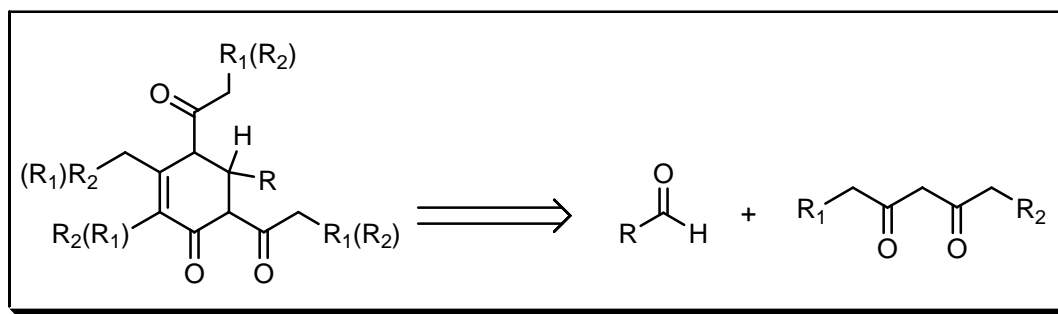
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

This reaction involves the condensation of an aldehyde with a 1,3-dicarbonyl compound to yield a 1,5-diketone. This compound undergoes an internal aldol condensation, followed by the loss of water to give an unsaturated ketone of cyclohexane.

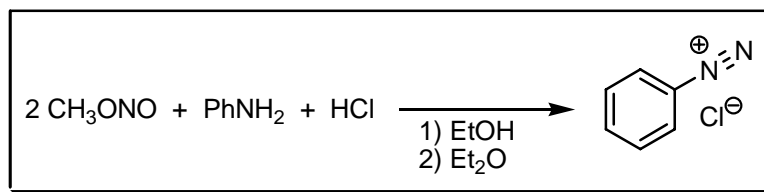
## REFERENCES :

- 1) E. Knoevenagel, *Liebigs Ann. Chem.*, 1894, **281**, 25.
- 2) H. Nitta; K. Takimoto; I. Ueda, *Chem. Pharm. Bull.*, 1992, **40**, 858.
- 3) U. Kuhl; U. Holzgrabe, *Monath. Chem.*, 2001, **132**, 407.

## COMMENTS :

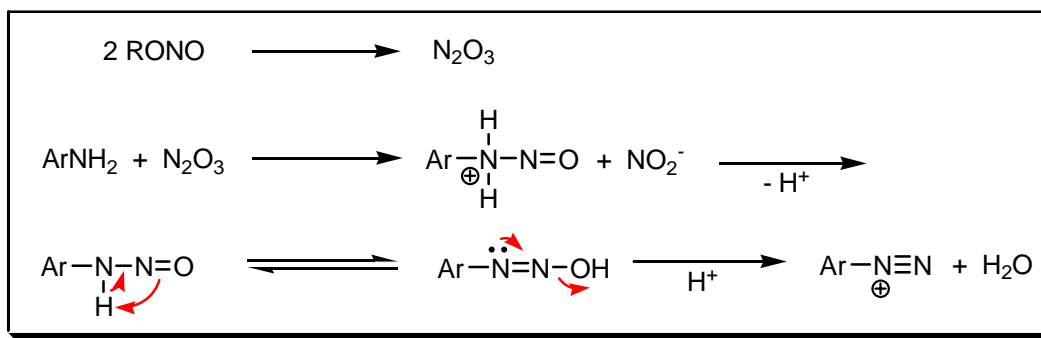
## KNOEVENAGEL DIAZOTATION

### EXAMPLE :

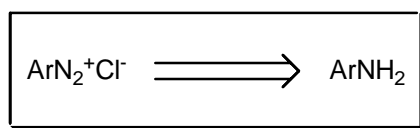




### MECHANISM :



### DISCONNECTION :



### NOTES :

This method relates to the diazotisation of primary aromatic amines by the addition of an alkyl nitrite to an ethanolic solution or suspension of the amine salt followed by precipitation of the diazonium salt with ether. Other media can replace ethanol. See also **Balz – Schiemann**, **Cadogan** arylation, **Craig** exchange, **Demjanov** rearrangement, **Gattermann** diazo, **Gattermann** sulphinic acid, **Griess** deamination, **Körner – Contardi**, **Meerwein** arylation, **Sandmeyer** diazonium, **Schwechten** and **Witt** diazotation reactions.

### REFERENCES :

**March** : 635

**Smith – March** : 816

**Smith** : 197

**Smith 2<sup>nd</sup>** : 1057

**Org. React.** : 2, 262

1) P. Griess, *Liebigs Ann. Chem.*, 1858, **106**, 123.

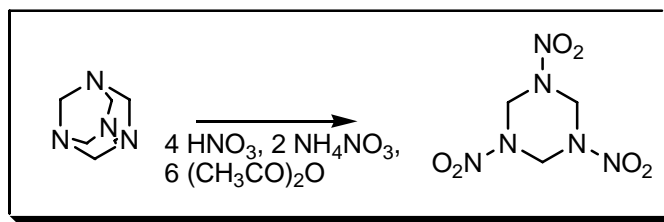
2) E. Knoevenagel, *Ber. Dtsch. Chem. Ges.*, 1890, **23**, 2994.

### COMMENTS :

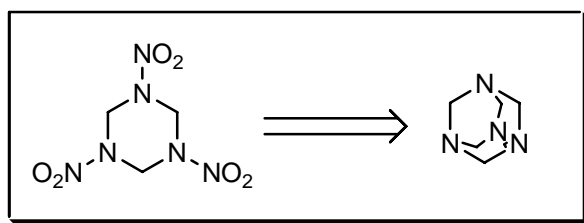
## KNOFFLER – BACHMANN CYCLONITE SYNTHESIS

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### EXAMPLE :



### DISCONNECTION :



### NOTES :

This process is essentially a combination of the **Ebele – Schiessler – Ross** and the **Hale** methods. Hexamethylenetetramine dinitrate reacts with ammonium nitrate, nitric acid and acetic anhydride to yield cyclonite. The reaction is also known as the K-method. See also **Ebele – Schiessler – Ross**, **Hale** and **Wolfram** reactions.

### REFERENCES :

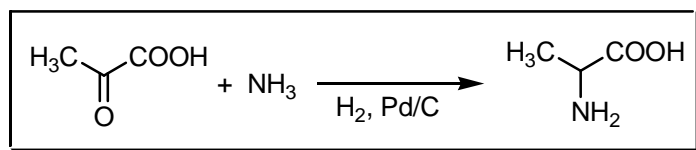
- 1) W.E. Bachmann; J.C. Sheehan, *J. Am. Chem. Soc.*, 1949, **71**, 1842.
- 2) C.J. McHugh; W.E. Smith; R. Lacey; D. Graham, *Chem. Commun.*, 2002, 2514.

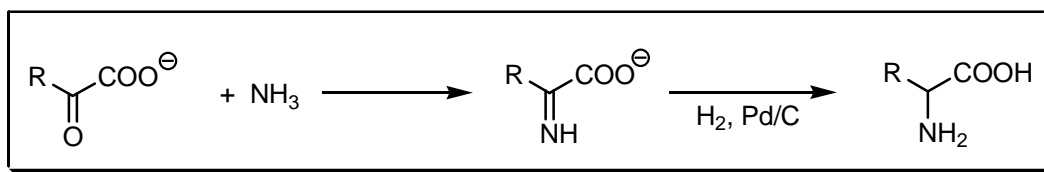
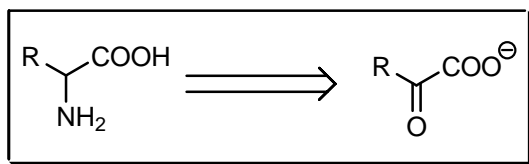
### COMMENTS :

## KNOOP – OESTERLIN AMINO ACID SYNTHESIS

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### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

Amino acids are obtained by the catalytic reduction of keto-acids in the presence of ammonia. Catalysts such as palladium on coal and Raney nickel may be employed.

**REFERENCES :**

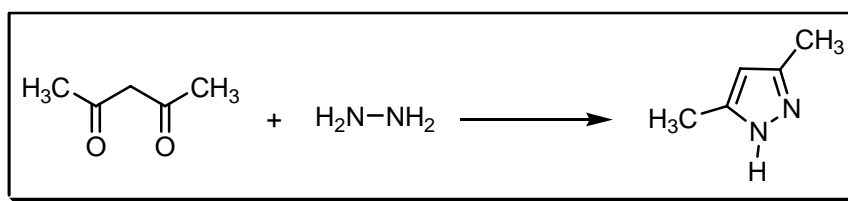
Houben – Weyl : 11/2, 311

- 1) F. Knoop; H. Oesterlin, *Hoppe Seylers Zeit. Physiol. Chem.*, 1925, **148**, 294.
- 2) H.R.V. Arnstein; R. Bentley, *J. Chem. Soc., Quat. Rev.*, 1950, **4**, 186.
- 3) C.W. Huffman; W.G. Skelly, *Chem. Rev.*, 1963, **63**, 625.

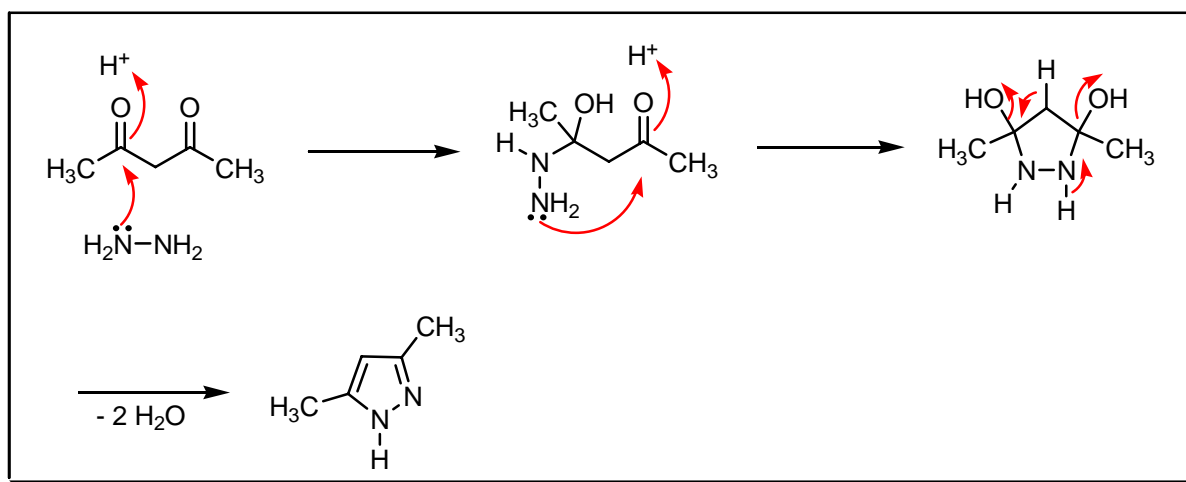
**COMMENTS :**

# KNORR PYRAZOLE SYNTHESIS

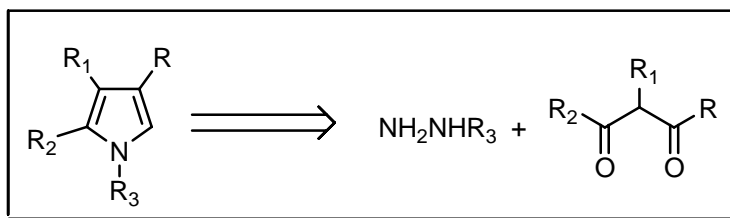
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Pyrazoles are obtained by the condensation of 1,3-dicarbonyl compounds with hydrazines. See also **Balbiano** and **von Pechmann** reactions.

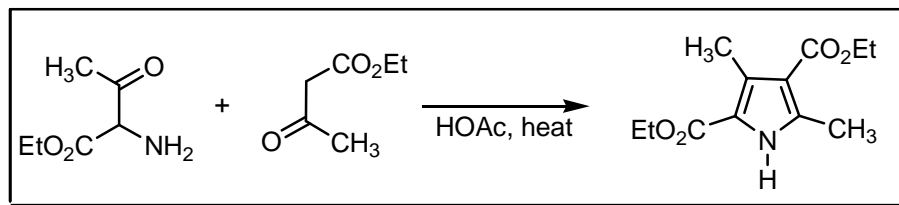
## REFERENCES :

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- 2) L. Claisen, *Liebigs Ann. Chem.*, 1894, **278**, 261.
- 3) A.R. Katritzky; F.W. Maine, *Tetrahedron*, 1964, **20**, 299.
- 4) E. Garcia-Egido; V. Spikmans; S.Y.F. Wong; B.H. Warrington, *Lab on a Chip*, 2003, **3**, 73.

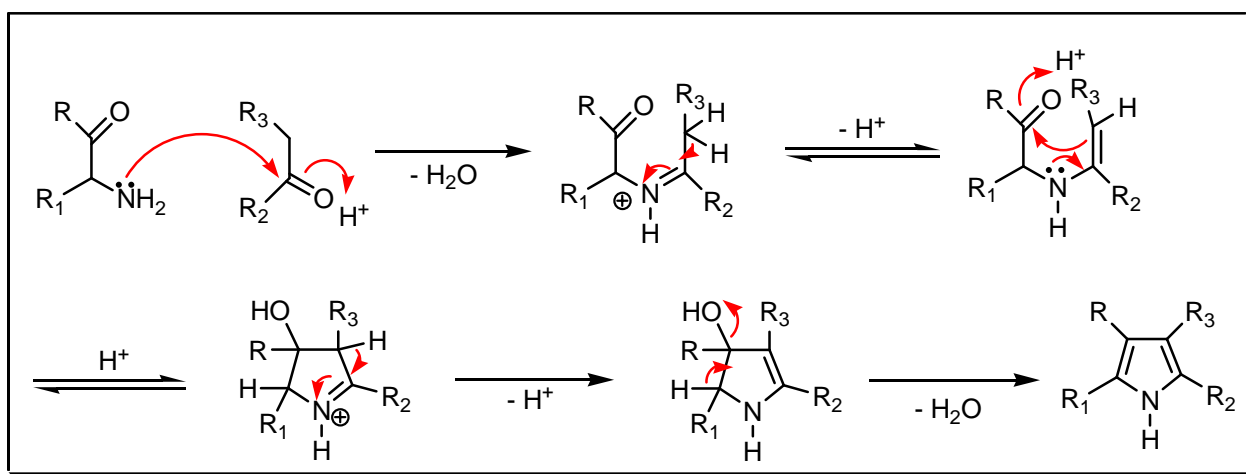
COMMENTS :

## KNORR PYRROLE SYNTHESIS

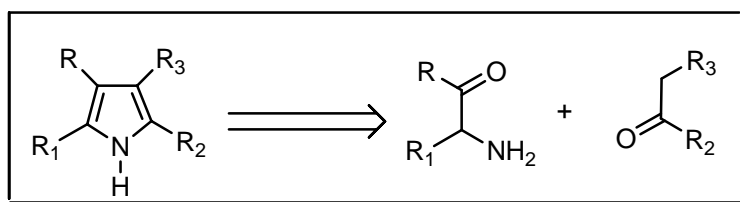
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

Pyrrole derivatives are prepared by the condensation of 1,3-diketones with  $\alpha$ -amino-ketones, which can be obtained from oximino-ketones. This reaction is a modification of the **Feist – Bénary** reaction. See also **Barton – Zard**, **Clauson–Kaas**, **Feist – Bénary**, **Fischer – Fink**, **Grob – Camenisch**, **Hantzsch** pyrrole, **Harries** pyrrole, **Kenner**, **Miller – Plöchl**, **Paal – Knorr**, **Padwa**, **Piloty – Robinson**, **Schwanert**, **Trofimov** and **Zav'yalov** reactions.

## REFERENCES :

Smith : 1021

Smith 2<sup>nd</sup> : 847, 849

Houben – Weyl : E6a, 624

Org. Synth. : 15, 17; 21, 67

Org. Synth. Coll. Vol. : 2, 202; 3, 513

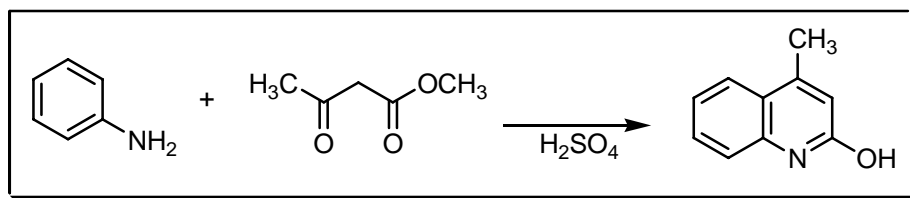
Science of Synthesis : 9, 469

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- 1) L. Knorr, *Ber. Dtsch. Chem. Ges.*, 1884, **17**, 1635.
  - 2) E. Baltazzi; L.I. Krimen, *Chem. Rev.*, 1963, **63**, 516.
  - 3) H. Rapoport; J. Harbuck, *J. Org. Chem.*, 1971, **36**, 853.
  - 4) E. Fabiano; B.T. Golding, *J. Chem. Soc., Perkin Trans. 1*, 1991, 3371.
  - 5) J.M. Hanby; J.C. Hodges, *Heterocycles*, 1993, **35**, 843.
  - 6) Y. Zhang; Y.Z. Jiang; X.T. Liang, *Chin. J. Chem.*, 1997, **15**, 371.
  - 7) T.D. Lash, *Tetrahedron*, 1998, **54**, 359.
  - 8) J.A. Bastian; T.D Lash, *Tetrahedron*, 1998, **54**, 6299.
  - 9) A. Alberola; A.G. Ortega; M.L. Sadaba; C. Sanudo, *Tetrahedron*, 1999, **55**, 6555.
  - 10) I. Elghamry, *Synth. Commun.*, 2002, **32**, 897.
  - 11) R.K. Bellingham; J.S. Carey; N. Hussain; D.O. Morgan; P. Oxley; L.C. Powling, *Org. Proc. Res. Dev.*, 2004, **8**, 279.
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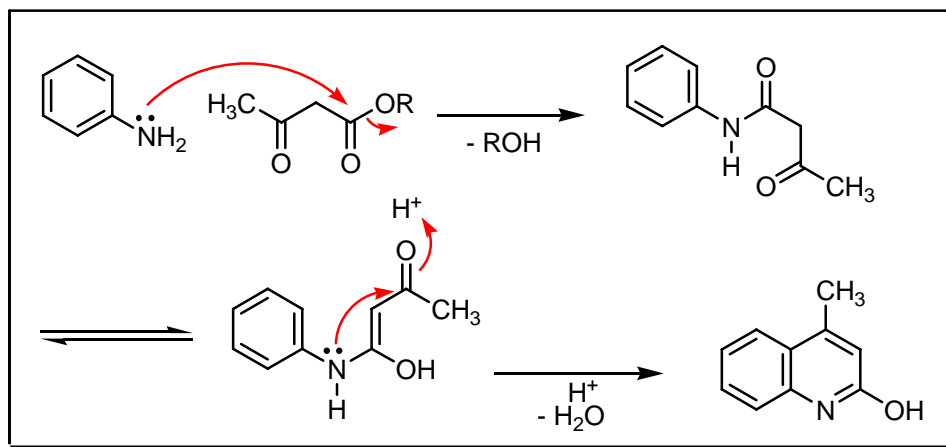
## COMMENTS :

## KNORR QUINOLINE SYNTHESIS

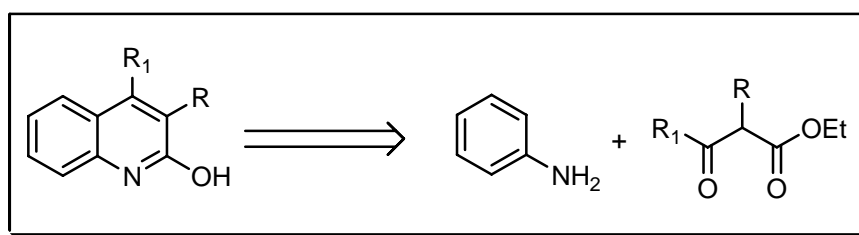
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The condensation of a  $\beta$ -ketoester with an aryl amine gives the anilide which is cyclised by concentrated sulfuric acid to a 2-hydroxyquinoline. See also **Allan – Loudon**, **von Baeyer – Drewson** quinoline, **Camps, Combes** quinoline, **Conrad – Limpach**, **Doebner** quinoline, **Doebner – von Miller**, **Foulds – Robinson**, **Friedländer**, **Meth–Cohn**, **von Niementowski** quinoline, **Pfitzinger – Borsche**, **Riehm** quinoline and **Skraup** quinoline reactions.

### REFERENCES :

Smith : 1334

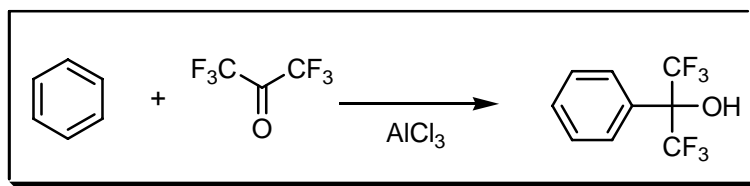
Smith 2<sup>nd</sup> : 1097

- 1) L. Knorr, *Liebigs Ann. Chem.*, 1886, **236**, 69.
- 2) F.W. Bergstrom, *Chem. Rev.*, 1944, **35**, 77.
- 3) A.J. Hodgkinson; B. Staskum, *J. Org. Chem.*, 1969, **34**, 1709.
- 4) P. Lopez–Alvarado; C. Avendano; J.C. Menendez, *Synthesis*, 1998, 186.

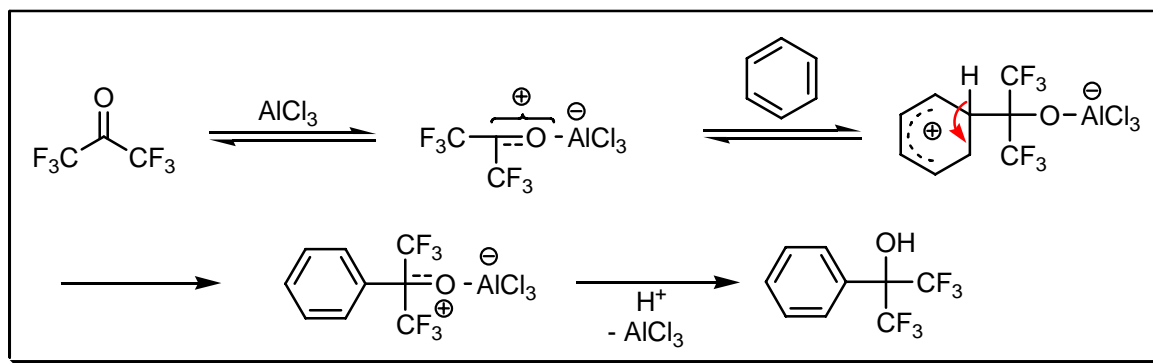
### COMMENTS :

## KNUNYANTS FLUORO ALKYLATION

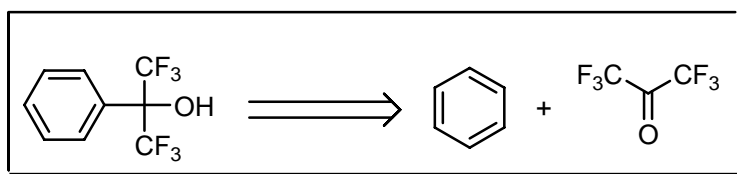
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This is the fluoroalkylation of aromatics using hexafluoroacetone. See also **Friedel – Crafts** and **Swarts** reactions.

### REFERENCES :

**Org. Synth.** : 63, 154

**Org. Synth. Coll. Vol.** : 7, 251

1) I.L. Knunyants; C. Ching-Yun; N.P. Gambaryan; E.M. Rokhlis, *Zh. Vses. Chim. Obsh.*, 1960, **5**, 114.

2) B.S. Farah; E.E. Gilbert; J.P. Sibilia, *J. Org. Chem.*, 1965, **30**, 998.

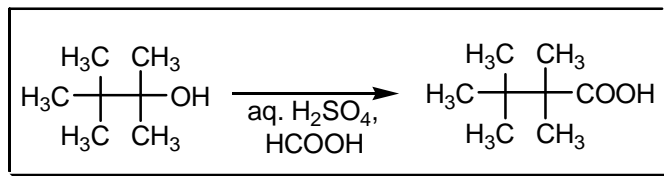
3) A.V. Fokin, *J. Fluorine Chem.*, 1993, **65**, R11.



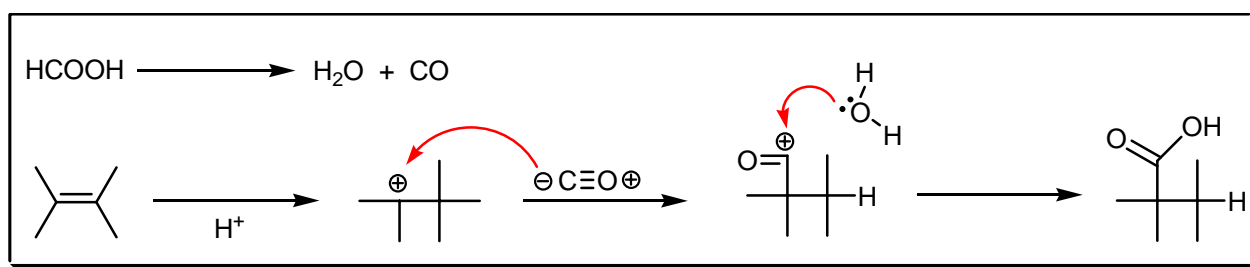
## COMMENTS :

## KOCH – HAAF REACTION

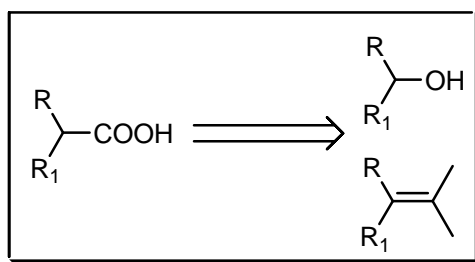
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This is the hydrocarboxylation of alcohols and alkenes. If formic acid is used as the source of carbon monoxide and water, the reaction can be done at atmospheric pressure and room temperature. The acid-catalysed hydrocarboxylation of an alkene with carbon monoxide and water under pressure is known as the **Koch** reaction. See also **Koch** reaction.

### REFERENCES :

March : 485, 808

Smith – March : 564, 1035

Smith : 1307

Smith 2<sup>nd</sup> : 1076

Houben – Weyl : E5, 302, 315; E19c, 367

Org. React. : 17, 213

Org. Synth. : 44, 1; 46, 72

Org. Synth. Coll. Vol. : 5, 20, 739

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1) H. Koch, *Brennst. Chem.*, 1955, **36**, 321.

2) H. Koch; W. Haaf, *Liebigs Ann. Chem.*, 1958, **618**, 251.

3) Y. Takahashi; N. Yoneda; H. Nagai, *Chem. Lett.*, 1982, 1187.

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6) C. Leonte; E. Carp, *Rev. Roum. Chim.*, 1989, **34**, 1241.

7) J.L. Emert; D.C. Dankworth; A. Gutierrez; D.J. Martella; S.P. Rucker; J.P. Stokes; W. Thaler; A. Worku; A.B. Padias; H.K. Hall, *Macromolecules*, 2001, **34**, 2766.

8) H. Mori; A. Mori; Q. Xu; Y. Souma, *Tetrahedron Lett.*, 2002, **43**, 7871.

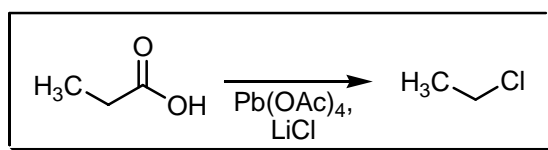
9) T. Li; N. Tsumori; Y. Souma; Q. Xu, *Chem. Commun.*, 2003, 2070.

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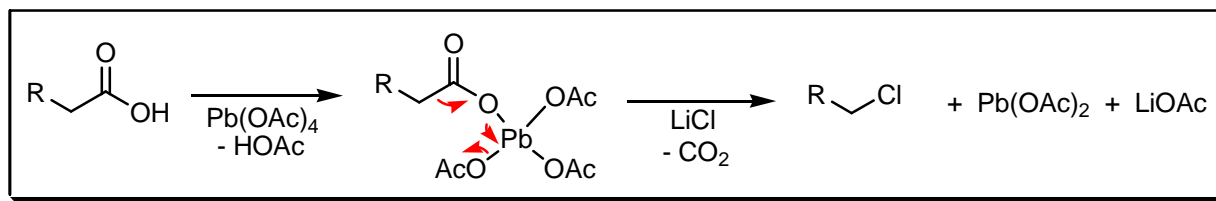
## COMMENTS :

## KOCHI DECARBOXYLATION

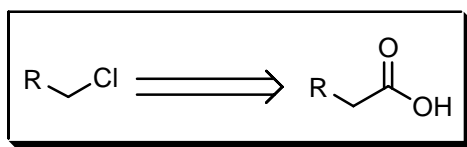
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The oxidative decarboxylation of carboxylic acids with lead(IV) acetate and lithium chloride. See also **Hunsdiecker – Borodine** and **Krapcho** reactions.

## REFERENCES :

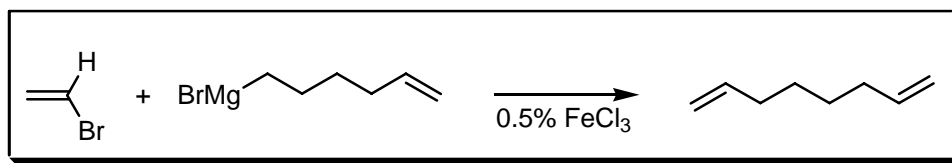
**Org. React.** : **19**, 279

- 1) J.K. Kochi, *J. Am. Chem. Soc.*, 1965, **87**, 2500.
- 2) M. Mannier; J.P. Aycard, *Can. J. Chem.*, 1979, **57**, 1257.
- 3) G.M. Strunz; L. Ya, *Can. J. Chem.*, 1992, **70**, 1317.

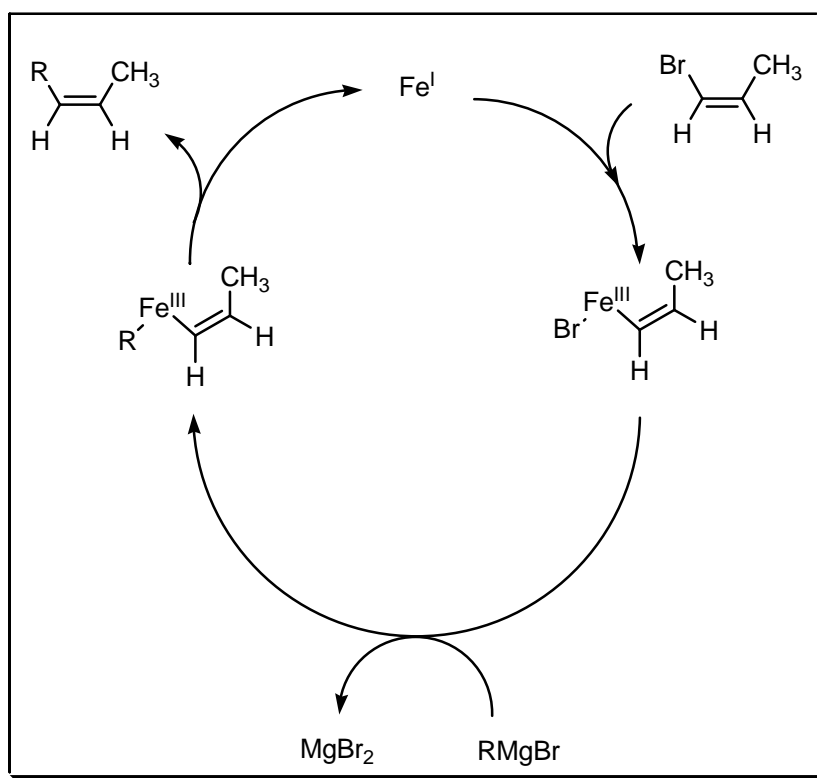
## COMMENTS :

## KOCHI REACTION

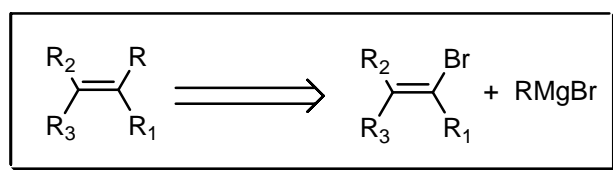
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The mechanism can be explained by an oxidative addition of 1-bromoalkene to iron(I) followed by exchange with the organomagnesium bromide and reductive elimination. In order to maintain the stereospecificity the oxidative addition should occur with retention. Copper(I) and silver(I) can also be used for cross-coupling and homo coupling, respectively.

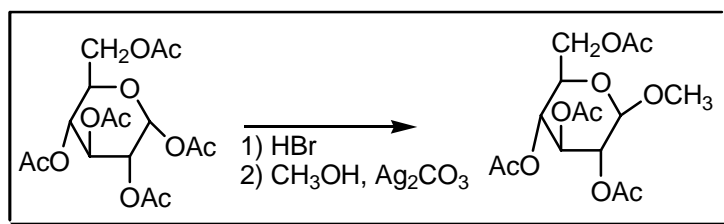
## REFERENCES :

- 1) M. Tamura; J.K. Kochi, *J. Am. Chem. Soc.*, 1971, **93**, 1487.
- 2) M. Tamura; J.K. Kochi, *Synthesis*, 1971, 303.
- 3) R.S. Smith; J.K. Kochi, *J. Org. Chem.*, 1976, **41**, 502.
- 4) G.A. Molander; B.J. Rahn; D.C. Shubert; S.E. Bonde, *Tetrahedron Lett.*, 1983, **24**, 5449.
- 5) J.K. Kochi, *J. Organomet. Chem.*, 2002, **653**, 11.
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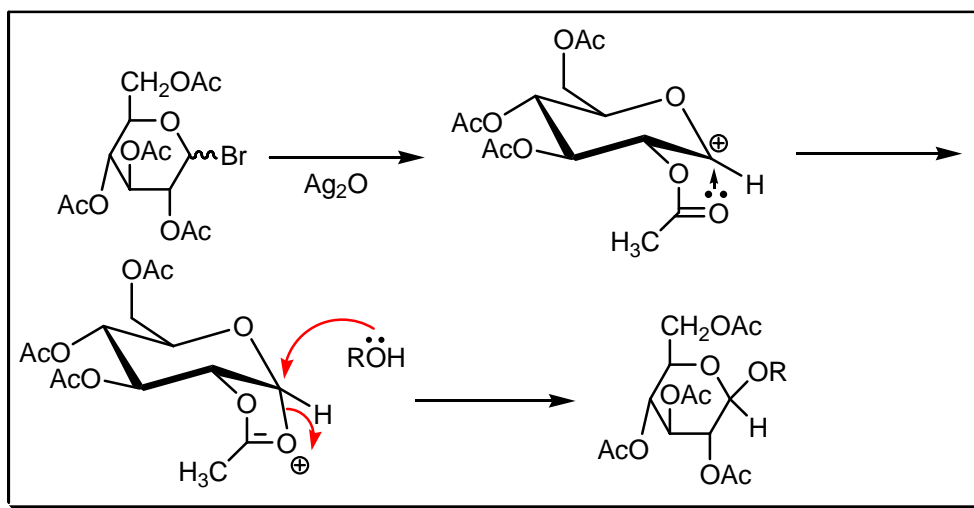
COMMENTS :

## KOENIGS – KNORR SYNTHESIS

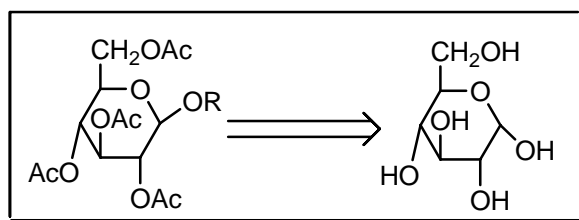
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

α and β-Acetylglycosyl bromides on treatment with alcohols and phenols in the presence of excess silver carbonate or oxide yield β-acetylglycosides, which may be deacetylated in alkaline solution. The **Zemplen – Helferich** modification uses Hg(CN)<sub>2</sub> or Hg(OCOCH<sub>3</sub>)<sub>2</sub>. The **Bredereck** modification works with tertiary esters of primary alcohols in

nitromethane in the presence of silver perchlorate, while the **Schroeder** modification is carried out in the presence of mercury oxide and mercury bromide. See also **Fischer** glycosidation, **Kahne** glycosidation, **Michael** glycosidation and **Schmidt** glycosidation reactions.

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#### REFERENCES :

Org. Synth. : **22**, 1

Org. Synth. Coll. Vol. : **3**, 11

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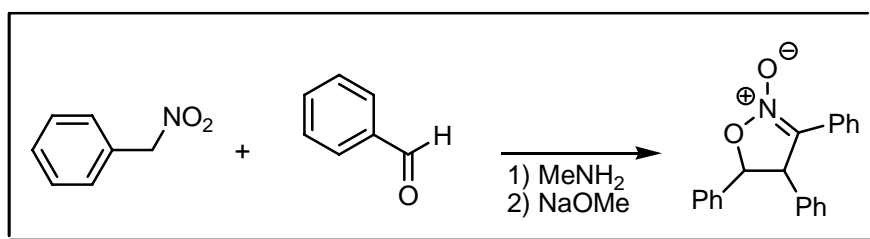
- 1) W. Koenigs; E. Knorr, *Ber. Dtsch. Chem. Ges.*, 1901, **34**, 957.
  - 2) A.S. Perlin, *Can. J. Chem.*, 1963, **41**, 399.
  - 3) F. Imperato, *J. Org. Chem.*, 1976, **41**, 3478.
  - 4) A. Miliua; J. Greiner; J.G. Riess, *New. J. Chem.*, 1991, **15**, 337.
  - 5) J. Tamura; R. Terayama; T. Shimadate, *J. Carbohydr. Chem.*, 1993, **12**, 893.
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  - 7) M.C.Z. Kasuya; L.X. Wang; Y.C. Lee; M. Mitsuki; H. Nakajima; Y. Miura; T. Sato; K. Hatanaka; S. Yamagata; T. Yamagata, *Carbohydr. Res.*, 2000, **329**, 755.
  - 8) G. Desmares; D. Lefebvre; G. Renevret; C. Le Drian, *Helv. Chim. Acta*, 2001, **84**, 880.
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  - 10) F. Stazi; G. Palmisano; M. Turconi; S. Clini; M. Santagostino, *J. Org. Chem.*, 2004, **69**, 1097.
- 

#### COMMENTS :

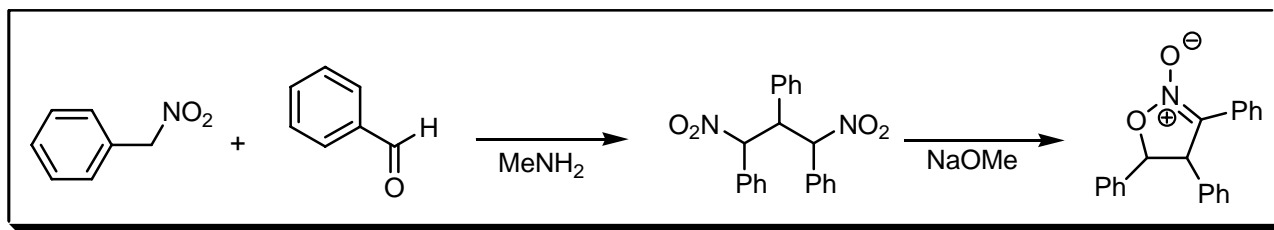
### KOHLER ISOXAZOLE-N-OXIDE SYNTHESIS

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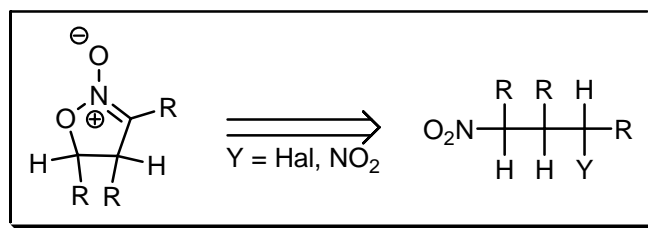
#### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The base-catalysed cyclisation of 2-isoxazole-2-oxides from 1,3-dinitroalkanes or 1-halo-3-nitro-alkanes.

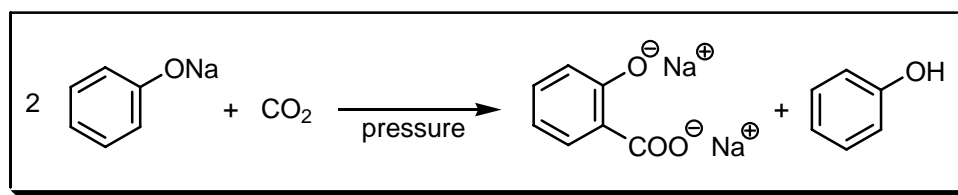
## REFERENCES :

- 1) E.P. Kohler; G.R. Barrett, *J. Am. Chem. Soc.*, 1924, **46**, 2105.
- 2) E.P. Kohler; N.K. Richtmyer, *J. Am. Chem. Soc.*, 1928, **50**, 3092.
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- 4) L.I. Smith, *Chem. Rev.*, 1938, **23**, 193.
- 5) A. Dornow; F. Boberg, *Liebigs Ann. Chem.*, 1952, **578**, 94.
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- 7) A.T. Nielsen; T.G. Archibald, *J. Org. Chem.*, 1969, **34**, 984.

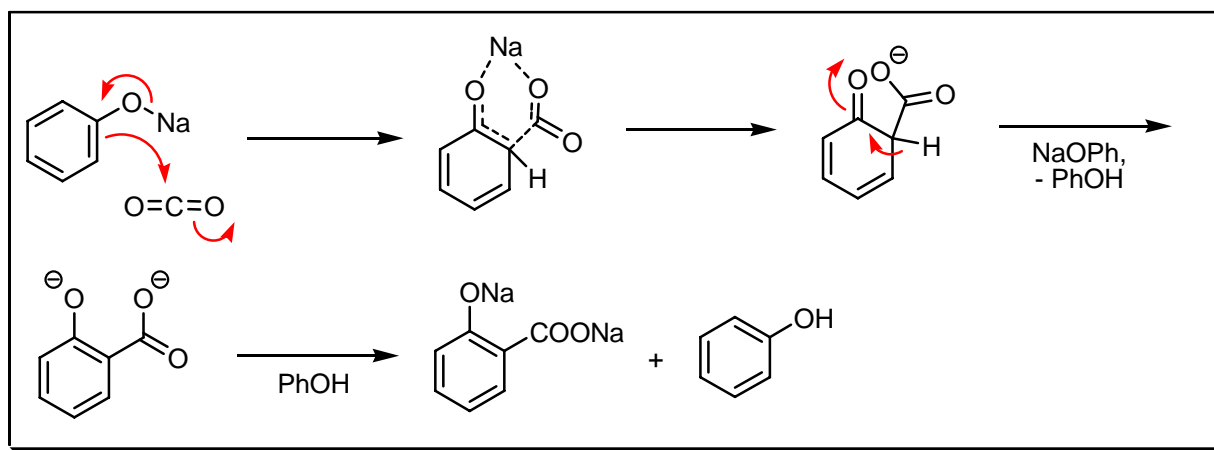
## COMMENTS :

## KOLBE – SCHMITT REACTION

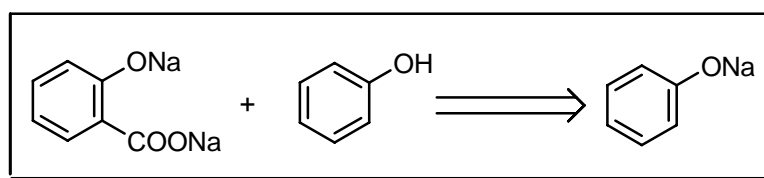
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The production of phenolic acid (salicylic acid) by the action of carbon dioxide under pressure on phenoxides. The carboxylation occurs mostly in the *ortho* position. In the **Marasse** modification the phenol is heated with potassium carbonate and carbon dioxide under pressure. See also **Kekulé** and **Reimer – Tiemann** reactions.

### REFERENCES :

March : 546

Smith – March : 718

Houben – Weyl : 8, 372; E5, 322

Org. Synth. : 10, 94

Org. Synth. Coll. Vol. : 2, 557

1) H. Kolbe, *Liebigs Ann. Chem.*, 1860, **113**, 125.



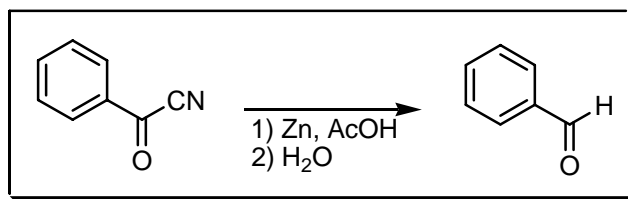
- 2) H. Kolbe, *J. Prakt. Chem.*, 1875, **120**, 151.  
3) R. Schmitt, *J. Prakt. Chem.*, 1885, **31**, 397.  
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**COMMENTS :**

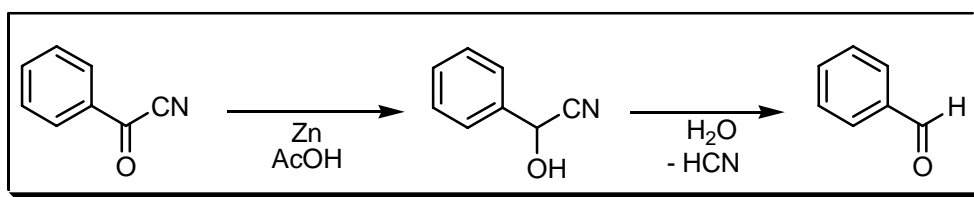
## KOLBE ALDEHYDE SYNTHESIS

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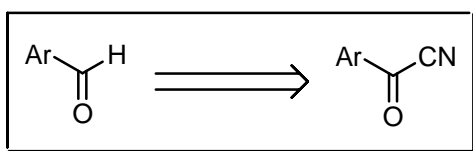
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

Aromatic aldehydes are produced by treatment of aroyl cyanides with zinc dust. The cyanohydrin thus formed is hydrolysed. See also **Claisen – Mauthner – Bouveault** reaction.

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## REFERENCES :

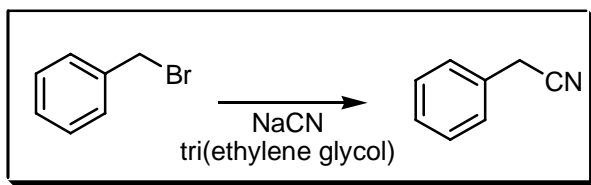
- 1) H. Kolbe, *Liebigs Ann. Chem.*, 1856, **98**, 344.
- 2) Tadeus; I. Reichstein, *Helv. Chim. Acta*, 1930, **13**, 1275.

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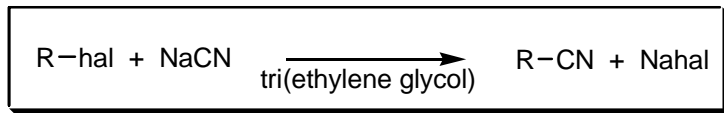
## COMMENTS :

## KOLBE CYANIDE ALKYLATION

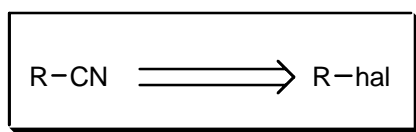
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The formation of a nitrile by heating a mixture of water and alcohol with an alkali cyanide and an alkyl halide. See also **Pelouze** reaction.

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## REFERENCES :

- Houben – Weyl** : **8**, 290; **E19a**, 6  
**Org. Synth.** **18**, 50  
**Org. Synth. Coll. Vol.** : **2**, 376

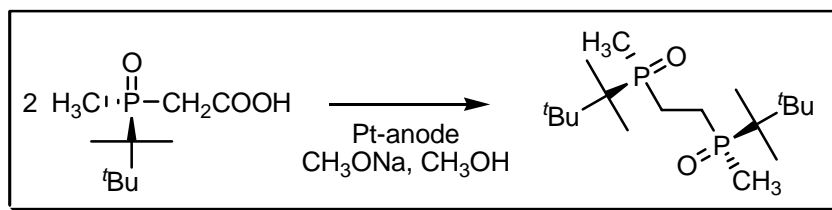
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- 1) F. Wöhler; J. von Liebig, *Liebigs Ann. Chem.*, 1832, **3**, 267.

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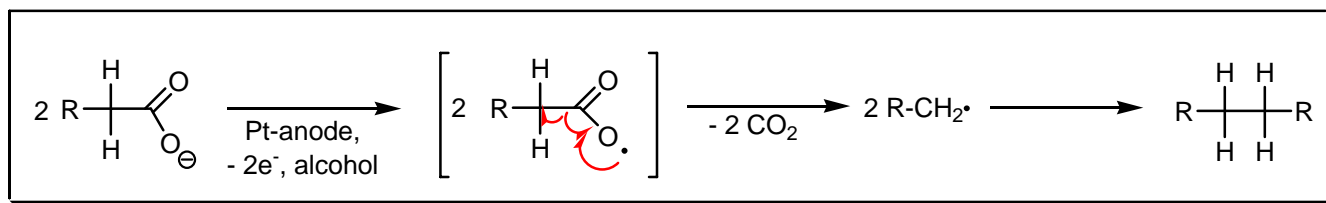
**COMMENTS :**

## KOLBE ELECTROLYTIC SYNTHESIS

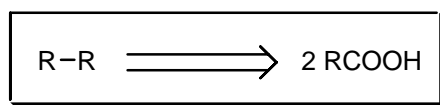
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

This reaction relates to the synthesis of hydrocarbons by the electrolysis of aqueous solutions of alkali salts of aliphatic acids. The decomposition of two alkylcarboxyl anions into carbon dioxide and the dimerisation of two alkyl radicals are involved. There is also a photo-Kolbe reaction. See also **Crum Brown – Walker** and **Hofer – Moest** reactions.

**REFERENCES :**

**March** : 729

**Smith – March** : 942

Smith : 1417

Smith 2<sup>nd</sup> : 1167

Houben – Weyl : 8, 500; E19a, 56

Org. Synth. : 41, 24, 33; 60, 1

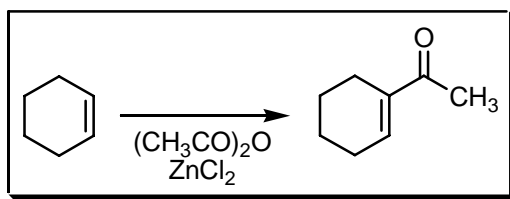
Org. Synth. Coll. Vol. : 5, 445, 463; 7, 181

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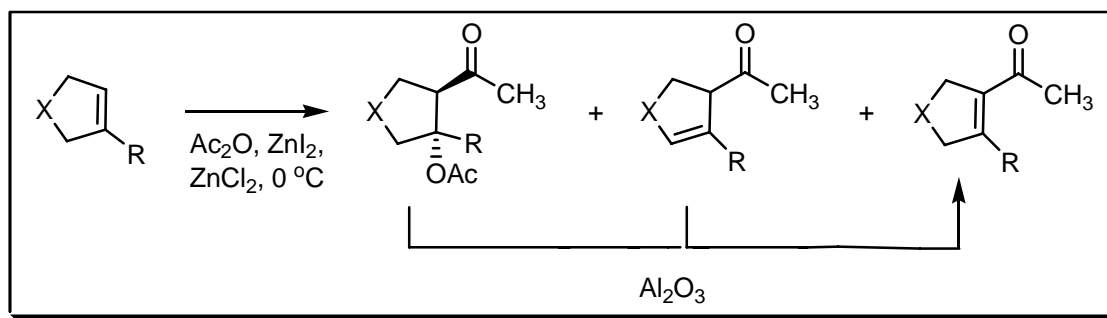
#### COMMENTS :

### KONDAKOFF OLEFIN REACTION

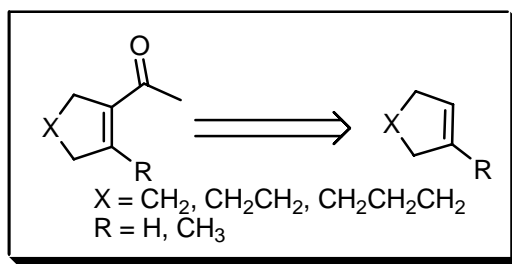
#### EXAMPLE :



#### MECHANISM :



## DISCONNECTION :



## NOTES :

Cyclic olefins condense in the presence of zinc or stannic chloride, with aliphatic acids or anhydrides.

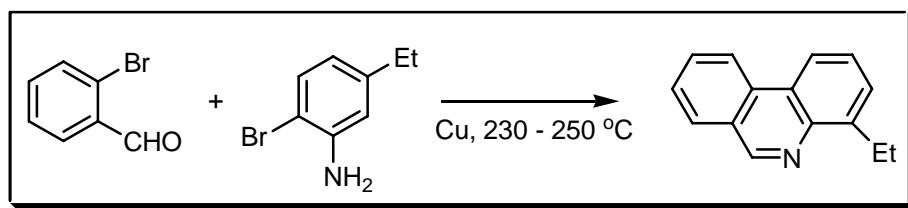
## REFERENCES :

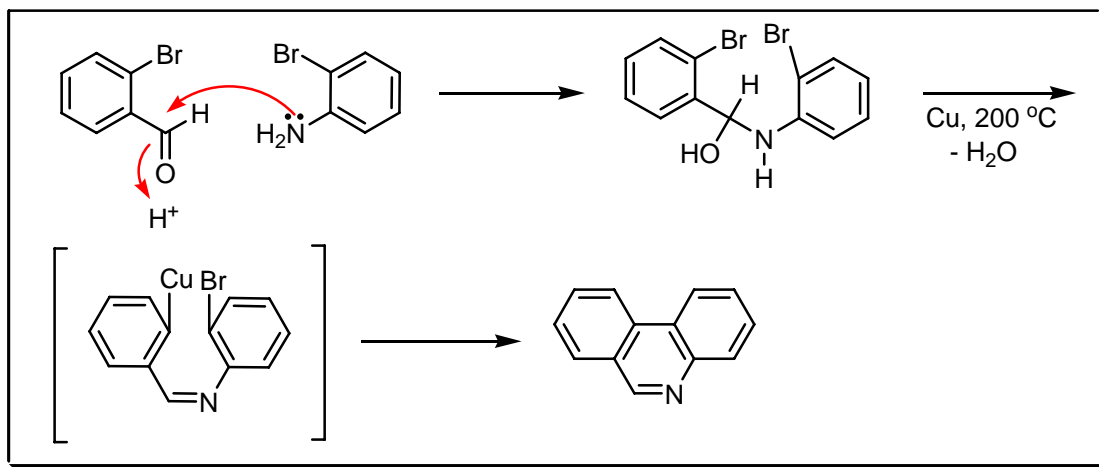
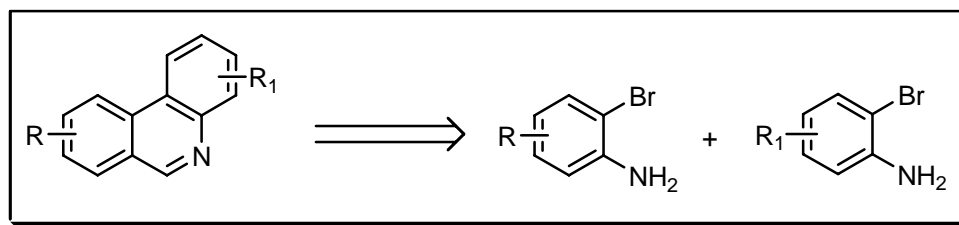
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## COMMENTS :

## KONDO – UYEO SYNTHESIS

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

Phenanthridines are obtained by heating an *o*-bromobenzaldehyde and an *o*-bromoaniline with copper powder at  $230 - 250\text{ }^\circ\text{C}$ . See also **Ullmann** diaryl reaction.

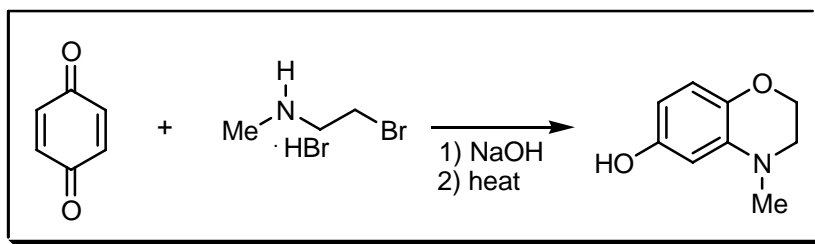
**REFERENCES :**

H. Kondo; S. Uyeo, *Ber. Dtsch. Chem. Ges.*, 1937, **70**, 1087.

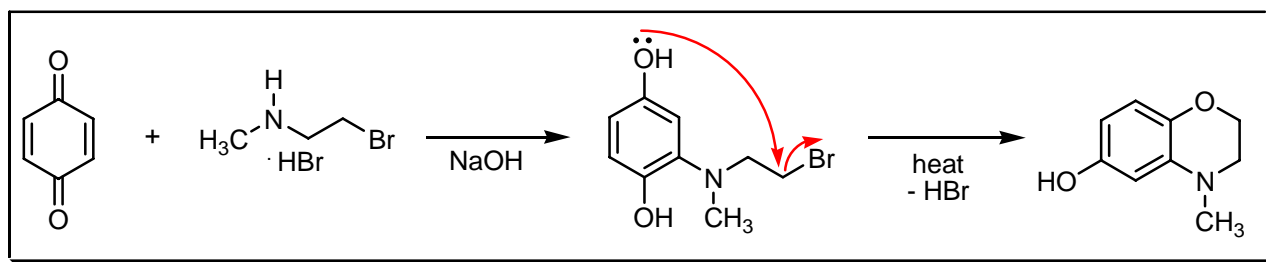
**COMMENTS :**

# KÖNIG BENZOXAZINE SYNTHESIS

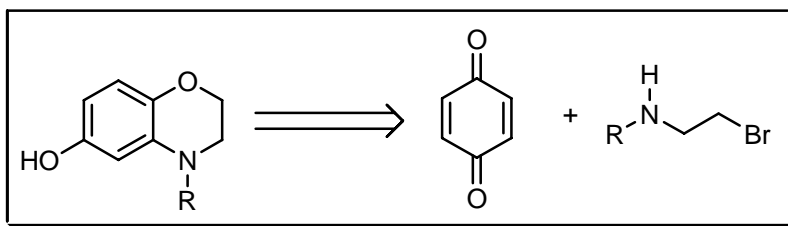
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The benzoxazine synthesis from quinones and 2-alkyl or aryl amino ethanol. The open compounds (non-cyclised) show some interesting thermochromic, piezochromic, solvatochromic and fluorescent properties.

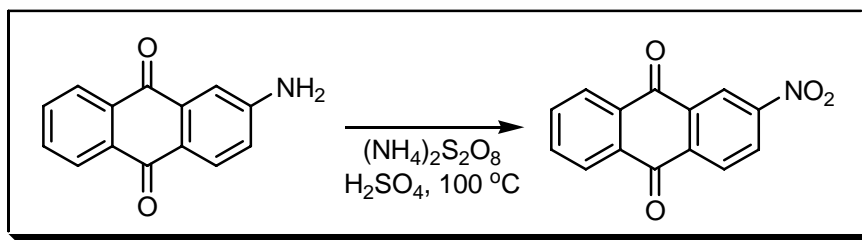
## REFERENCES :

- 1) K.-H. König, *Chem. Ber.*, 1959, **92**, 257.
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- 3) J.H. Day, *Chem. Rev.*, 1963, **63**, 65.
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- 5) K.D. McMurtrey; G.D. Daves, jr., *J. Org. Chem.*, 1970, **35**, 4252.

## COMMENTS :

## KOPETSCHNI CONVERSION

### EXAMPLE :



### NOTES :

Oxidation of aminoanthraquinones to nitroanthraquinones is effected by peracids. In some cases a nitroso derivative is obtained. Acetic acid can facilitate the reaction through the formation of peracetic acid.

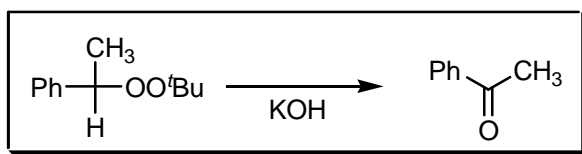
### REFERENCES :

E. Kopetschni, *German Patent*, 363930. (*Chem. Abs.*, 1924, **18**, 991.)

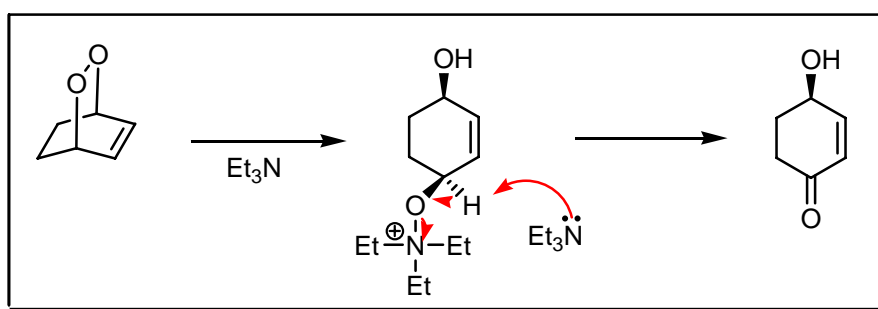
### COMMENTS :

## KORNBLUM – DELAMARE REARRANGEMENT

### EXAMPLE :

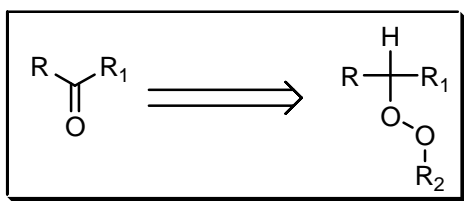


### MECHANISM :





## DISCONNECTION :



## NOTES :

The decomposition of dialkyl peroxides by base-catalysed rearrangement. The endoperoxides should have  $\alpha$ -protons to undergo the reaction. The reaction depends on the strength of the base used.

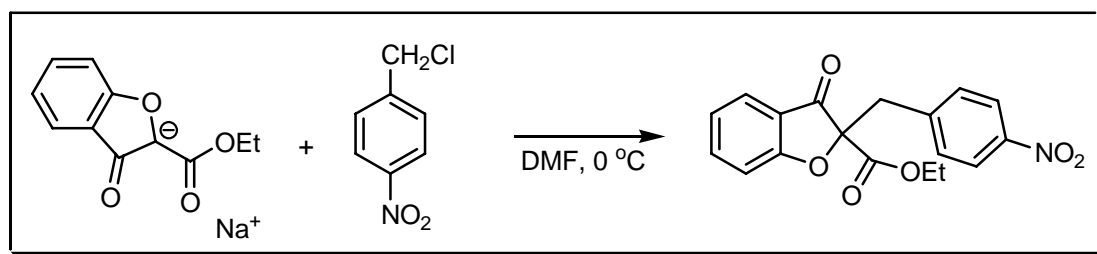
## REFERENCES :

- 1) N. Kornblum; H.E. DeLaMare, *J. Am. Chem. Soc.*, 1951, **73**, 880.
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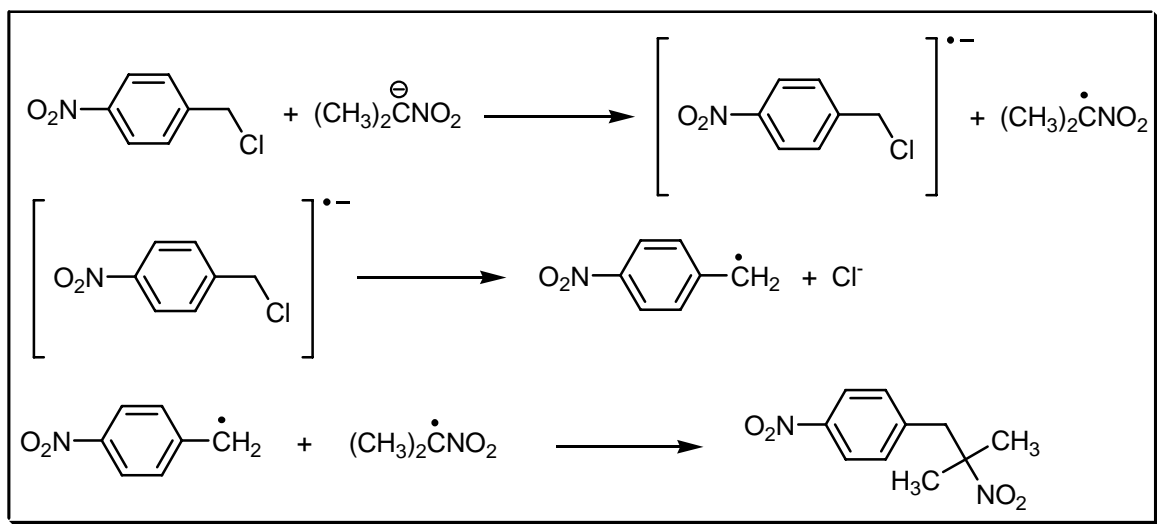
## COMMENTS :

## KORNBLUM – RUSSELL REACTION

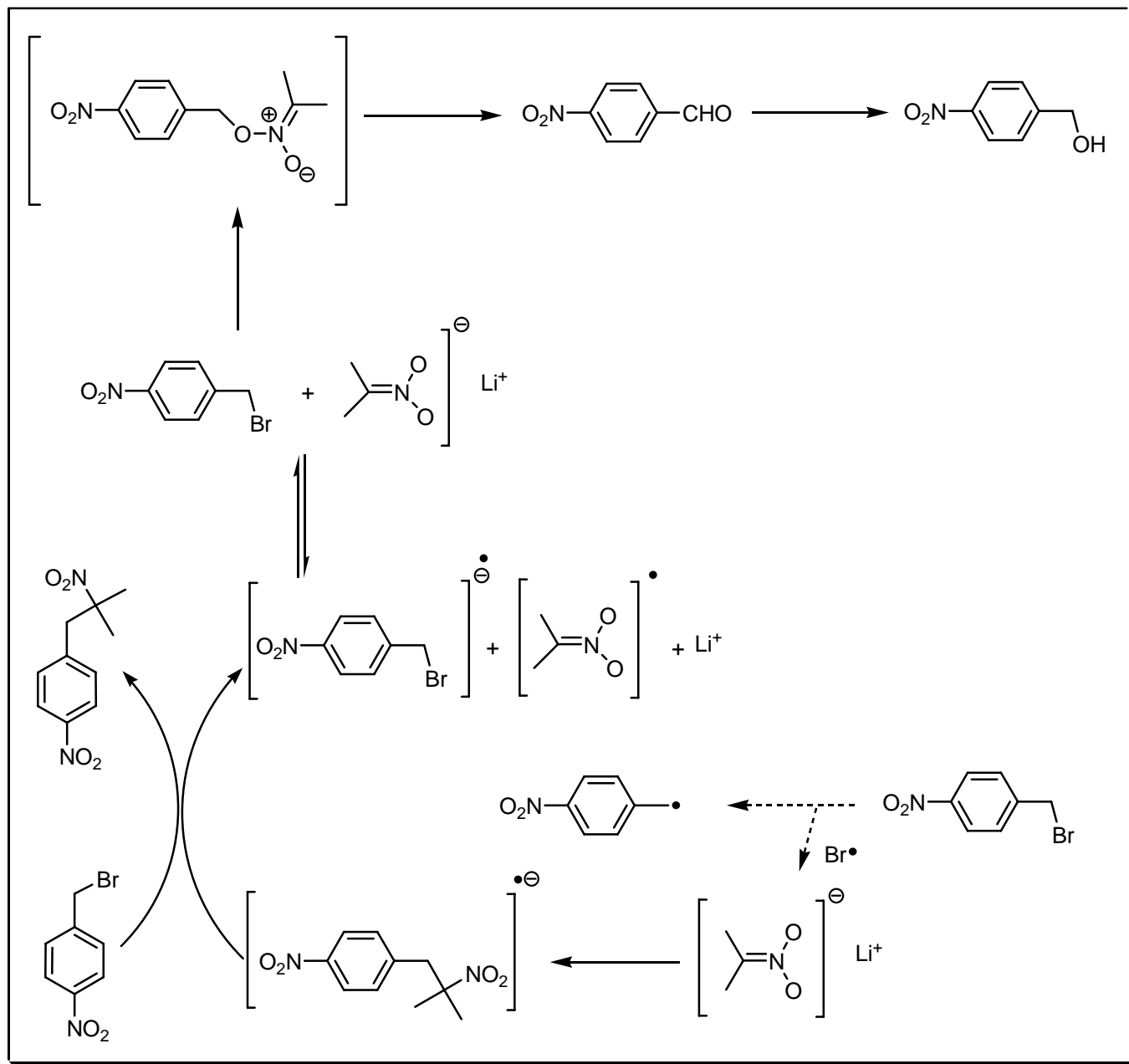
### EXAMPLE :



# MECHANISM :



# Luche :



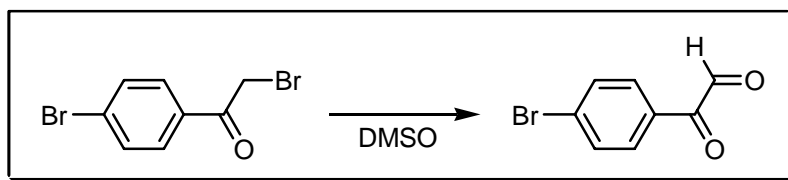
**NOTES :**

Normally O-alkylation ( $S_N2$ ) takes place between nitronate anions and alkyl halides. However, C-alkylation of nitronate anions *via* a radical chain reaction takes place when *para*-nitrobenzyl chlorides are used. **Luche et al.** discovered that sonification can influence the C/O alkylation ratio.

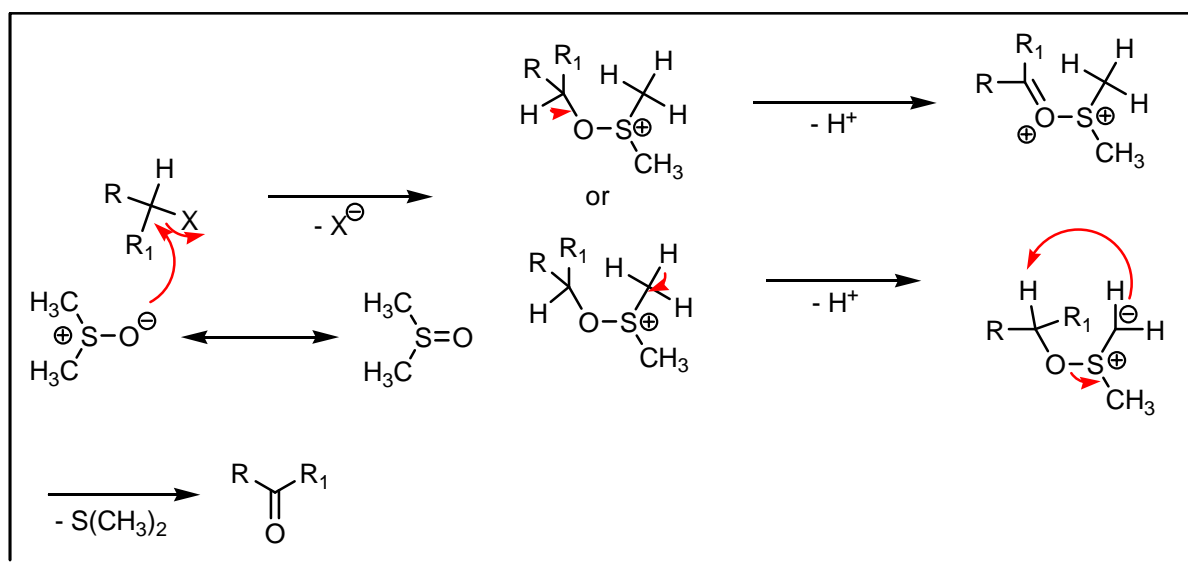
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**REFERENCES :**

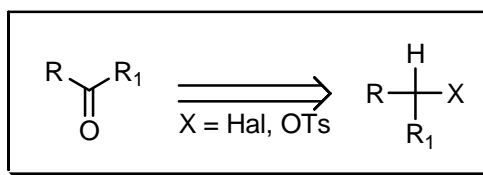
- 1) N. Kornblum; G.W. Urry; R.C. Kerber, *J. Am. Chem. Soc.*, 1964, **86**, 3904.
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  - 6) M.J. Dickens; J.-L. Luche, *Tetrahedron Lett.*, 1991, **32**, 4709.
- 

**COMMENTS :****KORNBLUM ALDEHYDE SYNTHESIS****EXAMPLE :**

## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of aldehydes from primary alkyl halides or tosylates, using dimethyl sulfoxide as oxidant. There are several variations of this reaction. The silver-assisted oxidation and the amine oxide assisted oxidation (sometimes called **Ganem** oxidation) are the best known variations. See also **Kröhnke – Ortoleva – King**, **Pfitzner – Moffatt** and **Swern** reactions.

## REFERENCES :

**Smith – March** : 1535

**Houben – Weyl** : **E3**, 248

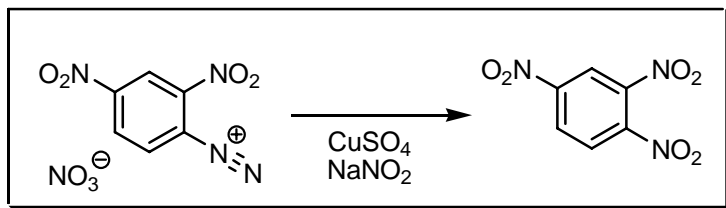
**Org. React.** : **39**, 297

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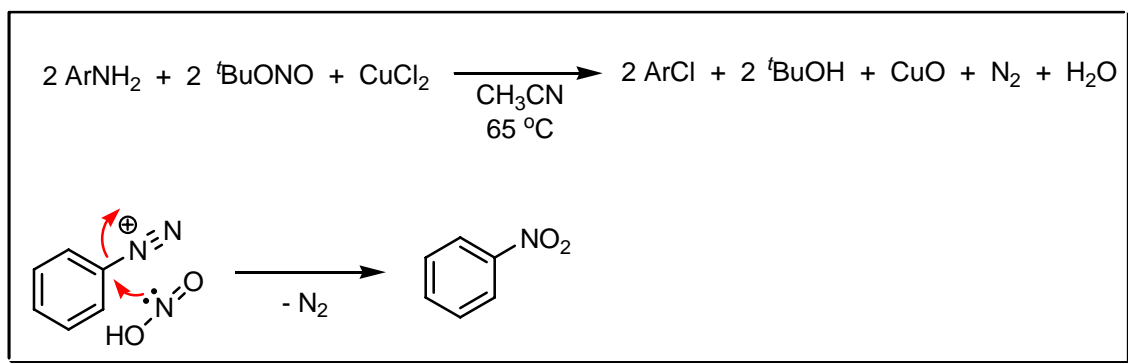
COMMENTS :

## KÖRNER – CONTARDI REPLACEMENT

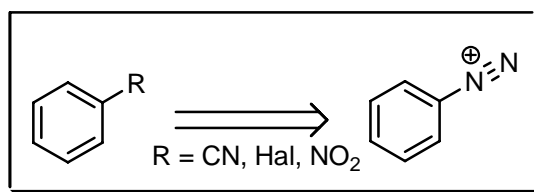
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The replacement of diazonium groups in aromatic compounds by halo, cyano or similar groups under the influence of cupric salts. It is limited to negatively substituted diazo-compounds. The reaction has been improved by **Suzuki** *et al.* See also **Balz – Schiemann**, **Cadogan** arylation, **Craig** exchange, **Demjanov** rearrangement, **Gattermann** diazo, **Gattermann** sulphinic acid, **Griess** deamination, **Knoevenagel** diazotation, **Meerwein** arylation, **Sandmeyer** diazonium, **Schwechten** and **Witt** diazotation reactions.

## REFERENCES :

Houben – Weyl : **5/3**, 846; **5/4**, 438

Org. Synth. : **19**, 40; **28**, 52

Org. Synth. Coll. Vol. : **2**, 225; **3**, 341

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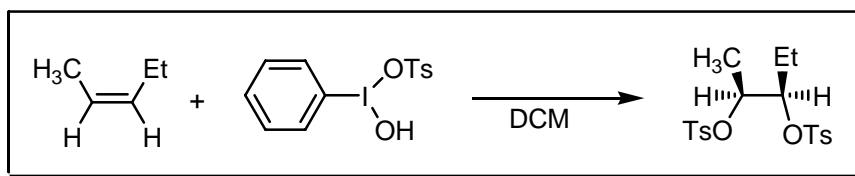
- 1) T. Sandmeyer, *Ber. Dtsch. Chem. Ges.*, 1884, **17**, 1633.
  - 2) T. Sandmeyer, *Ber. Dtsch. Chem. Ges.*, 1884, **17**, 2650.
  - 3) G. Körner; A. Contardi, *Atti. Accad. Nazl. Lincei*, 1914, **23II**, 464.
  - 4) H.H. Hodgson, *Chem. Rev.*, 1947, **40**, 251.
  - 5) M.P. Doyle, *J. Org. Chem.*, 1977, **42**, 2426.
  - 6) A.P. Krapcho; S.N. Haydar, *Heterocycl. Commun.*, 1998, **4**, 291.
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## COMMENTS :

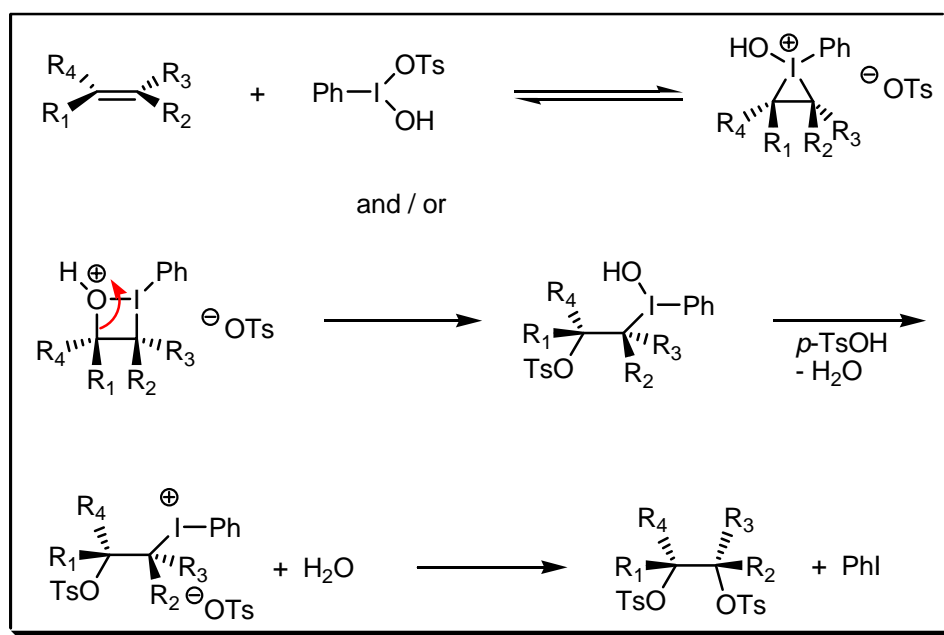
## KOSER TOSYLATION

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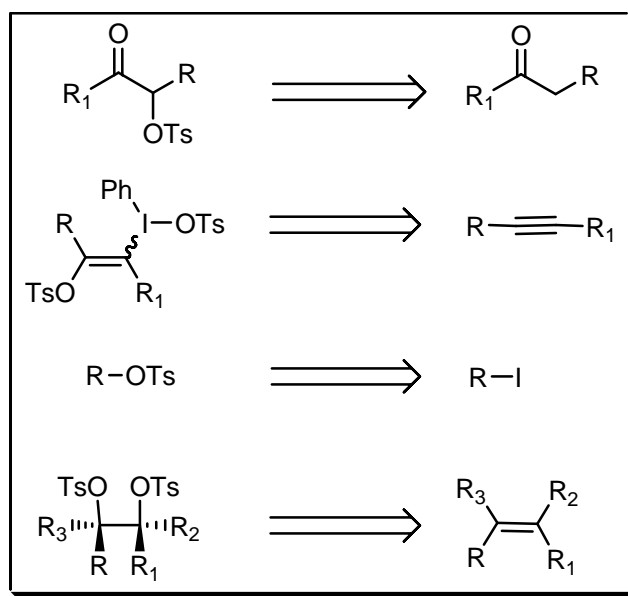
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The *vic*-bis tosylation of alkenes using [hydroxy(tosyloxy)iodo]benzene (HTIB) which is a moderate electrophile on iodine. HTIB can be used for oxytosylation, dioxytosylation, phenyliodination, solvohyperiodination and several other oxidative transformations. See also **McNelis** rearrangement.

## REFERENCES :

Org. Synth. : 70, 215

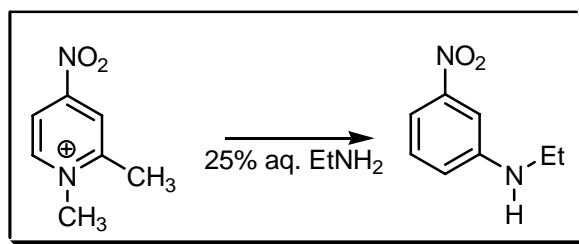
Org. Synth. Coll. Vol. : 9, 477

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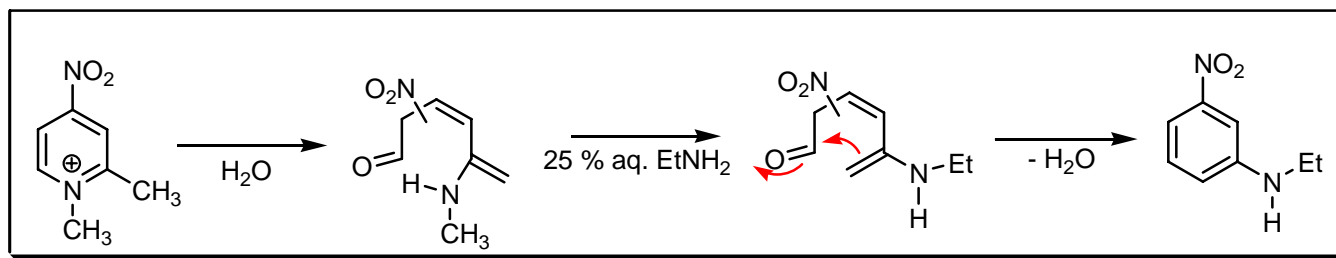
**COMMENTS :**

## KOST – SAGITULLIN REARRANGEMENT

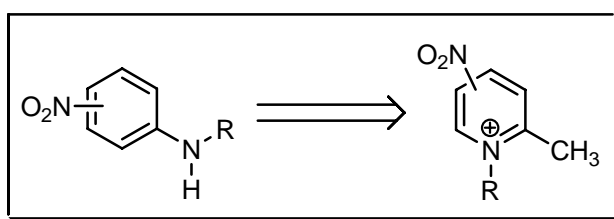
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**





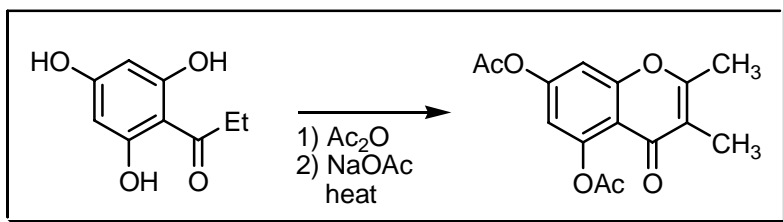
**NOTES :**

Nitropyridinium salts react with primary and secondary amines to afford alkyl or dialkyl anilines as a result of the recyclisation of the pyridine nucleus. The alkyl amine or dialkyl amine group is included in the final product at the open form stage.

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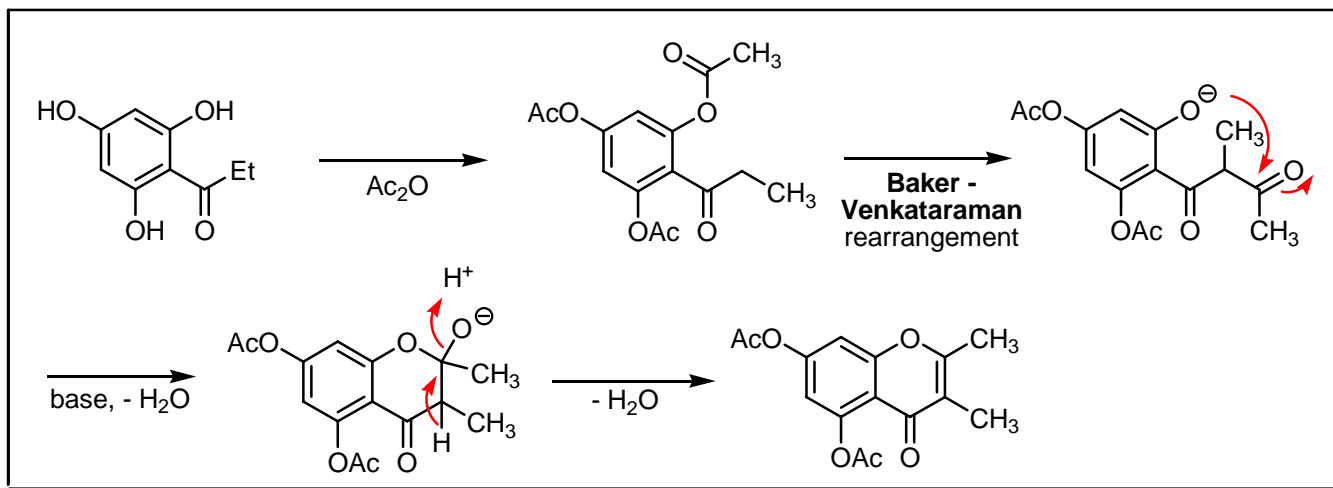
**REFERENCES :**

- 1) R.S. Sagitullin; S.P. Gromov; A.N. Kost, *Tetrahedron*, 1978, **34**, 2213.
  - 2) A.N. Kost; R.S. Sagitullin; S.P. Gromov, *Heterocycles*, 1977, **7**, 997.
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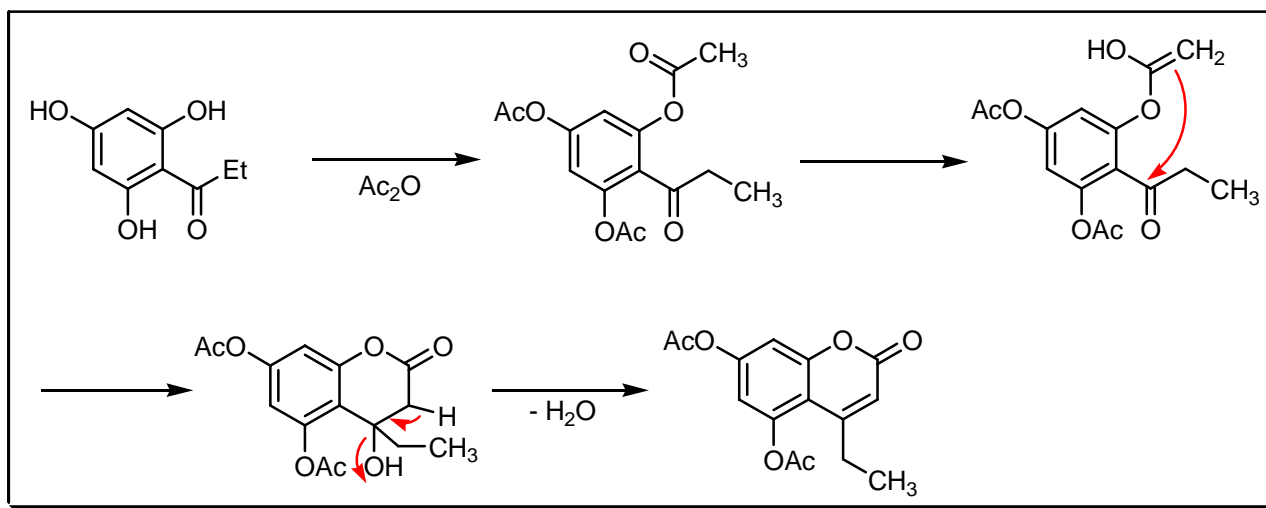
**COMMENTS :****von KOSTANECKI (ALLAN – ROBINSON) ACYLATION****EXAMPLE :**

## MECHANISM :

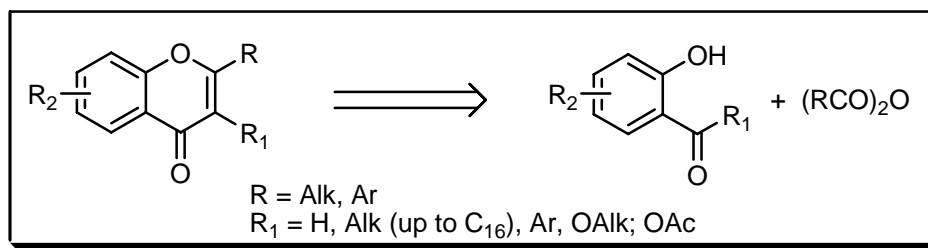
Allan – Robinson :



von Kostanecki :



## DISCONNECTION :



## NOTES :

*o*-Hydroxyketones when heated with acid anhydrides in the presence of the sodium or potassium salts of the corresponding acids form chromones, flavones or isoflavones. See also **Baker – Venkataraman** and **Bargellini** reactions.

## REFERENCES :

Org. React. : **8**, 59

Org. Synth. : **32**, 72; **46**, 28

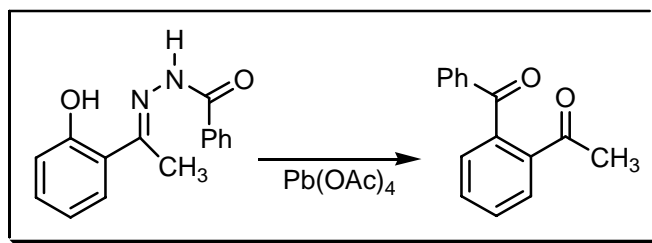
Org. Synth. Coll. Vol. : **4**, 478; **5**, 251

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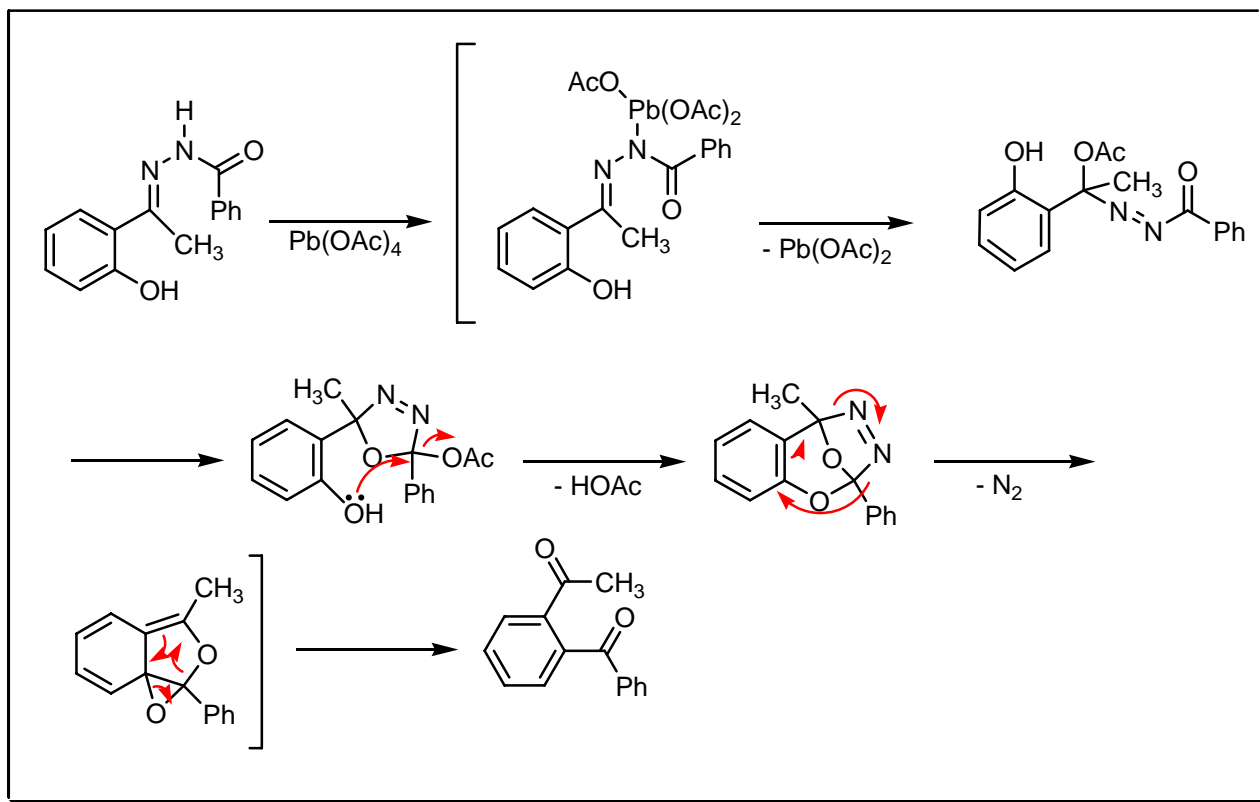
## COMMENTS :

## KOTALI – TSOUNGAS REACTION

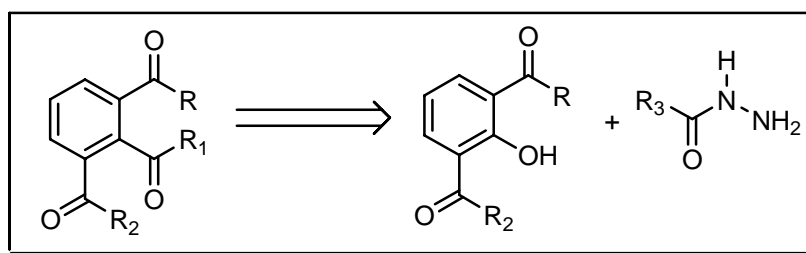
### EXAMPLE :



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

The lead tetraacetate forms an  $\alpha$ -azoacetate with a hydrazone. Cyclisation to a 1,3,4-oxadiazoline, with migration of the acetoxy group, followed by the displacement of the acetoxy by the phenolic hydroxyl affords a tricyclic intermediate. Nitrogen eliminates and an epoxy-isobenzofuran is formed. Ring-opening after rearrangement gives the product. The exact mechanism is still under investigation. Triacylbenzenes and 2-acylbenzaldehydes can also be made by this method.

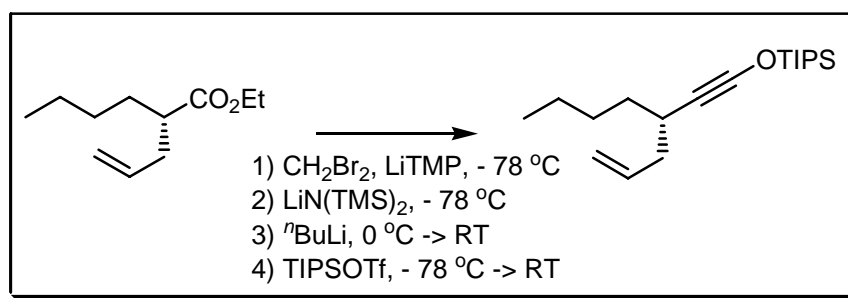
## REFERENCES :

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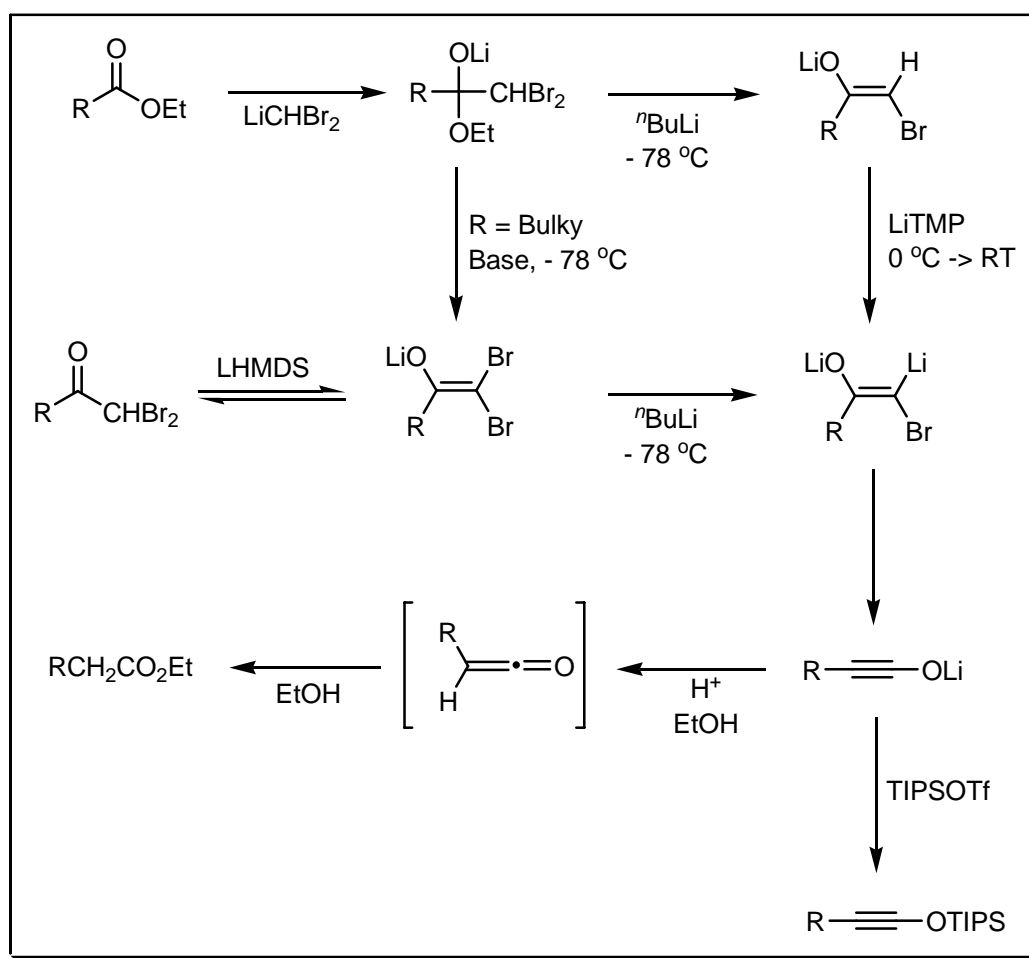
COMMENTS :

## KOWALSKI ESTER HOMOLOGATION

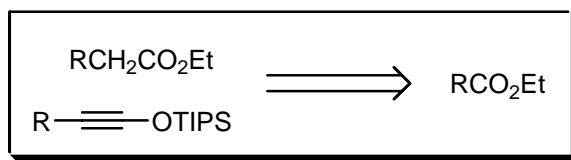
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

This reaction is a general method for the direct homologation of esters. The reaction is isoelectronic with the **Hofmann** rearrangement. See also **Arndt – Eistert**, **Buchner – Curtius – Schlotterbeck**, **Clibbens – Nierenstein**, **Colvin**, **Corey – Fuchs** and **Hofmann** rearrangement reactions.

## REFERENCES :

**Org. Synth.** : **71**, 146

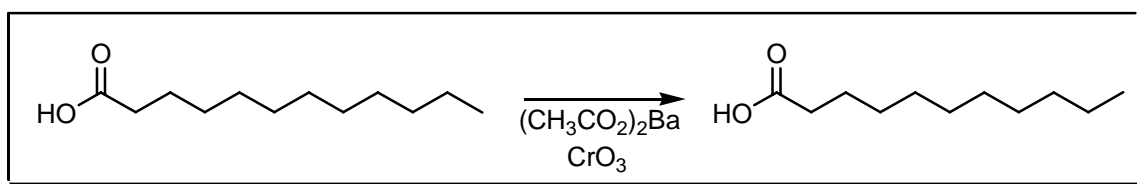
**Org. Synth. Coll. Vol.** : **9**, 426

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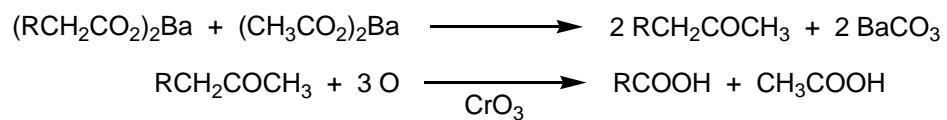
## COMMENTS :

## KRAFFT DEGRADATION

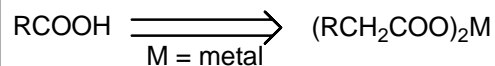
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This method for the transformation of a higher fatty acid into its next lower homologue involves the formation of the corresponding methyl ketone by dry distillation of the alkaline earth salt with the corresponding acetate. The methyl ketone is oxidised by chromic acid. See also **Barbier – Wieland – Locquin**, **Gallagher – Hollander**, **Hoehn – Mason** and **Miescher** reactions.

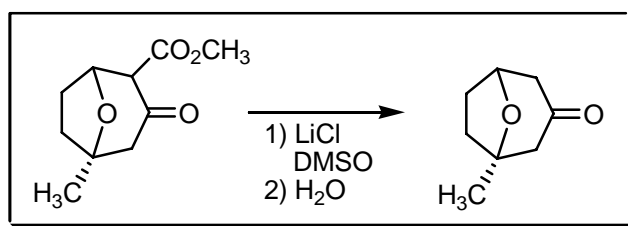
### REFERENCES :

- 1) F. Krafft, *Ber. Dtsch. Chem. Ges.*, 1879, **12**, 1664.
- 2) F. Krafft, *Ber. Dtsch. Chem. Ges.*, 1879, **12**, 1668.

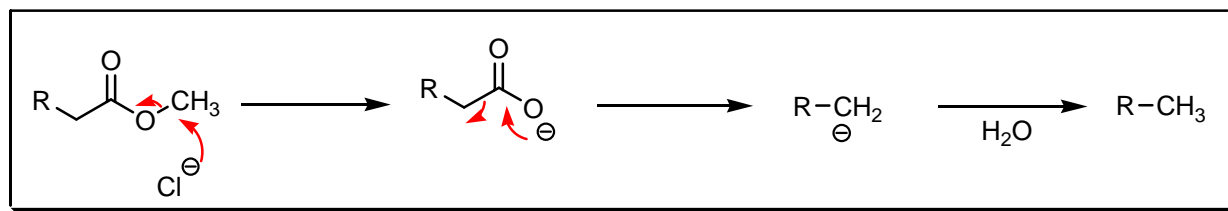
### COMMENTS :

## KRAPCHO DECARBOXYLATION

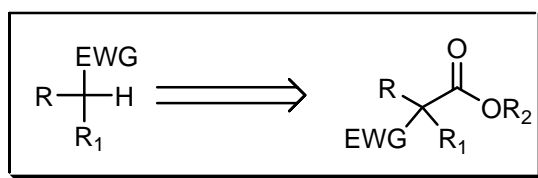
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

A mild procedure for the decarboxylation of methyl- or ethyl esters of carboxylic acids who normally bear an electron withdrawing group in the  $\alpha$ -position. A wide variety of metal salts (e.g. NaCN, LiCl, NaBr,  $\text{Na}_2\text{CO}_3 \cdot 10\text{H}_2\text{O}$ ) can be used in a dipolar aprotic solvent. See also **Kochi** decarboxylation.

### REFERENCES :

March : 629

Smith – March : 808

Smith 2<sup>nd</sup> : 143

Org. React. : 24, 187

Org. Synth. : 75, 195

Org. Synth. Coll. Vol. : 10, 2328

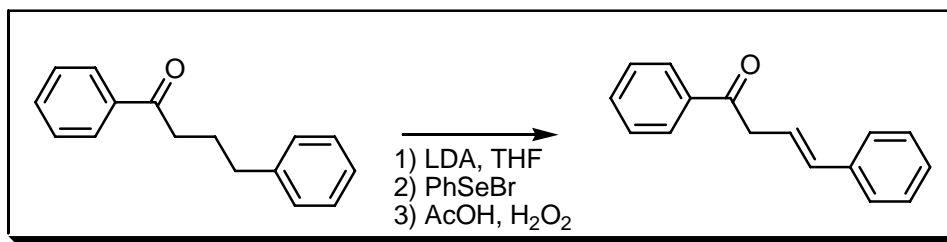
- 1) A.P. Krapcho; A.J. Lovey, *Tetrahedron Lett.*, 1973, **14**, 957.
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### COMMENTS :

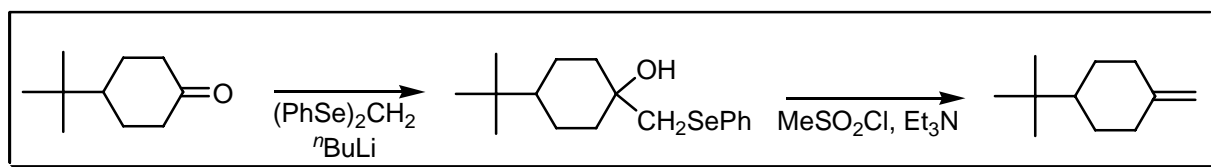


## KRIEF – REICH – CHOW OLEFINATION

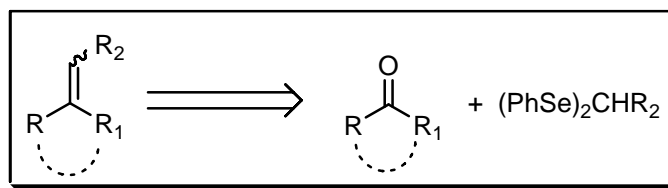
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The synthesis of olefins by stereospecific reductive elimination of  $\beta$ -hydroxyalkyl selenides using MeSO<sub>2</sub>Cl, HClO<sub>4</sub> or P<sub>2</sub>I<sub>4</sub>. See also **Corey – Kwiatkowski**, **Eastwood**, **Horner – Wadsworth – Emmons**, **Julia – Paris – Kocienski – Lythgoe**, **McMurry**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Nysted**, **Paquette**, **Petasis** reaction, **Peterson**, **Ramberg – Bäcklund**, **Still – Gennari**, **Takeda**, **Tebbe** and **Wittig olefination** reactions.

### REFERENCES :

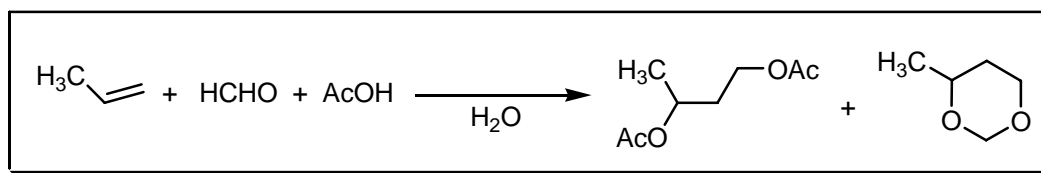
Org. React. : 44, 1

- 1) W. Dumont; P. Bayet; A. Krief, *Angew. Chem., Int. Ed. Engl.*, 1974, **13**, 804.
- 2) J.N. Denis; W. Dumont; A. Krief, *Tetrahedron Lett.*, 1976, **17**, 453.
- 3) H.J. Reich; F. Chow; S.K. Shah, *J. Am. Chem. Soc.*, 1979, **101**, 6638.
- 4) T.K. Sarkar; S.K. Ghosh, *Tetrahedron Lett.*, 1987, **28**, 2061.
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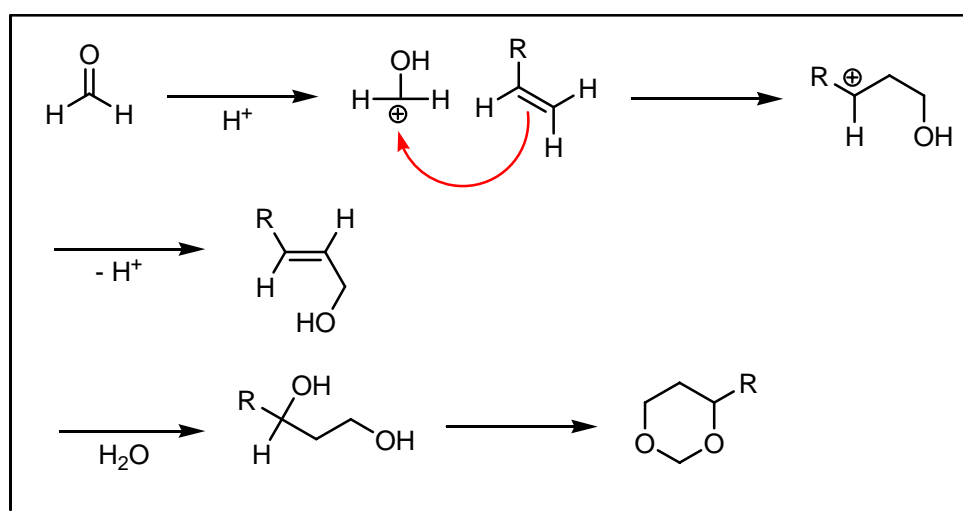
COMMENTS :

## KRIEWITZ – PRINS ADDITION

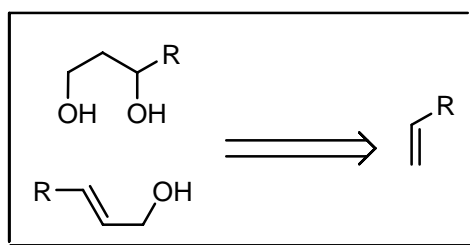
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

Aliphatic aldehydes, especially formaldehyde, condense with olefins in the presence of dilute mineral acids to give 1,3-glycols and *m*-dioxanes. A little explored variation has been reported by **Nussbaumer** and **Fráter**. There are also aza-**Prins** reactions. See also **Ritter** reaction.

## REFERENCES :

March : 820, 967

Smith – March : 1241

Smith : 1310

Smith 2<sup>nd</sup> : 1079

Houben – Weyl : 4/2, 45; 6/3, 265; E3, 641; E19c, 324, 336

Org. Synth. : 33, 72

Org. Synth. Coll. Vol. : 4, 786

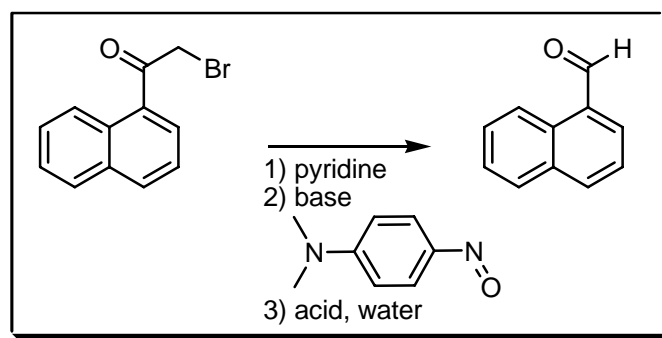
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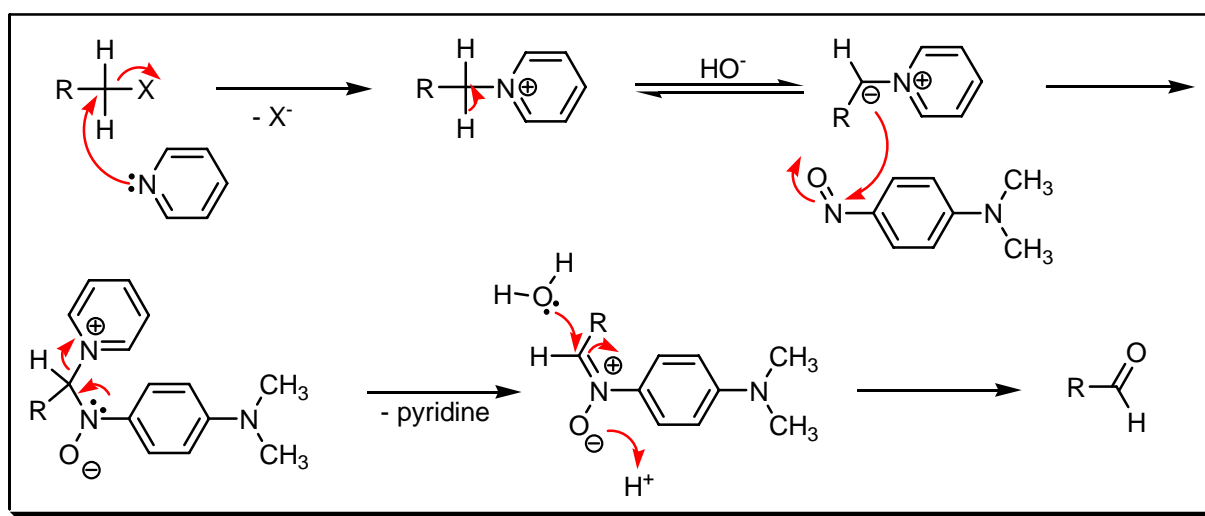
## COMMENTS :

## KRÖHNKE – ORTOLEVA – KING ALDEHYDE SYNTHESIS

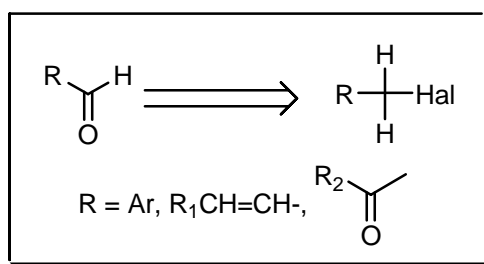
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Halogen compounds of the general formulae  $ArCH_2Hal$ ,  $RCH=CHCH_2Hal$  and  $RCOCH_2Hal$  are converted into quaternary pyridinium compounds which react with *p*-nitrosodimethylaniline to give nitrones. The latter on acid hydrolysis yield aldehydes. In the **Ortoleva – King** variant pyridine and iodine are used. See also **Duff – Bills**, **Kornblum**, **Sommelet** and **Utzinger** reactions.

## REFERENCES :

March : 1194

Smith – March : 1536

Houben – Weyl : **10/4**, 375; **E3**, 231, 402; **E6b**, 387; **E7a**, 530; **E7b**, 321; **E8a**, 414; **E14b**, 1484; **E15**, 938

Org. React. : **8**, 203

Org. Synth. : **46**, 81

Org. Synth. Coll. Vol. : **5**, 825

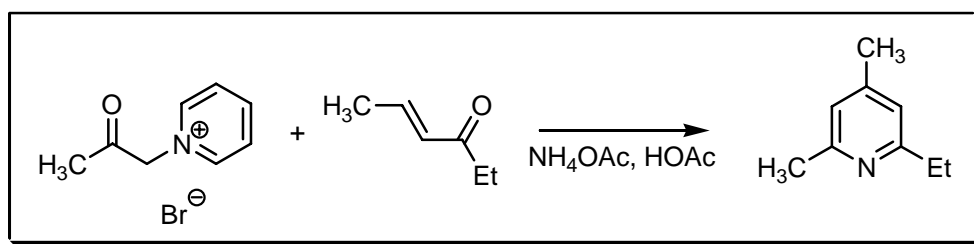
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## COMMENTS :

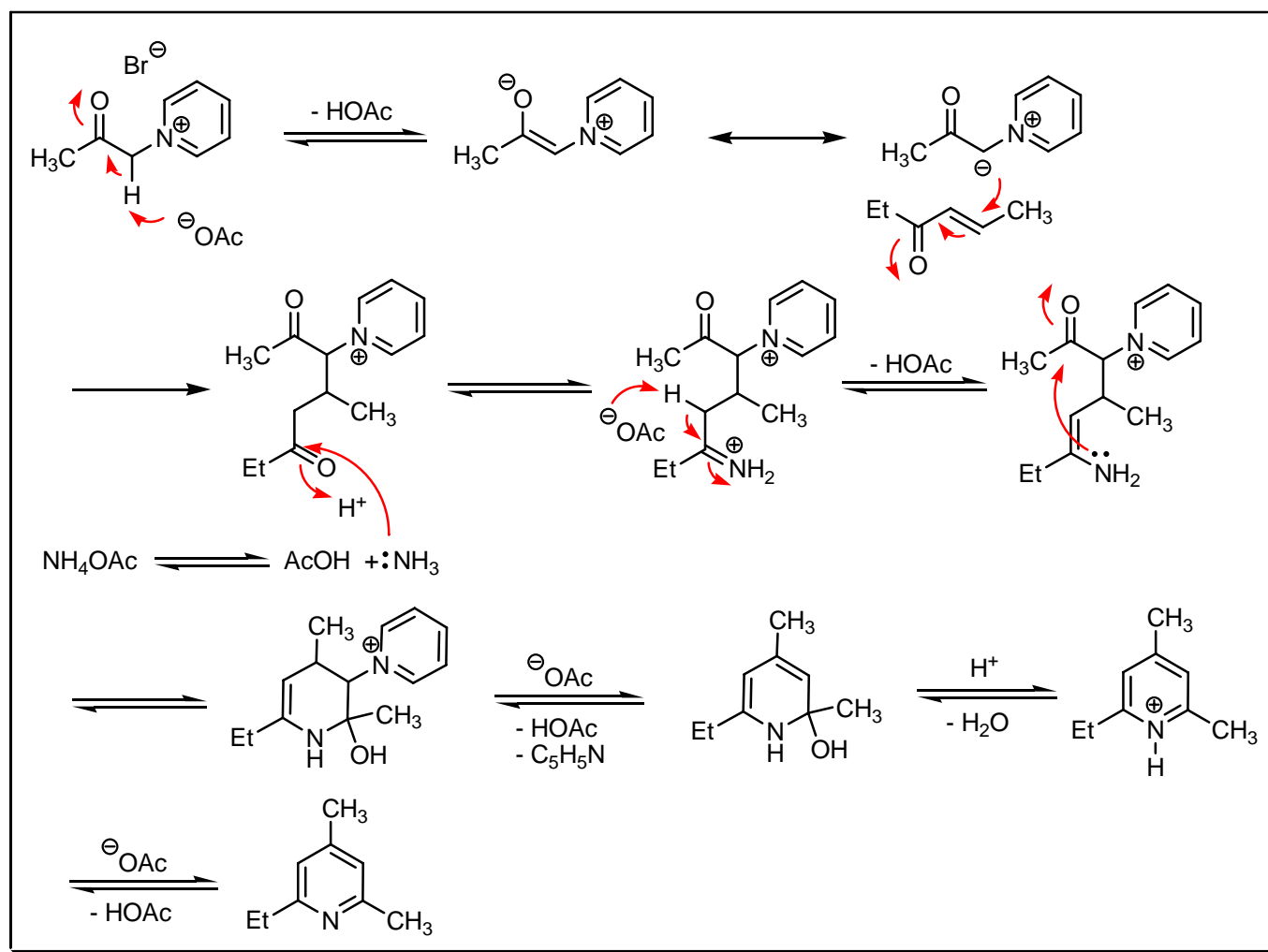
## KRÖHNKE PYRIDINE SYNTHESIS

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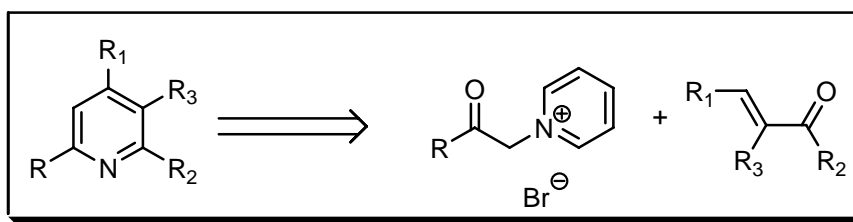
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

$\alpha$ -Pyridinium methyl ketones salts react with  $\alpha,\beta$ -unsaturated ketones to afford pyridines.

## REFERENCES :

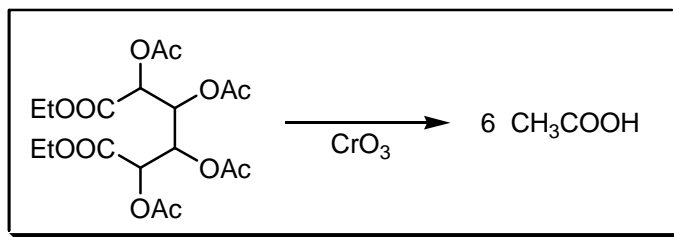
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- 2) W. Zecher; F. Kröhnke, *Chem. Ber.*, 1961, **94**, 698.
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- 4) T.R. Kelly; Y.-J. Lee; R.J. Mears, *J. Org. Chem.*, 1997, **62**, 2774.

**COMMENTS :**

**KUHN – ROTH OXIDATION**

---

**EXAMPLE :**



**NOTES :**

The substance is oxidised with sulfuric acid – chromic acid mixture under conditions such that C-methyl groups forms acetic acid which is distilled off and titrated. The method has rather limited use nowadays.

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**REFERENCES :**

**Smith :** 315

**Smith 2<sup>nd</sup> :** 276

**Houben – Weyl :** 2, 274

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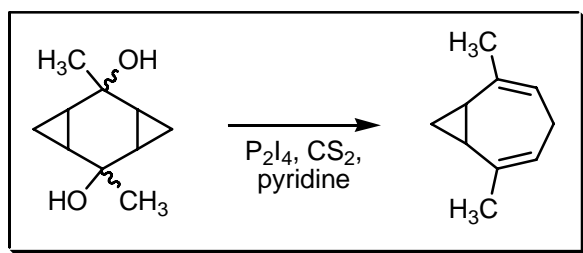
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- 

**COMMENTS :**

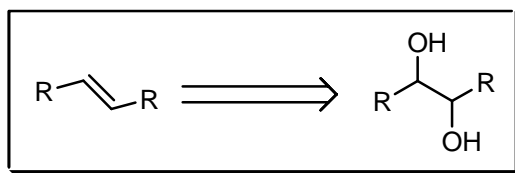
## KUHN – WINTERSTEIN REACTION

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### EXAMPLE :



### DISCONNECTION :



### NOTES :

The *trans* olefin formation (**Grob**-type fragmentation) from glycols using  $P_2I_4$ . This is a useful reaction for the preparation of polyenes. See also **Corey – Winter** reaction.

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### REFERENCES :

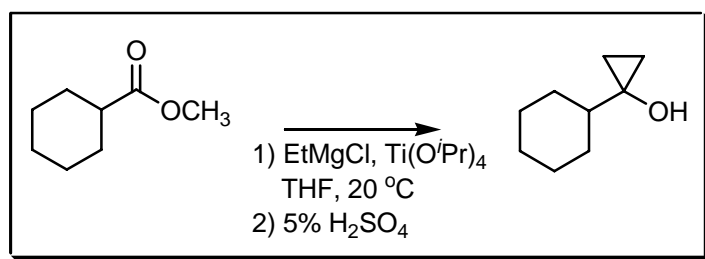
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### COMMENTS :

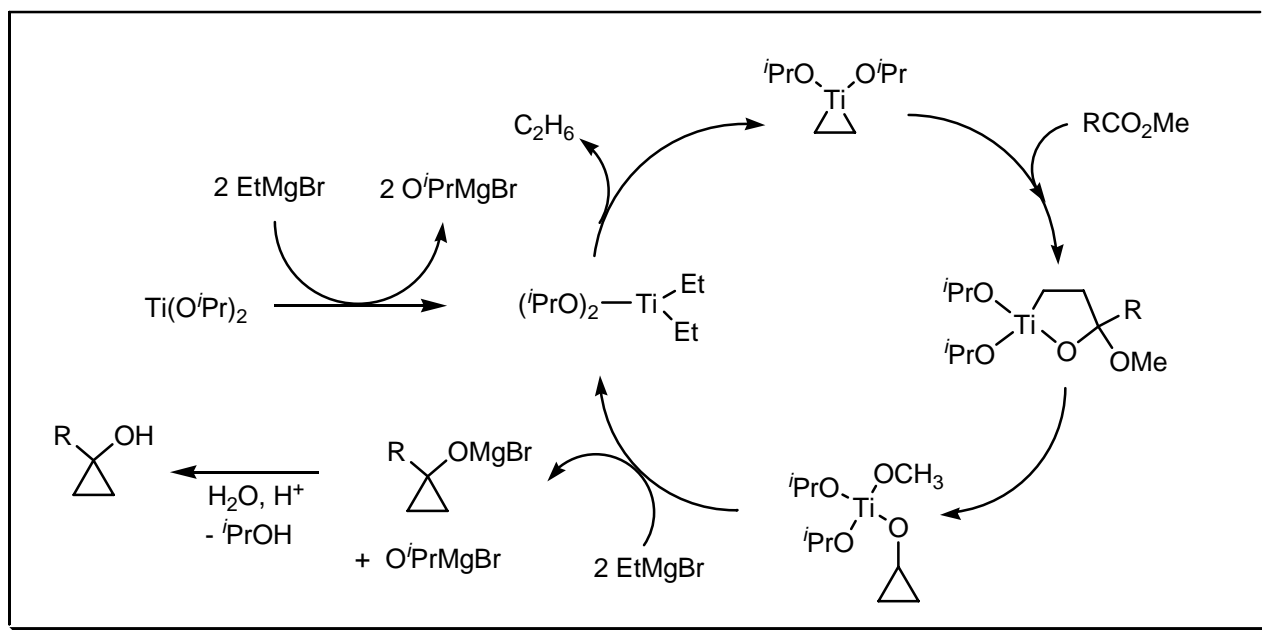


## KULINKOVICH REACTION

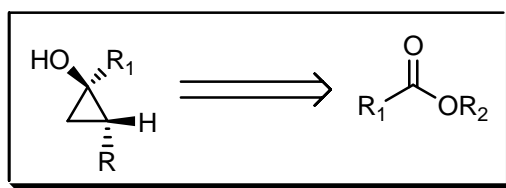
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

An efficient way of preparing hydroxycyclopropanes by treatment of carboxylic esters with a suitable **Grignard** reagent in the presence of titanium tetraisopropoxide. The proposed key intermediate is the titanacyclopropane. This intermediate is formed by 2 equivalents of **Grignard** reagent and titanium tetraisopropoxide. The thermally unstable intermediate undergoes β-hydride elimination and reductive elimination to give ethane and the titanacyclopropane. This reaction can be catalytic or non-catalytic. The reaction has been modified by **Corey et al.**

## REFERENCES :

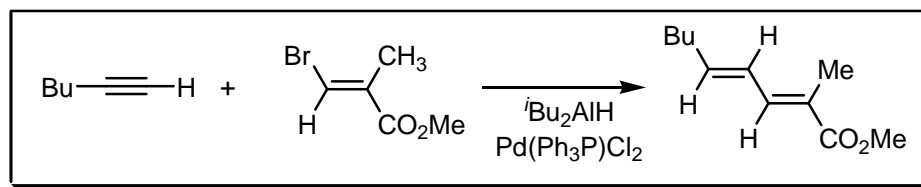
Org. Synth. : 80, 111

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## COMMENTS :

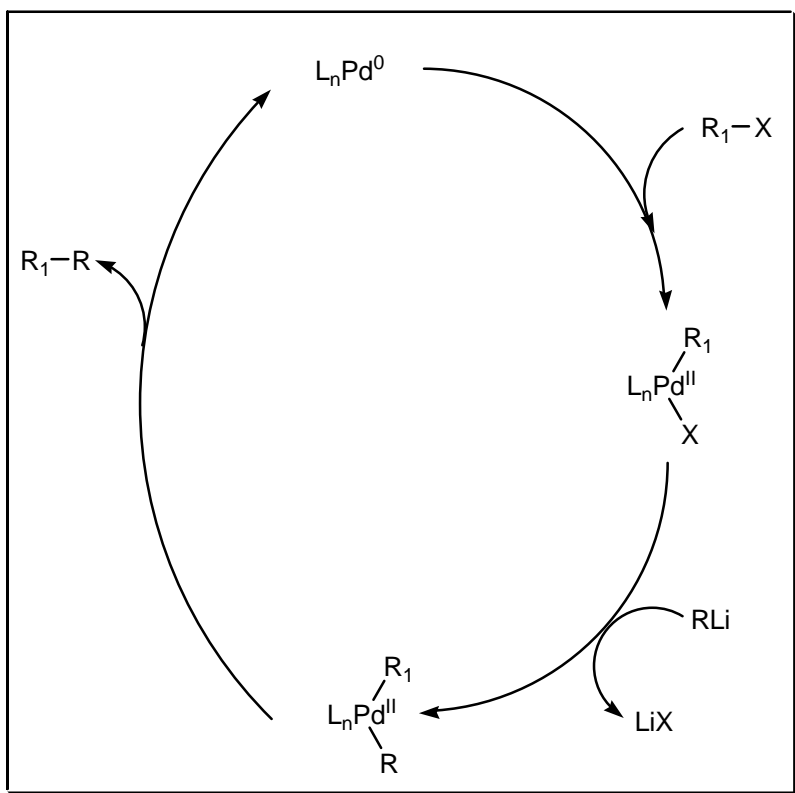
## KUMADA – TAMAO – CORRIU CROSS-COUPLING

### EXAMPLE :

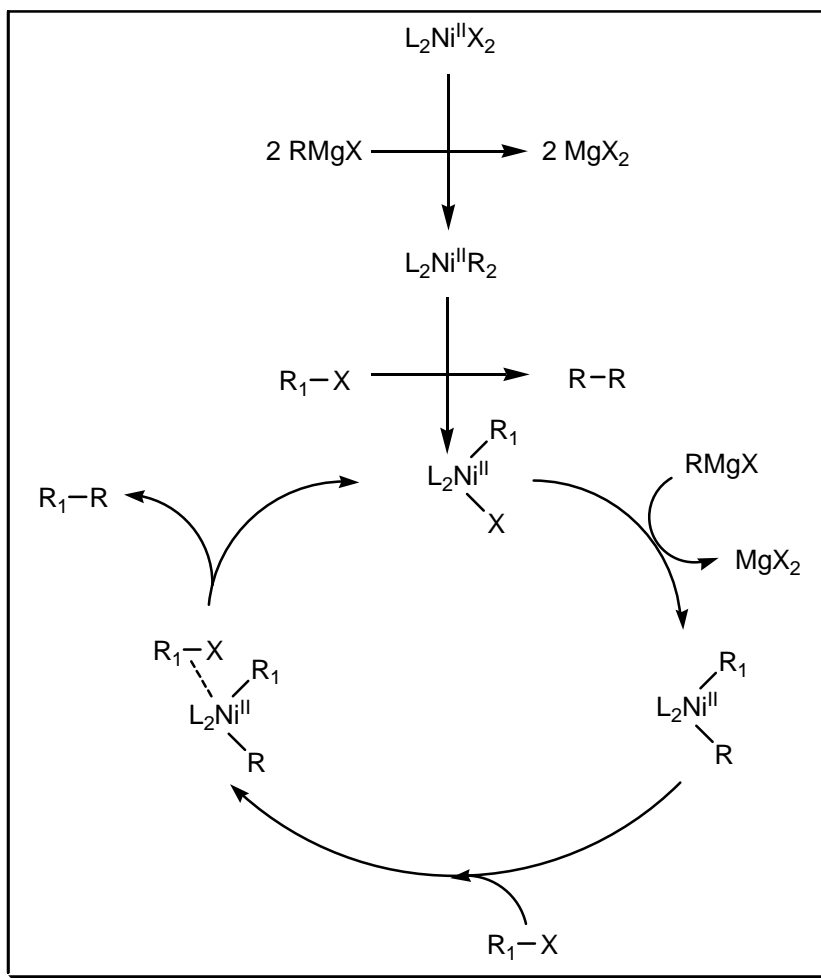


**MECHANISM :**

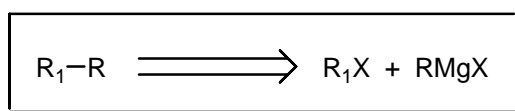
**Pd-catalysed :**



### Nickel-catalysed :



### DISCONNECTION :



### NOTES :

Nickel and palladium complexes catalyse the reaction of organometallic reagents (Al, Mg, Zn, Zr, Li) with alkenyl or aryl halides to afford cross-coupled products. In the asymmetric version mostly secondary alkyl **Grignard** reagents are used. Good results are obtained using P,N or N,S-type of ligands (*tert*-Leuphos, valphos or homomethpos). Much less recognised is the work done by **Felkin** in this area. **Negishi** introduced the use of zinc, which increased the scope of this reaction to cross coupling of acyl chlorides, thioesters and **Reformatsky** reagents. See also **Murahashi** cross-coupling and **Negishi** reaction.

### REFERENCES :

Smith – March : 537

Org. Synth. : 58, 127

Org. Synth. Coll. Vol. : 6, 407

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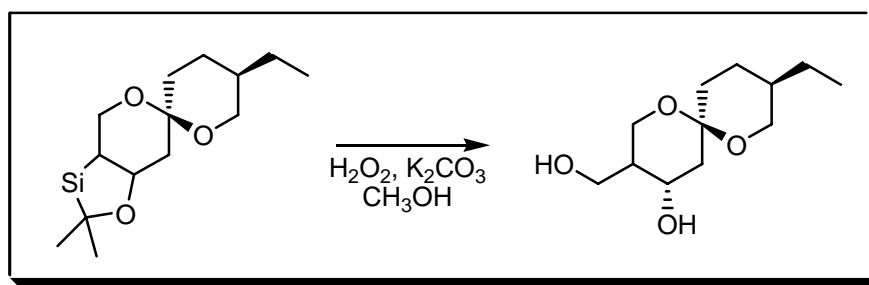
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**COMMENTS :**

## KUMADA – TAMAO – FLEMING STEREOSELECTIVE HYDROXYLATION

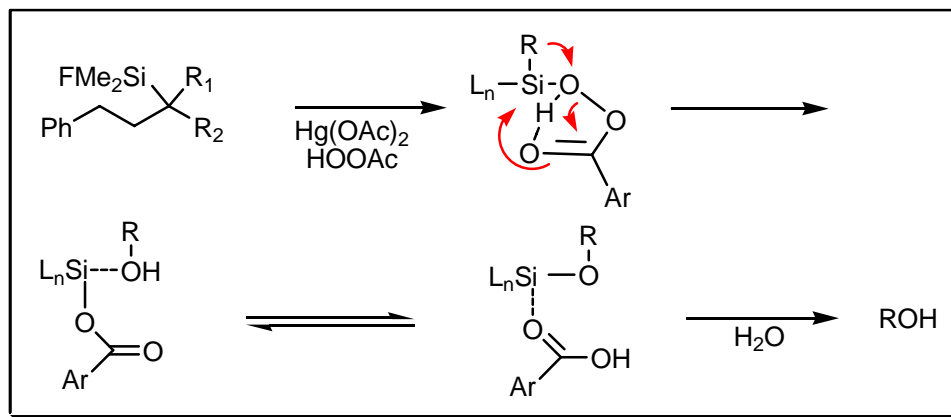
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**EXAMPLE :**

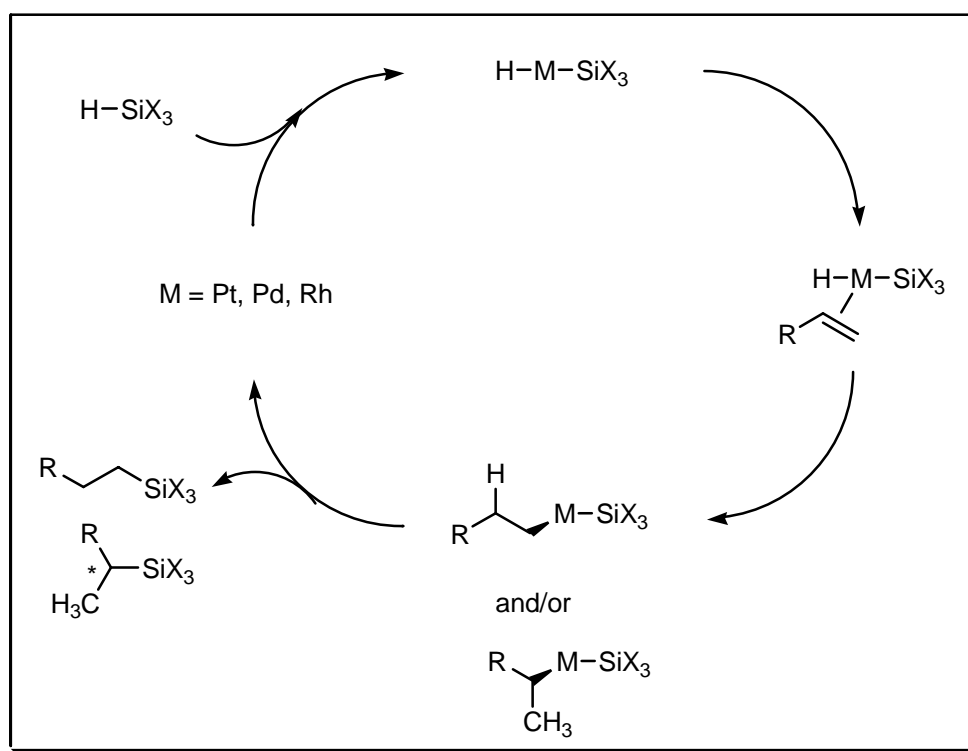


## MECHANISM :

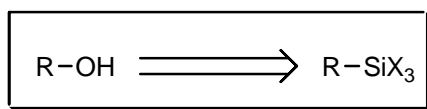
### Fleming :



### Catalytic hydrosilylation :



### DISCONNECTION :



### NOTES :

This is the oxidative cleavage of the silicon – carbon bond. The **Kumada – Tamao** method uses hydrogen peroxide potassium hydrogenfluoride and requires at least one electron-withdrawing group on the silicon atom. While the **Fleming** method is a two-step method using mercury acetate and peroxyacetic acid. There are 12 main silyl groups available for oxidation in the literature. See also **Stork – Nishiyama** radical cyclisation.

## REFERENCES :

Smith 2<sup>nd</sup> : 277, 968

Org. Synth. : 69, 96; 73, 94

Org. Synth. Coll. Vol. : 8, 315; 9, 539

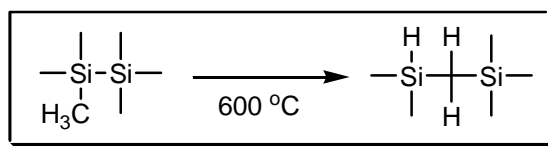
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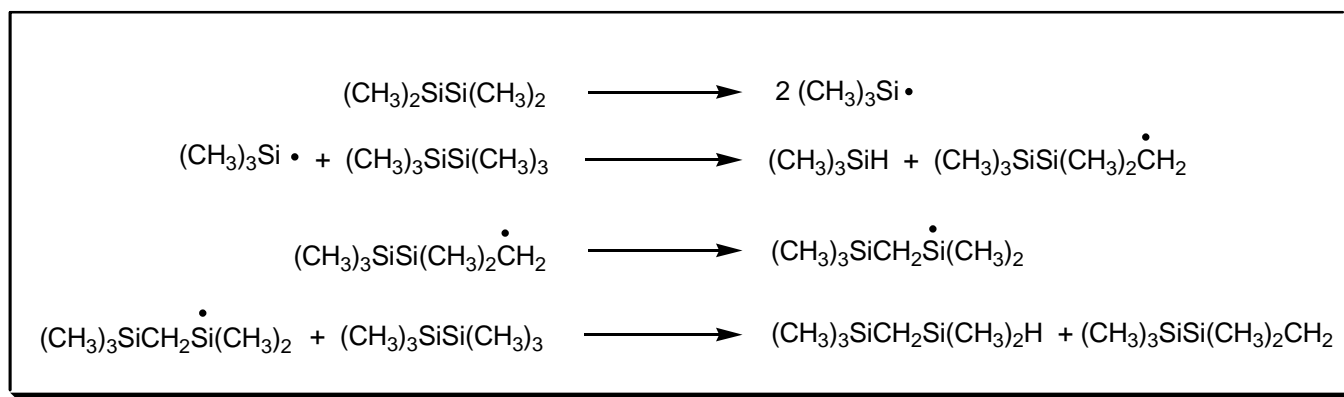
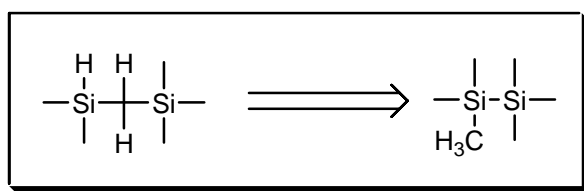
## COMMENTS :

## KUMADA REARRANGEMENT

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### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

This is the carbosilane formation under destruction of silicon-silicon bonds. This occurs at temperature above 325 °C.

**REFERENCES :**

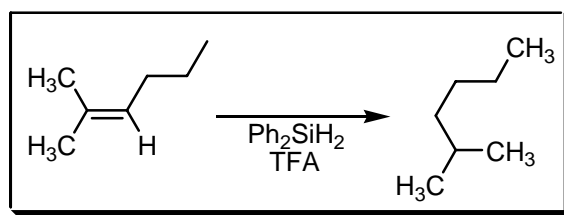
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**COMMENTS :**

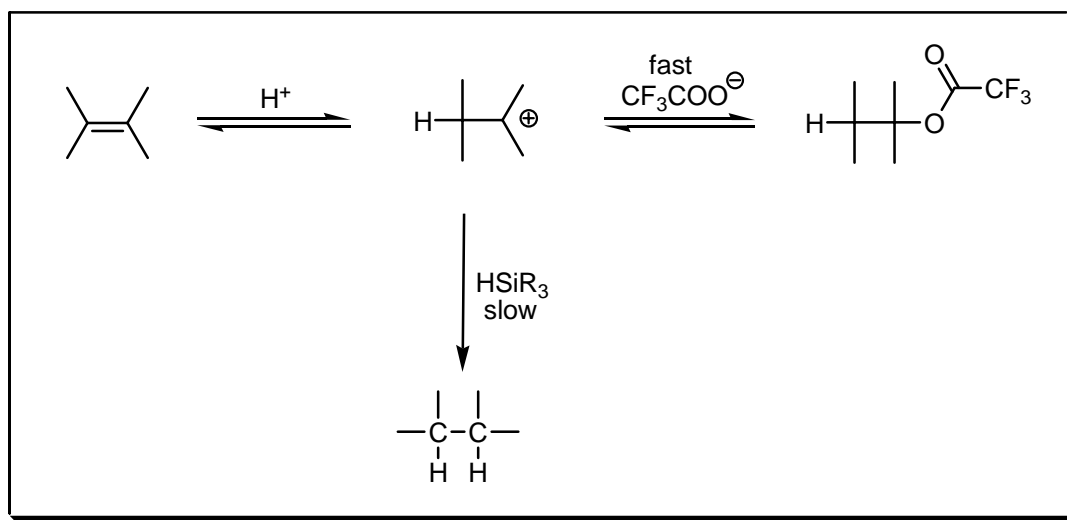


## KURSANOV – PARNES IONIC HYDROGENATION

### EXAMPLE :



### MECHANISM :



### NOTES :

A non-catalytic hydrogenation of  $\text{C}=\text{C}$ ,  $\text{C}=\text{O}$ ,  $\text{C}=\text{N}$  bonds and hydrogenolysis of  $\text{C}-\text{OH}$ ,  $\text{C}-\text{hal}$ , under the action of a proton donor and a hydride ion donor, normally trifluoroacetic acid and organo silanes. Under these conditions  $\text{COOH}$ ,  $\text{COOR}$ ,  $\text{CONR}_2$ ,  $\text{CN}$ ,  $\text{NO}_2$ ,  $\text{SO}_3\text{R}$ , aromatic rings do not hydrogenate. The hydrogenation of tetra-substituted alkenes often proceeds stereoselectively.

### REFERENCES :

Org. Synth. : 60, 108

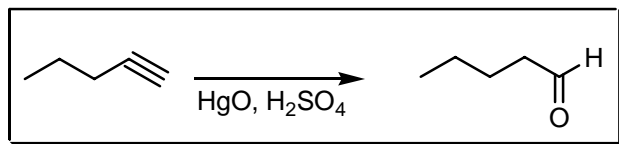
Org. Synth. Coll. Vol. : 7, 393

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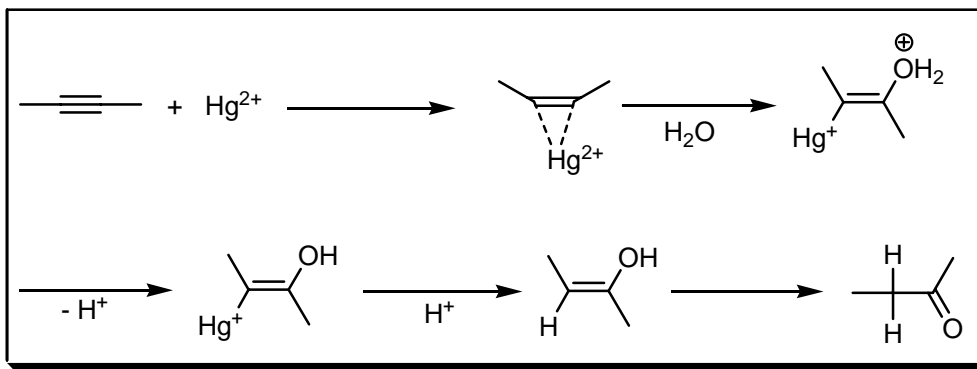
COMMENTS :

## KUTSCHEROFF – DENIGÈS HYDRATION

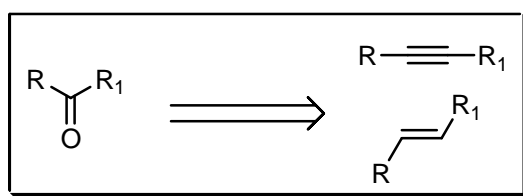
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The addition of water to a triple bond (**Kutscheroff**) or to a double bond (**Denigès**) under mercury salt catalysis. See also **Nieuwland** and **Reppe** carbonylation reaction.

REFERENCES :

March : 762

Smith – March : 995

Houben – Weyl : E3, 243

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- 

**COMMENTS :**



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**L**

LADENBURG – VYSHNEGRADSKIĬ HYDROGENATION · 1061  
LADENBURG CONIINE SYNTHESIS · 1062  
LADENBURG REARRANGEMENT · 1063  
LADENBURG RING-CLOSURE · 1064  
LANDAUER – RYDON SYNTHESIS · 1065  
LANDER REARRANGEMENT · 1066  
LAPWORTH CONDENSATION (BENZIN CONDENSATION) ·  
1067  
LAROCK FLUOREN-9-ONE-2 SYNTHESIS · 1071  
LAROCK FLUORENE SYNTHESIS · 1069  
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LEY OXIDATION · 1099  
LIEBEN IODOFORM REACTION · 1100  
LIEBESKIND – SROGL REACTION · 1102  
LIEBIG BENZYLIC ACID REARRANGEMENT · 1103  
LIEPA COUPLING · 1105  
LIMAYE SYNTHESIS · 1106  
LINDSEY PORPHYRIN SYNTHESIS · 1107  
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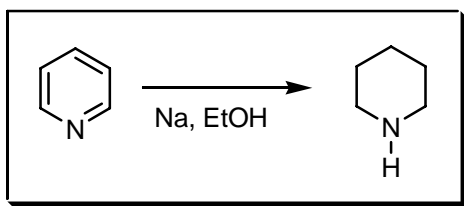
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**S**

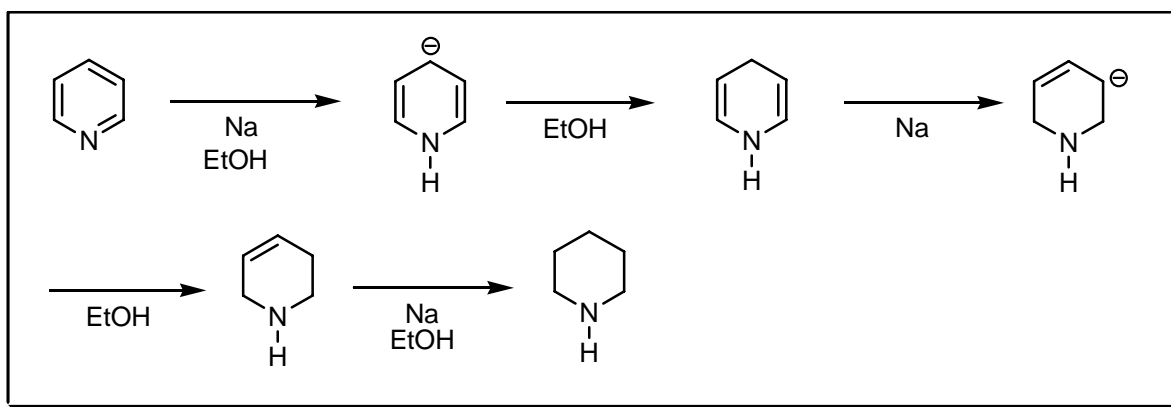
SCHOELLER MODIFICATION · 1087

## LADENBURG – VYSHNEGRADSKIĀ HYDROGENATION

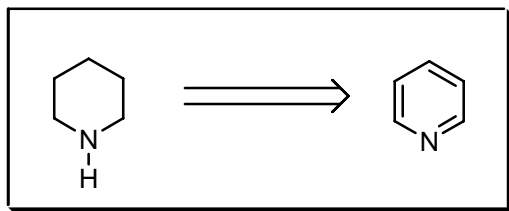
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The classic example is the use of sodium in ethanol for the hydrogenation of pyridine to piperidine. Other primary alcohols can be used as solvent. See also **Birch** and **Mendius** reactions.

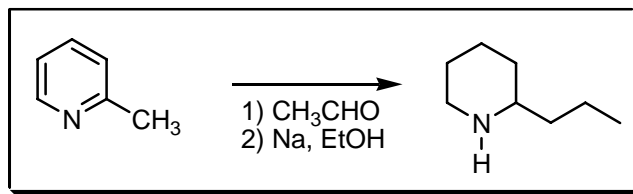
### REFERENCES :

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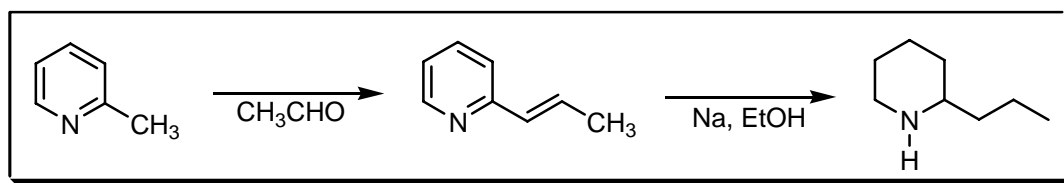
COMMENTS :

## LADENBURG CONIINE SYNTHESIS

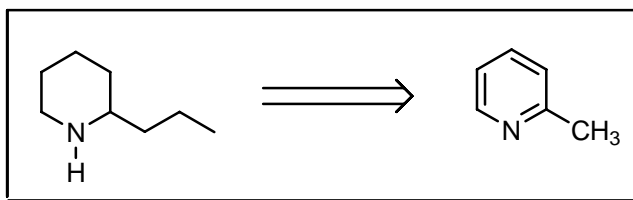
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

$\alpha$ -Picoline is condensed with acetaldehyde and the resulting 2-propenylpyridine is reduced with sodium in ethanol. See also **Ladenburg – Vysnegradskii** reaction.

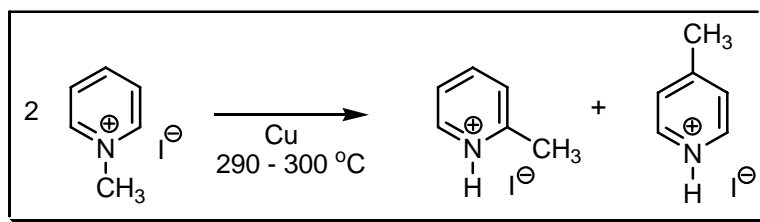
REFERENCES :

- 1) A. Ladenburg, *Ber. Dtsch. Chem. Ges.*, 1886, **19**, 439
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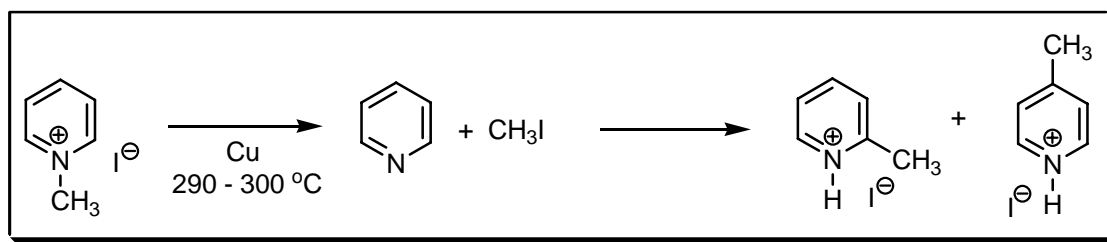
COMMENTS :

## LADENBURG REARRANGEMENT

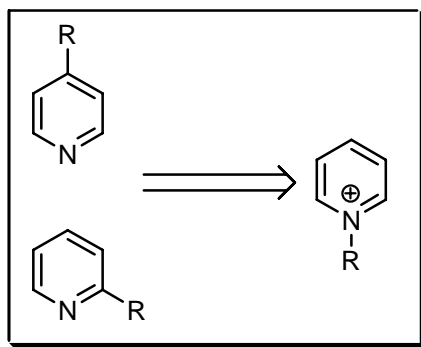
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

*N*-alkyl or benzyl pyridinium halides rearrange on heating to give a mixture of  $\alpha$ - and  $\gamma$ -alkylpyridinium halides. See also **Hofmann – Martius – Reilly**, **Reissert** and **Sommelet – Hauser** reactions.



## REFERENCES :

Houben – Weyl : E7b, 633

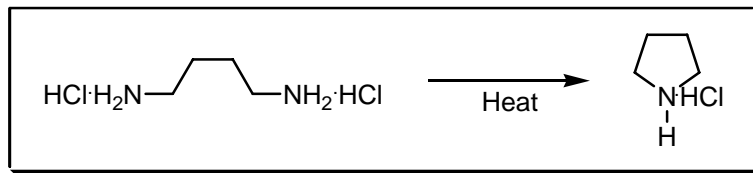
Org. React. : 7, 99

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## COMMENTS :

## LADENBURG RING-CLOSURE

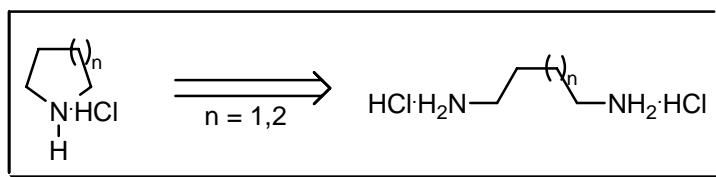
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

Dry distillation of the hydrochlorides of tetramethylene-1,4-diamine and pentane-1,5-diamine leads to ring-closure affording pyrrolidines and piperidines. See also **Hofmann – Löffler – Freytag** reaction.

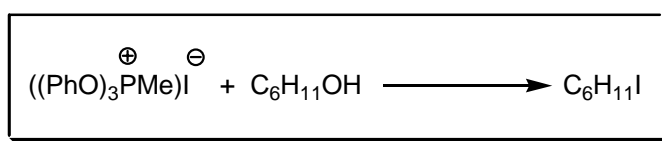
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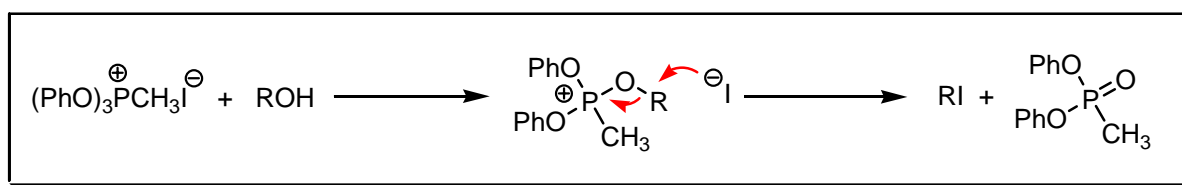
## COMMENTS :

## LANDAUER – RYDON SYNTHESIS

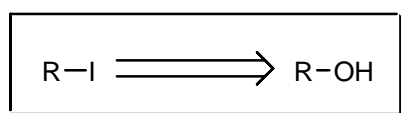
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

Triphenylphosphite methiodide and derivatives react with alcohols to afford the iodo derivative. See also **Appel**, **Blum**, **Darzens** method and **Miller** synthesis reactions.

## REFERENCES :

Org. Synth. : **31**, 33; **51**, 44

Org. Synth. Coll. Vol. : **4**, 325; **6**, 830

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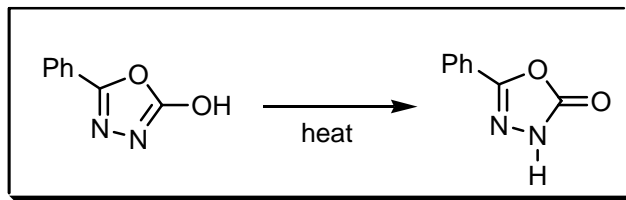
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## COMMENTS :

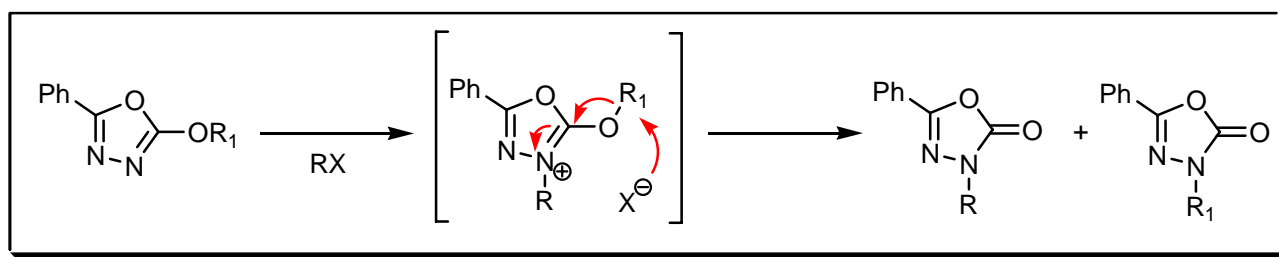
## LANDER REARRANGEMENT

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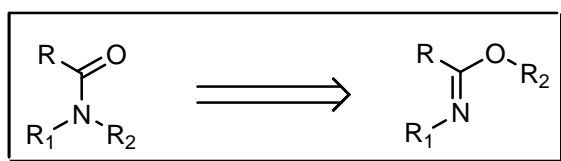
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



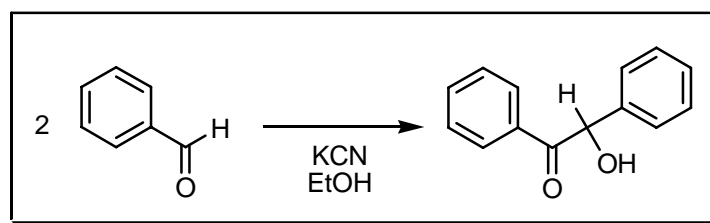
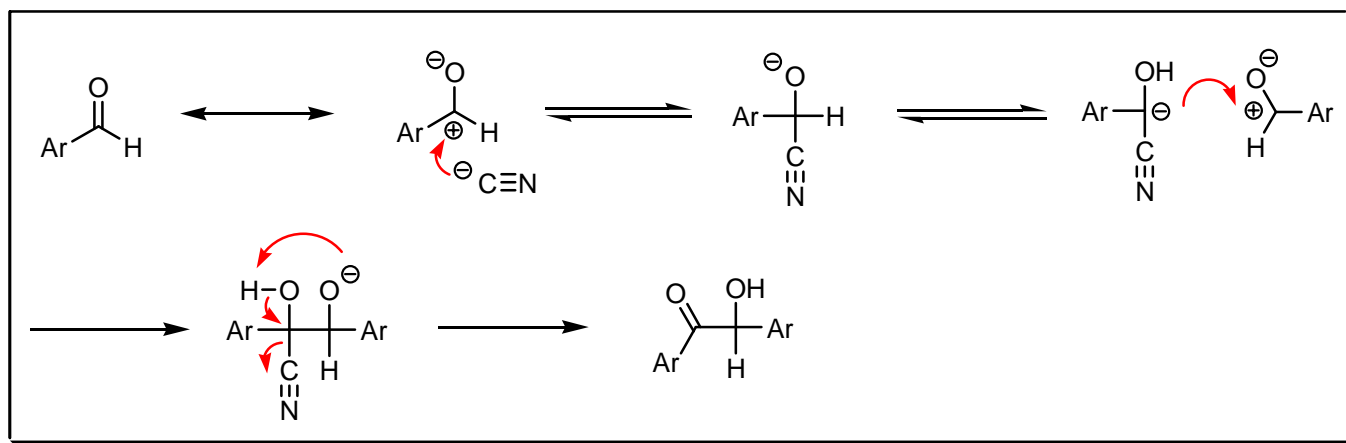
**NOTES :**

The thermal *intermolecular* rearrangement of aliphatic imino-ethers to afford substituted amides.

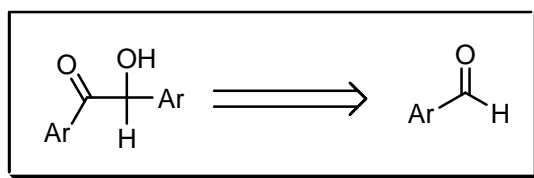
**REFERENCES :**

Houben – Weyl : E8c, 631

- 1) G.D. Lander, *J. Chem. Soc.*, 1903, **83**, 406.
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**COMMENTS :****LAPWORTH CONDENSATION (BENZOIN CONDENSATION)****EXAMPLE :****MECHANISM :**

## DISCONNECTION :



## NOTES :

The reversible condensation of two aromatic aldehyde molecules or one aromatic aldehyde and a glyoxal to afford an  $\alpha$ -hydroxy ketone. The reaction is catalysed by the cyanide ion (*via* cyanohydrins). Deactivating groups on the aromatic ring can inhibit this reaction. There is a thiazolium-ion catalysed reaction known.

## REFERENCES :

**March** : 969

**Smith – March** : 1243

**Org. React.** : **4**, 269

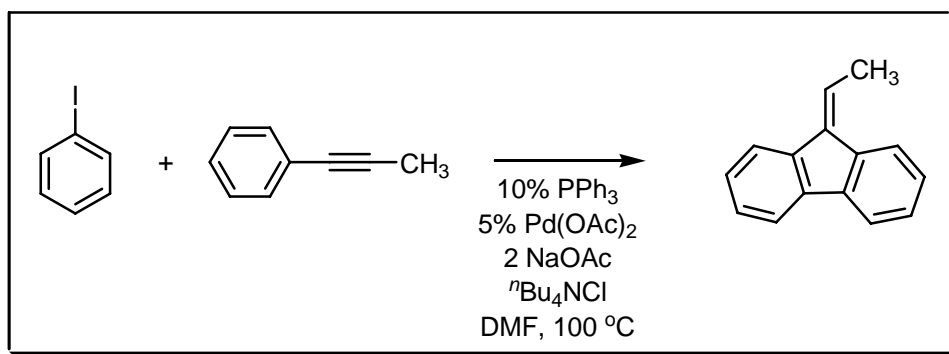
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## COMMENTS :

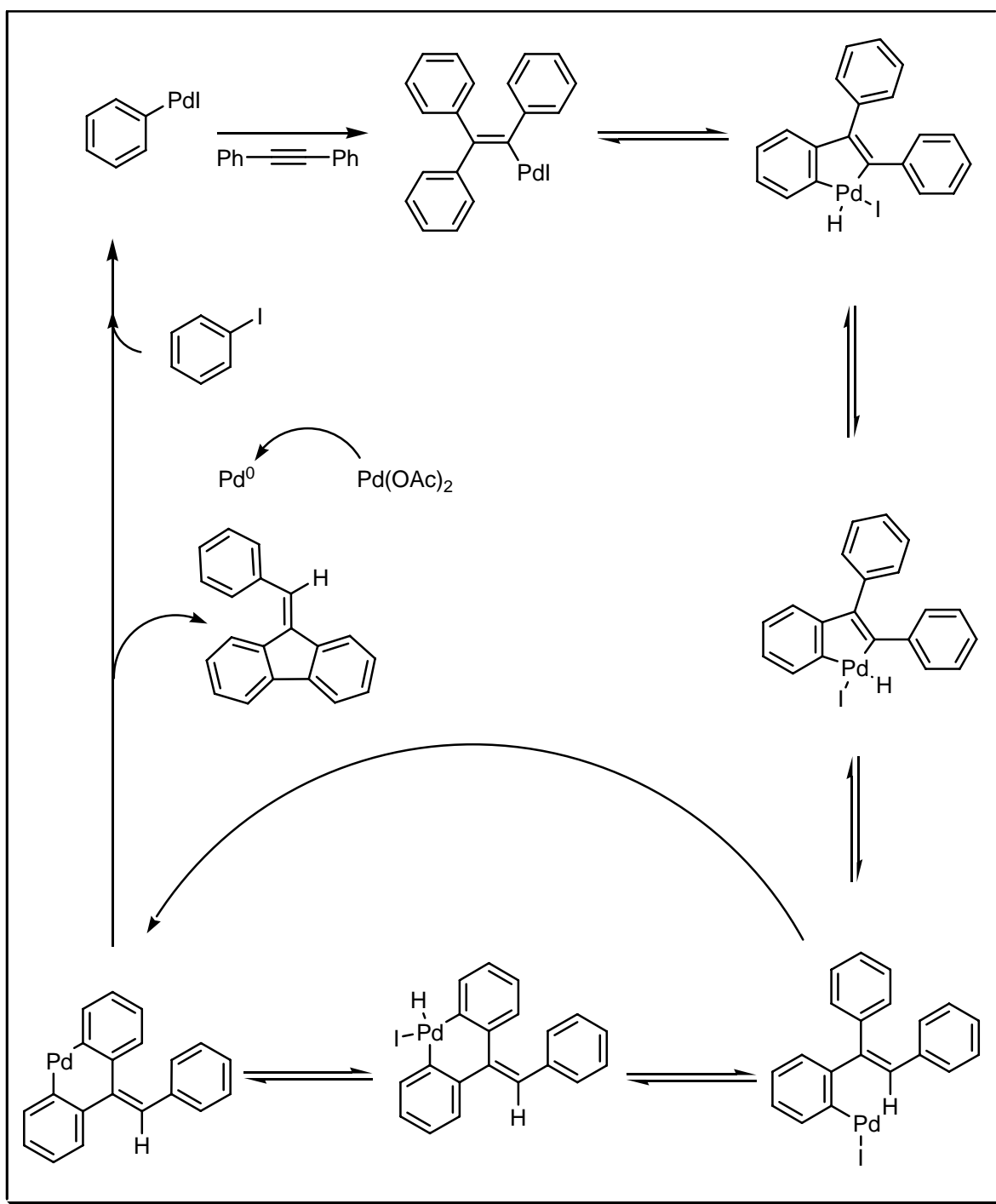
## LAROCK FLUORENE SYNTHESIS

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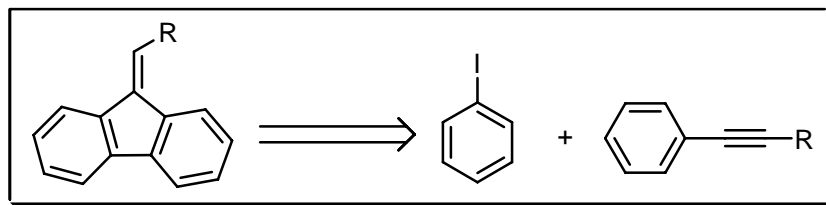
EXAMPLE :



**MECHANISM :**



**DISCONNECTION :**



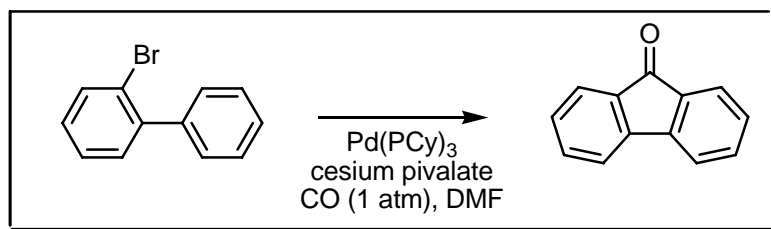
**NOTES :**

In the presence of a palladium catalyst and NaOAc, aryl iodides react with 1-aryl-1-alkynes to afford 9-alkylidene-9*H*-fluorenes. This process appears to involve (1) oxidative addition of the aryl iodide to Pd(0), (2) alkyne insertion, (3) rearrangement of the resulting vinylic palladium intermediate to an arylpalladium species, and (4) aryl-aryl coupling with simultaneous regeneration of the Pd(0) catalyst. See also **Graebe – Ullmann**, **Mascarelli** and **Ullmann** reactions.

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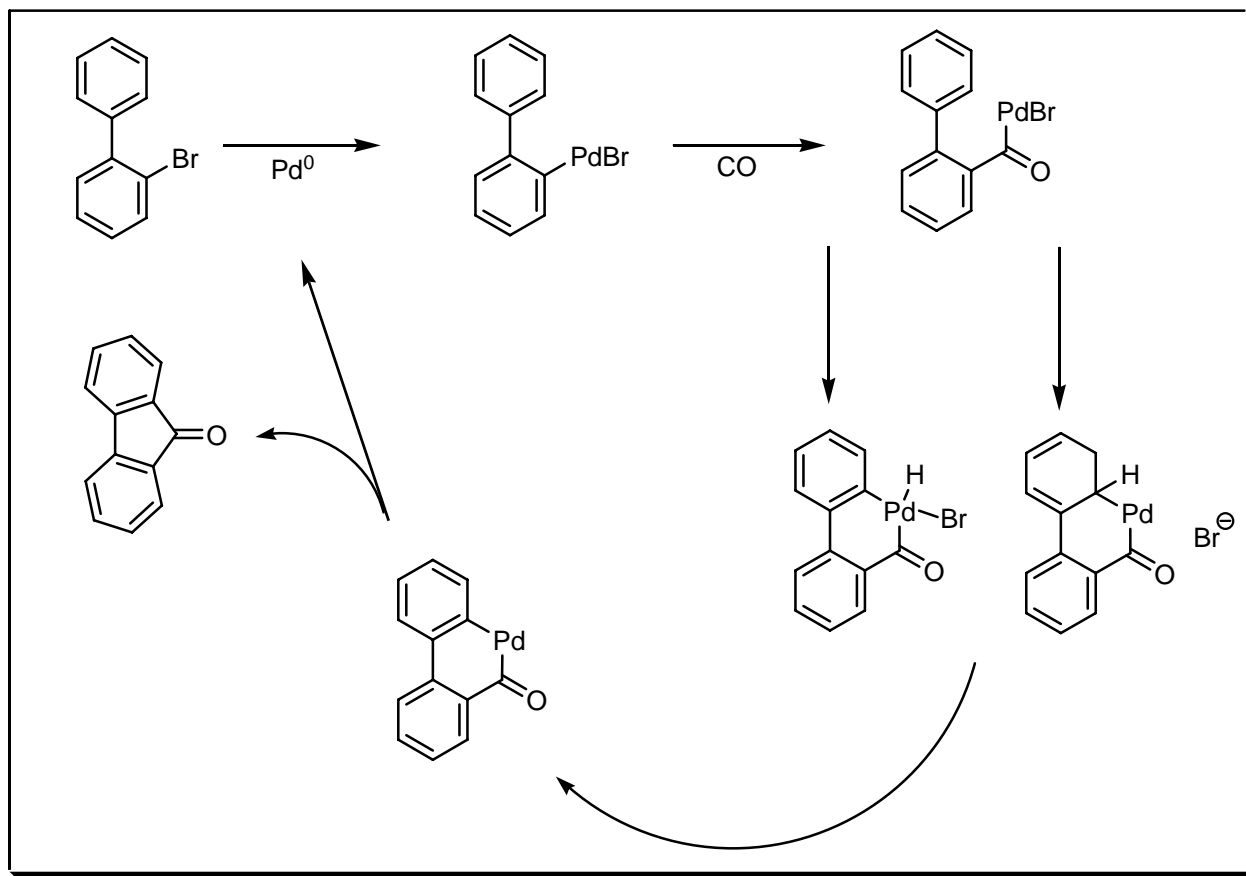
**REFERENCES :**

- 1) Q. Tian; R.C. Larock, *Org. Lett.*, 2000, **2**, 3329.
  - 2) R.C. Larock; Q. Tian, *J. Org. Chem.*, 2001, **66**, 7372.
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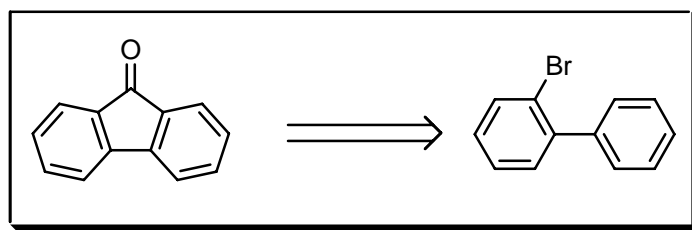
**COMMENTS :****LAROCK FLUOREN-9-ONE SYNTHESIS****EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

Another synthesis of fluoren-9-ones based on the palladium-catalysed cyclocarbonylation of *ortho*-halobiaryls. Fluoren-9-ones containing fused isoquinoline, indole, pyrrole, thiophene, benzothiophene and benzofuran rings can be prepared. The same type of chemistry can also be applied to vinylic halides. See also **Larock** fluorene and **Ullmann** fluorenone reactions.

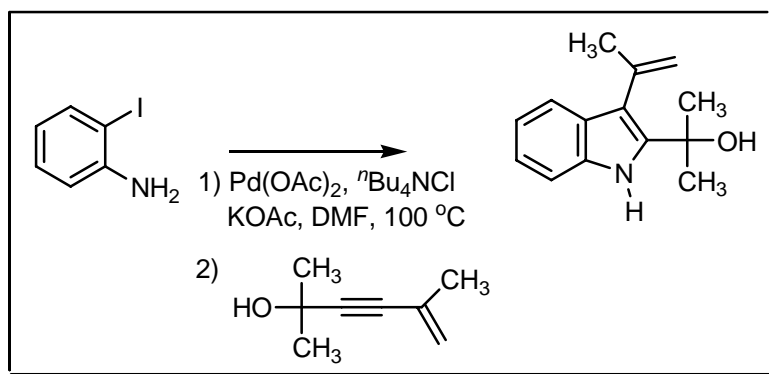
## REFERENCES :

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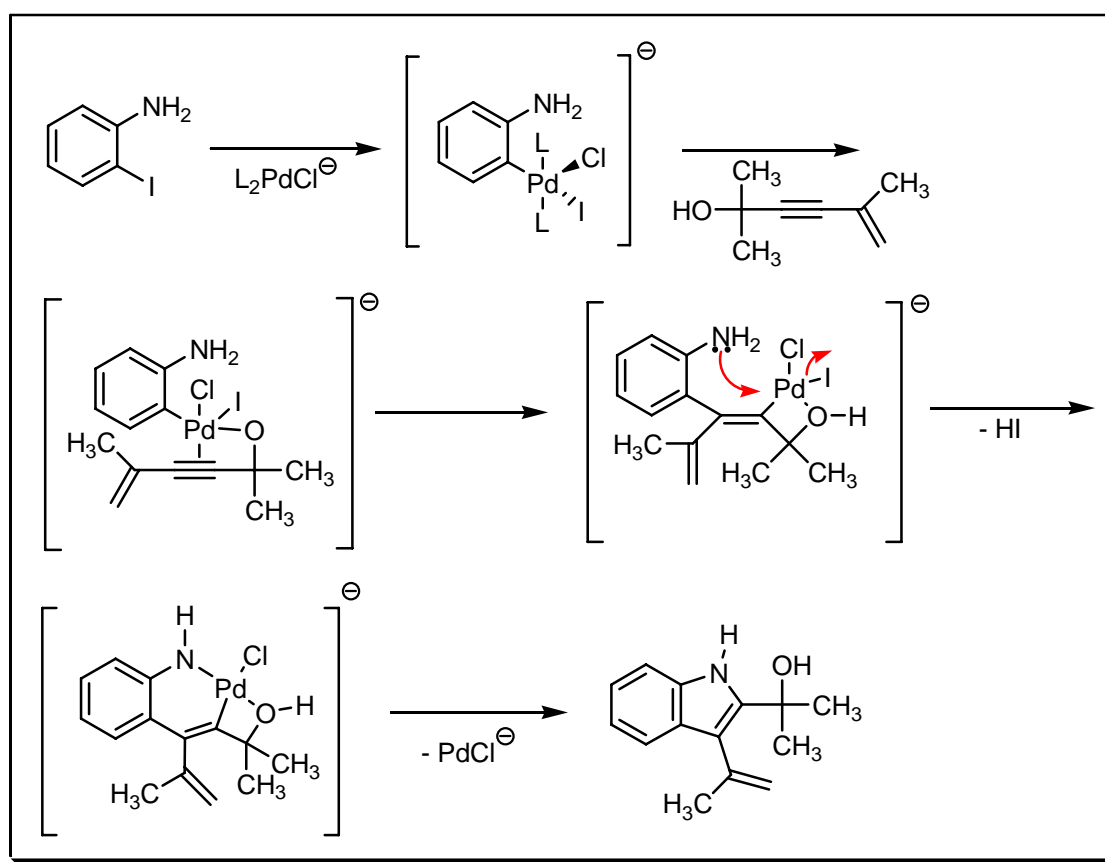
COMMENTS :

## LAROCK INDOLE SYNTHESIS

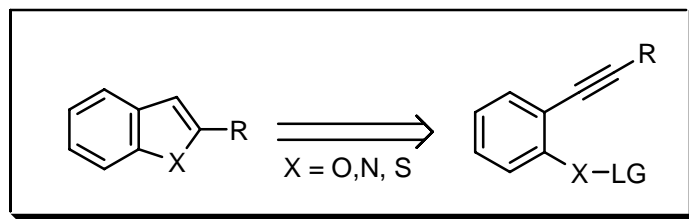
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

An indole synthesis *via* a palladium-catalysed heteroannulation of internal alkynes using *o*-iodoaniline and its derivatives. The use of imines will result in isoquinolines and pyridines, the use of iodothioanisole will result in benzo[*b*]thiophenes. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

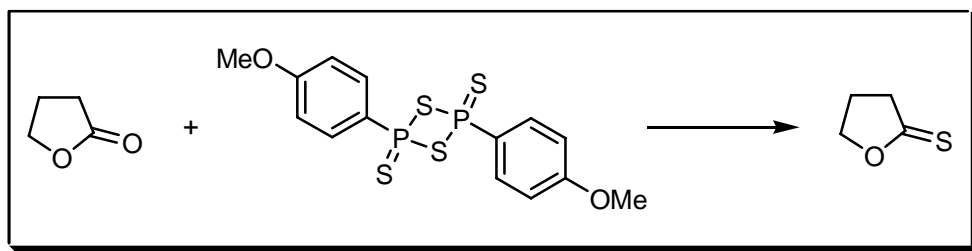
## REFERENCES :

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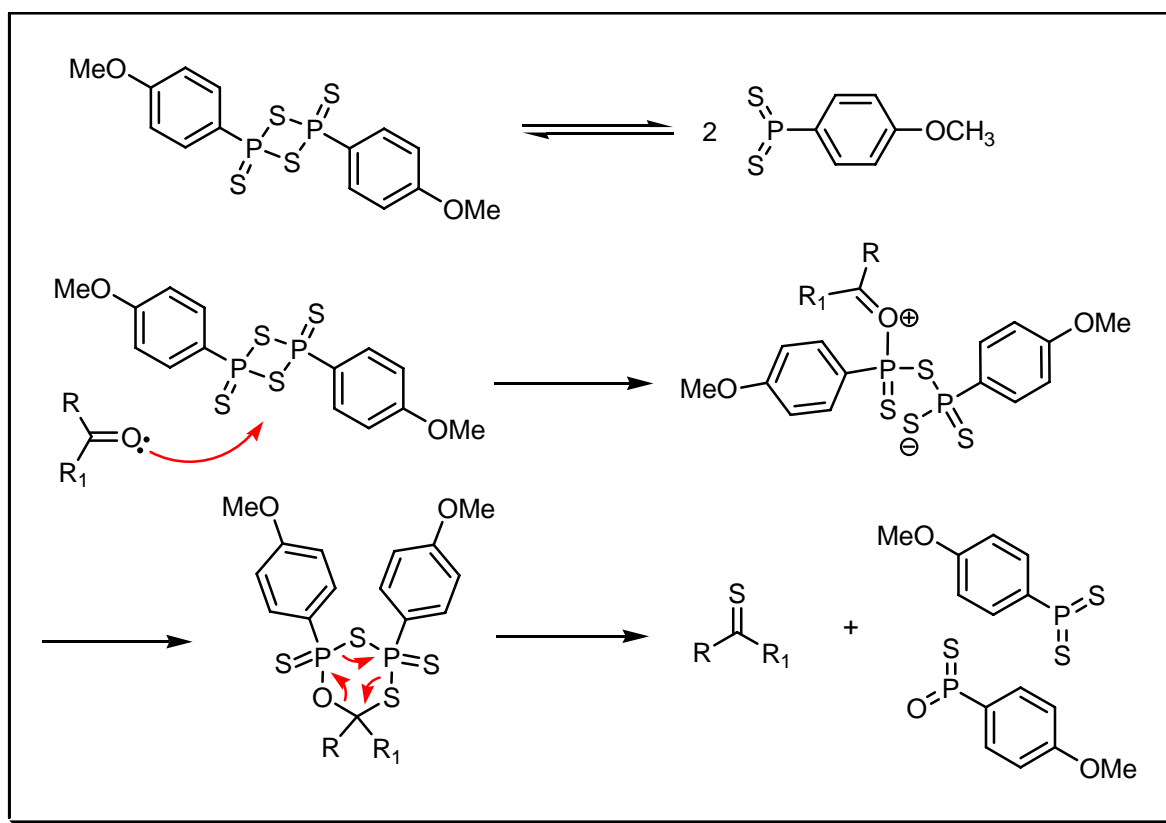
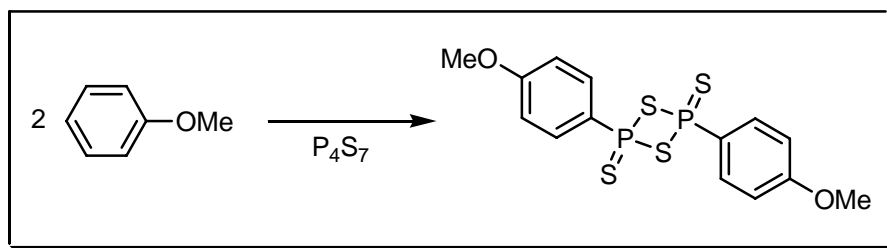
## COMMENTS :

## LAWESSON THIOCARBONYLATION

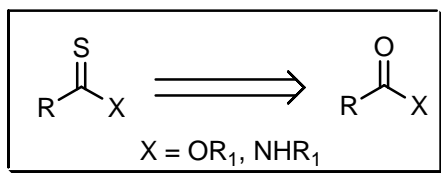
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

Reagents for the synthesis of thiamides, and thiaesters from the corresponding carbonyl compounds using 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulfide (**Lawesson** reagent). Sometimes insolubility problems are encountered, instead of **Lawesson** reagent phenyl phosphoro tetrathionate can be used.

## REFERENCES :

**March** : 406, 420, 893

**Smith – March** : 496, 509, 1184, 1331

**Org. Synth.** : **62**, 158

**Org. Synth. Coll. Vol.** : **7**, 372

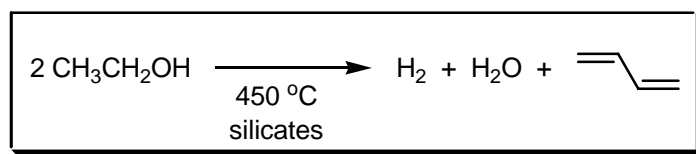
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## COMMENTS :

## LEBEDEV BUTADIENE PROCESS

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### EXAMPLE :



### NOTES :

Butadiene (20%) is obtained by the catalytic ( $\text{Al}_2\text{O}_3 + \text{ZnO}$ , silicates) pyrolysis of ethanol. Many side-products are formed at the same time. Acetaldehyde is presumed to be an intermediate in the pyrolysis. See also **Guerbet**, **Ostromyslenskii** and **Reppe** reactions.

### REFERENCES :

Houben – Weyl : 4/2, 216

1) S.V. Lebedeff, *J. Allg. Chem.*, 1933, **3**, 698.

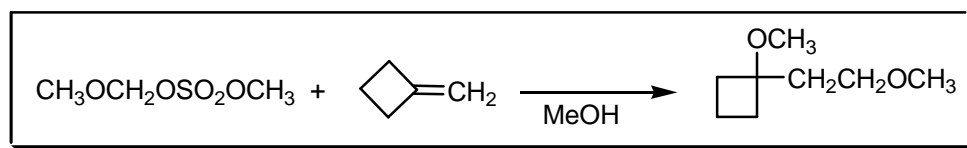
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### COMMENTS :

## LEBEDEV METHOXYMETHYLATION

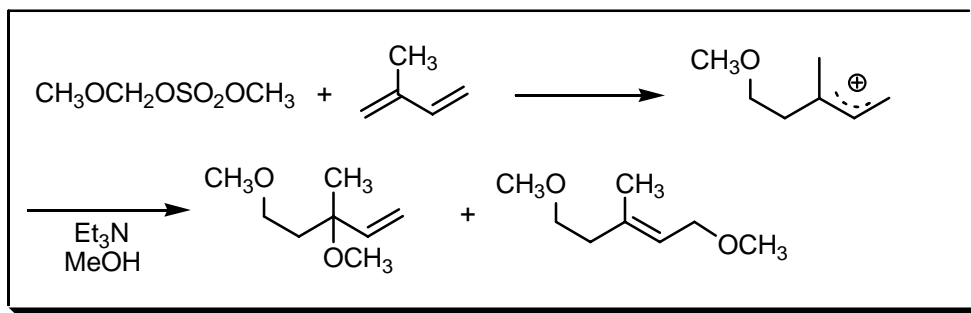
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### EXAMPLE :

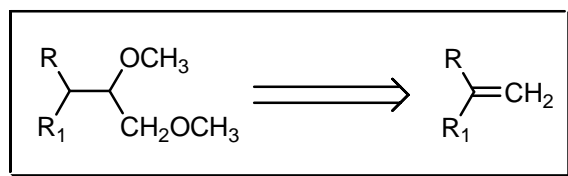


### MECHANISM :





#### DISCONNECTION :



#### NOTES :

Methoxymethyl methyl sulphate (MOM-MSF) is used as an electrophilic reagent for methoxymethylation of alkenes.

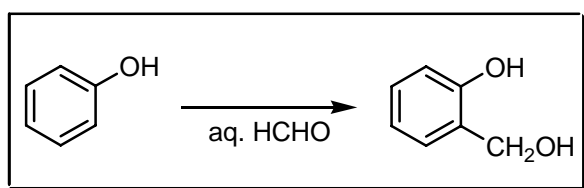
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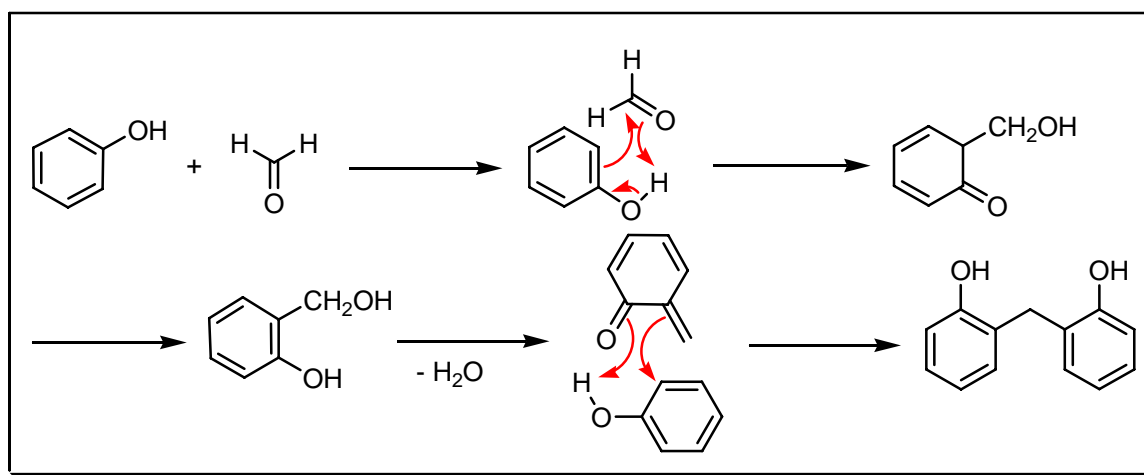
#### COMMENTS :

### LEDERER – MANASSE REACTION

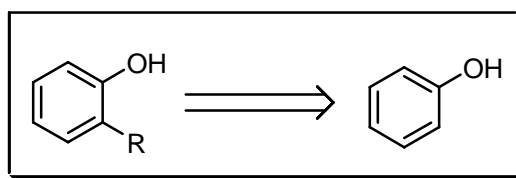
#### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Phenols condense with aqueous formaldehyde in acid or alkaline solution to yield hydroxybenzyl alcohols. Polymeric structures are very easily formed. See also **Baekeland** and **von Baeyer** reactions.

## REFERENCES :

**March** : 548

**Smith – March** : 719

**Houben – Weyl** : 14/2, 193; **E3**, 641

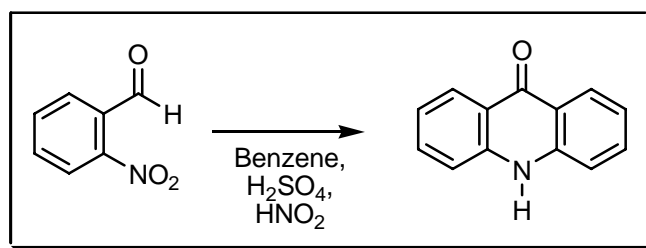
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## COMMENTS :

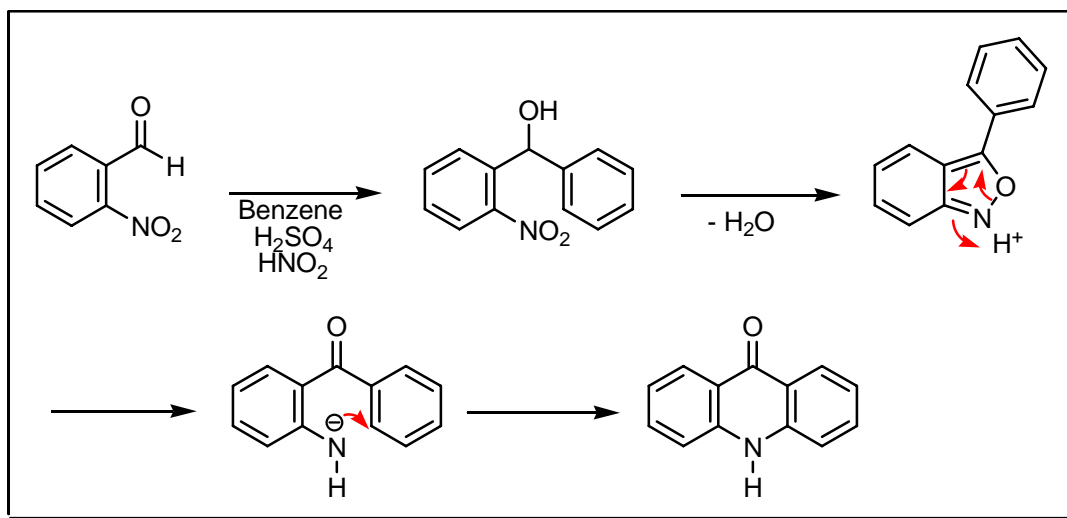


## LEHMSTEDT – TANASESCU REACTION

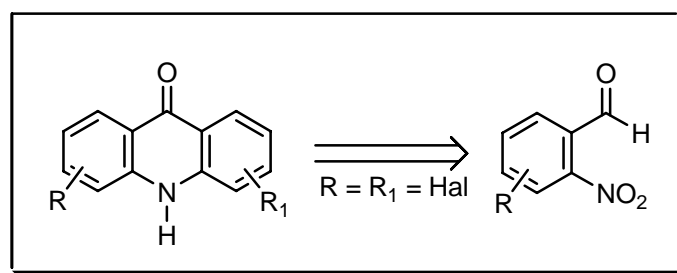
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

o-Nitrobenzaldehydes and benzene (or a halogenated benzene) condense in concentrated sulfuric acid containing a trace of nitrous acid to yield acridones.

### REFERENCES :

Houben – Weyl : E7b, 120, 139; E8a, 379, 438

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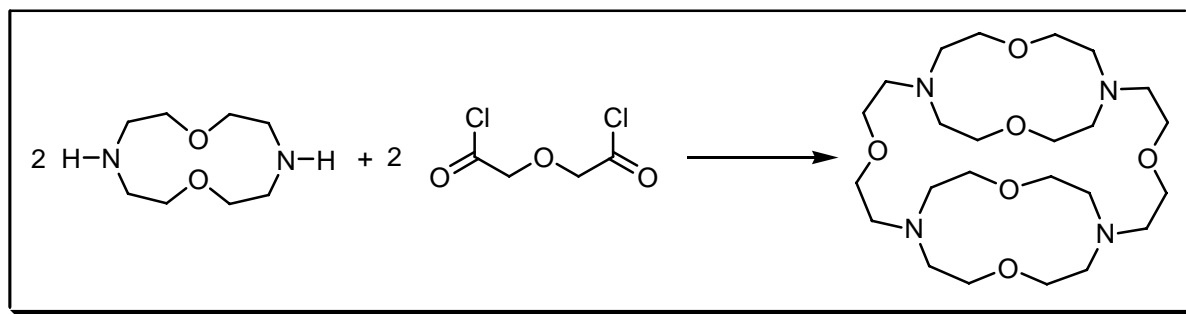
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**COMMENTS :**

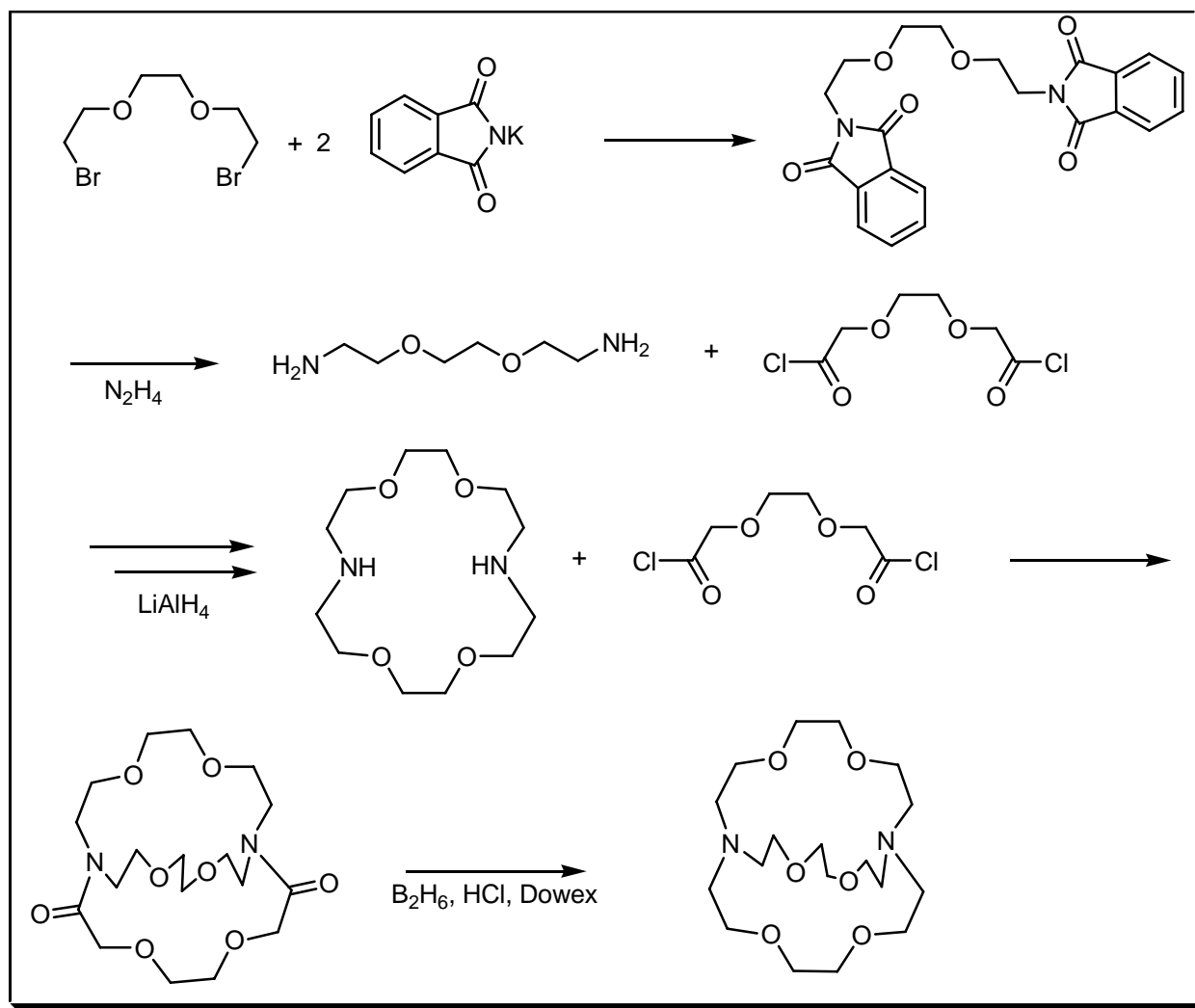
## LEHN CRYPTAND SYNTHESIS

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**EXAMPLE :**



## MECHANISM :



## NOTES :

The synthesis of diaza-polyoxa-macrobicyclic compounds (cryptands).

## REFERENCES :

March : 82

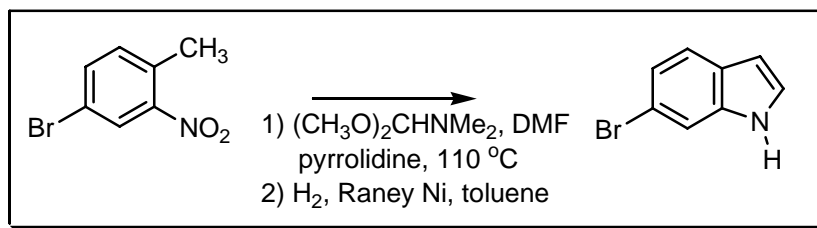
Smith – March : 105

- 1) J. Cheney; J.-M. Lehn; J.P. Sauvage; M.E. Stubbs, *J. Chem. Soc., Chem. Commun.*, 1972, 1100.
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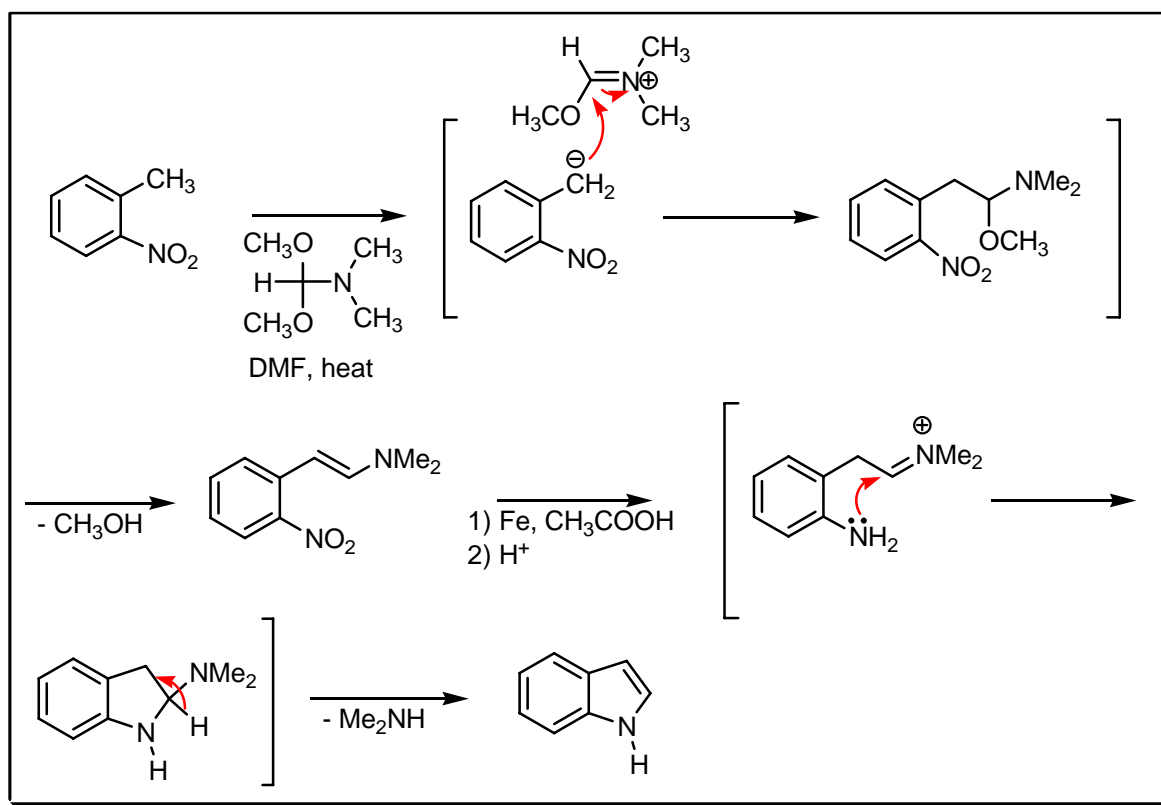
COMMENTS :

LEIMGRUBER – BATCHO ENAMINE / INDOLE SYNTHESIS

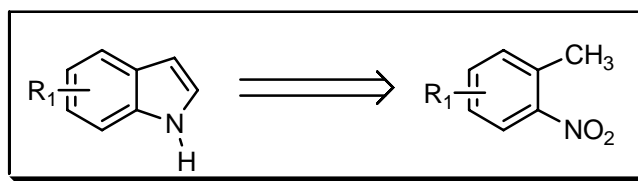
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The first step is the formation of the **Leimgruber – Batcho** enamine using hot DMF DMA and this enamine can be isolated. The reduction of the nitro group leads directly to the indole with the loss of dimethylamine. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

## REFERENCES :

**Org. Synth.** : **63**, 214

**Org. Synth. Coll. Vol.** : **7**, 34

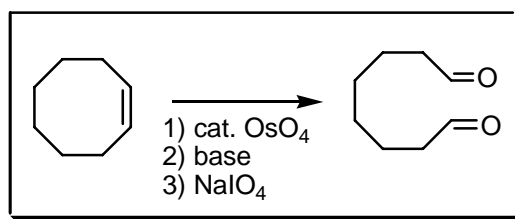
**Science of Synthesis** : **10**, 408, 421

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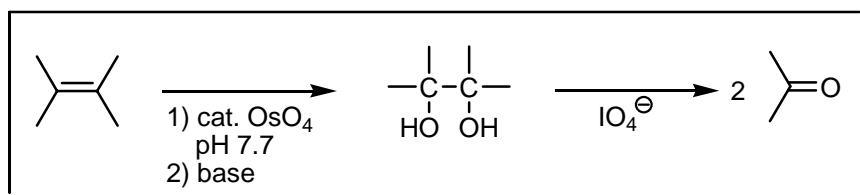
## COMMENTS :

## LEMIEUX – JOHNSON CLEAVAGE

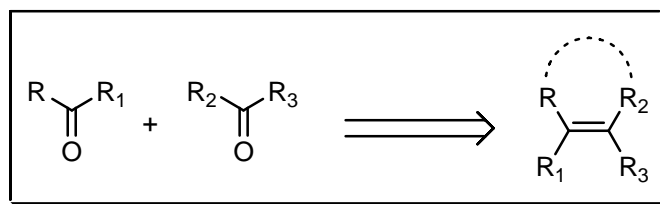
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The olefin is treated at room temperature with sodium metaperiodate and catalytic amounts of osmium tetroxide to afford aldehydes or ketones. The reaction can also be applied to the determination of isopropylidene groups. The **Lemieux – von Rudloff** oxidation uses sodium metaperiodate and catalytic amounts of potassium permanganate or ruthenium oxide or trichloride to afford carboxylic acids. See also **Barry**, **Criegee** glycol cleavage, **Djerassi – Rylander**, **Fischer** and **Hudson – Hirst** reactions.

### REFERENCES :

**March** : 1180

**Smith** : 301

**Smith 2<sup>nd</sup>** : 265

**Org. Synth.** : **68**, 41; **72**, 1, 6; **74**, 1; **78**, 123

**Org. Synth. Coll. Vol.** : **8**, 377; **9**, 39, 450, 454; **10**, 2617

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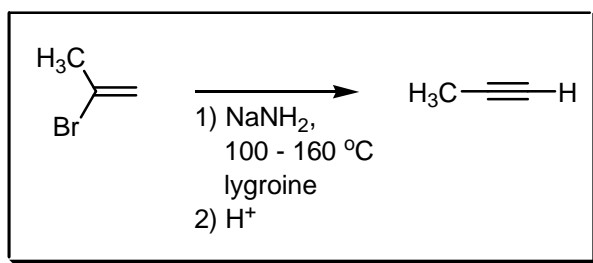
**COMMENTS :**

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**LESPIEAU – BOURGEL SYNTHESIS**

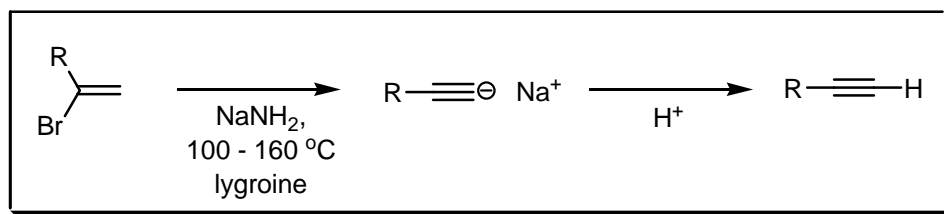
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**EXAMPLE :**



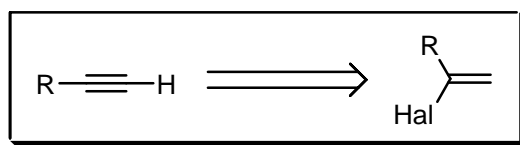
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**MECHANISM :**



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**DISCONNECTION :**



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**NOTES :**

The synthesis of monosubstituted ethynes by dehydrobromination of ethenes. The reaction also proceeds with halogen products as RCHXCH<sub>2</sub>X, RCH<sub>2</sub>CH<sub>2</sub>X and RCX<sub>2</sub>CH<sub>3</sub>. See also **Kendall – Mattox** reaction.

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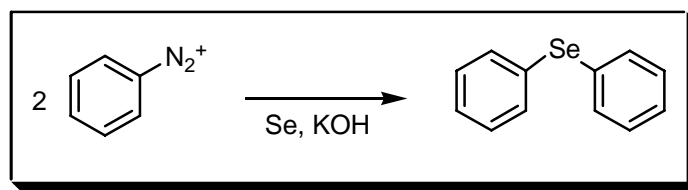
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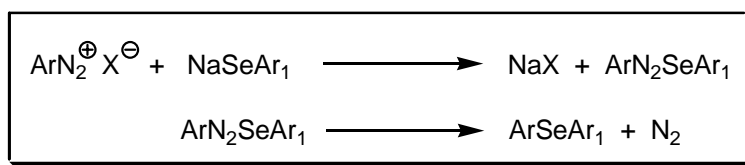
**COMMENTS :**

**LESSER – WEIß SYNTHESIS**

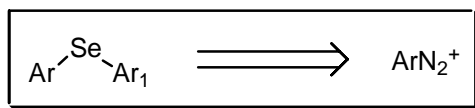
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

Diazo-compounds on treatment with alkali yield diazonium aryl selenides as intermediate compounds, which at room temperature lose nitrogen to yield diaryl selenides. Higher temperatures are sometimes needed. In the **Schoeller** modification aryl selenides are obtained by the interaction of solutions of diazonium salts with an alkaline solution of potassium polyselenide.



## REFERENCES :

Houben – Weyl : **9**, 995

Org. Synth. : **18**, 27

Org. Synth. Coll. Vol. : **2**, 238

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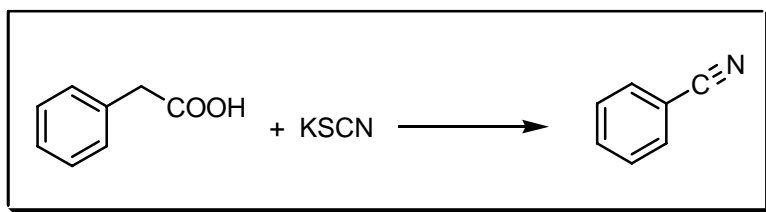
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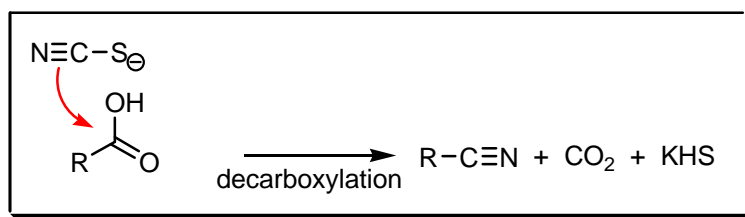
## COMMENTS :

## LETTS NITRILE SYNTHESIS

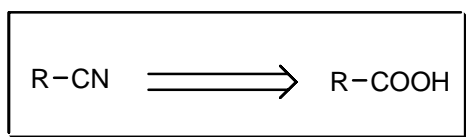
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

Nitriles are obtained by the fusion of an organic acid or the metallic salt of an organic aromatic acid with potassium or lead thiocyanate. Lead, barium or potassium ferrocyanide, lead cyanate, and silver cyanide have been used in the reaction. The reaction fails with amino-, nitro-, or hydroxyl benzoic acids. Aliphatic acids give low yields.

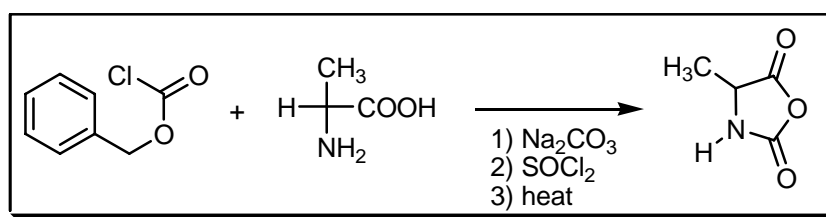
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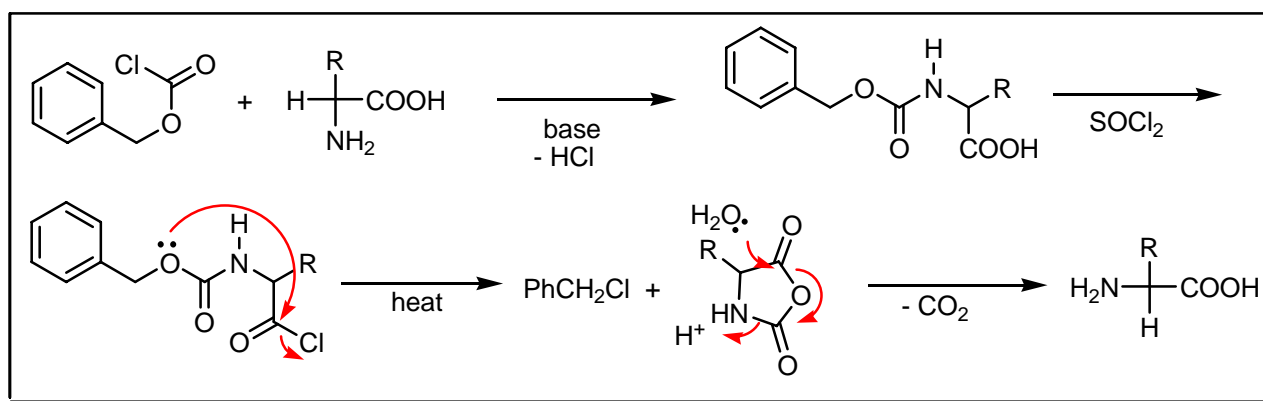
## COMMENTS :

## LEUCHS (LEUCHS – BERGMANN) PEPTIDE SYNTHESIS

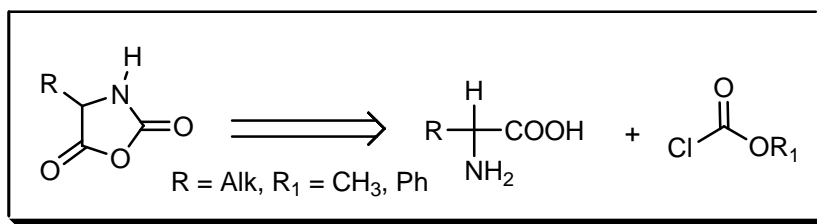
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

Benzyl chloroformate reacts with glycine or a substituted glycine to give the *N*-carbobenzyloxy- $\alpha$ -amino-acid, the acid chloride of which yields benzyl chloride and an oxazolid-2,5-dione on heating. The latter forms polypeptides on heating or treatment with water or organic bases. See also **Bergmann** azlactone peptide, **Bergmann – Zevars**, **Fischer** peptide and **du Vigneaud** reactions.

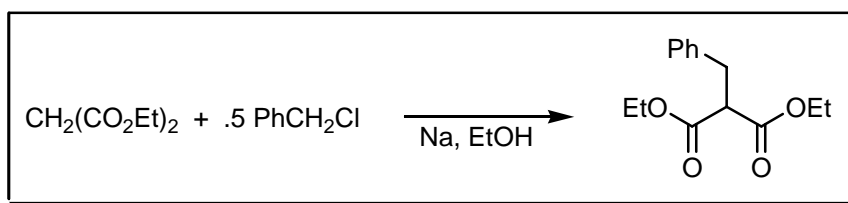
## REFERENCES :

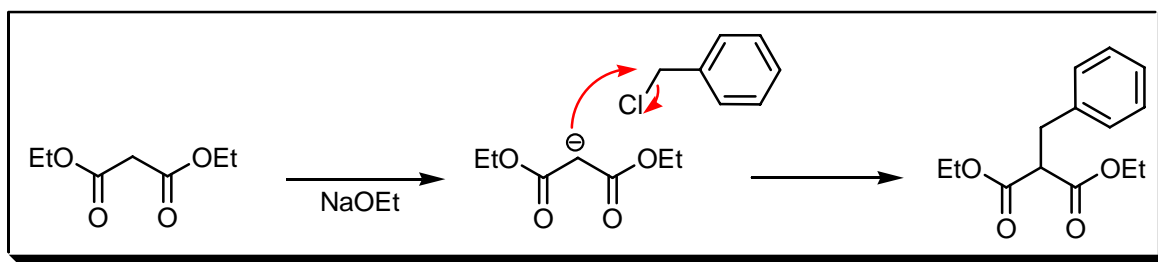
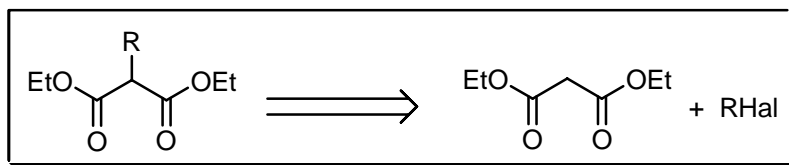
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- 5) H. Dahn; J.A. Garbarino; C. O'Murchu, *Helv. Chim. Acta*, 1970, **53**, 1370.

## COMMENTS :

## LEUCHS ALKYLATION

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

To ensure monoalkylation an excess of ethyl acetoacetate or diethyl malonate is treated with an aryl or alkyl halide and ethanolic sodium ethoxide.

**REFERENCES :**

**March :** 464

**Smith – March :** 548

**Smith :** 878

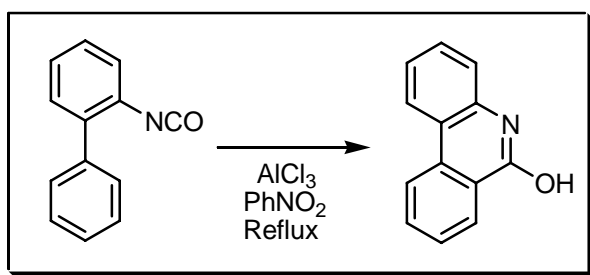
**Smith 2<sup>nd</sup> :** 733

H. Leuchs, *Ber. Dtsch. Chem. Ges.*, 1911, **44**, 1507.

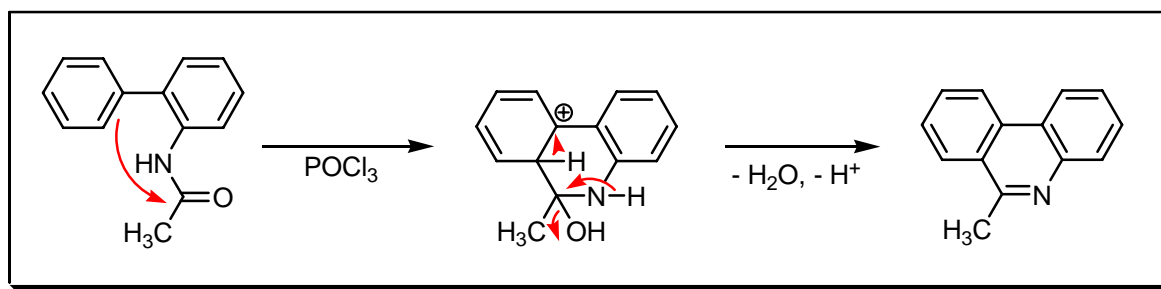
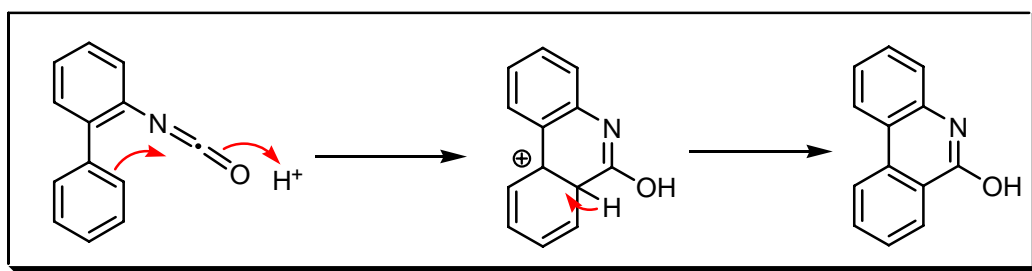
**COMMENTS :**

## LEUCKART – PICTET – HUBERT (MORGAN – WALLS) REACTION

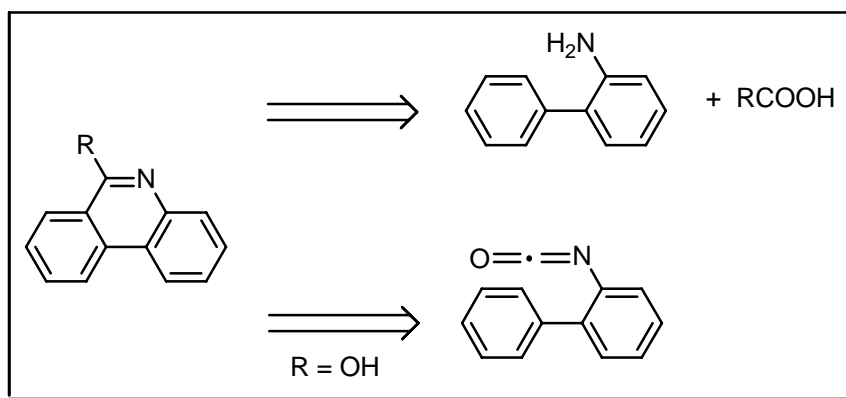
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The Lewis acid catalysed amidation of aryls by isocyanates (**Leuckart**) or by amides (**Pictet – Hubert**), affording to phenanthridines. See also **Bischler – Napieralski** and **Morgan – Walls** reactions.

## REFERENCES :

Smith : 1347

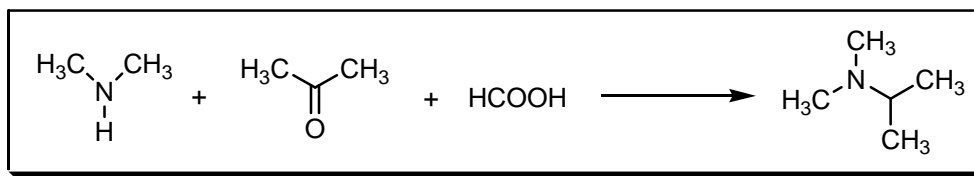
Smith 2<sup>nd</sup> : 1108

- 1) R. Leuckart, *Ber. Dtsch. Chem. Ges.*, 1885, **18**, 873.
- 2) A. Pictet; A. Hubert, *Ber. Dtsch. Chem. Ges.*, 1896, **29**, 1182.
- 3) C.T. Morgan; L.P. Walls, *J. Chem. Soc.*, 1931, 2447.
- 4) C.T. Morgan; L.P. Walls, *J. Chem. Soc.*, 1932, 2225.
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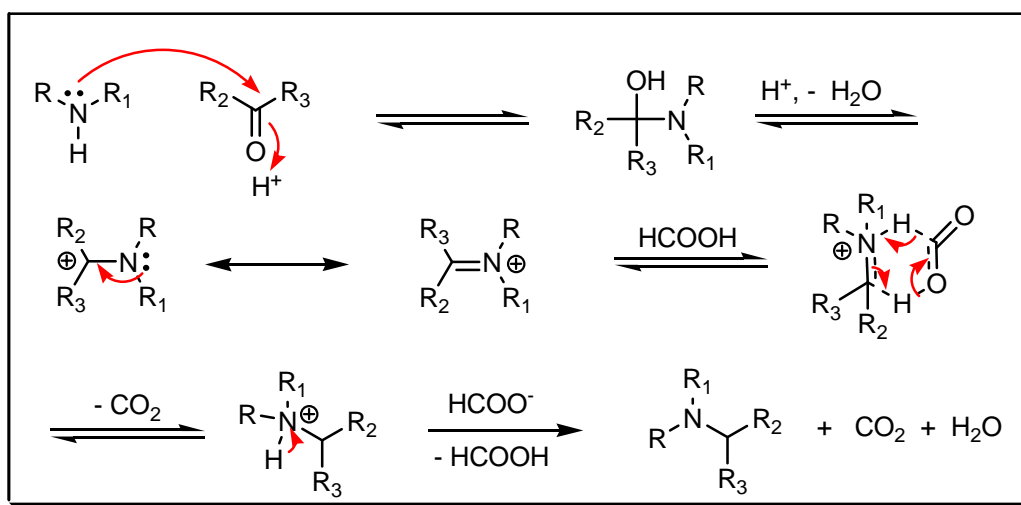
## COMMENTS :

## LEUCKART – WALLACH REACTION

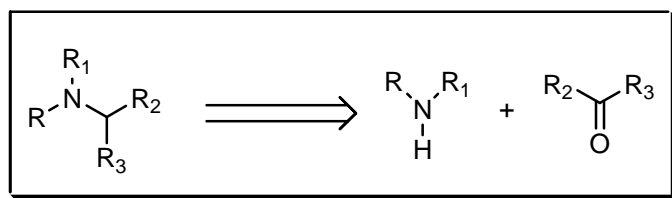
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

Carbonyl compounds are converted into amines (often as their formyl derivatives), when heated with ammonium formate or formamide. In addition to primary amines, secondary (formyl derivatives) and tertiary amines (formates) are formed in small amounts. Primary and secondary amine formates react similarly to ammonium formate. The reaction has been extended to the preparation of tertiary amines by treatment of ketones with dialkylformamide in the presence of formic acid and magnesium chloride. With the use of Cp<sup>+</sup>Rh(III) complexes this reaction can be made catalytic. When the reaction is done in the presence of excess formic acid it is referred to as the **Leuckart – Wallach** reaction, when formaldehyde and formic acid is used it is known as the **Eschweiler – Clarke** reaction. See also **Eschweiler – Clarke** reaction.

## REFERENCES :

**March** : 899

**Smith – March** : 1188

**Houben – Weyl** : 11/1, 648; **E16d**, 1082

**Org. React.** : 5, 301

**Org. Synth.** : 17, 76

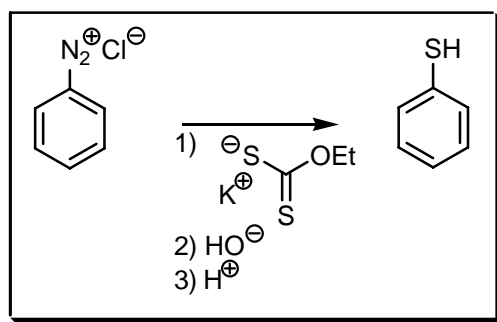
**Org. Synth. Coll. Vol.** : 2, 503

- 1) R. Leuckart, *Ber. Dtsch. Chem. Ges.*, 1885, **18**, 2341.
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- 3) R. Baltly; O. Kauder, *J. Org. Chem.*, 1951, **16**, 173.
- 4) A. Lukasiewicz, *Tetrahedron*, 1963, **19**, 1789.
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- 7) A.M. Bellini; E. Mencini; M.P. Quaglio; M. Guarneri; A. Fini, *Steroids*, 1991, **56**, 395.
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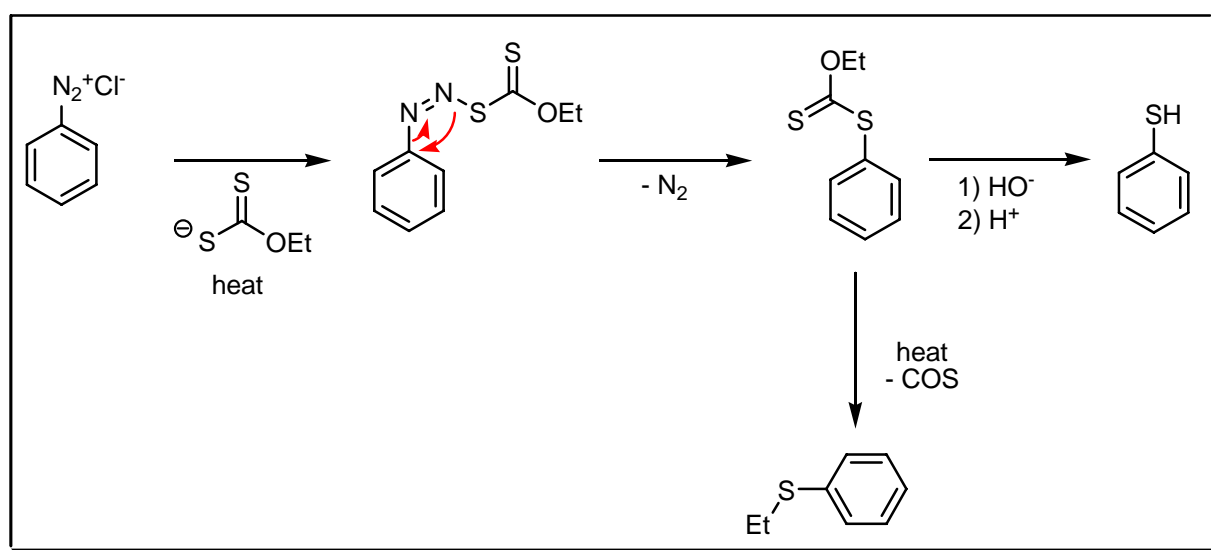
## COMMENTS :

## LEUCKART THIOPHENOL REACTION

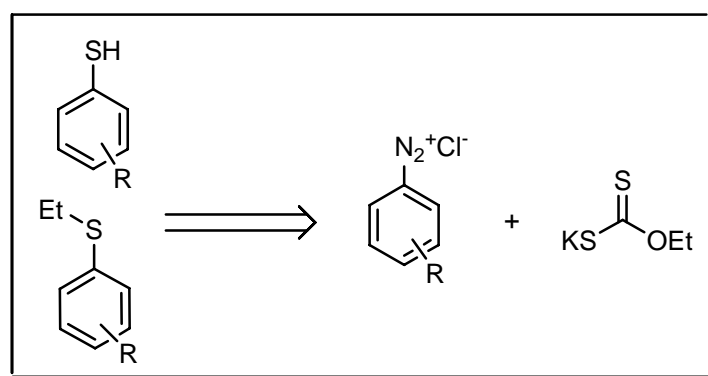
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Aromatic diazo-compounds react with potassium alkyl xanthates to yield aromatic xanthates in slightly acidic cuprous solution, which form thiophenols or aryl thioethers on warming.



## REFERENCES :

Houben – Weyl : **9**, 12

Org. Synth. : **27**, 81

Org. Synth. Coll. Vol. : **3**, 809

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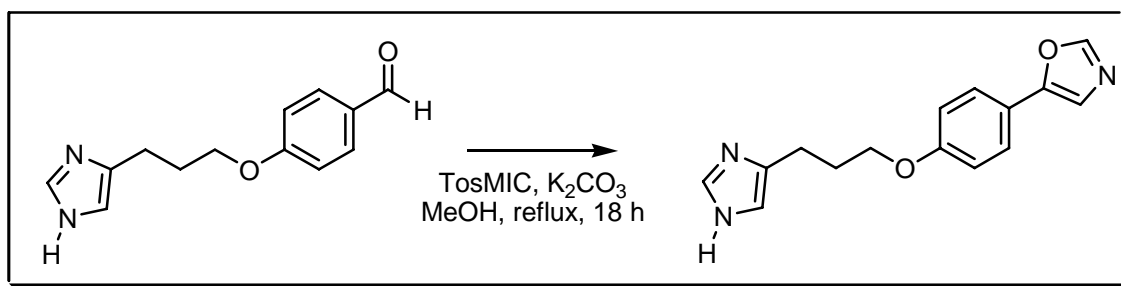
- 1) R. Leuckart, *J. Prakt. Chem.*, 1890, **41**, 179.
  - 2) D.S. Tarbell; M.A. McCall, *J. Am. Chem. Soc.*, 1952, **74**, 48.
  - 3) T. Schaefer; J.D. Baleja; G.H. Penner, *Can. J. Chem.*, 1985, **63**, 2471.
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## COMMENTS :

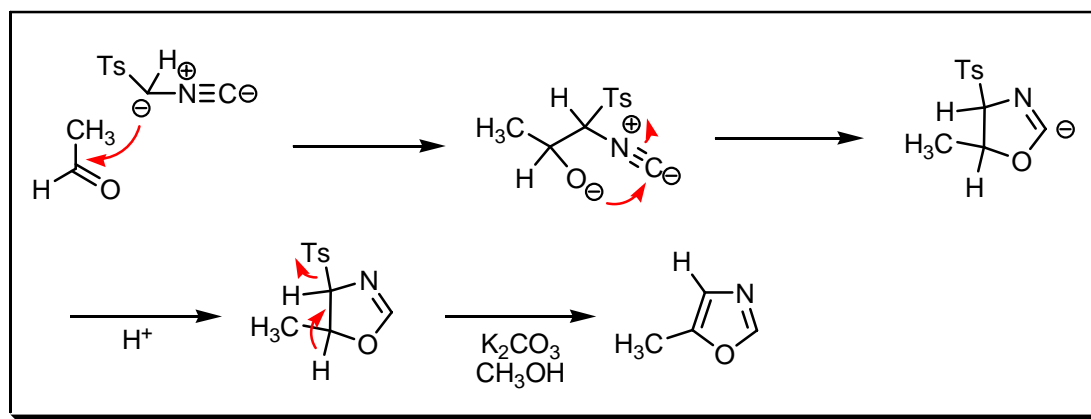
## van LEUSEN OXAZOLE SYNTHESIS

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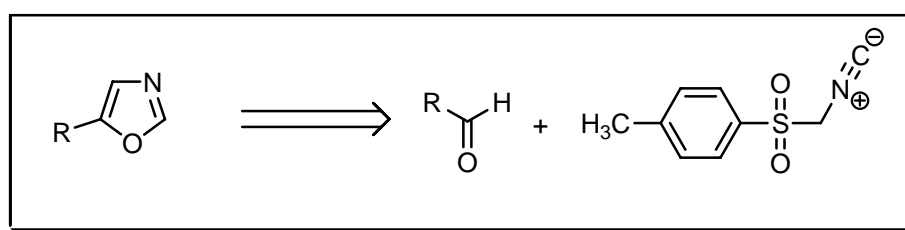
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Tosylmethylisocyanide (TosMIC), one of the most versatile reagent in organic synthesis, reacts under base catalysis in methanol with aldehydes to afford 4,5-dihydro-1,3-oxazoles which after elimination of sulfinic acid are converted into oxazoles. In general this reagent reacts in non-protic solvents with ketones and aldehydes to afford the nitrile.

## REFERENCES :

March : 949, 1041

Smith : 674

Smith 2<sup>nd</sup> : 572

Org. React. : 57, 417

Org. Synth. : 77, 198

Org. Synth. Col. Vol. : 10, 2382

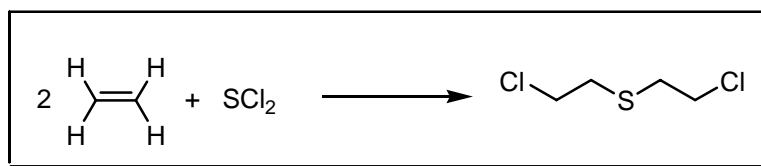
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- 7) P. Radha Krishna; V.V. Ramana Reddy; G.V.M. Sharma, *Synlett*, 2003, 1619.

**COMMENTS :**

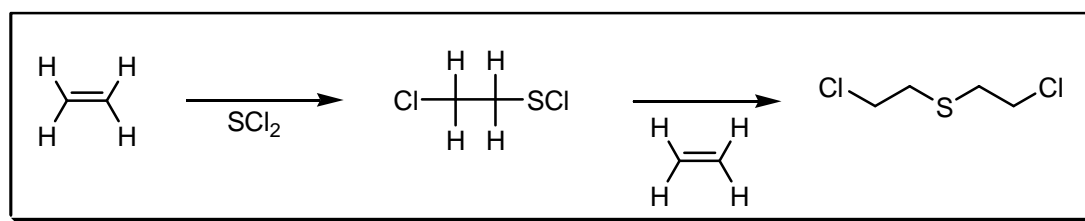
**LEVINSTEIN PROCESS**

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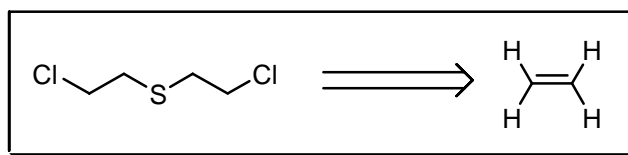
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

The synthesis of vesicant agent H (mustard gas). It contains around 30% sulfur. After distillation it is called agent HD.

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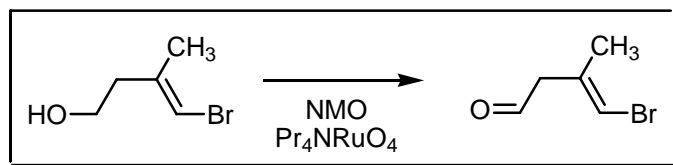
**REFERENCES :**

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  - 6) R.C. Fuson; W.E. Parham, *J. Org. Chem.*, 1946, **11**, 482.
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  - 8) W.A. Felsing; C.A. Hunting; S.D. Fell, *J. Am. Chem. Soc.*, 1948, **70**, 1966.
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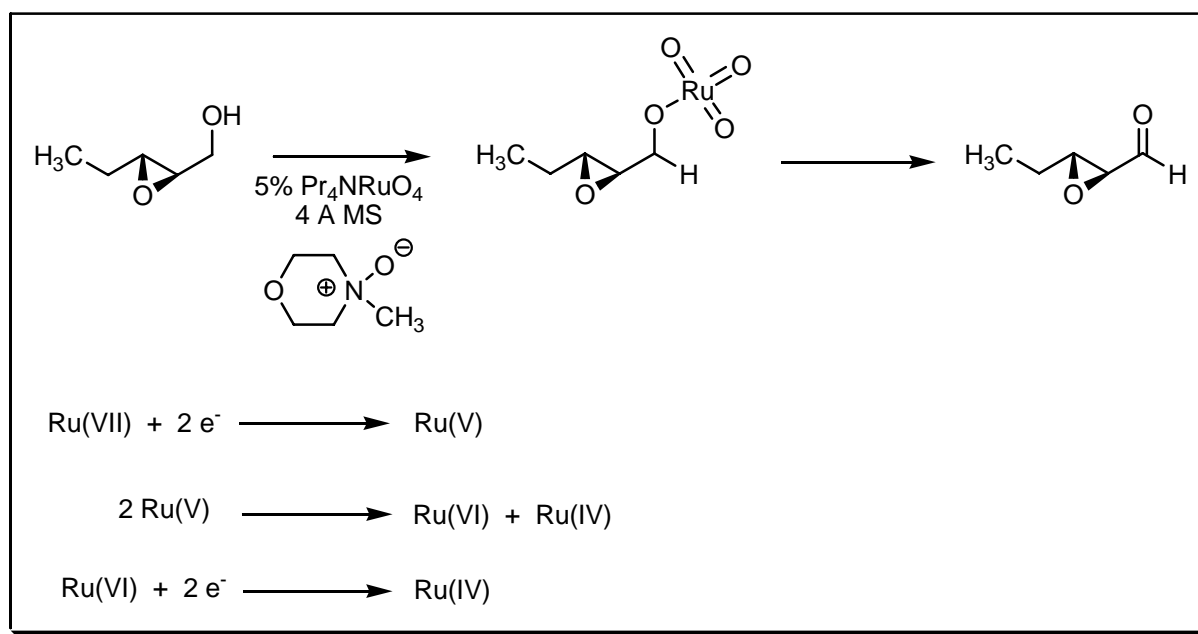
## COMMENTS :

## LEY OXIDATION

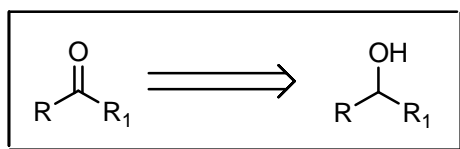
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The oxidation of alcohols with tetra-*n*-propylammonium perruthenate and *N*-methylmorpholine. Many other functional groups are tolerated. *N*-methylmorpholine-*N*-oxide is used as the stoichiometric oxidant for recycling the catalyst. Primary alcohols are oxidised to aldehydes. Over-oxidation to the carboxylic acid is rare although can be induced by

omitting the molecular sieves used to remove water from the reaction. See also **Anelli**, **Ball – Goodwin – Morton**, **Collins**, **Corey – Kim**, **Corey – Schmidt**, **Corey – Suggs**, **David – Thieffry**, **Delépine**, **Dess – Martin**, **Einhorn** oxidation, **Fétizon**, **Jones** oxidation, **Maurer – Drefahl**, **Mukaiyama** oxidation, **Nicolaou**, **Oppenauer**, **Parikh – von Doering**, **Pfitzner – Moffatt**, **Sarett**, **Swern** and **Uemura** reactions.

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#### REFERENCES :

Smith 2<sup>nd</sup> : 211

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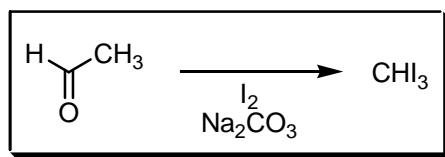
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#### COMMENTS :

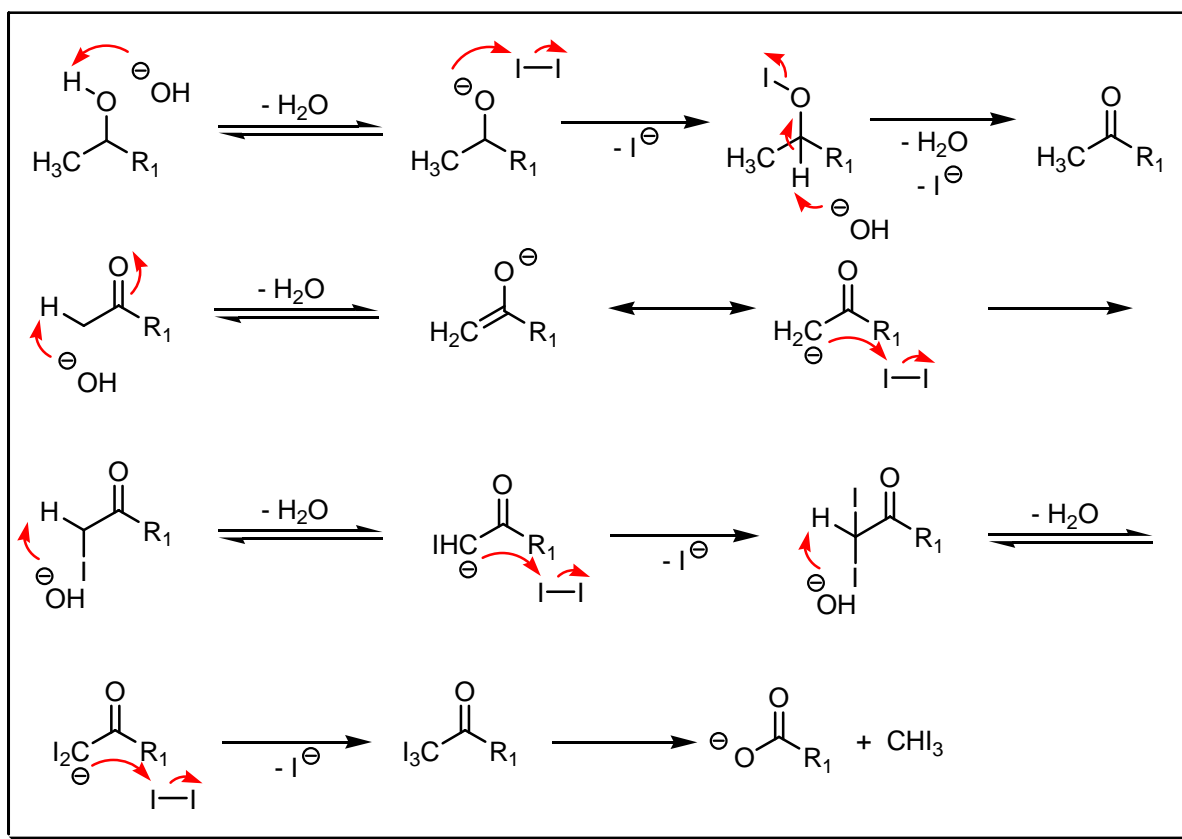
### LIEBEN IODOFORM REACTION

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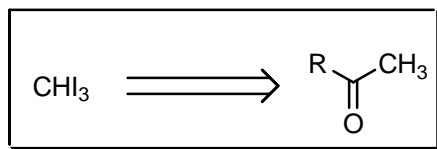
#### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Haloforms are obtained by the action of alkali hypohalites on acetaldehyde or methyl ketones, or their halogenated derivatives or on groups capable of being converted into these under the experimental conditions. The mechanism of the reaction is very complex. It is dependent on the structure of the substrate and the specific reaction conditions.

## REFERENCES :

Smith : 961

Smith 2<sup>nd</sup> : 799

Houben – Weyl : 2, 939

Org. Synth. : 69, 238

Org. Synth. Coll. Vol. : 8, 254

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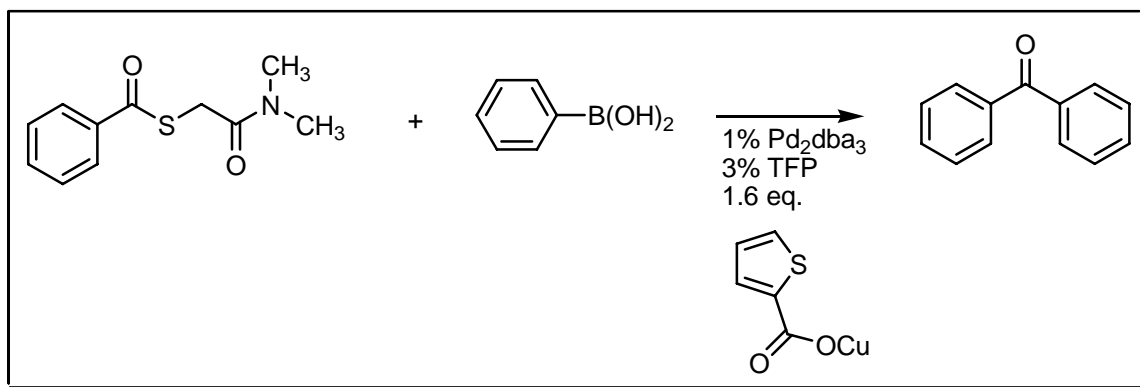
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**COMMENTS :**

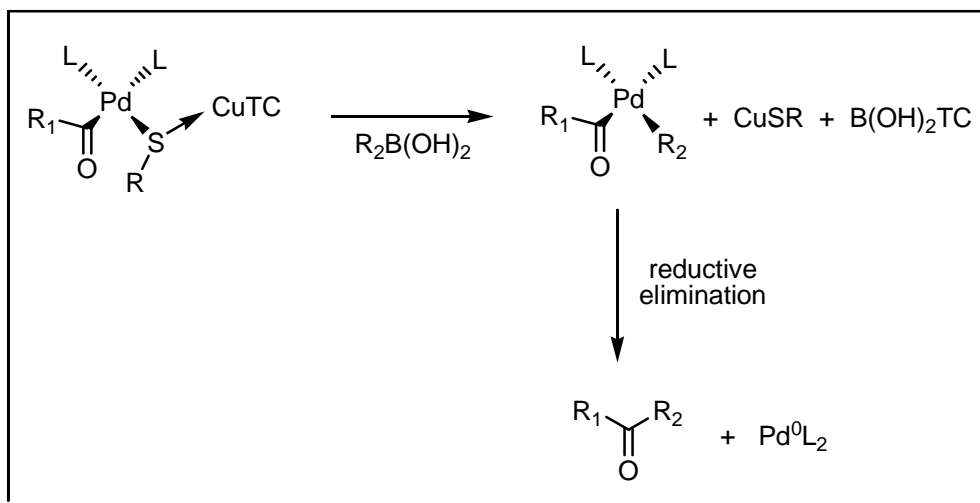
## LIEBESKIND – SROGL REACTION

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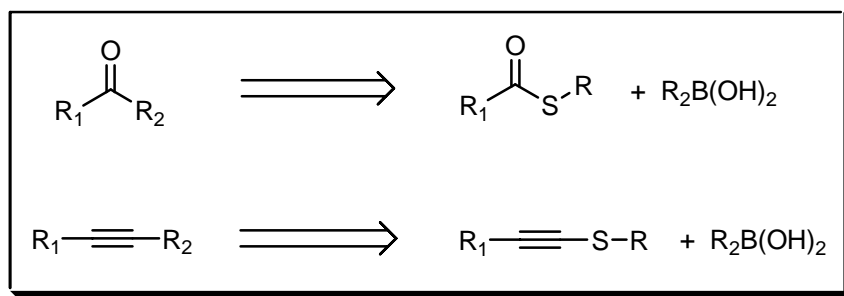
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

The palladium-catalysed cross-coupling of thioalkyne derivatives and thiol esters with boronic acids in the presence of copper(I) thiophene-2-carboxylate (CuTC) under neutral conditions. Both the copper cation and the carboxylate anion are critical to the reaction. The exact details of the mechanism are not known. See also **Sonogashira – Hagihara** and **Suzuki – Miyaura** reactions.

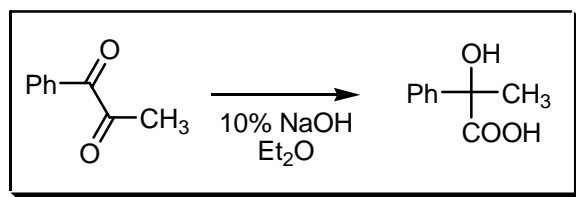
## REFERENCES :

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- 4) L.S. Liebeskind; J. Srogl, *Org. Lett.*, 2002, **4**, 979.
- 5) C. Savarin; J. Srogl; L.S. Liebeskind, *Org. Lett.*, 2002, **4**, 4309.
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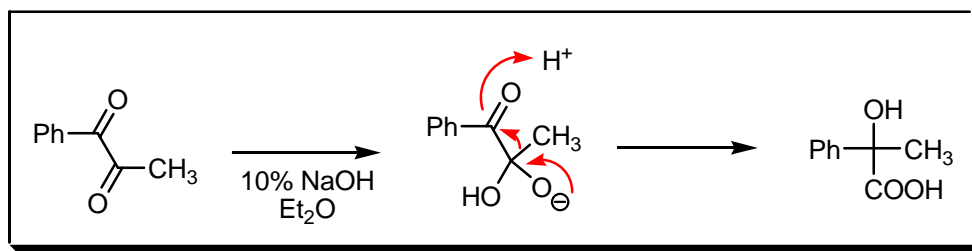
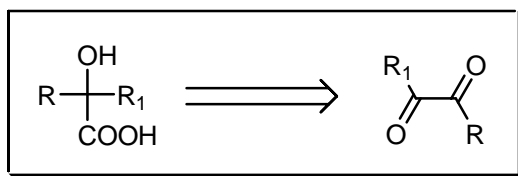
## COMMENTS :

## LIEBIG BENZYLIC ACID REARRANGEMENT

### EXAMPLE :





**MECHANISM :****DISCONNECTION :****NOTES :**

The base-induced transformation of an  $\alpha$ -diketone into the salt of an  $\alpha$ -hydroxyacid.

**REFERENCES :**

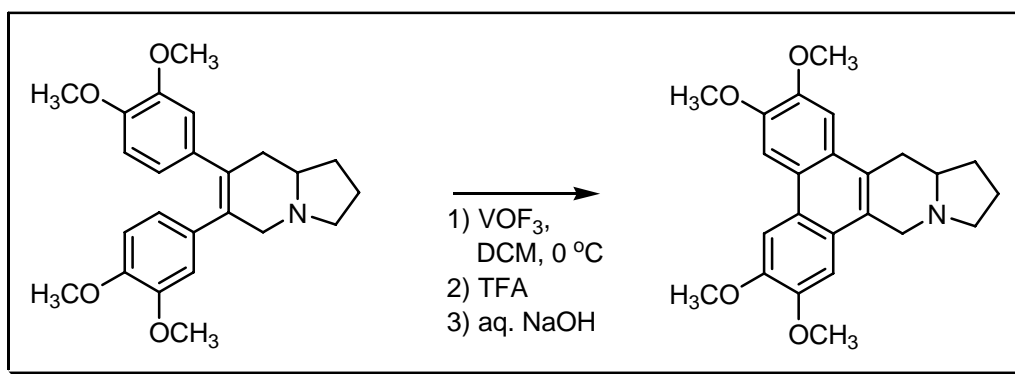
- 1) J. von Liebig, *Liebigs Ann. Chem.*, 1838, **25**, 27.
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- 4) A. Novelli; J.R. Barrio, *Tetrahedron Lett.*, 1969, **10**, 3671.
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**COMMENTS :**

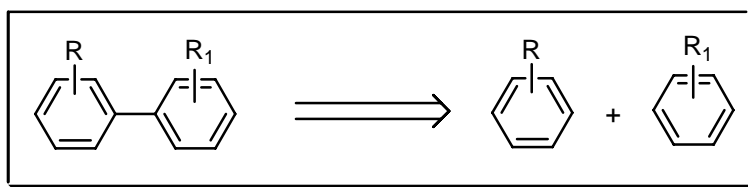
## LIEPA COUPLING

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### EXAMPLE :



### DISCONNECTION :



### NOTES :

The *intramolecular* coupling between mainly phenolic aromatic nuclei in the presence vanadium oxytrifluoride.

### REFERENCES :

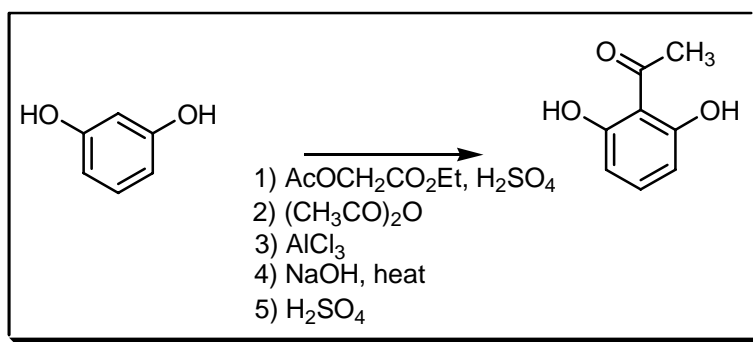
Smith 2<sup>nd</sup> : 1183

- 1) S.M. Kupchan; A.J. Liepa; V. Kameswaran; R.F. Bryan, *J. Am. Chem. Soc.*, 1973, **95**, 6861.
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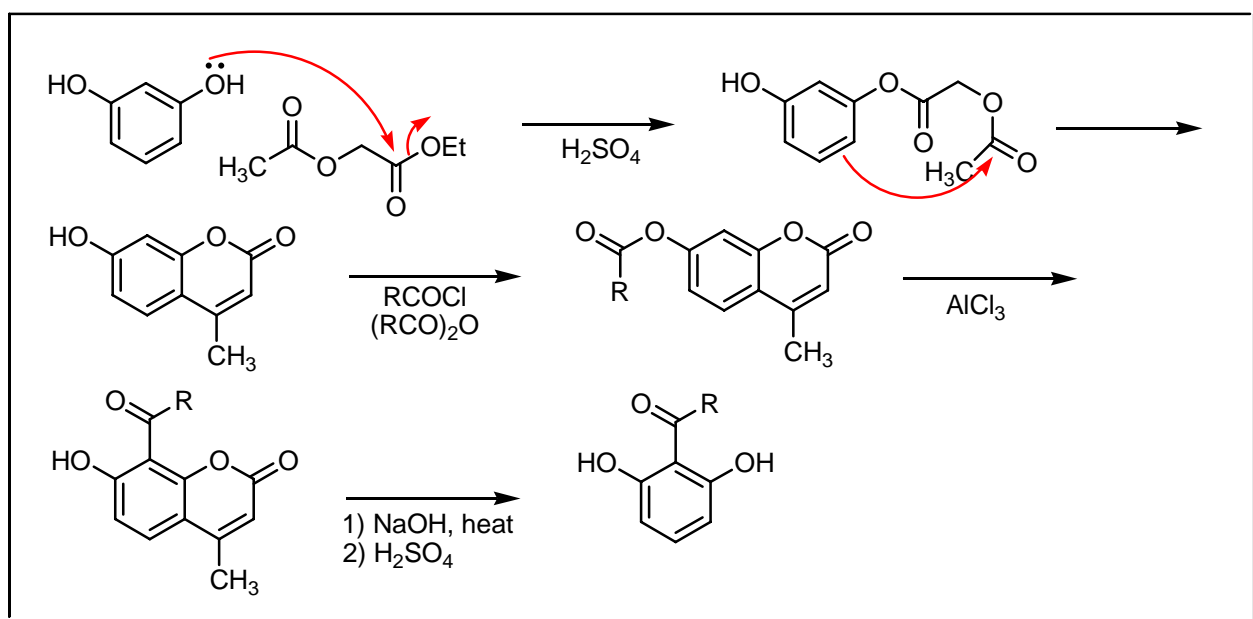
### COMMENTS :

## LIMAYE SYNTHESIS

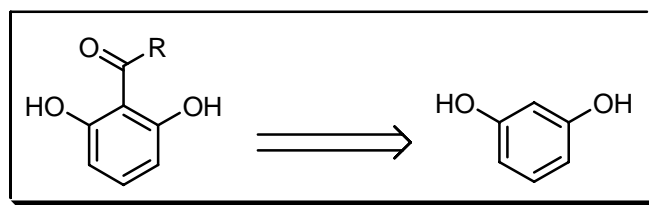
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The synthesis of 2-acylresorcinols via a **Fries** rearrangement. See also **Fries** rearrangement.

## REFERENCES :

Org. Synth. : **21**, 22

Org. Synth. Coll. Vol. : **3**, 281

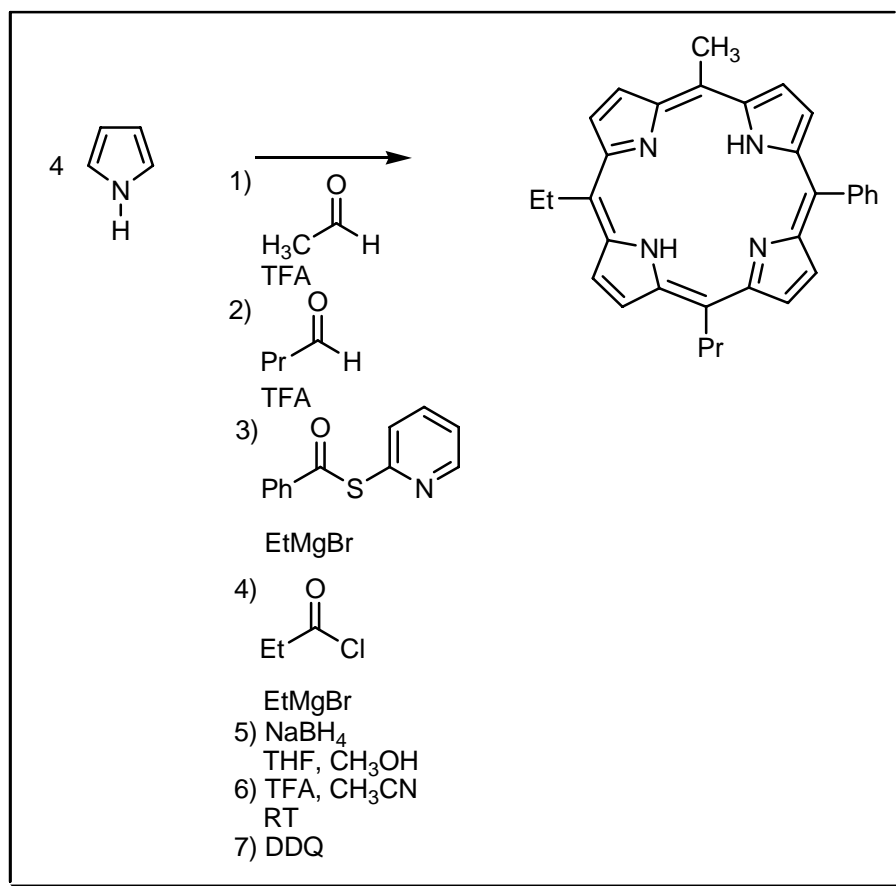
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2) W. Baker, *J. Chem. Soc.*, 1934, 1953.

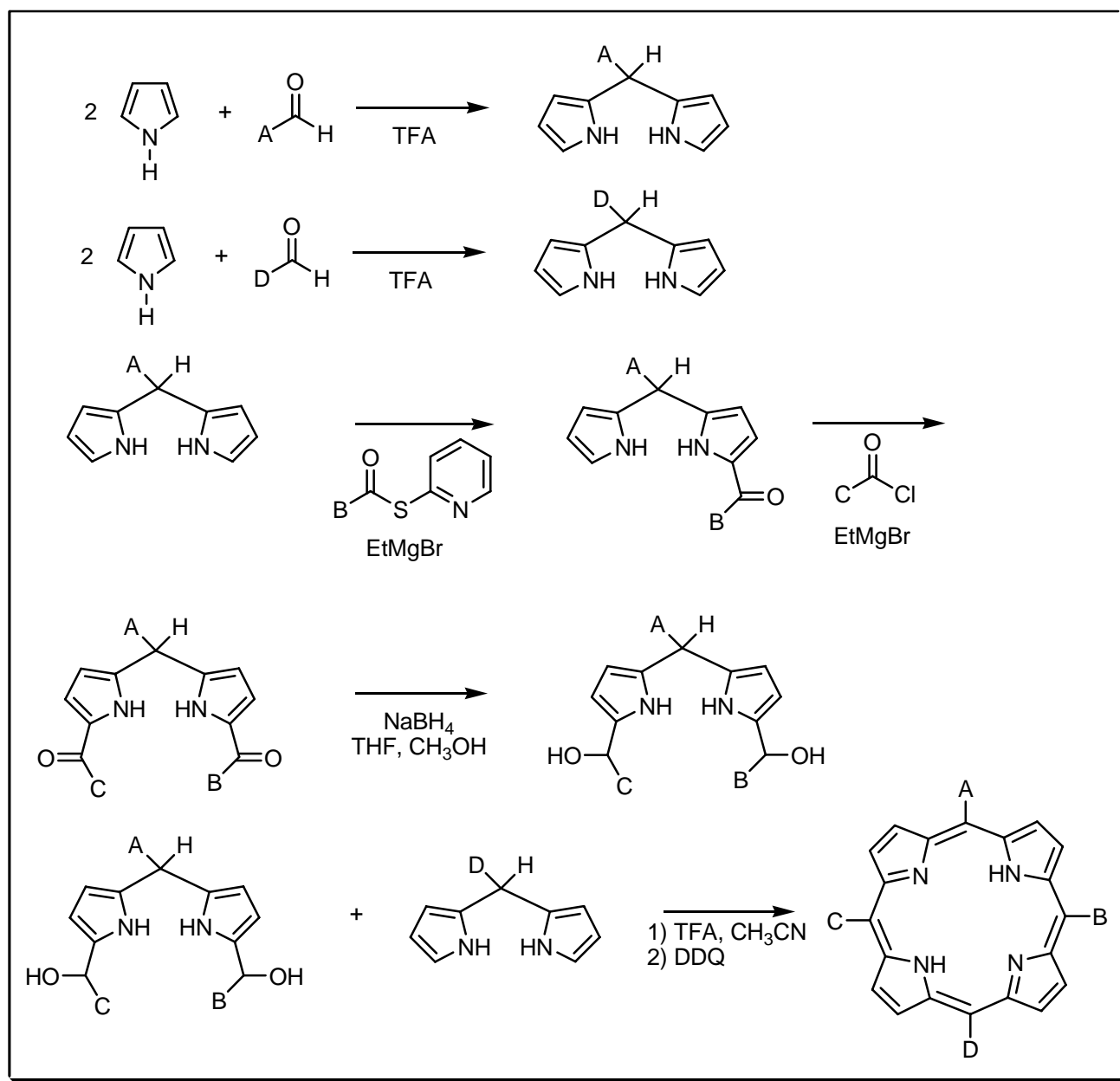
## COMMENTS :

## LINDSEY PORPHYRIN SYNTHESIS

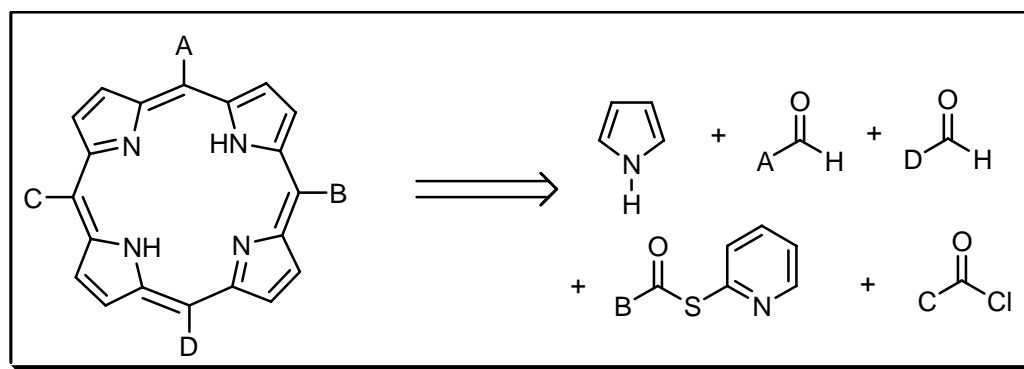
### EXAMPLE :



# MECHANISM :



# DISCONNECTION :



## NOTES :

**Lindsey** developed two main synthetic routes to porphyrins. The most interesting one is the synthesis of porphyrins bearing four different substituents. The key components in this synthesis are the dipyrromethanes. See also **Adler – Longo, MacDonald, Rothmund** and **Taniguchi** reactions.

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## REFERENCES :

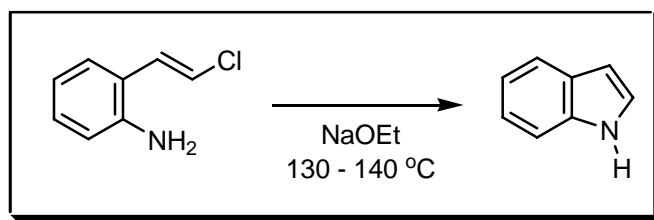
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## COMMENTS :

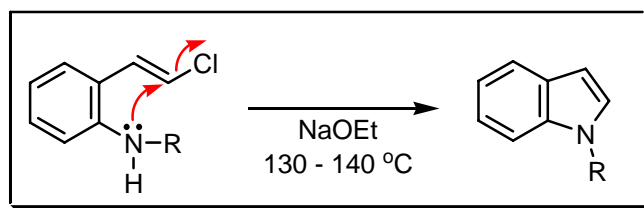
## LIPP INDOLE SYNTHESIS

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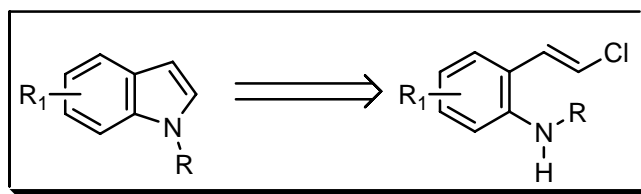
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

*o*-Amino- $\omega$ -chlorostyrenes on treatment with sodium ethoxide at 130 – 140 °C yield indoles. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

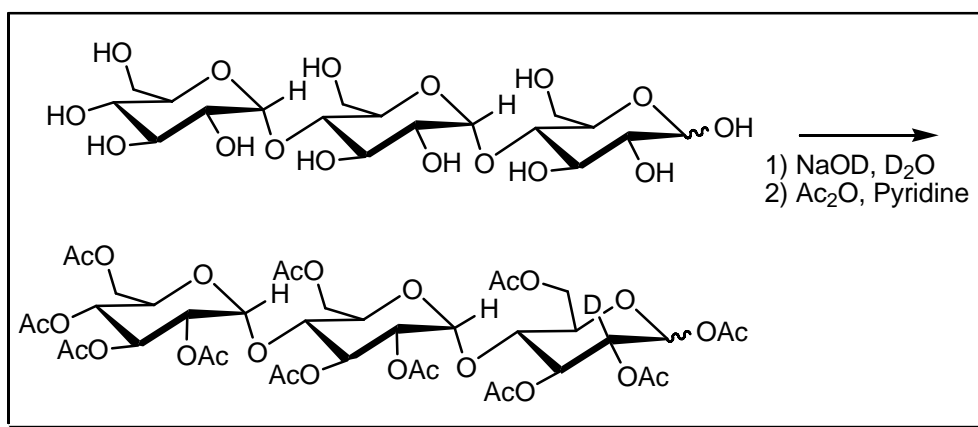
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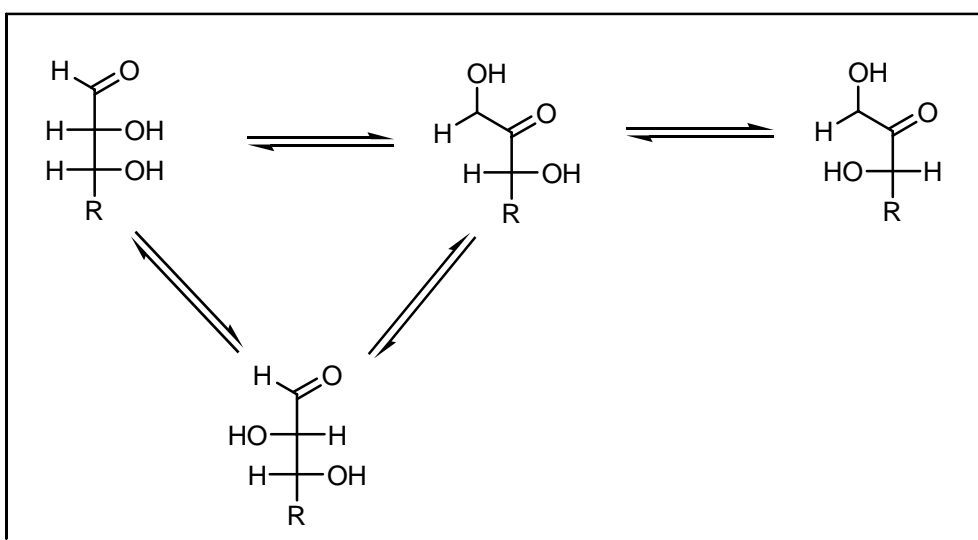
## COMMENTS :

## LOBRY de BRUIN – van EKENSTEIN TRANSFORMATION

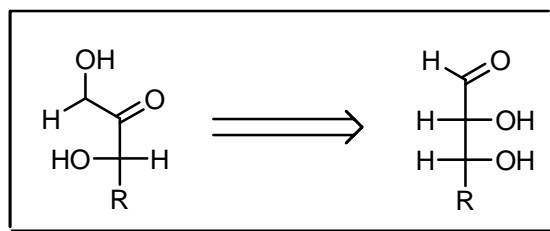
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The treatment of an aqueous solution of an aldose or ketose sugar with dilute aqueous alkali yields an equilibrium mixture of the epimeric aldose sugars and the related ketose sugar, which gives the same osazone.



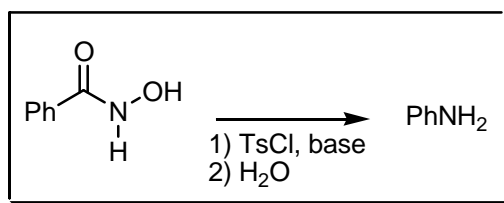
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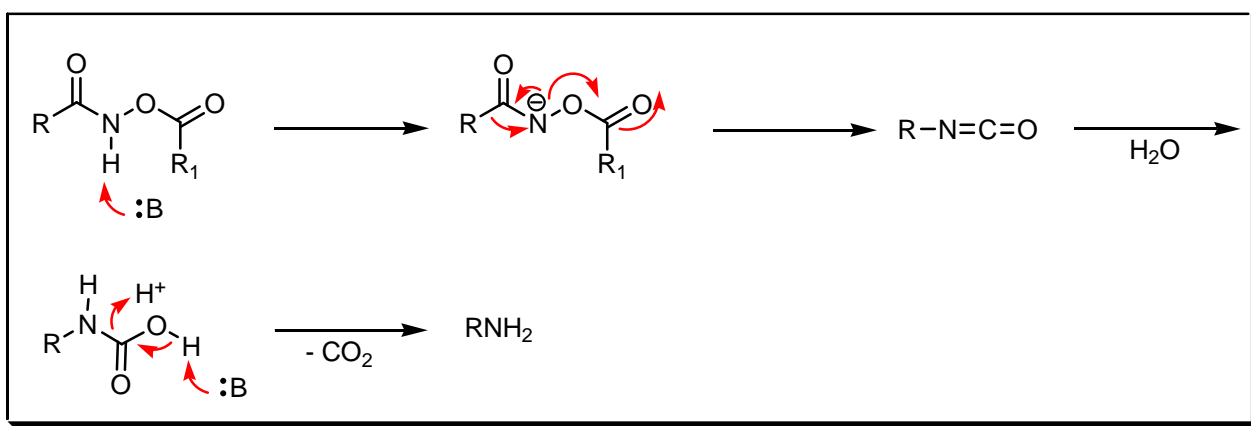
## COMMENTS :

## LOSSEN REARRANGEMENT

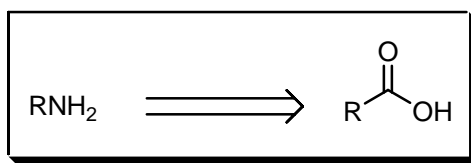
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



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## NOTES :

Hydroxamic acids or their acyl derivatives undergo rearrangement to form isocyanates either thermally or when treated with thionyl chloride or alkali. The isocyanates may react further with the components in the system. See also **Beckmann**, **Curtius**, **Hofmann** rearrangement, **Schmidt** rearrangement, **Tiemann** rearrangement and **Wolff** reactions.

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**March** : 1054, 1093

**Smith – March** : 1380, 1413

**Houben – Weyl** : **10/4**, 232; **E3**, 527; **E16d**, 1098

**Org. React.** : **3**, 267, 337

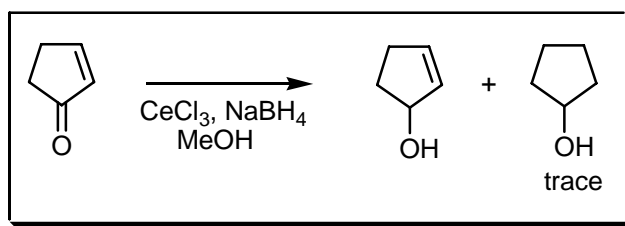
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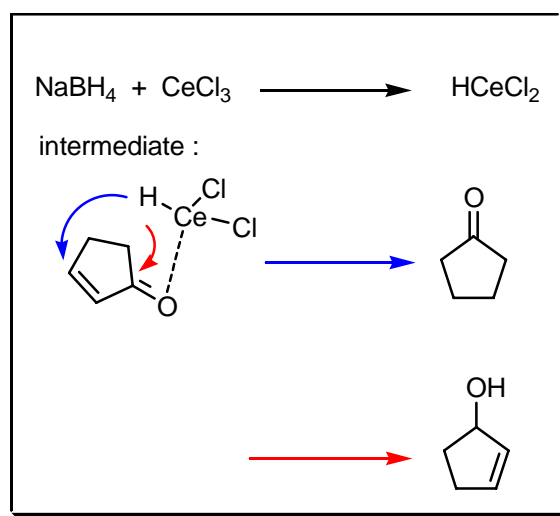
## COMMENTS :

## LUCHE REDUCTION

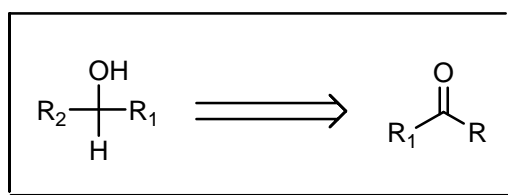
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The addition of cerium salts to  $\text{NaBH}_4$  gives very chemoselective 1,2-reduction of conjugated aldehydes and ketones. If the complex is formed irreversibly hydride transfer is under kinetic control (1,2-addition). If however the complex forms reversibly the reaction is under thermodynamic control (1,4-reduction). The exact mechanism is complicated. It is believed that an alkoxy borohydride is the active species. The cerium catalyses the formation of this species and increases the electrophilicity of the carbonyl atom.

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Smith – March : 1197

Smith 2<sup>nd</sup> : 330, 365

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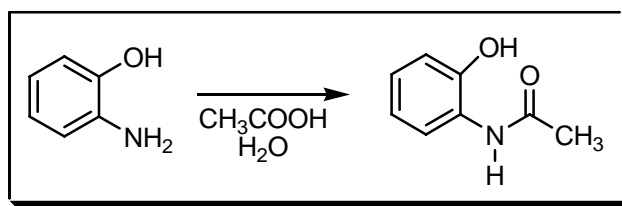
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**COMMENTS :**

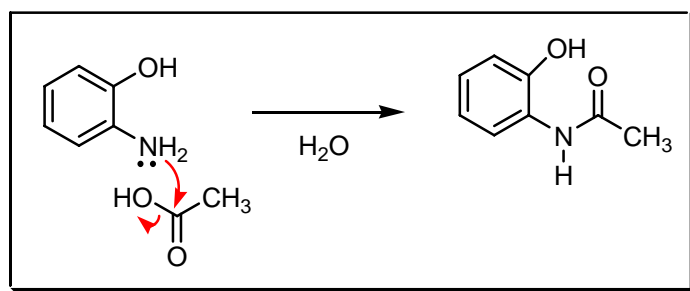
## LUMIÈRE – BARBIER ACETYLATION

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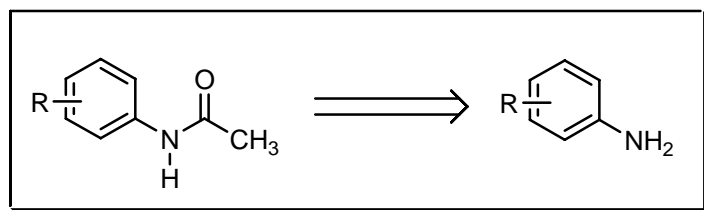
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**

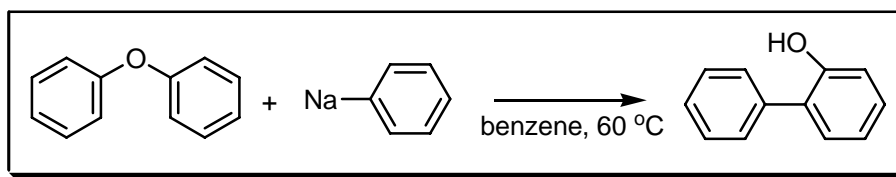
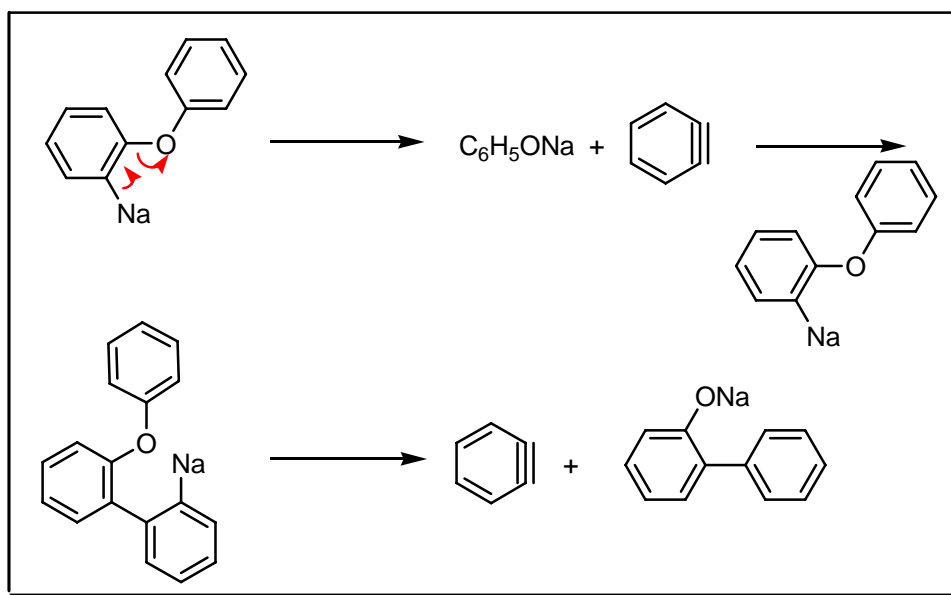


**NOTES :**

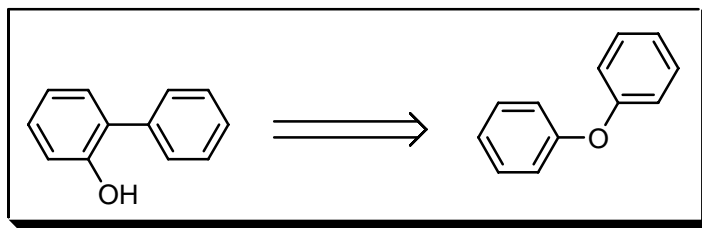
Aromatic amines are acetylated using a solution of acetic anhydride in cold water. See also **Chattaway** acetylation, **Einhorn** acylation, **Galat – Elion**, **Schotten – Baumann** and **Weinreb** reactions.

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**COMMENTS :****LÜTTRINGHAUS REARRANGEMENT****EXAMPLE :****MECHANISM :**

**DISCONNECTION :**



**NOTES :**

Diarylethers are rearranged to the *o*-arylphenol with phenyl sodium under anaerobic conditions.

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**COMMENTS :**

**M**

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**F**

FUKUYAMA – MITSUNOBU REACTION · 1212

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**H**

HOULIHAN MODIFICATION · 1123

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**M**

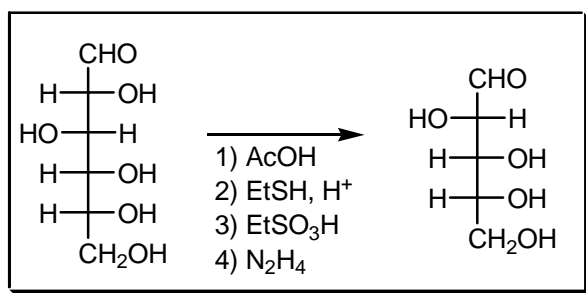
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MACDONALD PORPHYRIN SYNTHESIS · 1121  
MADELUNG INDOLE SYNTHESIS · 1122  
MAGNUS INDOLE SYNTHESIS · 1124  
MAITLAND – JAPP REACTION · 1125  
MAJETICH ANNULATION · 1127  
MAKAROV–ZEMLYANSKIĬ – PROKIN SYNTHESIS · 1128  
MAŁOŚZA VICARIOUS NUCLEOPHILIC SUBSTITUTION · 1128  
MALAPRADE REACTION · 1130  
MANN ETHER DEALKYLATION · 1131  
MANNICH REACTION · 1133  
MANSUY – EVANS REACTION · 1135  
MAQUENNE SYNTHESIS · 1136  
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MARTIN INDOLE SYNTHESIS · 1142  
MARTINET SYNTHESIS · 1143  
MASAMUNE MACROLACTONISATION · 1145  
MASCARELLI FLUORENE SYNTHESIS · 1146  
MATHEWS DRY HYDROLYSIS · 1147  
MATTESON REACTION · 1149  
MAURER – DREFAHL SYNTHESIS · 1151  
MAYER SYNTHESIS · 1152  
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McFADYEN – STEVENS REACTION · 1158  
McLAFFERTY REARRANGEMENT · 1159  
McMURRY OLEFINATION · 1161  
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MEER ter REACTION · 1164  
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MEERWEIN ARYLATION · 1166  
MEERWEIN METHYLATION · 1168  
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MENSCHUTKIN REACTION · 1177  
MENTZER PYRONE SYNTHESIS · 1178  
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METH–COHN QUINOLINE SYNTHESIS · 1180  
MEYER – HARTMANN SYNTHESIS · 1182  
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MEYER REACTION · 1189  
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MICHAEL CONDENSATION · 1193  
MICHAEL GLYCOSIDATION · 1195  
MICHAELIS – BECKER – NYLÉN PHOSPHONYLATION · 1196  
MIDLAND REDUCTION · 1197  
MIESCHER DEGRADATION · 1199  
MIGITA – SANO SYNTHESIS · 1200  
MILAS HYDROXYLATION OF OLEFINS · 1202  
MILLER – PLÖCHL SYNTHESIS · 1203  
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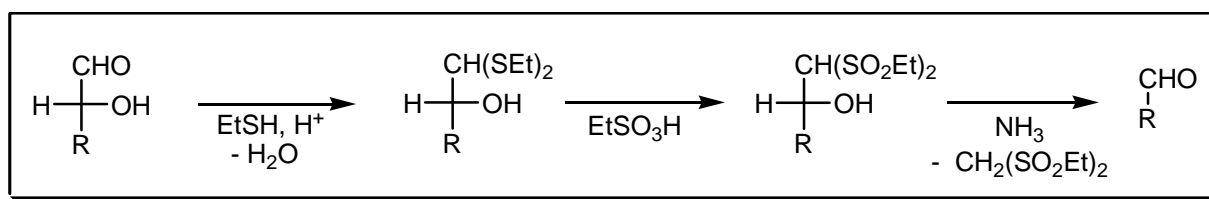


## MACDONALD – FISCHER SUGAR DEGRADATION

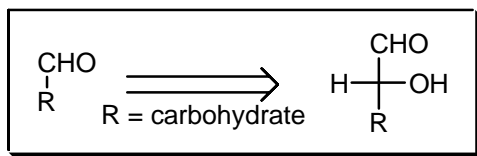
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

An aldose is condensed with ethylmercaptan and hydrochloric acid to a mercaptal followed by oxidation with e.g. perpropionic acid to a disulfone. The disulfone is cleaved with ammonia. See also **Ruff – Fenton** and **Wohl** reactions.

### REFERENCES :

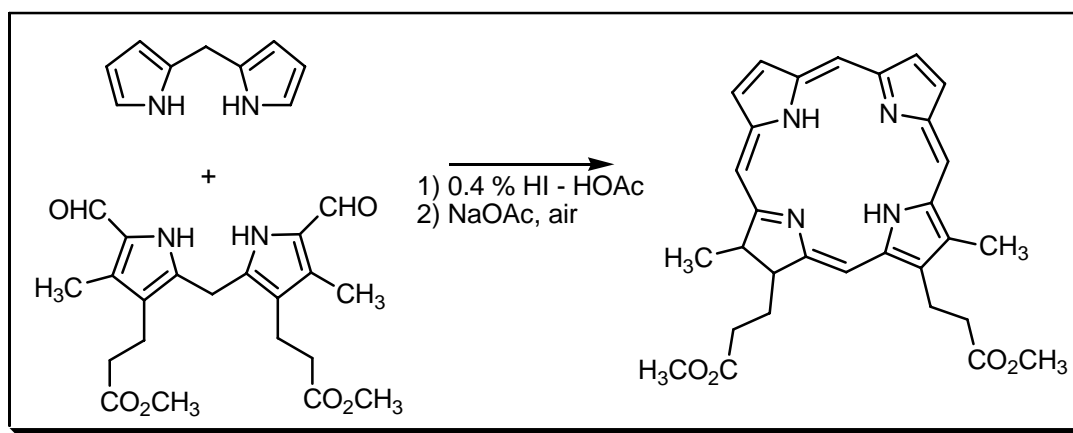
Houben – Weyl : E11, 1248

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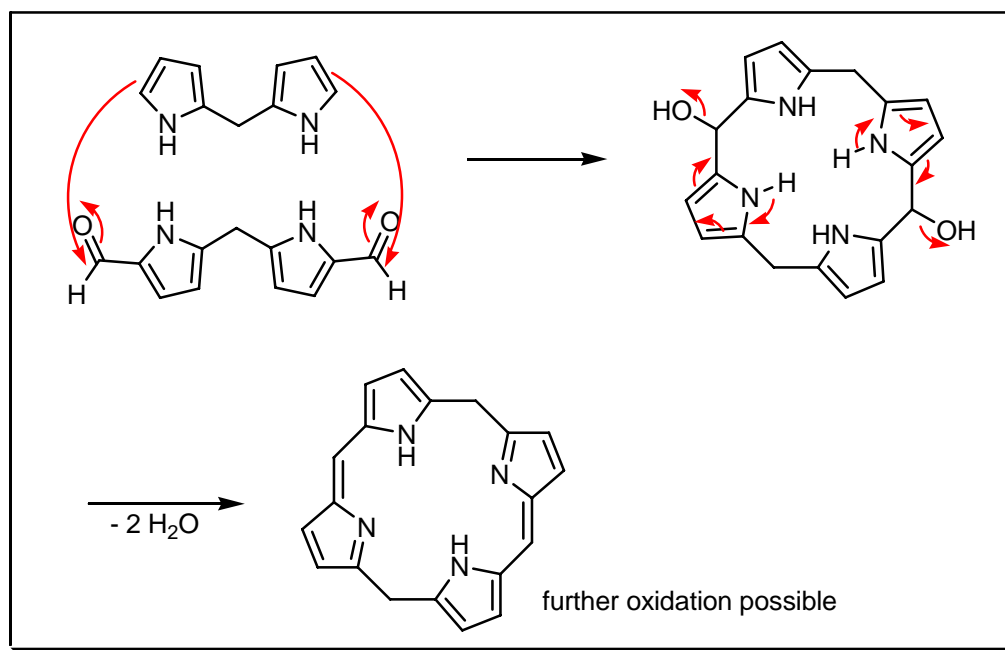
COMMENTS :

MACDONALD PORPHYRIN SYNTHESIS

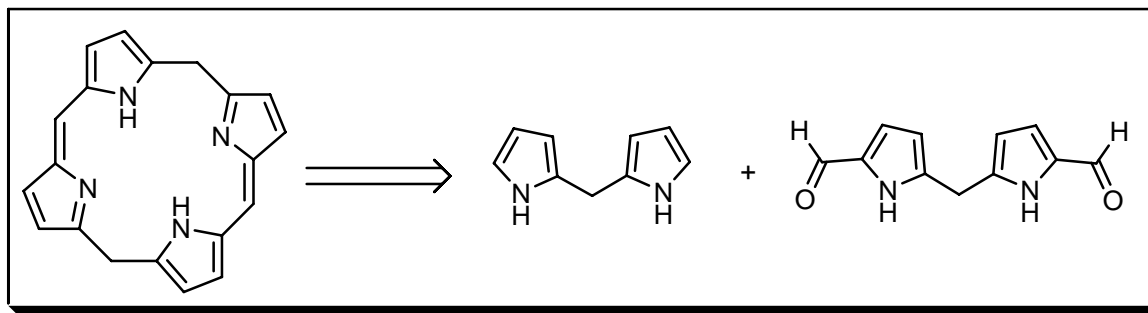
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The porphyrin synthesis from dipyrromethanes. This reaction is normally used for the synthesis of porphyrins with  $C_2$  symmetry. See also **Adler – Longo, Lindsey, Rothmund** and **Taniguchi** reactions.

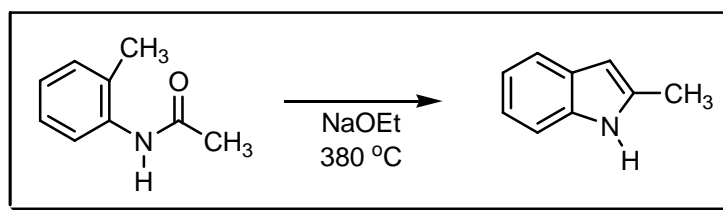
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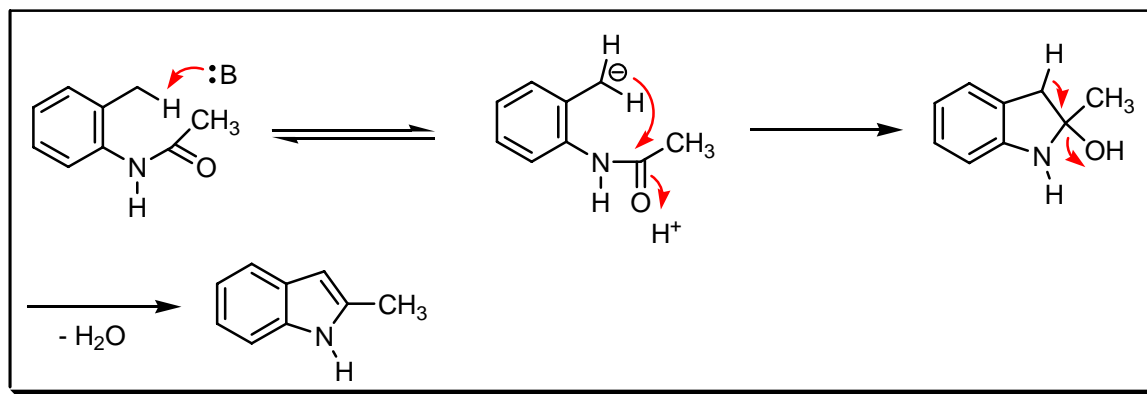
## COMMENTS :

## MADELUNG INDOLE SYNTHESIS

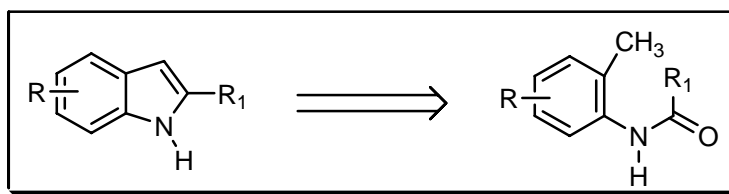
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Indoles are obtained by heating *N*-acyl-*o*-toluidines originally at high temperature with a base, e.g. alkali alkoxide, sodamide, in the absence of air. The **Houlihan** modification (through lithiation) is preferred above the classic reaction. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

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**Org. Synth. Coll. Vol.** : **3**, 479

**Science of Synthesis** : **10**, 443

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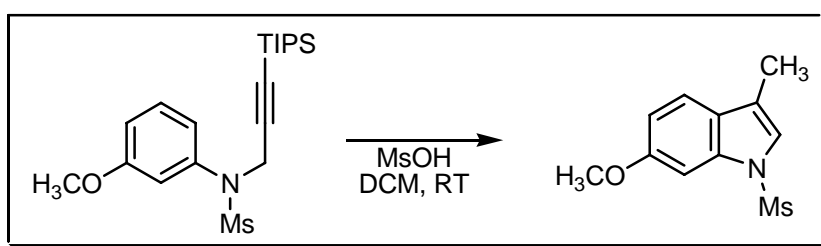
**COMMENTS :**

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**MAGNUS INDOLE SYNTHESIS**

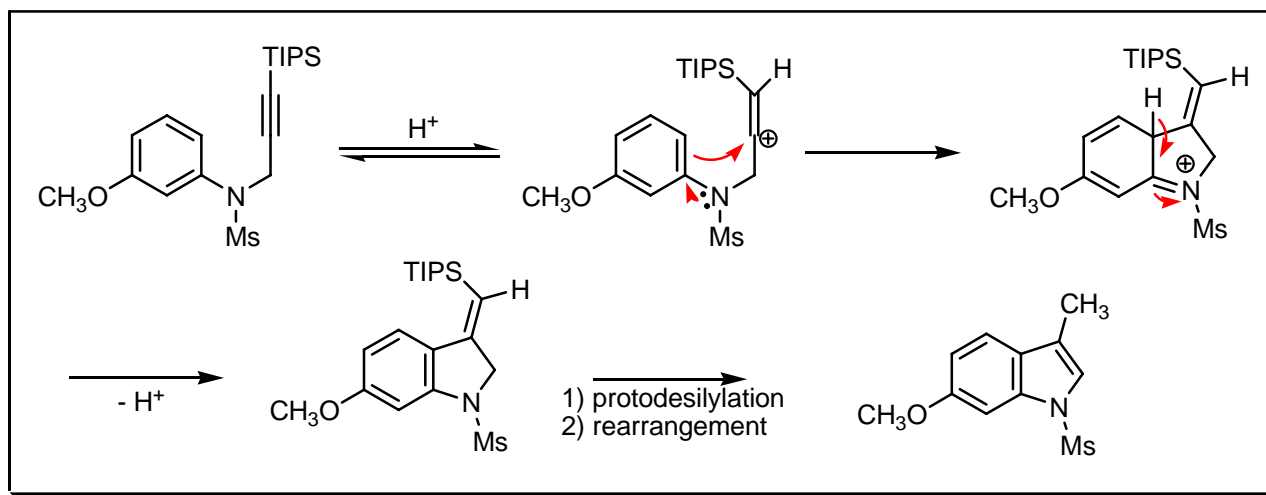
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**EXAMPLE :**



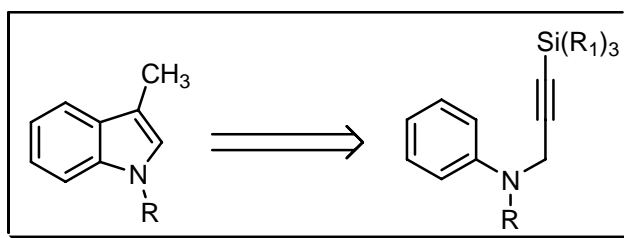
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**MECHANISM :**



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**DISCONNECTION :**



## NOTES :

3-Methyl indoles are formed after treating triisopropylsilylprop-2-ynylanilines with methanesulfonic acid. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

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## REFERENCES :

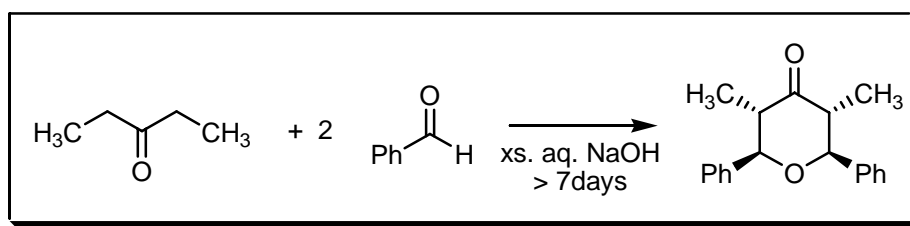
- 1) P. Magnus; I.S. Mitchell, *Tetrahedron Lett.*, 1998, **39**, 4595.
  - 2) G.W. Gribble, *J. Chem. Soc., Perkin Trans. 1*, 2000, 1045.
- 

## COMMENTS :

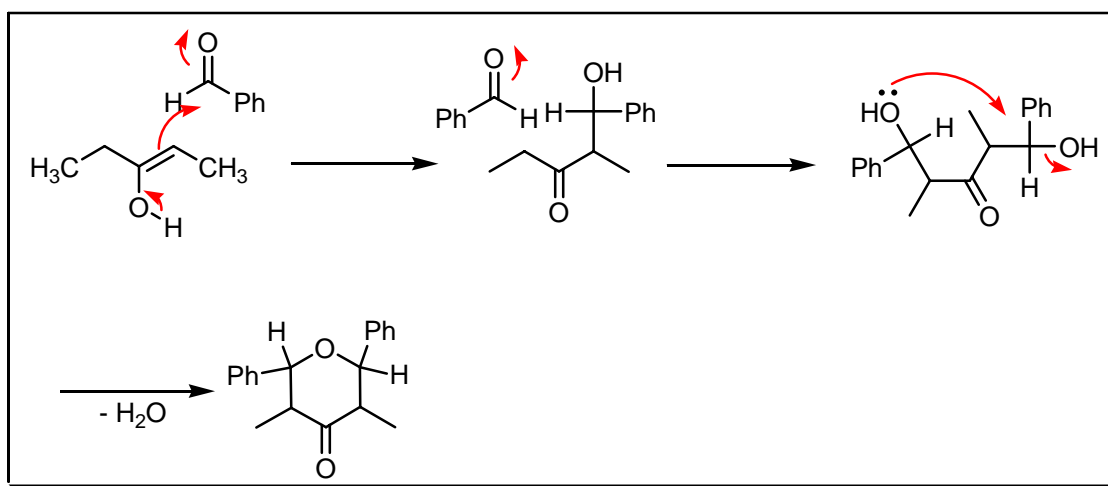
## MAITLAND – JAPP REACTION

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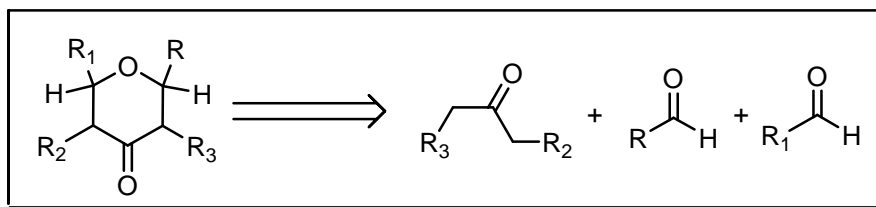
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Single diastereoisomers of THP products can be prepared from a ketone and 2 molecules of aldehydes. Several catalytic variants have been published.

## REFERENCES :

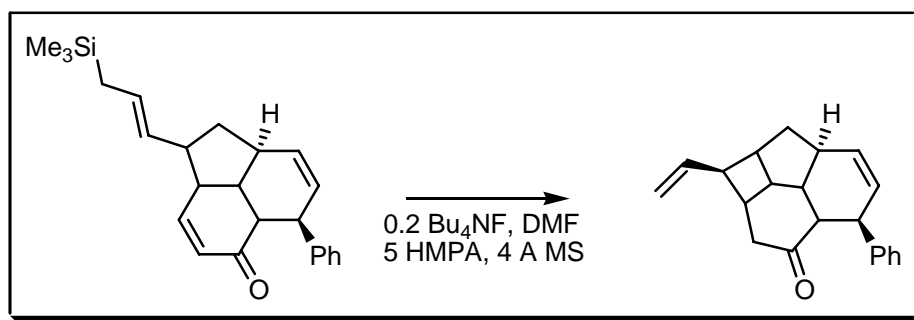
- 1) F.R. Japp; W. Maitland, *J. Chem. Soc.*, 1904, **85**, 1473.
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- 6) P.A. Clarke; W.H.C. Martin; J.M. Hargreaves; C. Wilson; A.J. Blake, *Chem. Commun.*, 2005, 1061.
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## COMMENTS :

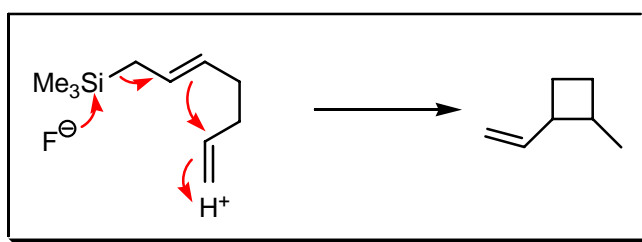
## MAJETICH ANNULATION

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### EXAMPLE :



### MECHANISM :



### NOTES :

This is an *intramolecular* **Hosomi – Sakurai** reaction to set-up different ring sizes (4, 5, 6, 7, 8). See also **Hosomi – Sakurai** reaction.

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### REFERENCES :

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  - 2) G. Majetich; A.M. Casares; D. Chapman; M. Behnke, *J. Org. Chem.*, 1986, **51**, 1753.
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  - 4) S.A. May; P.A. Grieco; H.-H. Lee, *Synlett*, 1997, 493.
- 

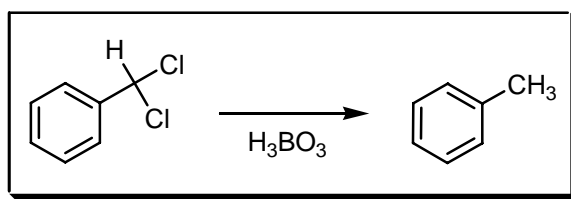
### COMMENTS :



## MAKAROV–ZEMLYANSKIĬ – PROKIN SYNTHESIS

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### EXAMPLE :



### NOTES :

1-(Dichloromethyl)benzene is selectively hydrolysed by boric acid. Benzyl chloride or benzotrichloride are unaffected.

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### REFERENCES :

Ya.Ya. Makarov–Zemlyanskiĭ; S.S. Prokin, *J. Appl. Chem. (USSR)*, 1936, **9**, 2207. (*Chem. Abs.*, 1937, **31**, 4659.)

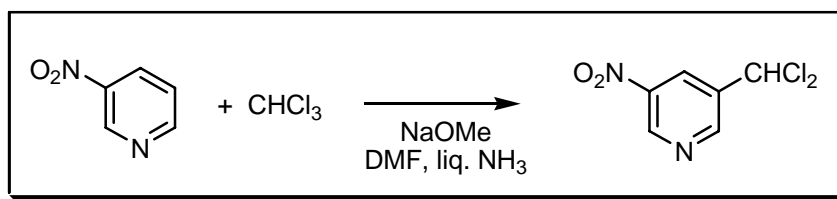
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### COMMENTS :

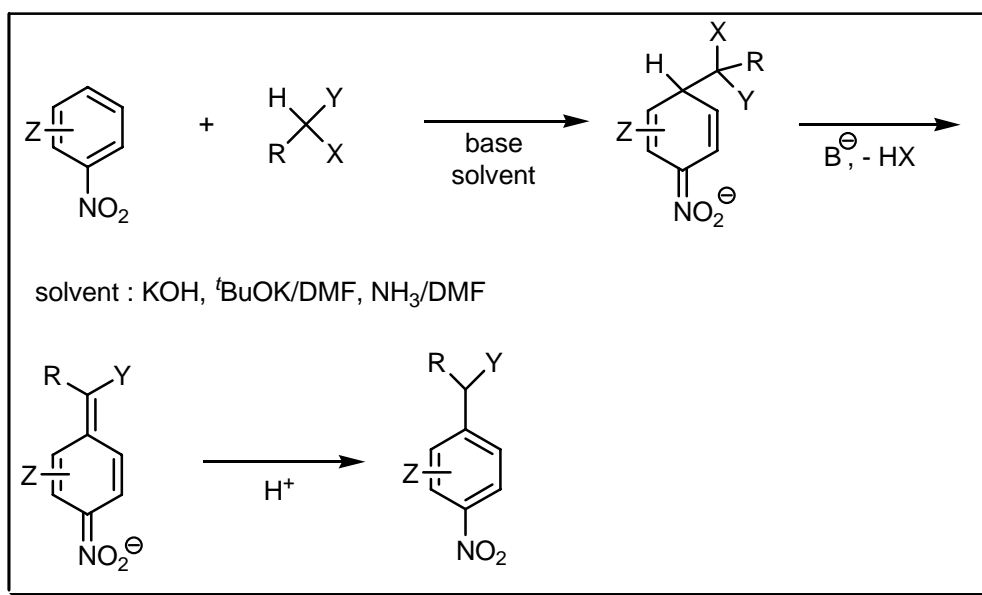
## MAKOSZA VICARIOUS NUCLEOPHILIC SUBSTITUTION

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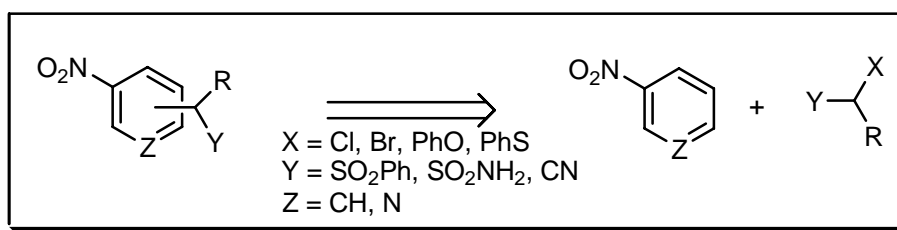
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The nucleophilic substitution of hydrogen in the *ortho* or *para* position of arenes, heteroarenes or nitro derivatives of these compounds. The mechanism goes *via* an addition- $\beta$ -elimination pathway. This synthesis can also be used to make indoles.

## REFERENCES :

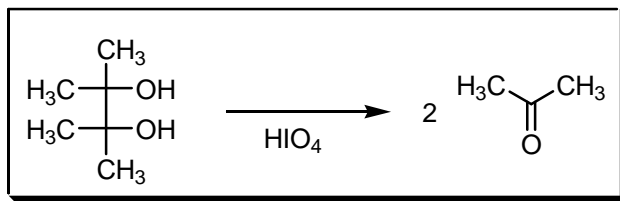
**Science of Synthesis** : 10, 437, 454, 459, 544

- 1) J. Goliński; M. Mąkosza, *Tetrahedron Lett.*, 1978, **32**, 3495.
- 2) T. Glinka; M. Mąkosza, *J. Org. Chem.*, 1983, **48**, 3860.
- 3) M. Mąkosza; J. Winiarski, *Acc. Chem. Res.*, 1987, **20**, 282.
- 4) M. Mąkosza, *Synthesis*, 1991, 103.
- 5) M. Mąkosza; R. Podraza, *Eur. J. Org. Chem.*, 2000, 193.
- 6) N.J. Lawrence; J. Liddle; S.M. Bushell; D.A. Jackson, *J. Org. Chem.*, 2002, **67**, 457.
- 7) T. Lemek; M. Mąkosza; D.S. Stephenson; H. Mayr, *Angew. Chem., Int. Ed.*, 2003, **42**, 2793.

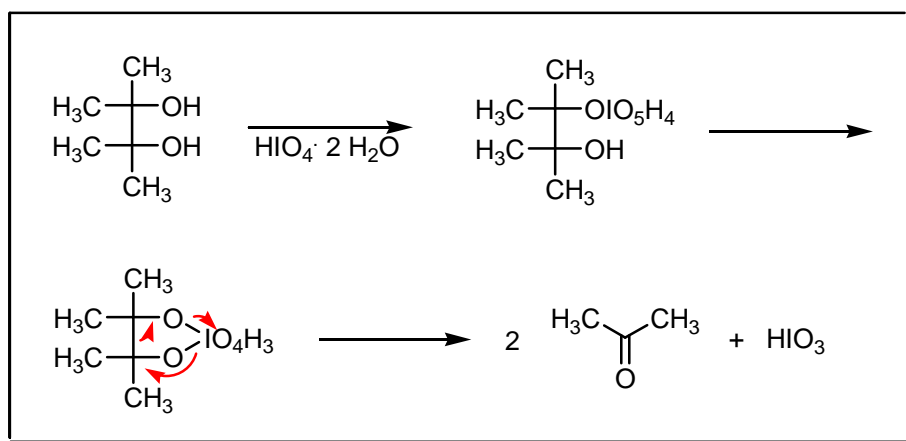
COMMENTS :

## MALAPRADE REACTION

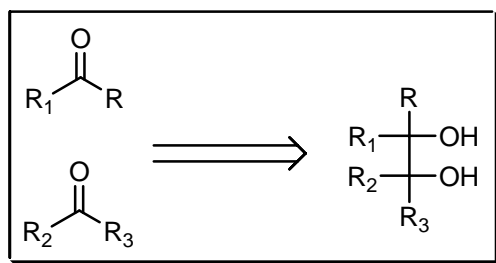
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

$\alpha$ -Glycols undergo quantitative fission at room temperature when treated with periodic acid or its salts. Aldehydes are the normal products but the central carbon of a glycerol residue yields formic acid. Cleavage also occurs with compounds with hydroxyl and amino groups attached to adjacent carbon atoms, with  $\alpha$ -hydroxyaldehydes or ketones,

and with 1,2-diketones. See also **Barry**, **Criegee** glycol cleavage, **Djerassi – Rylander**, **Fischer**, **Hudson – Hirst**, and **Lemieux – Johnson** reactions.

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#### REFERENCES :

**March** : 1174

**Smith – March** : 1519

**Houben – Weyl** : **E3**, 510

**Org. React.** : **2**, 341

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1) L. Malaprade, *Bull. Soc. Chim. Fr.*, 1928, **43**, 683.

2) G.H. Schenk, *J. Chem. Educ.*, 1962, **39**, 32.

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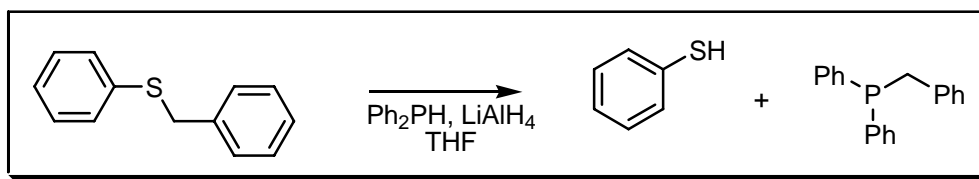
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#### COMMENTS :

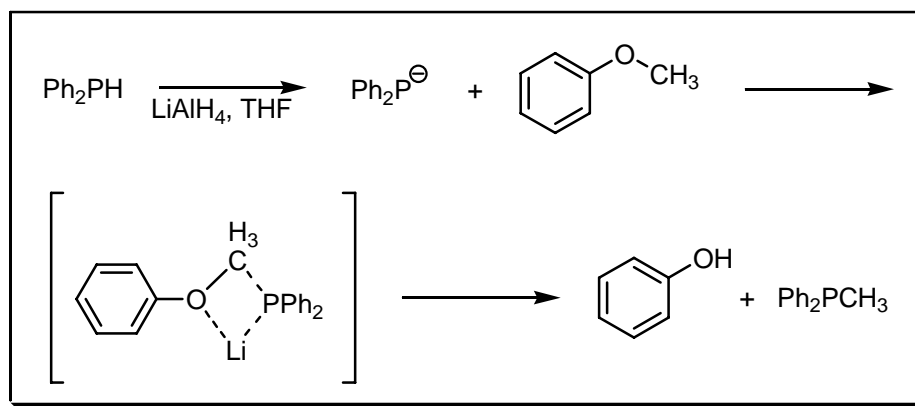
### MANN ETHER DEALKYLATION

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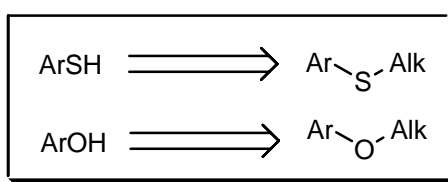
#### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The dealkylation of certain alkyl aryl sulfides and ethers by arsenide ions or diaryl phosphides. The last reaction is much faster than the first one. See also **Gustus** cleavage, **Prey** and **Stoermer** dealkylation.

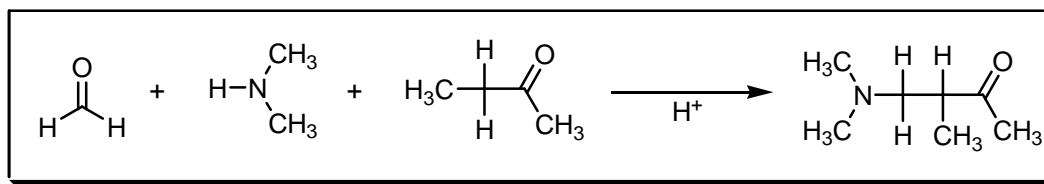
### REFERENCES :

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- 4) G. Vériot; A. Collet, *Acros Organics Acta*, 1995, **1**, 40.

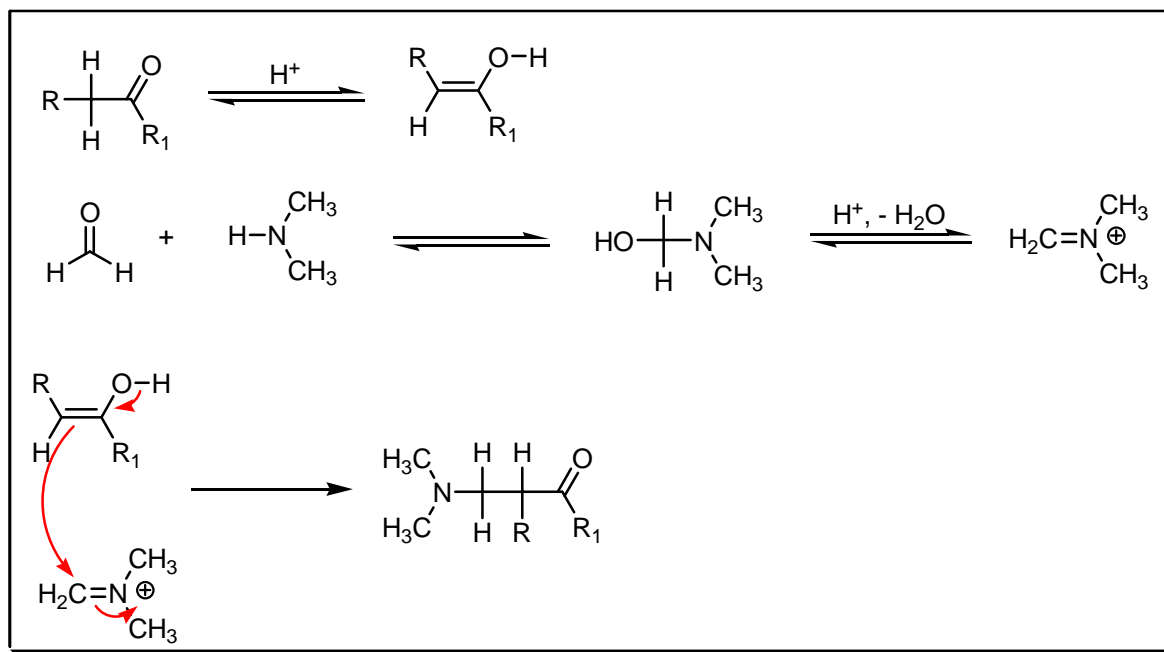
### COMMENTS :

## MANNICH REACTION

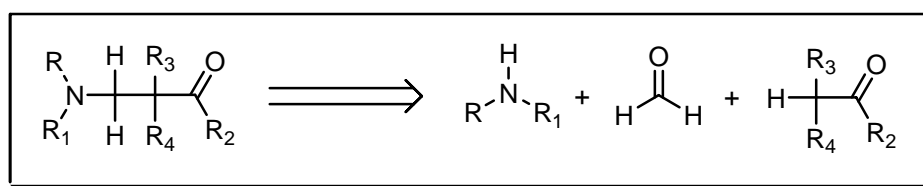
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The condensation of ammonia or a primary or secondary amine usually as the hydrochloride, with formaldehyde and a compound containing at least one reactive hydrogen atom, e.g. acetophenone, in which the hydrogen is replaced by aminomethyl or substituted aminomethyl. **List et al.** introduced a proline-catalysed direct asymmetric three-component **Mannich** reaction. Lewis acid catalysed examples are also known. See also **Asinger**, **Betti**, **Cheney**, **Einhorn – Tscherniac** and **Pictet – Sprengrer** reactions.

### REFERENCES :

**March** : 900

**Smith – March** : 1189

**Smith** : 958

**Smith 2<sup>nd</sup>** : 868

**Houben – Weyl** : **4/2**, 32; **11/1**, 731; **E3**, 642; **E6a**, 100; **E6b**, 1091; **E8c**, 129, 361; **E8d**, 446; **E11**, 781; **E16d**, 1058

**Org. React.** : **1**, 303; **7**, 99

**Org. Synth.** : **23**, 30; **35**, 78; **37**, 18, 52, 73; **57**, 95, 102; **59**, 153

**Org. Synth. Coll. Vol.** : **3**, 305; **4**, 281, 515, 626, 816; **6**, 474, 981, 987

**Science of Synthesis** : **10**, 517, 520, 534, 583, 595, 600, 682

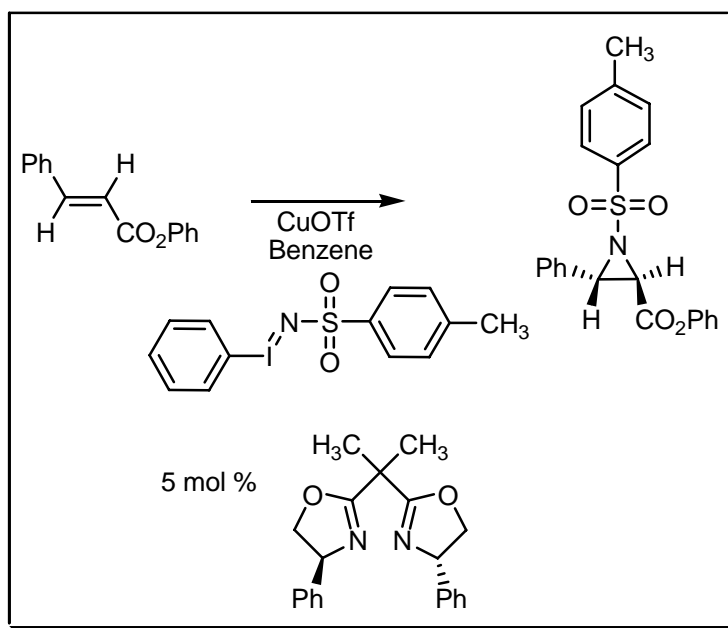
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- 

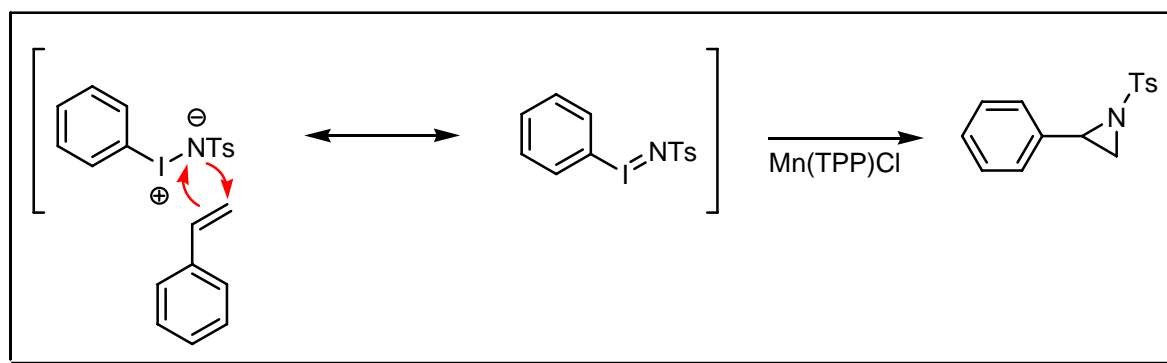
**COMMENTS :**

## MANSUY – EVANS REACTION

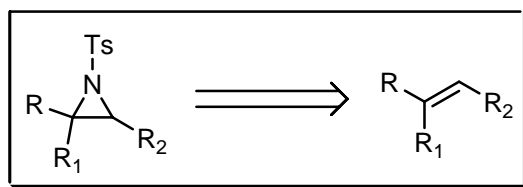
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

**Mansuy** *et al.* investigated the Fe(III) and Mn(III)-derived porphyrin catalysts in the aziridination of olefins employing (*N*-(*p*-tolylsulfonyl)imino)phenyliodine as the nitrene precursor. **Evans** *et al.* extended the scope of this reaction to include both electron-rich and electron-deficient olefins. His study has demonstrated that Cu(I) and Cu(II) chiral bis(oxazoline) complexes are excellent ligands for this reaction. See also **Blum** aziridine, **Gabriel – Marckwald** –



**Cromwell** ethylenimine method, **Hassner** azide aziridine, **Hoch – Campbell**, **Scheiner** and **Wenker** ring-closure reactions.

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## REFERENCES :

**Smith – March** : 1057

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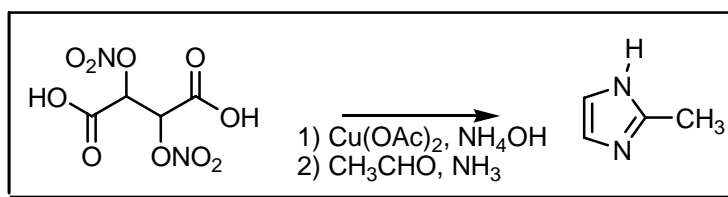
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- 

## COMMENTS :

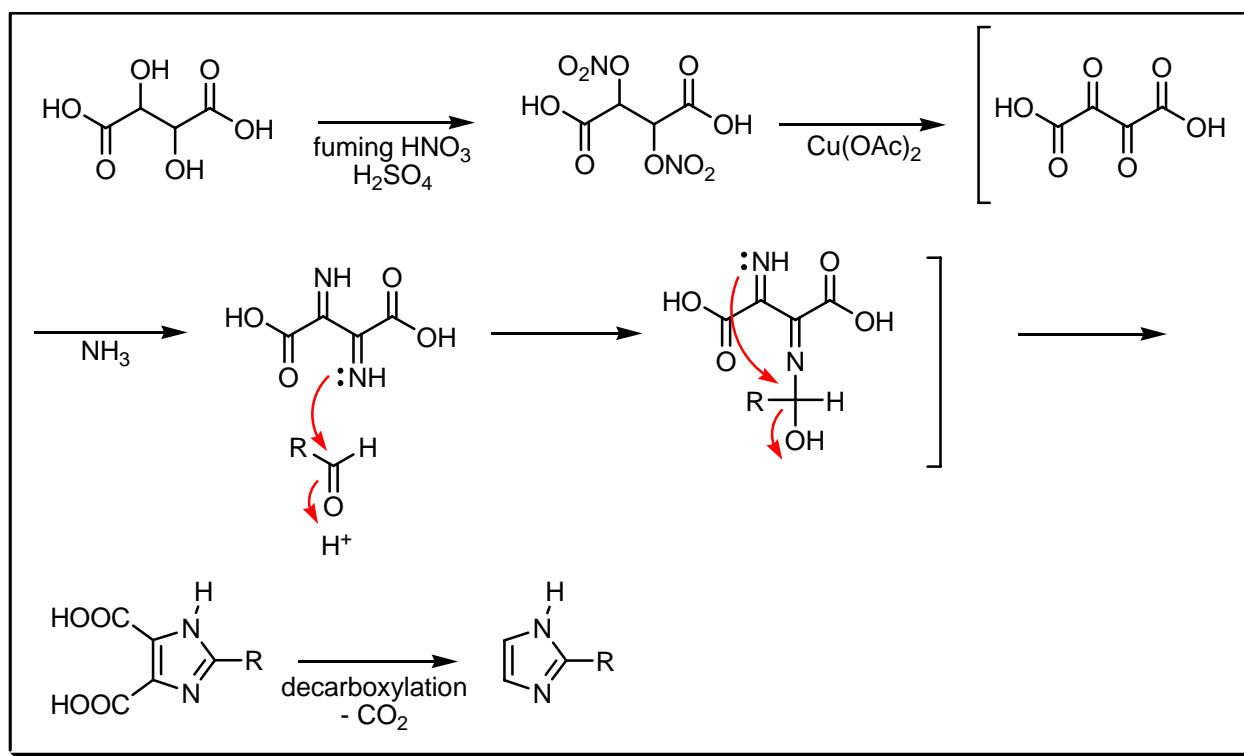
## MAQUENNE SYNTHESIS

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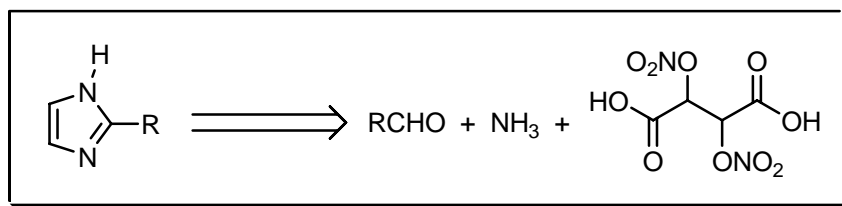
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

This reaction is a modification of the **Debus – Radziszewski** reaction and is very similar to the **Weidenhagen** reaction. See also **Akabori – Neuberg – Fischer**, **Brackeen**, **Bredereck**, **Wallach** imidazole and **Weidenhagen** reactions.

## REFERENCES :

Houben – Weyl : **E8c**, 9, 13, 97

Org. Synth. : **22**, 65

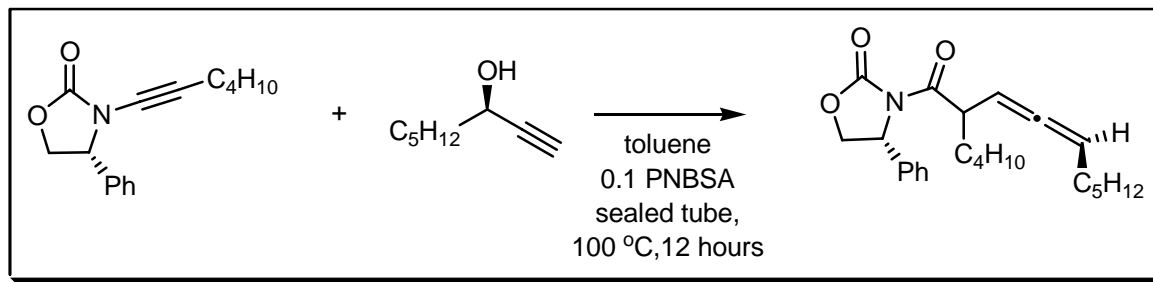
Org. Synth. Coll. Vol. : **3**, 471

Maquenne, *Ann. Chim. (Paris)*, 1891, **24**, 522.

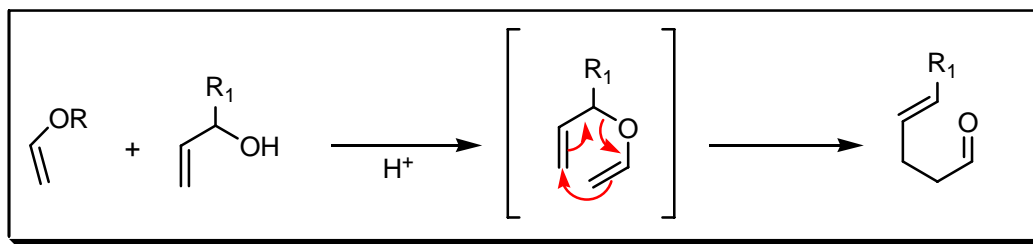
COMMENTS :

MARBET – SAUCY MODIFICATION

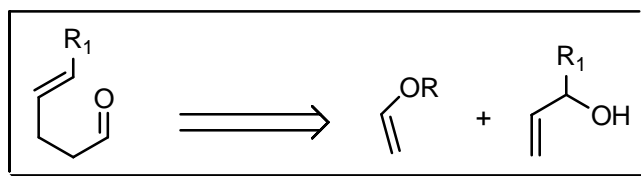
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The acid-catalysed reaction of allylic alcohols and vinyl ethers, the *in situ* formed ether undergoes the **Claisen** rearrangement. See also **Belluš – Claisen** rearrangement, **Carroll (Kimel – Cope)**, **Cope**, **Eschenmoser – Meerwein – Claisen** rearrangement, **Ficini – Claisen**, **Johnson – Claisen** and **Overman** rearrangement reactions.

REFERENCES :

Smith : 1240

Smith 2<sup>nd</sup> : 1022

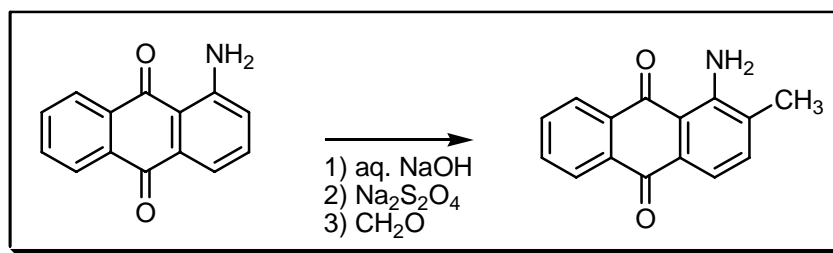
- 1) G. Saucy; L.H. Chopard–dit–Jean; W. Guex; G. Ryser; O. Isler, *Helv. Chim. Acta*, 1958, **41**, 160.
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- 

**COMMENTS :**

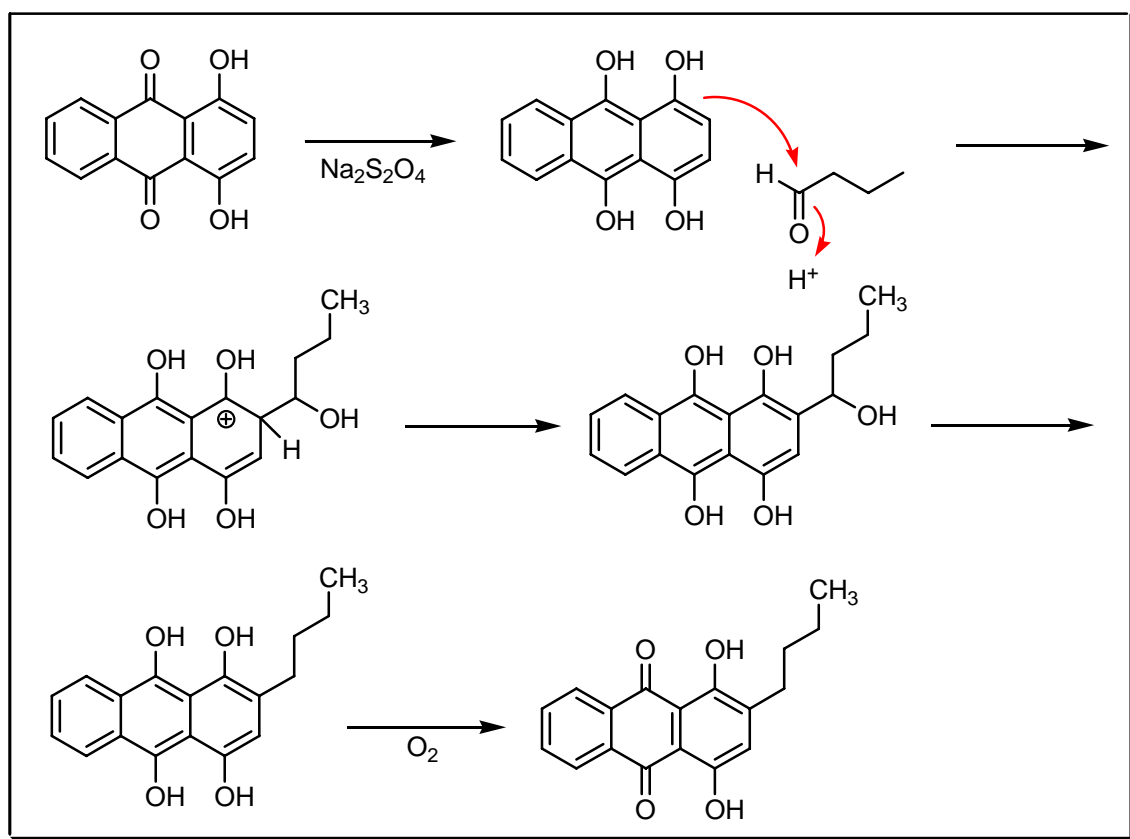
## MARSCHALK AROMATIC ALKYLATION

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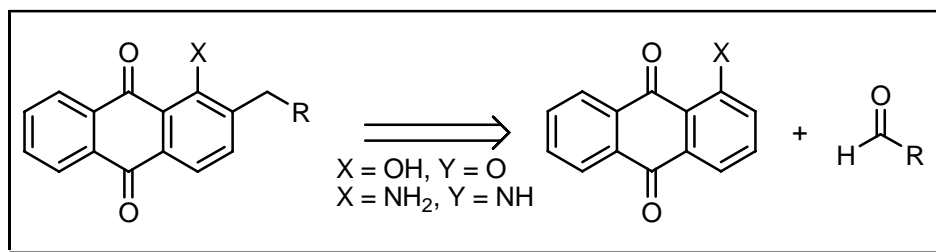
**EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

The alkylation of quinines or aminoquinones with aldehydes. Sodium dithionite reduction of 1-hydroxy- or aminoanthraquinones to their leuco-forms, followed by condensation with aldehydes to yield the 2-alkylated anthraquinones. 2-Hydroxyanthraquinones yield 1-alkylated products.

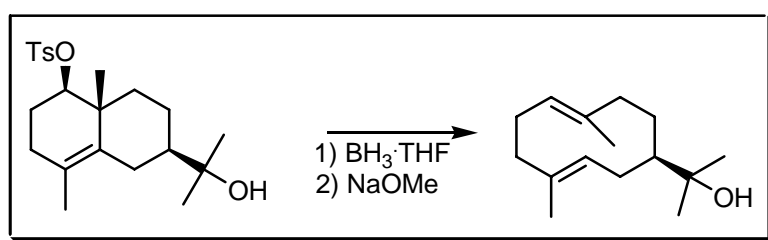
## REFERENCES :

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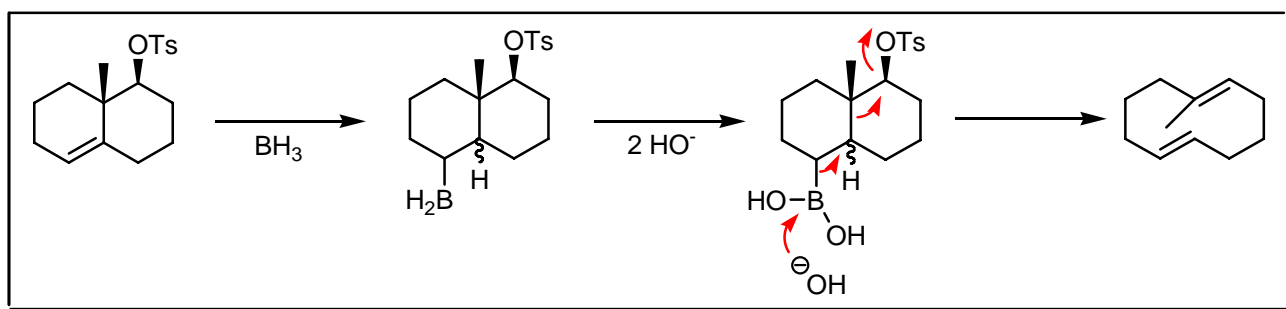
**COMMENTS :**

**MARSHALL – MINNAARD FRAGMENTATION**

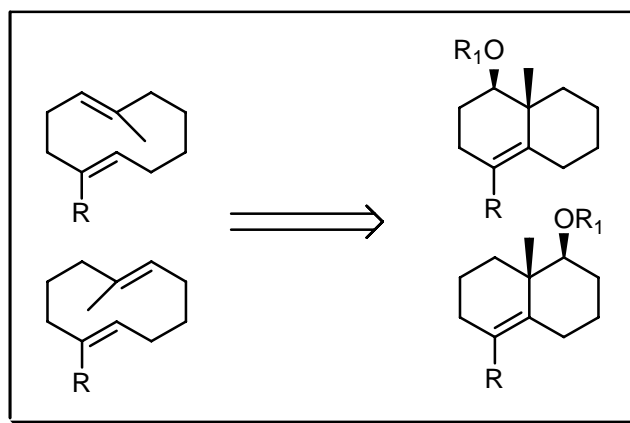
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

This is a diene synthesis *via* a boronate **Grob** fragmentation. See also **Grob** fragmentation and **Wharton** fragmentation.

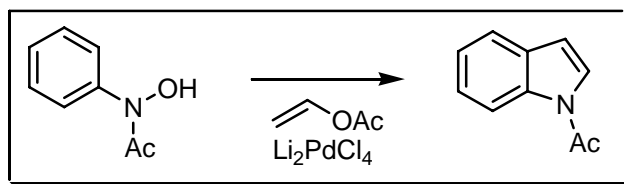
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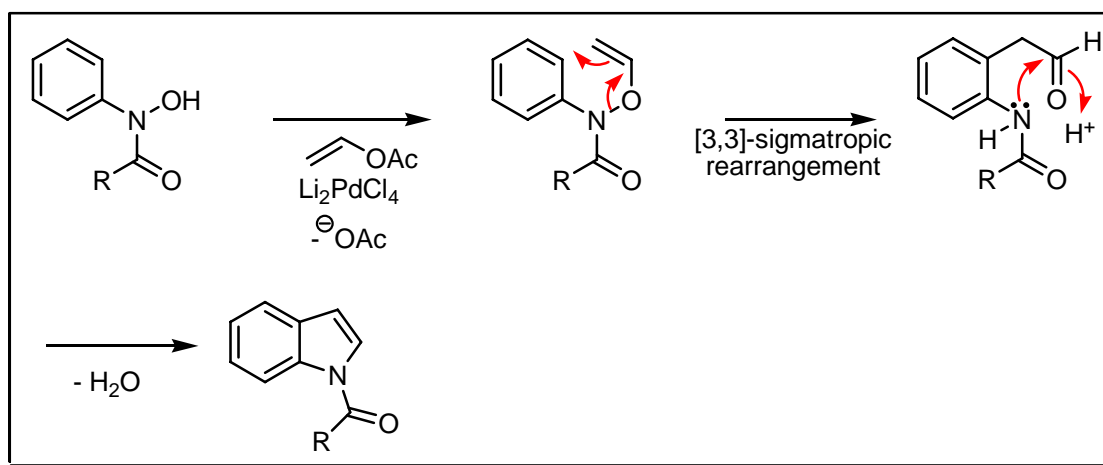
## COMMENTS :

## MARTIN INDOLE SYNTHESIS

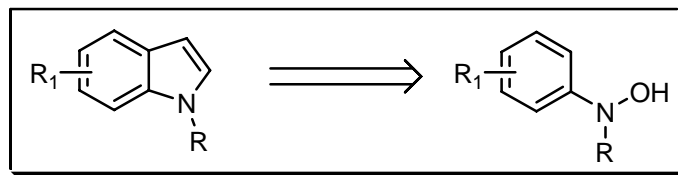
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

*N*-phenylhydroxamic acids react with vinyl acetate in the presence of  $\text{Li}_2\text{PdCl}_4$  to give 2,3-unsubstituted *N*-acylindoles via hetero-**Cope** rearrangement of the intermediate *N*-phenyl-*O*-vinylhydroxylamine. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

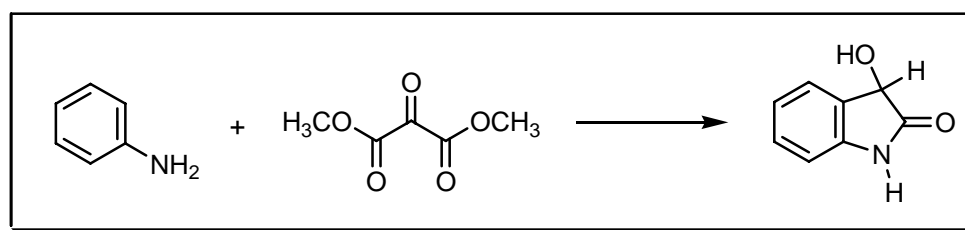
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## COMMENTS :

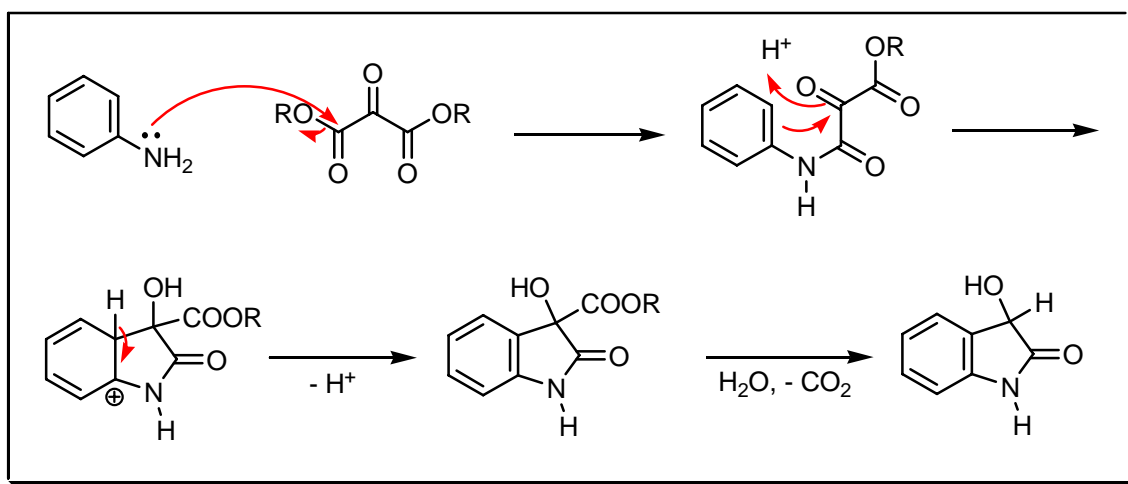
## MARTINET SYNTHESIS

### EXAMPLE :

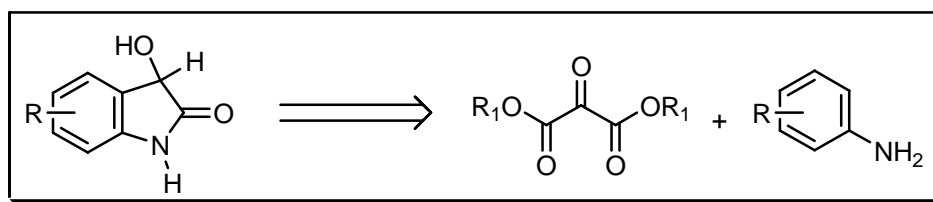




### MECHANISM :



### DISCONNECTION :



### NOTES :

Alkyl oxomalonate condenses with primary or secondary arylamine to yield a dioxindole-3-carboxylate, which with alkali in the absence of oxygen yields the dioxindole. See also **von Baeyer** oxindole, **Brunner**, **Gassman** oxindole, **Hinsberg** oxindole, **Neber – Bosset** and **Stollé** reactions.

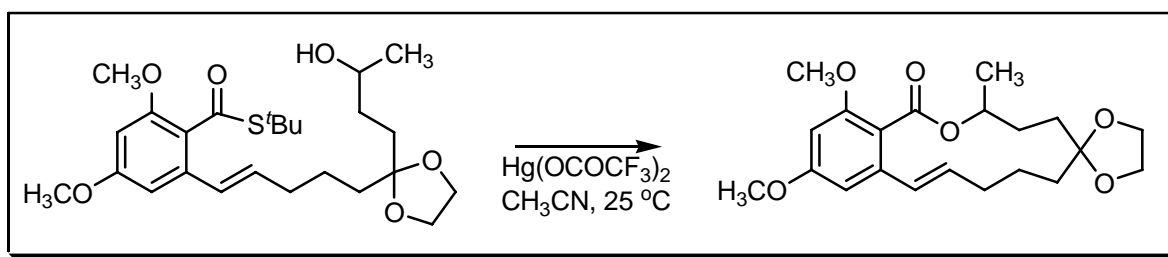
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### COMMENTS :

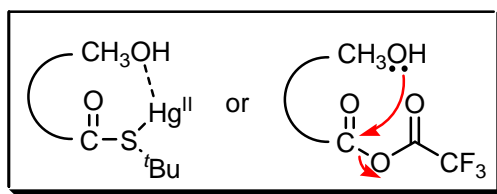
# MASAMUNE MACROLACTONISATION

## EXAMPLE :

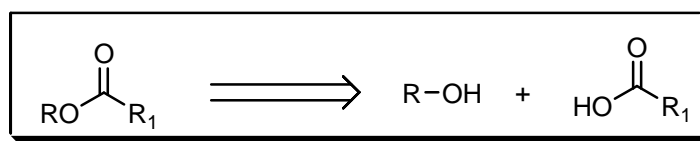


## MECHANISM :

### Proposed intermediate :



## DISCONNECTION :



## NOTES :

In this macrolactonisation the activating effect of the thiol ester is used. A rapid lactonisation occurs when *S*-*tert*-butyl thioester of hydroxyl acid reacts with an electrophilic Hg(II)-compound. The mechanism has not been fully clarified. See also **Corey – Nicolaou**, **Diels – Alder**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Kita**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolkiewicz**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

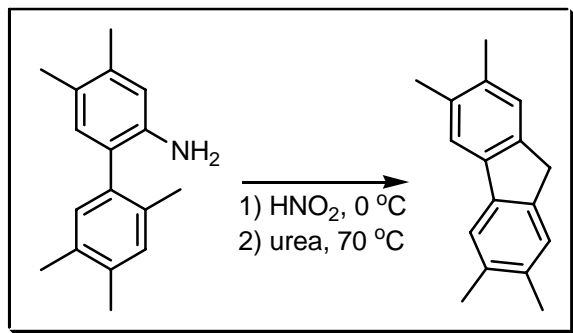
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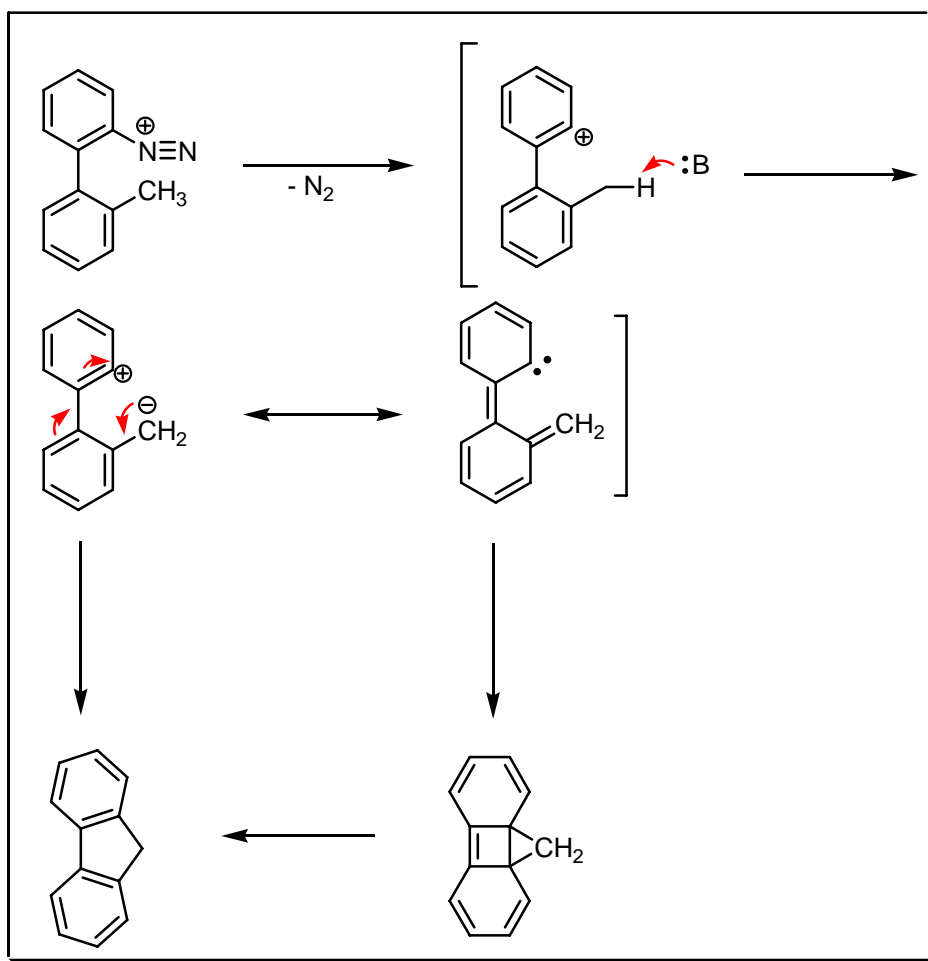
COMMENTS :

## MASCARELLI FLUORENE SYNTHESIS

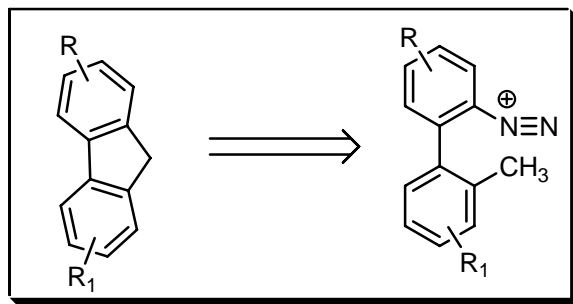
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of fluorenes from 2-amino-2'-alkylbiphenyls *via* diazonium salts. See also **Gomberg – Bachmann – Hey**, **Graebe – Ullmann**, **Larock fluorene**, **Pschorr** and **Ullmann fluorenone** reactions.

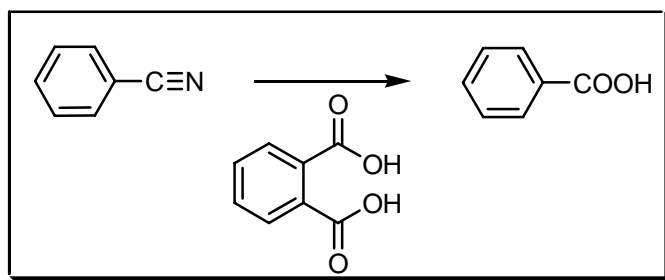
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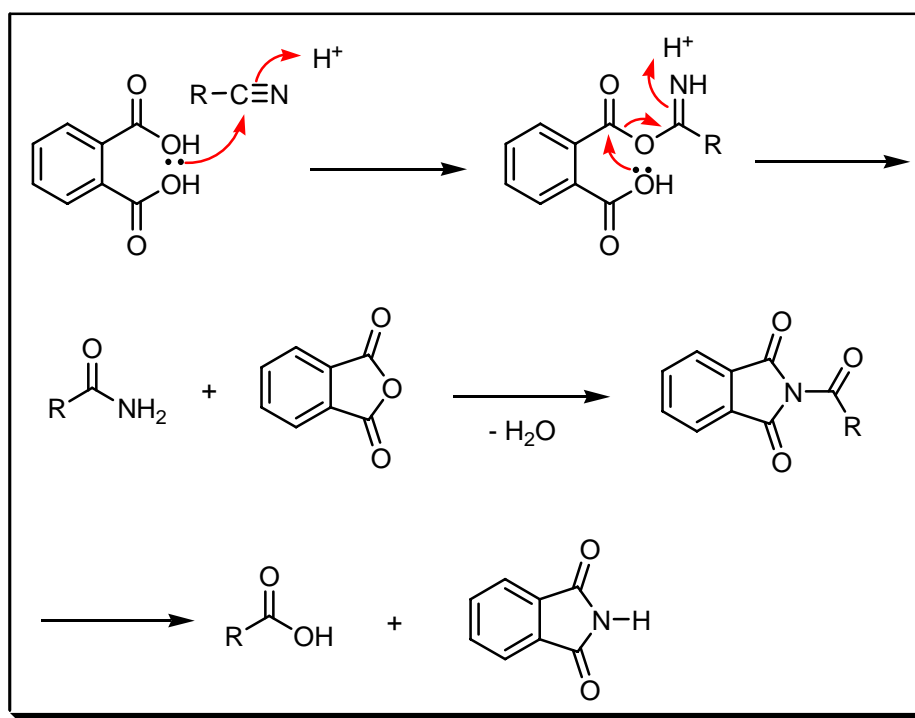
## COMMENTS :

## MATHEWS DRY HYDROLYSIS

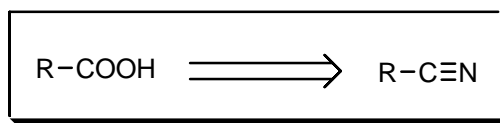
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

This is a one-pot preparation of carboxylic acids ideally under microwave conditions from their corresponding nitriles or amides by a dry hydrolysis process using phthalic acid or anhydride.

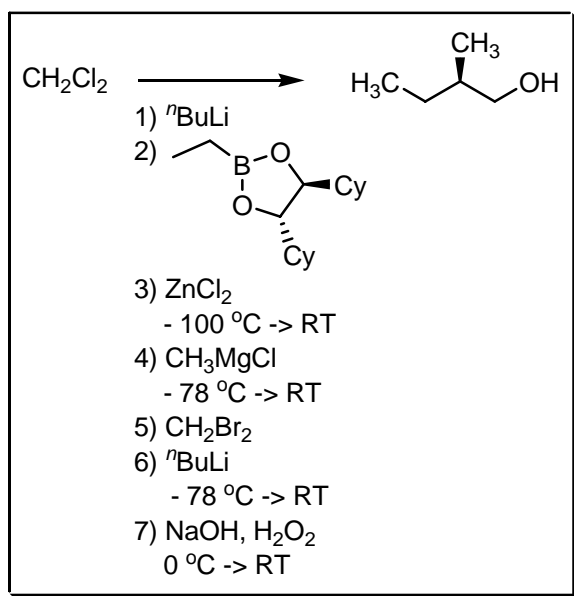
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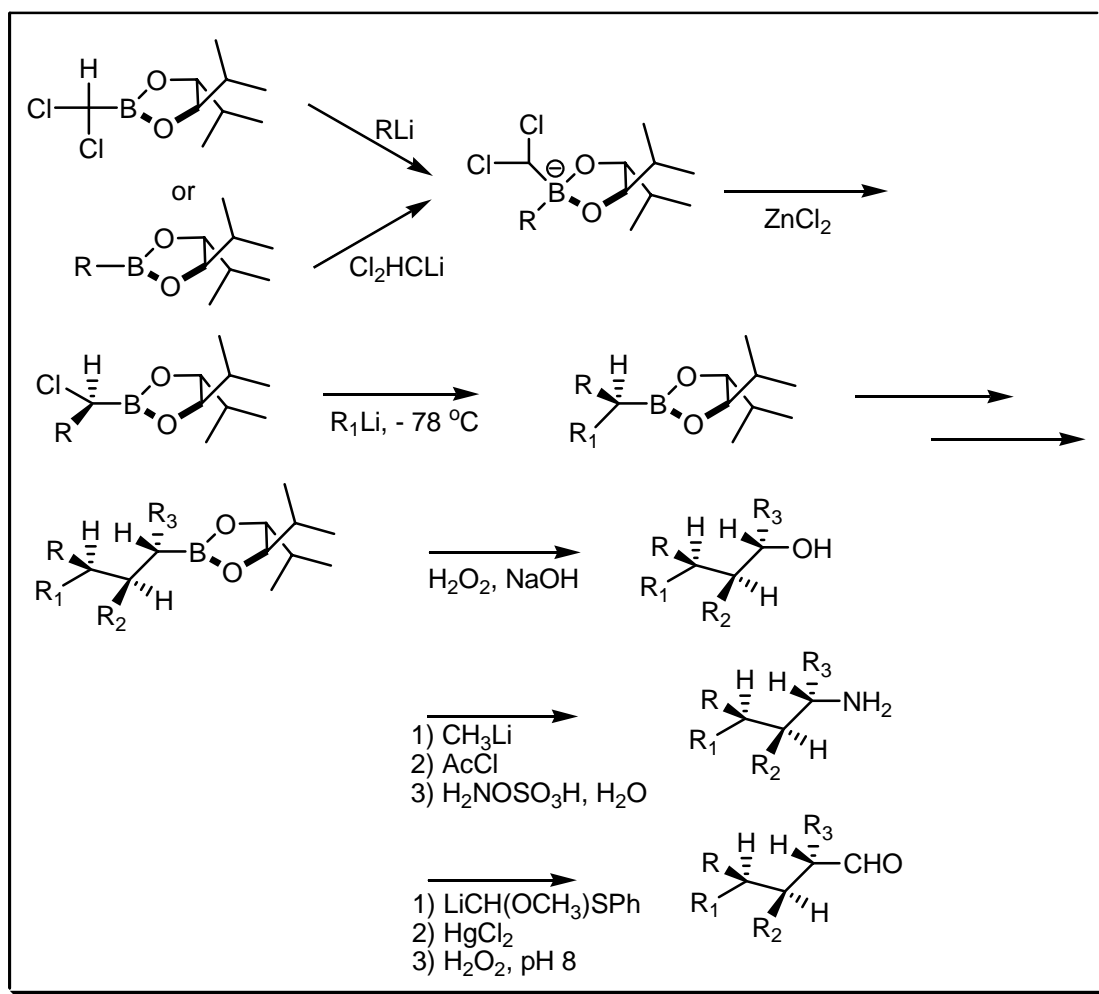
## COMMENTS :

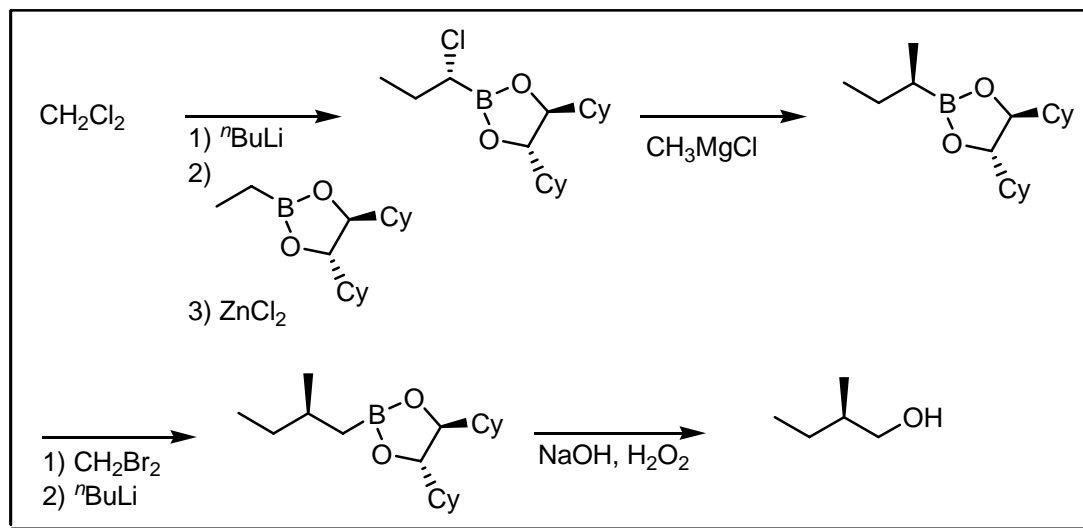
## MATTESON REACTION

### EXAMPLE :

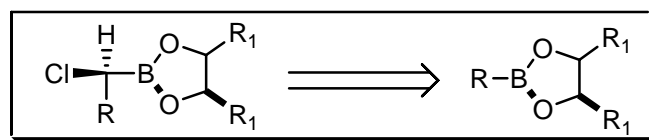


### MECHANISM :





#### DISCONNECTION :



#### NOTES :

The use of boronate esters of chiral  $\text{C}_2$ -symmetrical 1,2-diols for the enantioselective synthesis of a variety of chiral compounds using an one carbon-chain extension. The rearrangement after the addition of zinc chloride is high diastereoselective. This suggests that the zinc cation might complex with one of the boronic ester oxygens. See also **Duthaler – Hafner, Ibuka – Yamamoto, Roush – Hoffmann – Yamamoto and Thomas** reactions.

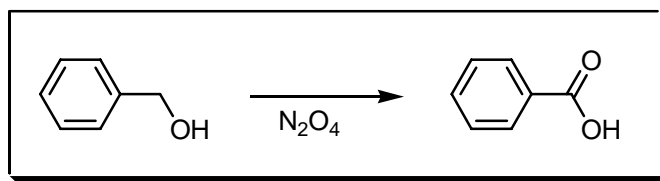
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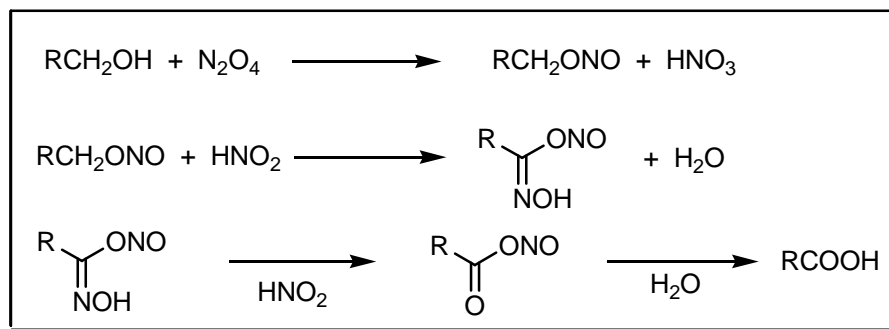
#### COMMENTS :

## MAURER – DREFAHL SYNTHESIS

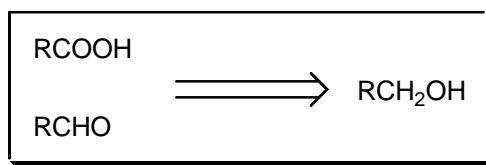
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The oxidation of primary or secondary aliphatic or aromatic alcohols by dinitrogen tetroxide to aldehydes or carboxylic acids. The reaction is of value in carbohydrate chemistry. The dinitrogen tetroxide reacts explosively with glycol and glycerol. See also **Anelli**, **Ball – Goodwin – Morton**, **Collins**, **Corey – Kim**, **Corey – Schmidt**, **Corey – Suggs**, **David – Thieffry**, **Delépine**, **Dess – Martin**, **Einhorn** oxidation, **Fétizon**, **Jones** oxidation, **Ley**, **Mukaiyama** oxidation, **Nicolaou**, **Oppenauer**, **Parikh – von Doering**, **Pfitzner – Moffatt**, **Pinnick**, **Sarett**, **Swern** and **Uemura** reactions.

### REFERENCES :

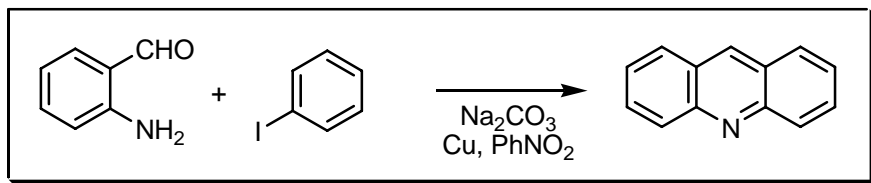
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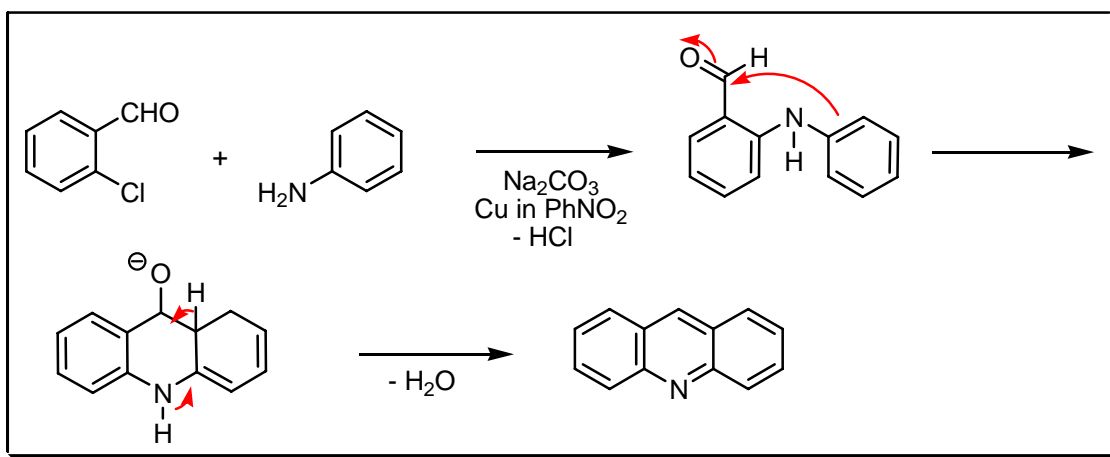
**COMMENTS :**

**MAYER SYNTHESIS**

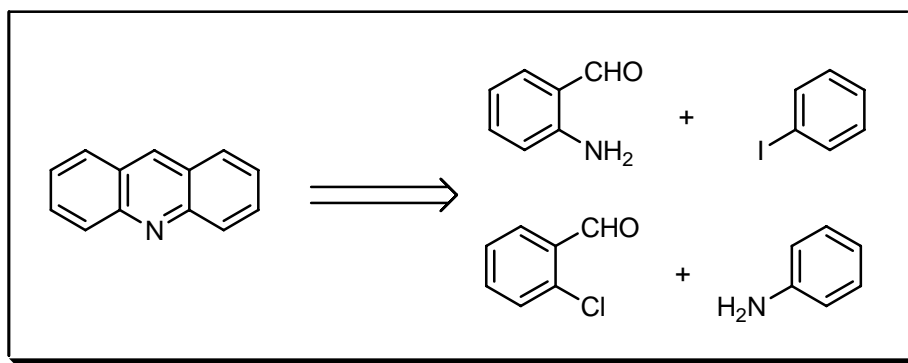
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

o-Aminobenzaldehyde is condensed with a halogenobenzene in the presence of alkali and copper in nitrobenzene or naphthalene as a solvent. The diphenylamine-aldehyde, thus formed is cyclised by concentrated sulfuric acid to an

acridine. The diphenylamine-aldehydes may also be prepared from *o*-halogenobenzaldehydes and aromatic amines preferably *o*-nitroamines. 1-Amino-antraquinones react also with *o*-chloro benzaldehydes. See also **Kondo – Uyeyo** and **Ullmann diaryl** reactions.

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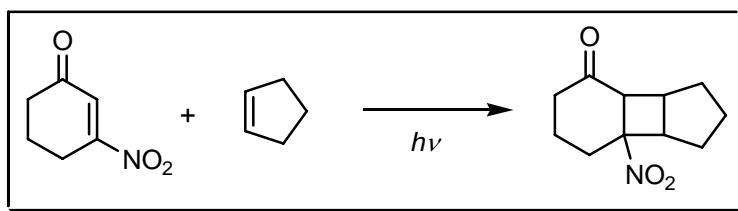
#### COMMENTS :

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### de MAYO REACTION

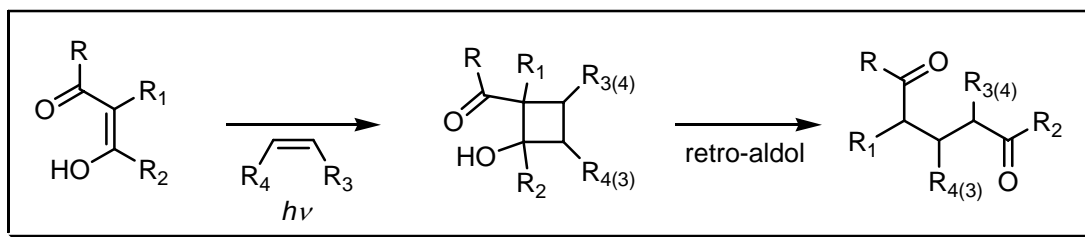
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#### EXAMPLE :



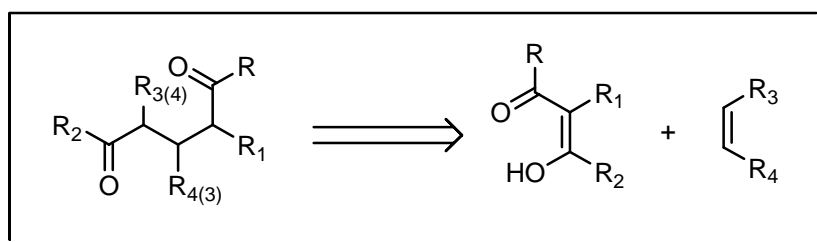
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#### MECHANISM :



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#### DISCONNECTION :



## NOTES :

The photo-addition of enol derivatives of 1,3-diketones and derivatives to olefins. With 1,3-diketones a retro-aldol type reaction occurs to afford 1,5-diketones.

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## REFERENCES :

Houben – Weyl : 4/5b, 924

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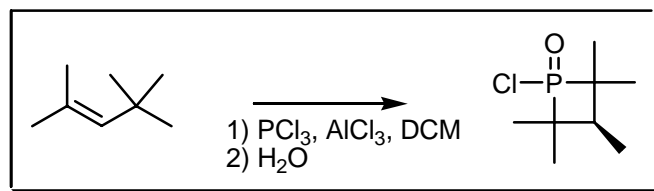
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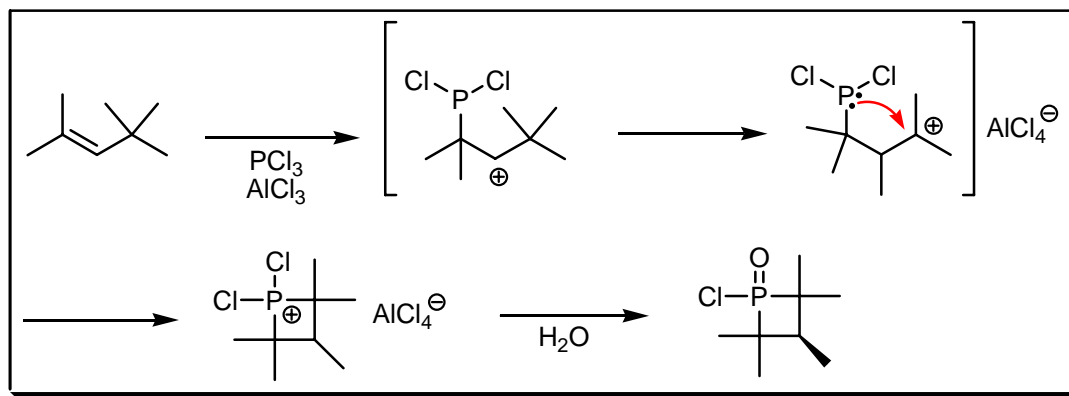
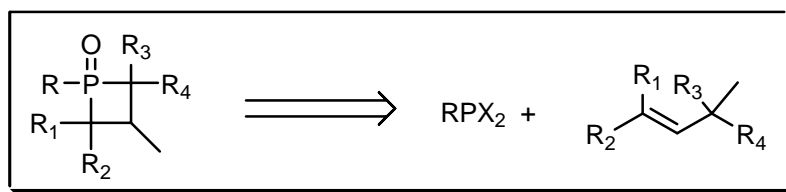
## COMMENTS :

## McBRIDE REACTION

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### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

An olefin phosphorylation procedure based on the reaction of electron-rich olefinic double bonds with  $\text{PCl}_3$ , in the presence of  $\text{AlCl}_3$  via a carbocationic intermediate. See also **Zinovev – Soborovski (Clayton – Jensen)** reaction.

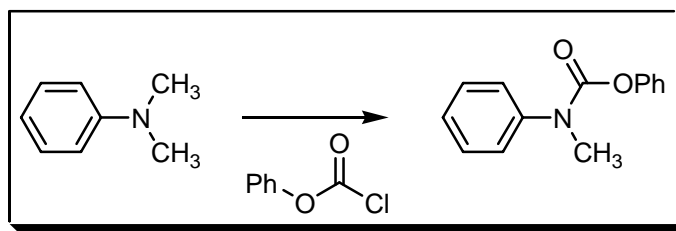
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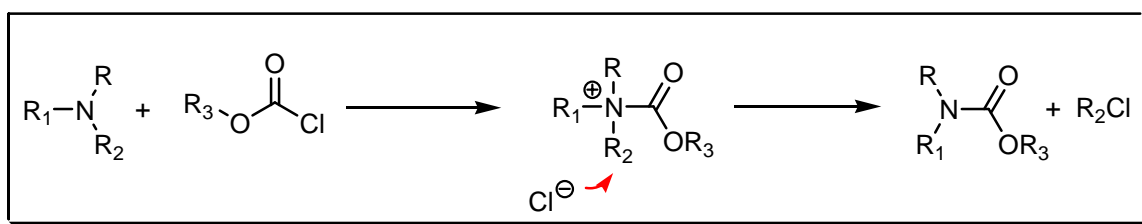
**COMMENTS :**

## McCLUSKEY FRAGMENTATION

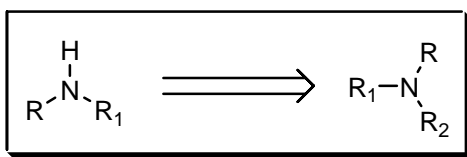
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The *N*-dealkylation of tertiary amines under mild conditions using chloroformates. Hydrolysis of the carbamate derivative affords the secondary amines. See also **von Braun** degradation.

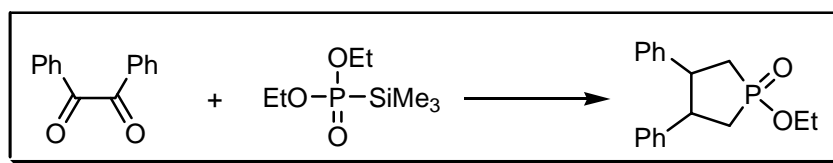
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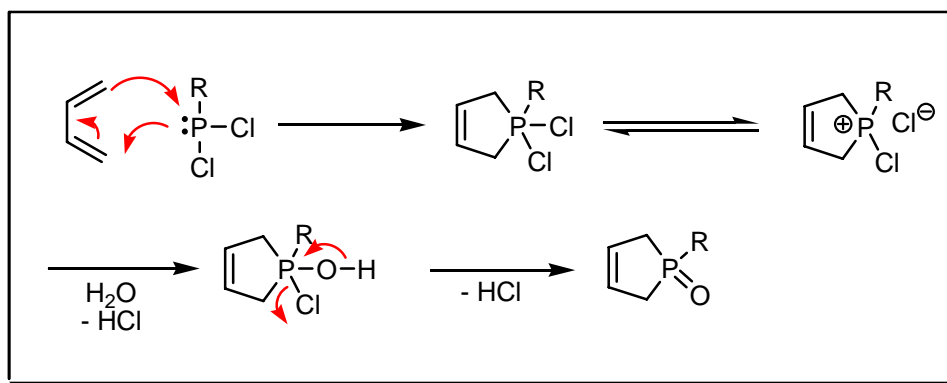
### COMMENTS :

## McCORMACK – KUKHTIN – RAMIREZ PHOSPHOLE SYNTHESIS

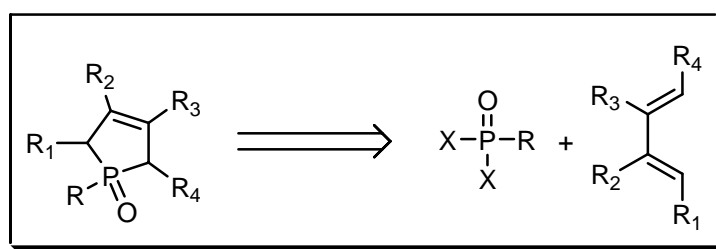
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The formation of phospholes from butadienes (**McCormack**) or of dioxaphospholes from 1,2-diketones (**Kukhtin – Ramirez**). See also **Allen – Millar – Mathey** rearrangement.

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**Org. Synth. Coll. Vol.** : **5**, 501, 787

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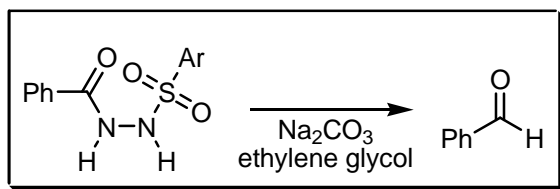
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**COMMENTS :**

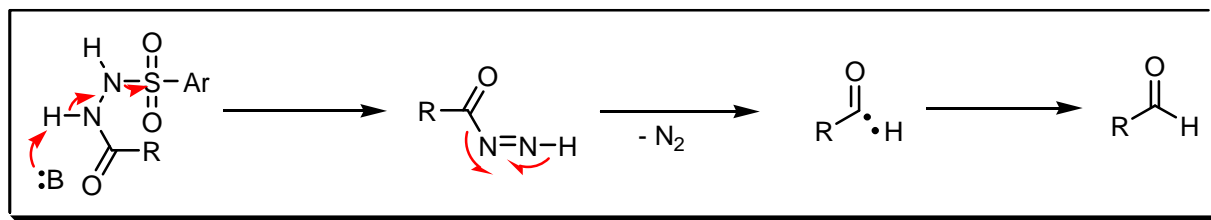
## McFADYEN – STEVENS REACTION

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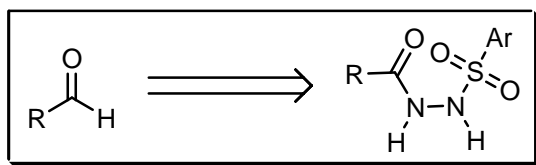
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

An acid is converted into a hydrazide, which on treatment with benzene- or *p*-toluenesulfonyl chloride gives an arylsulfonacylhydrazide. This yields on treatment with sodium carbonate in ethylene glycol an aldehyde. This reaction only works on aromatic aldehydes and aliphatic aldehydes with no  $\alpha$ -hydrogen atoms. See also **Kalb – Gross** and **Wuyts** reactions.

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## REFERENCES :

March : 448

Smith – March : 534

Houben – Weyl : 7/1, 297; E3, 470; E6a, 986; E6b, 437; E11, 622

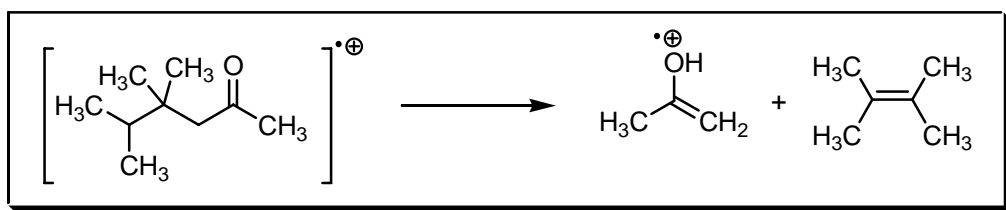
Org. React. : 8, 218

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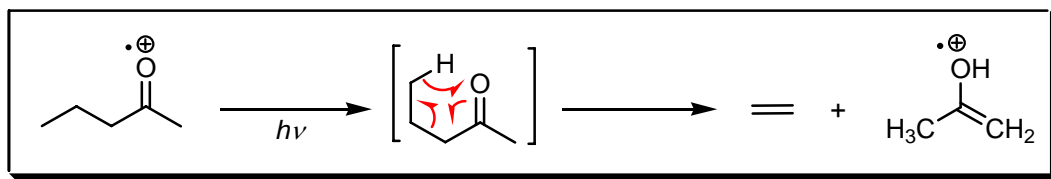
## COMMENTS :

## McLafferty REARRANGEMENT

### EXAMPLE :

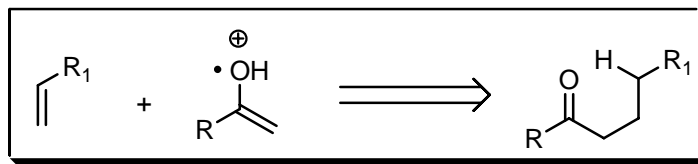


### MECHANISM :





## DISCONNECTION :



## NOTES :

Electron-impact-induced cleavage of carbonyl compounds having a hydrogen in the  $\gamma$ -position, to an enolic fragment and an olefin. See also **Norrish type II** reaction.

## REFERENCES :

Smith : 1404

Smith 2<sup>nd</sup> : 1156

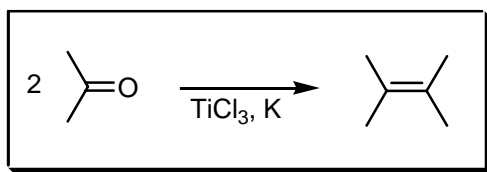
Houben – Weyl : E19a, 71

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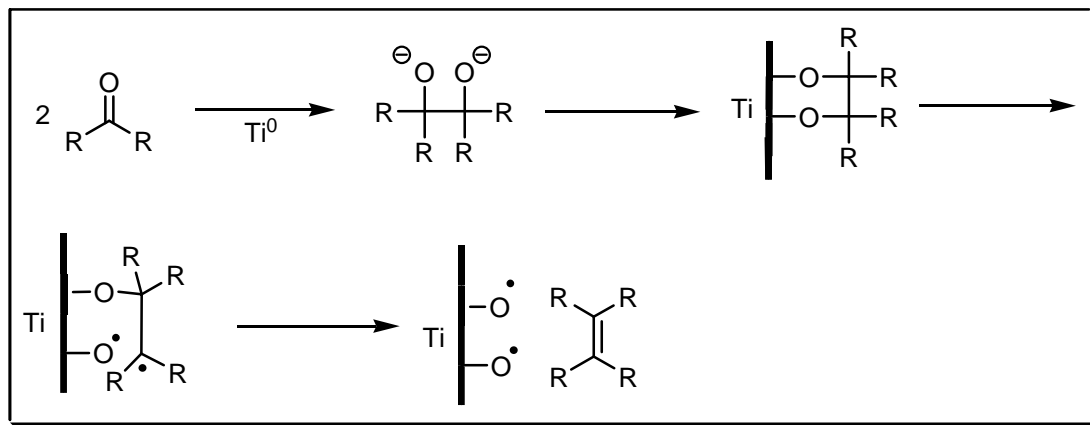
## COMMENTS :

## McMURRY OLEFINATION

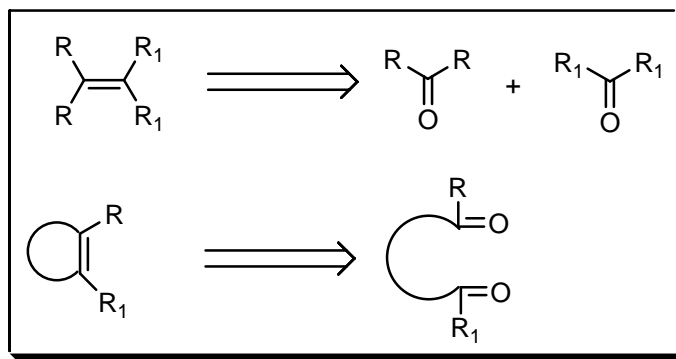
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The formation of olefins by coupling or cross coupling of ketones, mediated by low valent titanium in the presence of e.g.  $\text{K}$ ,  $\text{LiAlH}_4$ . The coupling of enol ethers of 1,3-dicarbonyl compounds is also possible. See also **Corey – Kwiatkowski**, **Eastwood**, **Fürstner**, **Horner – Wadsworth – Emmons**, **Julia – Paris – Kocienski** – **Lythgoe**, **Krief** – **Reich** – **Chow**, **Nozaki – Hiyama – Kishi** (**Takai – Utimoto**), **Paquette**, **Petasis** reaction, **Peterson**, **Ramberg** – **Bäcklund**, **Still** – **Gennari**, **Takeda**, **Tebbe** and **Wittig** olefination reactions.

### REFERENCES :

March : 1227

Smith – March : 1561

Smith : 1446

Smith 2<sup>nd</sup> : 1192, 1247

Org. Synth. : 60, 113; 76, 142

Org. Synth. Coll. Vol. : 7, 1

Science of Synthesis : 9, 220, 502; 10, 382, 2346

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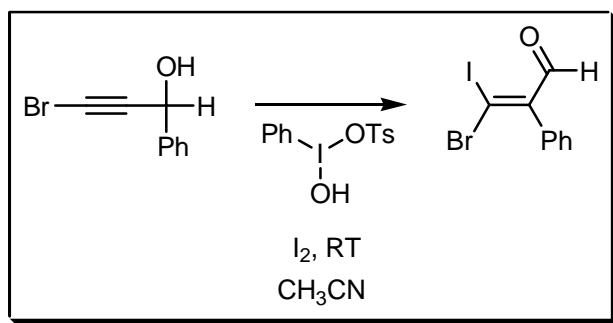
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#### COMMENTS :

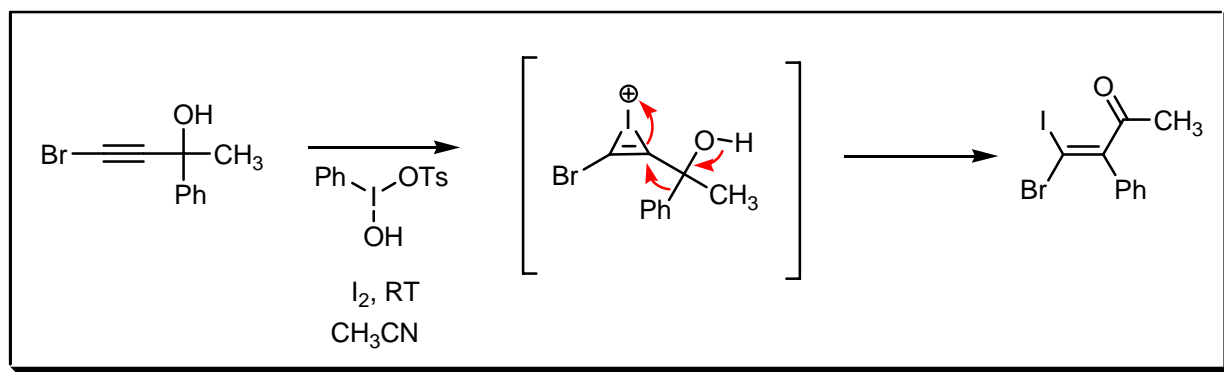
### McNELIS REARRANGEMENT

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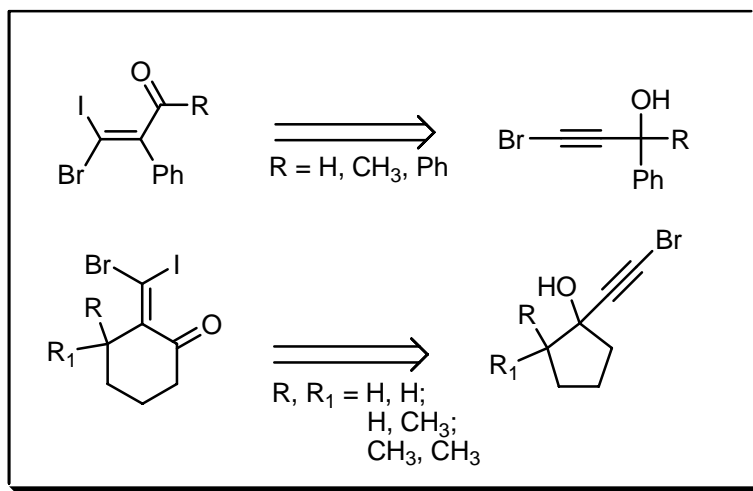
#### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The rearrangement of haloethynylcarbinols to β,β-dihaloenones using [hydroxyl(tosyloxy)iodo]benzene (HTIB), molecular iodine or *N*-iodosuccinimide (NIS). HTIB is employed stoichiometrically with iodine or catalytically with NIS and functions as a Lewis acid, activating iodine and NIS as I<sup>+</sup>. The reaction is very successful in the ring-expansion of cyclic systems. See also **Koser** tosylation.

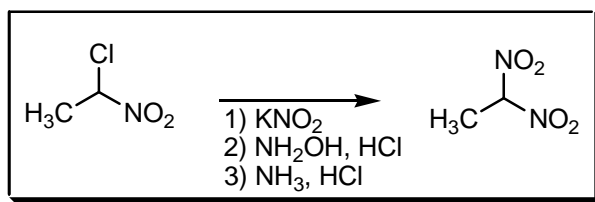
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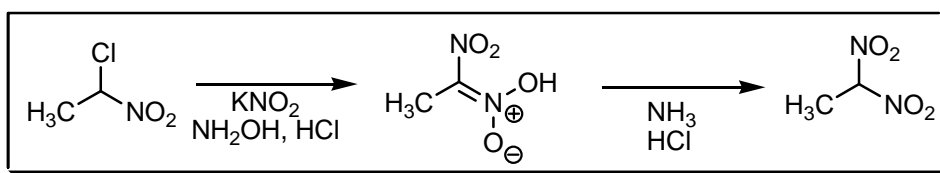
COMMENTS :

ter MEER REACTION

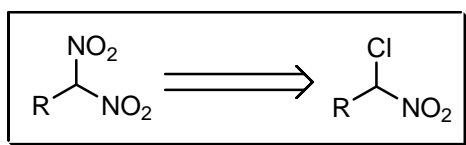
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The *gem* dinitro derivatives are prepared from chloronitro compounds.

REFERENCES :

Org. Synth. : 37, 23

Org. Synth. Coll. Vol. : 4, 372

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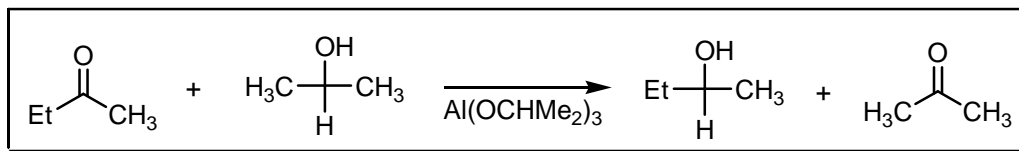
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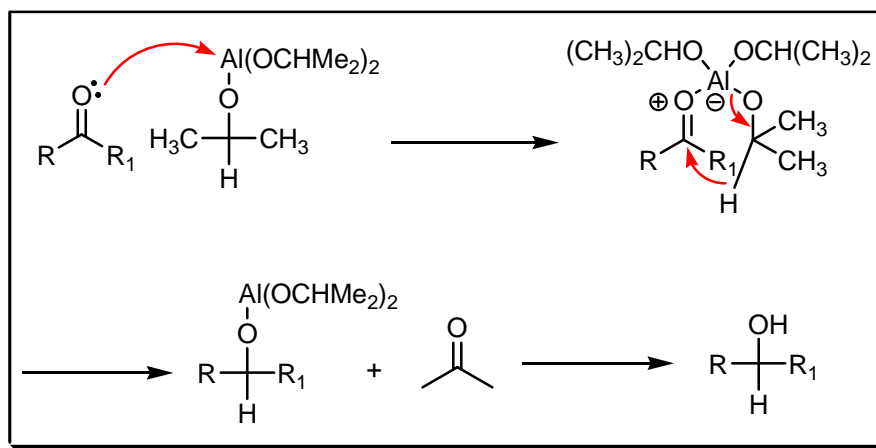
COMMENTS :

## MEERWEIN – PONNDORF – VERLEY REDUCTION

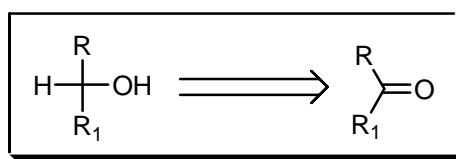
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

Carbonyl compounds are reduced to alcohols by treatment with aluminium or zirconium alkoxides in the corresponding alcohol, which itself is oxidised. The oxidation product is removed as formed to displace the equilibrium in the required direction. Asymmetric reduction are known, see **Evans** *et al.* See also **Bouveault – Blanc**, **Kerp**, **Noyori** hydrogenation, **Oppenauer** and **Tishchenko – Claisen** reactions.

REFERENCES :

**March** : 913; 917

Smith – March : 1199

Smith : 472

Smith 2<sup>nd</sup> : 212, 407, 604

Houben – Weyl : 4/2, 85; 7/1, 186

Org. React. : 2, 178; 6, 207

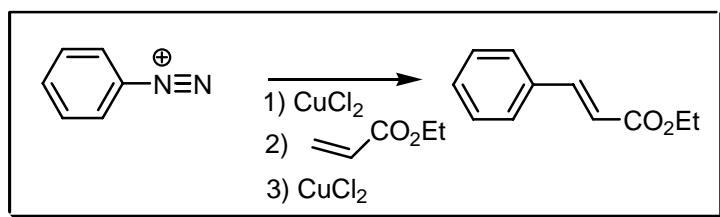
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## COMMENTS :

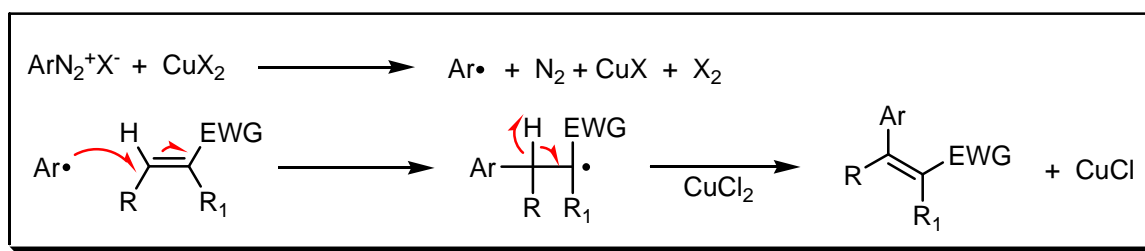
## MEERWEIN ARYLATION

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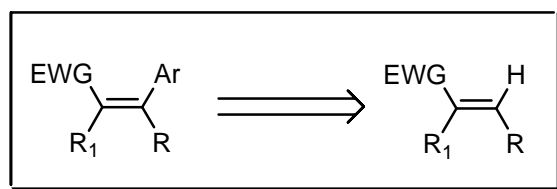
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Diazonium compounds, or nitrosoacylanilides react in acetone solution usually in the presence of a cupric or cuprous catalyst, with compounds containing activated or polarised ethylenic bonds ( $\alpha,\beta$ -unsaturated carbonyl compounds) to yield  $\alpha$ -halo- $\beta$ -arylalkanes. A free-radical pathway is most likely. Certain olefins give products corresponding to the dehydrohalogenated adduct. See also **Balz – Schiemann**, **Cadogan** arylation, **Craig** exchange, **Demjanov** rearrangement, **Gattermann** diazo, **Gattermann** sulfinic acid, **Griess** deamination, **Knoevenagel** diazotation, **Körner** – **Contardi**, **Sandmeyer** diazonium, **Schwechten** and **Witt** diazotation reactions.

## REFERENCES :

March : 716

Smith – March : 928

Smith : 1435

Smith 2<sup>nd</sup> : 1184

Houben – Weyl : 4/2, 134; 5/3, 992; E16a, 1098

Org. React. : 11, 189; 24, 225

Org. Synth. : 51, 1

Org. Synth. Coll. Vol. : 6, 21

Science of Synthesis : 9, 246; 10, 412

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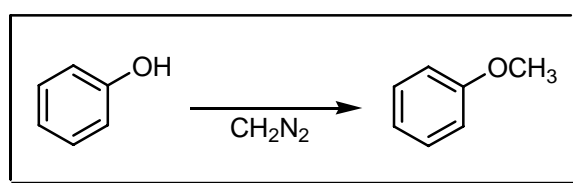
**COMMENTS :**

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**MEERWEIN METHYLATION**

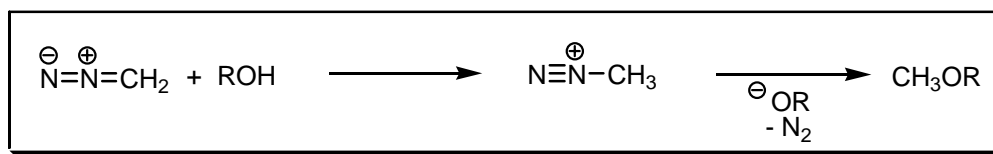
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**EXAMPLE :**



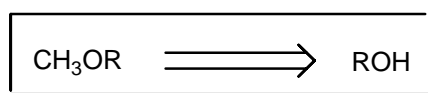
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**MECHANISM :**



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**DISCONNECTION :**



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**NOTES :**

Diazomethane is of value in the methylation of hydroxyl groups, which are activated by neighbouring groups. Polar compounds act as catalysts in the methylation by diazomethane of non-activated hydroxyl groups. Suitable catalysts are  $\text{HBF}_4$ ,  $\text{ZnCl}_2$ ,  $\text{FeCl}_2$ ,  $\text{MgCl}_2$ ,  $\text{Al}(\text{OEt})_3$ ,  $\text{B}(\text{OEt})_3$ . See also **Claisen** carbonate alkylation, **Fischer** glycosidation, **Hakomori**, **Haworth** methylation, **Irvine – Purdie**, **Meerwein** methylation, **Robertson – Robinson** and **Williamson** reactions.

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**REFERENCES :**

**March** : 388

**Smith – March** : 479

**Smith 2<sup>nd</sup>** : 544

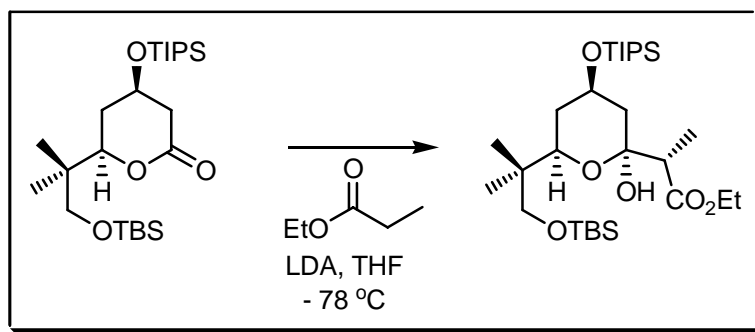
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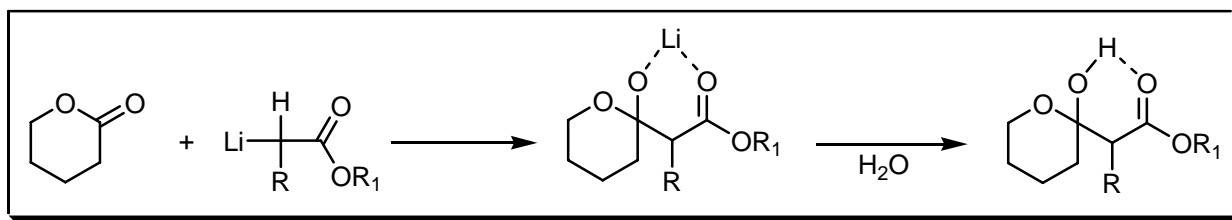
COMMENTS :

MEINWALD REACTION

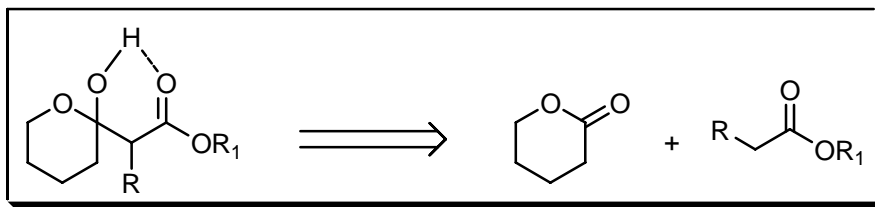
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

Stabilised anions, such as ester enolates and enolates of phosphononitriles, condense with lactones to afford single addition products.

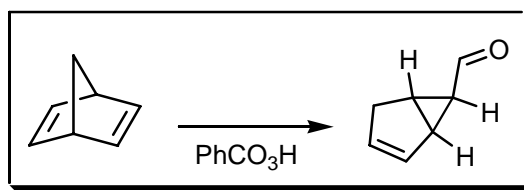
## REFERENCES :

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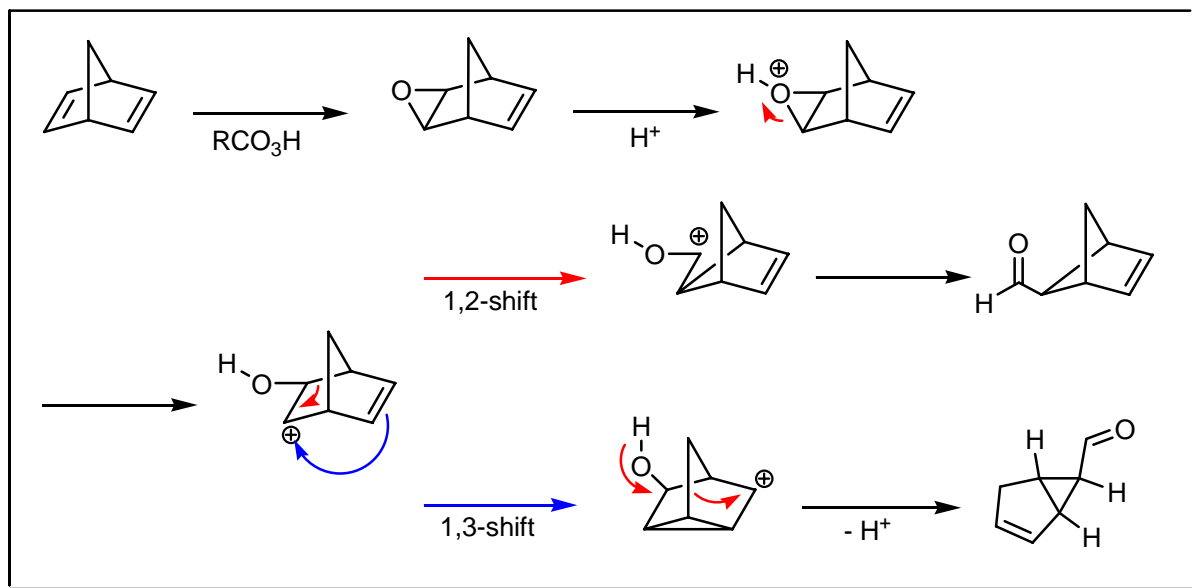
## COMMENTS :

## MEINWALD REARRANGEMENT

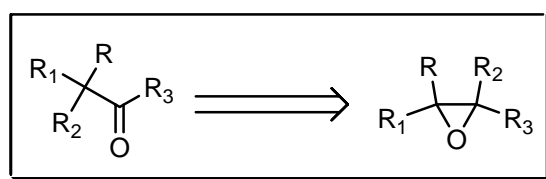
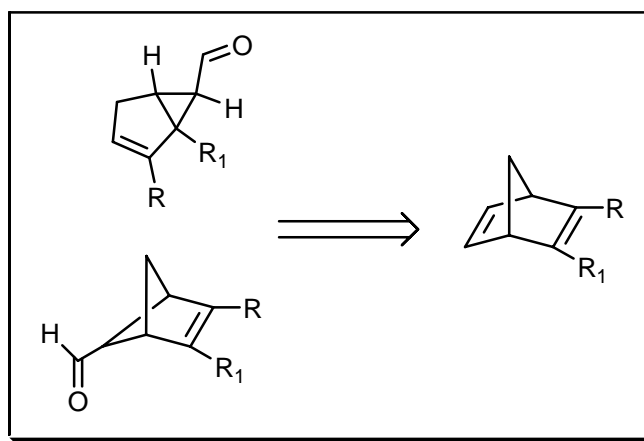
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The classic reaction is the peracid oxidation of norbornadiene. Nowadays the name is used for the synthetic route to aldehydes and ketones from epoxides. See also **von Baeyer – Villiger** and **Noyori** rearrangements.

## REFERENCES :

**Smith – March** : 1398

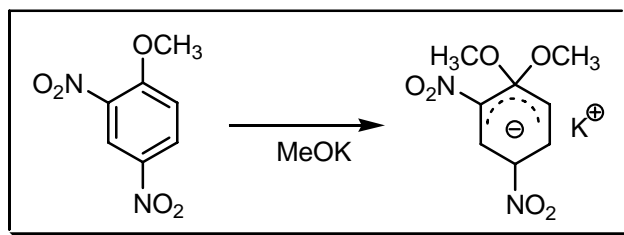
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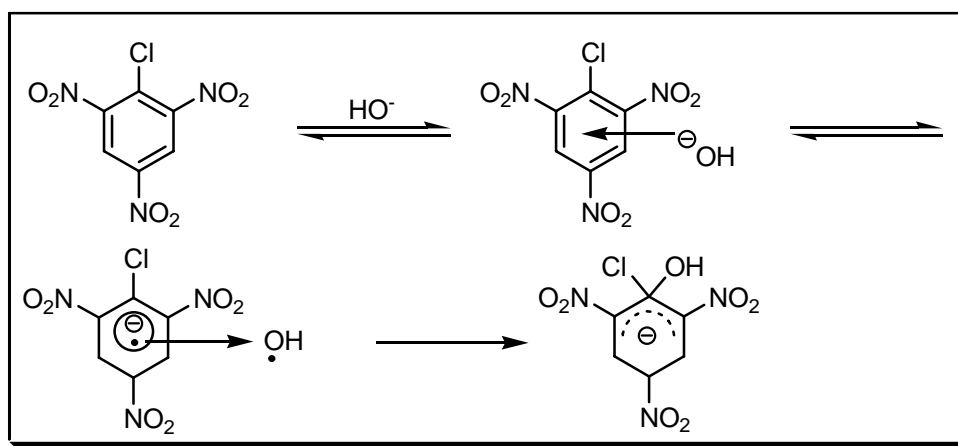
**COMMENTS :**

## MEISENHEIMER – JANOVSKY SYNTHESIS

**EXAMPLE :**



**MECHANISM :**



**NOTES :**

The adduct is formed from a polynitroaromatic compound in alkaline solution with alkoxide or hydroxide (**Meisenheimer**) or with acetone (**Janovsky**) by S<sub>N</sub>Ar mechanism. The reaction is also known as the **Meisenheimer – Jackson** reaction. See also **Zimmermann** reaction.

## REFERENCES :

March : 642

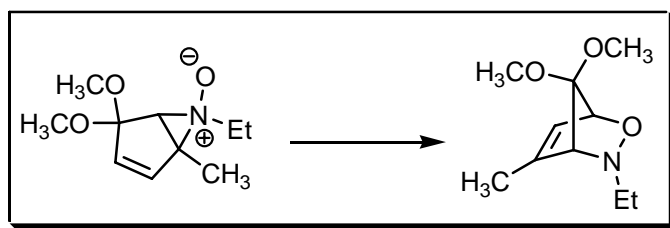
Smith – March : 851

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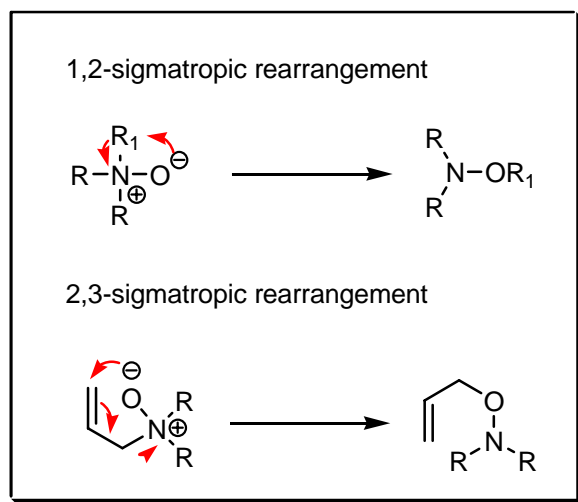
## COMMENTS :

## MEISENHEIMER REARRANGEMENT

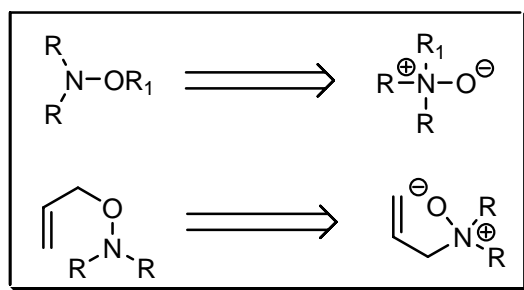
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The formation of *O,N,N*-trisubstituted hydroxylamines from tertiary amine oxides via [1,2]-R group migration, or [2,3]-sigmatropic rearrangement when  $R_1$  = allyl. See also **Boekelheide**, **Mislow – Bravermann – Evans**, **Sommelet – Hauser** and **Wittig** reactions.

## REFERENCES :

**March** : 1102

**Smith – March** : 1420

**Houben – Weyl** : E16a, 304

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- 6) S.G. Davies; G.D. Smyth, *Tetrahedron: Asymmetry*, 1996, **7**, 1001.
- 7) J.M. Molina; R. El-Bergmi; J.A. Dobado; D. Portal, *J. Org. Chem.*, 2000, **65**, 8574.
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9) C.S. Penkett; I.D. Simpson, *Tetrahedron Lett.*, 2001, **42**, 3029.

10) E.J. Williams; P.W. Kenny; J.G. Kettle; P.G. Mwashimba, *Tetrahedron Lett.*, 2004, **45**, 3693.

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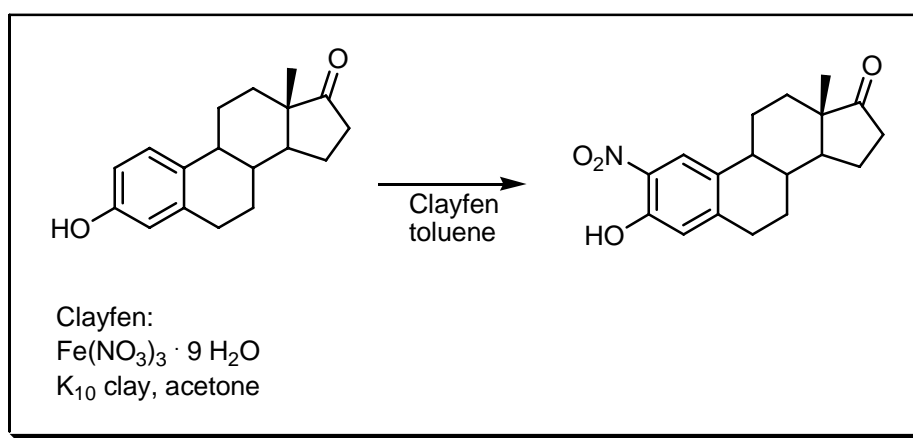
**COMMENTS :**

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**MENCKE – LASZLO NITRATION OF PHENOLS**

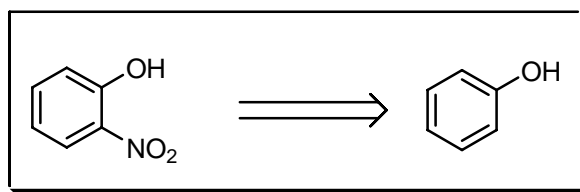
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**EXAMPLE :**



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**DISCONNECTION :**



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**NOTES :**

*Ortho* nitration of phenols by metal nitrates (mainly  $\text{Fe}(\text{NO}_3)_3$ ) or alkyl nitrates catalysed by bentonite clay (Clayfen). In the classic **Mencke** reaction copper(II) nitrate and acetic acid anhydride was used.

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## REFERENCES :

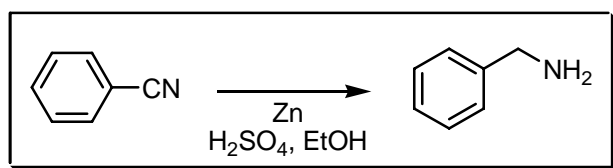
- 1) J.B. Mencke, *Recl. Trav. Chim. Pays-Bas*, 1925, **44**, 141.
- 2) W. Davey; J.R. Gwilt, *J. Chem. Soc.*, 1950, 204.
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- 5) P. Laszlo, *Pure Appl. Chem.*, 1990, **63**, 2027.
- 6) T.J. Kwok; K. Jayasuriya; R. Damavarapu; B.W. Brodman, *J. Org. Chem.*, 1994, **59**, 4942.

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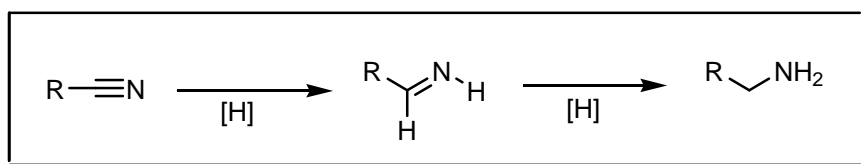
## COMMENTS :

## MENDIUS REDUCTION

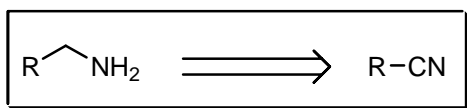
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Nitriles are reduced by *in situ* prepared hydrogen to primary amines by zinc and alcoholic sulfuric acid. There are many reducing agents for nitriles available, e.g. LiAlH<sub>4</sub>. See also **Ladenburg – Vysnegradskii** reaction.

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## REFERENCES :

March : 918

Smith – March : 1204

Smith : 440

Smith 2<sup>nd</sup> : 316

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O. Mendius, *Liebigs Ann. Chem.*, 1862, **121**, 129.

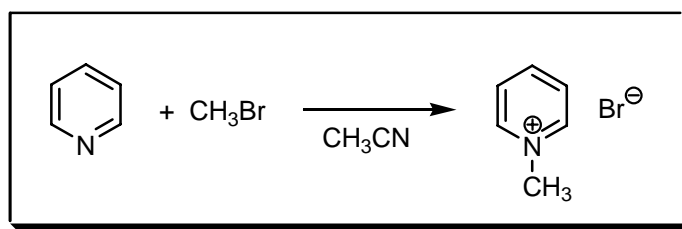
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COMMENTS :

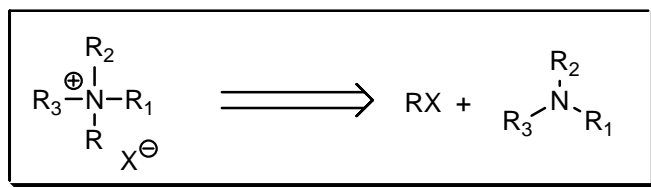
## MENSCHUTKIN REACTION

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EXAMPLE :



DISCONNECTION :



NOTES :

This reaction involves the formation of tetra-alkylammonium halides from alkyl halides and tertiary amines, particularly in relation to solvent effects. See also **Hofmann** degradation.

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REFERENCES :

March : 411

Smith – March : 499

Smith : 1142

Smith 2<sup>nd</sup> : 950

Houben – Weyl : 11/2, 593

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- 4) G. Wenz; F. Wolf; M. Wagner; S. Kubrik, *New J. Chem.*, 1993, **17**, 729.
- 5) J.-L.M. Abboud; R. Notario; J. Betran; M. Sola, *Prog. Phys. Org. Chem.*, 1993, **19**, 1.
- 6) H.D. Jenkins; E.J. Kelly; C.J. Samuel, *Tetrahedron Lett.*, 1994, **35**, 6543.
- 7) H. Castejon; K.B. Wiberg, *J. Am. Chem. Soc.*, 1999, **121**, 2139.
- 8) J.H. Markgraf; P.K. Sangani; R.J. Manalasan; S.A. Snyder; R.P. Thummel, *J. Chem. Res.*, 2000, 561.
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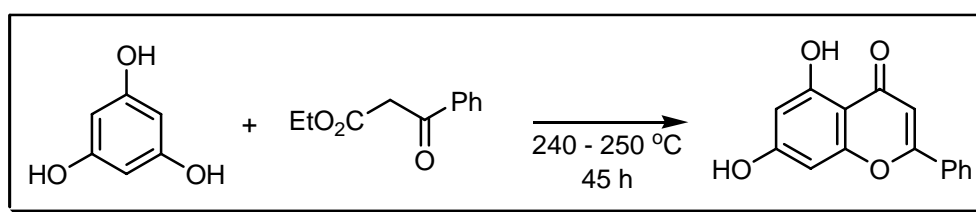
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**COMMENTS :**

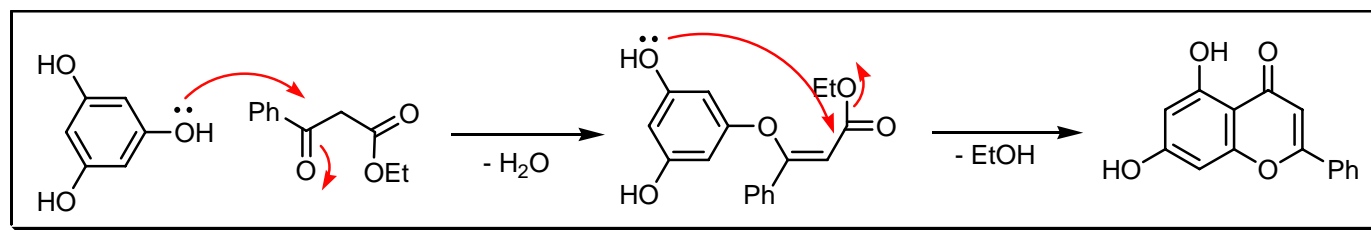
**MENTZER PYRONE SYNTHESIS**

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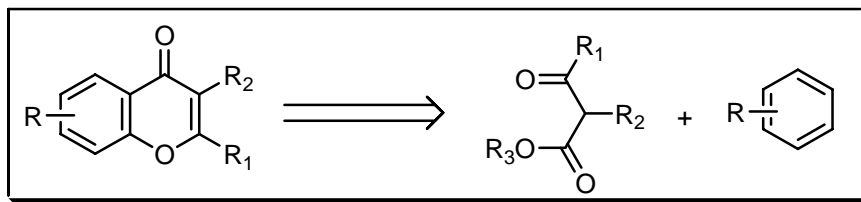
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

Benzopyranone is synthesised from phenols and  $\beta$ -ketoesters or unsaturated acids. This reaction is uncatalysed and it is assumed that the first step is the etherification at high temperature to give the phenoxyacrylic ester. The reaction has been enhanced by the use of microwaves. See also **Anschütz** hydroxycoumarin, **Knoevenagel** coumarin, **Pauly – Lockemann**, **Pechmann**, **Perkin**, **Simonis** and **Skraup – Priglinger** reactions.

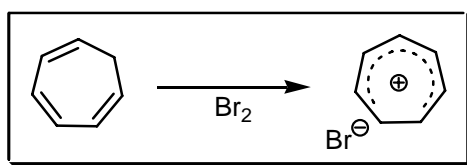
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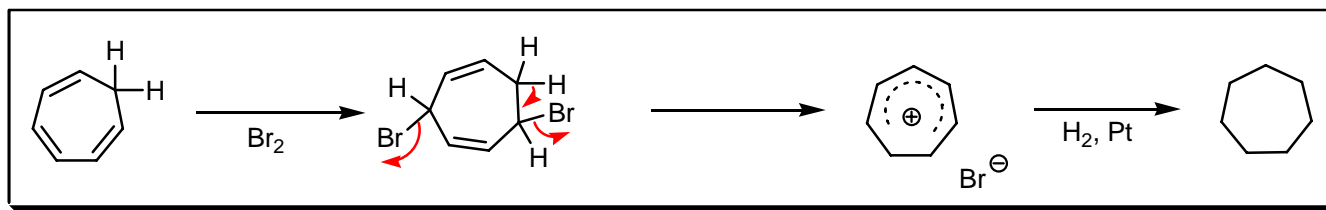
## COMMENTS :

## MERLING – von DOERING SYNTHESIS

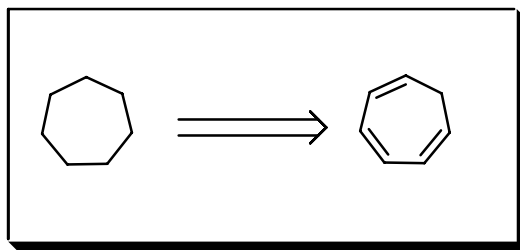
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

Tropilidene is treated with one equivalent of bromine to give dibromotropilidene, which on distillation *in vacuo* yields the tropylium ion. Hydrogenation of the tropylium ion will afford cycloheptane.

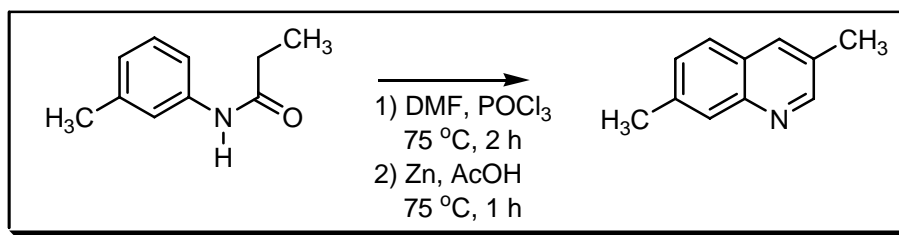
## REFERENCES :

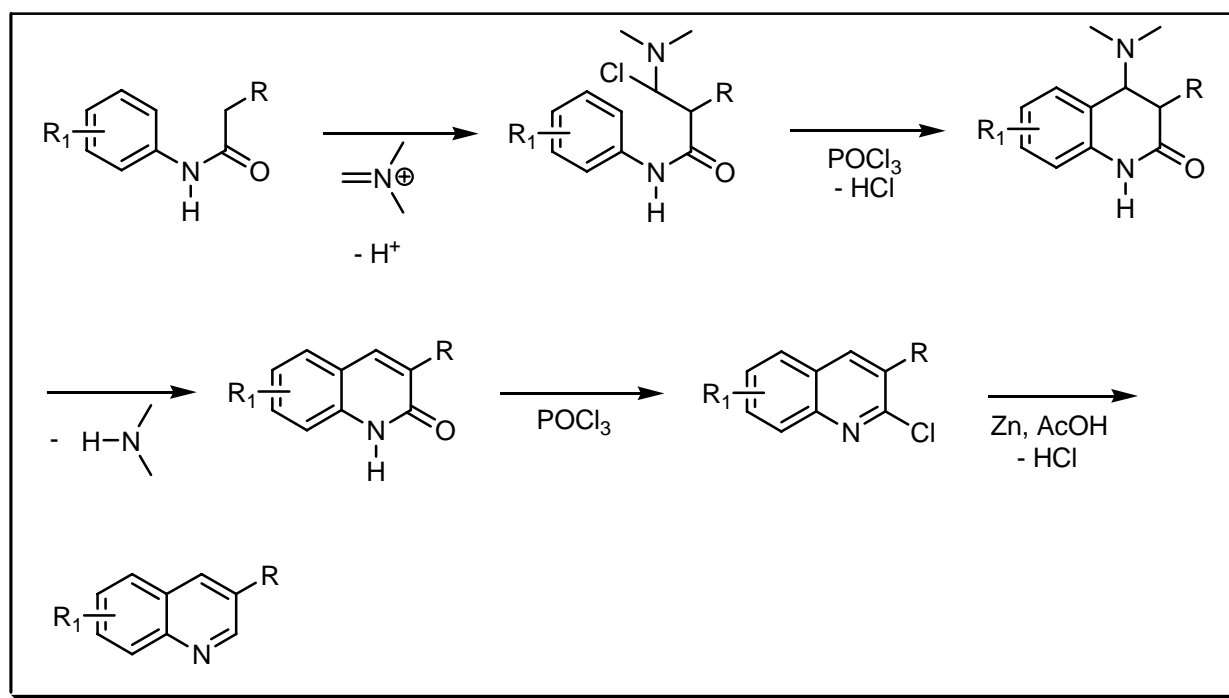
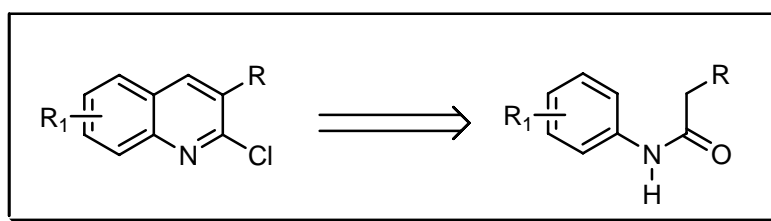
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## COMMENTS :

## METH-COHN QUINOLINE SYNTHESIS

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

Acetanilide is converted under **Vilsmeier – Haack – Viehe** conditions followed by cyclisation and amine expulsion into 2-quinolone which reacts with  $\text{POCl}_3$  to give 3-substituted-2-chloro-quinolines, which can be dechlorinated with zinc in acetic acid. See also **Allan – Loudon**, **von Baeyer – Drewson** quinoline, **Camps, Combes** quinoline, **Conrad – Limpach**, **Doebner** quinoline, **Doebner – von Miller**, **Foulds – Robinson**, **Friedländer**, **Knorr** quinoline, **von Niementowski** quinoline, **Pfitzinger – Borsche**, **Riehm** quinoline, **Skraup** quinoline and **Vilsmeier – Haack – Viehe** reactions.

**REFERENCES :**

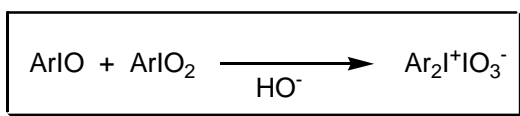
O. Meth-Cohn; S. Rhouati; B. Tarnowski, *Tetrahedron Lett.*, 1979, **20**, 4885.

**COMMENTS :**

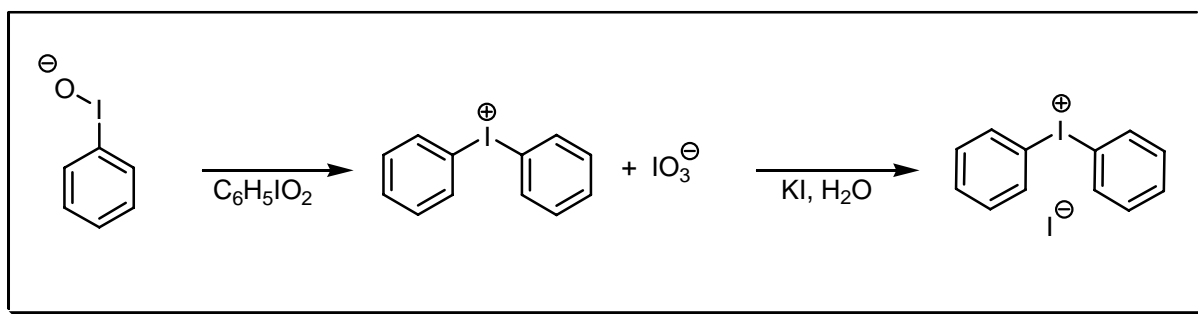
## MEYER – HARTMANN SYNTHESIS

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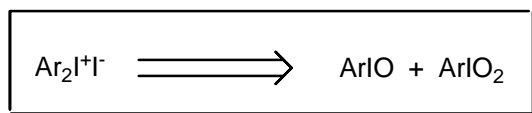
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Aryliodoso compounds react with aryliodoxy compounds in the presence of alkali to yield diaryliodonium iodates.

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### REFERENCES :

Houben – Weyl : E16d, 143

Org. Synth. : 22, 52, 70

Org. Synth. Coll. Vol. : 3, 355, 484

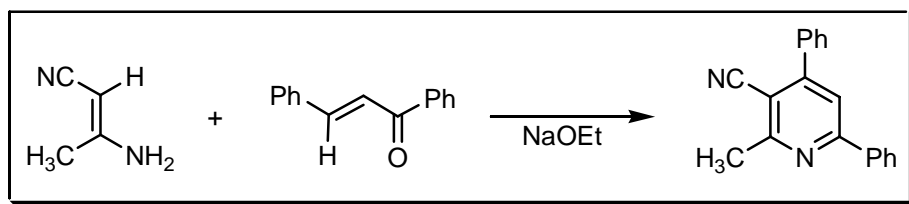
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  - 2) I. Mason; E. Race; F.E. Pounder, *J. Chem. Soc.*, 1935, 1669.
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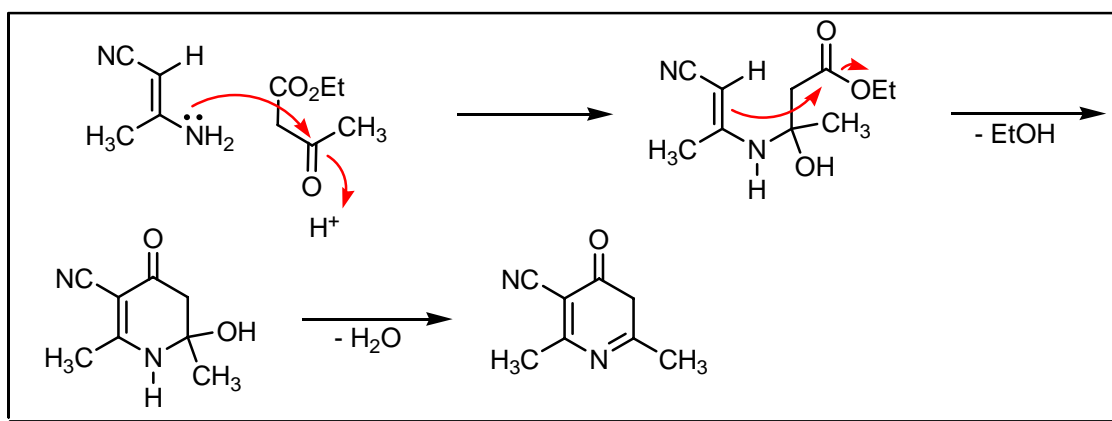
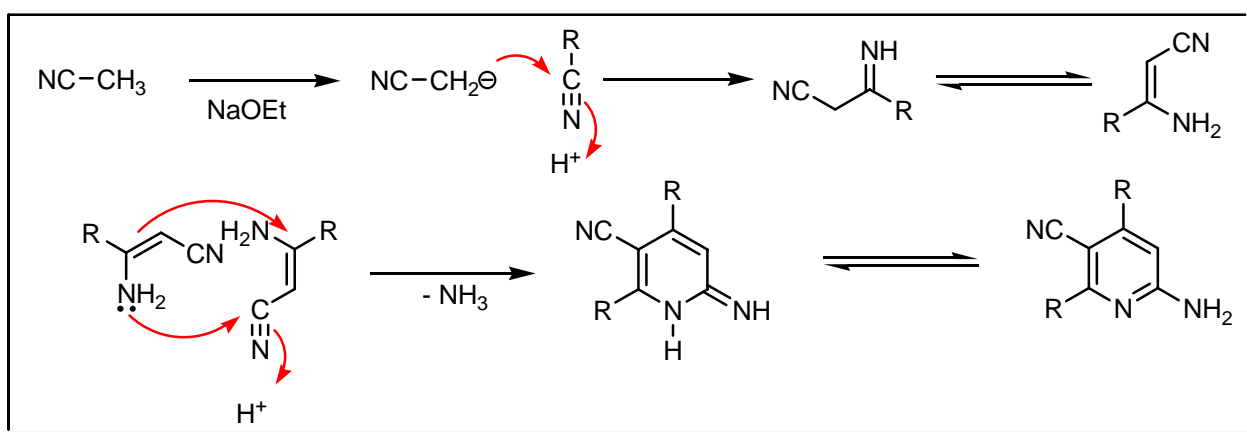
COMMENTS :

## von MEYER – MOHR SYNTHESIS

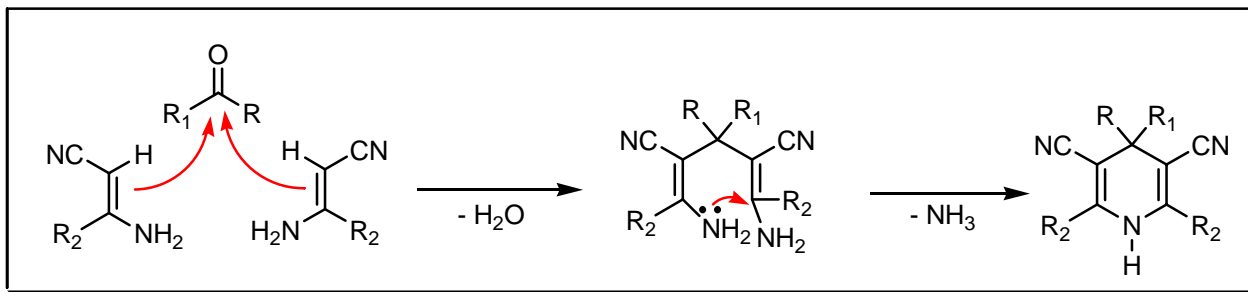
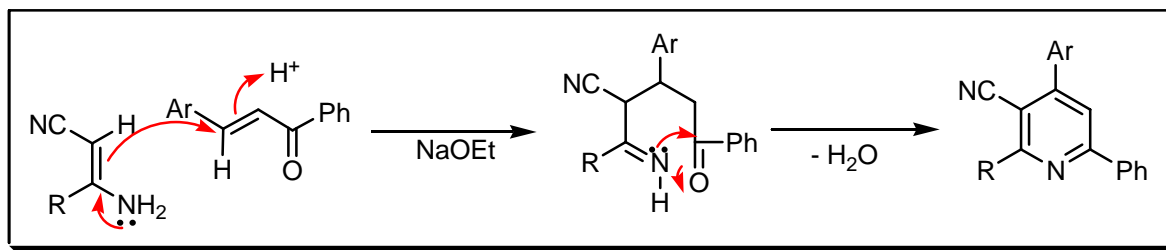
EXAMPLE :



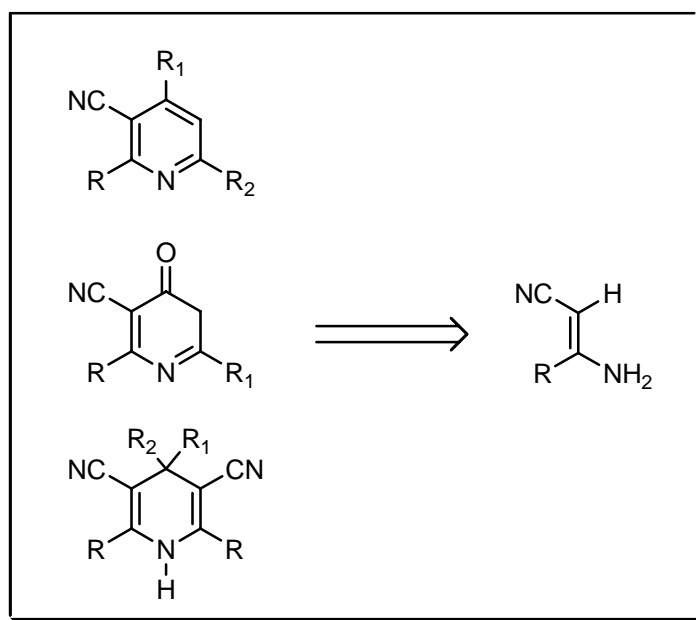
MECHANISM :







#### DISCONNECTION :



#### NOTES :

Acetonitrile undergoes a base-catalysed condensation with itself or another nitrile to form a dinitrile. These dinitriles react with a variety of compounds (1,3-diketones, arylideneacetophenones, aldehydes and ketones.) in the presence of acids or bases to yield pyridine derivatives. See also **Bohlmann – Rahtz**, **Chichibabin** pyridine, **Gattermann – Skita**, **Guareschi – Thorpe**, **Hantzsch – Beyer**, **Petrenko–Kritschenko**, **Riehm** pyridine and **Wakatsuki – Yamazaki – Bönnemann** reactions.

#### REFERENCES :

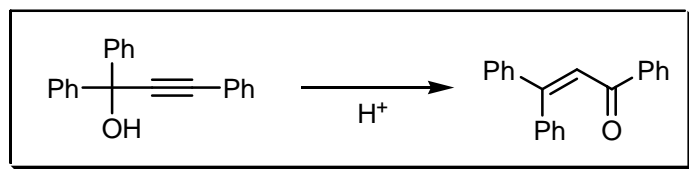
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6) A. Courts; V. Petrow, *J. Chem. Soc.*, 1952, 334.

**COMMENTS :**

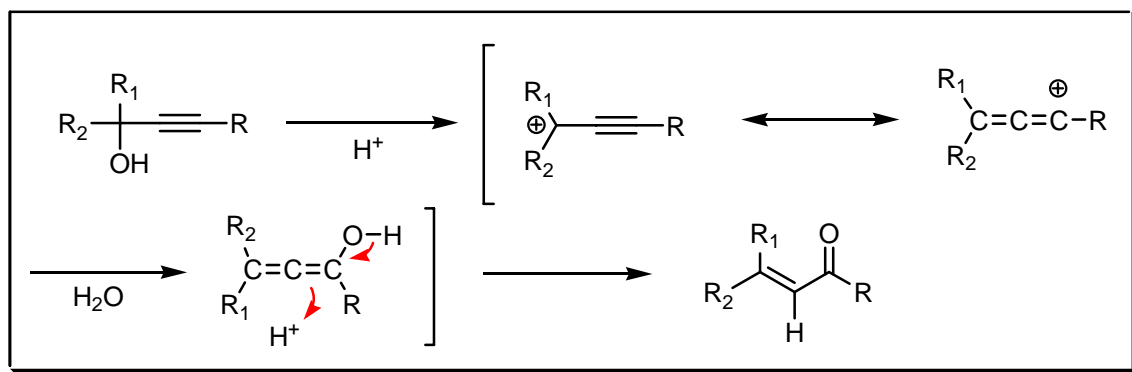
## MEYER – SCHUSTER REARRANGEMENT (RUPE REACTION)

**EXAMPLE :**

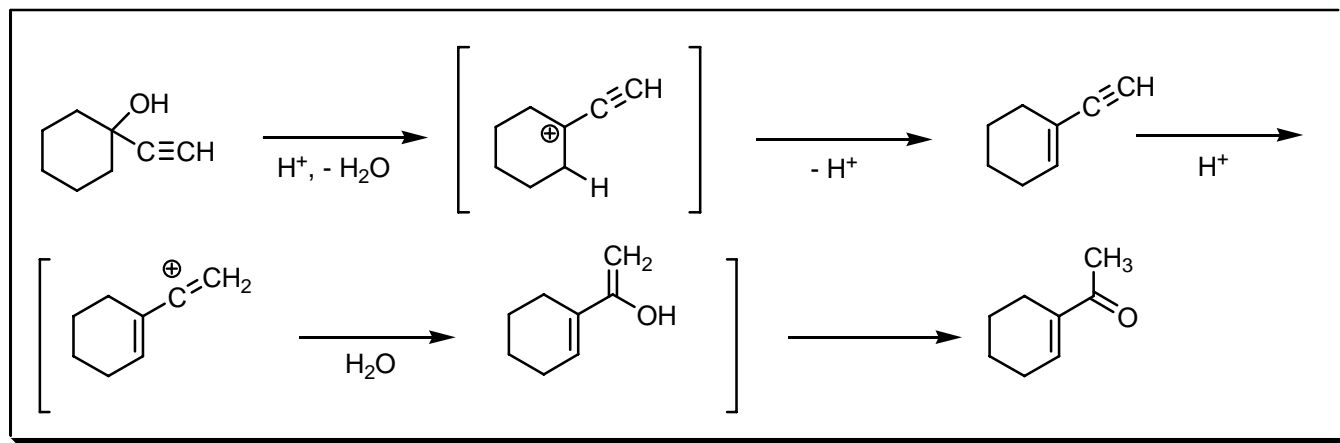


**MECHANISM :**

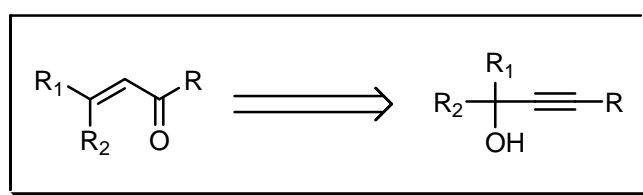
**Meyer – Schuster :**



## Rupe :



## DISCONNECTION :



## NOTES :

The acid-catalysed rearrangement of secondary and tertiary  $\alpha$ -acetylenic alcohols to  $\alpha,\beta$ -unsaturated carbonyl compounds. Aldehydes result when the acetylenic group is terminal, ketones when it is internal. The conversion of tertiary alkylacetylenic carbinols with a terminal acetylenic group to predominantly  $\alpha,\beta$ -unsaturated ketones and not the expected aldehydes, is referred to as the **Rupe** rearrangement.

## REFERENCES :

**March** : 330

**Smith – March** : 423

**Houben – Weyl** : 4/2, 54; 7/1, 109; **E15**, 3206, 3345; **E19c**, 199

**Org. Synth.** : 29, 1

**Org. Synth. Coll. Vol.** : 3, 22

- 1) K.H. Meyer; K. Schuster, *Ber. Dtsch. Chem. Ges.*, 1922, **55**, 819.
- 2) H. Rupe; K. Glenz, *Liebigs Ann. Chem.*, 1924, **436**, 195.
- 3) B. Gredy, *Ann. Chim (Paris)*, 1935, **4**, 5.
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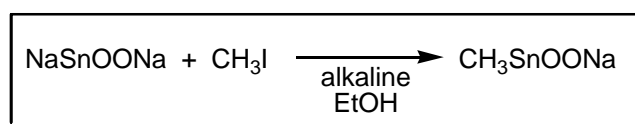
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**COMMENTS :**

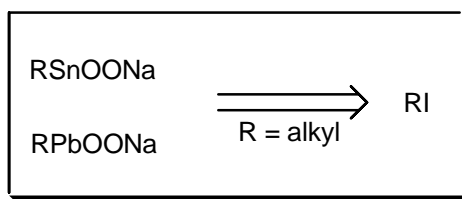
## MEYER ALKYLATION REACTION

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**EXAMPLE :**



**DISCONNECTION :**



**NOTES :**

Preparation of alkylstannonic acids by reacting alkali stannite with an alkyl iodide. When applied to alkali arsenites or plumbites the reaction yields alkylarsonic and alkylplumbonic acids, respectively.

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**REFERENCES :**

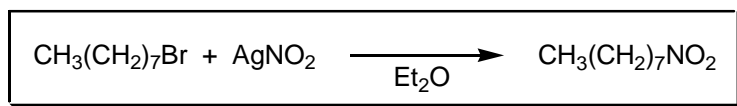
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  - 2) J.G.F. Druce, *J. Chem. Soc.*, 1918, **113**, 715.
  - 3) W.R. Cullen, *Adv. Organomet. Chem.*, 1966, **4**, 148.
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**COMMENTS :**

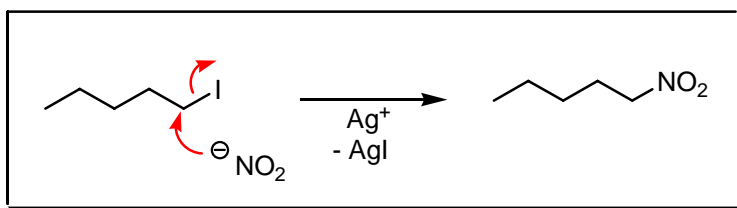
## MEYER NITROALKANE REACTION

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### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Aliphatic nitrites and nitro-compounds are obtained by treating alkyl halides with metallic nitrites. The steric outcome of this reaction depends on substrate and solvent. The transition state is both  $\text{S}_{\text{N}}1$  and  $\text{S}_{\text{N}}2$  in character.

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### REFERENCES :

Org. React. : **12**, 101

Org. Synth. : **34**, 37

Org. Synth. Coll. Vol. : **4**, 368

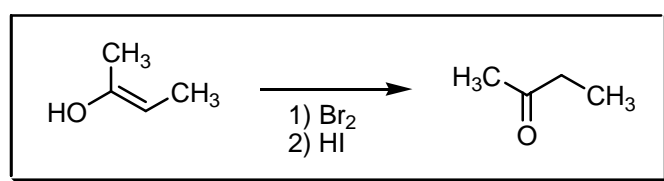
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  - 4) N. Levy; J.D. Rose, *J. Chem. Soc., Quat. Rev.*, 1947, **1**, 358.
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  - 6) J.K. Stille; E.D. Vessel, *J. Org. Chem.*, 1960, **25**, 478.
  - 7) R.C. Kerber; G.W. Urry; N. Kornblum, *J. Am. Chem. Soc.*, 1965, **87**, 4520.
  - 8) N. Kornblum; W.J. Jones; D.E. Hardies, *J. Am. Chem. Soc.*, 1966, **88**, 1704.
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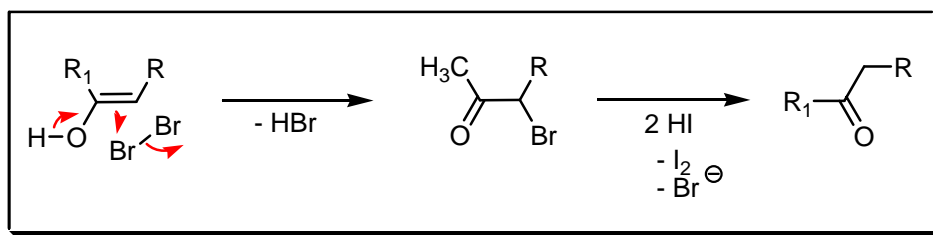
COMMENTS :

## MEYER REACTION

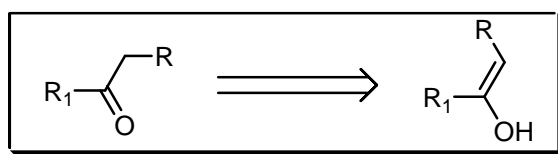
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The addition of bromine on an enolic double bond, followed by treatment with hydrogen iodide will give a ketone. This reaction is used to determine the enol ratio in a keto/enol mixture. It is based on the reaction of only the enol with an alcoholic bromine solution. This can be done by direct titration or indirect titration, see Houben – Weyl for more details.

REFERENCES :

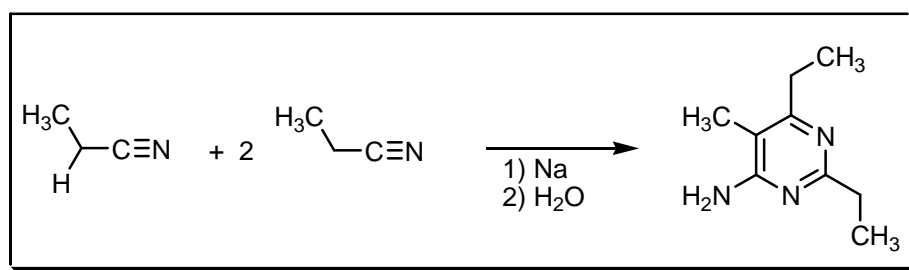
Houben – Weyl : 2, 388

- 1) K.H. Meyer, *Liebigs Ann. Chem.*, 1911, **380**, 212.
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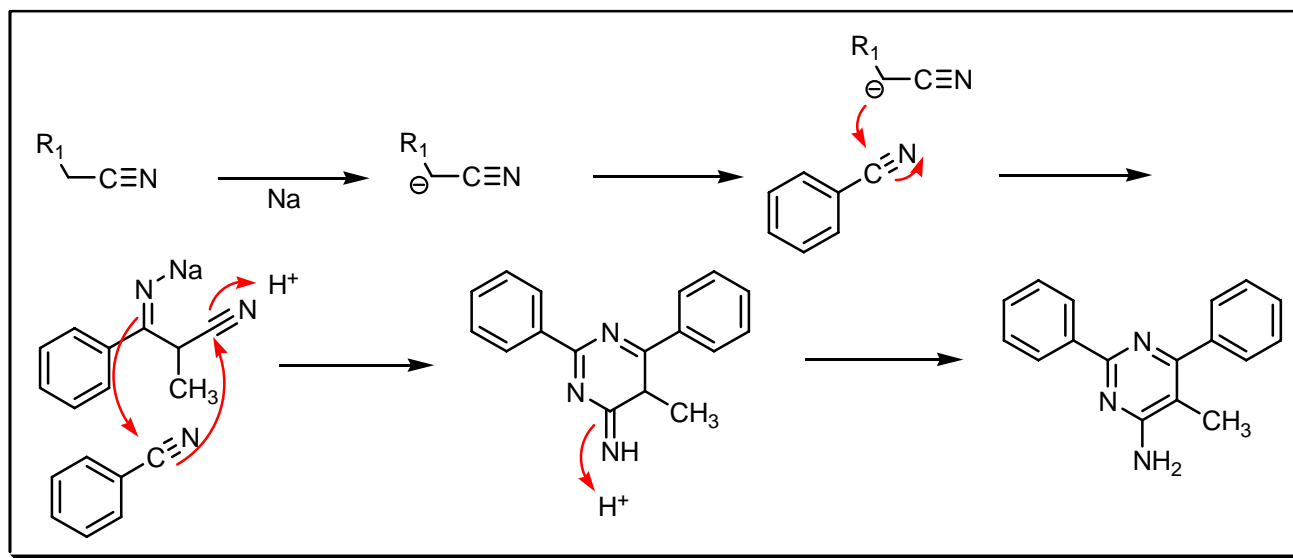
**COMMENTS :**

## von MEYER PYRIMIDINE SYNTHESIS

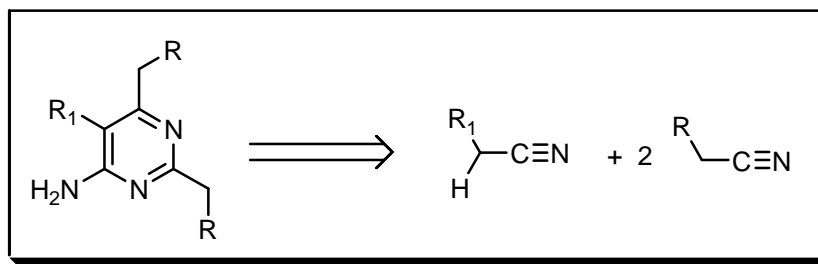
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

Aliphatic nitriles in diethyl ether solution react in the presence of sodium to yield the imide of the  $\beta$ -ketonitrile, the reaction proceeds probably *via* the sodium salt. Under vigorous conditions amino pyrimidines are formed (sodium, 150 °C).

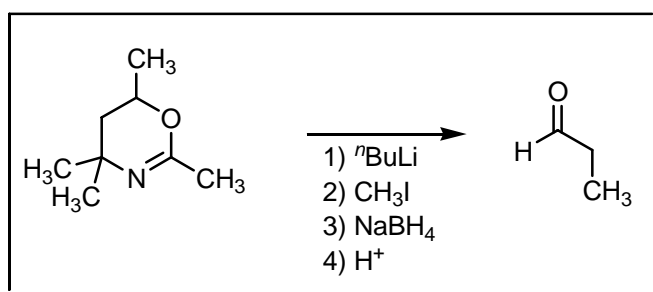
## REFERENCES :

- 1) E. von Meyer, *J. Prakt. Chem.*, 1888, **38**, 336.
- 2) E. von Meyer, *J. Prakt. Chem.*, 1889, **39**, 188.

## COMMENTS :

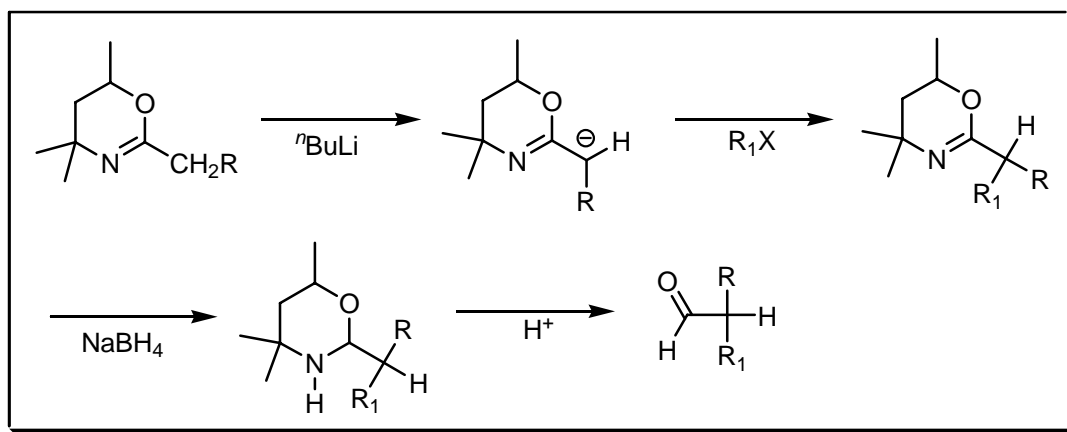
## MEYERS ALDEHYDE SYNTHESIS

### EXAMPLE :

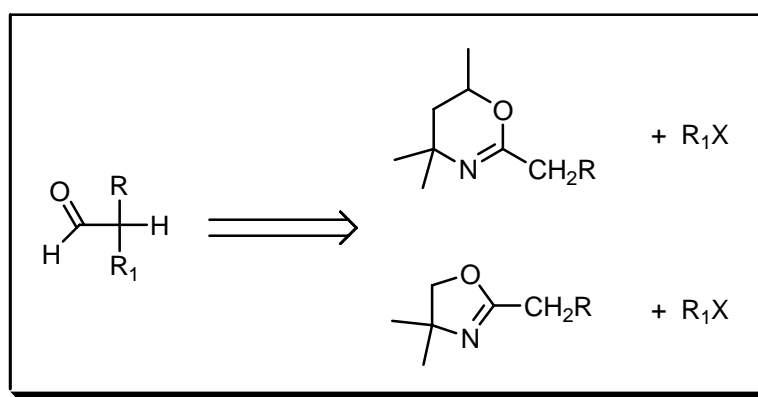




## MECHANISM :



## DISCONNECTION :



## NOTES :

Synthesis of aldehydes from alkyl halides and  $\alpha$ -lithio derivatives of dihydro-1,3-oxazines or 2-oxazolines which are used as carbanionic synthons.

## REFERENCES :

March : 478

Smith – March : 558

Smith : 916

Smith 2<sup>nd</sup> : 762

Org. Synth. : 51, 24; 54, 42

Org. Synth. Coll. Vol. : 6, 64, 905

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2) A.I. Meyers; A. Nabeya; H.W. Adickes; J.M. Fitzpatrick; G.R. Malone; I.R. Politzer, *J. Am. Chem. Soc.*, 1969, **91**, 764.

3) A.I. Meyers; A. Nabeya; H.W. Adickes; I.R. Politzer; G.R. Malone; A.C. Kovelesky; R.L. Nolen; R.C. Portnoy, *J. Org. Chem.*, 1973, **38**, 36.

4) A.I. Meyers; N. Nazarenko, *J. Org. Chem.*, 1973, **38**, 175.

5) A.I. Meyers; H. Harre; R. Garland, *J. Am. Chem. Soc.*, 1984, **106**, 1146.

6) A.I. Meyers, *Tetrahedron*, 1992, **48**, 2589.

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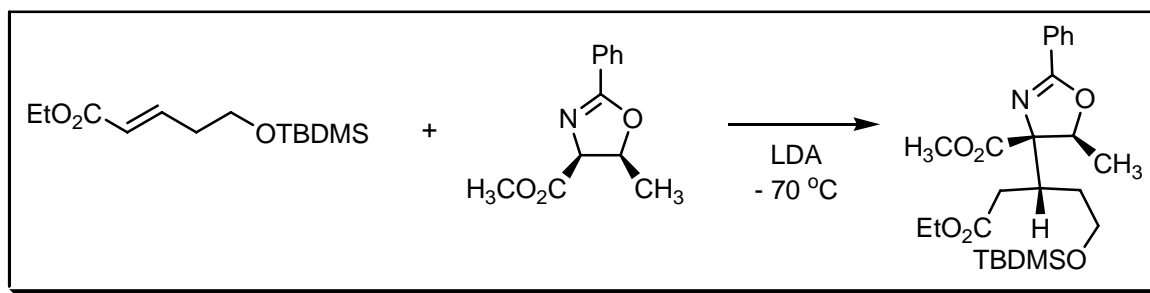
## COMMENTS :

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## MICHAEL CONDENSATION

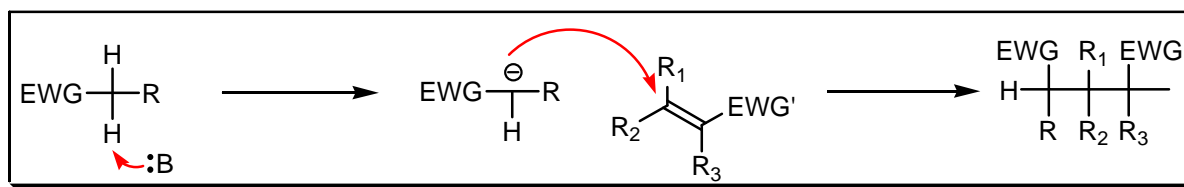
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### EXAMPLE :



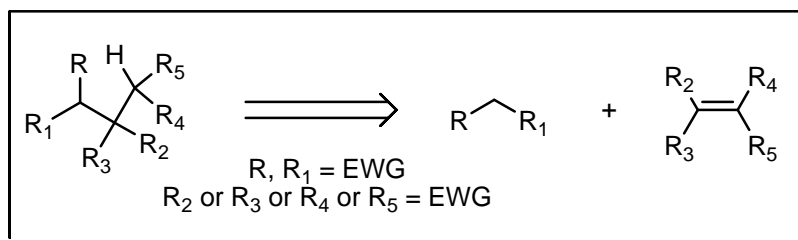
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### MECHANISM :



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### DISCONNECTION :



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### NOTES :

The base-catalysed reaction between an acceptor compound containing an activated double or triple bond and a donor compound containing an active  $\alpha$ -hydrogen atom, which results in the apparent addition of the component parts of the donor to the multiple bond of the acceptor. It is believed that the carbanion formed from the donor in alkaline

solution attacks the more positive end of the polarised system of the acceptor yielding an anion which after treatment with water yields the ultimate adduct. Less generally is the base-catalysed addition of a pseudo-acidic ketone, ester, nitrile, nitro-compound or sulfone to the  $\alpha,\beta$ -double bond of a conjugated unsaturated ketone, ester or nitrile. The anionic part of the pseudo-acidic addendum attaches to the  $\beta$ -end of the  $\alpha,\beta$ -double bond. *Intramolecular Michael* condensations have been effected and cyclic products obtained. In the abnormal *Michael* reaction rearranged products are produced. The reaction involves an equilibrium and reversal, to give the starting materials or different products, is possible. A proline-catalysed enantioselective *Michael* addition of ketones to nitrostyrene has been reported by **Enders** and **Seki**. Cerium(III) chloride catalyses the *Michael* addition of 1,3-dicarbonyl compounds to  $\alpha,\beta$ -unsaturated ketones. See also **d'Angelo**, **Carroll (Kimel – Cope)** rearrangement, **Corey – Nicolaou**, **Diels – Alder**, **Hajos – Parrish – Eder – Sauer – Wiechert**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Kita**, **Masamune**, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nagata**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Raphael**, **Robinson**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolkiewicz**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

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#### REFERENCES :

**March** : 795

**Smith – March** : 976, 1022

**Smith** : 956

**Smith 2<sup>nd</sup>** : 98, 522, 623, 636, 649, 676, 689, 794, 838, 1066

**Houben – Weyl** : **7/1**, 96; **E5**, 425, 1088, 1409, 1516; **E8d**, 765; **E16d**, 232

**Org. React.** : **10**, 179; **15**, 1; **19**, 1; **20**, 1; **46**, 1; **47**, 315

**Org. Synth.** : **4**, 29; **15**, 14; **26**, 24; **30**, 80; **32**, 86; **38**, 52; **39**, 52; **41**, 38; **49**, 121; **53**, 1; **55**, 99; **56**, 36; **58**, 158; **60**, 117; **63**, 26, 37; **64**, 27; **65**, 98; **66**, 37; **69**, 226

**Org. Synth. Coll. Vol.** : **1**, 272; **2**, 200; **3**, 286; **4**, 630, 652, 662, 776; **5**, 486, 1135; **6**, 31, 648, 666, 940; **7**, 50, 363, 368, 414; **8**, 87, 219, 444

**Science of Synthesis** : **9**, 195, 306, 312, 454, 472, 492; **10**, 136, 167, 556

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2) A. Michael, *J. Prakt. Chem.*, 1887, **35**, 349.

3) H. Wynberg; H.A.P. de Jongh, *Recl. Trav. Chim. Pays-Bas*, 1963, **82**, 202.

4) G.H. Posner; S.-B. Lu; E. Asirvatham, *Tetrahedron Lett.*, 1986, **27**, 659.

5) G.H. Posner; E. Asirvatham, *Tetrahedron Lett.*, 1986, **27**, 663.

6) D. Enders; J. Wiedemann; W. Bettray, *Synlett*, 1995, 369.

7) G. Batoli; M. Bosco; M.C. Bellucci; E. Marcantoni; L. Sambri; E. Torregiani, *Eur. J. Org. Chem.*, 1999, 617.

8) D. Enders; A. Seki, *Synlett*, 2002, 65.

9) R. Antonioletti; P. Bovicelli; S. Malancona, *Tetrahedron*, 2002, **58**, 589.

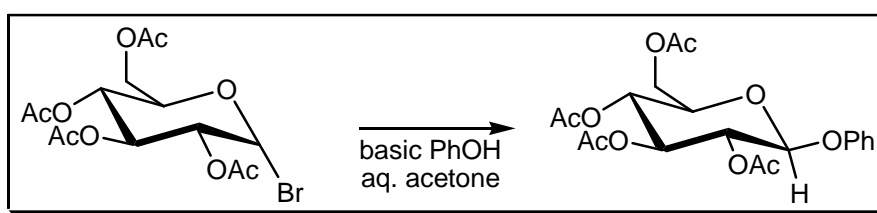
10) B. List, *Acc. Chem. Res.*, 2004, **37**, 548.

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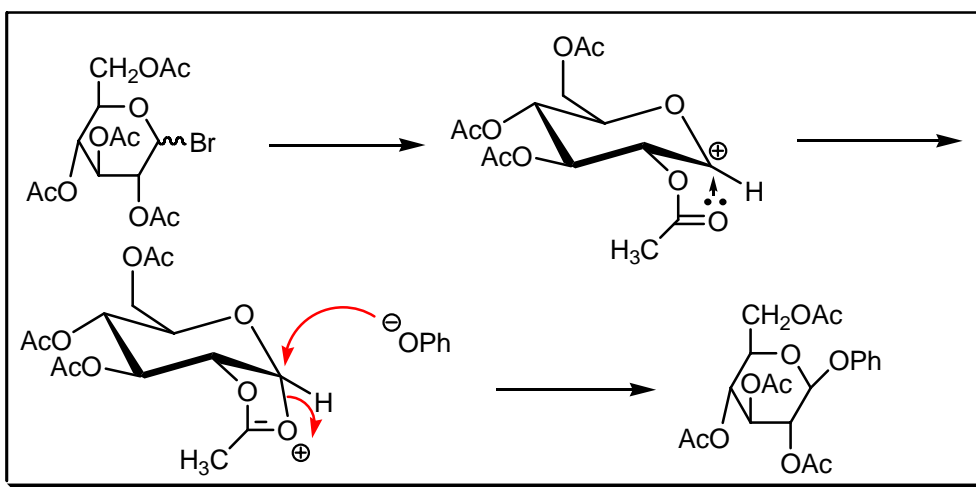
COMMENTS :

## MICHAEL GLYCOSIDATION

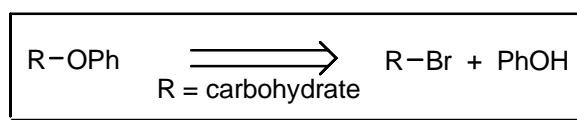
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

An acetohalogeno-sugar reacts with alkali phenoxide to yield the phenylglycoside. This method of glycoside synthesis was modified by **Koenigs** and **Knorr**. See also **Fischer** glycosidation, **Kahne** glycosidation and **Koenigs – Knorr** reactions.

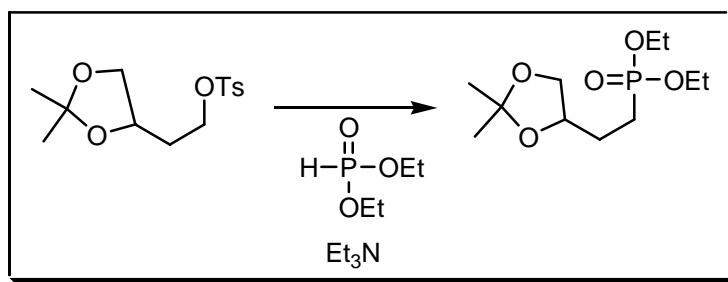
## REFERENCES :

- 1) A. Michael, *J. Am. Chem. Soc.*, 1879, **1**, 307.
- 2) W.J. Hickinbottom, *J. Chem. Soc.*, 1930, 1338.

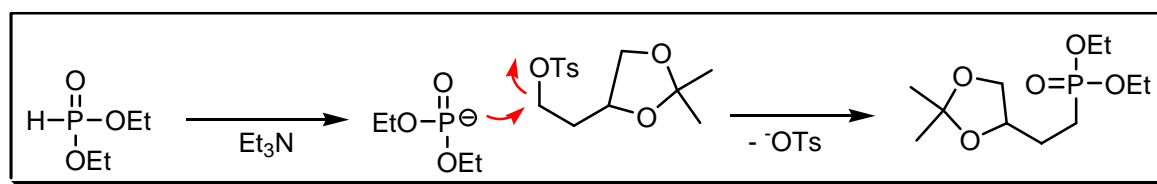
## COMMENTS :

## MICHAELIS – BECKER – NYLÉN PHOSPHONYLATION

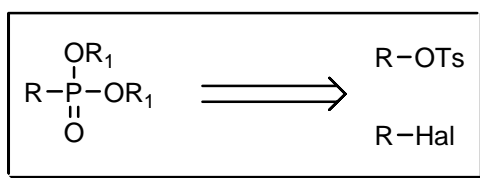
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The reaction is mainly used for the synthesis of phosphonates from alkyl halogens or tosylates. See also **Abramov**, **Allen**, **Arbuzov** (Michaelis – Arbuzov), **Atherton – Openshaw – Todd**, **Landauer – Rydon** and **Perkow** reactions.

## REFERENCES :

Houben – Weyl : E7b, 913

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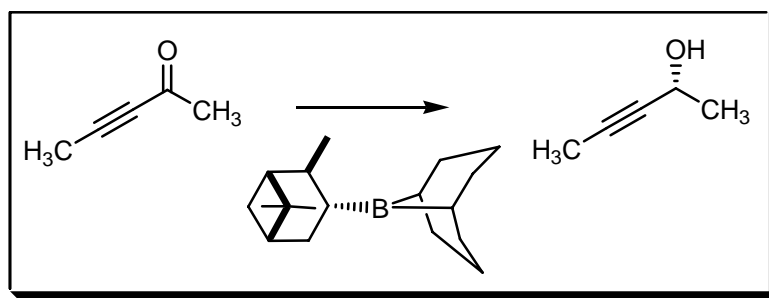
- 1) A. Michaelis; Th. Becker, *Ber. Dtsch. Chem. Ges.*, 1897, **30**, 1003.
  - 2) P. Nylén, *Ber. Dtsch. Chem. Ges.*, 1924, **57**, 1023.
  - 3) A.K. Bhattacharya; G. Thyagarajan, *Chem. Rev.*, 1981, **81**, 415.
  - 4) K.M. Kem; N.V. Nguyen; D.J. Cross, *J. Org. Chem.*, 1981, **46**, 5188.
  - 5) T. Kato; M. Tejima; H. Ebiiike; K. Achiwa, *Chem. Pharm. Bull.*, 1996, **44**, 1132.
  - 6) G.M. Ciszewski; J.A. Jackson, *Org. Prep. Proced. Int.*, 1999, **31**, 240.
  - 7) B. Iorga; F. Eymery; D. Carmichael; P. Savignac, *Eur. J. Org. Chem.*, 2000, 3103.
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## COMMENTS :

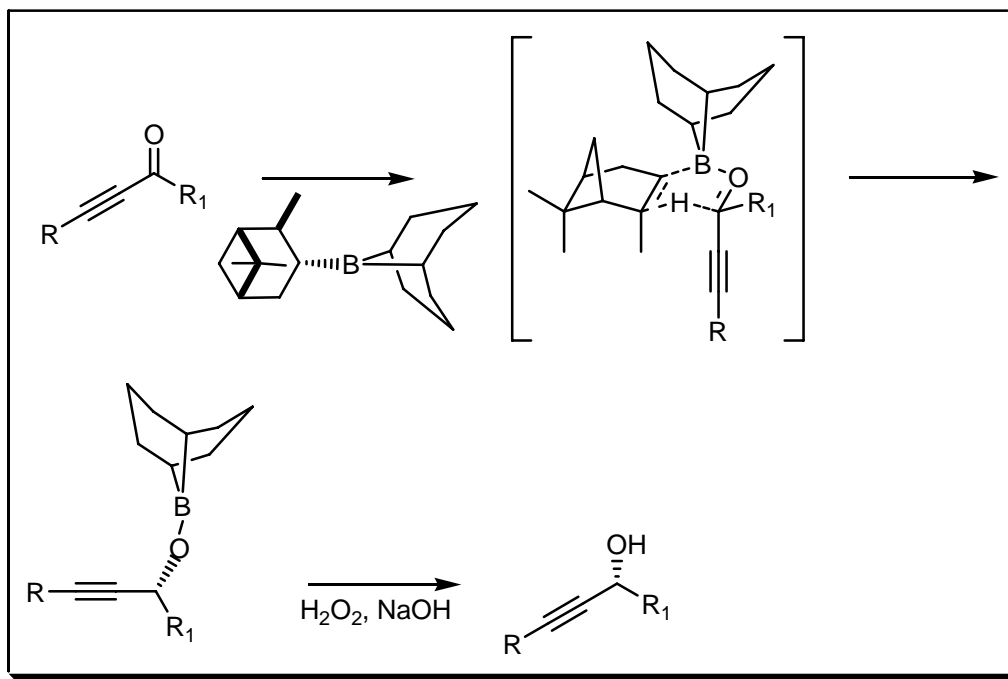
## MIDLAND REDUCTION

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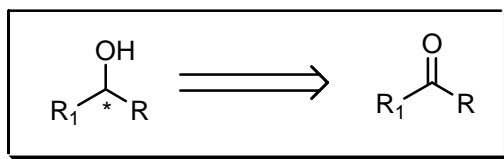
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Alpine-borane (*B*-isopinocampheyl-9-borabicyclo[3.3.1]nonane) reduces ketones asymmetrically. See also **Corey – Itsuno – Bakshi – Shibata**, **Horner – Knowles – Kagan** and **Noyori** hydrogenation.

## REFERENCES :

**March** : 915

**Smith – March 2<sup>nd</sup>** : 1201

**Smith 2<sup>nd</sup>** : 347

**Org. Synth.** : 63, 57

**Org. Synth. Coll. Vol.** : 7, 402

1) M.M. Midland; A. Tramontano; S.A. Zederic, *J. Am. Chem. Soc.*, 1979, **101**, 2352.

2) H.C. Brown; G.G. Pai; P.K. Jadhav, *J. Am. Chem. Soc.*, 1984, **106**, 1531.

3) M.M. Midland, *Chem. Rev.*, 1989, **89**, 1553.

4) V.K. Singh, *Synthesis*, 1992, 605.

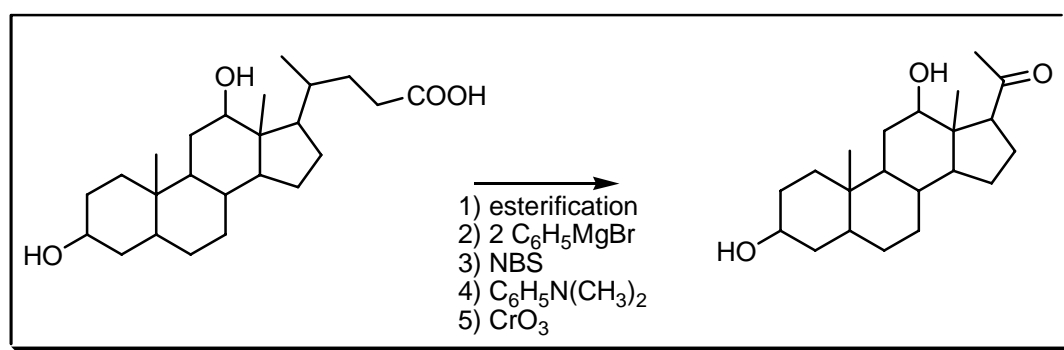
5) D.R. Williams; M.G. Fromhold; J.D. Earley, *Org. Lett.*, 2001, **3**, 2721.

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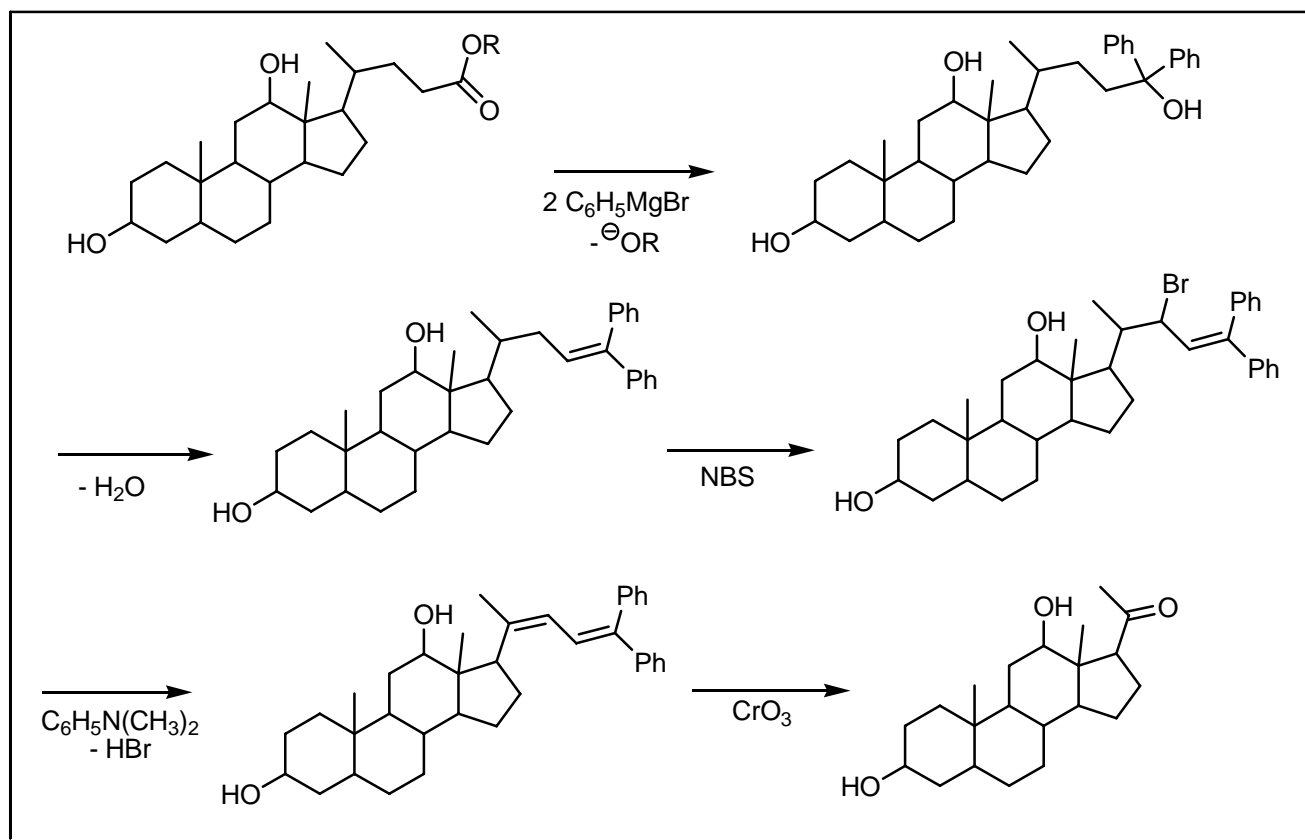
COMMENTS :

## MIESCHER DEGRADATION

EXAMPLE :

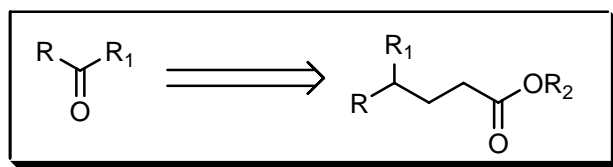


MECHANISM :





## DISCONNECTION :



## NOTES :

A modification of the **Barbier – Locquin – Wieland** reaction for the degradation of aliphatic acids side chains in which three carbons are eliminated at one time. Using *N*-bromosuccinimide in allyl bromide it is possible simultaneously to affect the  $\alpha$ -bromination, elimination of hydrogen bromide, and the bromination of the diene. See also **Barbier – Locquin – Wieland**, **Gallagher – Hollander**, **Hoehn – Mason**, **Krafft** and **Trost** oxidative decarboxylation reactions.

## REFERENCES :

Smith : 304

Smith 2<sup>nd</sup> : 267

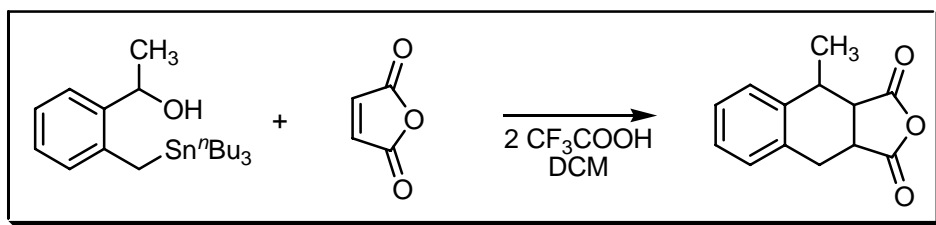
1) C. Meystre; H. Frey; A. Wettstein; K. Miescher, *Helv. Chim. Acta*, 1944, **27**, 1815.

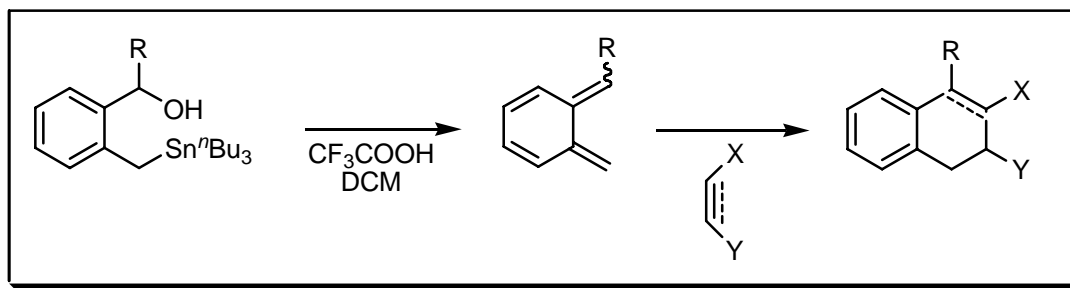
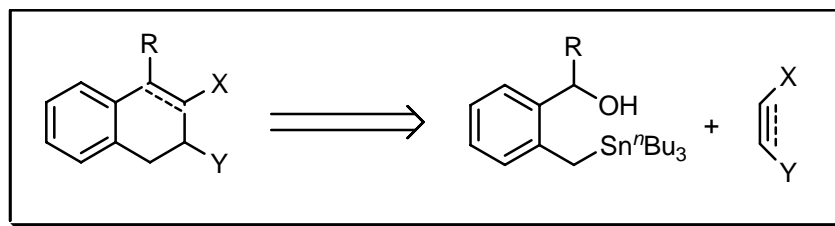
2) F.S. Spring, *J. Chem. Soc.*, 1950, 3355.

## COMMENTS :

## MIGITA – SANO SYNTHESIS

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

The proton induced [1,4]-elimination of O-(1-hydroxyalkyl)benzyltributylstannanes.

**REFERENCES :**

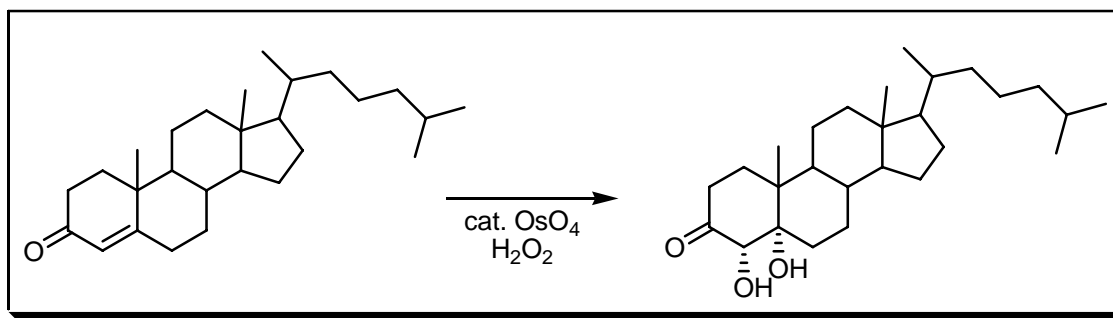
- 1) T. Kauffmann, *Angew. Chem., Int. Ed. Engl.*, 1982, **21**, 410.
- 2) H. Sano; H. Ohtsuka; T. Migata, *J. Am. Chem. Soc.*, 1988, **110**, 2014.

**COMMENTS :**

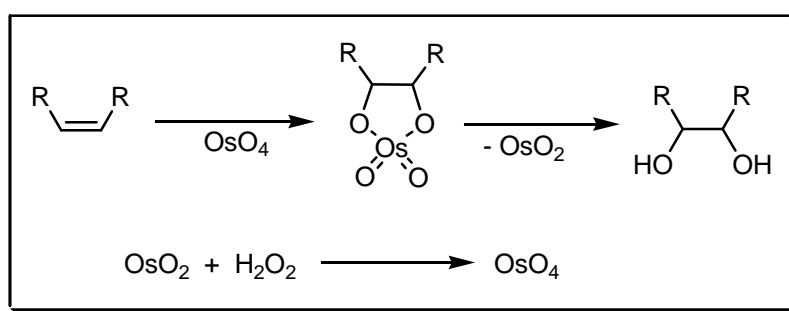
## MILAS HYDROXYLATION OF OLEFINS

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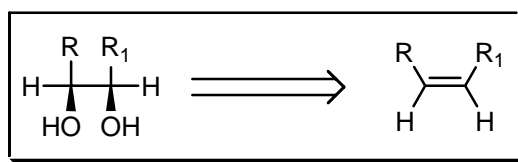
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The *syn* hydroxylation of a double bond to a 1,2-diol with hydrogen peroxide and catalytic amounts of  $\text{OsO}_4$  or  $\text{V}_2\text{O}_5$  as catalyst to reoxidise the osmium(4+). Ultraviolet light can also be used. See also **Criegee** osmium tetroxide, **Fenton**, **Prévost**, **Sharpless** dihydroxylation and **Woodward** dihydroxylation reactions.

### REFERENCES :

March : 822

Smith – March : 1048

Smith : 280

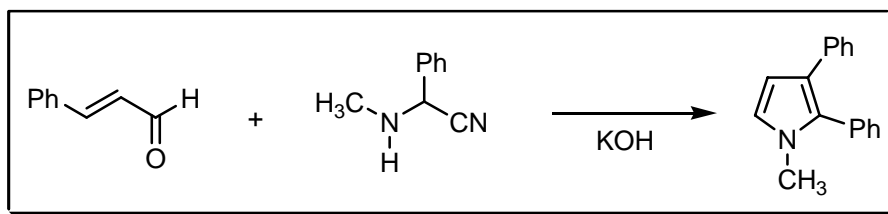
Smith 2<sup>nd</sup> : 248

Org. Synth. : 11, 46

Org. Synth. Coll. Vol. : 2, 302

- COMMENTS :**

**EXAMPLE :**



The reaction scheme illustrates the synthesis of 2,3-disubstituted pyrroles. It begins with the reaction of an  $\alpha,\beta$ -unsaturated aldehyde (with substituents  $R$  and  $H$ ) and a malononitrile derivative (with substituents  $R_1$  and  $R_2$ ) in the presence of  $KOH$ . This forms an intermediate where the aldehyde carbon is reduced to a secondary alcohol and the malononitrile nitrogen is protonated. Subsequent cyclization, indicated by red curved arrows, leads to a five-membered ring intermediate. This intermediate then undergoes dehydration ( $-H_2O$ ) and decarboxylation ( $-HCN$ ) to yield the final 2,3-disubstituted pyrrole product.

$$\text{R}_3\text{-C}_5\text{H}_3\text{(R)-N(R}_1\text{)-C}_2\text{(R}_2\text{)=C(R)-C(R)=C(R)-} \Rightarrow \text{R-CH=CH-C(=O)R}_3 + \text{R}_1\text{-NH-CH(R}_2\text{)-CN}$$

## NOTES :

Pyrrole is obtained by treating a mixture of an  $\alpha,\beta$ -unsaturated aldehyde and an aminoacetonitrile with potassium hydroxide. See also **Barton – Zard**, **Clauson–Kaas**, **Fischer – Fink**, **Grob – Camenisch**, **Hantzsch** pyrrole, **Harries** pyrrole, **Kenner**, **Knorr** pyrrole, **Paal – Knorr**, **Padwa**, **Piloty – Robinson**, **Schwanert**, **Trofimov** and **Zav'yalov** reactions.

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## REFERENCES :

**Houben – Weyl** : E6a, 672

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- 1) W. von Miller; I. Plöchl, *Ber. Dtsch. Chem. Ges.*, 1898, **31**, 2699.
  - 2) R.W.L. Clark; A. Lapworth, *J. Chem. Soc.*, 1907, **91**, 694.
  - 3) S. Borforß, *Ber. Dtsch. Chem. Ges.*, 1931, **64**, 1111.
  - 4) A. Treibs; R. Derra, *Liebigs Ann. Chem.*, 1954, **589**, 176.
  - 5) *Japan Patent*, 7338705. (*Chem. Abs.*, 1974, **80**, 133240.)

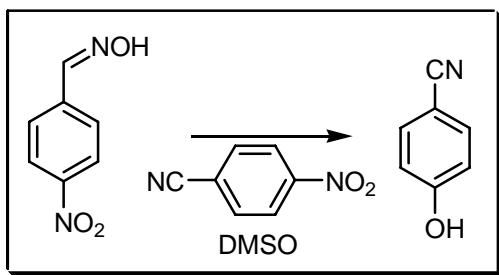
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## COMMENTS :

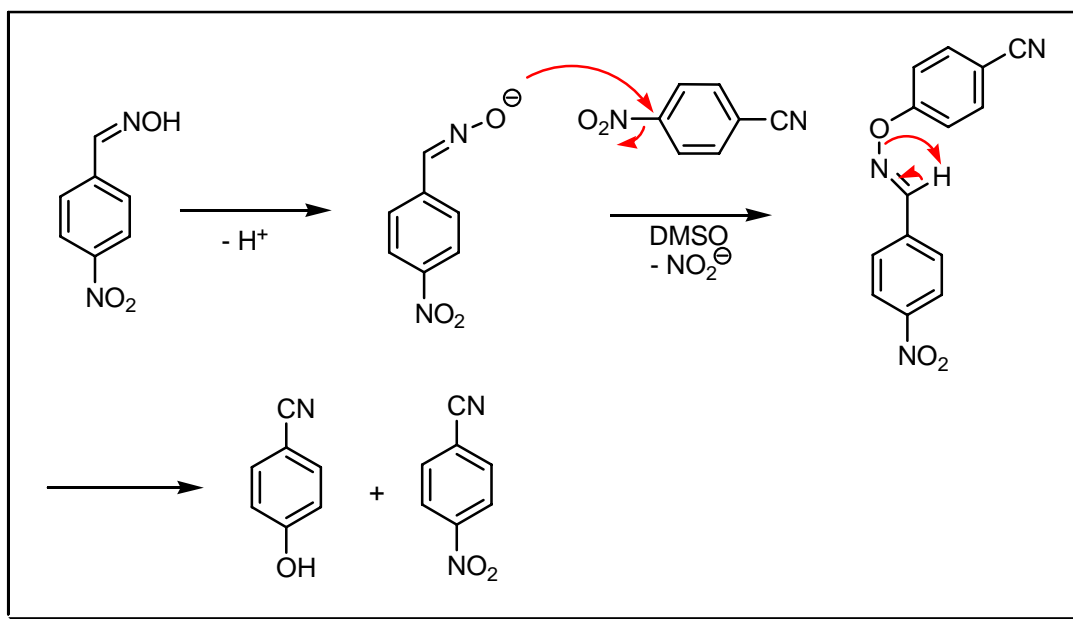
## MILLER – SNYDER ARYL CYANIDE SYNTHESIS

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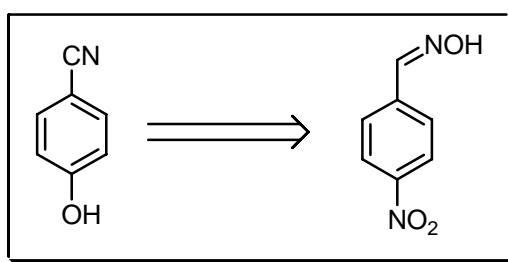
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Benzonitriles are synthesised from aldehydes *via* oxime ethers. *p*-Cyanophenol can also be prepared from *p*-nitrobenzaldehyde oxime and *p*-nitrobenzonitrile (sometimes used as a recyclable chain carrier.)

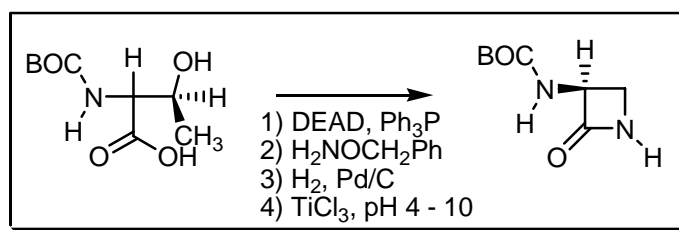
## REFERENCES :

- 1) R.D. Knudsen; H.R. Snyder, *J. Org. Chem.*, 1974, **39**, 3343.
- 2) M.J. Miller; G.M. Loudon, *J. Org. Chem.*, 1975, **40**, 126.
- 3) R.D. Knudsen; A.G. Morrice; H.R. Snyder, *J. Org. Chem.*, 1975, **40**, 2878.
- 4) H.M.S. Kumar; B.V.S. Reddy; P.T. Reddy; J.S. Yadav, *Synthesis*, 1999, 586.
- 5) K.V.N. Srinivas; E.B. Reddy; B. Das, *Synlett*, 2002, 625.

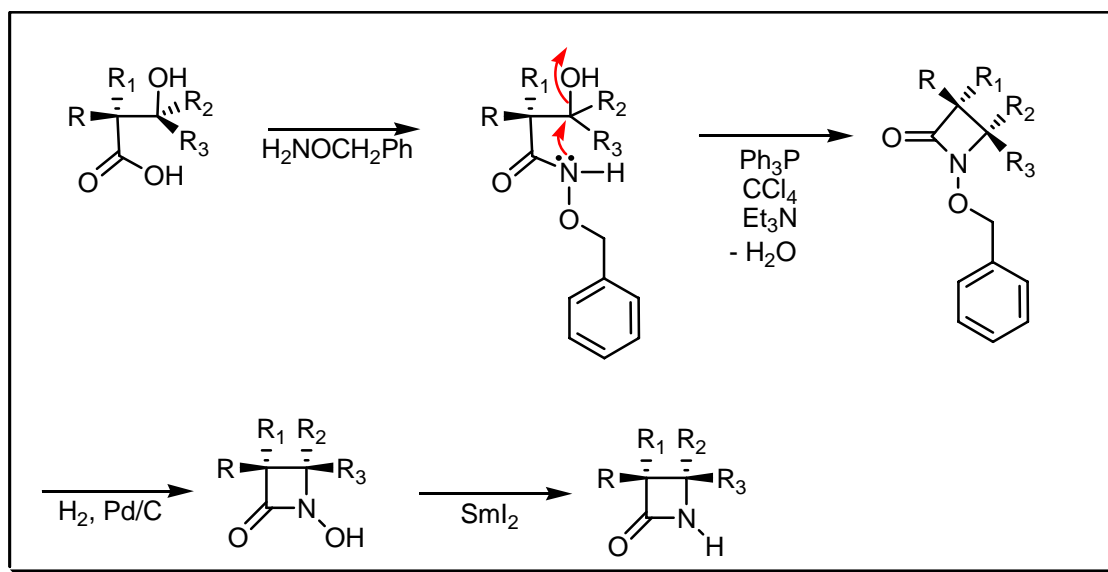
## COMMENTS :

## MILLER SYNTHESIS

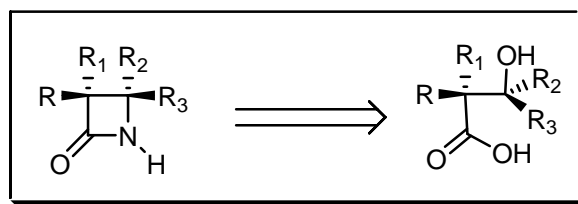
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

An efficient biomimetic  $\beta$ -lactam synthesis has been developed on the basis of cyclisation of substituted  $\beta$ -hydroxyhydroxamic acids. DEAD,  $\text{Ph}_3\text{P}$  or  $\text{Ph}_3\text{P}$ ,  $\text{CCl}_4$ ,  $\text{Et}_3\text{N}$  mediates the cyclisation. See also **Appel**, **Mitsunobu** and **Vorbrüggen – Krolakiewicz** reactions.

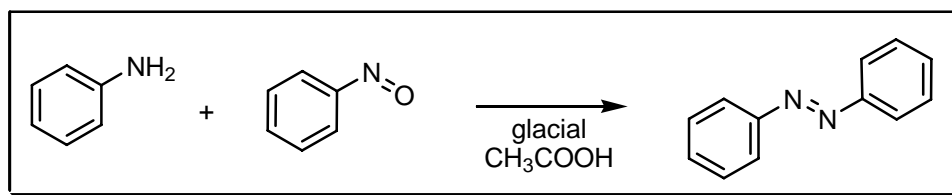
### REFERENCES :

- 1) M.J. Miller; P.G. Mattingly; M.A. Morrison; J.F. Kerwin, jr., *J. Am. Chem. Soc.*, 1980, **102**, 7026.
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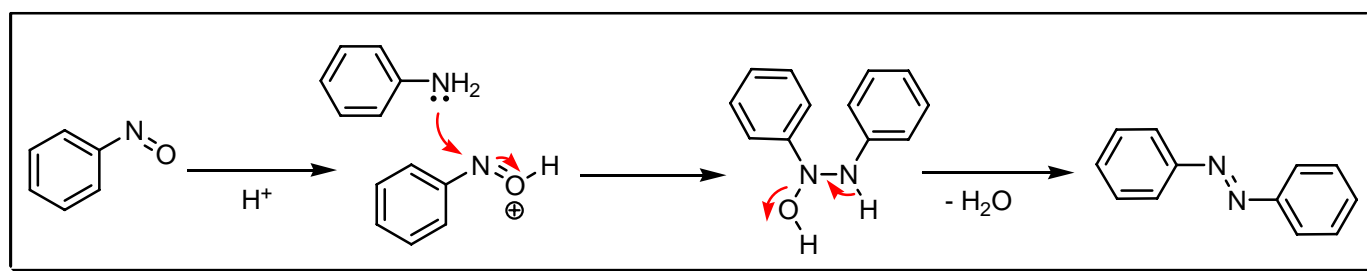
COMMENTS :

## MILLS SYNTHESIS

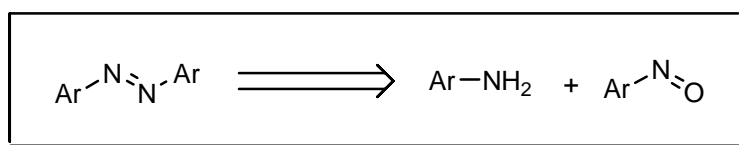
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The reaction between a primary arylamine and an aromatic nitroso compound in glacial acetic acid affords symmetrical or unsymmetrical azo compound. It is assumed that the intermediate is an *N*-anilinohydroxylamine.

REFERENCES :

March : 638

Smith – March : 818

1) C. Mills, *J. Chem. Soc.*, 1895, **67**, 925.

2) P. Ruggli; C. Pettijean, *Helv. Chim. Acta*, 1938, **24**, 711.



3) Y. Ogata; Y. Takagi, *J. Am. Chem. Soc.*, 1958, **80**, 3591.

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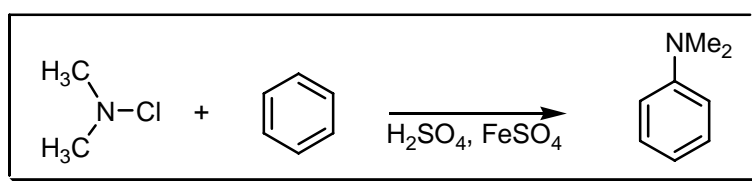
**COMMENTS :**

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**MINISCI AROMATIC AMINATION**

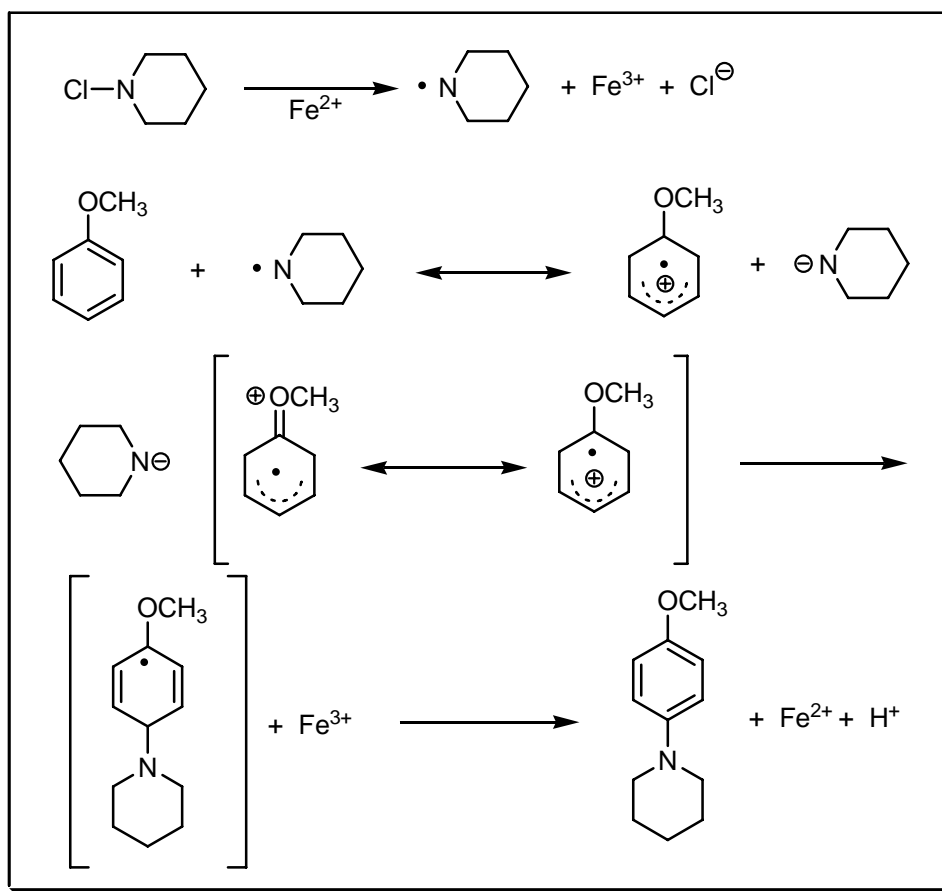
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**EXAMPLE :**

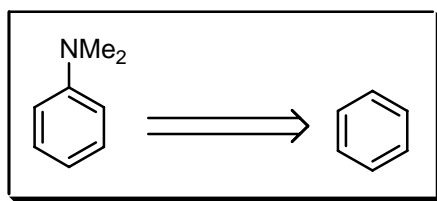


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**MECHANISM :**



## DISCONNECTION :



## NOTES :

The iron-catalysed free radical amination of aromatics or free radical carbamylation of protonated heterocycles. The majority of the reactions have been carried out in water or aqueous solutions.

## REFERENCES :

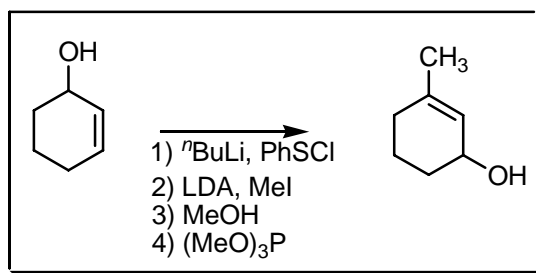
Houben – Weyl : **E5**, 1050; **E7b**, 583; **E16d**, 655

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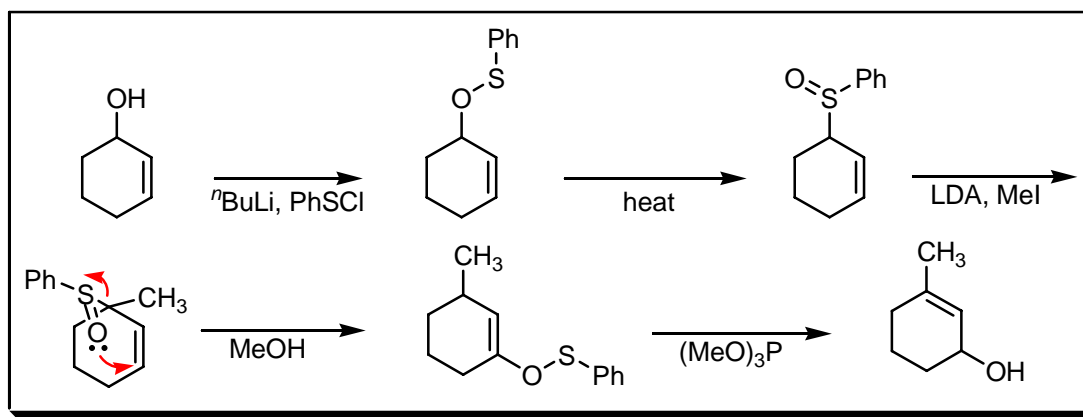
## COMMENTS :

## MISLOW – BRAVERMAN – EVANS REARRANGEMENT

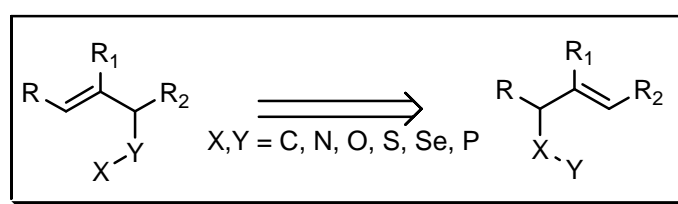
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The reversible [2,3]-sigmatropic rearrangement of allylic sulfoxides to allyl sulfenates which are cleaved by phosphites to allylic alcohols.

## REFERENCES :

March : 1143

Smith – March : 1455

Smith : 746

Smith 2<sup>nd</sup> : 631

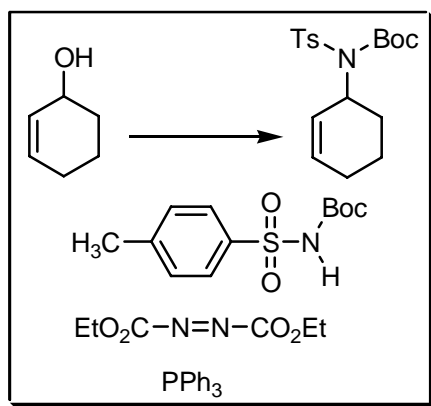
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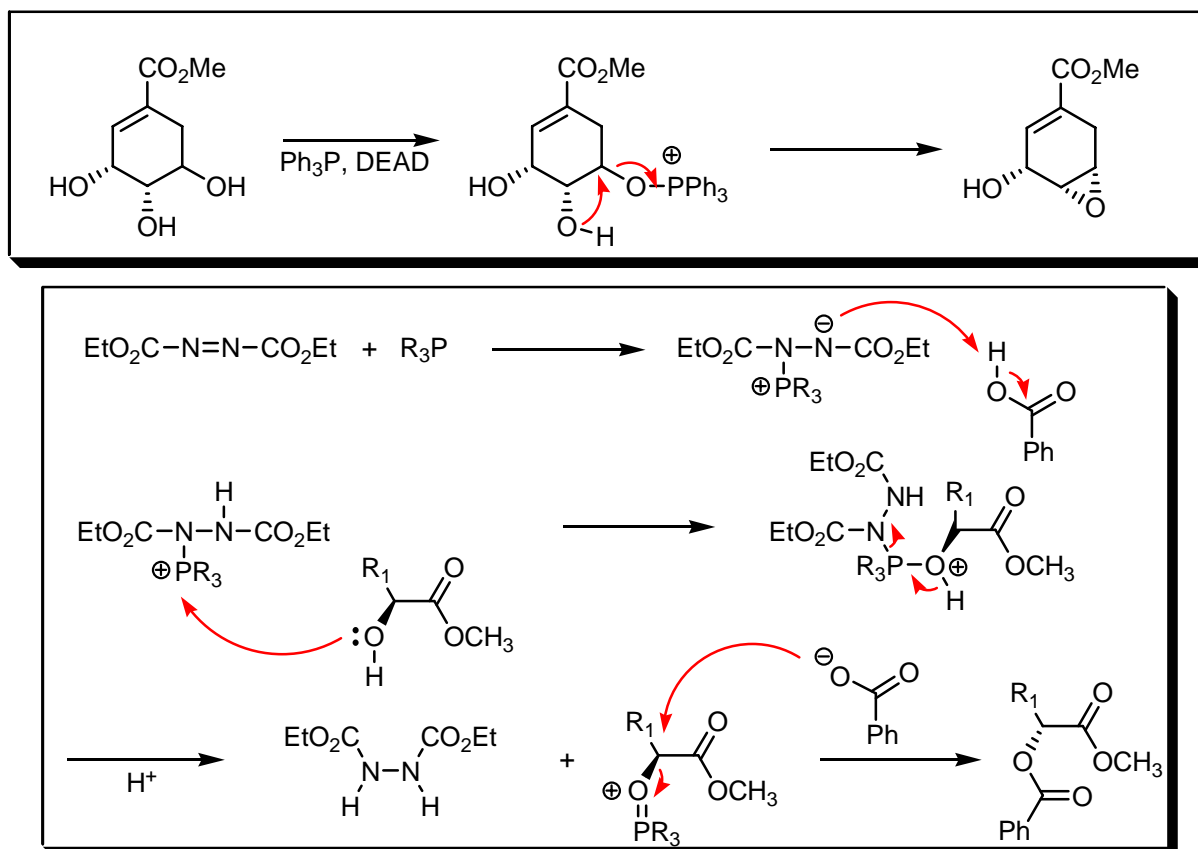
COMMENTS :

## MITSUNOBU REACTION

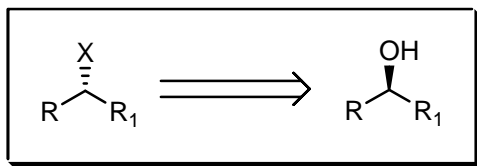
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The *inter*- and *intramolecular* nucleophilic displacement of alcohols with inversion (The **Mitsunobu** inversion) using diethylazodicarboxylate (DEAD)-triphenylphosphine or diisopropylazodicarboxylate (DIAD) – triphenylphosphine and a nucleophile. The **Mitsunobu** reaction can be used for ester, ether, imide, lactam, C-N, C-S, C-halogen, C-C formation and also for dehydration reactions. The use of a fluorous analogue of DEAD has been reported by **Dobbs et al.** Fukuyama uses **Mitsunobu** conditions in the preparation of secondary amines from primary amines. This reaction is also known under the name **Fukuyama – Mitsunobu** reaction. **Corey – Nicolaou**, **Diels – Alder**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Kita**, **Masamune**, **Michael** condensation, **Miller**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolakiewicz**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

## REFERENCES :

**March** : 396

**Smith – March** : 486, 502, 513

**Smith** : 138

**Smith 2<sup>nd</sup>** : 110, 495, 505, 1264

**Houben – Weyl** : **E6b**, 1122; **E16a**, 1266; **E16c**, 390, 443; **E16d**, 581, 726

**Org. React.** : **42**, 335

**Org. Synth.** : **73**, 110; **76**, 178

**Org. Synth. Coll. Vol.** : **9**, 607; **10**, 2350

**Science of Synthesis** : **10**, 51, 437

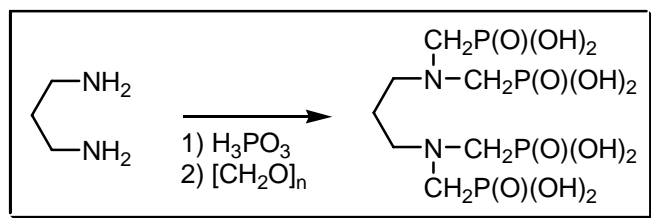
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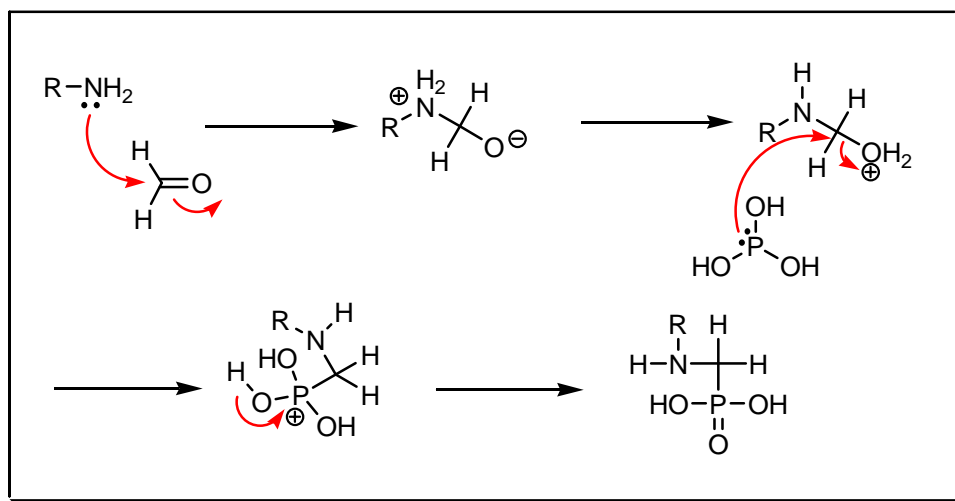
COMMENTS :

## MOEDRITZER – IRANI REACTION

EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

This is the one-step **Mannich**-like synthesis of aminoalkylphosphonates. See also **Kabachnik – Fields** and **Richman – Atkins** reactions.

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## REFERENCES :

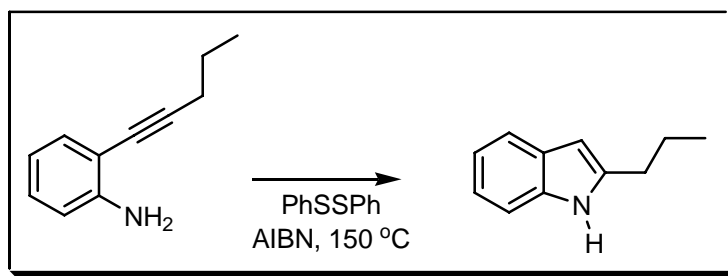
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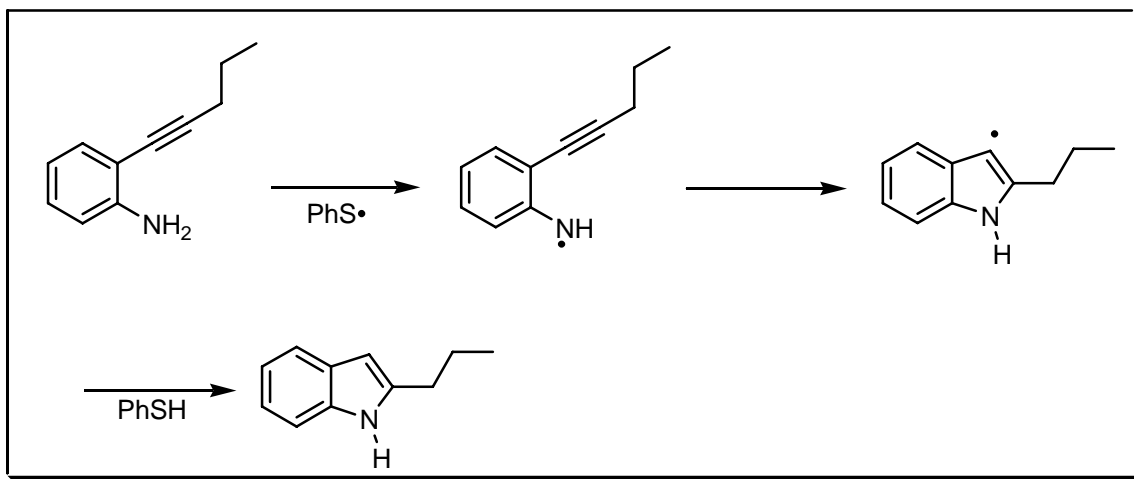
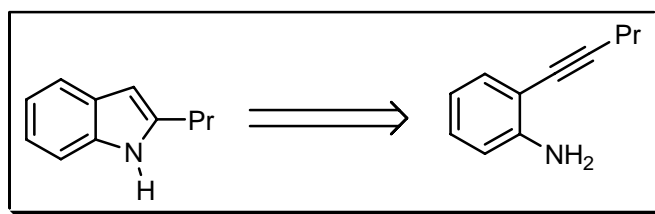
## COMMENTS :

## MONTEVECCHI INDOLE SYNTHESIS

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### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

1-(2-Aminophenyl)pent-1-yne can be cyclised to a 2-substituted indole by diphenyldisulfide. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman indole**, **Fischer indole**, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman indole**, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock indole**, **Leimgruber – Batcho**, **Lipp**, **Madelung indole**, **Magnus**, **Martin**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu indole**, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert indole**, **Saegusa indole**, **Schmid**, **Smith**, **Sugasawa indole**, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe heterocyclisation**, **Watanabe indole**, **Weerman indole**, **Wender**, **Widman**, **Yamamoto indole-1**, **Yamamoto indole-2** and **Yurovskaya** reactions.

**REFERENCES :**

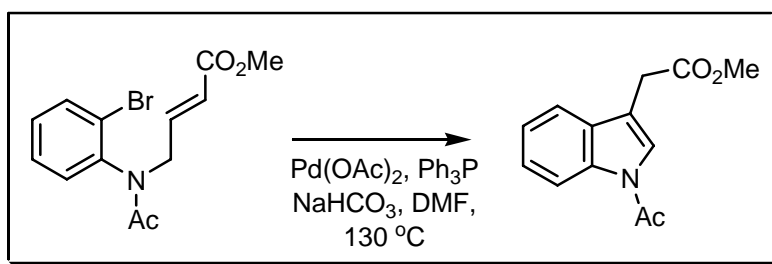
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**COMMENTS :**

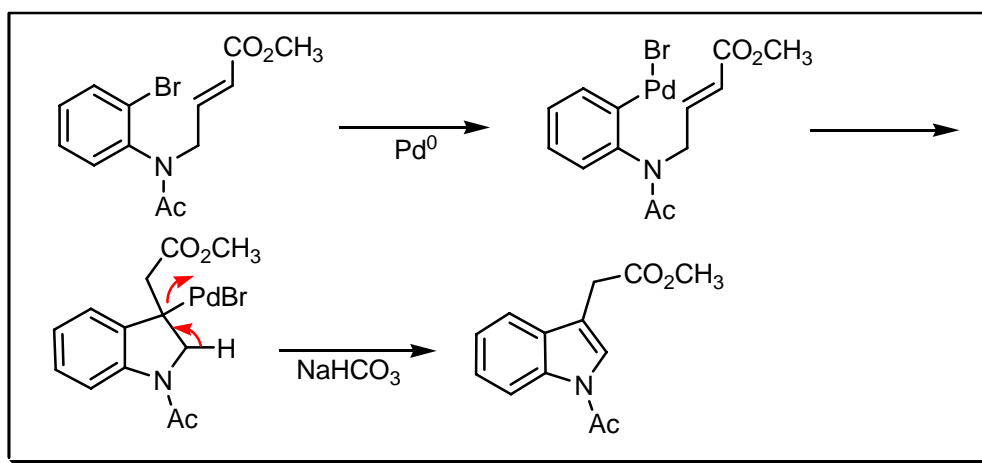
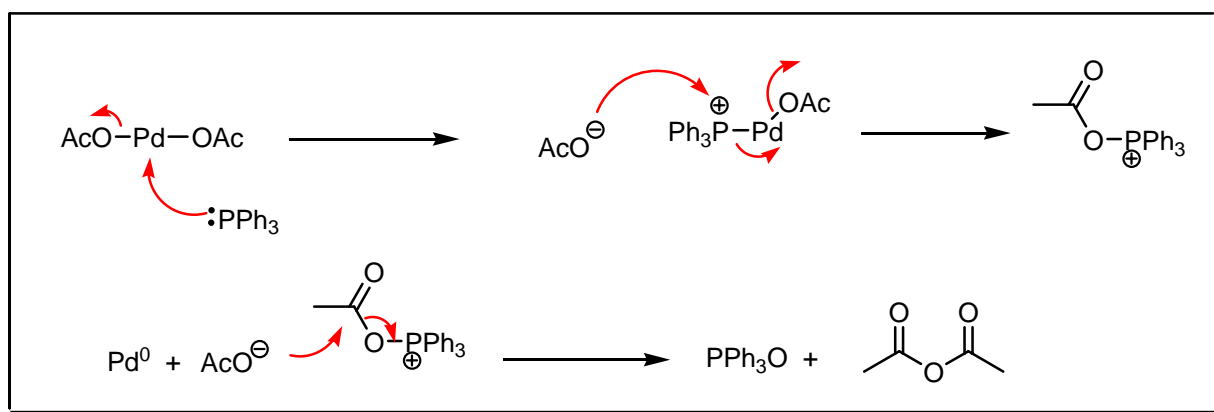


## MORI – BAN INDOLE SYNTHESIS

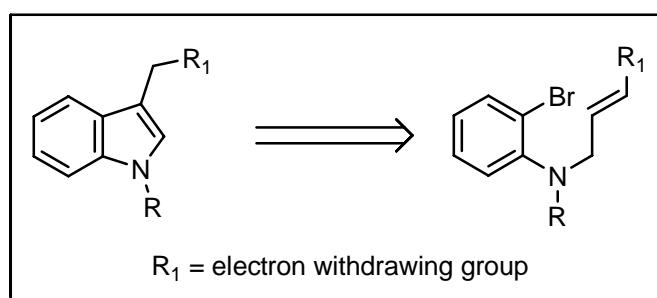
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The mechanism for the **Mori – Ban** indole formation is representative of many palladium-catalysed pyrrole annulation processes. The palladium atom can affect the cyclisation of the *o*-halo-*N*-allyl anilines to indoles under **Fujiwara – Heck** conditions. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

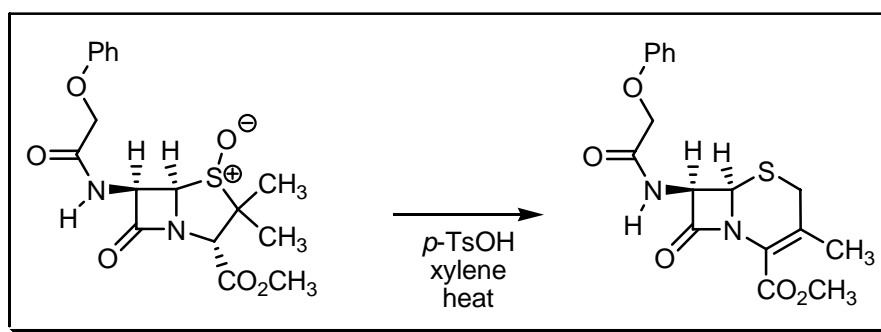
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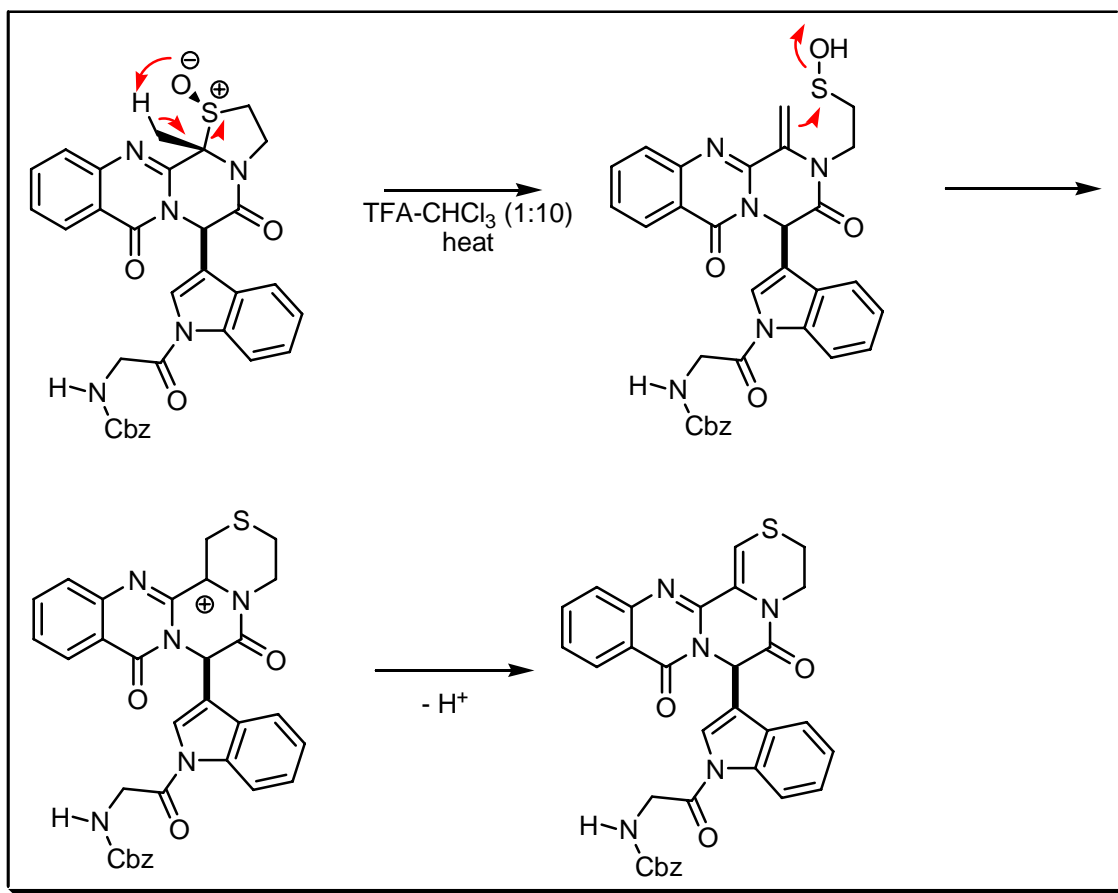
## COMMENTS :

## MORIN REARRANGEMENT

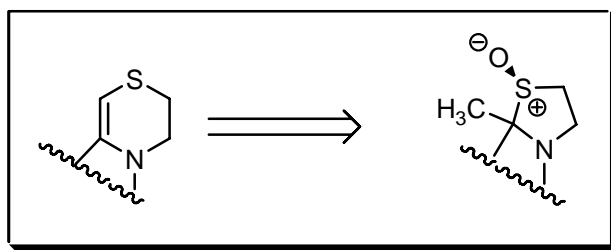
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The rearrangement of heterocyclic sulfoxides *via* an olefinic sulfenic acid, addition of this acid to an olefin affords after loss of a proton a sulfide. The reaction is mainly used for the ring-expansion of penams to cepems.

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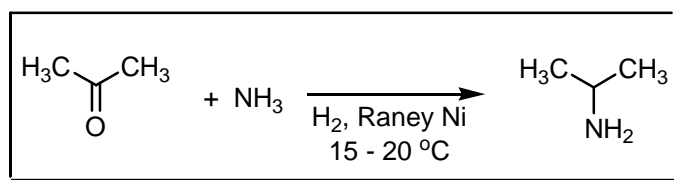
**COMMENTS :**

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## MOUREAU – MIGNONAC REACTION

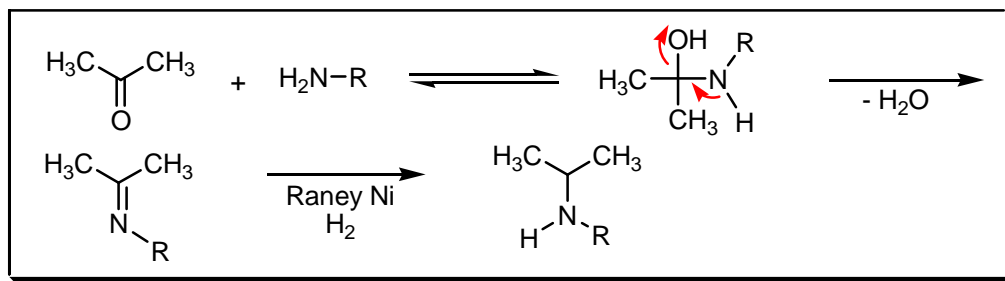
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**EXAMPLE :**



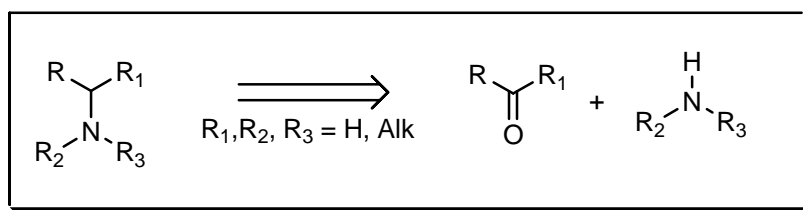
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**MECHANISM :**



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**DISCONNECTION :**



## NOTES :

Aldehydes and ketones are converted into amines by catalytic hydrogenation in ethanol containing one mole of ammonia or an amine (reductive alkylation). Also possible is the catalytic oxidation of aliphatic alcohols into aldehydes or ketones by heating in a stream of oxygen in the presence of nickel or silver. See also **Adkins – Peterson**, **Eschweiler – Clarke**, and **Leuckart – Wallach** reactions.

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## REFERENCES :

**March** : 898

**Smith – March** : 1187

**Houben – Weyl** : 4/2, 51

**Org. Synth.** : 23, 68; 27, 28

**Org. Synth. Coll. Vol.** : 3, 328, 717

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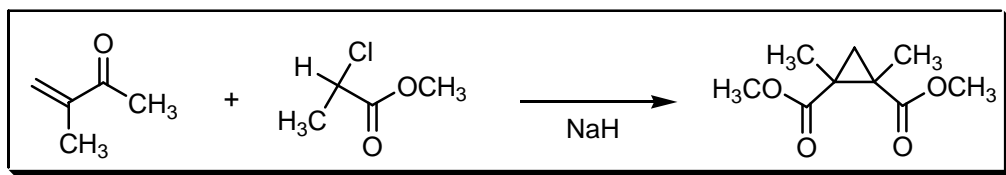
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## COMMENTS :

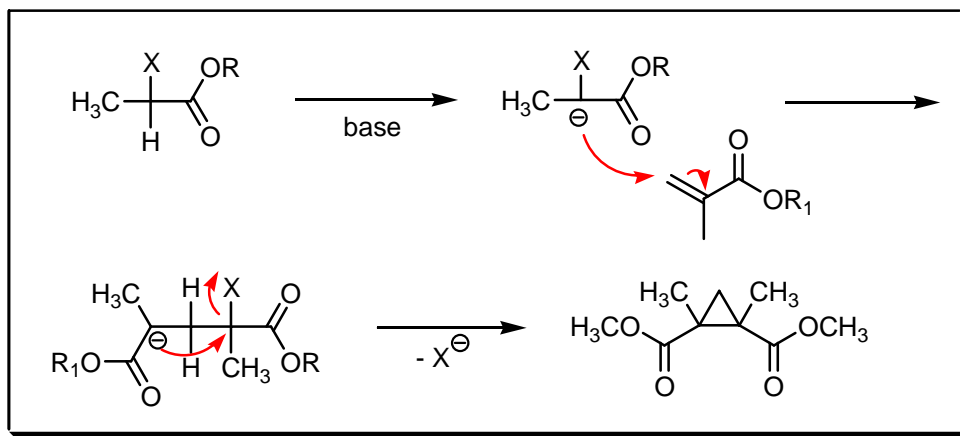
## MOUSSERON – FRAISSE – McCOY CYCLOPROPANATION

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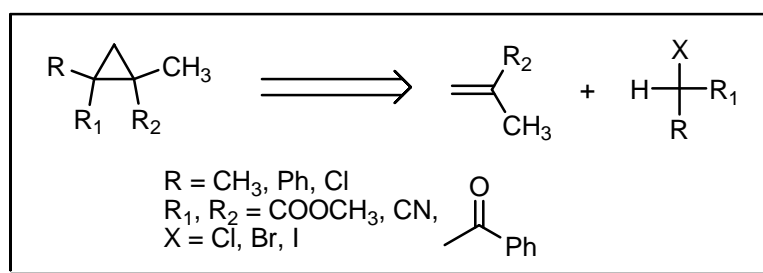
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The stereoselective preparation of substituted cyclopropanes by **Michael** addition. See also **Charette**, **Freund**, **Gustavson**, **Hass** cyclopropane, **Ipatiew**, **Nerdel** and **Simmons – Smith** reactions.

## REFERENCES :

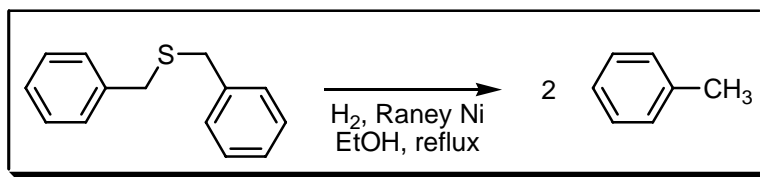
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## COMMENTS :

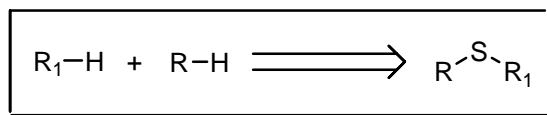
## MOZINGO DESULFURISATION

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### EXAMPLE :



### DISCONNECTION :



### NOTES :

Hydrogenolysis and desulfurisation is affected by treatment with Raney nickel, which normally contains hydrogen in a suitable solvent.

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### REFERENCES :

March : 728

Smith – March : 940

Org. Synth. : **21**, 15; **35**, 80; **56**, 15, 72

Org. Synth. Coll. Vol. : **3**, 181; **4**, 638; **6**, 581, 601

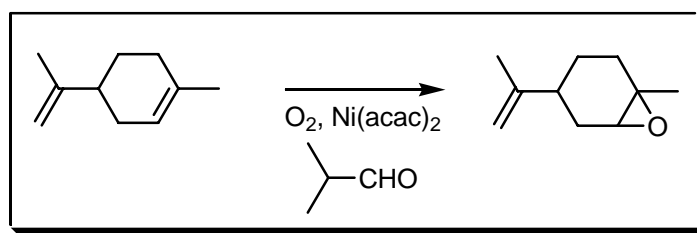
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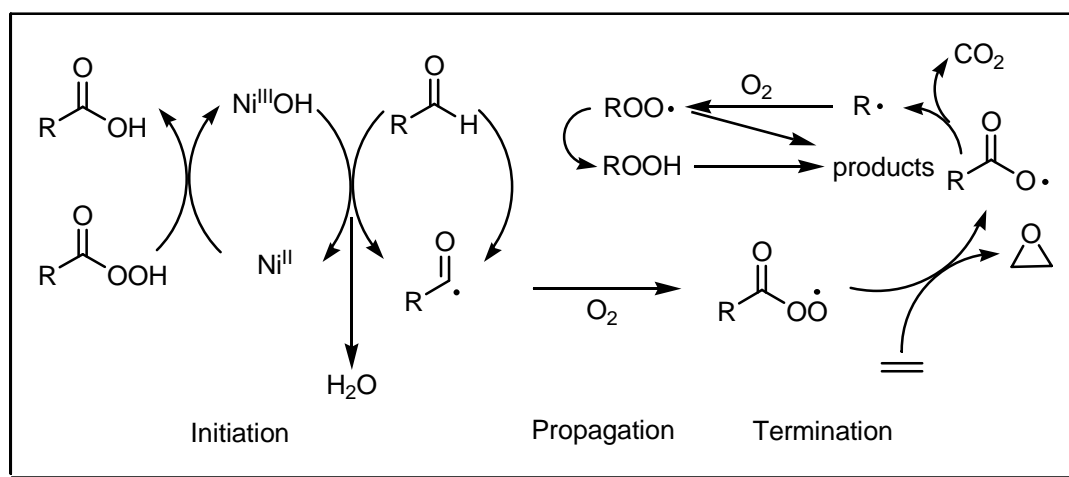
### COMMENTS :

## MUKAIYAMA – YAMADA EPOXIDATION

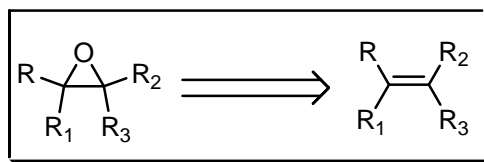
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Although more than stoichiometric amounts of the co-reacting aldehyde are needed, this reaction is very mild, done at room temperature and often display epoxide selectivities up to 100%. The reaction is complete within a few hours. The epoxidising species is the acylperoxy radical. For a detailed study on the mechanism see the work of **Wentzel et al.** See also **Buchner – Curtius – Schlotterbeck**, **Corey – Chaykovsky**, **Jacobsen – Katsuki**, **Juliá – Colonna**, **Katsuki – Sharpless**, **Prileschajew**, **Shi** and **Weitz – Scheffer** reactions.

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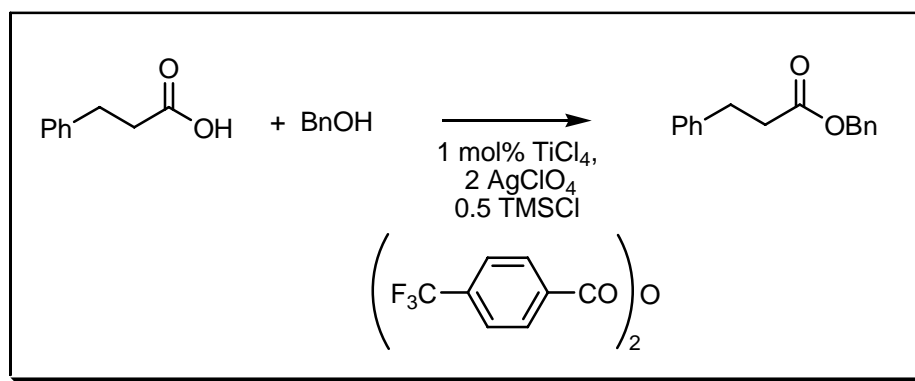


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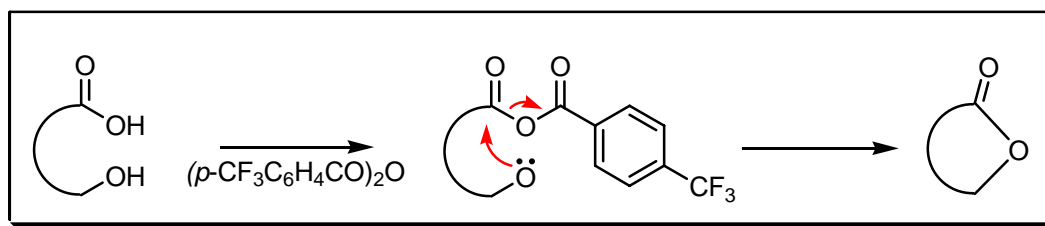
**COMMENTS :**

## MUKAIYAMA MACROLACTONISATION -1

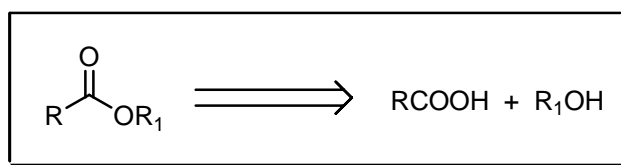
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

A method for the preparation of carboxylic esters from free carboxylic acids and alcohols by combined use of *p*-(trifluoromethyl)benzoic anhydride and a catalytic amount a titanium(IV) salt together with chlorotrimethylsilane. The method is very suitable for the preparation of cyclic lactone from  $\omega$ -hydroxy carboxylic acids. In later versions of this reaction medium-sized ring lactones are prepared by treating monomeric cyclic silylcarboxylates prepared *in situ* from  $\omega$ -hydroxy carboxylic acids and 1,2-bisdimethylsilylbenzene using  $\text{RhCl}(\text{PPh}_3)_3$  and  $\text{Me}_2\text{Si}(\text{OTf})_2$  as catalyst. See also **Corey – Nicolaou**, **Diels – Alder**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Kita**, **Masamune**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolikiewicz**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

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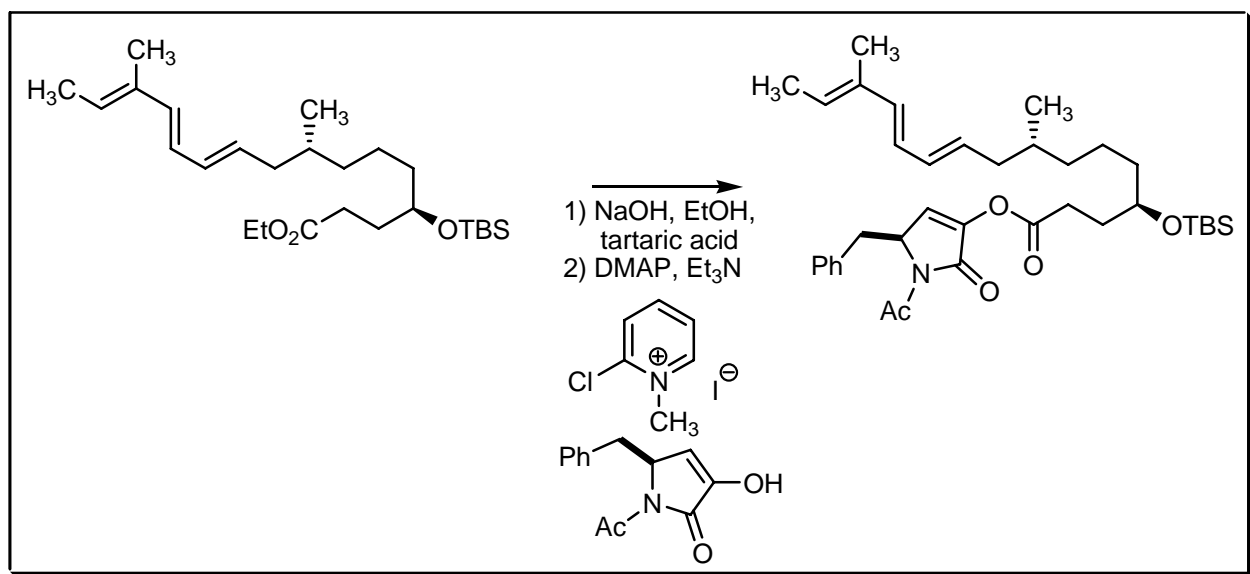
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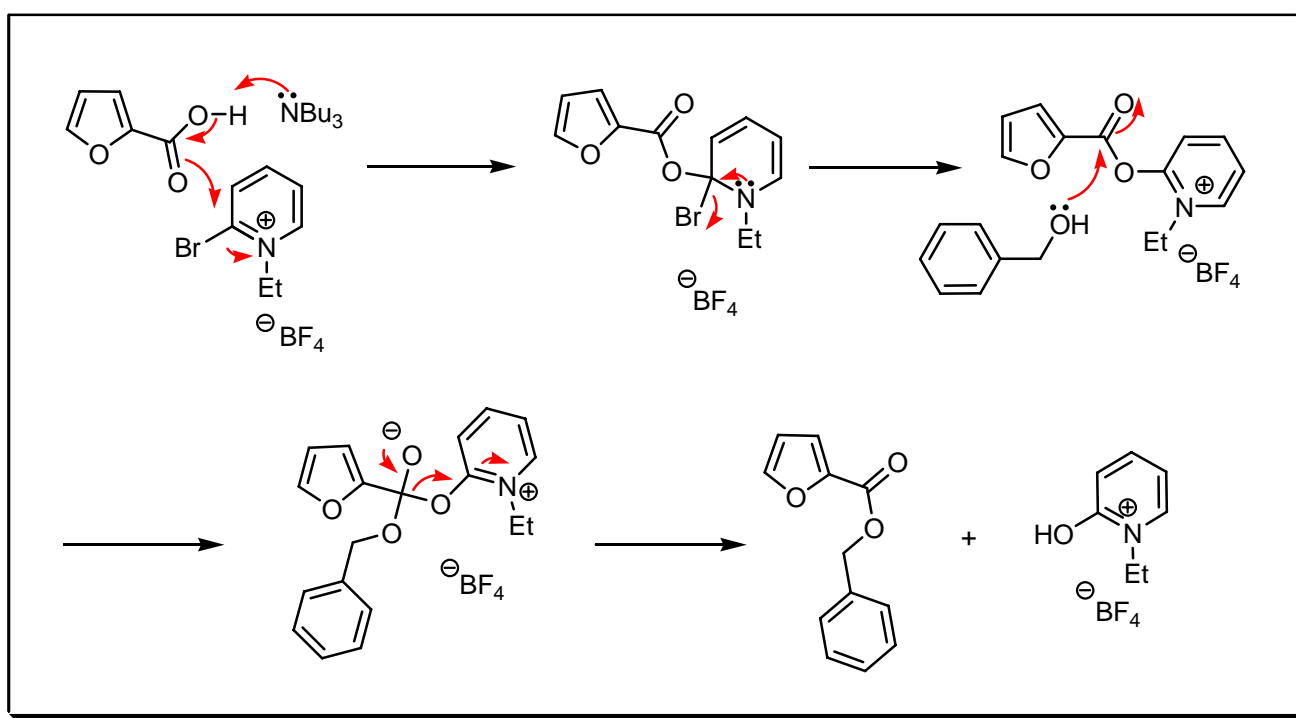
## COMMENTS :

## MUKAIYAMA MACROLACTONISATION - 2

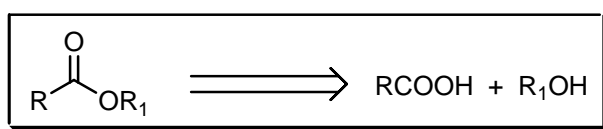
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The **Mukaiyama** reagent is used for the macrolactonisation of carboxylic acids and alcohols. Amides can also be formed using this reagent. See also **Corey – Nicolaou**, **Diels – Alder**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Kita**, **Masamune**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyaama – Kishi (Takai – Utimoto)**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolakiewicz**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

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## REFERENCES :

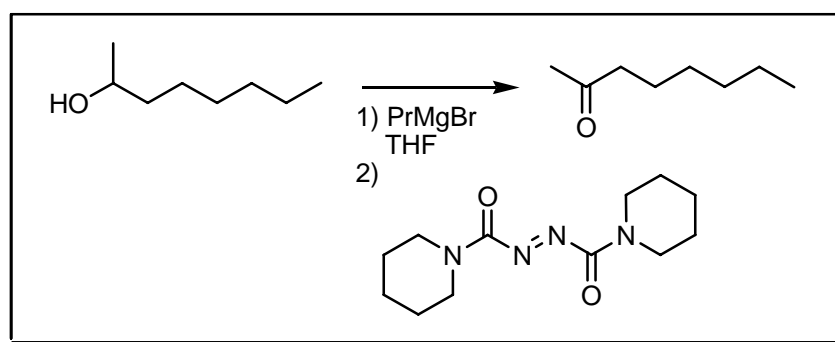
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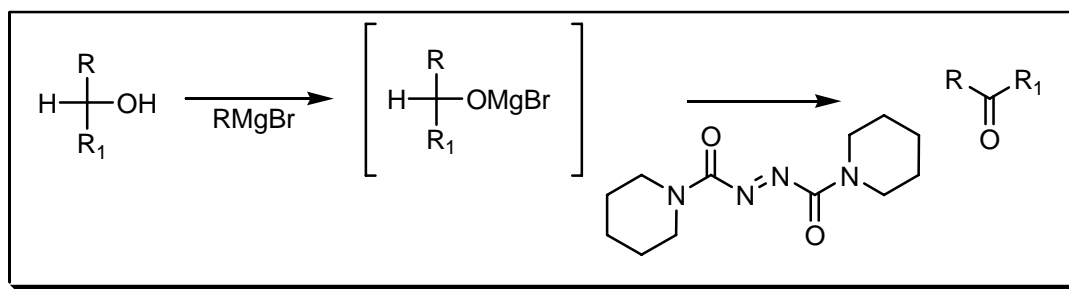
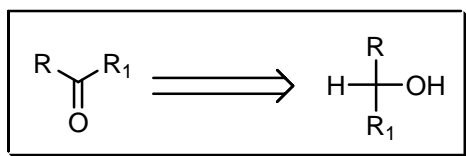
## COMMENTS :

## MUKAIYAMA OXIDATION

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### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

The oxidation of alcohols using a **Grignard** reagent and 1,1'-(azodicarbonyl)dipiperidine. See also **Anelli**, **Ball – Goodwin – Morton**, **Collins**, **Corey – Kim**, **Corey – Schmidt**, **Corey – Suggs**, **David – Thieffry**, **Delépine**, **Dess – Martin**, **Einhorn** oxidation, **Fétizon**, **Jones** oxidation, **Ley**, **Maurer – Drefahl**, **Nicolaou**, **Oppenauer**, **Parikh – von Doering**, **Pfitzner – Moffatt**, **Sarett**, **Swern** and **Uemura** reactions.

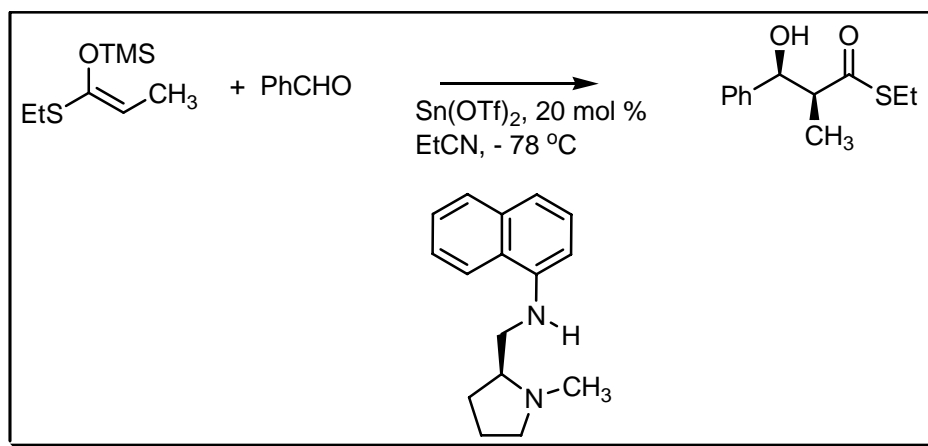
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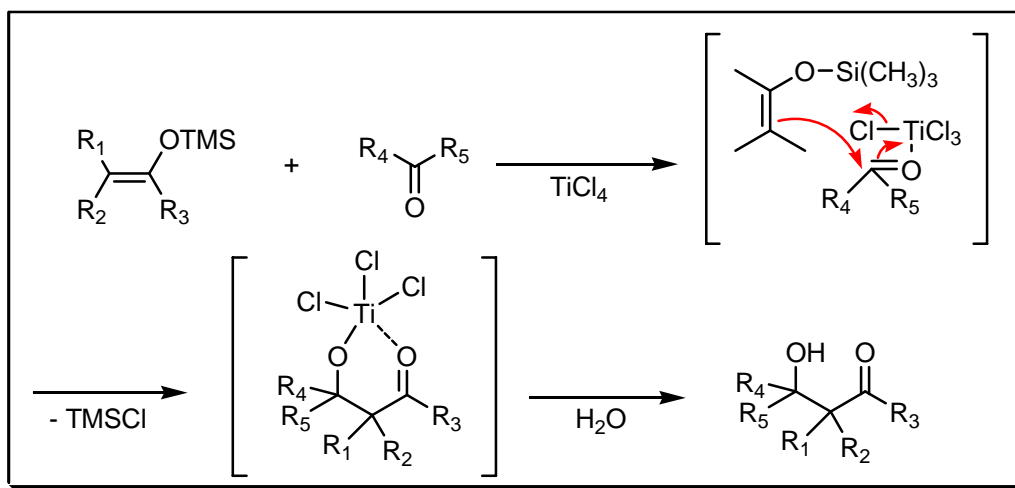
**COMMENTS :**

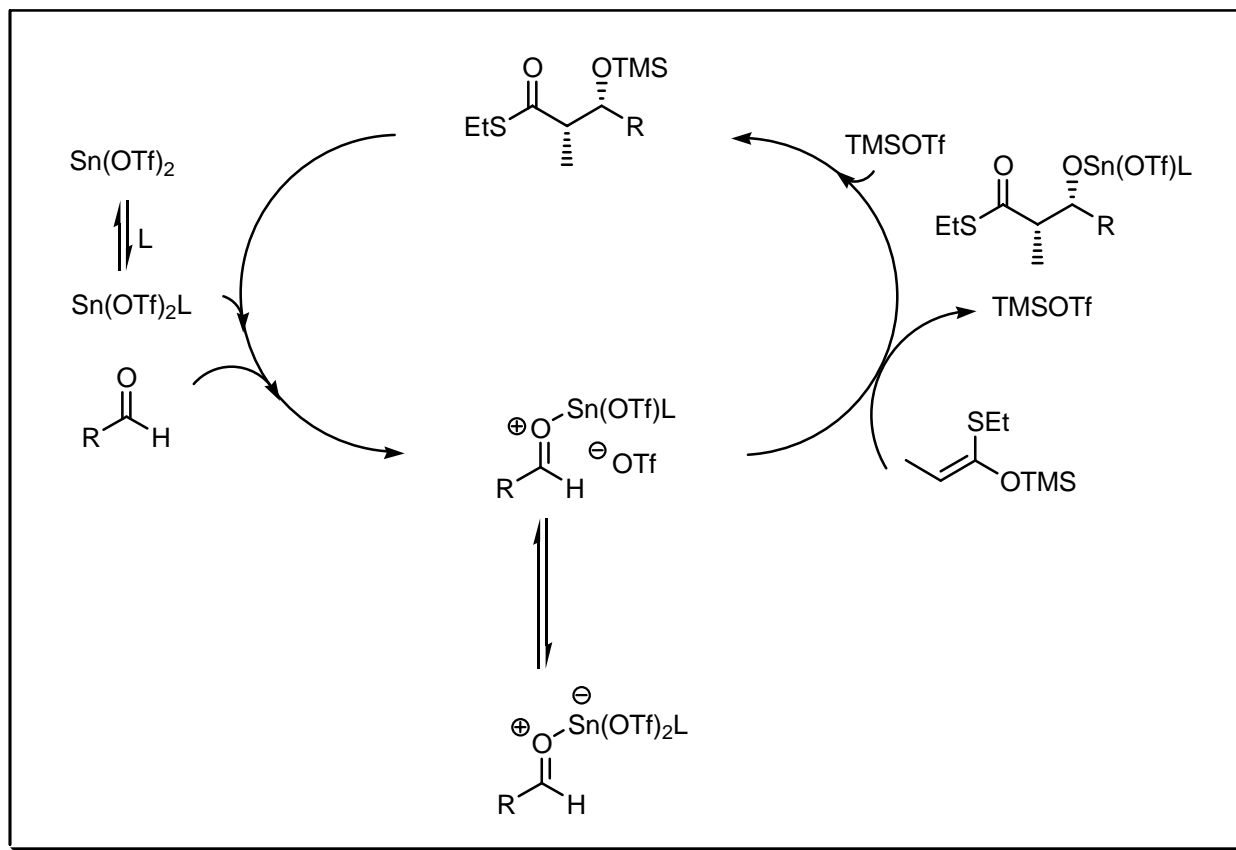
## MUKAIYAMA REACTION

### EXAMPLE :

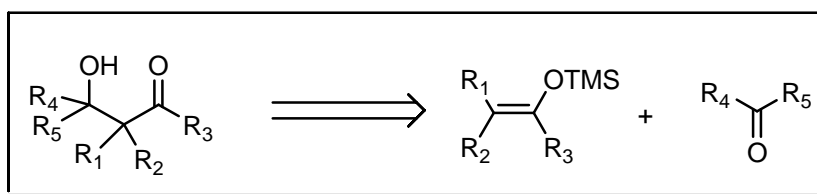


### MECHANISM :





#### DISCONNECTION :



#### NOTES :

Silyl enol ethers are not nucleophilic enough to undergo aldol reactions with aldehydes and ketones. However, if a Lewis acid is present which can complex to the aldehyde or ketone carbonyl, then the silyl enol ether can add in an aldol fashion or by addition of fluoride ion the silyl enol ether can add. The stereoselective aldol condensation is based on tin triflate and a chiral alkaloid. The method works best with thioester-derived silyl enol ethers. The addition of  $Bu_3SNF$  or  $Bu_3Sn(OAc)_2$  is in most cases crucial for asymmetric induction. This reaction is sometimes called a **Mukaiyama – Michael** reaction. Solvent-free reactions have been reported.

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March : 937

Smith – March : 1223

Smith : 908

Smith 2<sup>nd</sup> : 755, 775, 1132

Houben – Weyl : E16c, 390, 443

Org. React. : 28, 203, 46, 1

Org. Synth. : 65, 6

Org. Synth. Coll. Vol. : 8, 323

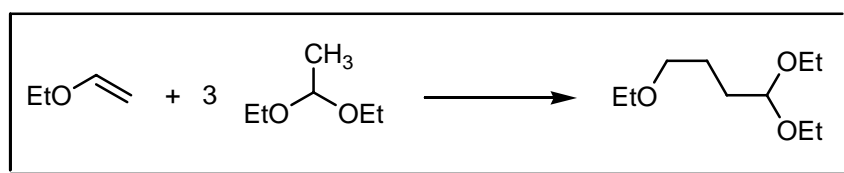
Science of Synthesis : 1, 992; 9, 477

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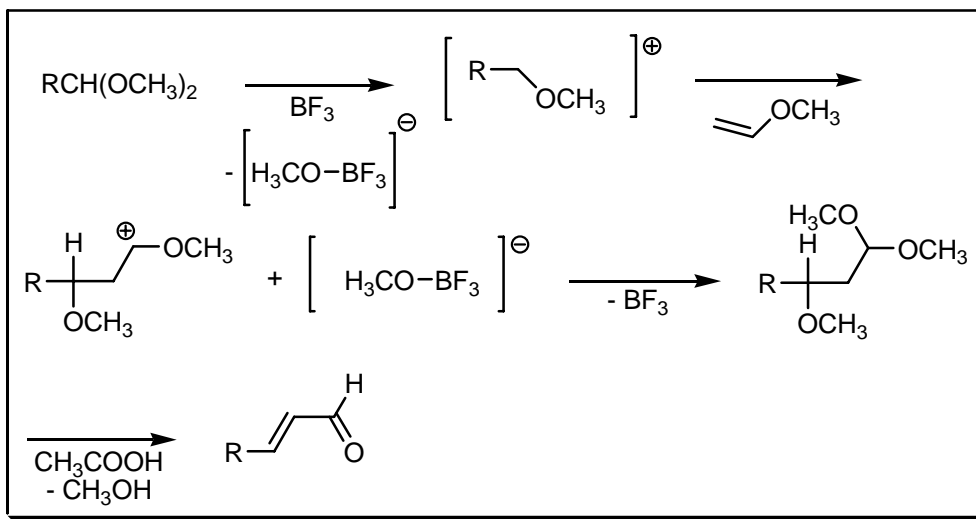
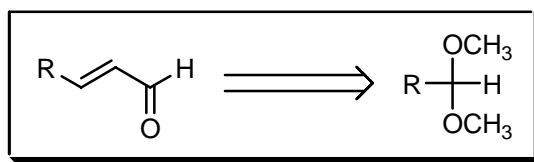
## COMMENTS :

## MÜLLER–CUNRADI CONDENSATION

### EXAMPLE :





**MECHANISM :****DISCONNECTION :****NOTES :**

The formation of a vinylaldehyde starting with an acetal that will be transformed to an acetal with an extra two carbon atoms.

**REFERENCES :**

Houben – Weyl : 6/3, 289; 7/1, 116

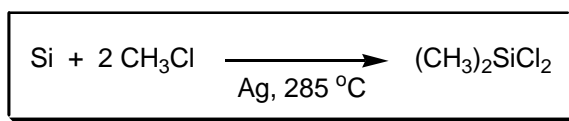
M. Müller–Cunradi; K. Pieroh, *U.S. Patent*, 1936, 2165962.

**COMMENTS :**

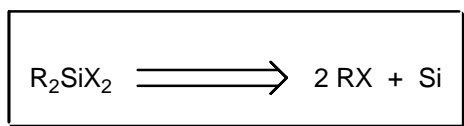
## MÜLLER – ROCHOW SYNTHESIS

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### EXAMPLE :



### DISCONNECTION :



### NOTES :

Alkyl- or aryl halides react in the liquid or vapour phase at about 300 °C with silicon preferably in the presence of a metallic catalyst (silver). The reaction takes place at the surface of the silicon.

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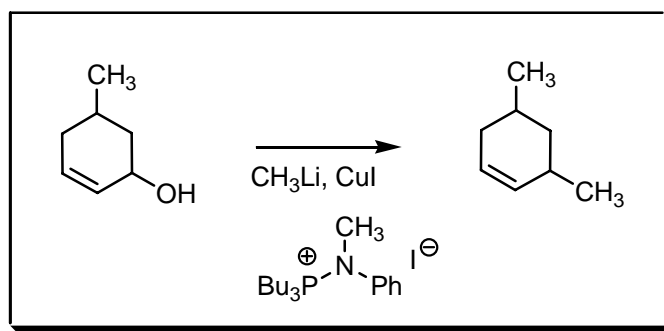
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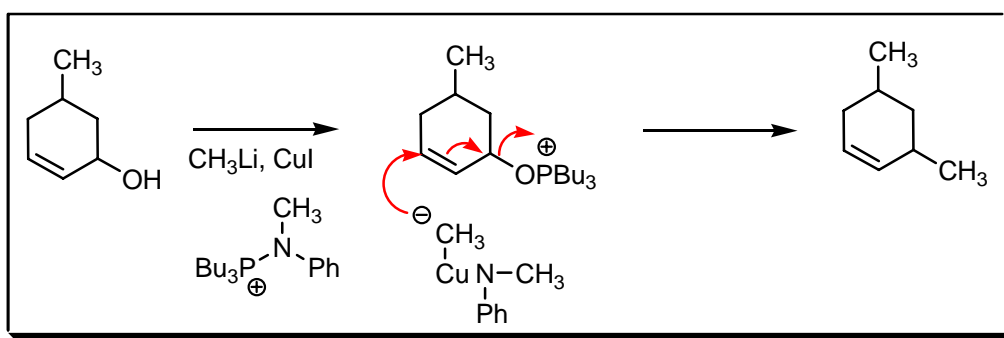
### COMMENTS :

## MURAHASHI ALLYLIC ALKYLATION

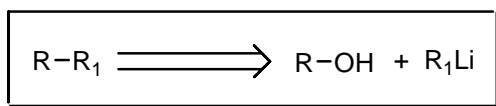
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The allylic alkylation of allyl alcohols in the presence of copper iodide and phosphinimines.

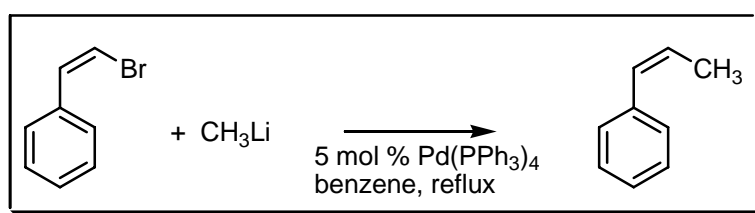
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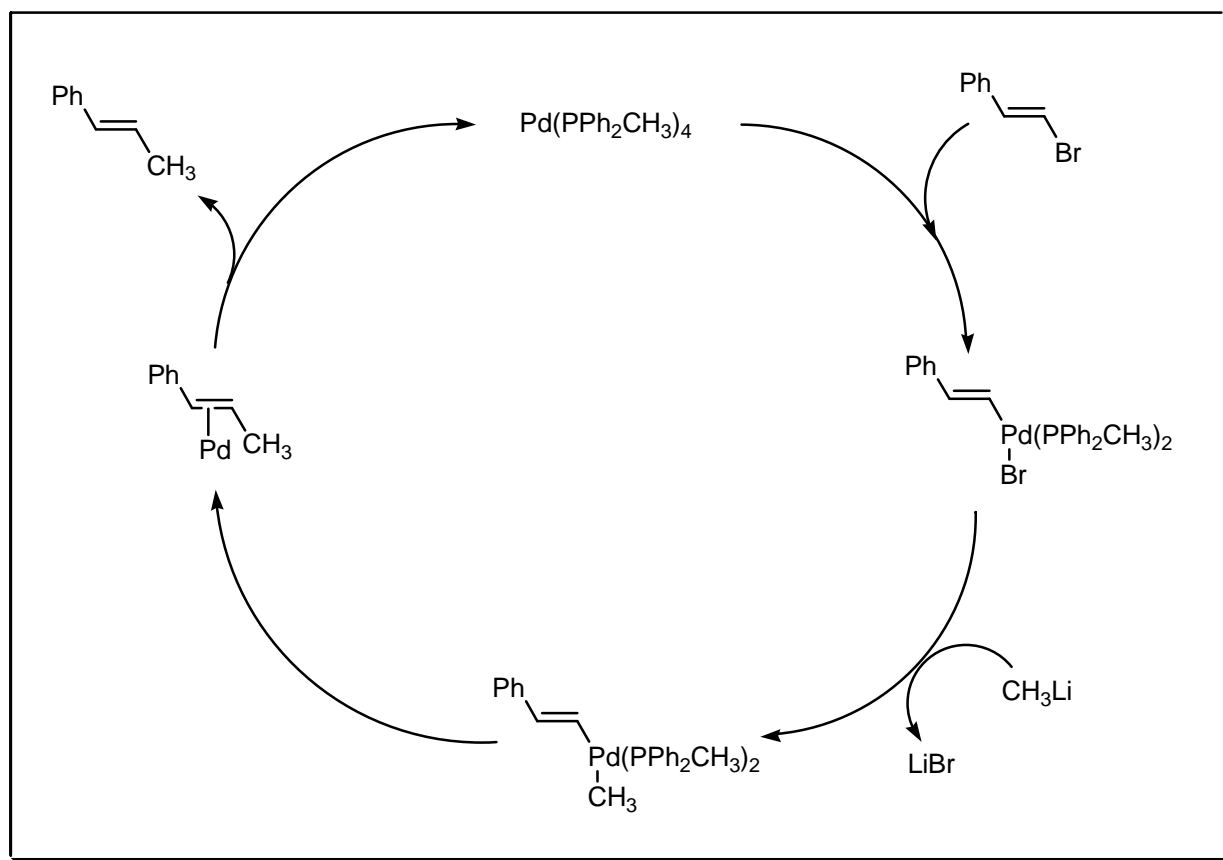
COMMENTS :

## MURAHASHI CROSS-COUPLING REACTION

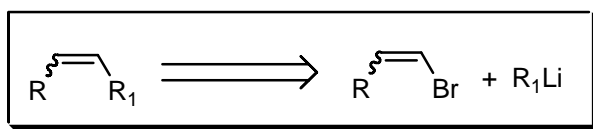
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The palladium cross-coupling using organolithium compounds. Nickel does not work well with organolithium compounds. Vinyl halides undergo the cross-coupling with organolithium compounds stereoselectively. The rate of the addition of the organolithium compound is crucial. Fast addition will produce  $\alpha$ -bromoalkenyl lithium species which will rearrange in a **Fritsch – Butenberg – Wiechell** fashion. See also **Fritsch – Butenberg – Wiechell** and **Kumada – Tamao – Corriu** cross – coupling reactions.

## REFERENCES :

**Org. Synth.** : **62**, 39

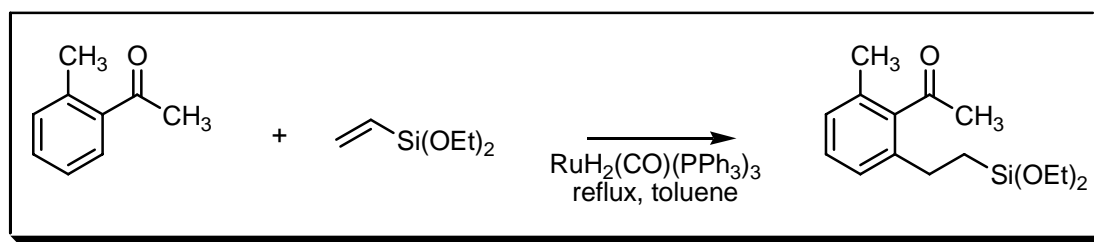
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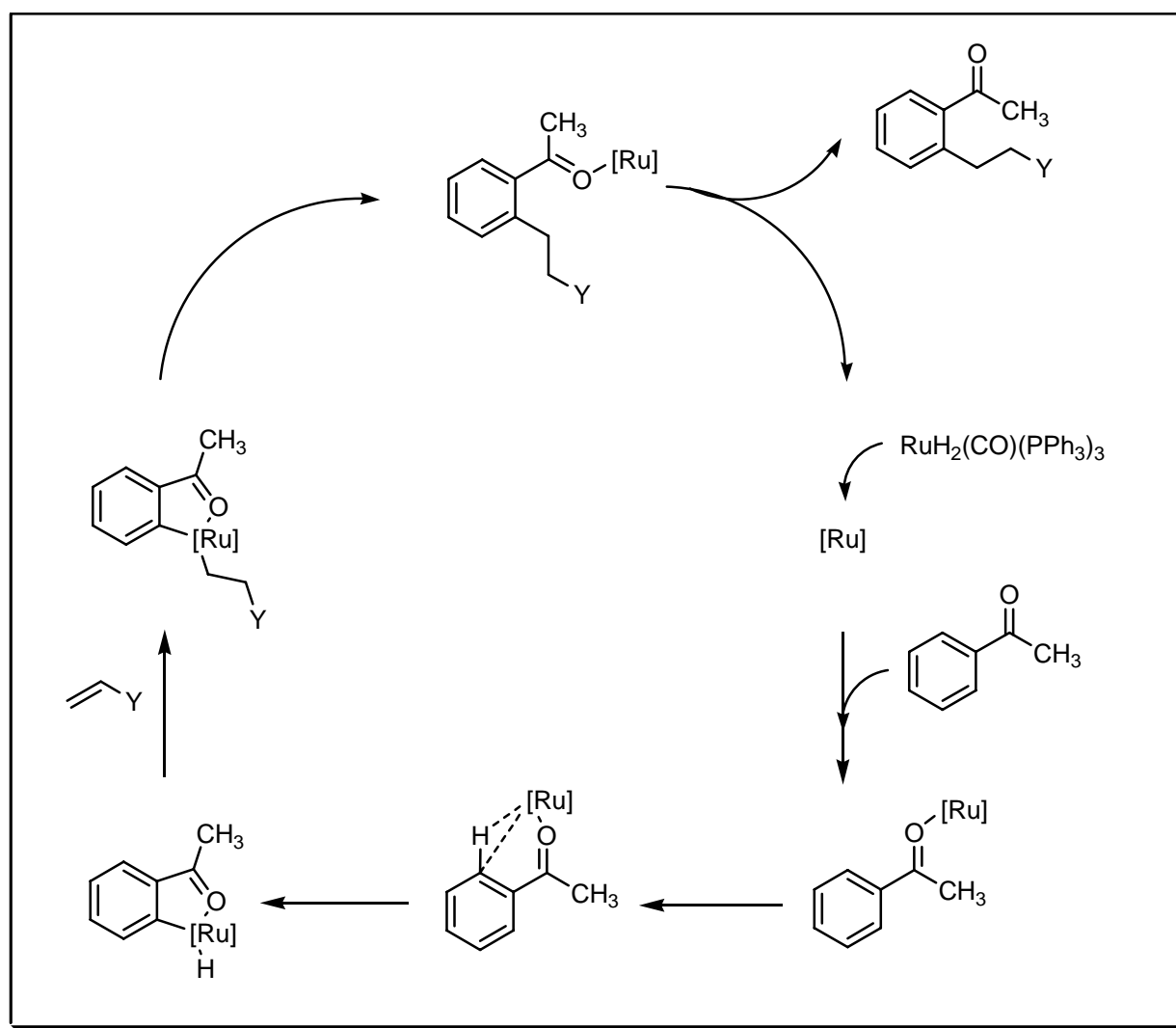
## COMMENTS :

## MURAI C-C BOND FORMATION

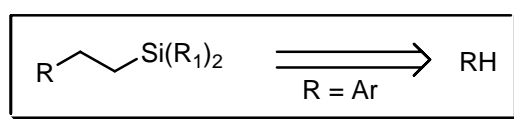
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

A catalytic carbon-carbon bond formation following C-H activation of an aromatic ketone, olefin, aromatic ester or imine. It is proposed that the regioselectivity for the activation  $\alpha$  to the ketone on the aromatic ring arises from coordination of the carbonyl to the ruthenium.

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## REFERENCES :

**Org. Synth.** : **80**, 104

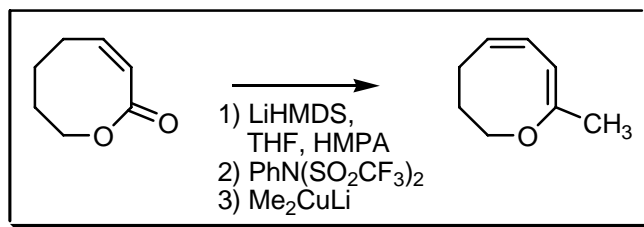
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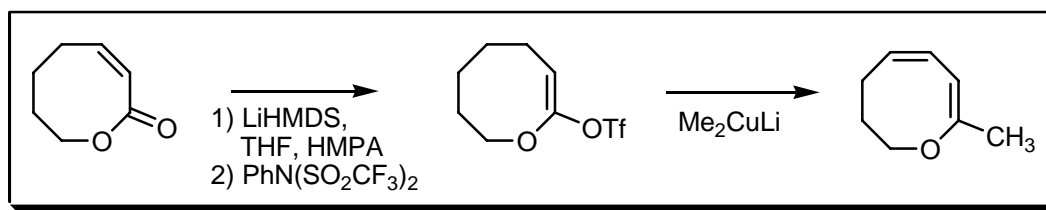
## MURAI COUPLING

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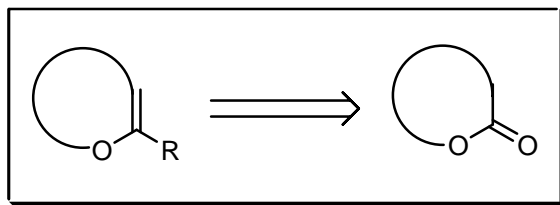
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Lactone enolates are treated with *N*-phenyl triflimide in the presence of THF and HMPA to afford the corresponding enol triflate which on reaction with lithium dialkylcuprates give rise to alkylated cyclic ethers.

### REFERENCES :

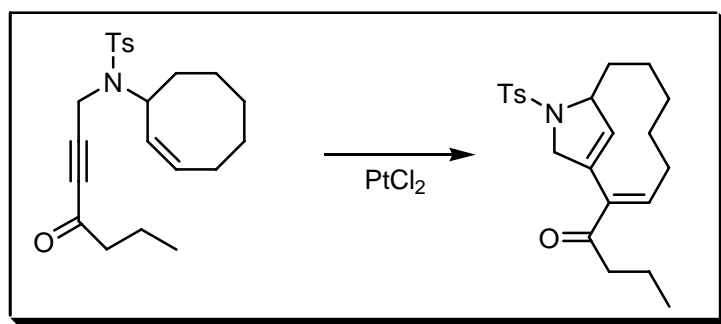
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### COMMENTS :

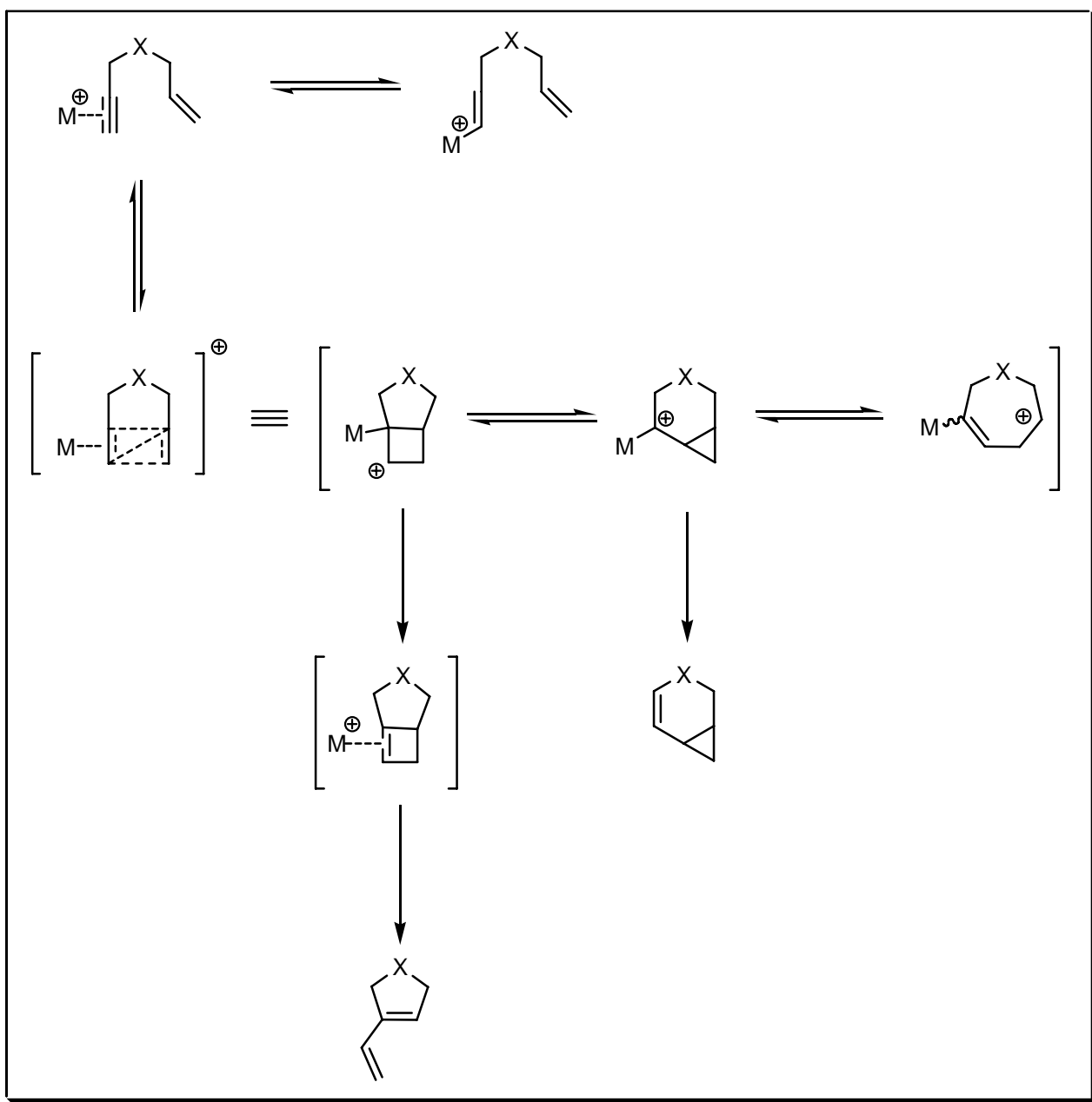


## MURAI REARRANGEMENT

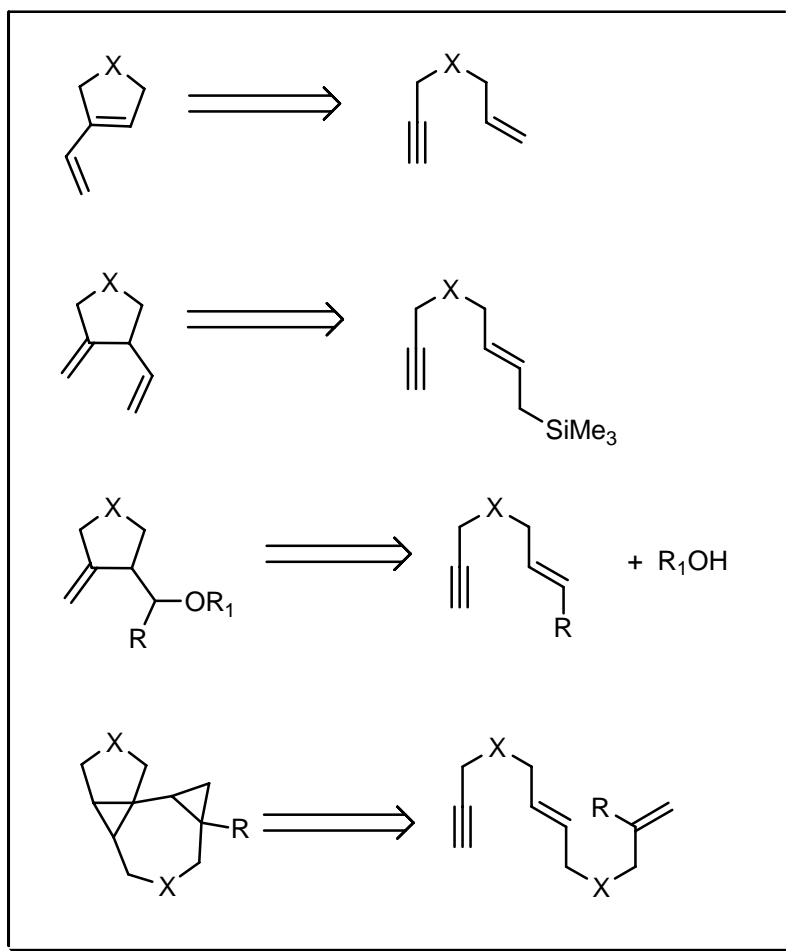
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

These are 4 different types of cycloisomerisation reactions of enynes catalysed by  $\text{PtCl}_2$ . All these reactions share a common mechanism comprising a cationic manifold triggered by the  $\pi$ -complexation of the  $\text{Pt(II)}$  onto the alkyne unit of the substrates. **Fürstner et al.** added an additional two cycloisomerisations processes. See also **Corey – Nicolaou**, **Diels – Alder**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Kita**, **Masamune**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolakiewicz**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

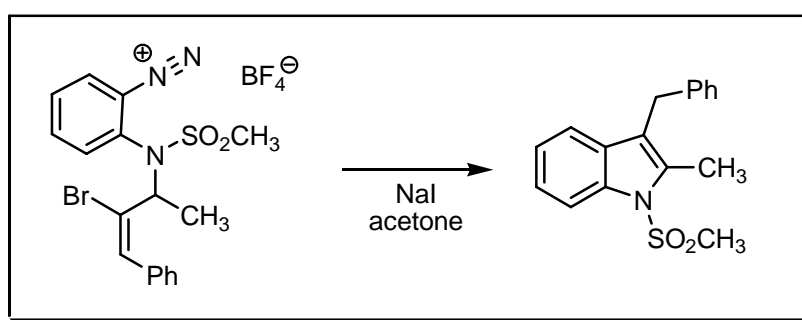
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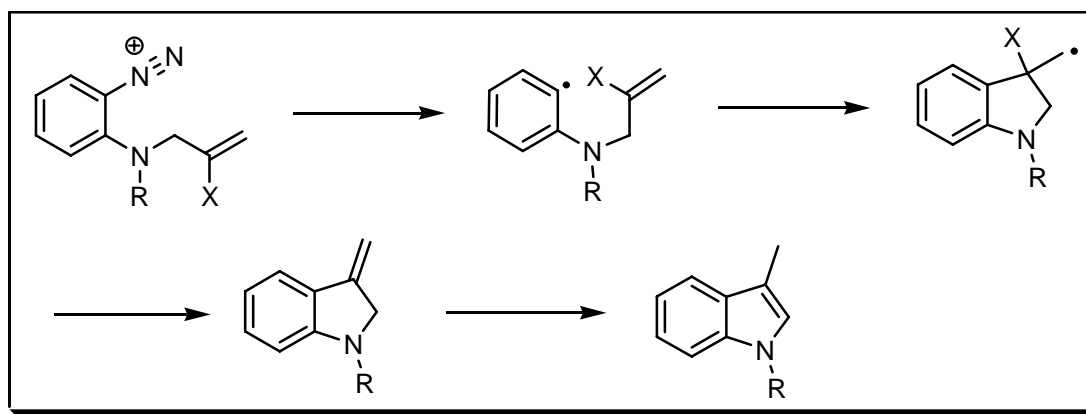
COMMENTS :

## MURPHY INDOLE SYNTHESIS

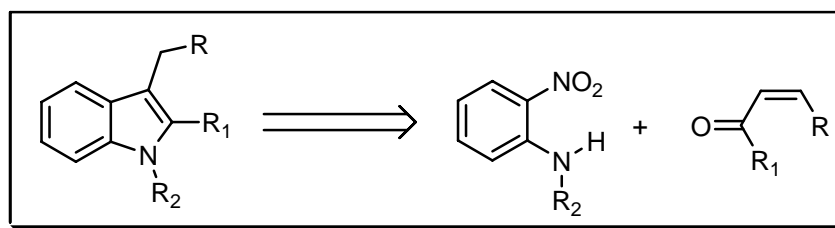
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

Aryl radical cyclisation (sodium iodide in acetone) onto appropriate vinyl bromides leads to a new route to indoles. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

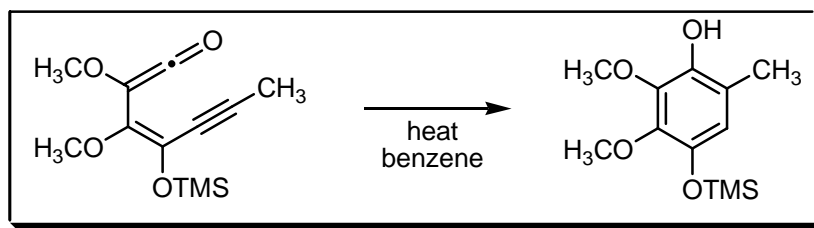
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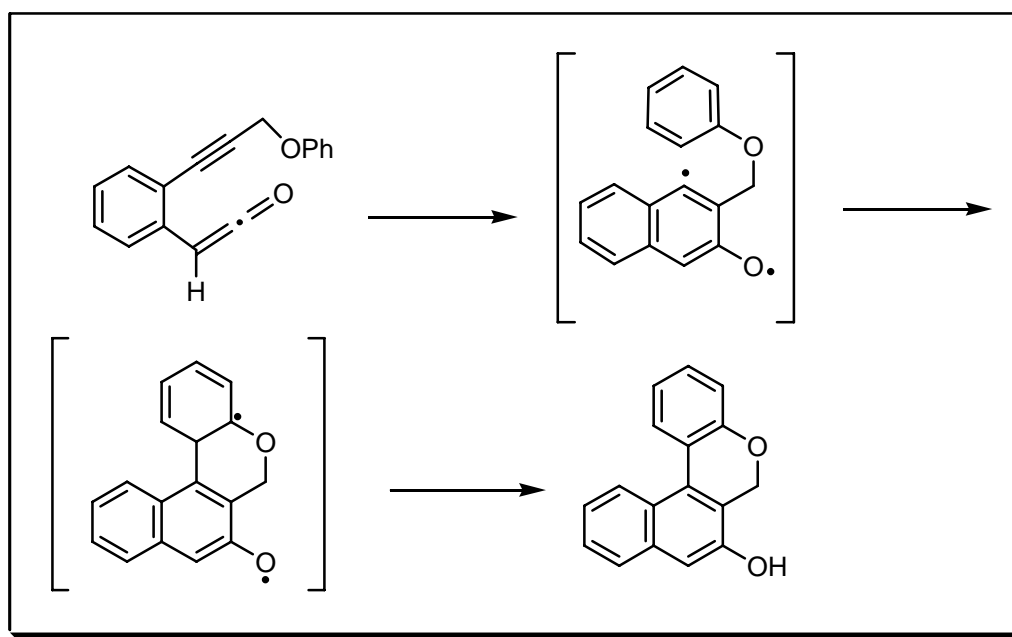
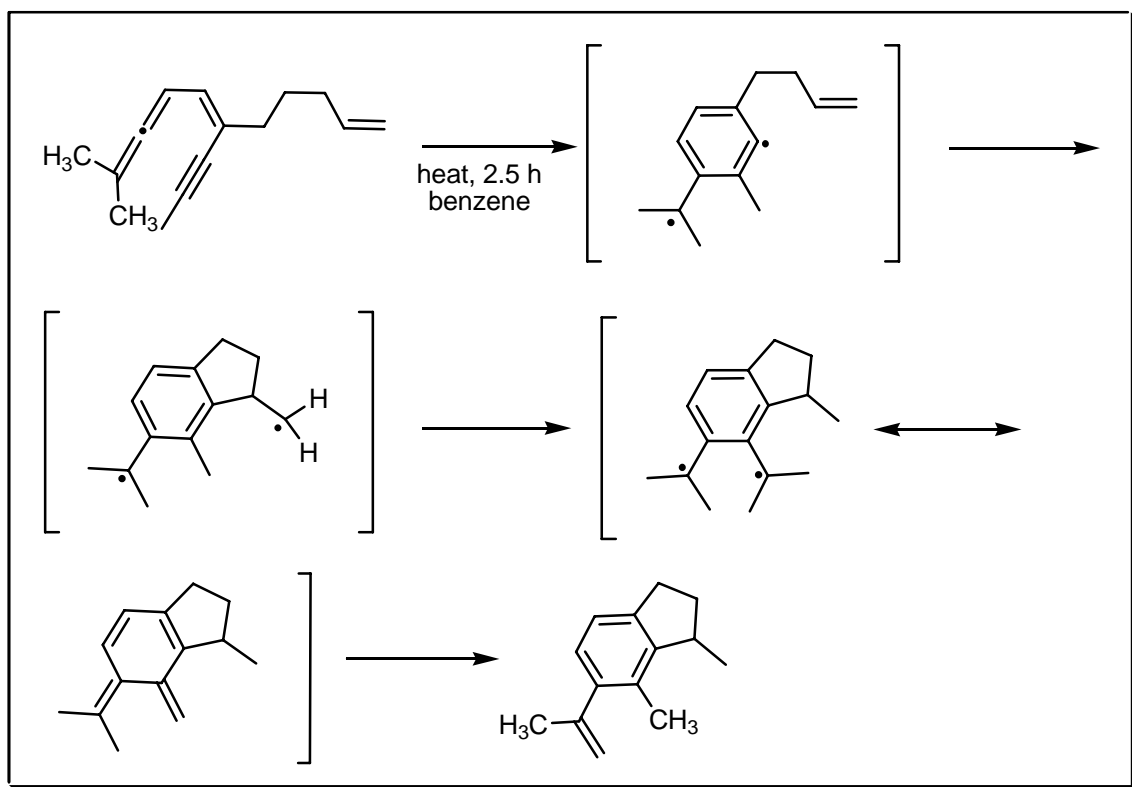
## COMMENTS :

## MYERS – MOORE – SAITO – SCHMITTEL CYCLISATION

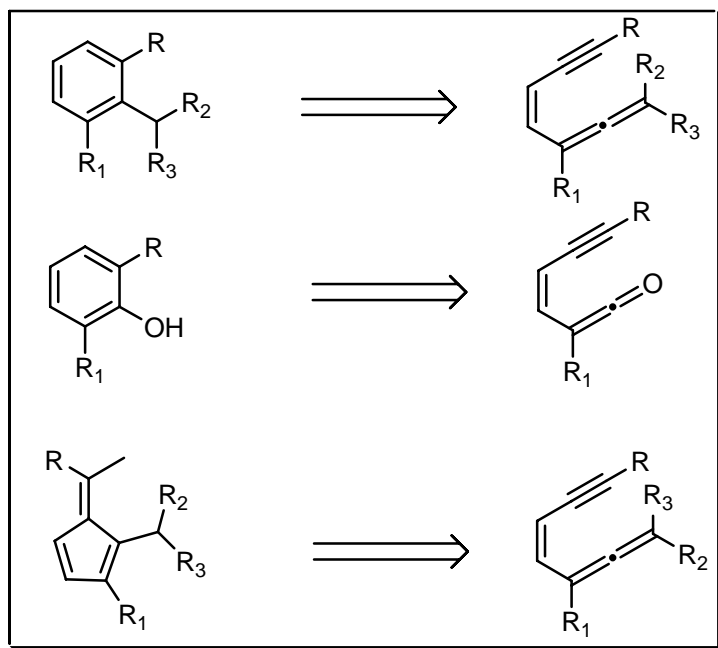
### EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

This reaction has been discovered in the natural product *neocarzinostatine*. The reactive structural element for the **Myers** cyclisation is an enyne allene, for the **Moore** cyclisation it is the reaction between enyne and ketenes. The **Myers** cyclisation reaction of enyne-allenes to  $\alpha,3$ -didehydrotoluenes provides a particularly attractive pathway to carbon biradicals for subsequent synthetic elaborations because the reaction occurs under mild thermal conditions and various synthetic routes to enyne-allenes with diverse chemical structures are becoming available. The **Moore** cyclisation is similar in producing biradicals containing an aryl and a phenoxy radical centre. The **Myers – Saito** cyclisation is between an enyne and an allene, the **Schmittel** cyclisation is a regioalternative of the **Myers – Saito** cyclisation, to give 5-membered rings. See also **Bergman – Masamune** cyclisation.

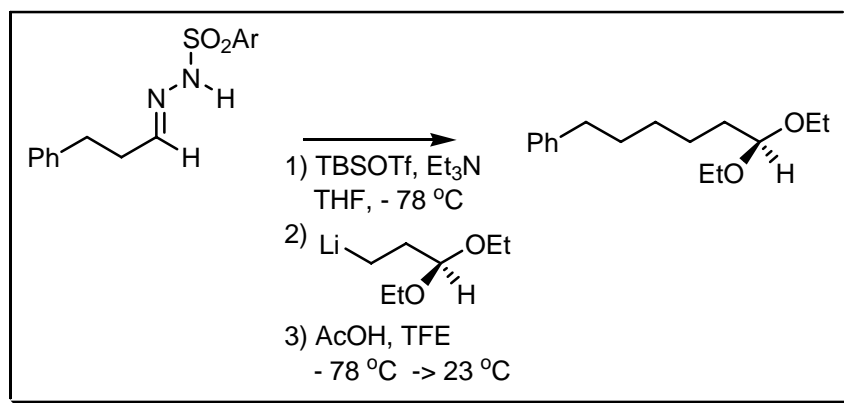
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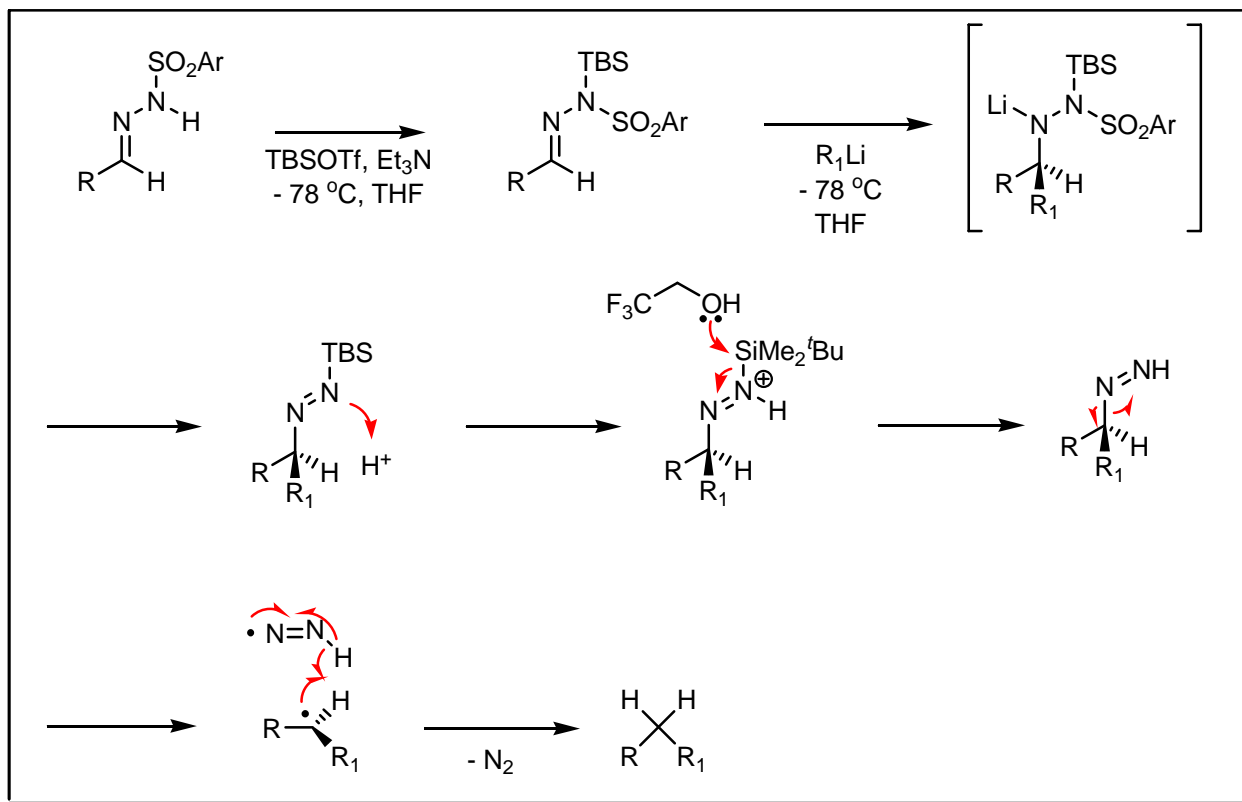
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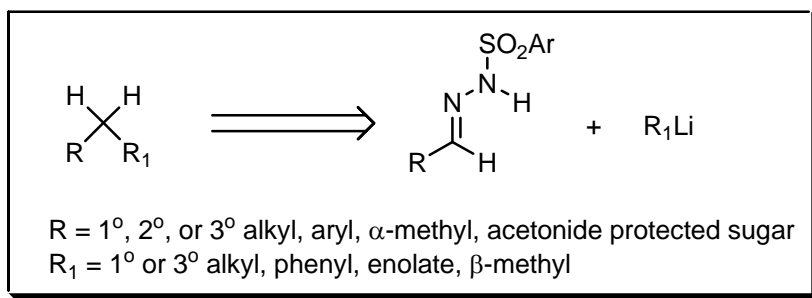
## MYERS REDUCTIVE COUPLING

**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :****NOTES :**

The highly efficient reductive coupling of aldehyde tosylhydrazones with alkyl lithium reagents. The elimination of nitrogen proceeds *via* a radical pathway.

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**COMMENTS :**



**N**

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**B**

BOECKMANN PROCEDURE · 1300

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**F**

FÜRSTNER PROCEDURE · 1300

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**N**

NAGARAJAN – KUMAR – RAO

MACROLACTONISATION · 1250

NAGATA HYDROCYANATION · 1251

NAITO INDOLE SYNTHESIS · 1253

NAMETKIN REARRANGEMENT · 1254

NATSUME INDOLE SYNTHESIS · 1256

NAZAROV CYCLISATION · 1257

NEBER – BOSSEL CINNOLINE / OXINDOLE  
SYNTHESIS · 1259

NEBER REARRANGEMENT · 1261

NEF REACTION · 1262

NEF SYNTHESIS · 1264

NEGISHI COUPLING · 1265

NENITZESCU ACYLATION · 1267

NENITZESCU INDOLE SYNTHESIS · 1269

NERDEL CYCLOPROPANE SYNTHESIS · 1271

NESMANJANOV FULVENE SYNTHESIS · 1272

NESMANJANOV METALLATION · 1273

NEWMAN – KARNES – KWART REARRANGEMENT  
· 1274

NEWMAN SYNTHESIS · 1275

NICHOLAS SYNTHESIS · 1277

NICKL SYNTHESIS · 1279

NICOLAOU OXIDATION · 1280

NIEMENTOWSKI von QUINAZOLONE REACTION ·  
1281

NIEMENTOWSKI von QUINOLINE SYNTHESIS ·  
1283

NIEUWLAND HYDRATION · 1284

NISHIMURA – CRISTESCU *N*-GLYCOSIDATION ·  
1285

NOLLER SYNTHESIS · 1286

NORD SYNTHESIS · 1288

NORRISH TYPE 1 REARRANGEMENT · 1290

NORRISH TYPE 2 REARRANGEMENT · 1291

NOYORI ANNULATION · 1293

NOYORI HYDROGENATION · 1295

NOYORI REARRANGEMENT · 1297

NOZAKI – HIYAMA – KISHI (TAKAI – UTIMOTO)  
REACTION · 1298

NUGENT – RAJANBABU EPOXIDE HOMOLYSIS ·  
1301

NYSTED REACTION · 1302

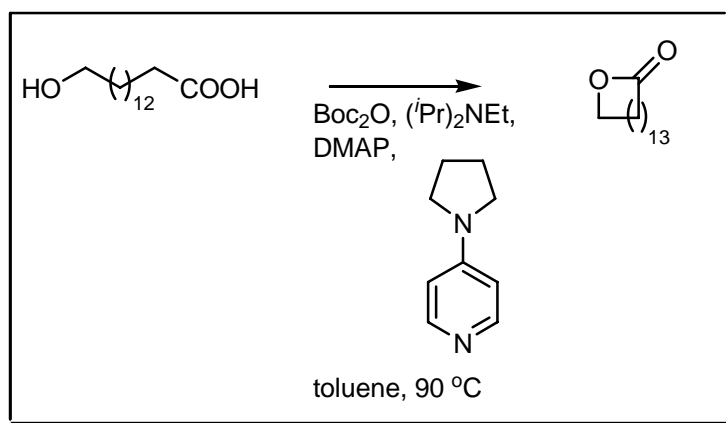
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**T**

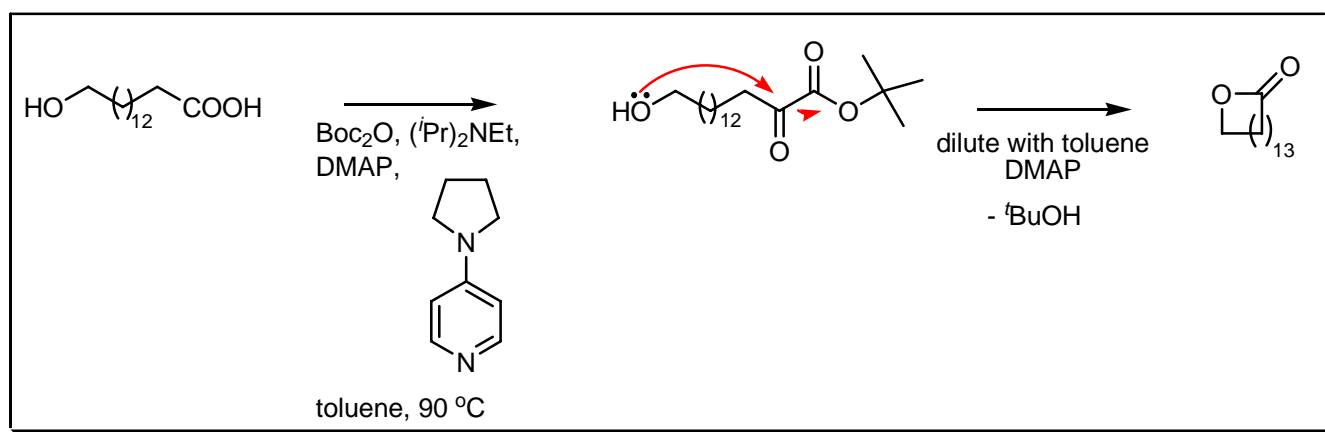
TAKAI – UTIMOTO REACTION · 1300

## NAGARAJAN – KUMAR – RAO MACROLACTONISATION

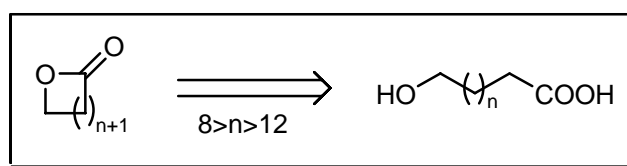
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

A useful way of making macrolides using mild reaction conditions (toluene,  $90^\circ\text{C}$ ), with low cost reagents (Boc anhydride, Hünigs base and 4-pyrrolidinopyridine). The reaction is also tolerant to olefinic bonds, easy work-up and no tedious purification necessary to remove the by-products. The exact reaction mechanism is not known. See also **Corey – Nicolaou**, **Diels – Alder**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Kita**, **Masamune**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Thorpe –**

**REFERENCES :**

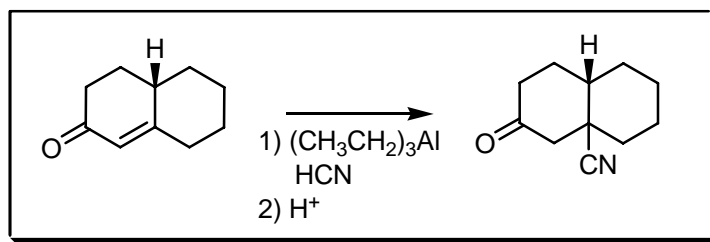
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**COMMENTS :**

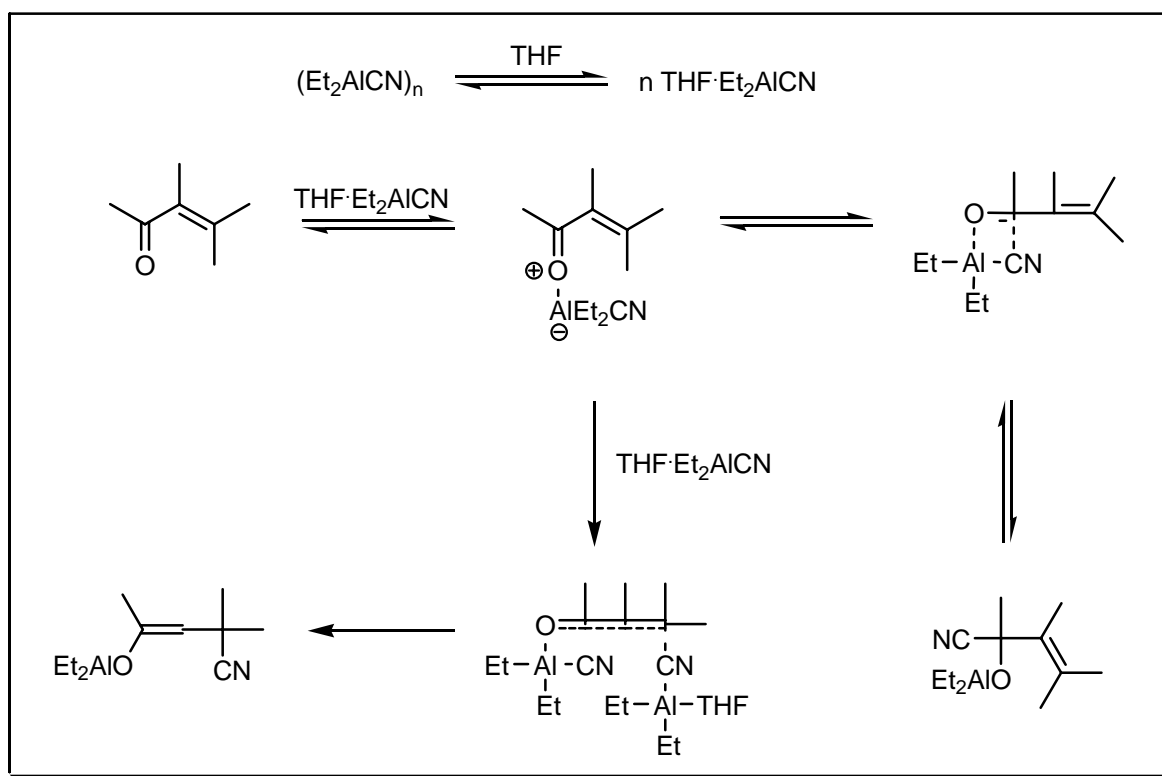
**NAGATA HYDROCYANATION**

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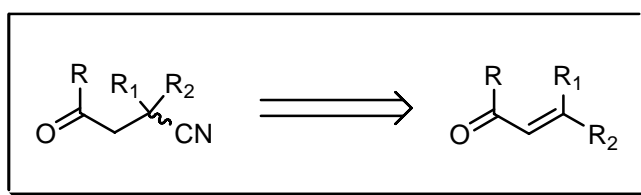
**EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

Alkylaluminium mediated 1,4-addition of hydrogen cyanide to  $\alpha,\beta$ -unsaturated carbonyl compounds. For more details about the mechanism see *J. Am. Chem. Soc.*, 1972, **94**, 4644. See also **Michael** reaction.

## REFERENCES :

**Org. React.** : **25**, 255

**Org. Synth.** : **52**, 90, 100

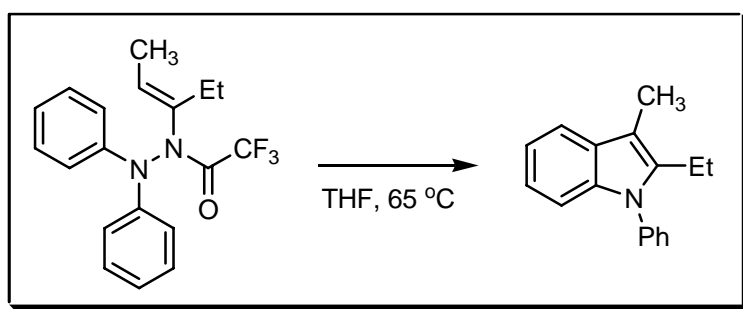
**Org. Synth. Coll. Vol.** : **6**, 14, 436

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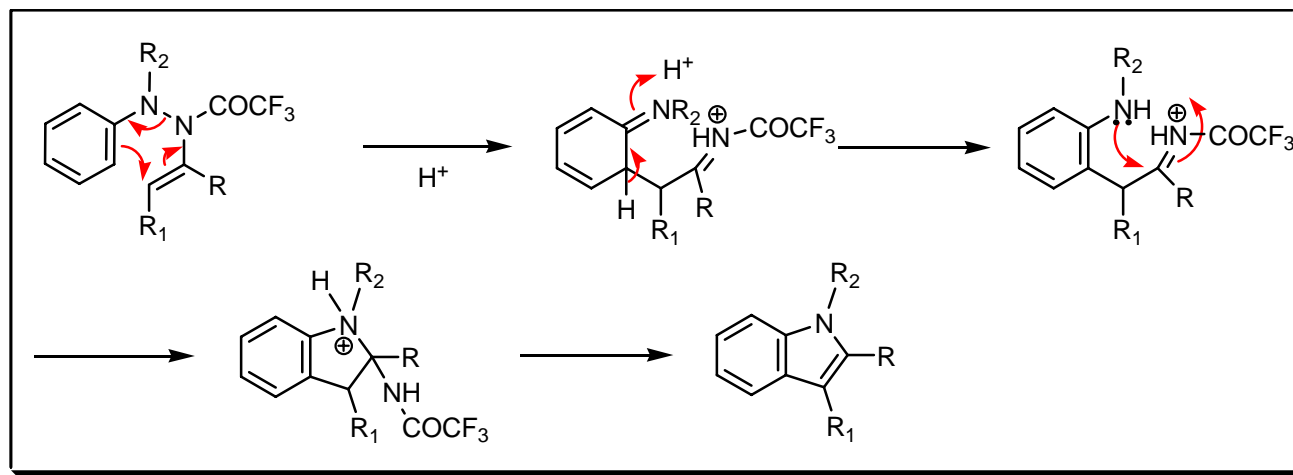
**COMMENTS :**

**NAITO INDOLE SYNTHESIS**

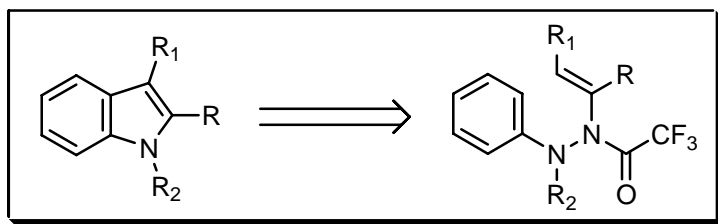
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

The thermal cyclisation of *N*-trifluoroacetyl enehydrazines to afford indoles under mild conditions via the **Fischer** indole reaction. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

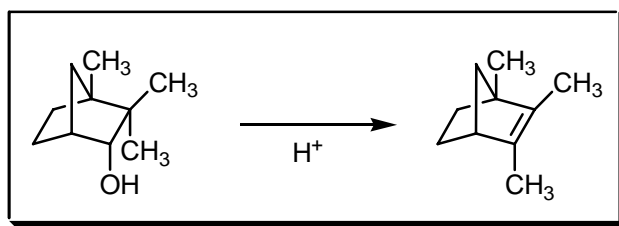
## REFERENCES :

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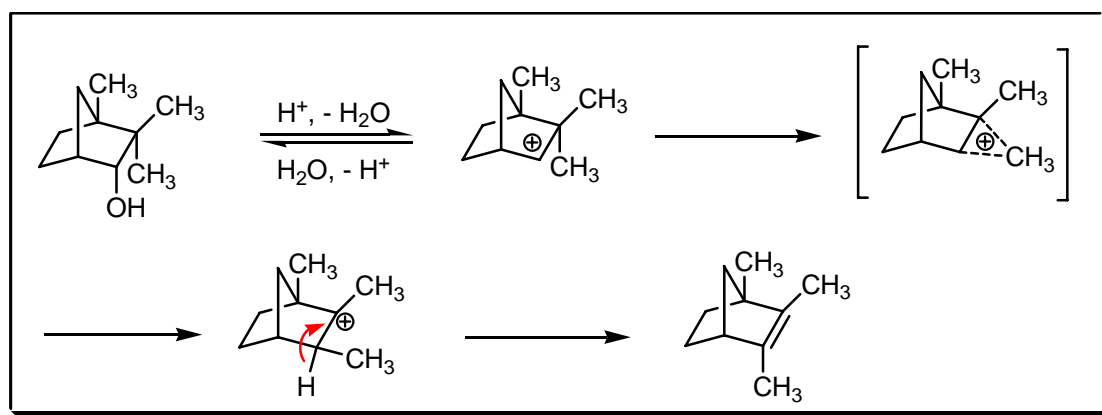
## COMMENTS :

## NAMETKIN REARRANGEMENT

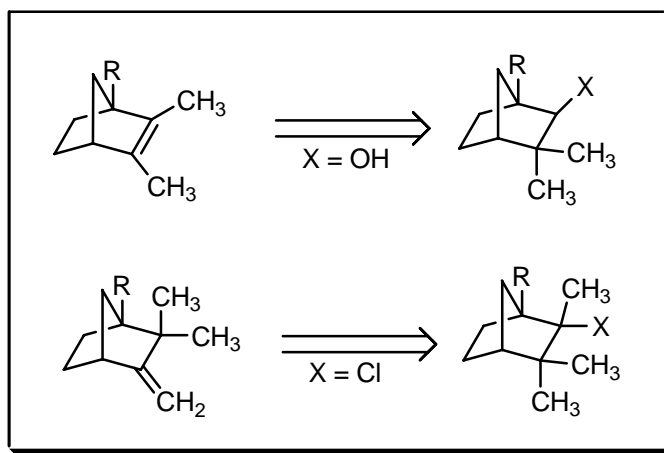
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

A retropinacolic rearrangement in the terpene series involving the formation of a carbonium ion, without variation in the ring structure. (As is involved in the racemisation of camphene hydrate by acidic reagents.) See also **Wagner – Meerwein** rearrangement.

## REFERENCES :

**March** : 1070

**Smith – March** : 1394

**Houben – Weyl** : 4/2, 16

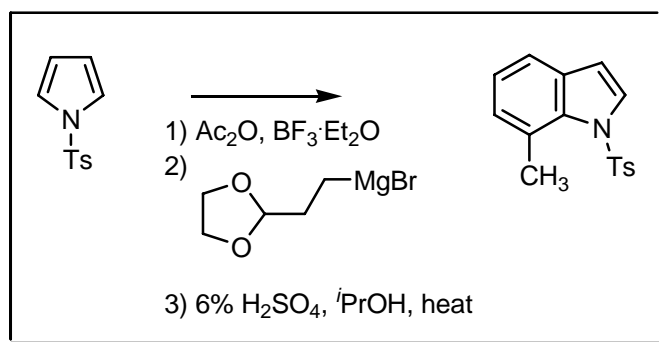
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## COMMENTS :

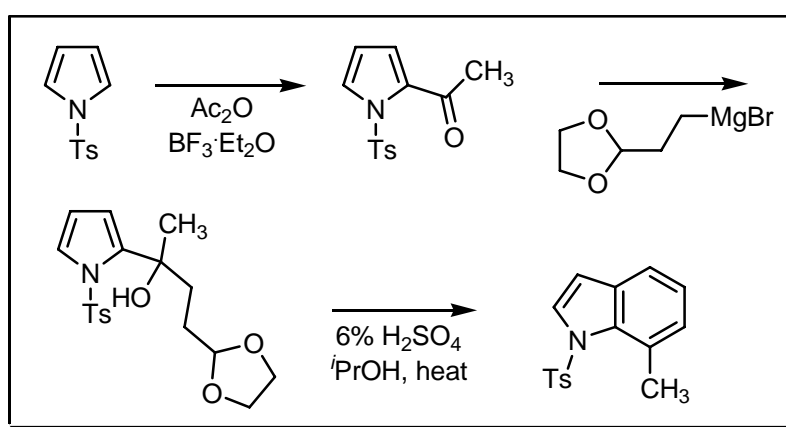


# NATSUME INDOLE SYNTHESIS

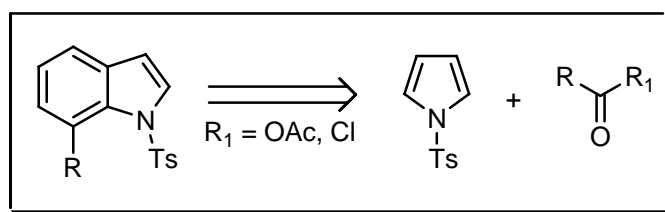
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The key step in this indole synthesis is the *intramolecular* electrophilic cyclisation of C-2 of the pyrrole ring, followed by the functionalisation. The Lewis acid ( $\text{AlCl}_3$ ,  $\text{BF}_3 \cdot \text{Et}_2\text{O}$ ) controls the initial site of the *intermolecular* electrophilic substitution. The indole ring can be functionalised in several positions around the ring. Several modifications have been reported in the literature. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**,

**Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

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#### REFERENCES :

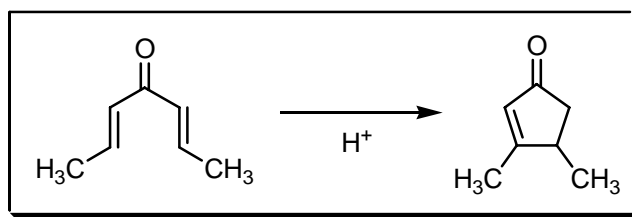
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#### COMMENTS :

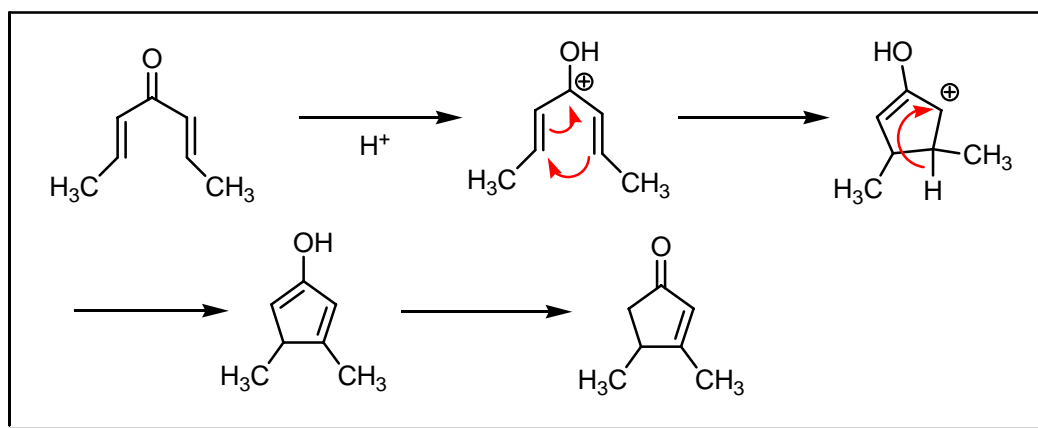
### NAZAROV CYCLISATION

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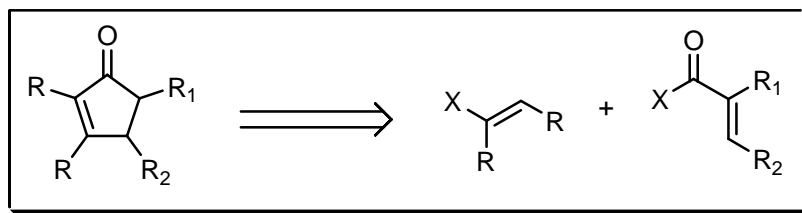
#### EXAMPLE :



#### MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of alicyclic five-membered rings by the cyclisation of a divinylacetylene or of a substituted alkyl vinyl ketone by strong acids or UV light. It is a  $4\pi$  electrocyclisation (via a carbocation intermediate), conrotatory in the presence of a protic acid or Lewis acid, disrotatory under photochemical conditions. Divinyl ketones and allyl compounds can also be employed. There is also a silicon-directed **Nazarov** cyclisation, and a retro-**Nazarov** reaction. See also **Noyori** annulation.

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Smith – March : 1021

Smith : 1308

Smith 2<sup>nd</sup> : 1077, 1133

Houben – Weyl : E19c, 345

Org. React. : 45, 1

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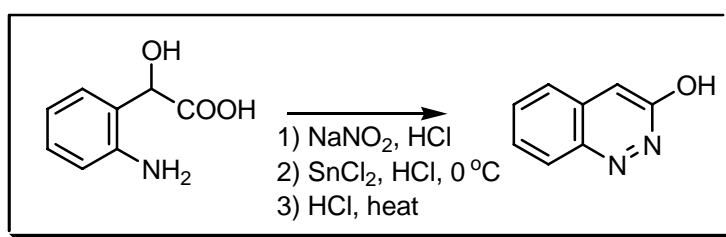
**COMMENTS :**

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**NEBER – BOSSEL CINNOLINE / OXINDOLE SYNTHESIS**

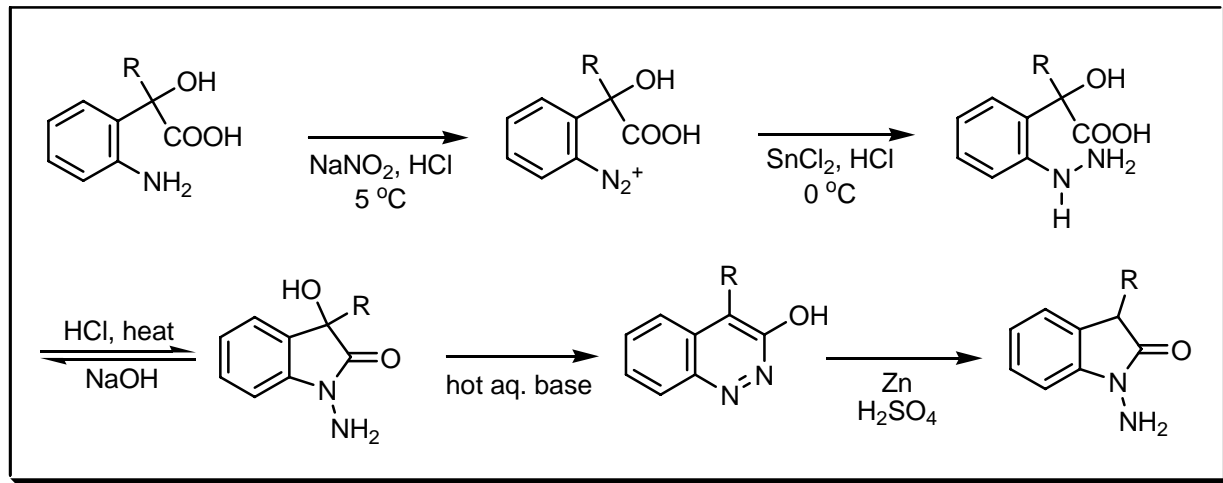
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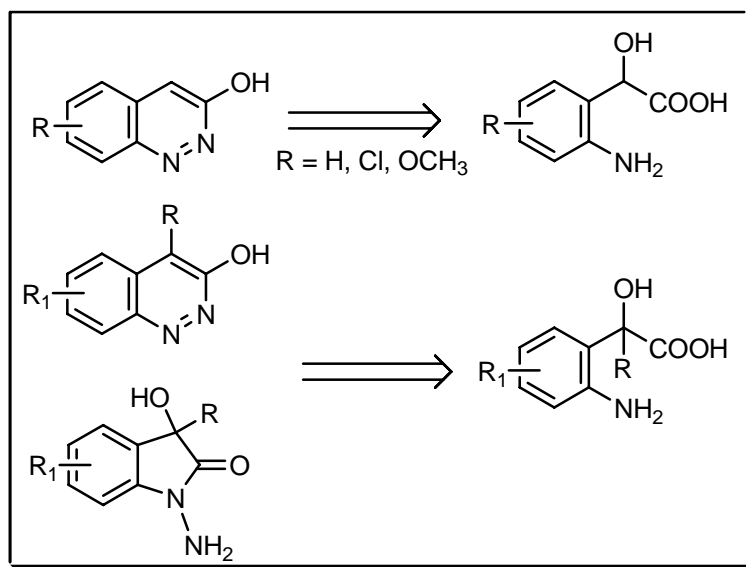


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**MECHANISM :**



## DISCONNECTION :



## NOTES :

The sodium salt of an *o*-aminomandelic acid is diazotised and the diazo compound is reduced by stannous chloride to the *o*-hydrazinomandelic acid. The latter is cyclised in acid solution to yield a 3-hydroxy-cinnoline.  $\alpha$ -Substituted derivatives may yield either 4-substituted 3-hydroxy-cinnolines or 3-substituted 1-aminodioxindoles. 1-Aminodioxindoles can also be obtained by reduction of the 3-hydroxy cinnoline or by thermal cyclisation of *o*-hydrazinophenylacetic acid. See also **von Baeyer** oxindole, **Brunner**, **Gassman** oxindole, **Hinsberg** oxindole, **Martinet**, **von Richter**, **Stollé – Becker** and **Widman – Stoermer** reactions.

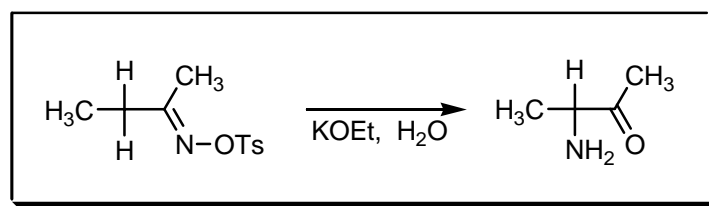
## REFERENCES :

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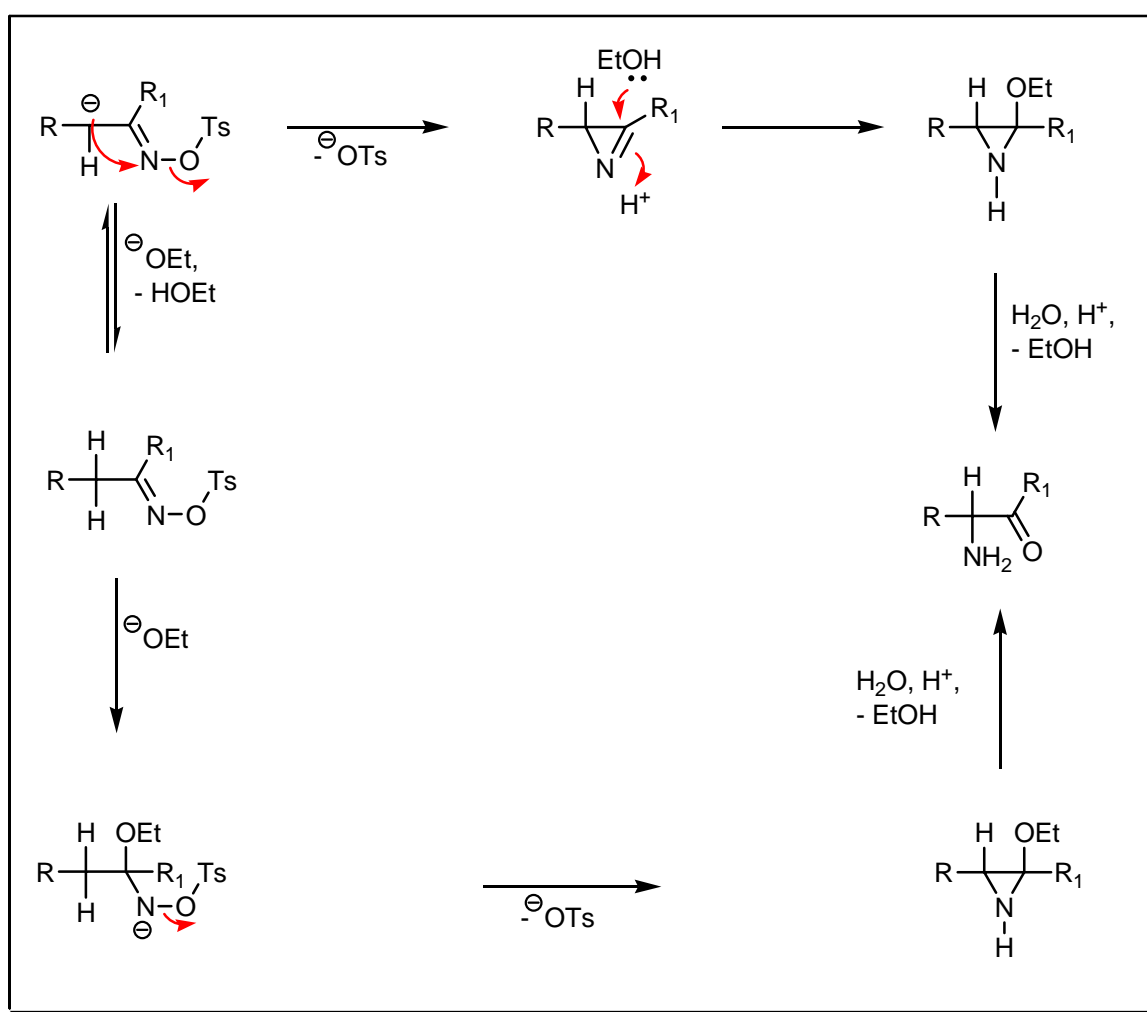
## COMMENTS :

## NEBER REARRANGEMENT

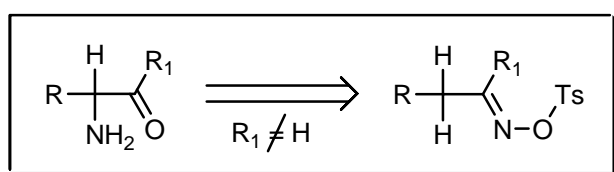
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

This is the base-induced rearrangement of O-acylated ketoximes to the corresponding  $\alpha$ -aminoketones. This reaction is important in the synthesis of heterocycles in which aminoketones are used as intermediates. See also **Beckmann** rearrangement.

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## REFERENCES :

**March** : 217

**Smith – March** : 288, 1410

**Houben – Weyl** : **11/1**, 903; **E5**, 528; **E7b**, 380; **E14b**, 431

**Org. Synth.** : **41**, 82; **64**, 19

**Org. Synth. Coll. Vol.** : **5**, 909; **7**, 149

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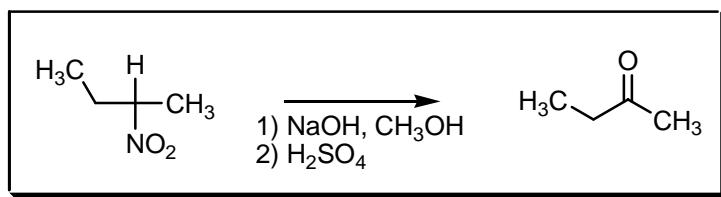
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## COMMENTS :

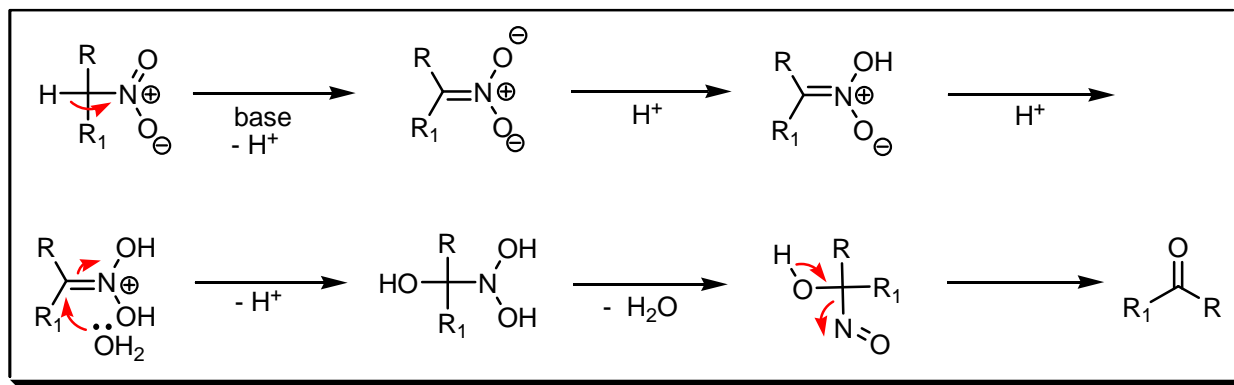
## NEF REACTION

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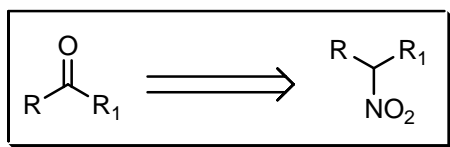
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Aliphatic primary and secondary nitro-compounds can be converted into aldehydes and ketones respectively by adding the alkali salts of the former to strong mineral acids. This is an important reaction for aldose chain extension. Modern versions of this reaction use LDA as base and MoOPh or Oxone as oxidant.

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March : 948

Smith – March : 1178, 1225

Smith : 899

Smith 2<sup>nd</sup> : 751

Houben – Weyl : **6a**, 641, 647; **7/2a**, 843; **E3**, 396, 587; **E14b**, 796, 857, 942; **E16d**, 368

Org. React. : **38**, 655

Science of Synthesis : **9**, 472

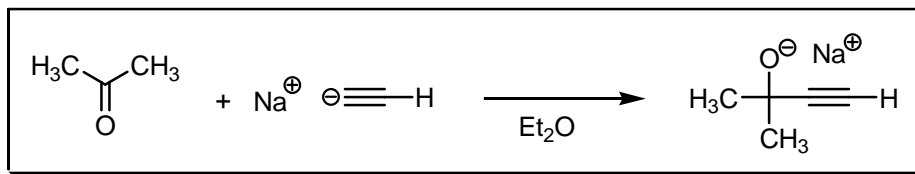
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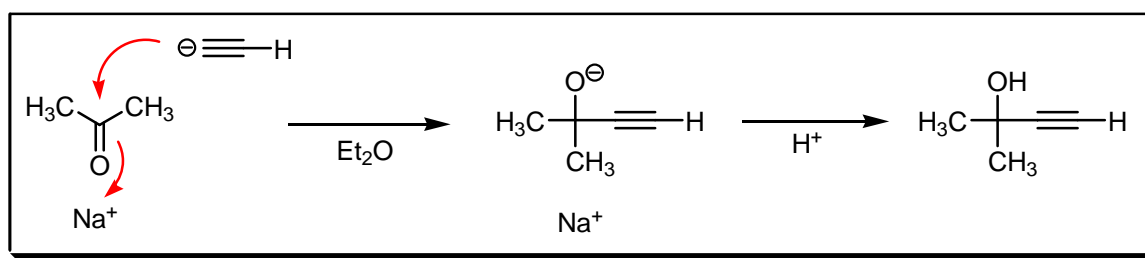
COMMENTS :

## NEF SYNTHESIS

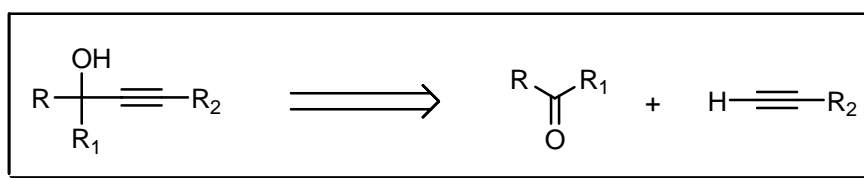
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

Acetylenic carbinols are obtained by treating ketones with the sodium or other metallic derivatives of an acetylenic hydrocarbon in ether or liquid ammonia. See also **Arens – van Dorp**, **Favorskii – Babayan**, **Inhoffen**, **Isler** and **Reppé** acetylene reactions.

REFERENCES :

Org. React. : **38**, 655

Org. Synth. : **20**, 40

Org. Synth. Coll. Vol. : **3**, 320

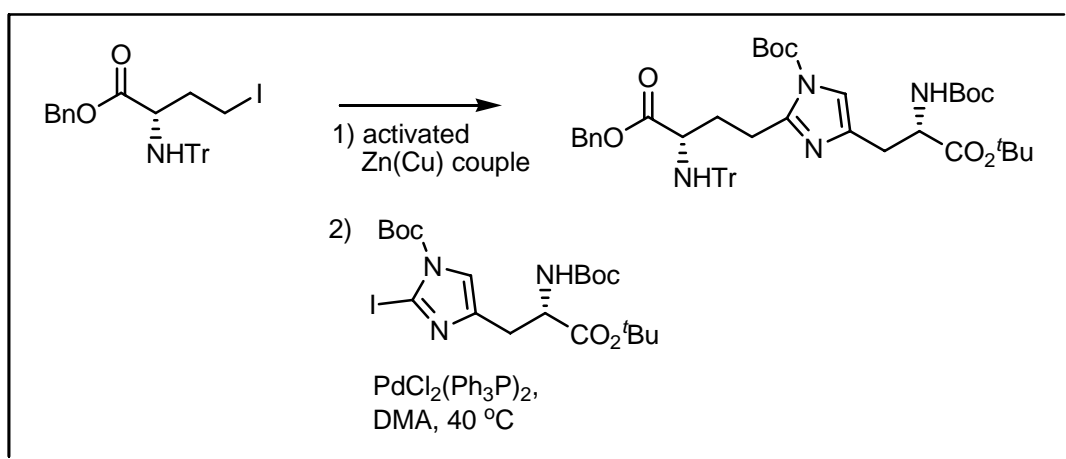
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**COMMENTS :**

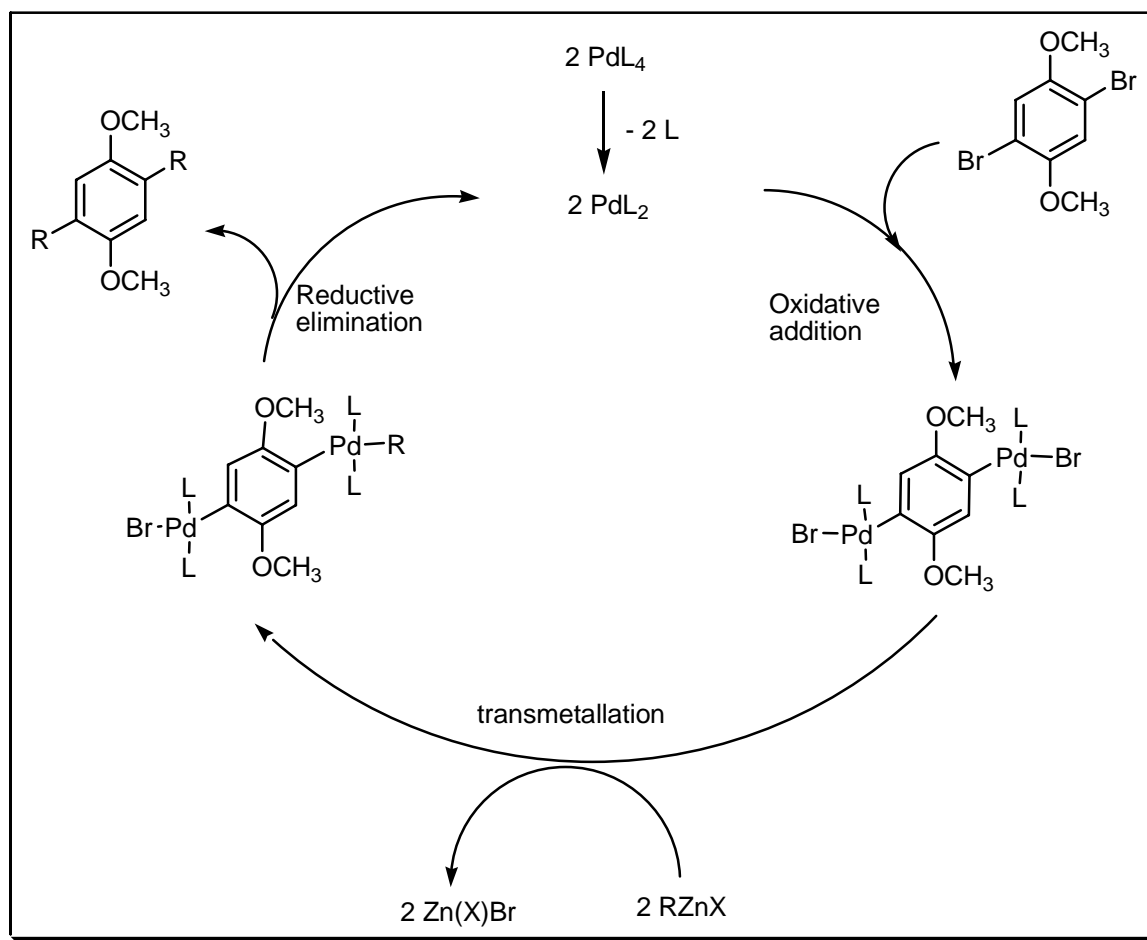
## NEGISHI COUPLING

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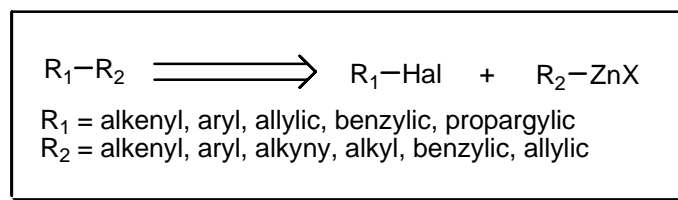
**EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

This is the palladium-catalysed cross-coupling between organozinc reagents and organohalides or triflates. It is compatible with many functional groups including ketones, esters, amines and nitriles. See also **Hayashi – Ito**, **Heck – Fujiwara – Mizoroki**, **Kochi**, **Kumada – Tamao – Corriu**, **McMurry**, **Murahashi**, **Stille – Kelly**, **Stille – Migita – Kosugi** and **Suzuki – Miyaura** reactions.

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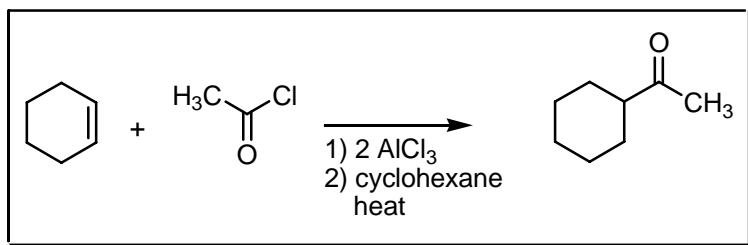
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**COMMENTS :**

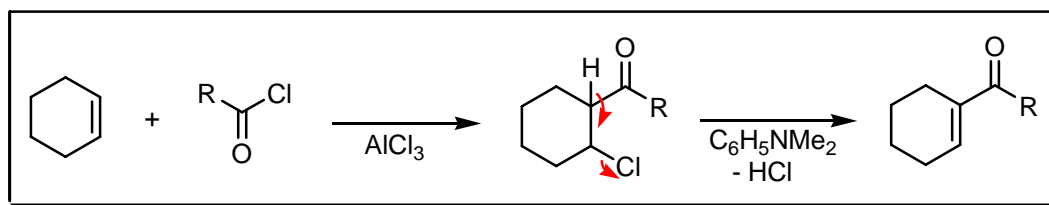
## NENITZESCU ACYLATION

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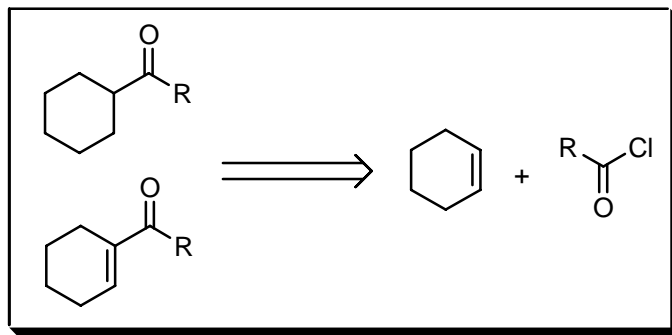
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

Acid chlorides condense with cyclo-olefins in the presence of acid catalysts to yield a chloro-ketone which readily loses hydrogen chloride to form an  $\alpha,\beta$ -unsaturated ketone. This method can be applied to ring formation. With C7 rings, ring contraction frequently occurs, cyclopentane and cyclohexane are however unchanged. See also **Friedel – Crafts** and **Scholl** reactions.

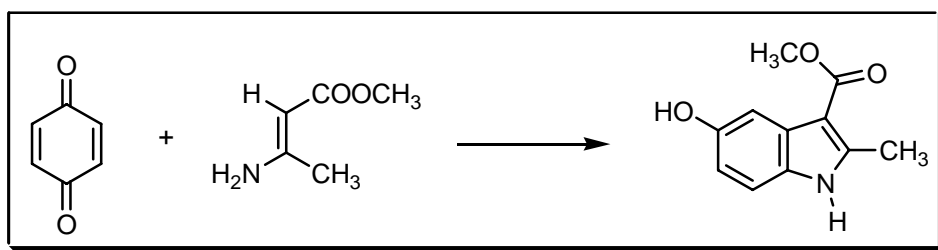
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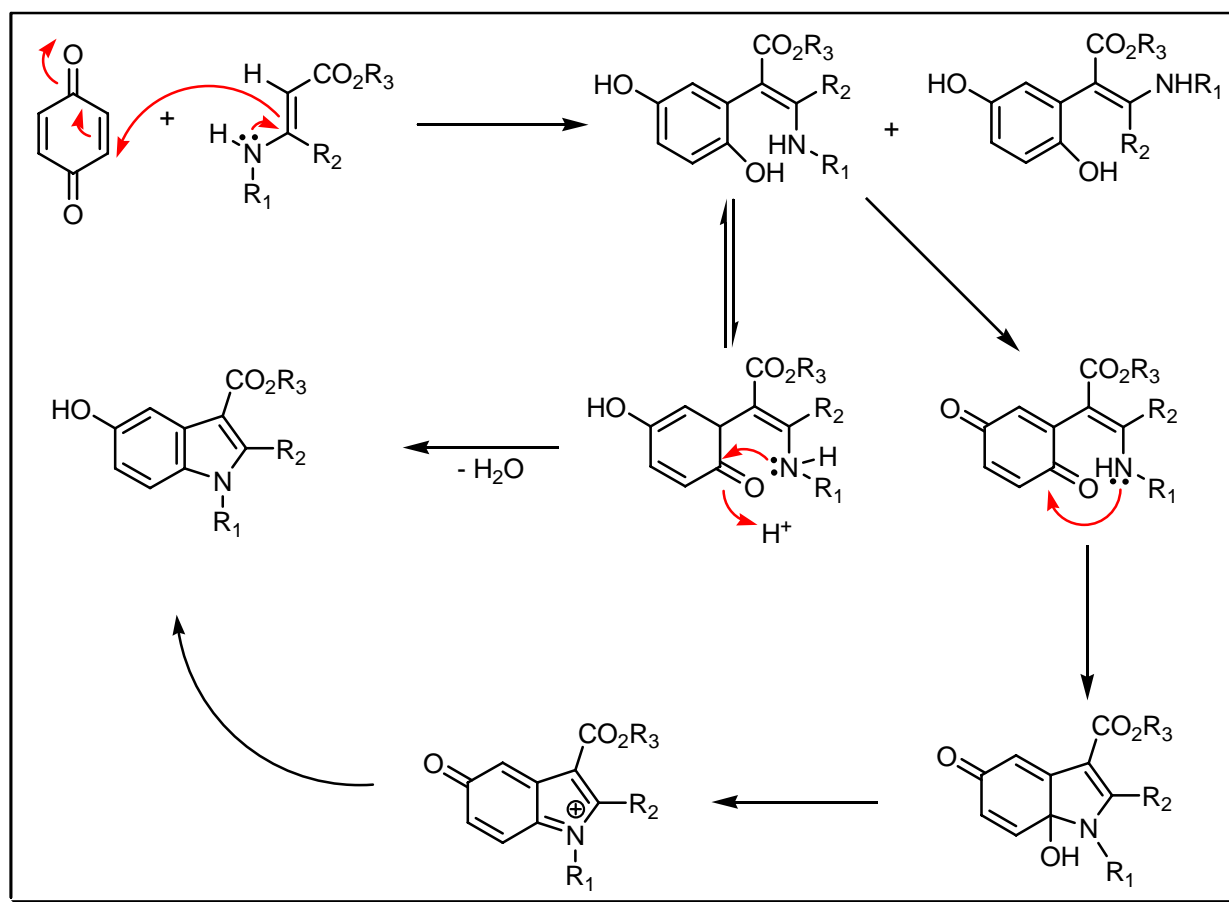
## COMMENTS :

## NENITZESCU INDOLE SYNTHESIS

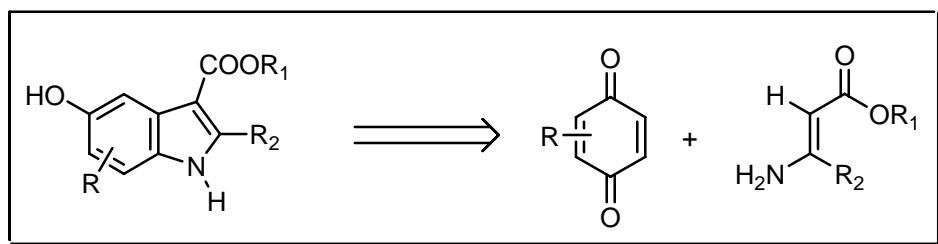
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

*p*-Benzoquinone reacts with ethyl  $\beta$ -aminocrotonate and certain of its *N*-monosubstituted derivatives to yield hydroxyindole esters. Also reduction of *o*, $\omega$ -dinitrostyrenes by iron in acetic acid or catalytically, yield indoles. **Bernier et al.** reported on the internal oxidation – reduction process in nitromethane. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

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## REFERENCES :

**Org. React.** : **20**, 337

**Science of Synthesis** : **10**, 401, 698

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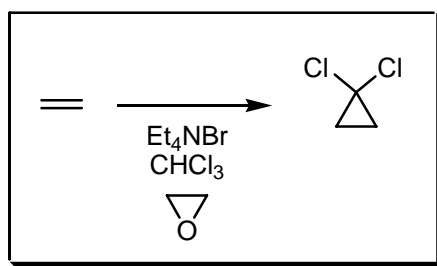
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## COMMENTS :

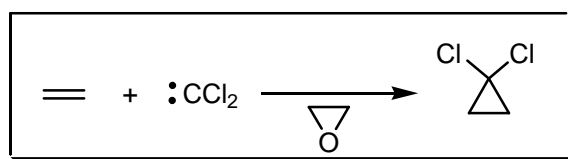
# NERDEL CYCLOPROPANE SYNTHESIS

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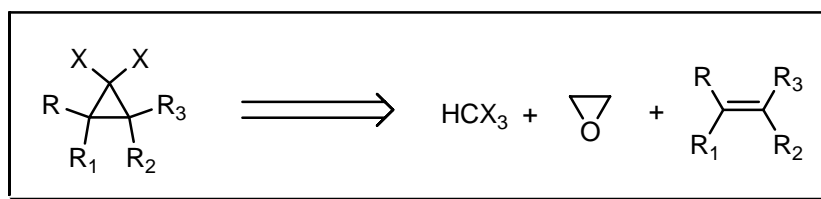
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The formation of 1,1-dihalo-cyclopropanes from olefins, trihalogenmethane and ethyleneoxide (Brönsted base) in the presence of a tetraalkylammonium or phosphonium salt. Dichlorocarbene is the active species. See also **Charette**, **Freund**, **Gustavson**, **Hass** cyclopropane, **Ipatiew** cyclopropane, **Mousseron – Fraisse – McCoy** and **Simmons – Smith** reactions.

## REFERENCES :

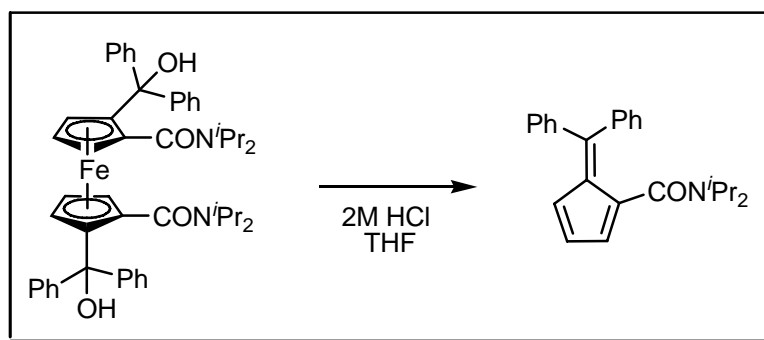
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## COMMENTS :

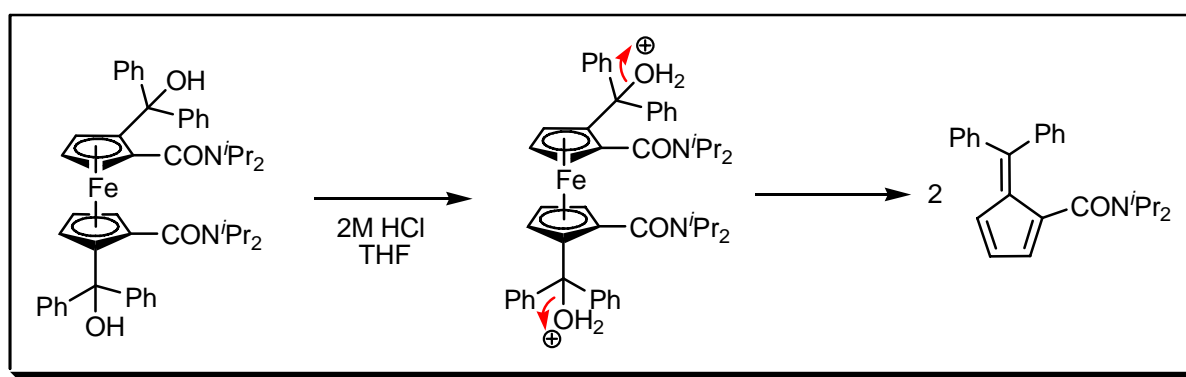


# NESMANJANOV FULVENE SYNTHESIS

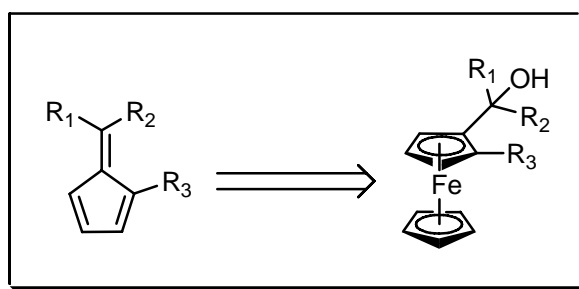
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The directed *ortho* metalation (Dom) fragmentation sequence to ring-substituted 6-aryl and 6,6-diaryl fulvenes with amide and phosphinyl ring substituents. See also **Thiele** reaction.

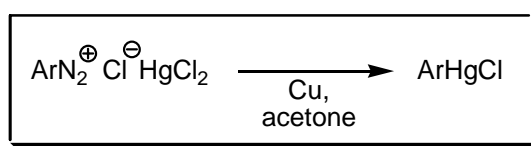
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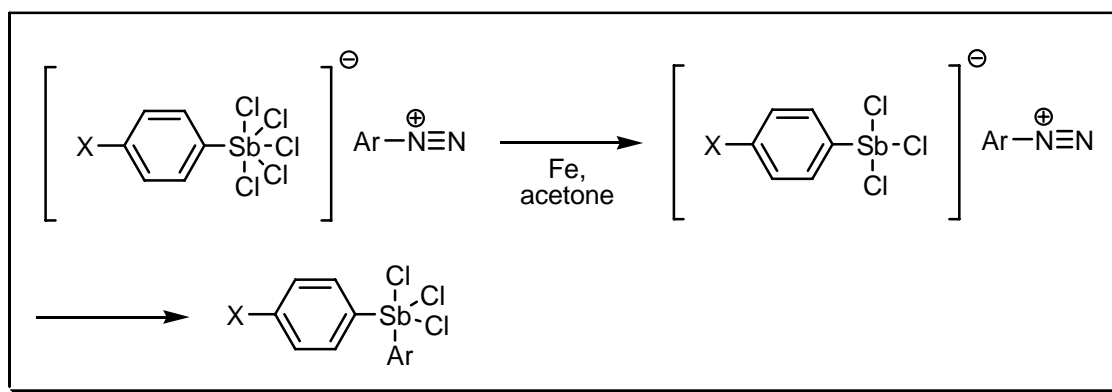
## COMMENTS :

## NESMANJANOV METALLATION

### EXAMPLE :



### MECHANISM :



### NOTES :

A benzenediazonium chloride reacts with mercuric chloride to yield a complex which when treated with a reducing agent (copper (iron) powder in acetone), gives an aryl mercuric chloride. If ammonia is present a diaryl mercury is obtained. The more electron donating X is, the faster the reaction proceeds. The halogen atom is abstracted first before the formation of the organometallic bond. Organo compounds of tin, arsenic, bismuth, thallium and lead can be similarly prepared.

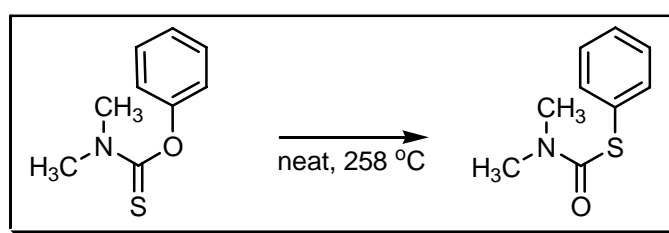
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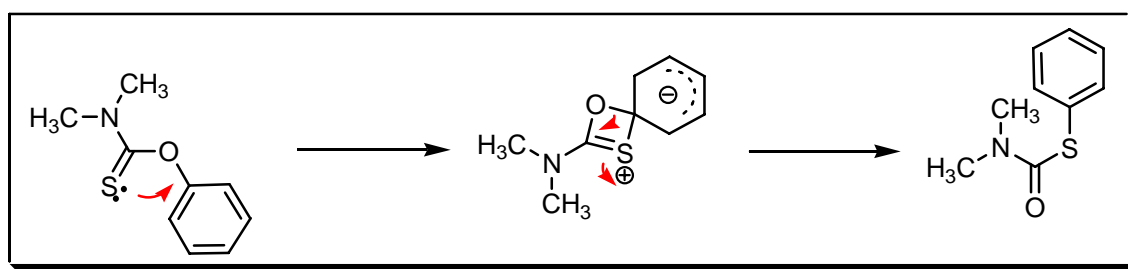
COMMENTS :

## NEWMAN – KARNES – KWART REARRANGEMENT

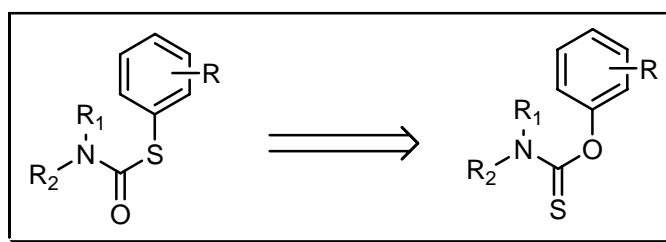
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

An aryl group migrates from an oxygen atom to a sulfur atom in an O-aryl *N,N*-dimethylthiocarbonate. Oxime thiocarbamates thermally rearrange to thio-oxime carbamates and this is thought to proceed through radical intermediates. See also **Beckmann** rearrangement, **Chapman** rearrangement, **Freudenberg – Schönberg**, **Hayashi** rearrangement and **Smiles** rearrangement reactions.

## REFERENCES :

Houben – Weyl : E5, 876

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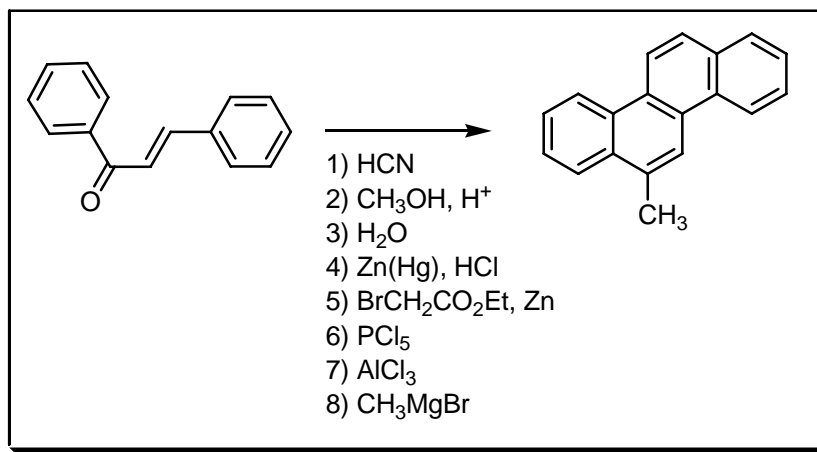
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## COMMENTS :

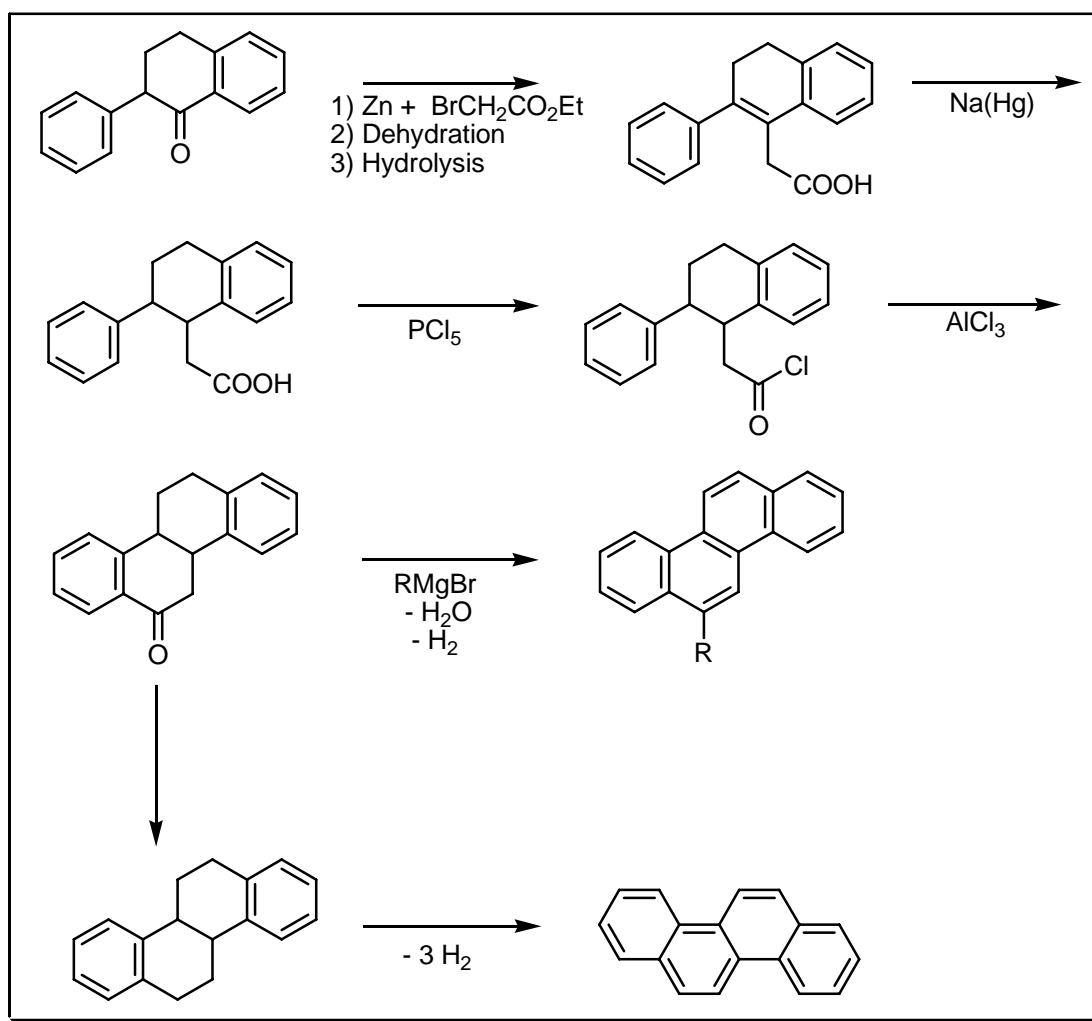
## NEWMAN SYNTHESIS

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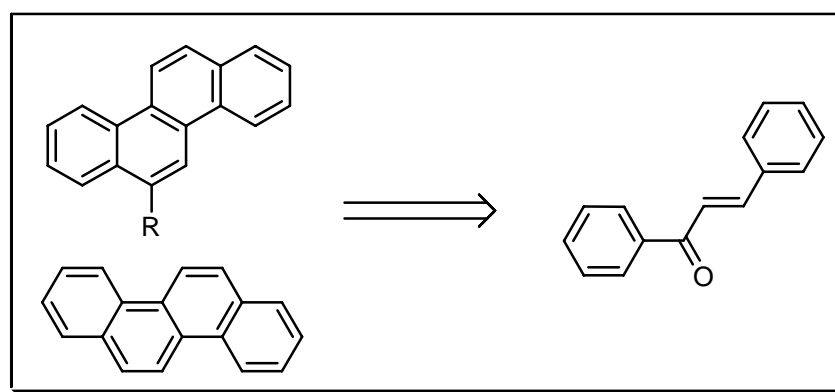
### EXAMPLE :



# MECHANISM :



# DISCONNECTION :



# NOTES :

The syntheses of chrysene and picene and their derivatives starting from 1,3-diphenylpropanone.

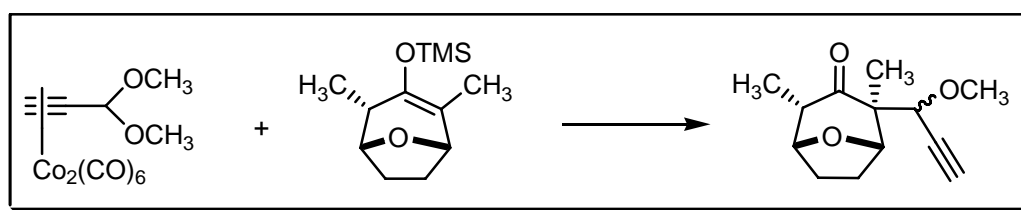
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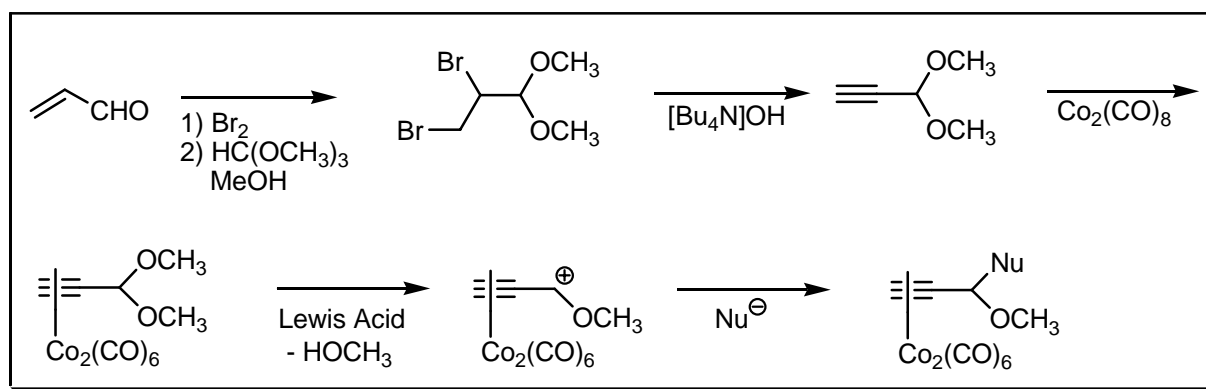
## COMMENTS :

## NICHOLAS SYNTHESIS

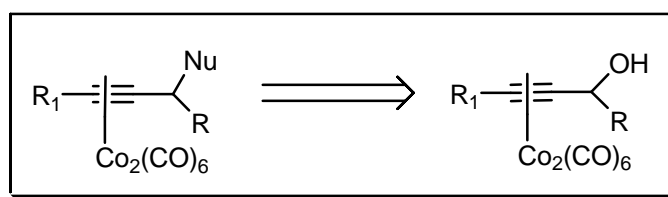
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The reaction between a propargyl cation stabilised as a dicobalt hexacarbonyl complex and a wide variety of nucleophiles is known as the **Nicholas** reaction. This reaction is very versatile and enables the introduction of different functional groups, especially by modification of the C-C triple bond, after demetallation. Thus, there have been many applications for this reaction leading recently to the synthesis of complex biologically active compounds. A heterobimetallic cobalt-molybdenum propargylium complex has been reported by **Jones et al.** See also **Pauson – Khand** reaction.

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## REFERENCES :

**Org. Synth.** : **67**, 141

**Org. Synth. Coll. Vol.** : **8**, 460

**Science of Synthesis** : **1**, 508

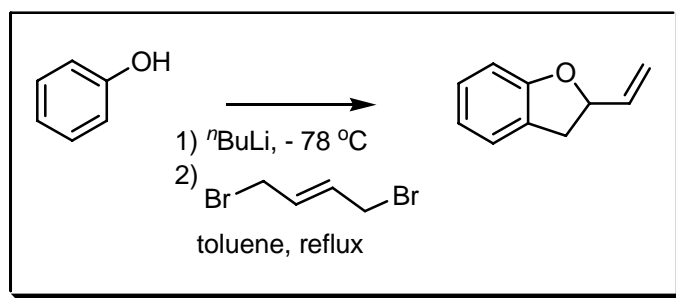
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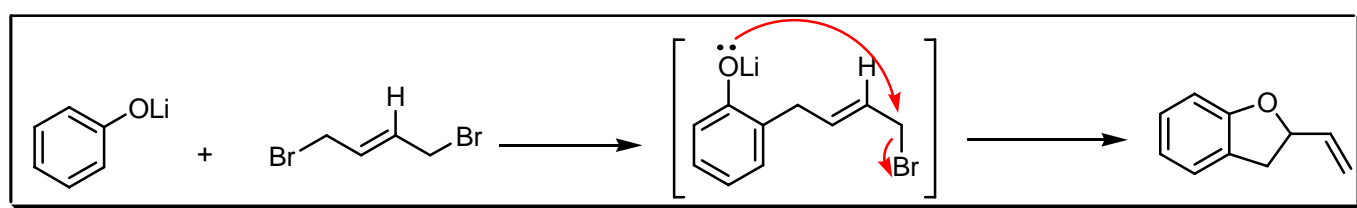
## COMMENTS :

# NICKL SYNTHESIS

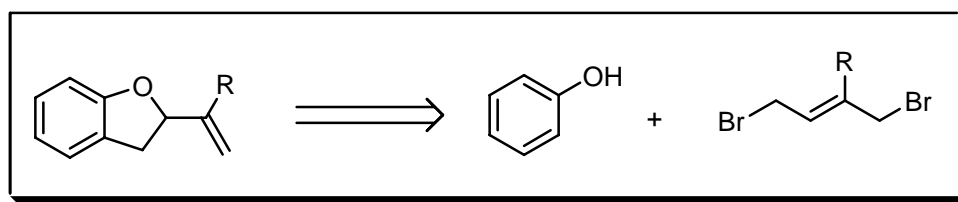
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The one-step heteroannulation of sodium phenolates with 1,4-dibromo-2-butenes to afford benzofurans. **Casiraghi et al.** critically examined this reaction.

## REFERENCES :

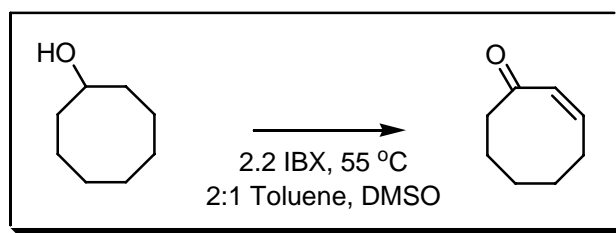
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- 3) S. Inoue; H. Kakoi; K. Okada; T. Goto, *Chem. Lett.*, 1979, 253.
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## COMMENTS :

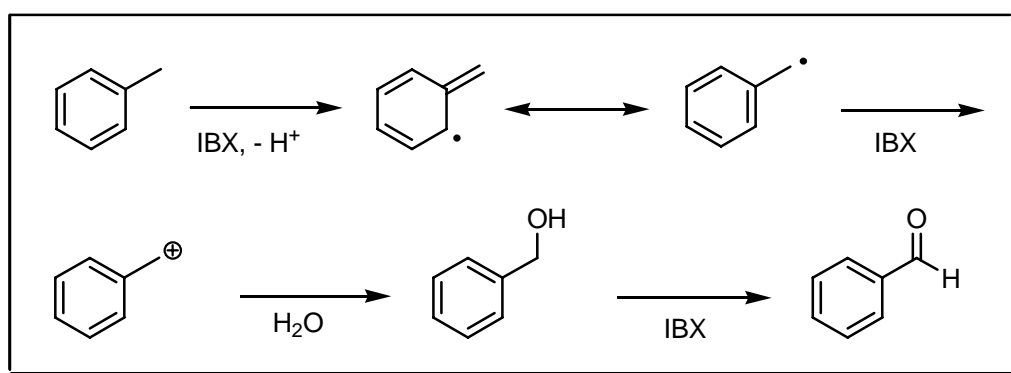
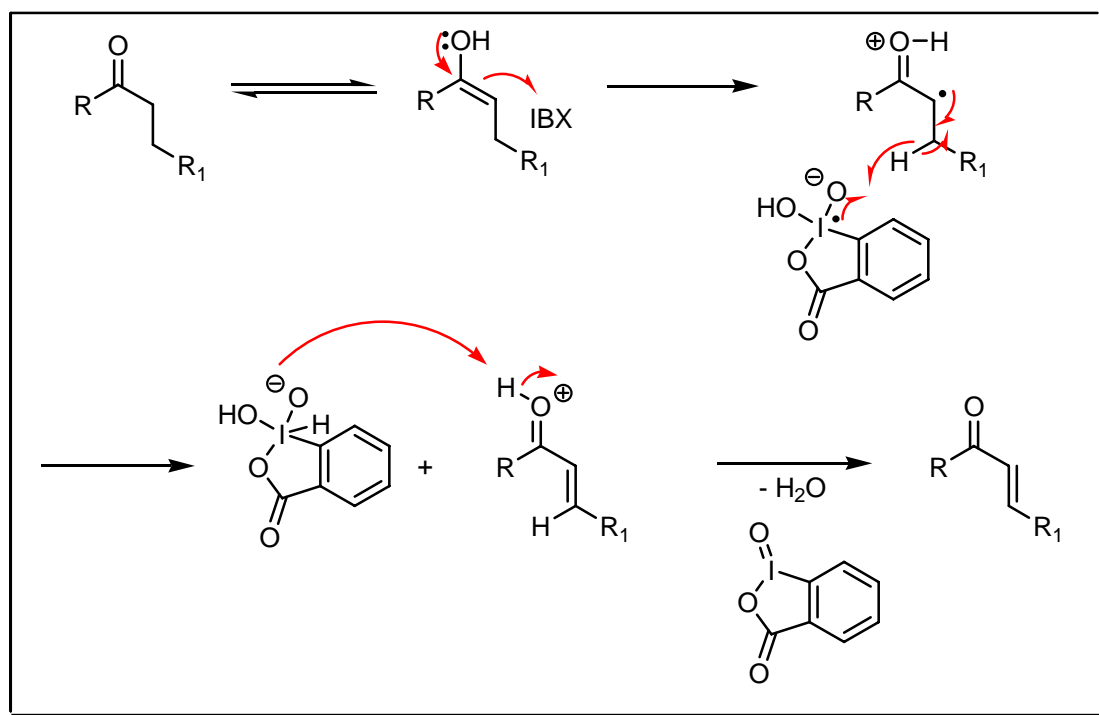


## NICOLAOU OXIDATION

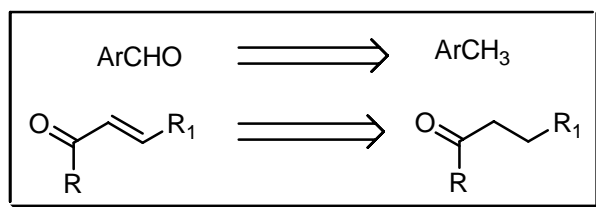
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The use of *ortho*-iodoxybenzoic acid as oxidising agent for the one-step synthesis of  $\alpha,\beta$ -unsaturated carbonyl compounds from saturated alcohols and carbonyl compounds. Under similar conditions carbons adjacent to aromatic systems can selectively be oxidised. See also **Anelli, Ball – Goodwin – Morton, Collins, Corey – Kim, Corey – Schmidt, Corey – Suggs, David – Thieffry, Delépine, Dess – Martin, Einhorn** oxidation, **Fétizon, Jones** oxidation, **Ley, Maurer – Drefahl, Mukaiyama** oxidation, **Oppenauer, Parikh – von Doering, Pfitzner – Moffatt, Pinnick, Sarett, Swern** and **Uemura** reactions.

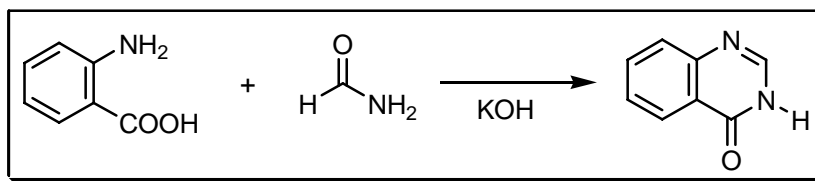
## REFERENCES :

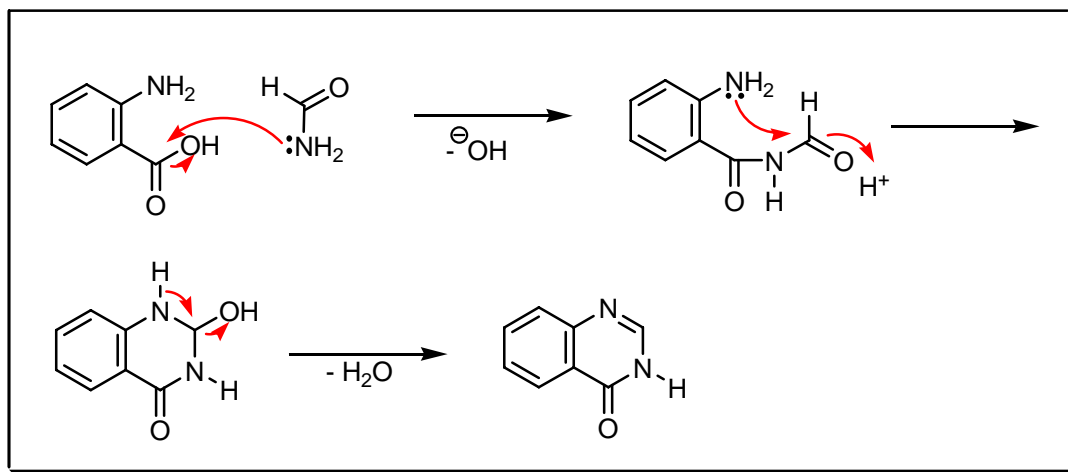
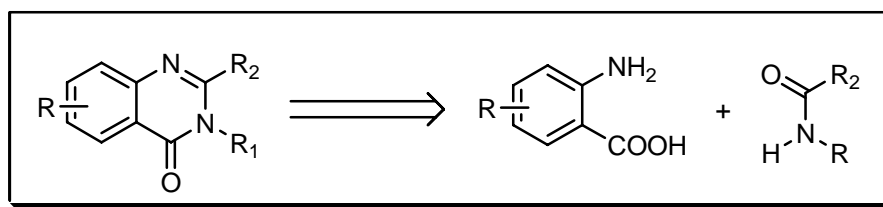
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- 4) K.C. Nicolaou; C.J.N. Mathison; T. Montagnon, *J. Am. Chem. Soc.*, 2004, **126**, 5192.
- 5) S. Kotha; S. Banerjee; K. Mandal, *Synlett*, 2004, 2043.
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## COMMENTS :

## von NIEMENTOWSKI QUINAZOLONE REACTION

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

Anthranilic acids or their esters react with amides to yield 4-keto-3,4-dihydroquinazolines. Variants of the essential synthesis, using amidines have been described.

**REFERENCES :**

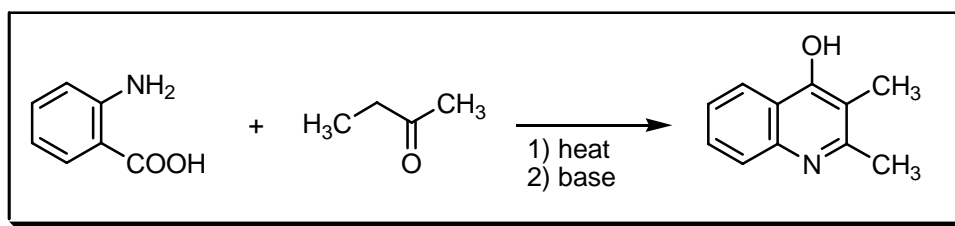
Houben – Weyl : E8b, 849

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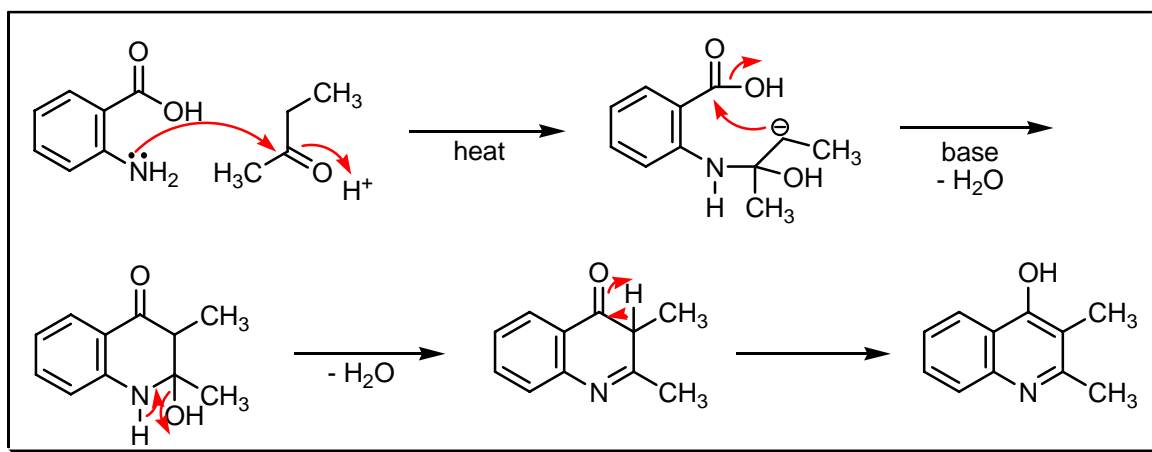
**COMMENTS :**

## von NIEMENTOWSKI QUINOLINE SYNTHESIS

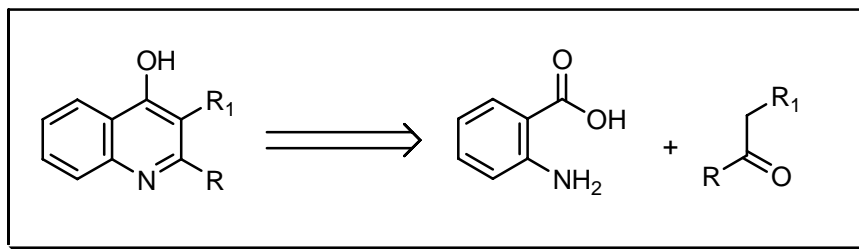
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This reaction involves the use of anthranilic acids in place of the *o*-amino-benzaldehydes used in the **Friedländer** synthesis of quinolines. See also **Allan – Loudon**, **von Baeyer – Drewson** quinoline, **Camps, Combes** quinoline, **Conrad – Limpach**, **Doebner** quinoline, **Doebner – von Miller**, **Foulds – Robinson**, **Friedländer**, **Knorr** quinoline, **Meth-Cohn**, **Pfitzinger – Borsche**, **Riehm** quinoline and **Skraup** quinoline reactions.

### REFERENCES :

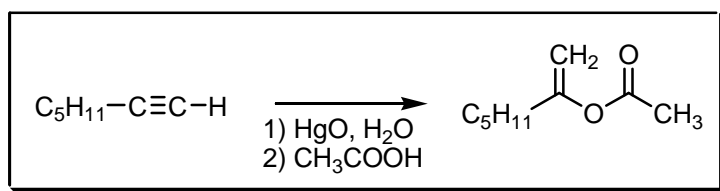
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- 3) T. Hisano, *Org. Prep. Proced. Int.*, 1973, **5**, 145.
- 4) E. Cuny; F.W. Lichtenthaler; A. Moser, *Tetrahedron Lett.*, 1980, **21**, 3029.

- 5) B.P. Suthar, *Indian J. Chem.*, 1982, **21B**, 588.  
6) R.J. Chong; M.A. Siddiqui; V. Snieckus, *Tetrahedron Lett.*, 1986, **27**, 5323.  
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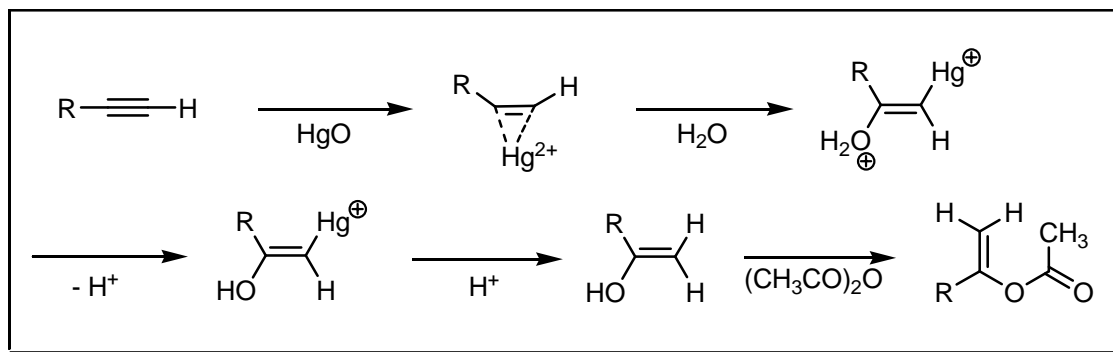
COMMENTS :

## NIEUWLAND HYDRATION

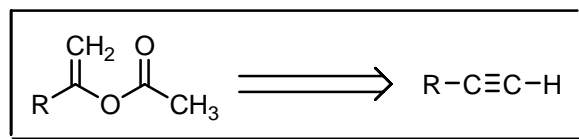
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The hydration and acylation of acetylenes using mercuric oxide and acetic acid or acetic anhydride. This method is very suitable for use on steroid derivatives. See also **Kutscheroff – Denigès** reaction and **Reppe** carbonylation.

## REFERENCES :

March : 762

Smith – March : 995

Houben – Weyl : E3, 243

Org. Synth. : 35, 1; 40, 88

Org. Synth. Coll. Vol. : 4, 13; 5, 1024

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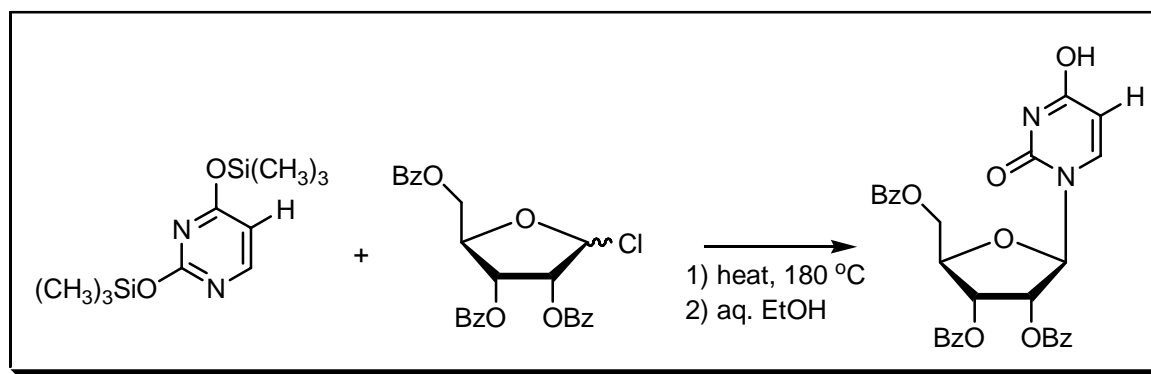
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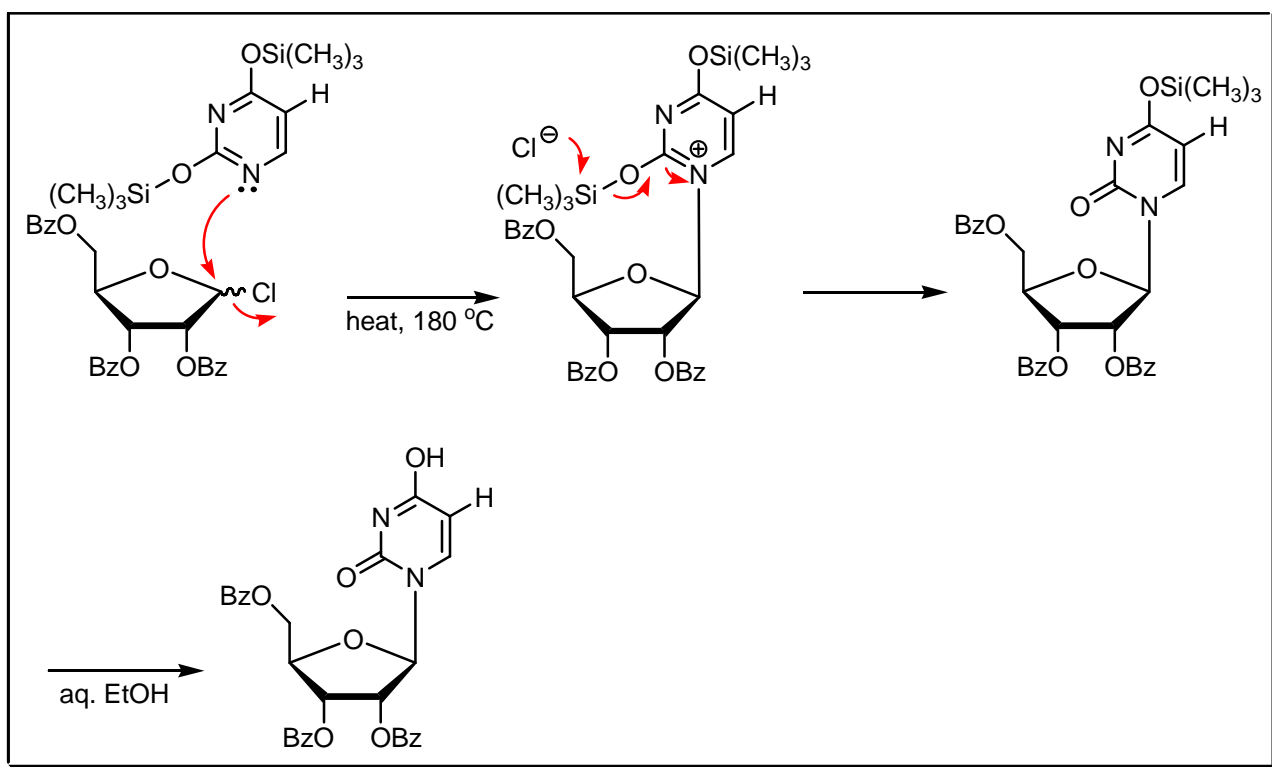
## COMMENTS :

## NISHIMURA – CRISTESCU N-GLYCOSIDATION

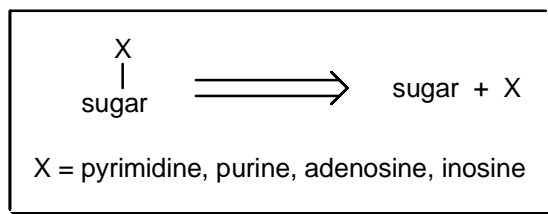
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of natural and synthetic nucleosides using trimethylsilyl derivatives of pyrimidines, adenosines, inosines and purines. The aqueous ethanol removes the trimethylsilyl protecting group on the hydroxyl. See also **Vorbrüggen** nucleoside synthesis.

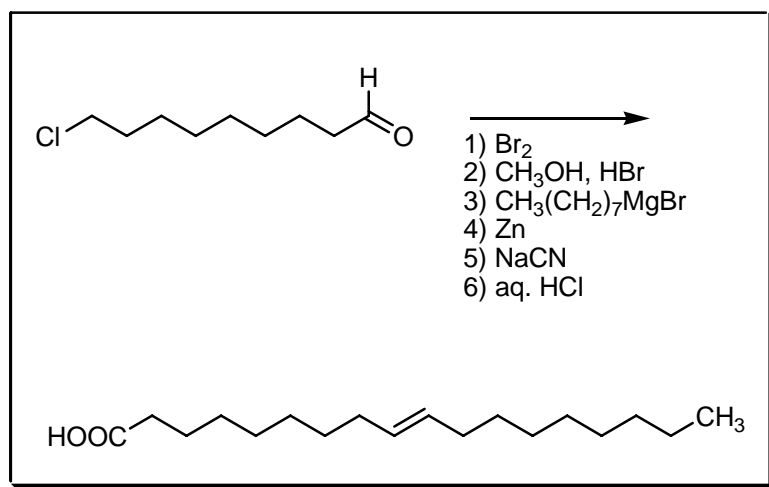
## REFERENCES :

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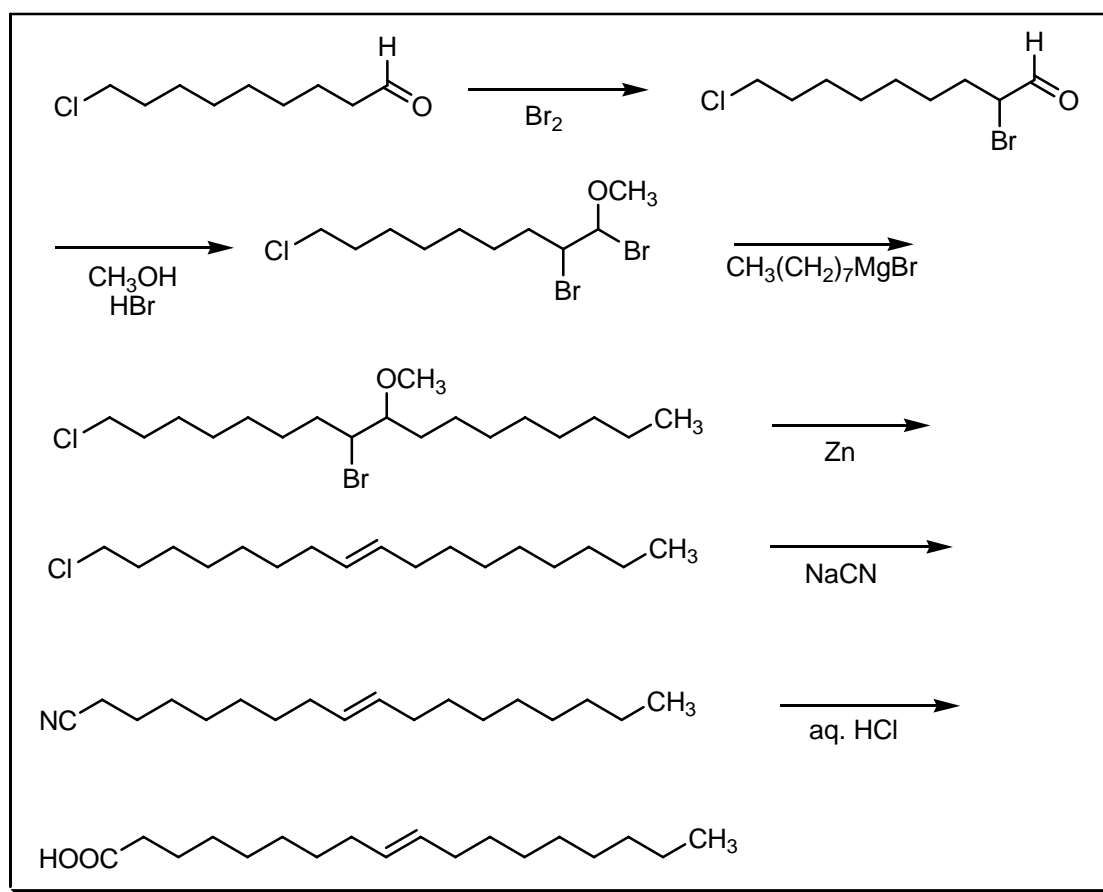
## COMMENTS :

## NOLLER SYNTHESIS

### EXAMPLE :

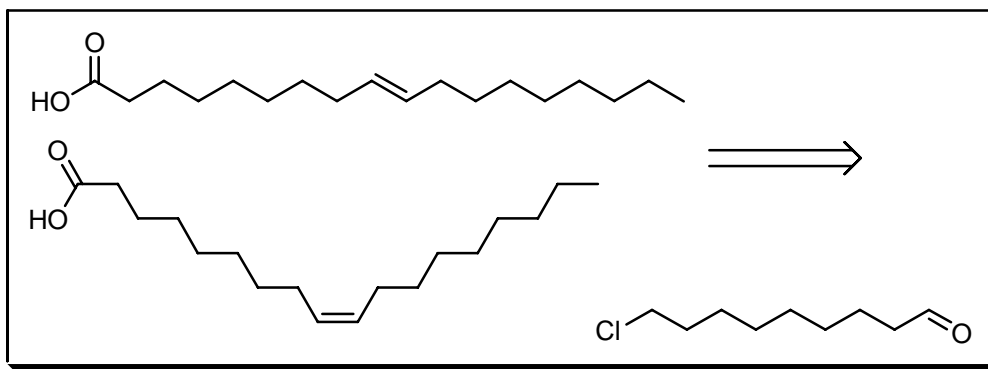


### MECHANISM :





## DISCONNECTION :



## NOTES :

This synthesis in which the position of the double bond is unambiguous is exemplified by the classic preparation of oleic acid and elaidic acid. See also **Baudart**, **Boord**, **Bowman**, **Kapp – Knoll** and **Robinson – Robinson** reactions.

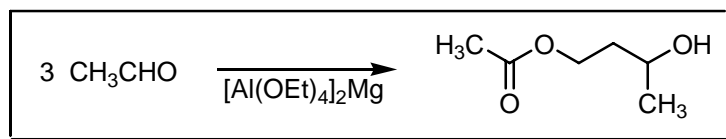
## REFERENCES :

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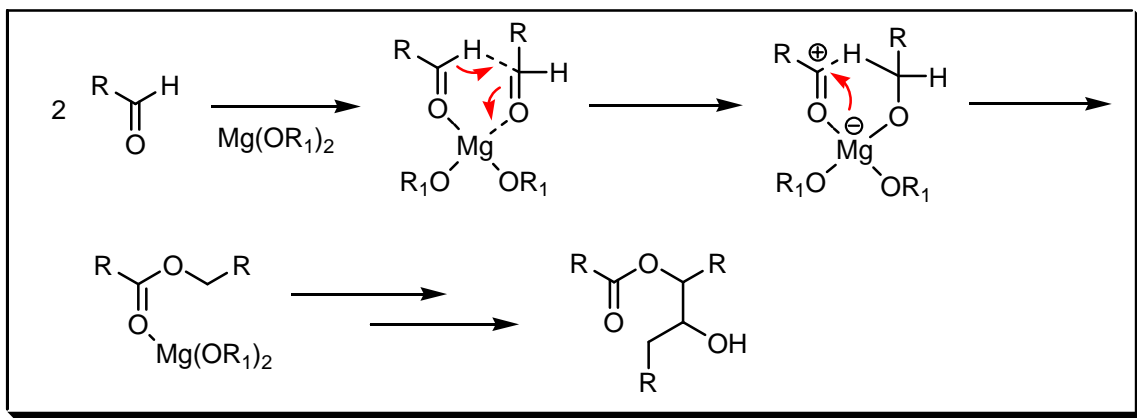
## COMMENTS :

## NORD SYNTHESIS

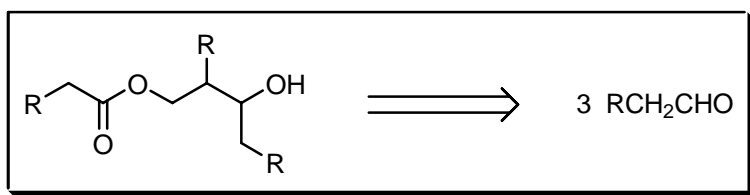
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Magnesium aluminium alkoxides and similar co-ordination catalysts produce a trimeric condensation of  $\alpha$ -methylenealdehydes to yield glycol esters. See also **Cannizzaro** and **Tishchenko – Claisen** reactions.

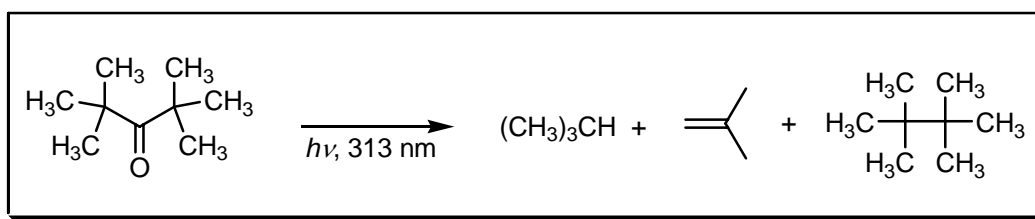
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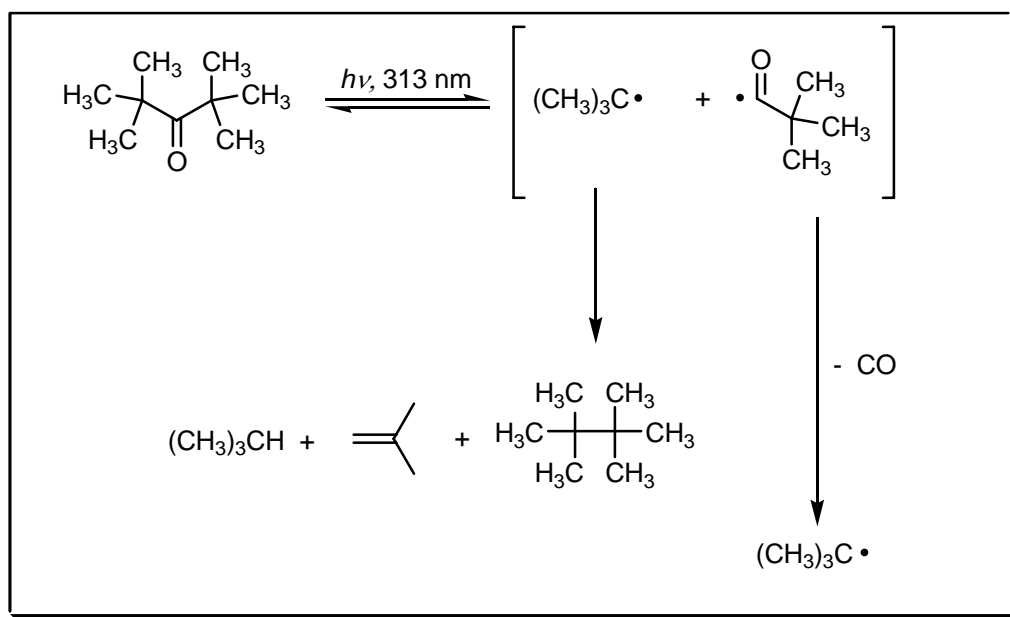
### COMMENTS :

## NORRISH TYPE 1 REARRANGEMENT

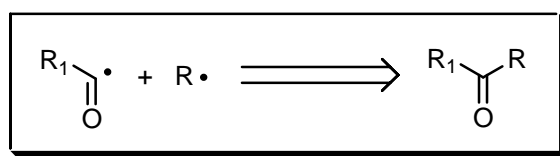
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The homolytic cleavage of the C-C bond which is  $\alpha$  to the carbonyl group is observed from  $(n, \pi^*)$  excited states for a number of ketones. This rearrangement can also be used for photolactonisations. See also **Norrish** type II reaction.

### REFERENCES :

March : 243, 1047

Smith – March : 318, 1354

Smith 2<sup>nd</sup> : 1155

Houben – Weyl : 4/5b, 1021, 1035

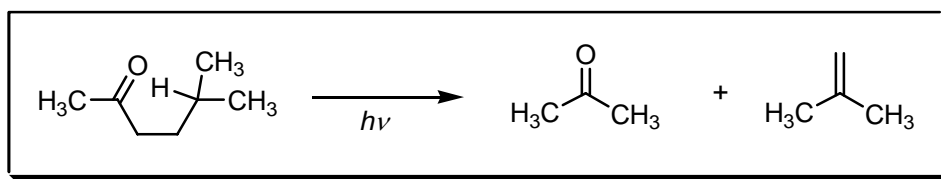
- 1) R.G.W. Norrish, *Trans. Faraday Soc.*, 1934, **30**, 103.
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**COMMENTS :**

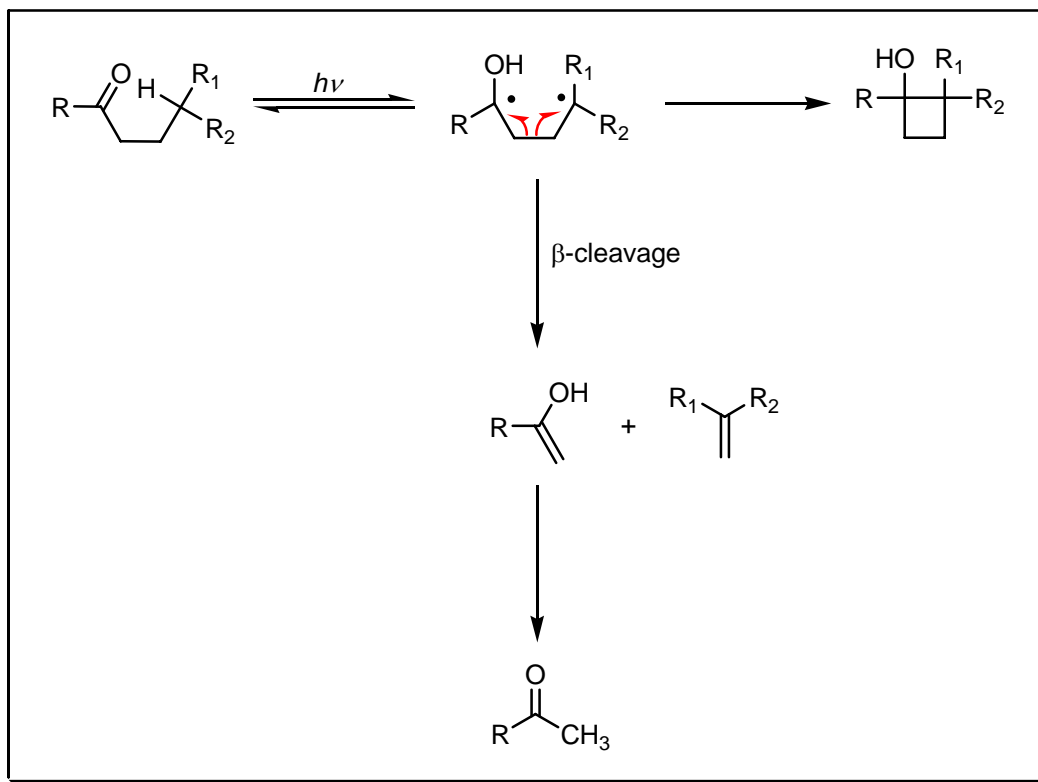
## NORRISH TYPE 2 REARRANGEMENT

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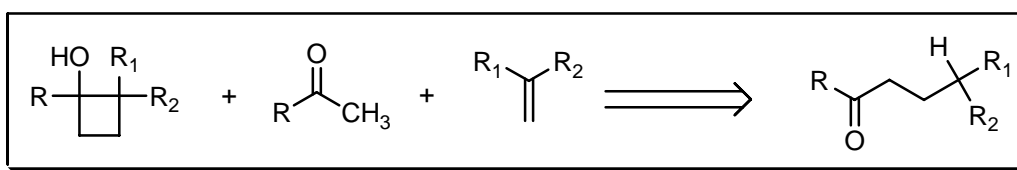
**EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

The principal photochemical reaction from the  $(n, \pi^*)$  excited state of ketones containing a hydrogen atom in the  $\gamma$ -position is *intramolecular* hydrogen abstraction. In the absence of steric constraints, a six-center cyclic transition state favours transfer of this hydrogen to the oxygen of the carbonyl group. The primary product of this reaction is a 1,4-biradical. See also **McLafferty** and **Norrish type 1** reactions.

## REFERENCES :

March : 243

Smith – March : 318, 1299

Smith 2<sup>nd</sup> : 1155

Houben – Weyl : 4/5b, 795, 892, 1017

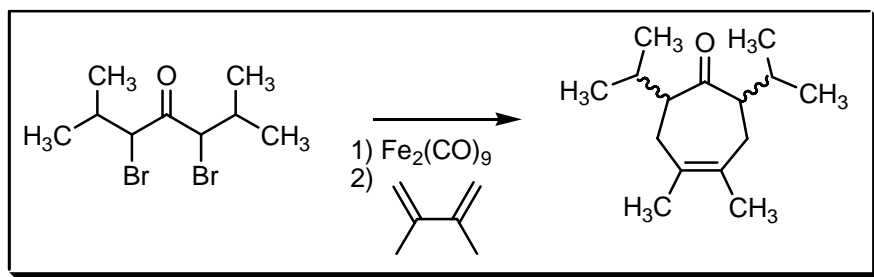
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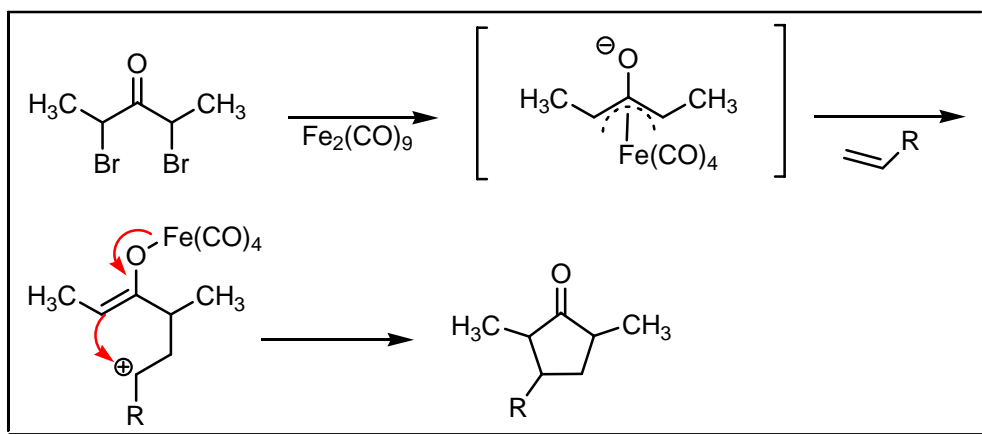
**COMMENTS :**

**NOYORI ANNULATION**

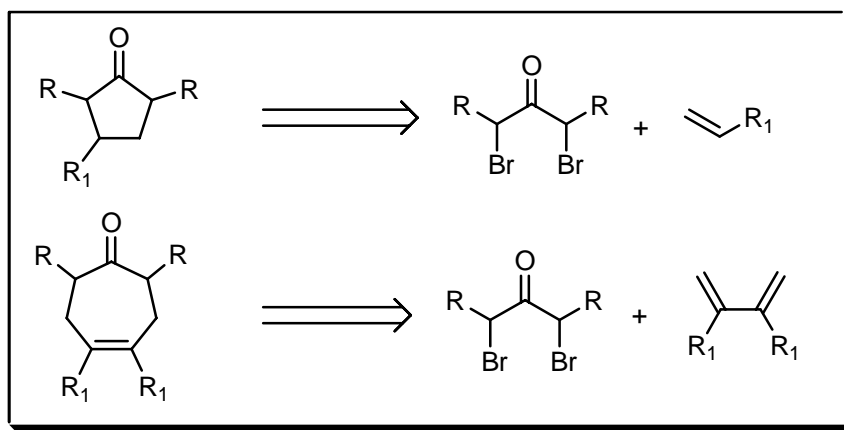
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

A useful carbon-bond forming reaction involving diiron nonacarbonyl with halo-carbonyl compounds. See also **Nazarov** reaction.

## REFERENCES :

Smith : 1372

Smith 2<sup>nd</sup> : 1133

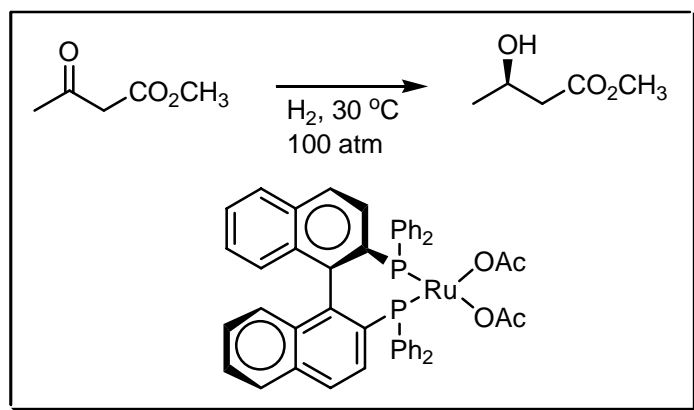
Org. React. : **29**, 163

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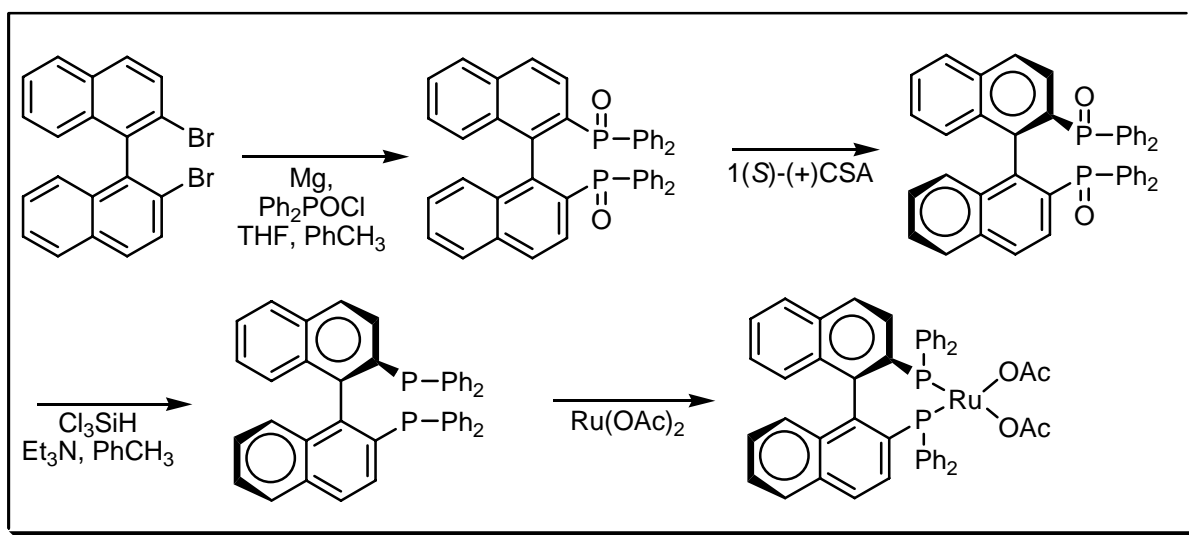
## COMMENTS :

## NOYORI HYDROGENATION

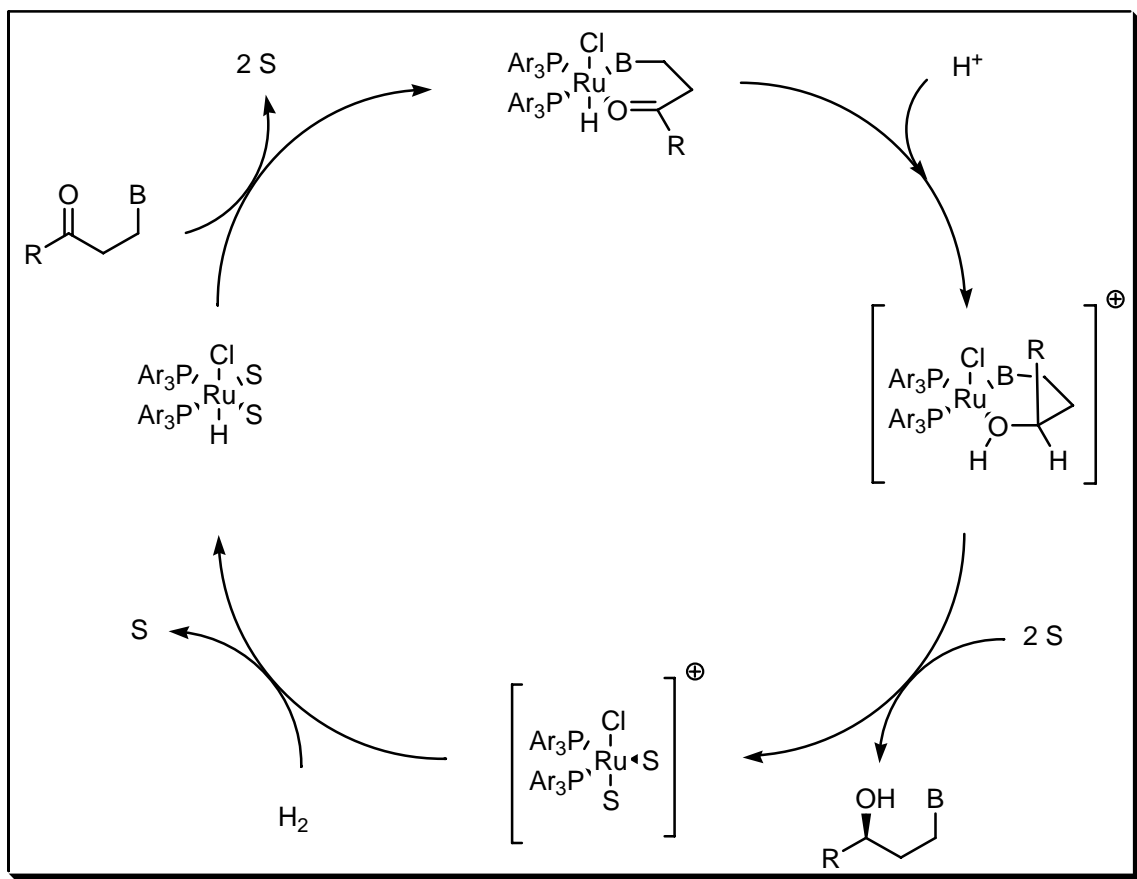
### EXAMPLE :



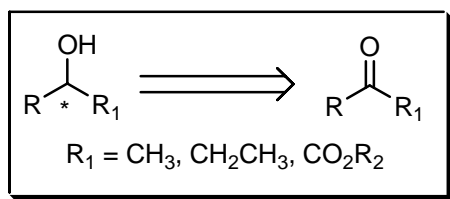
### MECHANISM :







#### DISCONNECTION :



#### NOTES :

The homogeneous chiral hydrogenation of unsaturated alcohols, or carboxylic acids, enamides, ketones in the presence of BINAP Ru or Rh complex as catalyst. There are three classes of catalytic systems. For enantioselective hydrogenation a diphosphine ligand or a diphosphine ligand with a diamine ligand can be used. For enantioselective hydrogen transfer a 1,2-diamine ligand is used. The **Noyori** catalysts are highly-efficient, work under mild-conditions and at 1 – 10 atmosphere of hydrogen pressure. See also **Corey – Itsuno – Bakshi – Shibata, Horner – Knowles – Kagan, Kerp** and **Midland** reactions.

#### REFERENCES :

March : 914

Smith – March : 1201

Org. Synth. : 67, 20; 72, 74; 77, 1

Org. Synth. Coll. Vol. : 8, 57; 9, 169

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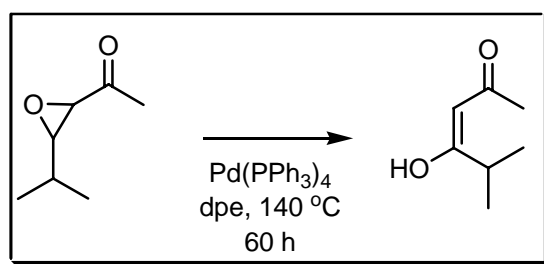
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**COMMENTS :**

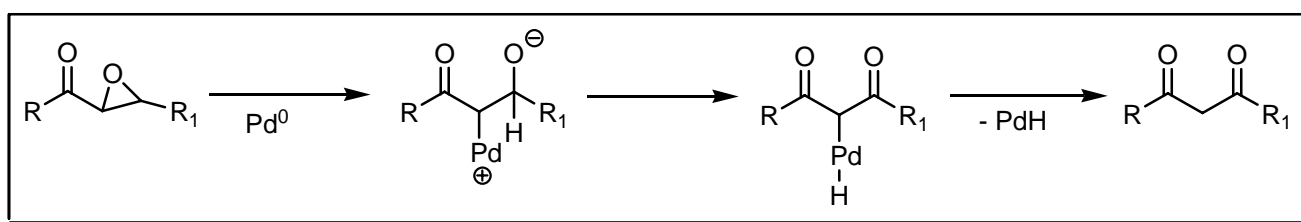
**NOYORI REARRANGEMENT**

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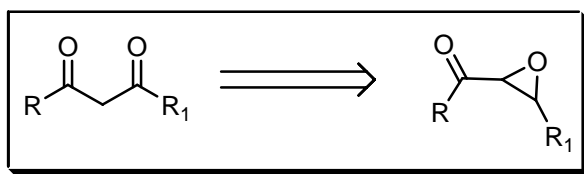
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

In the presence of 1,2-bis(diphenylphosphino)ethane catalytic amounts of palladium(0) isomerises cyclic and acyclic  $\alpha,\beta$ -epoxy ketones to  $\beta$ -diketones. Epoxy ketones containing an  $\alpha$ -alkyl group react only sluggish. Epoxy esters or nitriles do not react under these conditions. There are two reaction mechanisms proposed the most probable is outlined in the scheme.

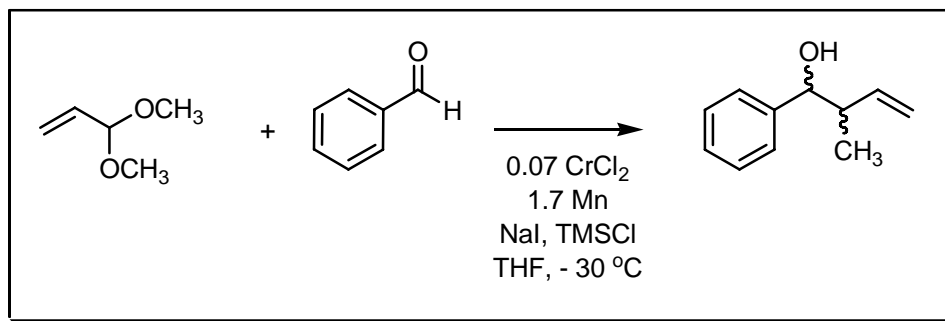
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## COMMENTS :

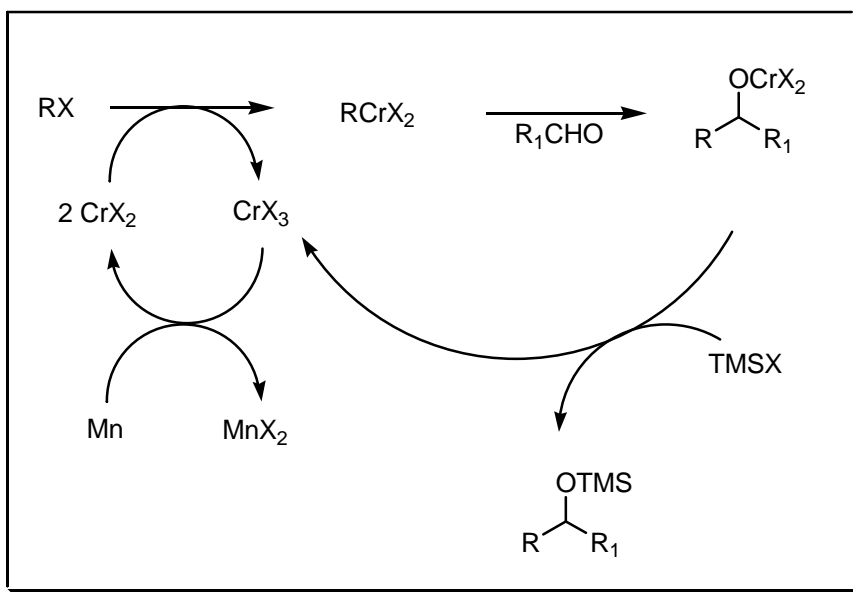
## NOZAKI – HIYAMA – KISHI (TAKAI – UTIMOTO) REACTION

### EXAMPLE :

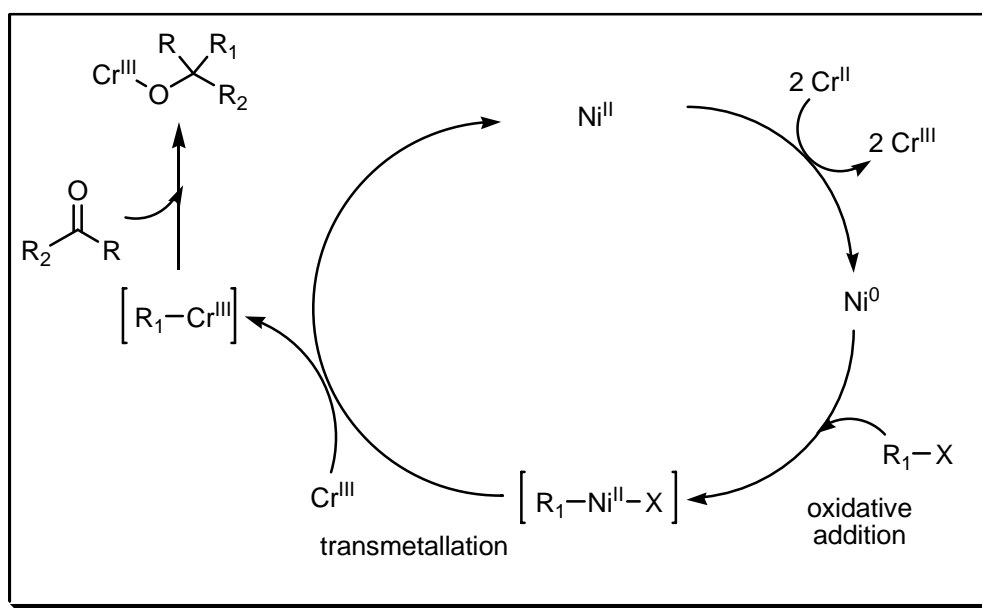


## MECHANISM :

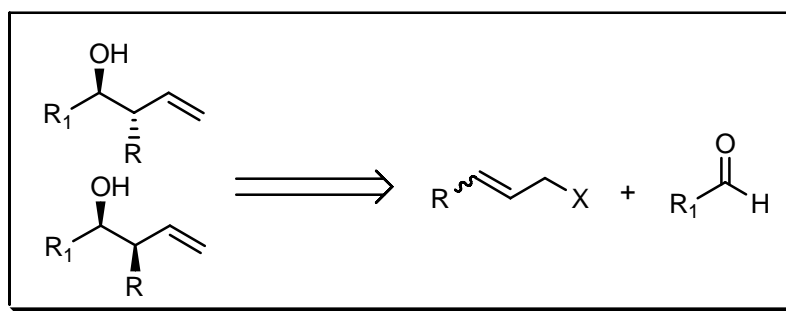
### Fürstner procedure :



### Nickel-catalysed :



## DISCONNECTION :



## NOTES :

The addition of vinyl, allyl, or aryl halides to aldehydes *via* an intermediate chromium(III) species is generally achieved by CrCl<sub>2</sub> with a catalytic amount of nickel chloride. The reaction can also be catalytic (**Fürstner** procedure Mn<sup>0</sup> and TMSCl or **Boeckmann** procedure Mn<sup>0</sup>, TMSCl and NaI) and enantioselective. The **Nozaki – Hiyama** reaction is the formation of homoallyl alcohols from allylhalogenides, tosylates or phosphates. The **Kishi** reaction uses vinyl- and arylhalogenides, while in the **Takai – Utimoto** reaction non-activated alkyl halogenides are used. See also **Corey – Kwiatkowski**, **Corey – Nicolaou**, **Diels – Alder**, **Eastwood**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Julia – Paris – Kocienski – Lythgoe**, **Keck** macrolactonisation, **Krief – Reich – Chow**, **Masamune**, **McMurry**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nysted**, **Paquette**, **Petasis** reaction, **Peterson**, **Ramberg – Bäcklund**, **Raphael**, **Roush**, **Růžička** large ring synthesis, **Schmidt** macrolactonisation, **Staab**, **Stacey**, **Steglich – Hassner**, **Still – Gennari**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Takeda**, **Tebbe**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolakiewicz**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

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**Org. Synth.** : **72**, 180

**Org. Synth. Coll. Vol.** : **9**, 472

**Science of Synthesis** : **1**, 34

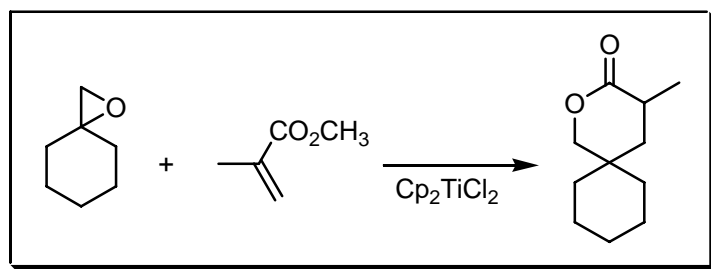
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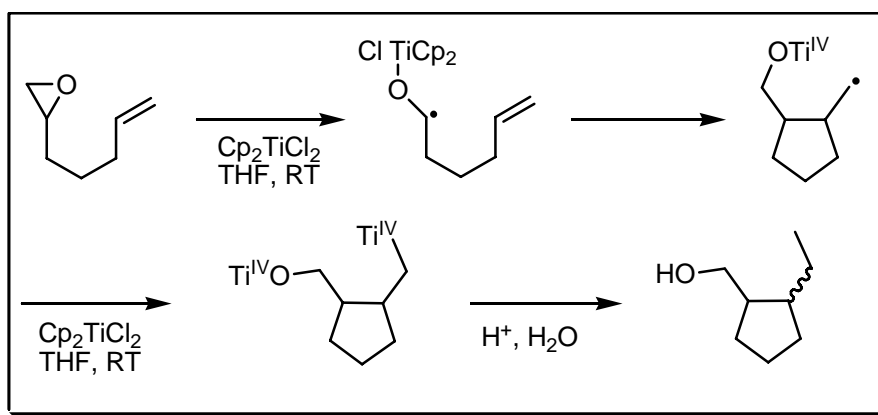
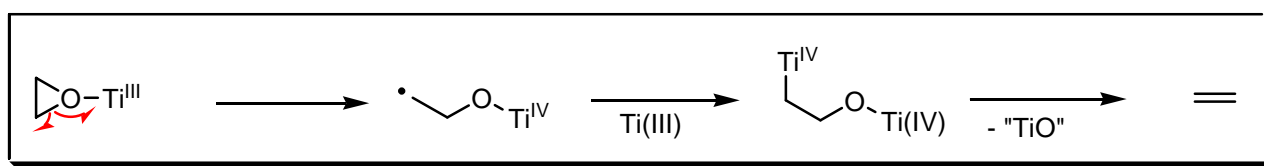
COMMENTS :

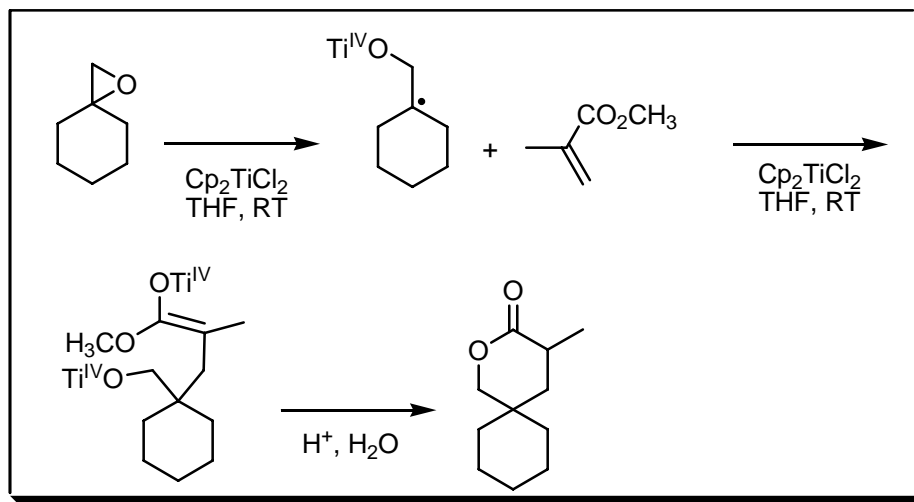
## NUGENT – RAJANBABU EPOXIDE HOMOLYSIS

EXAMPLE :



MECHANISM :





#### NOTES :

Bis(cyclopentadienyl)titanium(III) chloride reacts with epoxides by initial C-O homolysis. It has applications in all major classes of free radical chemistry, *inter*- and *intramolecular* addition to olefins, H-atom abstraction and electron-transfer reductions.

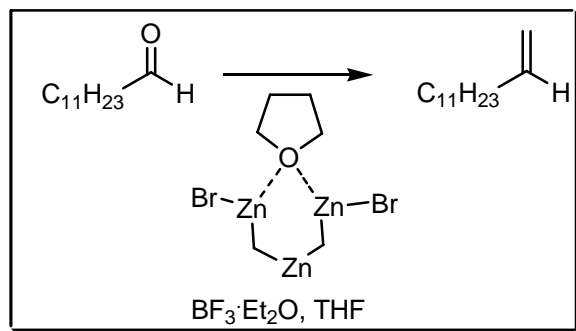
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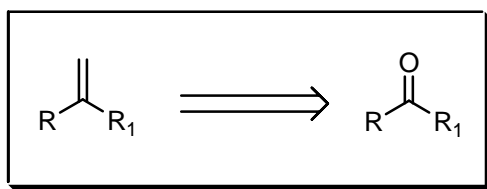
#### COMMENTS :

### NYSTED REACTION

#### EXAMPLE :



## DISCONNECTION :



## NOTES :

[Cyclo-dibromodi-μ-methylene(μ-tetrahydrofuran)trizinc] reacts with aldehydes in the presence of BF<sub>3</sub>·Et<sub>2</sub>O, whereas it reacts with ketones in the presence of BF<sub>3</sub>·Et<sub>2</sub>O and TiCl<sub>2</sub> or TiCl<sub>4</sub>, TiCl<sub>3</sub> to afford methylated products. The reactivity of this reagent itself and the role of the additives still has to be clarified. See also **Corey – Kwiatkowski, Eastwood, Horner – Wadsworth – Emmons, Julia – Paris – Kocienski – Lythgoe, Krief – Reich – Chow, Nozaki – Hiyama – Kishi (Takai – Utimoto), Paquette, Petasis reaction, Peterson, Ramberg – Bäcklund, Still – Gennari, Takeda, Tebbe and Wittig reactions.**

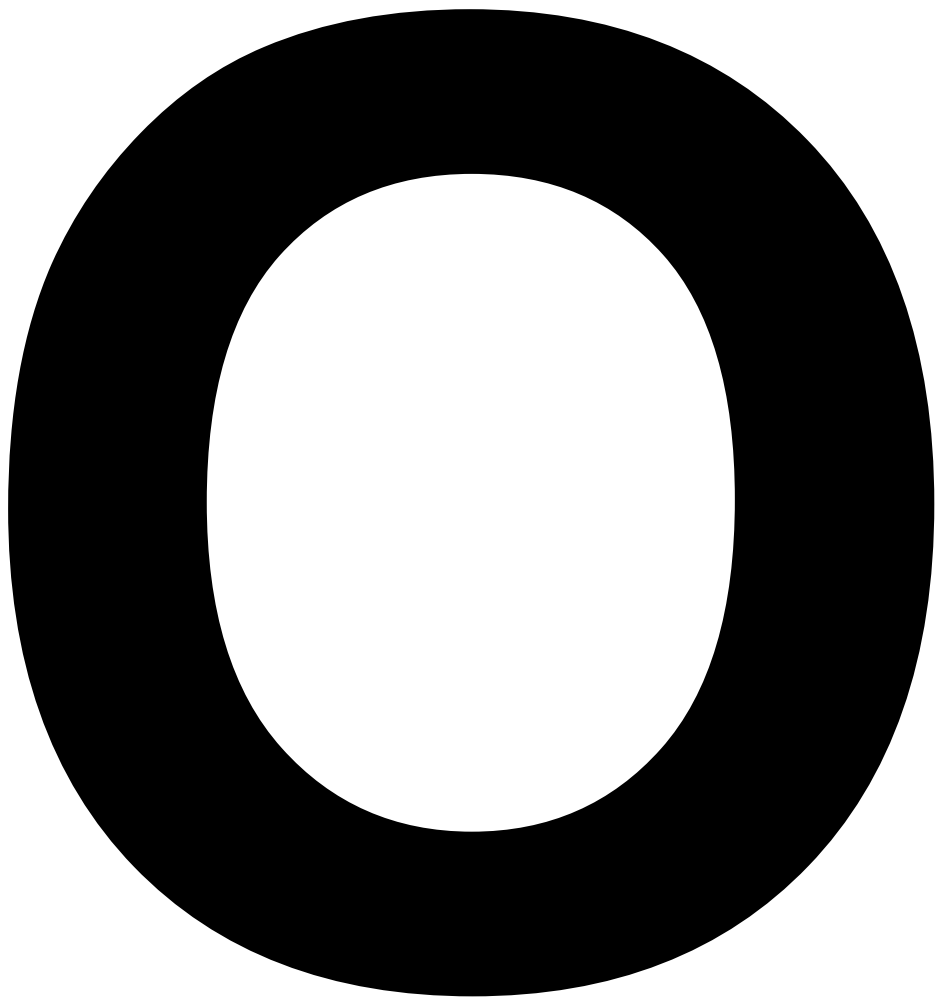
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## COMMENTS :





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## O

O'DONNELL AMINO ACID SYNTHESIS · 1306

OHLE CLEAVAGE · 1309

OHSHIRO – HIRAO REDUCTION · 1310

OLAH CROWDED OLEFIN SYNTHESIS · 1312

OLEKSYSZYN AMINOPHOSPHONIC ACID SYNTHESIS · 1314

OPPENAUER OXIDATION · 1315

OPPOLZER ALLYL ALCOHOL SYNTHESIS · 1317

ORTON HALOANILINE REARRANGEMENT · 1318

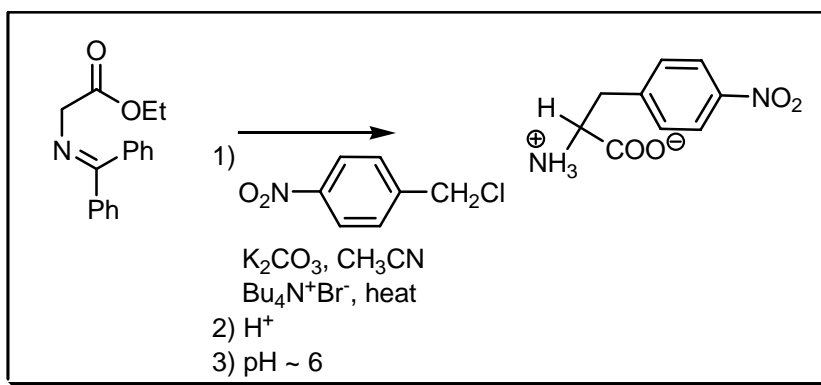
OSTROMYSLENSKI REACTION · 1320

OVERMAN PYRROLIDINE SYNTHESIS · 1321

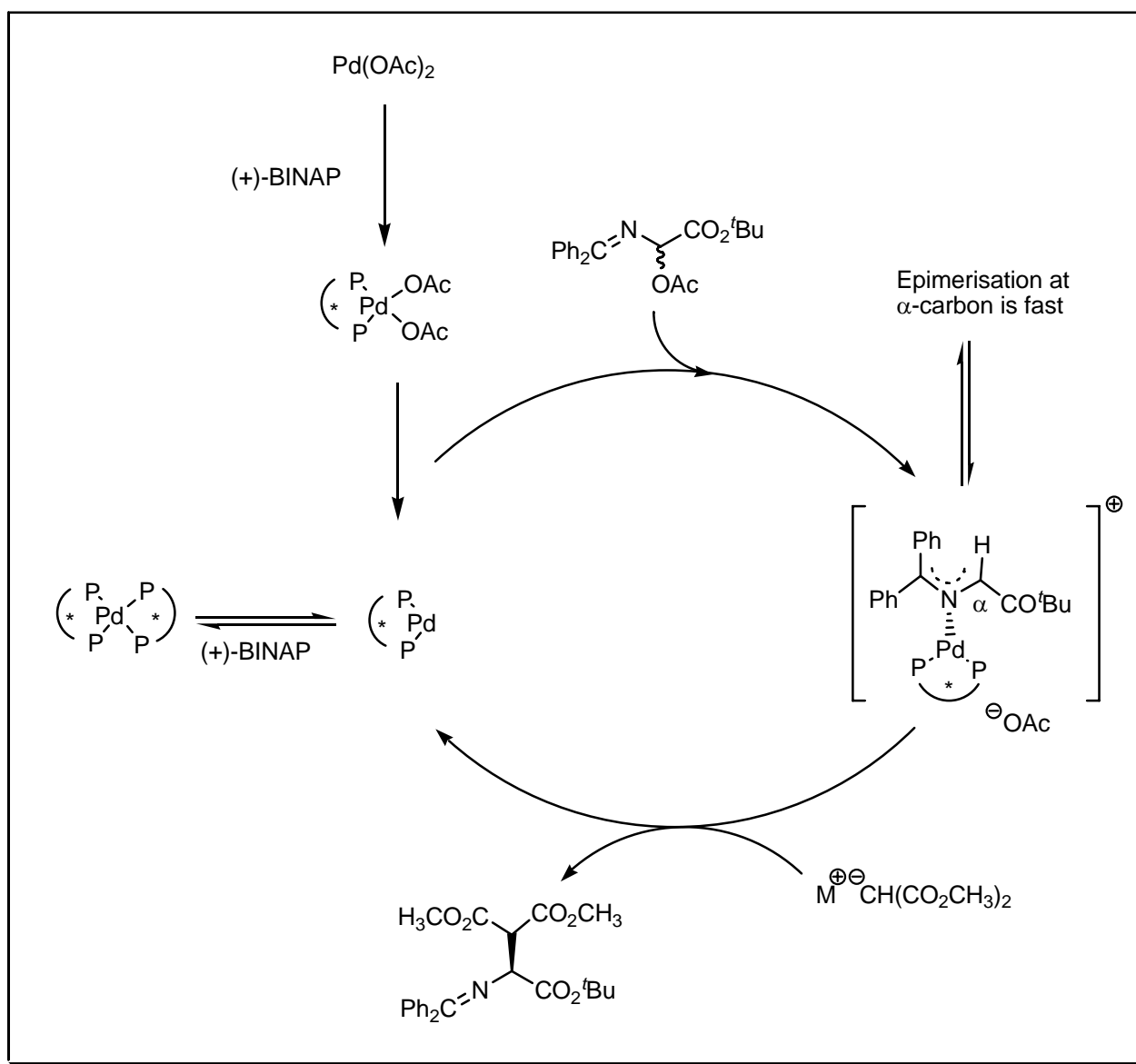
OVERMAN REARRANGEMENT · 1322

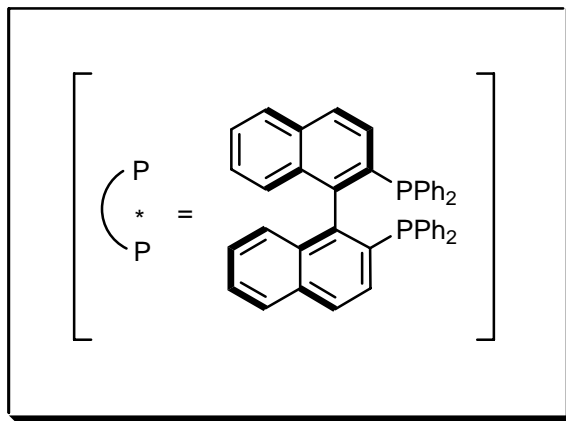
# O'DONNELL AMINO ACID SYNTHESIS

## EXAMPLE :

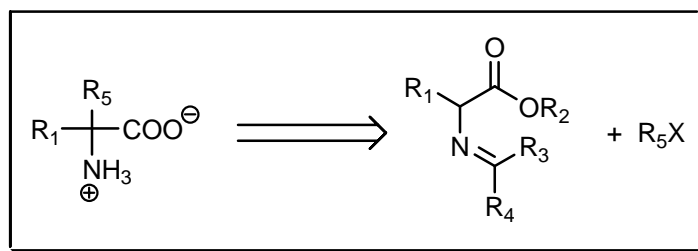


## MECHANISM :





## DISCONNECTION :



## NOTES :

**Schiff** bases of glycine can be alkylated in the presence of solid potassium carbonate in refluxing acetonitrile containing a phase transfer catalyst. Subsequent hydrolysis furnishes the corresponding  $\alpha$ -alkylated  $\alpha$ -amino acid. This method has developed into the enantioselective alkylation of **Schiff** base acetates with malonate stabilised carbon nucleophiles in the presence of palladium(II) acetate and (+)-BINAP as the chiral ligand. Organoboranes have also been used.

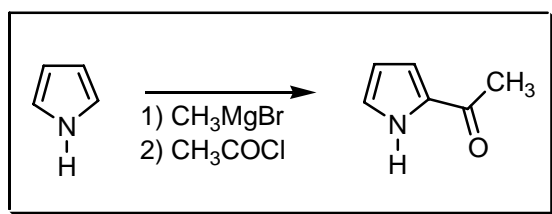
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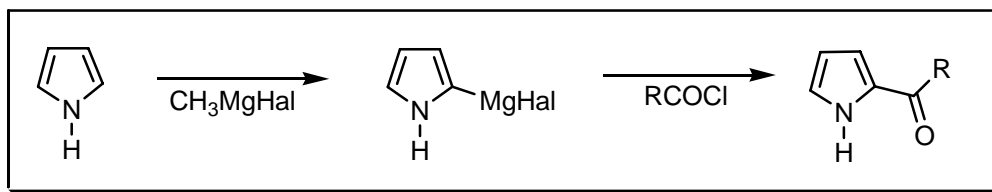
COMMENTS :

## ODDO SYNTHESIS

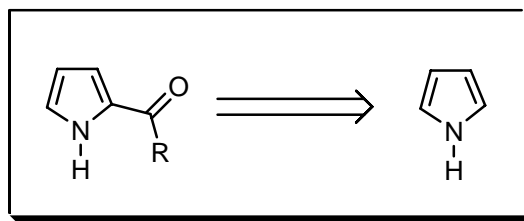
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

Pyrrole reacts with methylmagnesium halide to yield the 2-pyrrolyl magnesium halide, which with an acid chloride gives the ketone. 3-Indolyl ketones can be similarly obtained. See also **Friedel – Crafts** and **Grignard** reactions.

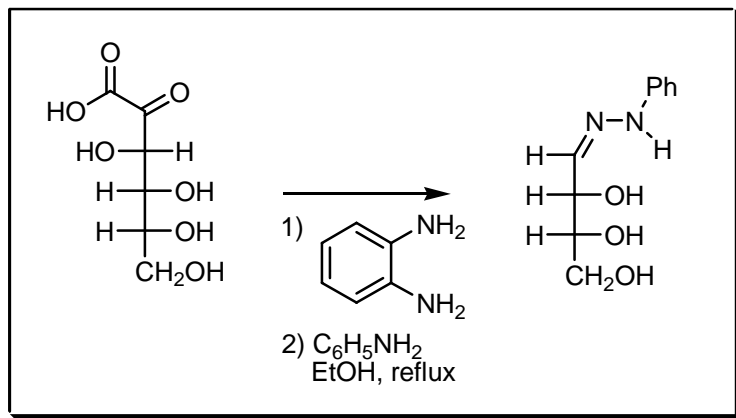
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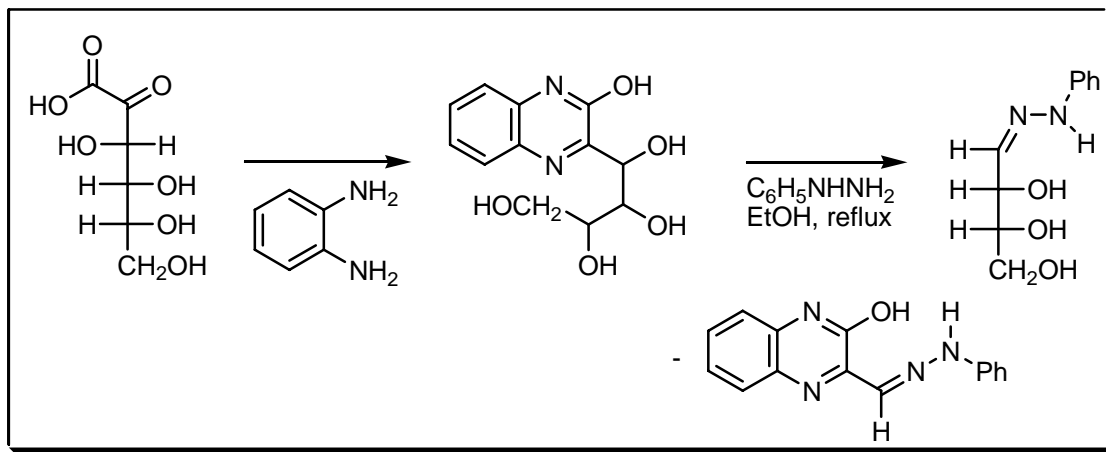
COMMENTS :

## OHLE CLEAVAGE

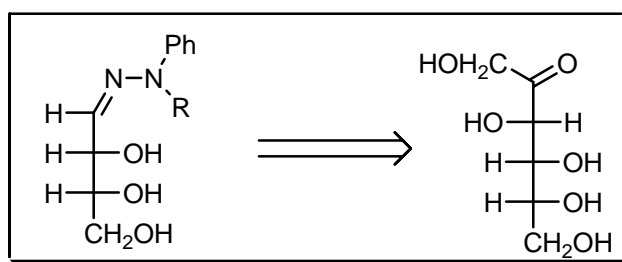
EXAMPLE :



MECHANISM :



DISCONNECTION :



**NOTES :**

A method for the decomposition of a hexose into three-carbon units in which the hexose is first converted into a hydroxytetrahydroxybutylquinoxaline. The latter is refluxed with an ethanolic solution of aniline or a hydrazine. The product varies with the nature of the reactant and the conditions. See also **Amadori**, **Barry** and **Fischer** phenylhydrazine and oxazone reactions.

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**REFERENCES :**

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**Smith – March** : 1195

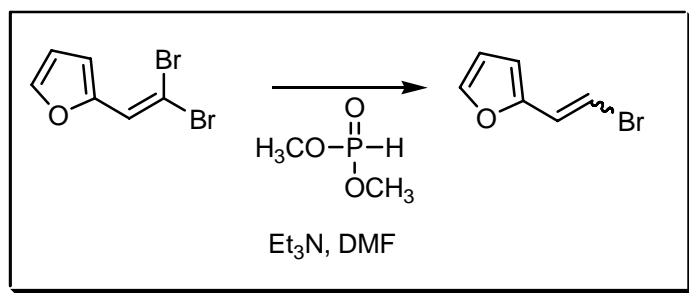
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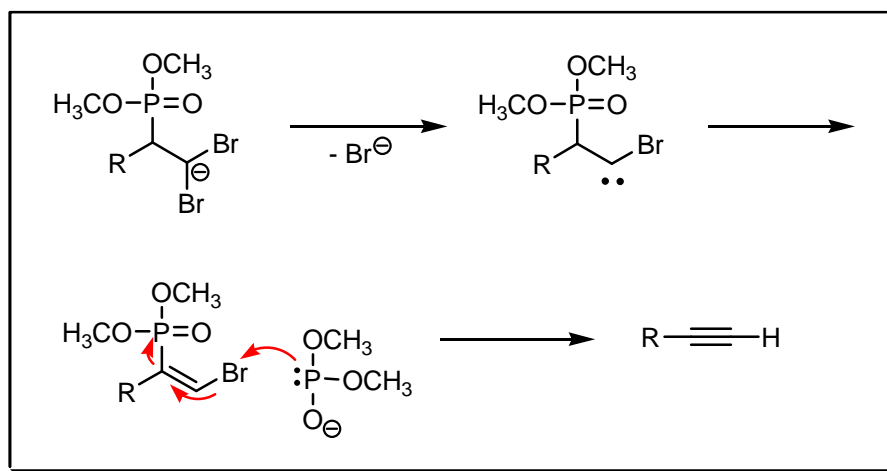
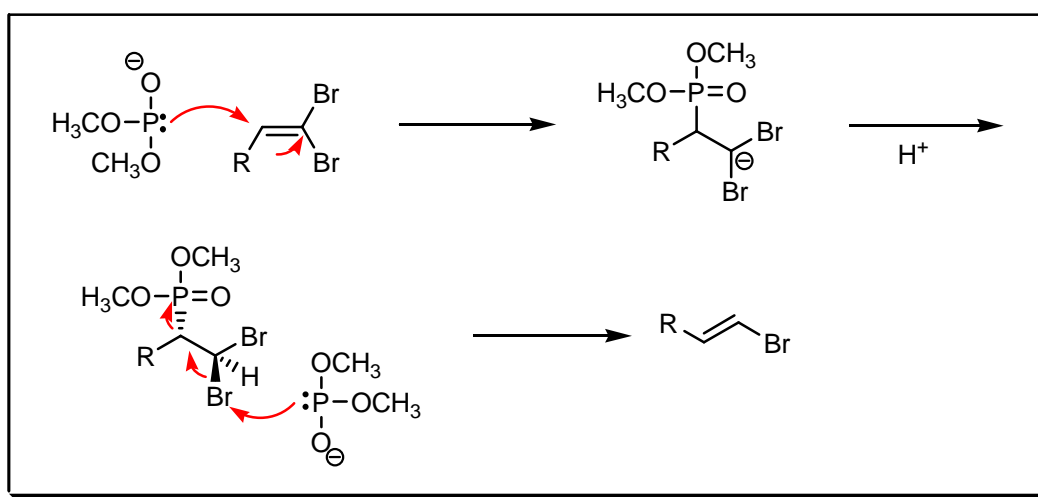
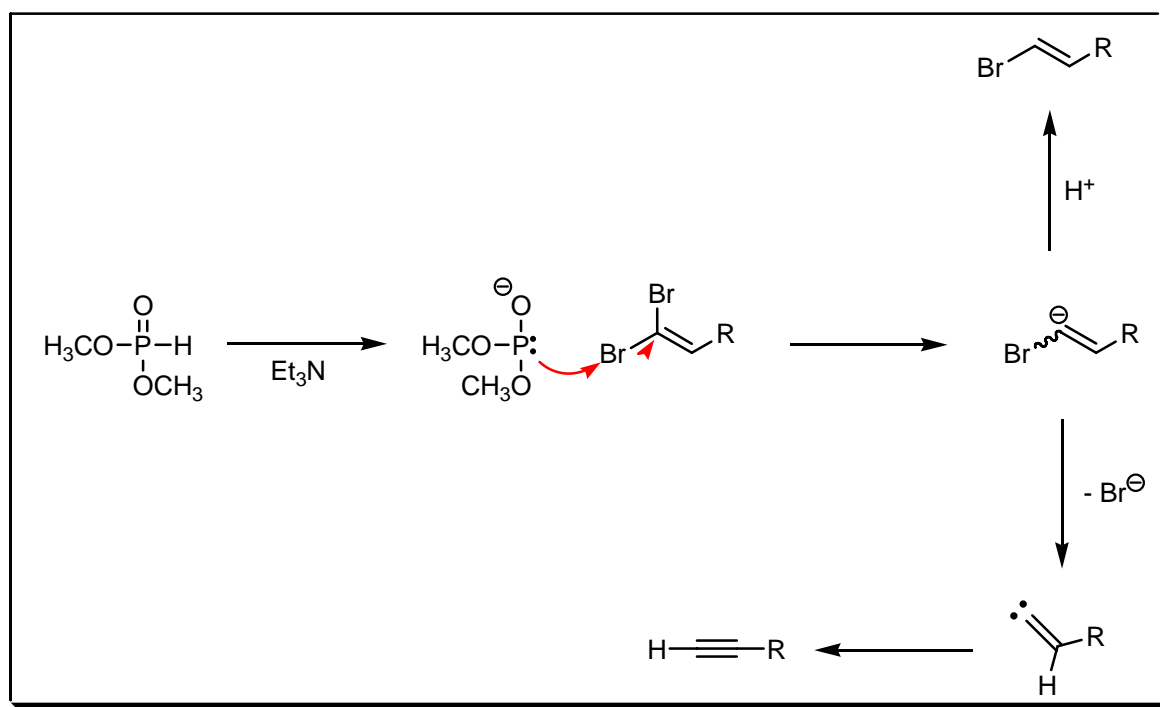
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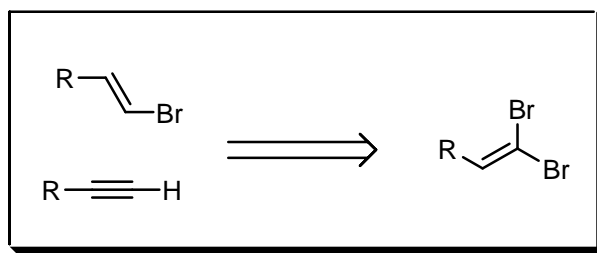
**COMMENTS :****OHSHIRO – HIRAO REDUCTION****EXAMPLE :**

MECHANISM :





## DISCONNECTION :



## NOTES :

The synthesis of vinyl bromides using reduction of the corresponding 1,1-dibromoalkenes with dimethylphosphite and triethylamine. In some cases large amounts of terminal acetylenic products were found.

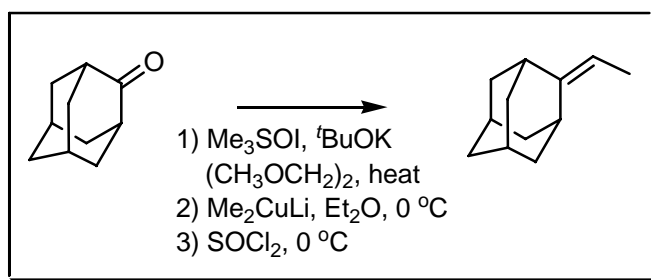
## REFERENCES :

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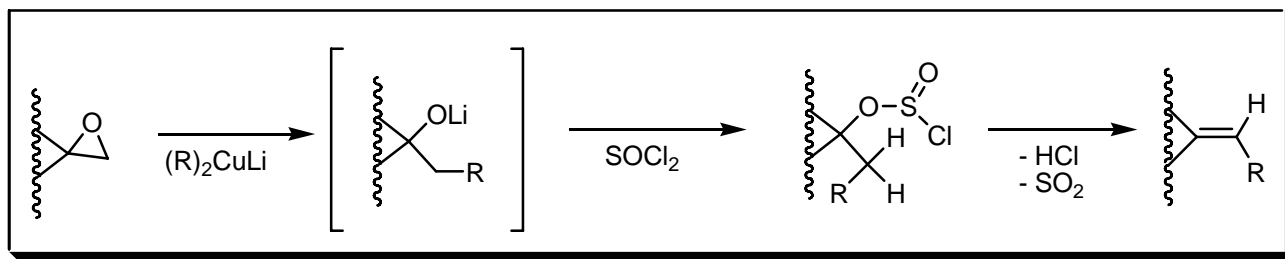
## COMMENTS :

## OLAH CROWDED OLEFIN SYNTHESIS

### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The procedure provides an alternative synthesis of crowded (alkylidene)polycycloalkanes from the readily available corresponding ketones using alkyl lithium and thionyl chloride, in cases where **Grignard** or **Wittig** methods are not useful. Alternatively, the epoxide can be formed under **Corey – Chaykovsky** conditions. See also **Corey – Chaykovsky**, **Corey – Kwiatkowski**, **Eastwood**, **Fürstner**, **Horner – Wadsworth – Emmons**, **Julia – Paris – Kocienski – Lythgoe**, **Krief – Reich – Chow**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Paquette**, **Petasis** reaction, **Peterson**, **Ramberg – Bäcklund**, **Still – Gennari**, **Takeda**, **Tebbe** and **Wittig** olefination reactions.

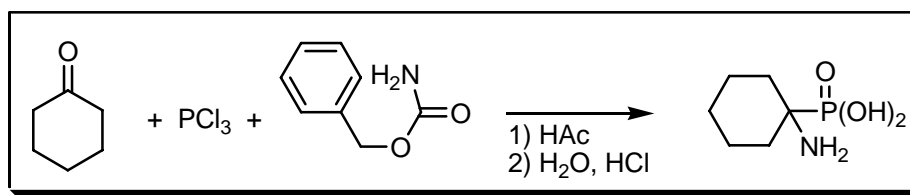
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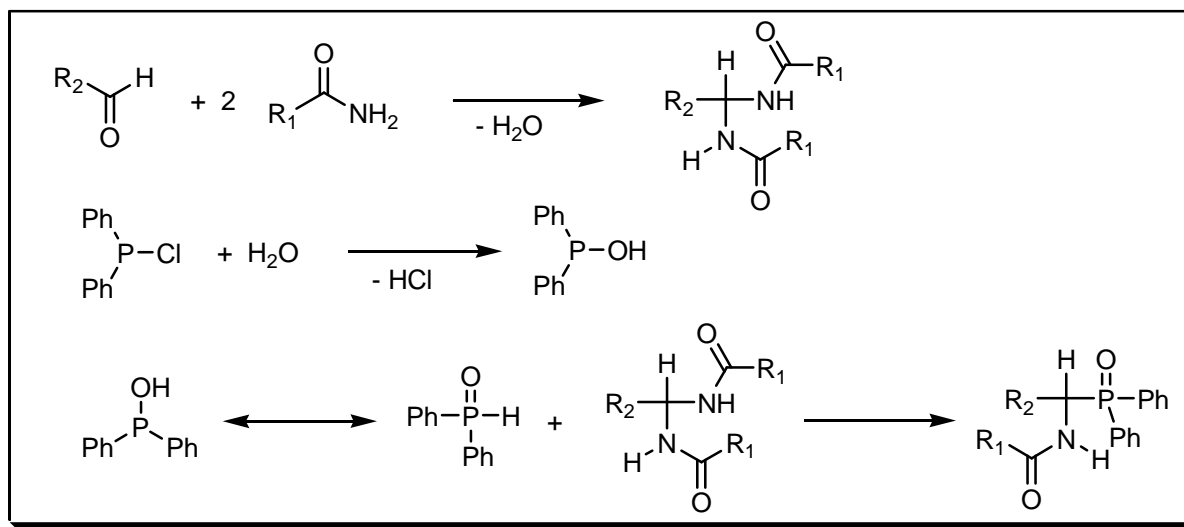
### COMMENTS :

# OLEKSYSZYN AMINOPHOSPHONIC ACID SYNTHESIS

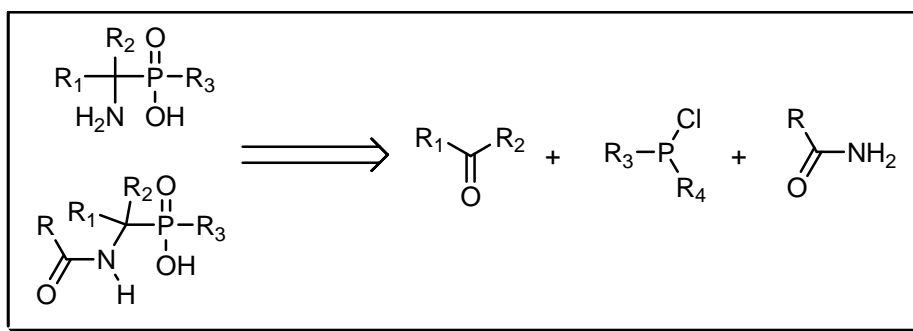
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of 1-aminoalkanephosphonic and 1-aminoalkanephosphinic acids from ketones or aldehydes, chlorophosphines and carbamates. There are several proposed mechanisms in the literature, the one by **Oleksyszyn** is shown here. See also **Kabachnik – Fields** reaction.

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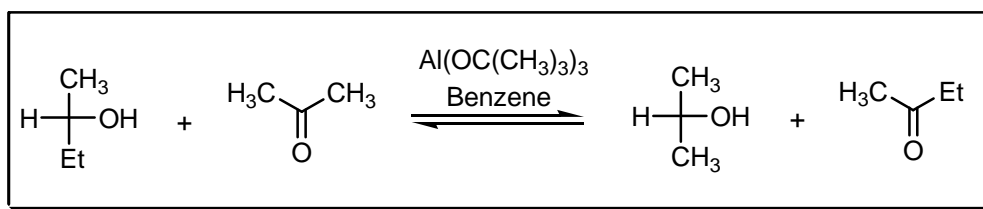
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**COMMENTS :**

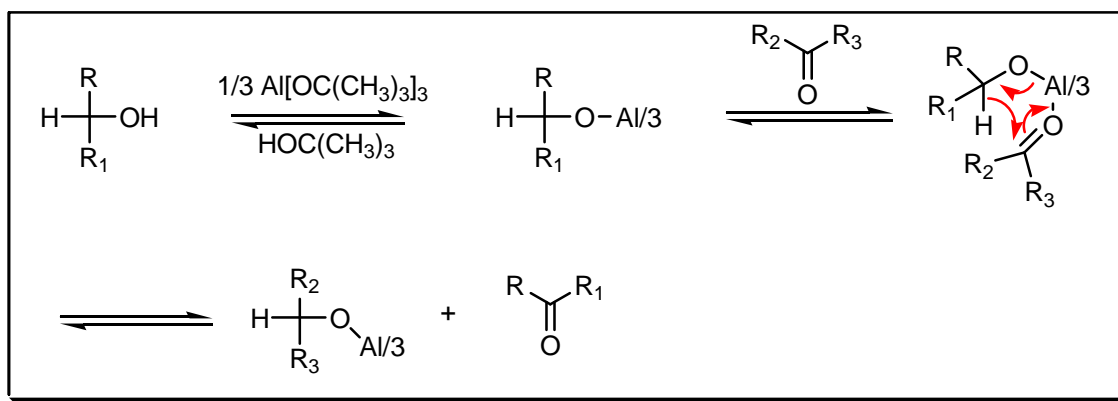
**OPPENAUER OXIDATION**

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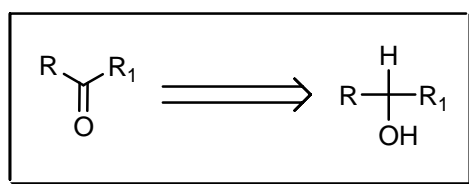
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

A reversal of the **Meerwein – Ponndorf – Verley** reaction involving the oxidation of a primary or secondary hydroxyl compound to the corresponding carbonyl compound, using aluminium alkoxide and an excess of acetone, benzophenone or other ketone which acts as a carbonyl hydrogen acceptor. Anisaldehyde and cinnamaldehyde have also been employed. See also **Anelli, Ball – Goodwin – Morton, Collins, Corey – Kim, Corey – Schmidt, Corey – Suggs, David – Thieffry, Delépine, Dess – Martin, Einhorn** oxidation, **Fétizon, Jones** oxidation, **Ley, Maurer – Drefahl, Mukaiyama** oxidation, **Nicolaou, Parikh – von Doering, Pfitzner – Moffatt, Sarett, Swern** and **Uemura** reactions.

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**Smith – March** : 1516

**Smith** : 243

**Smith 2<sup>nd</sup>** : 211, 407, 604

**Houben – Weyl** : **4/2**, 85, 121; **7/1**, 186; **E3**, 274

**Org. React.** : **2**, 178; **6**, 207

**Org. Synth.** : **21**, 8, 18

**Org. Synth. Coll. Vol.** : **3**, 48, 207

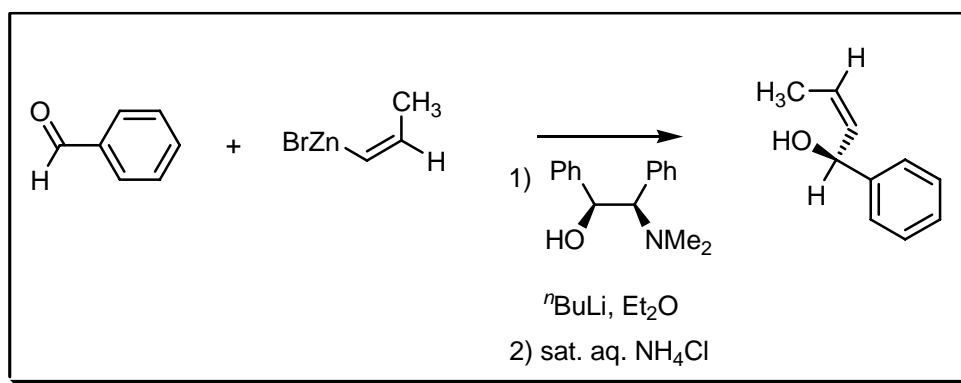
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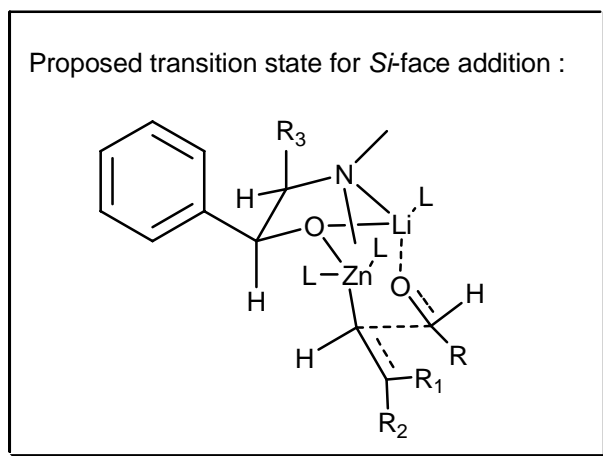
## COMMENTS :

# OPPOLZER ALLYL ALCOHOL SYNTHESIS

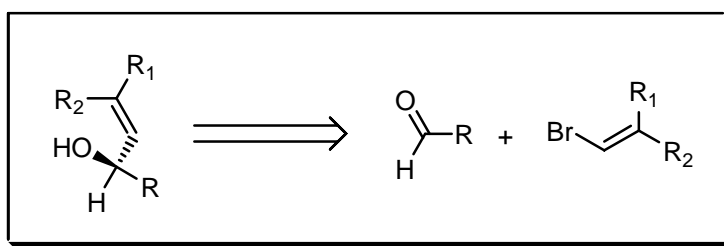
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

(*Z*)- and (*E*)-1-alkenylzinc bromides (starting from alkynes) react with aldehydes (highly *Si*-face selective addition) in the presence of lithiated (+)-*N*-methylephedrine or (+)-2-(*N,N*-dimethylamino)-1,2-diphenylethanol to afford secondary allyl alcohols in high optical purity (up to 98%).

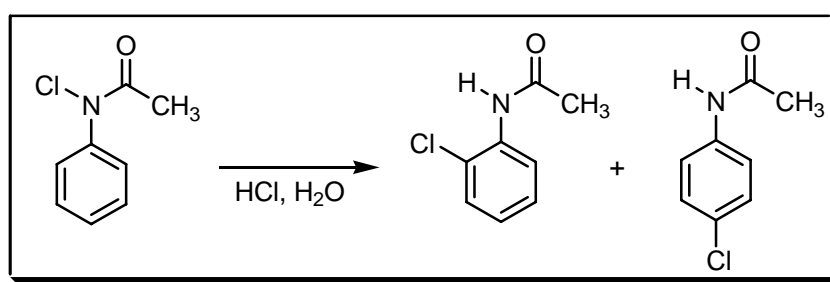
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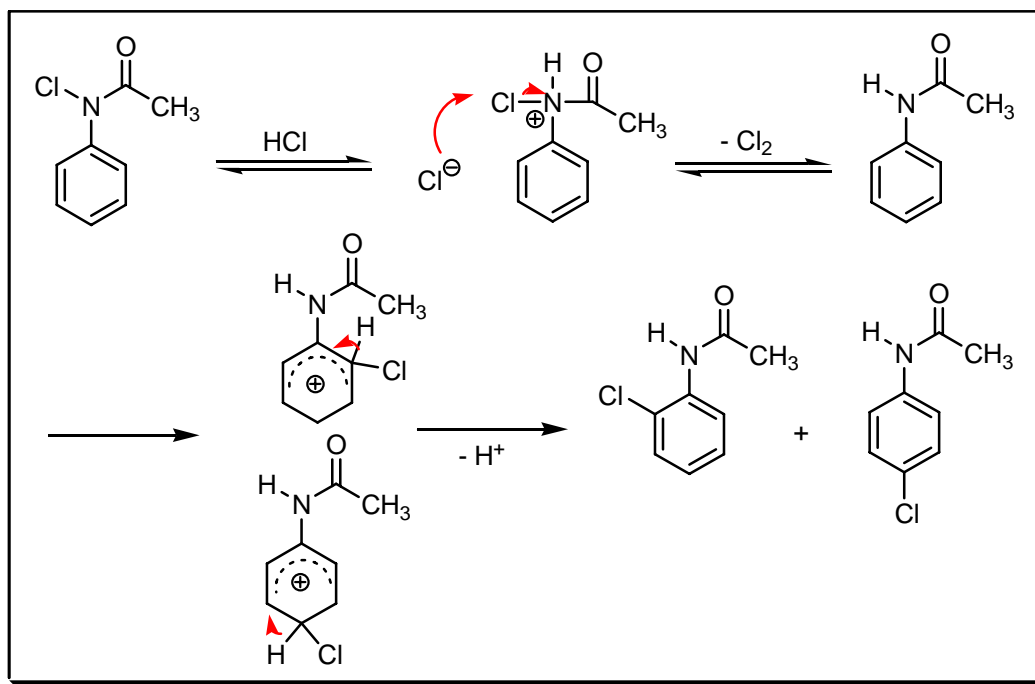
COMMENTS :

ORTON HALOANILINE REARRANGEMENT

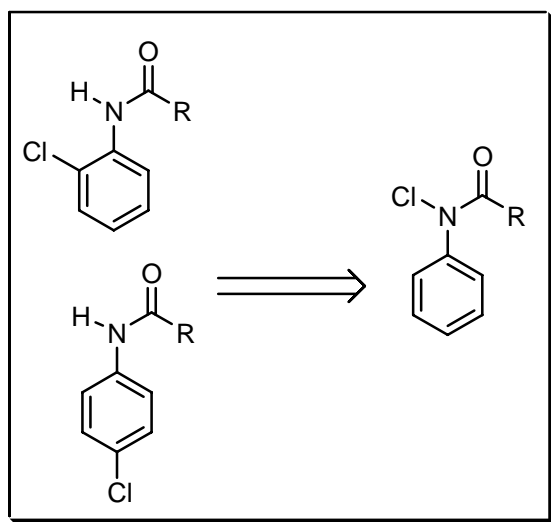
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The conversion of *N*-chloroacylamides into a mixture of *o*- and *p*-halogenoacylamides in the presence of hydrochloric acid (sometimes with iron(III) chloride) and usually in hydroxylic solvents (water, acetic acid), also photochemical rearrangement possible. See also **Chattaway** rearrangement, **Fischer – Hepp** rearrangement and **Hofmann – Martius (Reilly – Hickinbottom)** reaction.

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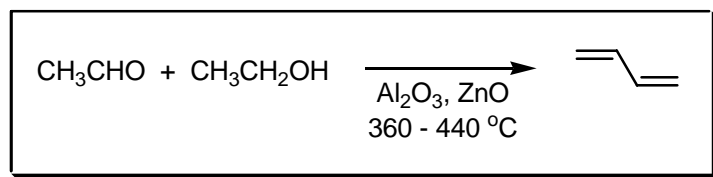
## COMMENTS :



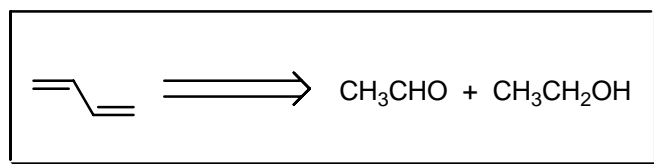
## OSTROMYSLENSKI REACTION

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### EXAMPLE :



### DISCONNECTION :



### NOTES :

This reaction comprises the high temperature catalytic condensation of acetaldehyde and ethanol to form butadiene, most likely *via* 1,3-butanediol. For more about the reaction mechanism see **Jones** *et al.* See also **Lebedev** and **Reppe** butadiene reactions.

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**Houben – Weyl** : 4/2, 216

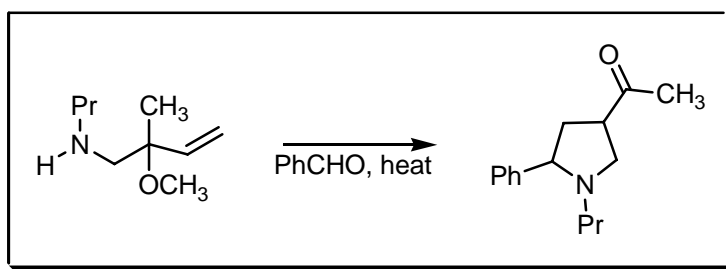
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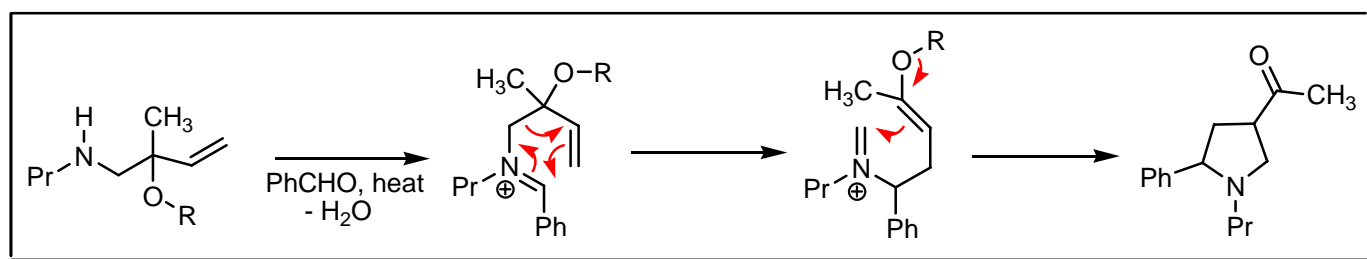
### COMMENTS :

# OVERMAN PYRROLIDINE SYNTHESIS

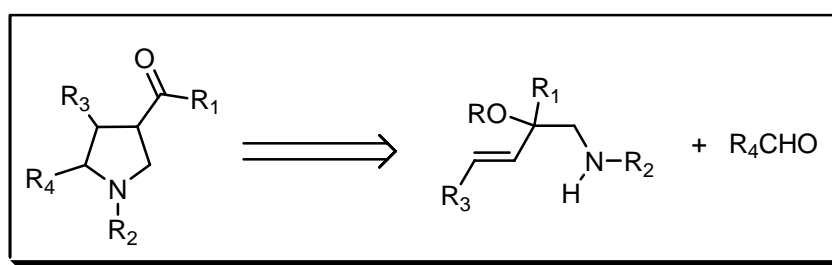
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The carbon – carbon bond formation via tandem **Mannich** condensation, followed by a cationic **aza-Cope** rearrangement of the homoallylamines, to afford pyrrolidines. See also **Cope** rearrangement and **Mannich** reaction.

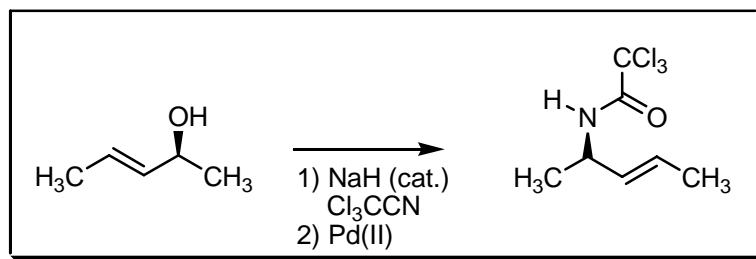
## REFERENCES :

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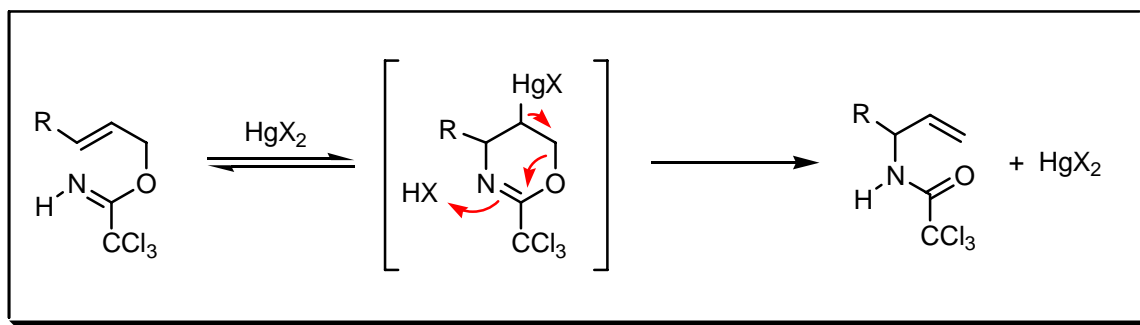
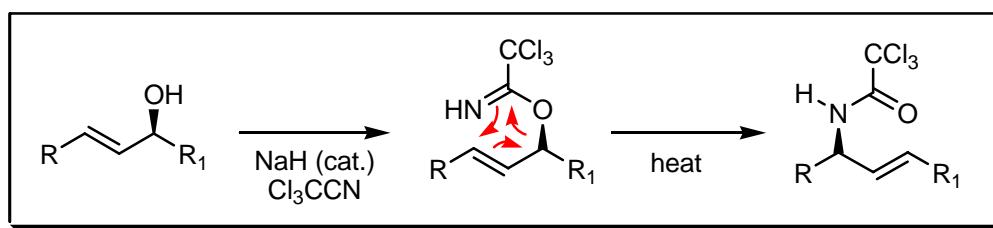
COMMENTS :

## OVERMAN REARRANGEMENT

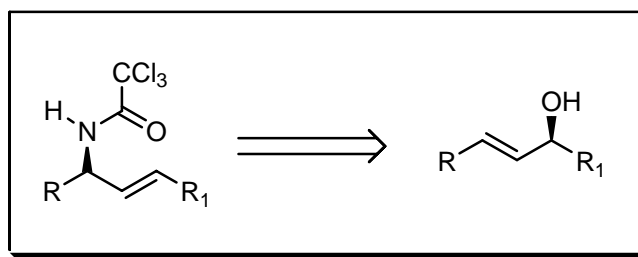
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

The formal [3,3]-sigmatropic rearrangement of the trichloroacetimidate of allylic alcohols to allylic trichloroacetamides, thereby transposing the hydroxyl and amino functions with high chirality transfer. An enormous rate acceleration is observed when the reaction is catalysed by mercuric(II) or palladium(II) salts. Contra-thermodynamic cases have also been reported. Excess of mercury salts and triphenyl phosphine are needed to overcome the thermodynamic preference. See also **Belluš – Claisen** rearrangement, **Carroll (Kimel – Cope)**, **Claisen (Claisen – Ireland)** rearrangement, **Cope**, **Eschenmoser – Meerwein – Claisen** rearrangement, **Ficini – Claisen**, **Johnson – Claisen** and **Marbet – Saucy** reactions.

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## COMMENTS :

P

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**B**

BOBBIT MODIFICATION · 1391

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**H**

HALBERKANN VARIANT · 1369

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**O**

OGLIALORO MODIFICATION · 1359

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**P**

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PADBURY – LINDWALL MODIFICATION · 1327  
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PUMMERER REARRANGEMENT · 1404

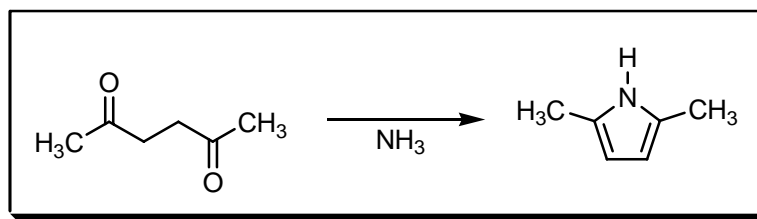
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**W**

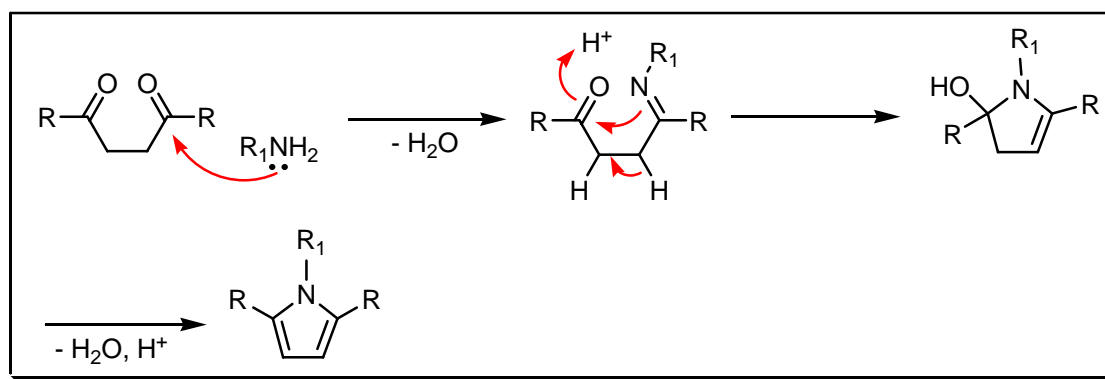
WALTHER MODIFICATION · 1369

## PAAL – KNORR PYRROLE SYNTHESIS

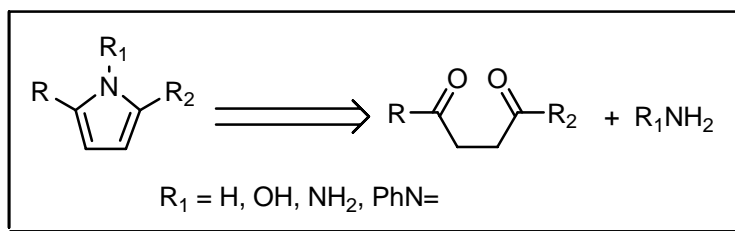
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The synthesis of pyrroles from 1,4-diketones, ammonia and certain amines, primary amines, hydroxylamine, glycine, hydrazine, and phenylhydrazine. In the presence of acid and without an amine source furans can be synthesised. Sometimes called the **Paal – Knorr** furan synthesis. See also **Barton – Zard**, **Clauson-Kaas**, **Fischer – Fink**, **Grob – Camenisch**, **Hantzsch** pyrrole, **Harries** pyrrole, **Kenner**, **Knorr** pyrrole, **Miller – Plöchl**, **Padwa**, **Piloty – Robinson**, **Schwanert**, **Trofimov** and **Zav'yalov** reactions.

### REFERENCES :

Houben – Weyl : **E6a**, 34, 64, 202, 205, 593; **E6b**, 467

Org. Synth. : **16**, 25

Org. Synth. Coll. Vol. : **2**, 219

Science of Synthesis : **9**, 207, 298, 455

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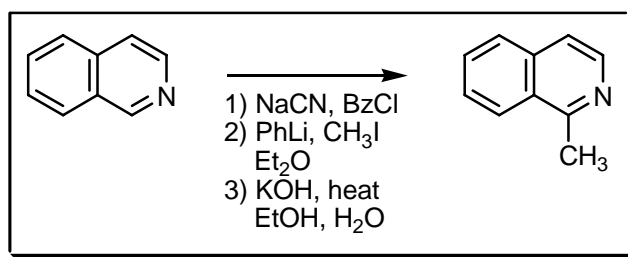
**COMMENTS :**

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**PADBURY – LINDWALL MODIFICATION**

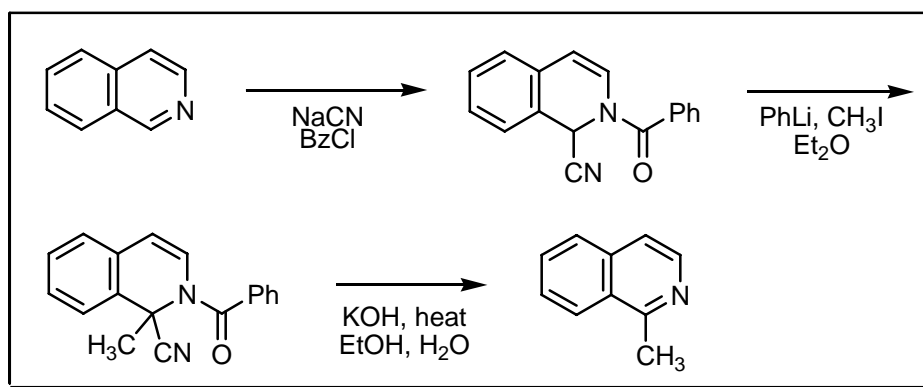
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**EXAMPLE :**



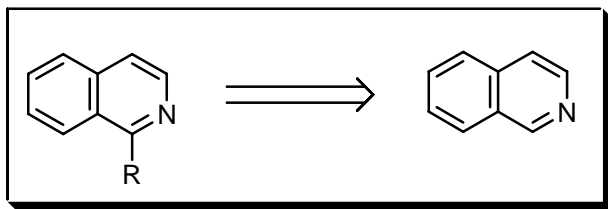
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**MECHANISM :**





## DISCONNECTION :



## NOTES :

This is a modification of the **Reissert – Grosheintz – Fischer** reaction, which employs isoquinoline. See also **Reissert – Henze** and **Reissert – Grosheintz – Fischer** reactions.

## REFERENCES :

**March** : 448

**Smith – March** : 533

**Houben – Weyl** : 7/1, 291

**Org. React.** : 7, 99; 8, 218

**Org. Synth.** : 38, 58; 56, 19

**Org. Synth. Coll. Vol.** : 4, 641; 6, 115

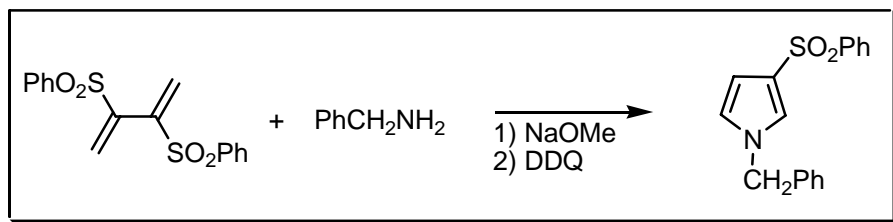
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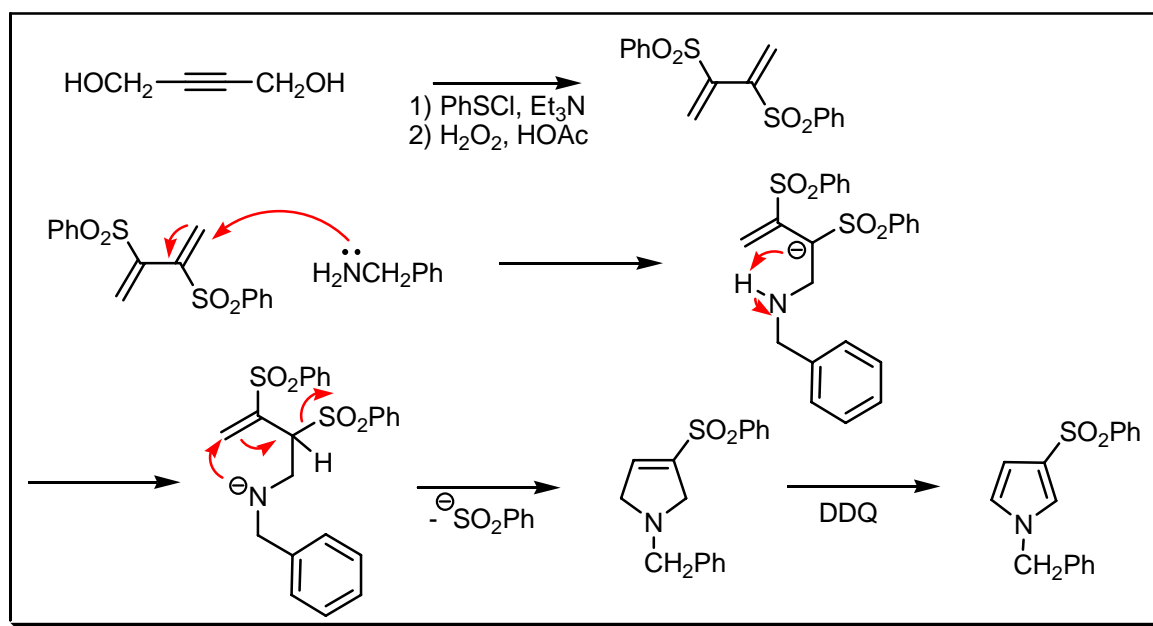
## COMMENTS :

## PADWA ANNULATION

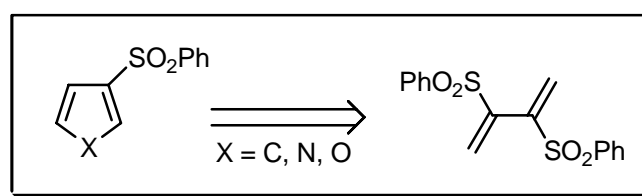
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The pyrrolines and pyrroles by [4+1] annulation of 2,3-bis(phenylsulfonyl)-1,3-butadiene and amines. Also 2,3-dihalo-1-phenylsulfonyl-1-propenes are used as versatile reagents for the annulation of furans and cyclopentenones. A versatile range of compounds undergoes the tandem addition – proton exchange addition reaction with 2,3-bis(phenylsulfonyl)-1,3-butadiene. See also **Barton – Zard**, **Clauson–Kaas**, **Fischer – Fink**, **Grob – Camenisch**, **Hantzsch** pyrrole, **Harries** pyrrole, **Kenner**, **Knorr** pyrrole, **Miller – Plöchl**, **Paal – Knorr**, **Piloty – Robinson**, **Schwanert**, **Trofimov** and **Zav'yalov** reactions.

## REFERENCES :

**Org. Synth.** : **74**, 147

**Org. Synth. Coll. Vol.** : **9**, 82

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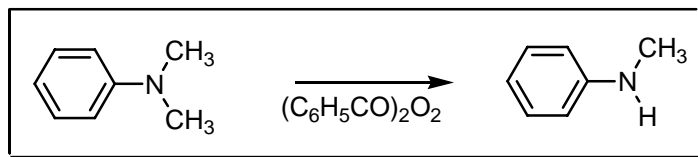
3) A. Padwa; M. Ishida; C.L. Muller; S.S. Murphree, *J. Org. Chem.*, 1992, **57**, 1170.

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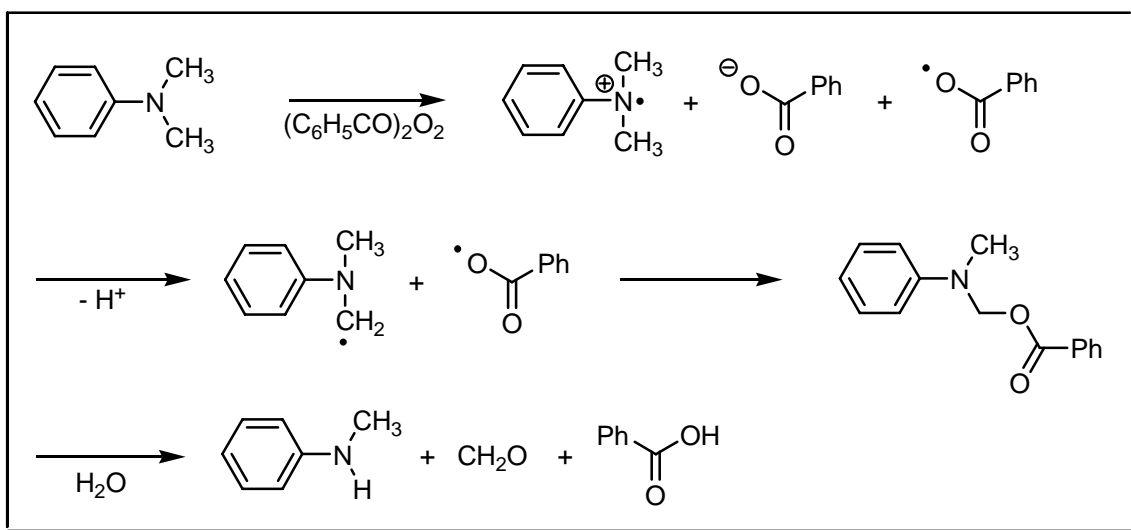
COMMENTS :

## de PAOLINI REACTION

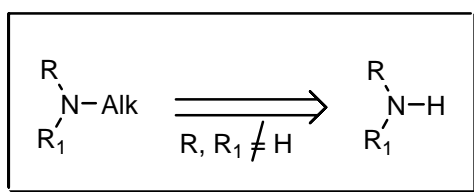
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The dealkylation of tertiary amines with diacylperoxides. It is not exactly understood if the reaction mechanism involves a radical mechanism or nucleophilic substitution or both. The radical mechanism is shown here.

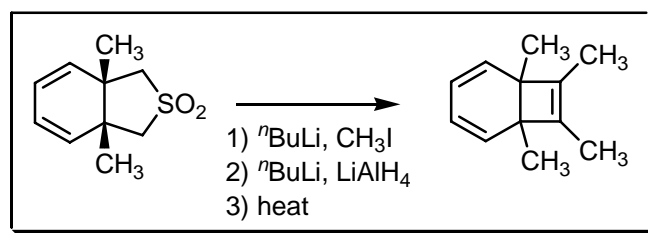
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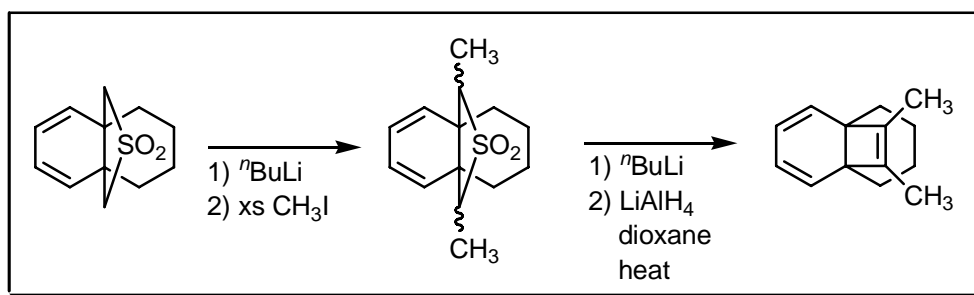
## COMMENTS :

## PAQUETTE OLEFIN SYNTHESIS

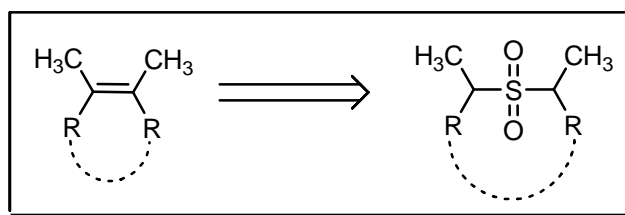
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The desulfonation of sulfones to alkenes (alternative to **Ramberg – Bäcklund**). See also **Corey – Kwiatkowski**, **Horner – Wadsworth – Emmons**, **Julia – Paris – Kocienski – Lythgoe**, **Krief – Reich – Chow**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Nysted**, **Petasis** reaction, **Peterson**, **Ramberg – Bäcklund**, **Still – Gennari**, **Takeda**, **Tebbe** and **Wittig** reactions.

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## REFERENCES :

**March** : 1030

**Smith – March** : 1354

**Org. Synth.** : **57**, 53

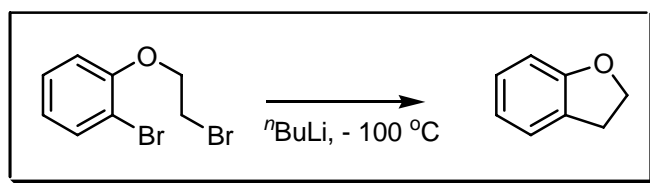
**Org. Synth. Coll. Vol.** : **6**, 482

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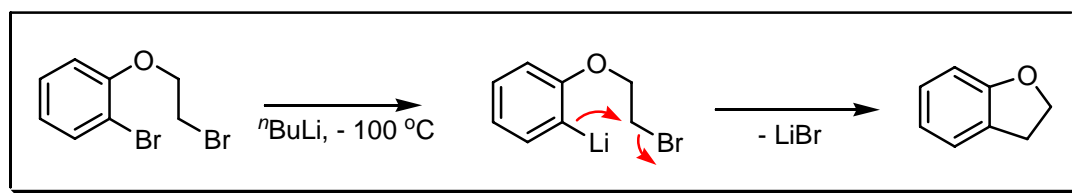
## COMMENTS :

## PARHAM CYCLIC ALKYLATION

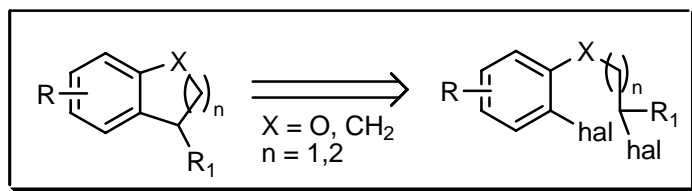
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The benzoheterocycle synthesis from di-halides using lithium bromine exchange. The halogen on the side chain can be replaced by a carboxylic acid. This reaction has been extended to a large range of heterocycles.

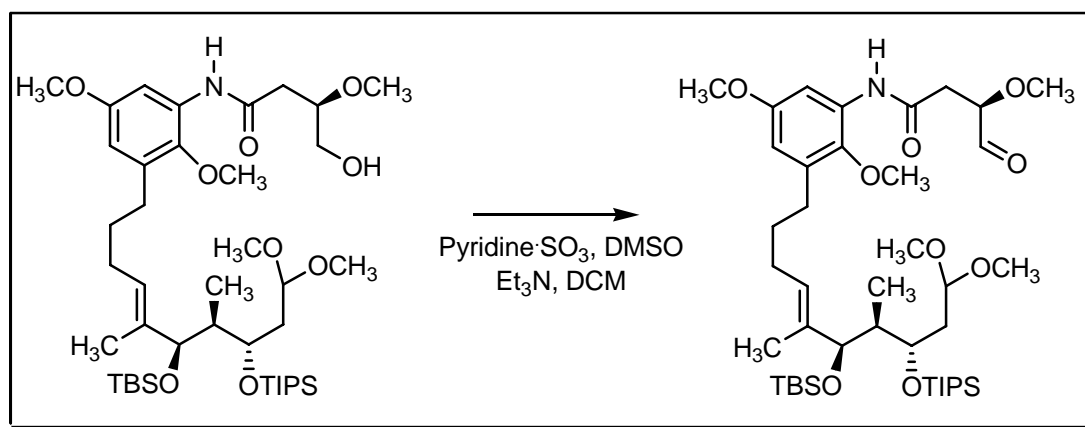
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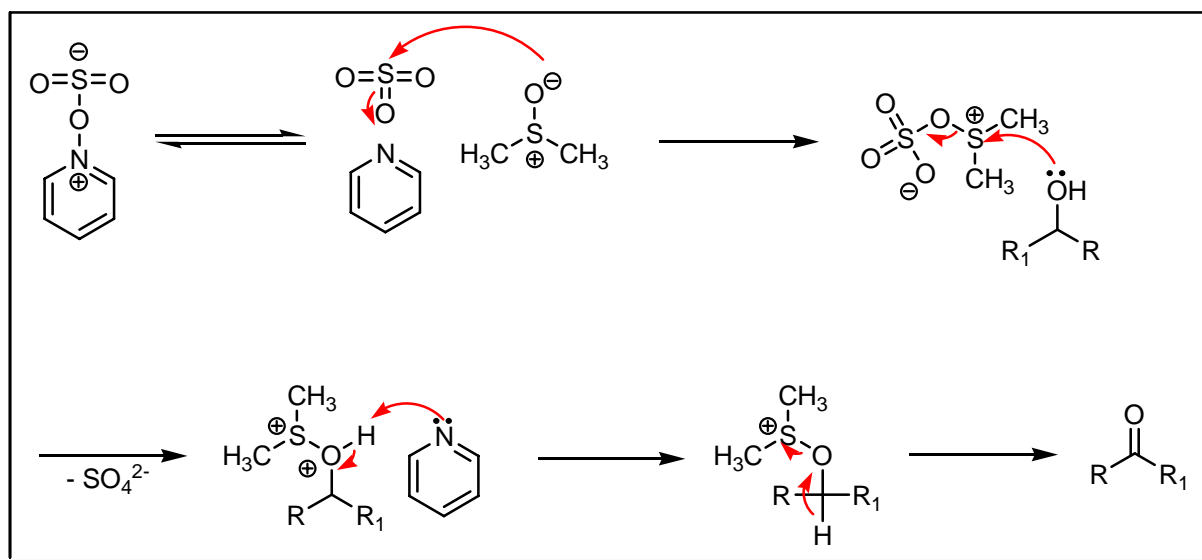
## COMMENTS :

## PARIKH – von DOERING OXIDATION

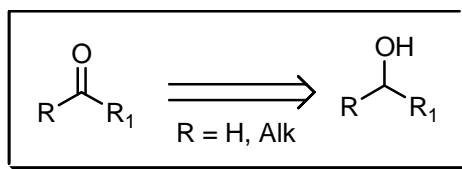
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The oxidation of primary or secondary alcohols, in a similar fashion as the **Pfitzner – Moffatt** oxidation. See also **Anelli**, **Ball – Goodwin – Morton**, **Collins**, **Corey – Kim**, **Corey – Schmidt**, **Corey – Suggs**, **David – Thieffry**, **Delépine**, **Dess – Martin**, **Einhorn** oxidation, **Fétizon**, **Jones** oxidation, **Ley**, **Maurer – Drefahl**, **Mukaiyama** oxidation, **Nicolaou**, **Oppenauer**, **Pfitzner – Moffatt**, **Pinnick**, **Sarett**, **Swern** and **Uemura** reactions.

## REFERENCES :

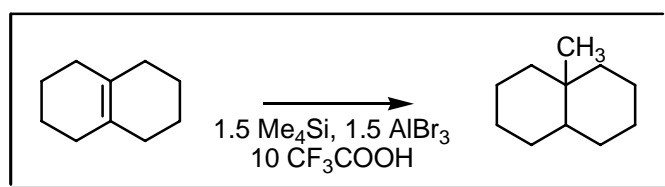
Smith – March : 1516

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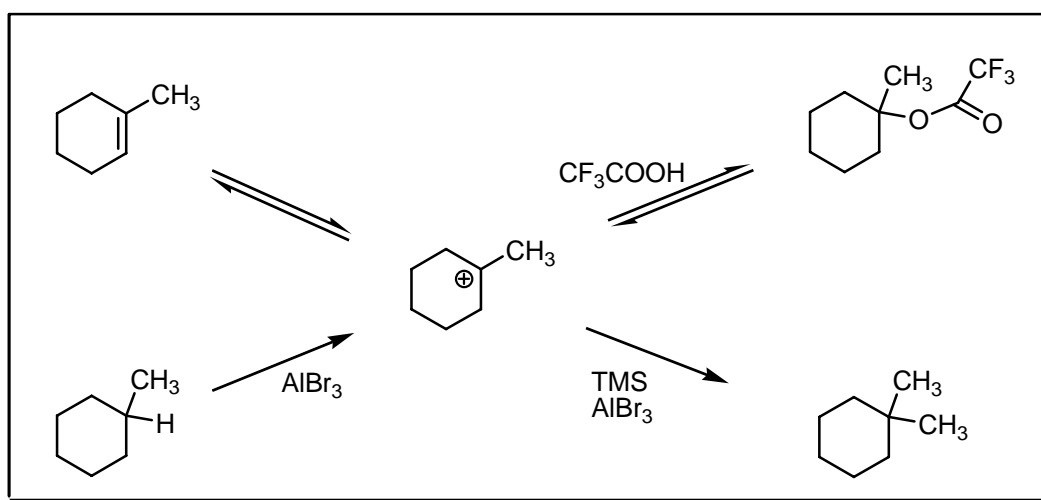
## COMMENTS :

## PARNES GEMINAL DIMETHYLATION

### EXAMPLE :

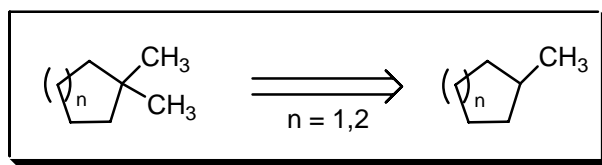


### MECHANISM :





## DISCONNECTION :



## NOTES :

The *gem*-dialkylation of cyclopentane or cyclohexane derivatives (vicinal dihalocyclohexanes or methylcyclohexane) with tetramethylsilane (TMS),  $\text{Me}_4\text{Ge}$ ,  $\text{Me}_4\text{Sn}$ ,  $\text{Me}_3\text{SnCl}$ ,  $\text{Pr}_4\text{Ge}$ ,  $\text{Pr}_4\text{Sn}$ ,  $\text{Bu}_4\text{Sn}$ , and  $\text{Bu}_4\text{Si}$  in the presence of  $\text{AlBr}_3$ .

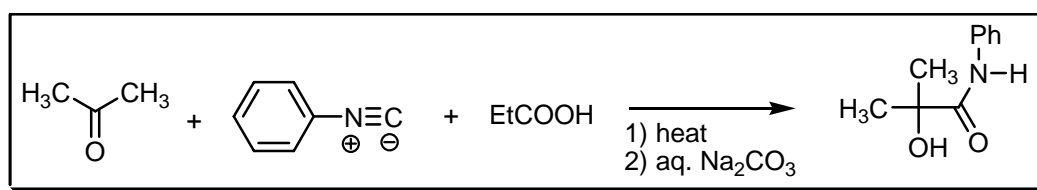
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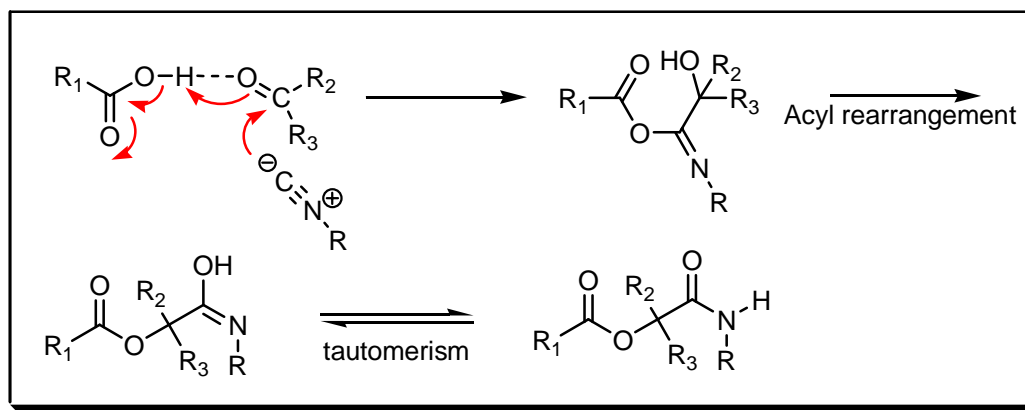
## COMMENTS :

## PASSERINI REACTION

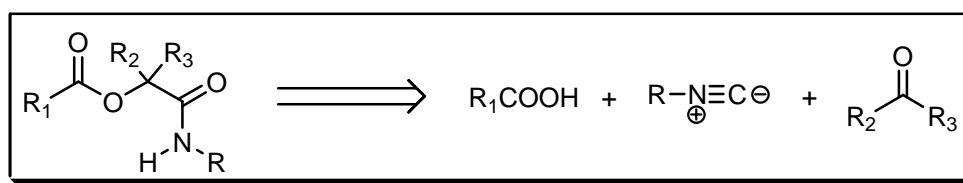
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Aldehydes and ketones react with aryl isocyanides in the presence of carboxylic acids to yield α-acyloxy-derivatives of *N*-arylamides. The use of trifluoroacetate esters gives milder hydrolysis conditions than for the normal esters. The reaction has been made catalytic and asymmetric by **Denmark** *et al.* Titanium tetrachloride assisted reactions are also known. See also **Ugi** reaction.

## REFERENCES :

**March** : 980

**Smith – March** : 1252

**Smith** : 676

**Smith 2<sup>nd</sup>** : 574

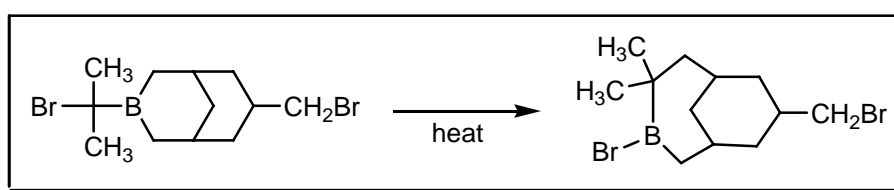
**Houben – Weyl** : **8**, 355; **E5**, 1067, 1651

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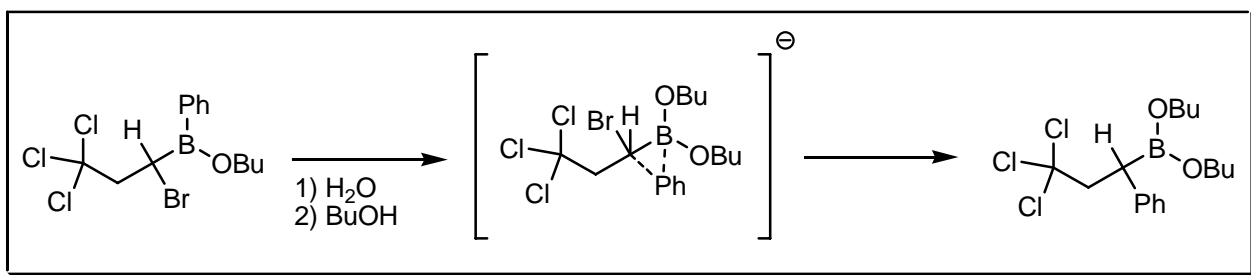
**COMMENTS :**

**PASTO – MATTESON REARRANGEMENT**

**EXAMPLE :**



**MECHANISM :**



**NOTES :**

The *intramolecular* rearrangement of  $\alpha$ -bromoorganoboranes, consisting in migration of the bromine atom to the boron and the reverse transition of the organic radical to the  $\alpha$ -carbon atom. Organoboron compounds formed by the hydroboration of enethiols, enols and vinyl halides also undergo a similar rearrangement.

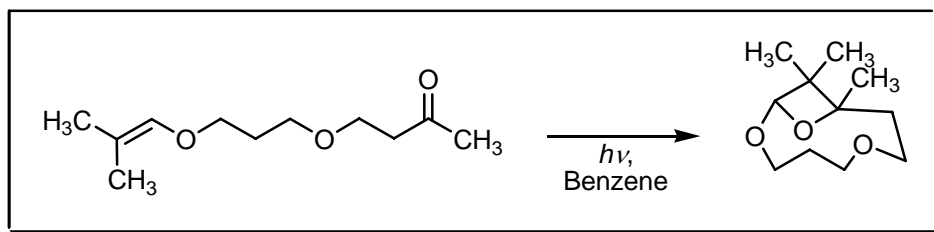
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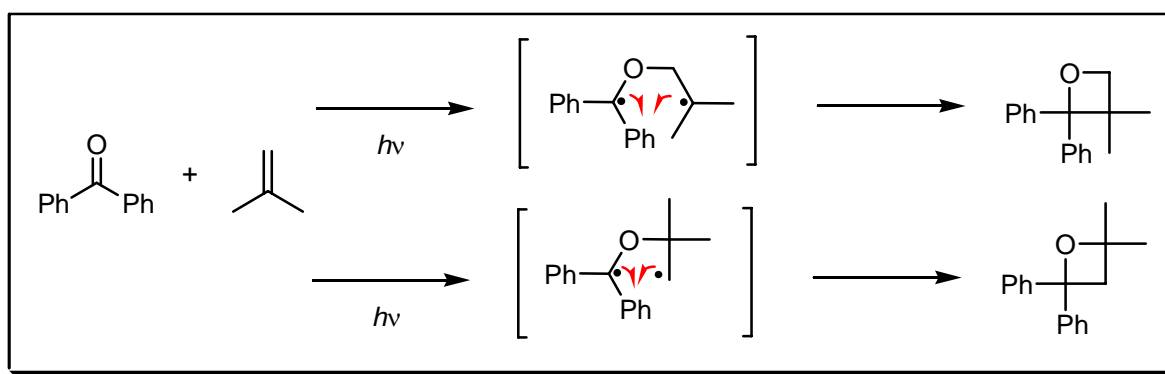
COMMENTS :

## PATERNÒ – BÜCHI REACTION

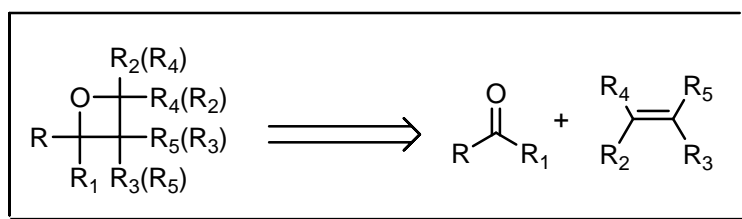
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The photochemical [2+2] cyclisation of carbonyls and olefins to oxetanes. The irradiation is usually carried out with light of the near UV region, in order to activate only the  $n \rightarrow \pi^*$  transition of the carbonyl function, thus generating excited carbonyl species. Depending on the substrate this can be in a singlet or triplet excited state. See also **Norrish type I** and **Norrish type II** reactions.

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March : 977

Smith – March : 1249

Smith : 1202

Smith 2<sup>nd</sup> : 994, 1218

Houben – Weyl : E3, 648; E15, 332

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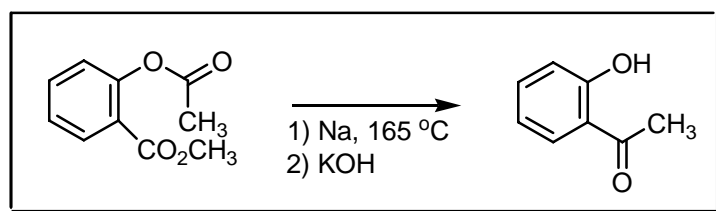
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## COMMENTS :

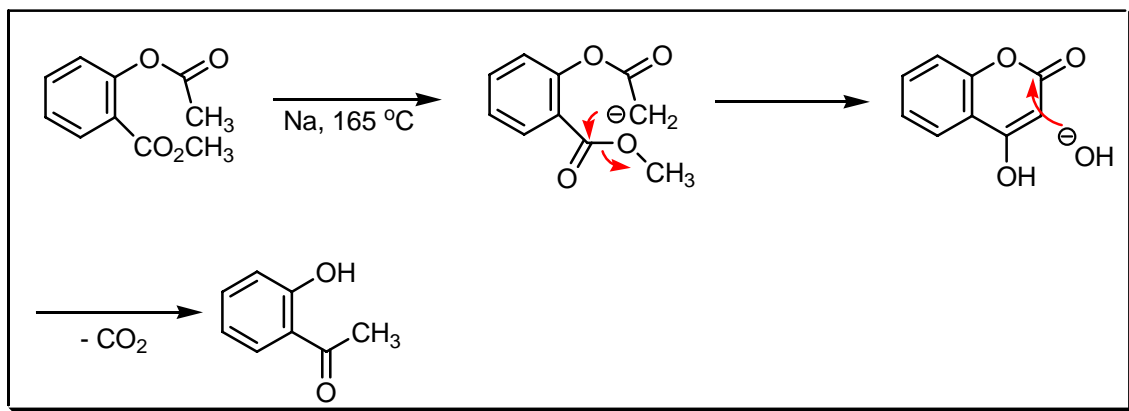
## PAULY – LOCKEMANN SYNTHESIS

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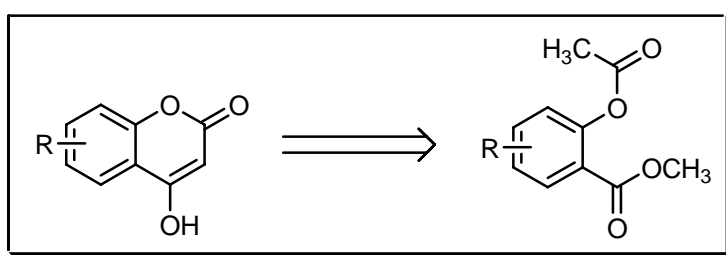
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Methyl o-acetoxybenzoates on treatment with sodium yield 4-hydroxycoumarins which may be hydrolysed. See also **Anschütz** hydroxycoumarin, **Bargellini**, **Boyd – Robinson**, **Knoevenagel** coumarin, **Mentzer**, **von Pechmann**, **von Pechmann – Duisberg**, **Perkin** coumarin and **Simonis** reactions.

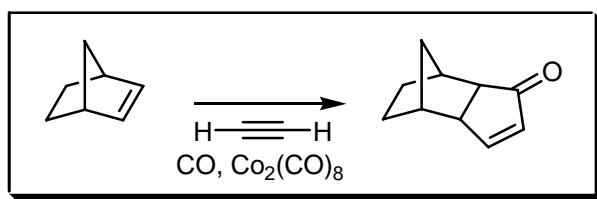
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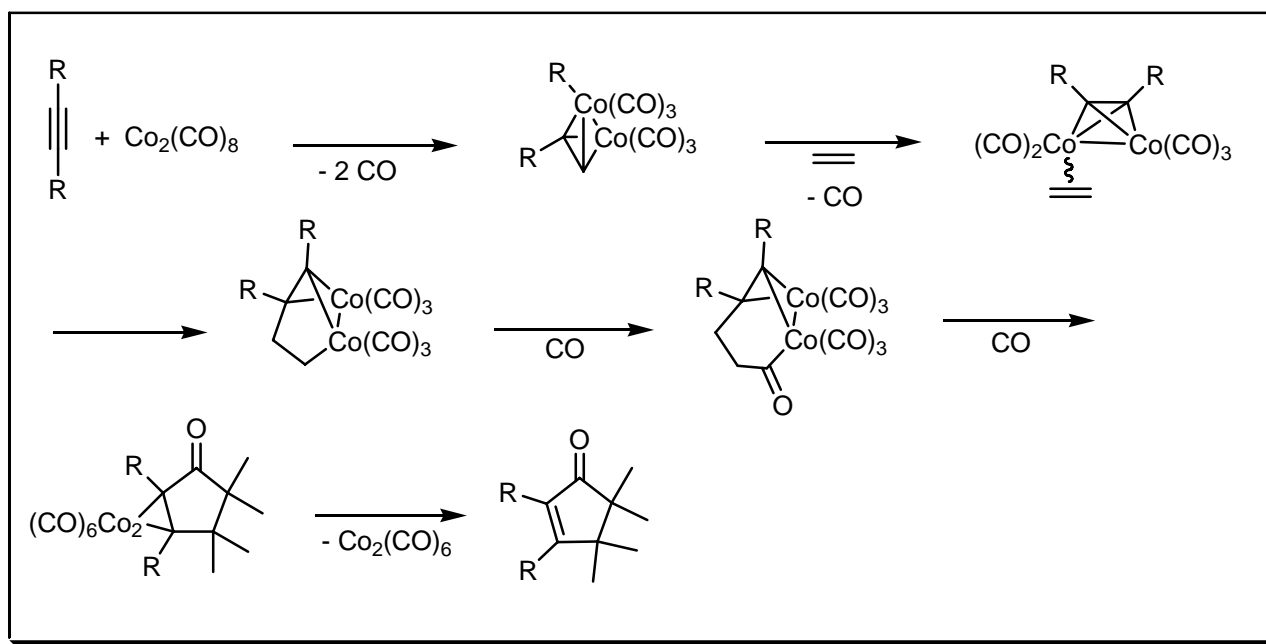
### COMMENTS :

## PAUSON – KHAND REACTION

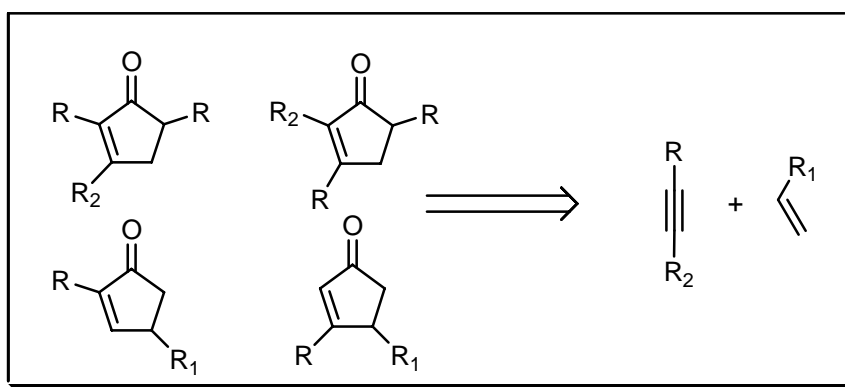
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The cyclopentenone synthesis from carbon monoxide, acetylene, and olefins. The reaction is cobalt carbonyl catalysed. The mechanism by **Magnus** is generally accepted. The reaction is also enantioselective if it is mediated by a chiral amine *N*-oxide or (*S*)-BINAP. Entrapped rhodium complexes can also catalyse this reaction. Faster reaction rates and higher yields can be obtained by using ultrasound, solid supports, phosphine oxides or acetonitrile as solvent. **Krafft**

*et al.* has published several anomalous **Pauson – Khand** reactions, while **Coogan** *et al.* has studied an overlooked byproduct of the reaction. See also **Nicholas** reaction.

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#### REFERENCES :

**Smith – March** : 1091

**Smith 2<sup>nd</sup>** : 1257

**Houben – Weyl** : **E18**, 341

**Org. React.** : **40**,1

**Org. Synth.** : **80**, 93

**Science of Synthesis** : **1**, 512, 596, 962

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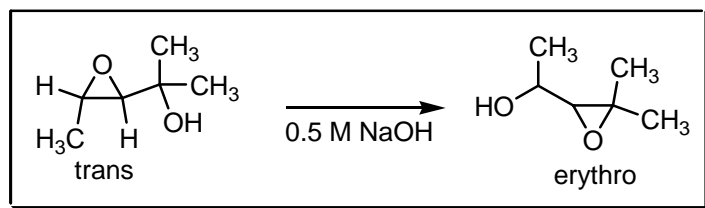
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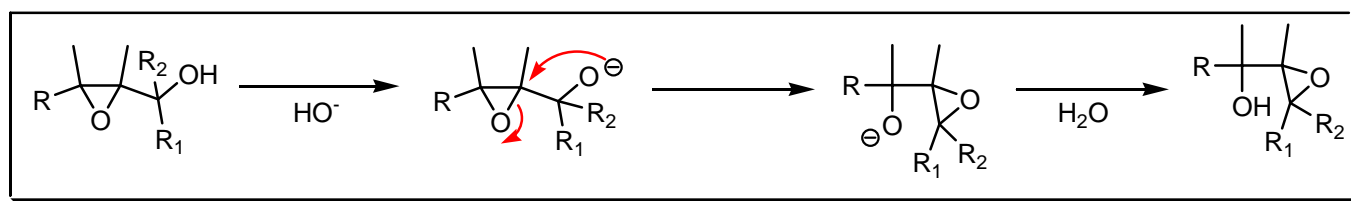
COMMENTS :

## PAYNE REARRANGEMENT

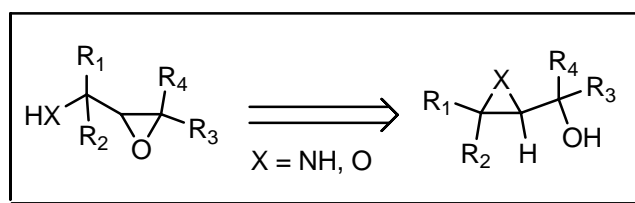
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The rearrangement of 2,3-epoxy alcohols to an isomeric one using a base. The configuration at C-2 of the epoxide ring will be inverted *via* an S<sub>N</sub>2 mechanism. The product can revert to the starting material under the same conditions. A mixture of compounds is normally obtained. The application of **aza-Payne** rearrangements has been used for the synthesis of homochiral 1,2-amino alcohols.

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Smith – March : 481

Smith 2<sup>nd</sup> : 229

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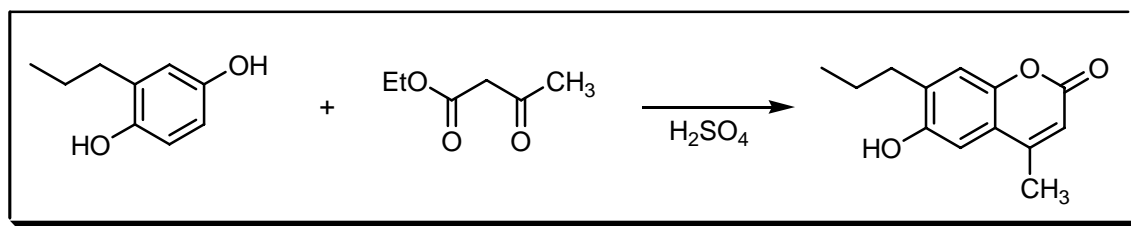
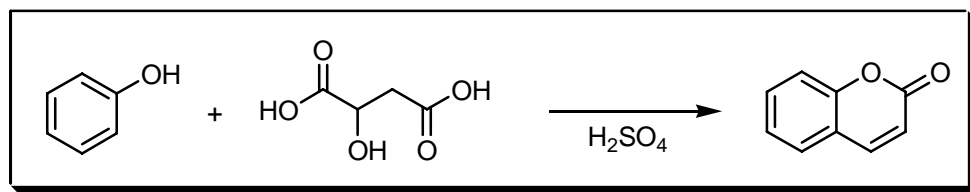
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**COMMENTS :**

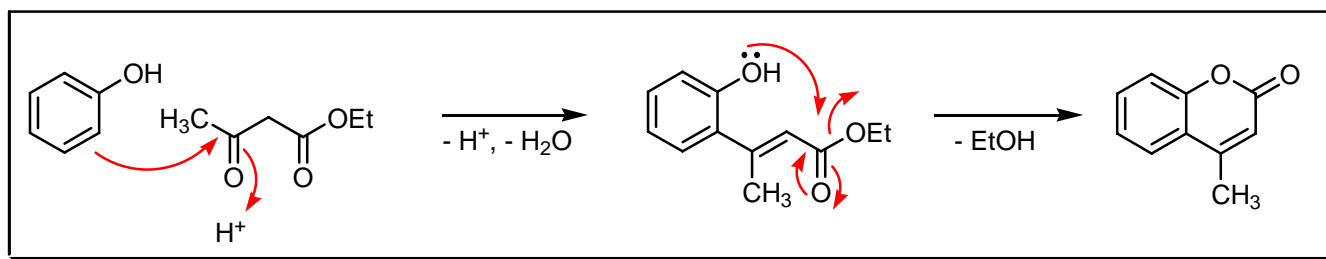
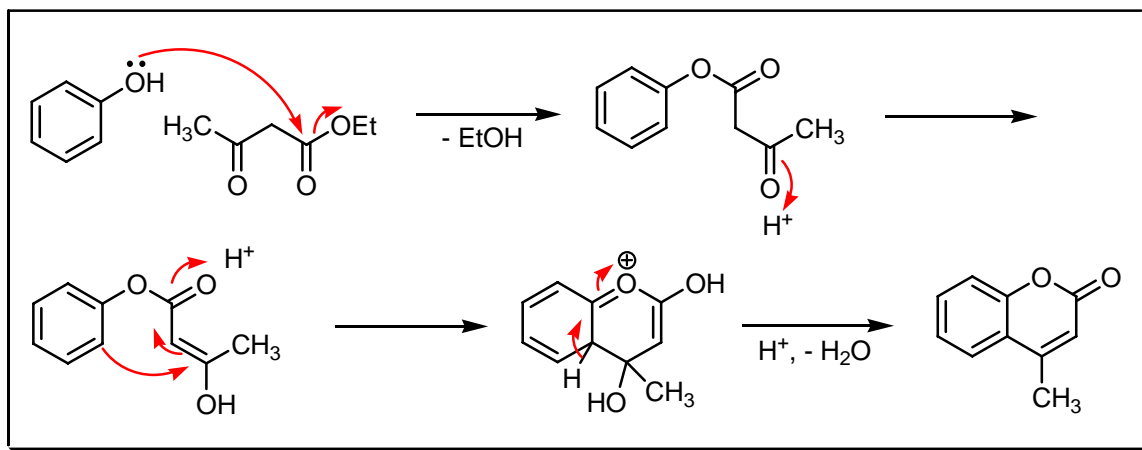
von PECHMANN – DUISBERG SYNTHESIS

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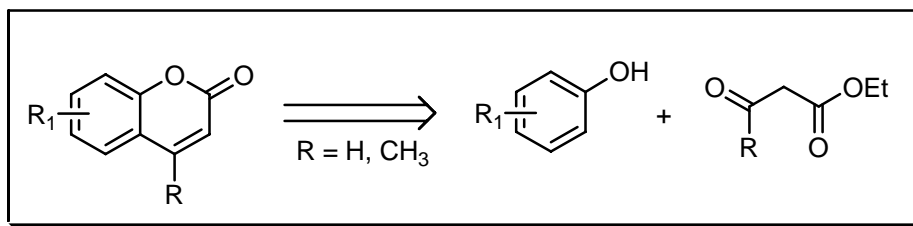
**EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

Coumarins are formed, when a mixture of a phenol and malic acid are heated with *e.g.* concentrated sulfuric acid. This is formally the **von Pechmann** synthesis. The **von Pechmann – Duisberg** synthesis is the coumarin synthesis from phenols and ethyl acetoacetate. There are several proposed mechanisms in the literature. See also **Anschütz** hydroxycoumarin, **Bargellini**, **Boyd – Robinson**, **Knoevenagel** coumarin, **Mentzer**, **von Pechmann**, **Pauly – Lockemann**, **Perkin** coumarin and **Simonis** reactions.

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Smith 2<sup>nd</sup> : 1109

Houben – Weyl : 6/2, 641

Org. React. : 7, 1

Org. Synth. : 24, 69

Org. Synth. Coll. Vol. : 3, 581

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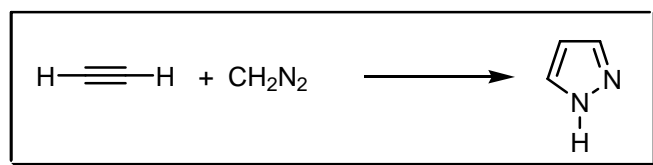
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**COMMENTS :**

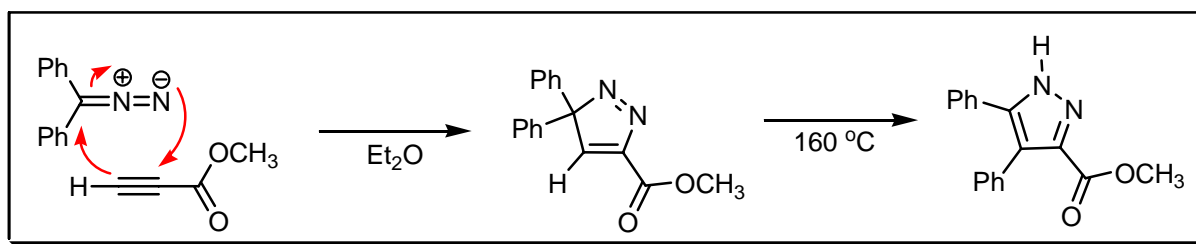
von PECHMANN PYRAZOLE SYNTHESIS

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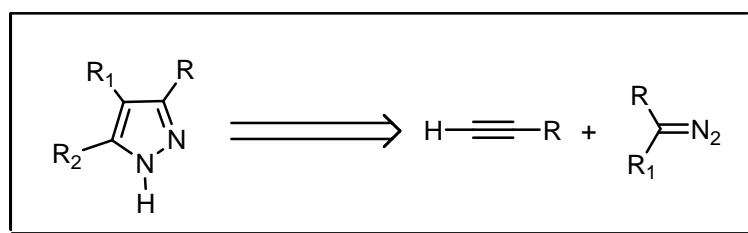
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

Pyrazole is obtained by treating acetylene with diazomethane derivatives in a 1,3-dipolar cycloaddition. See also **Balbiano** and **Knorr** pyrazole reactions.

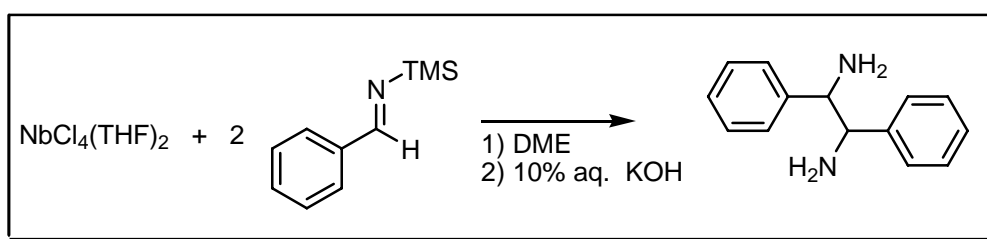
## REFERENCES :

- 1) E. Buchner, *Ber. Dtsch. Chem. Ges.*, 1889, **22**, 842.
- 2) H. von Pechmann, *Ber. Dtsch. Chem. Ges.*, 1898, **31**, 2950.
- 3) R. Huisgen, *Angew. Chem.*, 1963, **75**, 616.
- 4) T. Aoyama; S. Inoue; T. Shioiri, *Tetrahedron Lett.*, 1984, **25**, 433.
- 5) T. Asaki; T. Aoyama; T. Shioiri, *Heterocycles*, 1988, **27**, 343.
- 6) D.R. Sauer; S.W. Schneller, *J. Org. Chem.*, 1990, **55**, 5535.

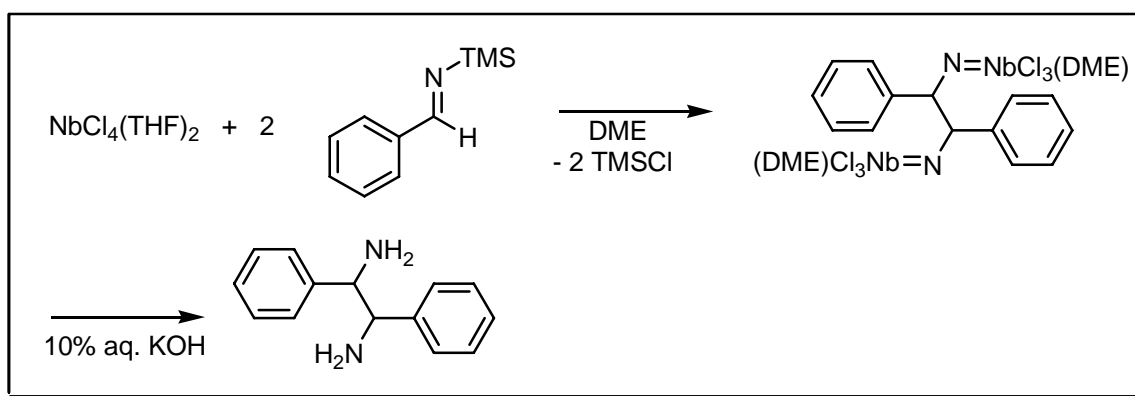
## COMMENTS :

## PEDERSEN COUPLING

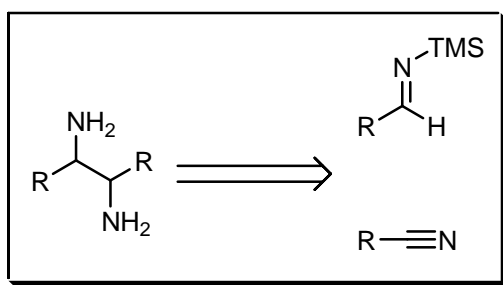
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The coupling of nitriles or N-(trimethylsilyl)imines promoted by niobium(I) reagent. See also **Fujiwara** lanthanide reaction.

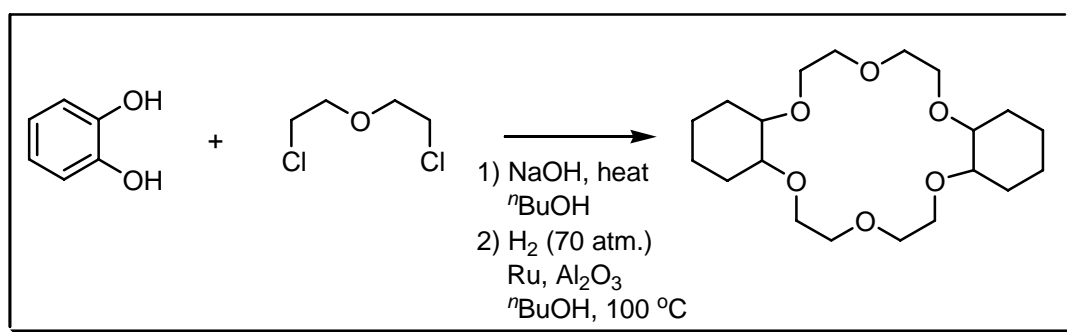
## REFERENCES :

- 1) L.E. Manzer, *Inorg. Chem.*, 1977, **16**, 525.
- 2) E.J. Roskamp; S.F. Pedersen, *J. Am. Chem. Soc.*, 1987, **109**, 3152.
- 3) J.B. Hartung, jr.; S.F. Pedersen, *Organometallics*, 1990, **9**, 1414.

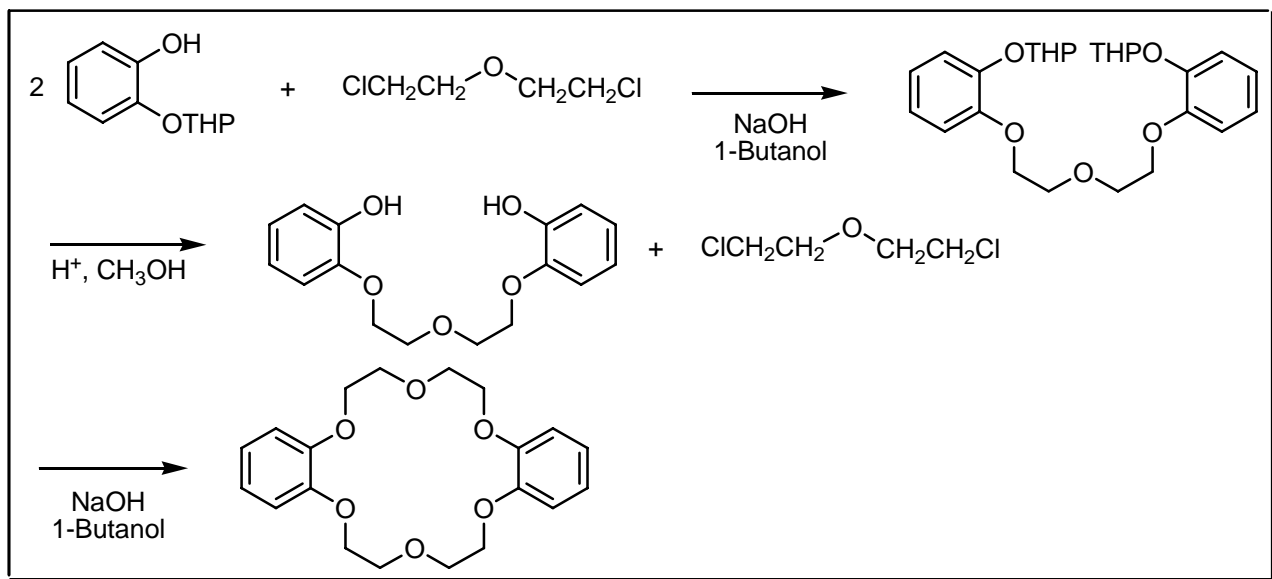
## COMMENTS :

## PEDERSEN CROWN ETHER SYNTHESIS

### EXAMPLE :



## MECHANISM :



## NOTES :

The crown ether formation and its use in substitutions, oxidations etc. The original crown ether discovered by **Pedersen** has six oxygen atoms exposed along the inside wall of the ring. When atoms of certain metallic elements such as sodium or potassium pass through the center of the ring, they attach themselves to the exposed oxygen atoms and fit like a key in a lock. The second scheme shows an example of the use of crown ethers.

## REFERENCES :

Org. Synth. : 52, 66; 57, 30

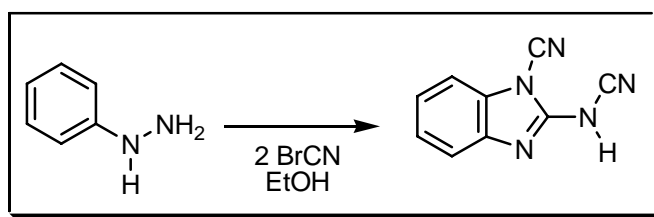
Org. Synth. Coll. Vol. : 6, 301, 395

- 1) A. Lüttringhaus; K. Ziegler, *Liebigs Ann. Chem.*, 1937, **528**, 155.
- 2) C.J. Pedersen, *J. Am. Chem. Soc.*, 1967, **89**, 2495.
- 3) C.J. Pedersen, *J. Am. Chem. Soc.*, 1971, **93**, 4684.
- 4) A.M. Kolodziejczyk; M. Manning, *J. Org. Chem.*, 1981, **46**, 1944.
- 5) K.E. Krakowiak; J.S. Bradshaw; D.J. Zamecka-Krakowiak, *Chem. Rev.*, 1989, **89**, 929.
- 6) Y. Machida; H. Nishi; K. Nakamura, *Chirality*, 1999, **11**, 173.

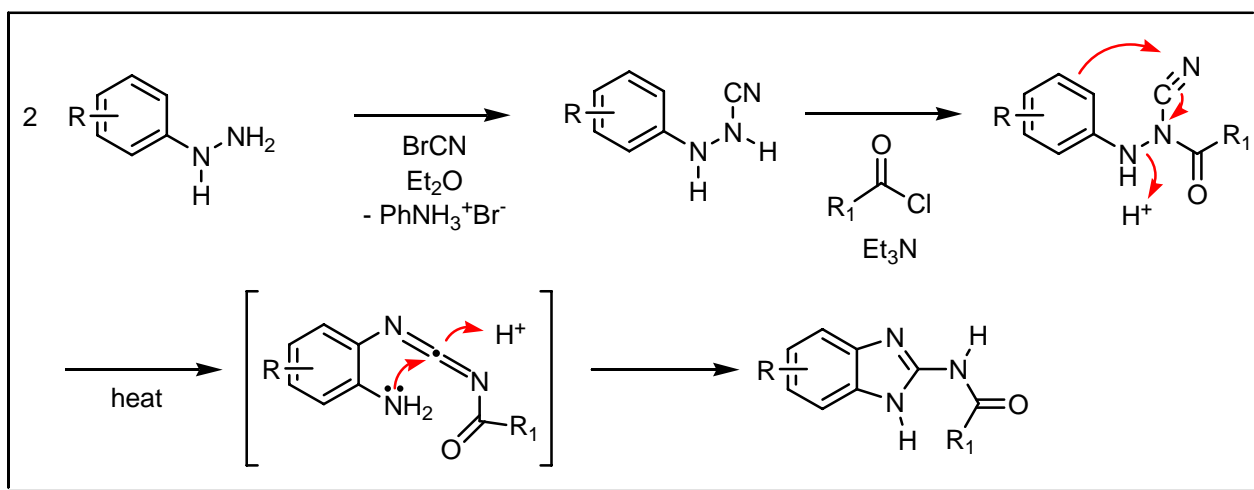
## COMMENTS :

# PELLIZZARI BENZIMIDAZOLE SYNTHESIS

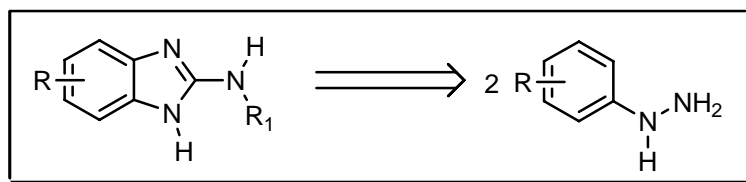
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The thermal rearrangement of 1-aryl-2-cyanohydrazines to afford 2-aminobenzimidazoles.

## REFERENCES :

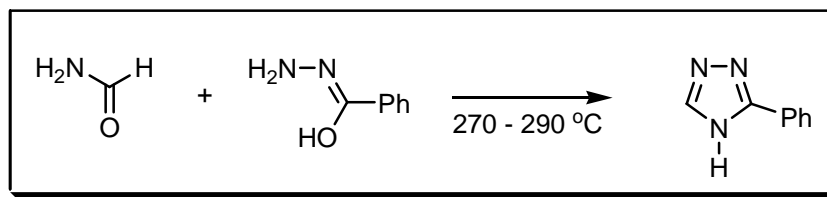
- 1) G. Pellizzari; A. Gaiter, *Gazz. Chim. Ital.*, 1918, **48**, 151.
- 2) C.W. Bird; C.K. Wong, *Tetrahedron Lett.*, 1974, **15**, 1251.
- 3) C.W. Bird; J. Cobb; S.C. Nyburg; A.W. Parkins, *Tetrahedron*, 1995, **51**, 13161.
- 4) M.T.V.L. Carvalho; A.M. Lobo; P.S. Branco; S. Prabhakar, *Tetrahedron Lett.*, 1997, **38**, 3115.



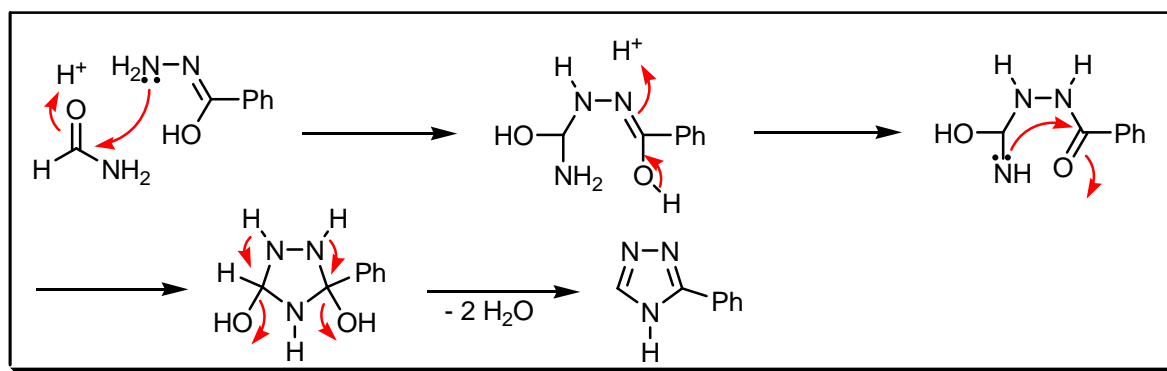
COMMENTS :

## PELLIZZARI REACTION

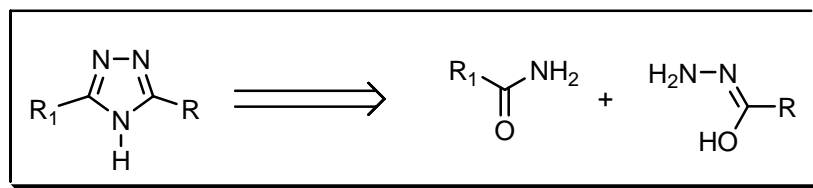
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The triazole will be formed during distillation of the hydrazide with the amide. See also **Einhorn – Brunner** reaction.

REFERENCES :

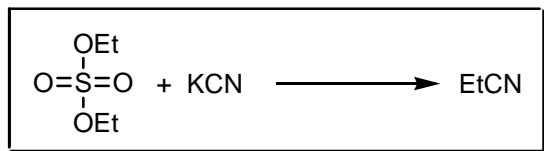
- 1) G. Pellizzari, *Gazz. Chim. Ital.*, 1911, **41/II**, 20.
- 2) K.T. Potts, *Chem. Rev.*, 1961, **61**, 87.
- 3) E.J. Browne; J.B. Polya, *J. Chem. Soc.*, 1962, 5149.

COMMENTS :

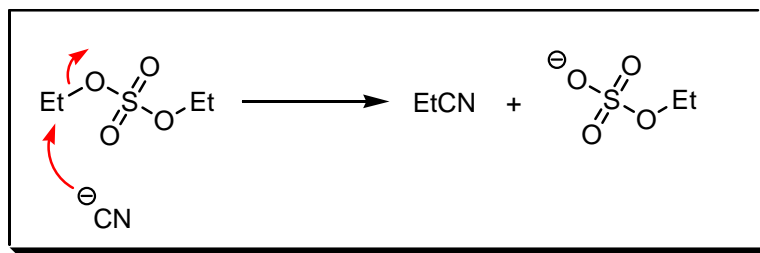
## PELOUZE SYNTHESIS

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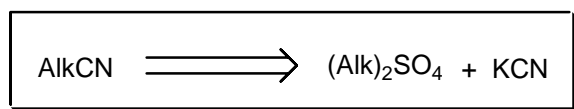
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The cyanide alkylation between potassium cyanide and alkyl sulfates. See also **Kolbe** cyanide reaction.

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REFERENCES :

Houben –Weyl : 8, 306

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1) J. Pelouze, *Liebigs Ann. Chem.*, 1834, **10**, 249.

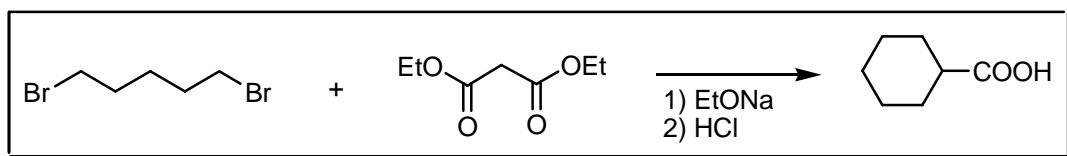
2) D.T. Mowry, *Chem. Rev.*, 1948, **42**, 189.

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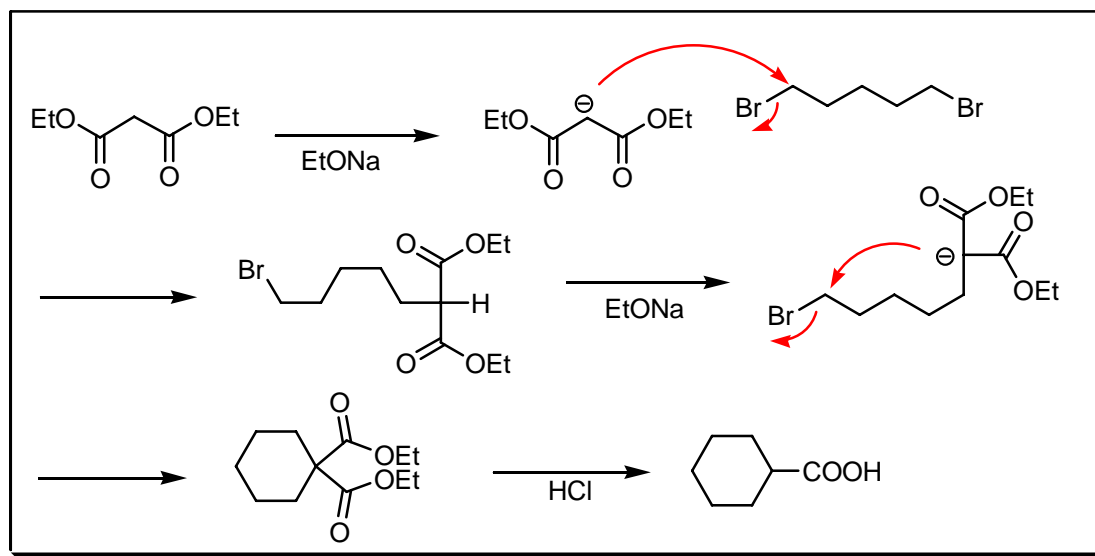
COMMENTS :

## PERKIN ALICYCLIC SYNTHESIS

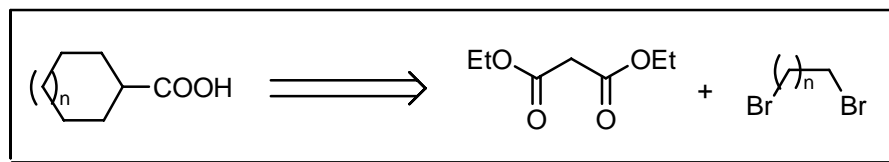
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The synthesis of cycloalkane carboxylic acids from  $\alpha,\omega$ -dihaloalkanes and sodium diethyl malonate. See also **Claisen** alkylation, **Freund** and **Knoevenagel** condensation reactions.

REFERENCES :

Smith : 880

Smith 2<sup>nd</sup> : 733

Org. Synth. : 23, 16

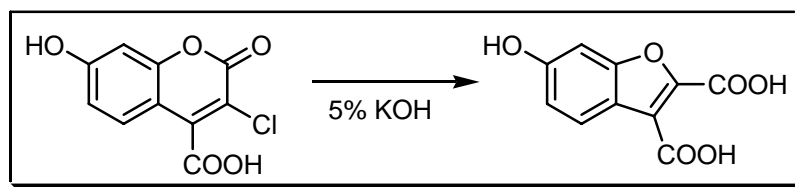
Org. Synth. Coll. Vol. : 3, 213

- 1) W.H. Perkin, jr., *Chem. Ber.*, 1883, **16**, 1793.
- 2) L.M. Rice; C.H. Crogan, *J. Org. Chem.*, 1961, **26**, 54.
- 3) M. Julia; M. Maumy, *Bull. Soc. Chim. Fr.*, 1969, 2415.
- 4) R. Fajgar; J. Pola, *J. Org. Chem.*, 1993, **58**, 7709.
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- 6) W. Dmowski; A. Wolniewicz, *J. Fluorine Chem.*, 2000, **102**, 141.

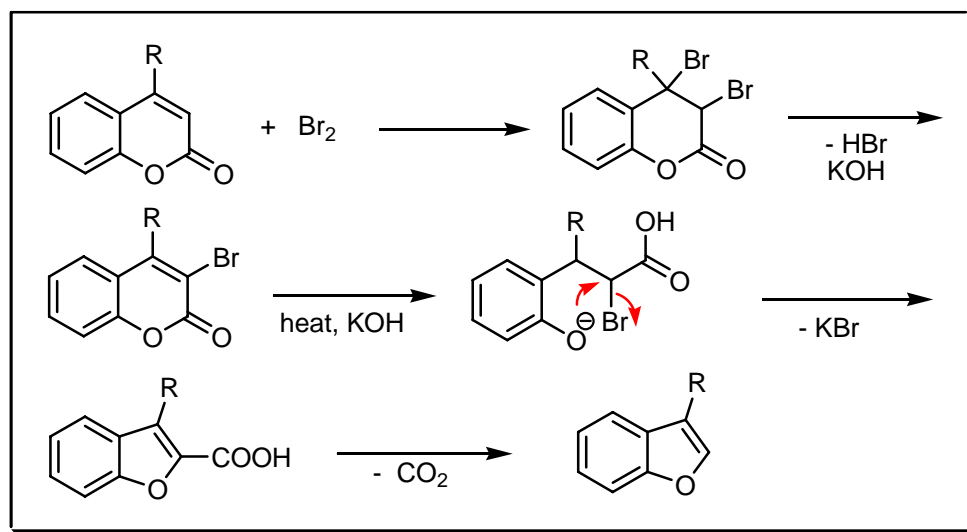
COMMENTS :

## PERKIN BENZOFURAN SYNTHESIS

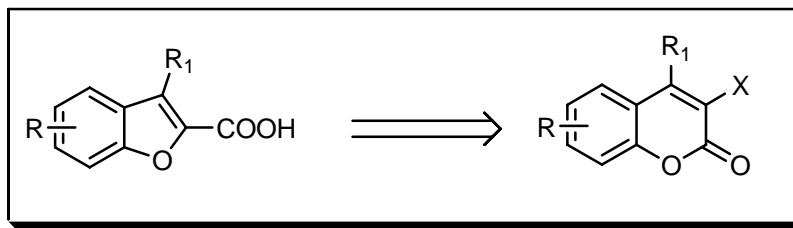
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The base-catalysed rearrangement of 3-halogen-substituted coumarins into the corresponding coumarone-2-carboxylic acid.

## REFERENCES :

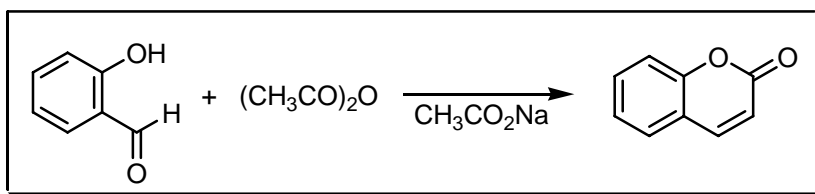
**Org. React.** : **1**, 210

- 1) W.H. Perkin, *J. Chem. Soc.*, 1870, **23**, 368.
- 2) W.H. Perkin, *J. Chem. Soc.*, 1871, **24**, 37.
- 3) B.B. Dey, *J. Chem. Soc.*, 1915, **107**, 1606.
- 4) G.W. Holton; G. Parker; A. Robertson, *J. Chem. Soc.*, 1949, 2049.
- 5) P. Cagniant; D. Cagniant, *Adv. Heterocycl. Chem.*, 1975, **18**, 337.
- 6) K. Bowden; S. Battah, *J. Chem. Soc., Perkin Trans. 2*, 1998, 1603.

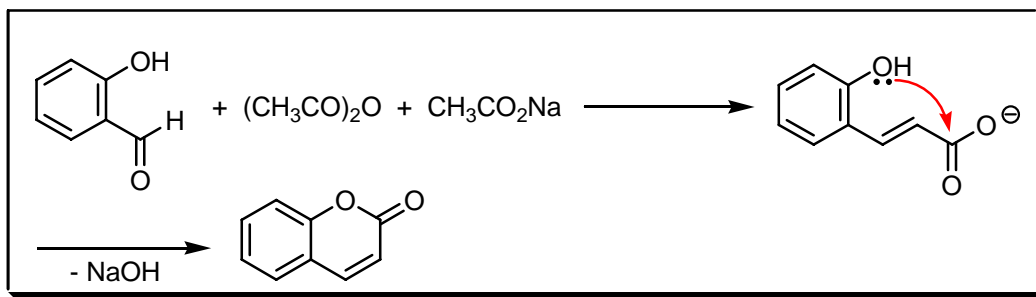
## COMMENTS :

## PERKIN COUMARIN SYNTHESIS

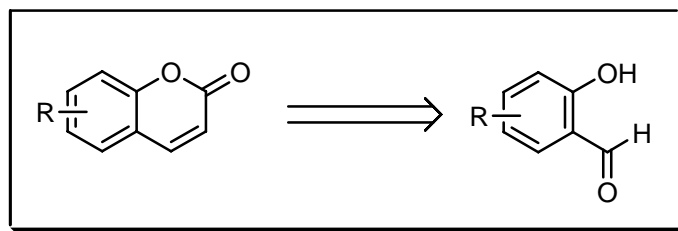
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Coumarins unsubstituted in the pyrone ring are obtained by heating an *o*-hydroxyaryl aldehyde with acetic anhydride and sodium acetate. See also **Anschütz** hydroxycoumarin, **Bargellini**, **Boyd – Robinson**, **Dieckmann – Meiser**, **Knoevenagel**, **Mentzer**, **Pauly – Lockemann**, **von Pechmann – Duisberg** and **Simonis** reactions.

### REFERENCES :

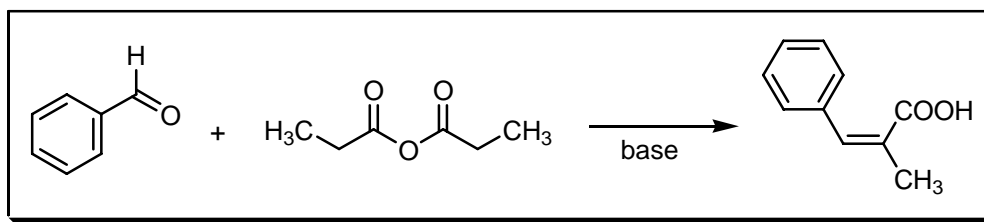
**Org. React.** : **1**, 210

- 1) W.H. Perkin, *J. Chem. Soc.*, 1868, **21**, 53.
- 2) W.H. Perkin, *J. Chem. Soc.*, 1868, **21**, 181.
- 3) S.M. Sethna; N.M. Shah, *Chem. Rev.*, 1945, **36**, 1.
- 4) J.A. Mahling; R.R. Schmidt, *Liebigs Ann. Chem.*, 1995, 467.
- 5) K. Felföldi; M. Sutyinsky; N. Nagy; I. Palinko, *Synth. Commun.*, 2000, **30**, 1543.

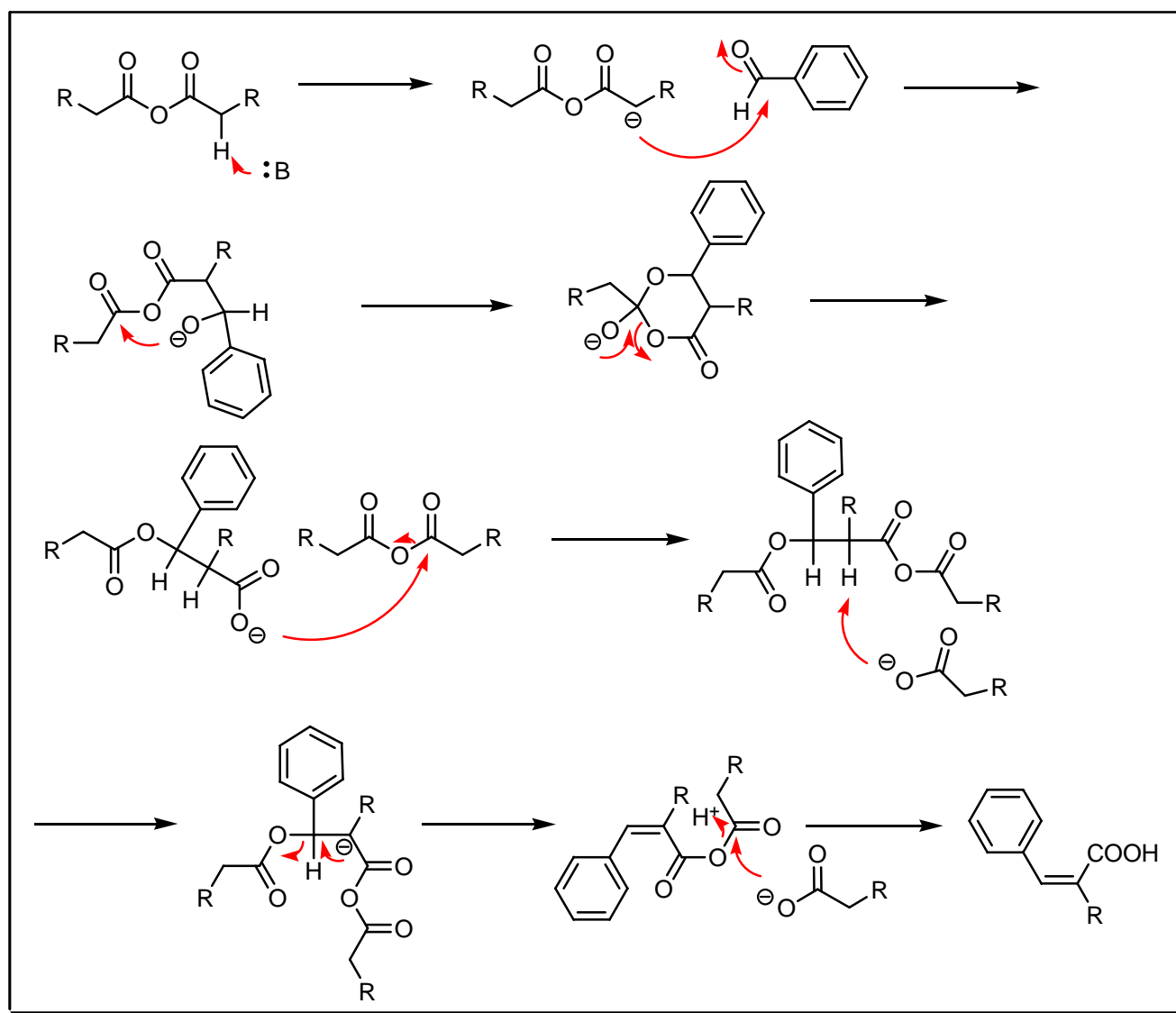
### COMMENTS :

## PERKIN REACTION

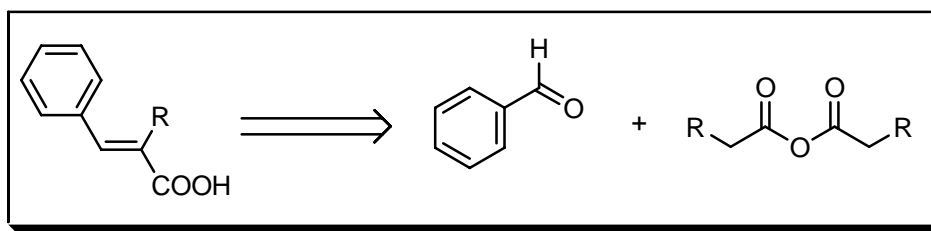
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

This aldol-type reaction involves the base-catalysed condensation of a carbonyl compound, or in a few cases an imine and an acid anhydride. The alkali salt of the acid can function as the base and amides can be employed instead of anhydrides. Sodium phenylacetate and acetic anhydride react with benzaldehydes to yield  $\alpha$ -phenylcinnamic acids. This is the **Ogialoro** modification of the **Perkin** reaction (*Gazz. Chim. Ital.*, 1878, **8**, 429). See also **Claisen** cinnamic, **Claisen – Schmidt**, **Doebner**, **Erlenmeyer – Plöchl**, **Knoevenagel**, **Perkin**, **Pschorr** and **Stobbe** reactions.

## REFERENCES :

**March** : 953

**Smith – March** : 1219, 1229

**Smith** : 894

**Smith 2<sup>nd</sup>** : 748

**Org. React.** : **1**, 210; **3**, 198

**Org. Synth.** : **33**, 70

**Org. Synth. Coll. Vol.** : **4**, 777

**Houben – Weyl** : **4/2**, 30; **8**, 442

**Science of Synthesis** : **10**, 48, 159, 278

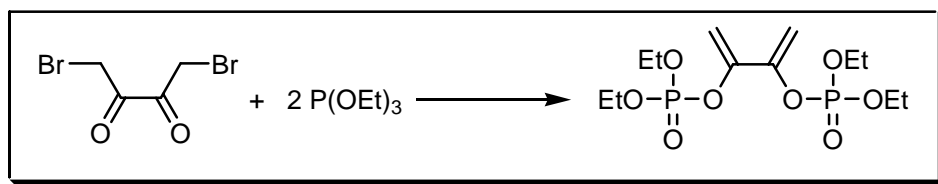
- 1) W.H. Perkin, *J. Chem. Soc.*, 1868, **21**, 53.
- 2) P.H. Leake, *Chem. Rev.*, 1956, **56**, 27.
- 3) R. Ketcham, *J. Chem. Educ.*, 1964, **41**, 565.
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- 5) G. Karminskizamola; L. Fiserjakic; M. Bajic, *Heterocycles*, 1985, **23**, 313.
- 6) A.Sr. Anjaneyulu; G.S. Rani; U.V. Mallavadhani; L.N. Murthy, *Indian J. Chem.*, 1990, **29B**, 219.
- 7) J.A. Mahling; R.R. Schmidt, *Liebigs Ann. Chem.*, 1995, 467.
- 8) K. Felfoldi; M. Sutyinszky; N. Naay; I. Palinko, *Synth. Commun.*, 2000, **30**, 1543.
- 9) D.V. Sevenard, *Tetrahedron Lett.*, 2003, **44**, 7119.

## COMMENTS :

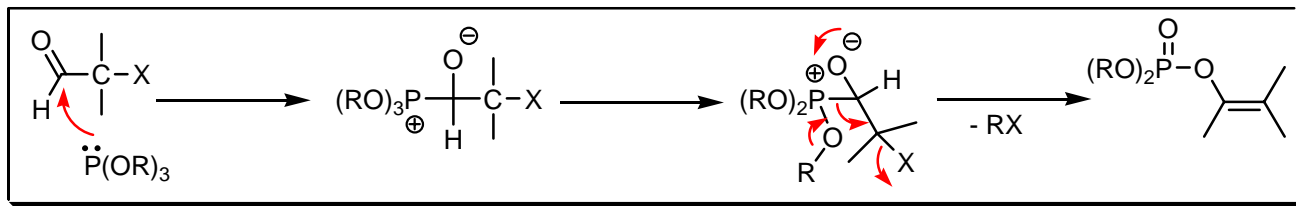


## PERKOW REACTION

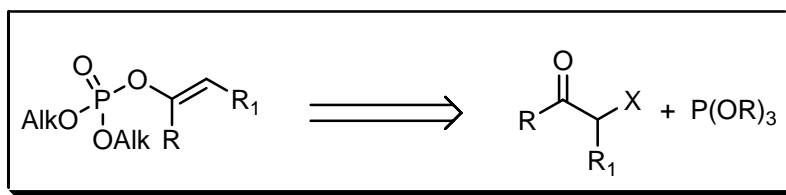
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The reaction of  $\alpha$ -haloketones with trialkyl phosphite to give ketophosphonate or vinylphosphate with a predominantly *E*-configuration. See also **Abramov**, **Arbusov (Michaelis – Arbuzov)** and **Michaelis – Becker – Nylén** reactions.

### REFERENCES :

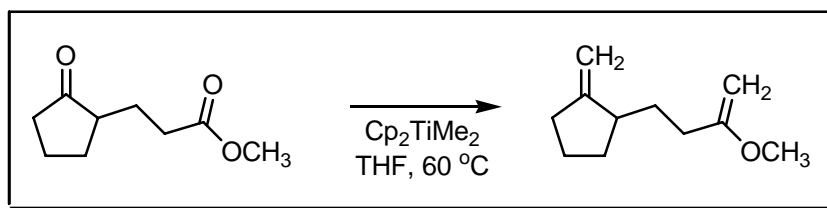
**Houben – Weyl** : 12/2, 348

- 1) W. Perkow; K. Ullerich; F. Meyer, *Naturwissenschaften*, 1952, **39**, 353.
- 2) W. Perkow, *Chem. Ber.*, 1954, **87**, 755.
- 3) F.W. Lichtenthaler, *Chem. Rev.*, 1961, **61**, 607.
- 4) I.J. Borowitz; S. Firstenberg; G.B. Horowitz; D. Schuessler, *J. Am. Chem. Soc.*, 1972, **94**, 1623.
- 5) M. Sekine; M. Nakajima; T. Hata, *J. Org. Chem.*, 1981, **46**, 4030.
- 6) J. Thiem; D. Rasch, *Nucleosides, Nucleotides*, 1985, **4**, 487.
- 7) P.N. Nagar, *Phosphorus Sulfur*, 1993, **79**, 207.
- 8) T. Janecki; R. Bodalski, *Heteroatom Chem.*, 2000, **11**, 115.

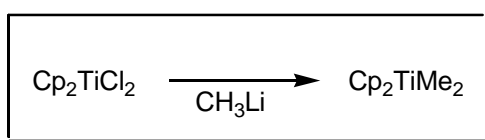
COMMENTS :

## PETASIS REACTION

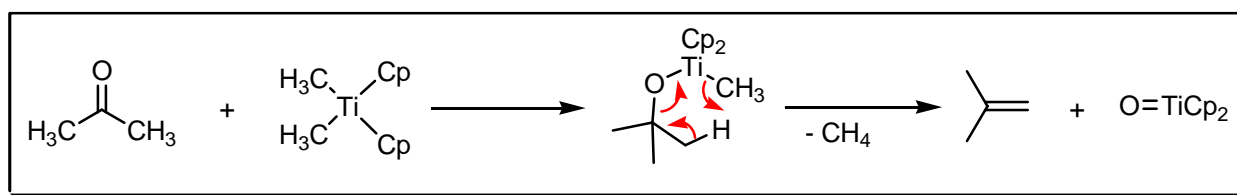
EXAMPLE :



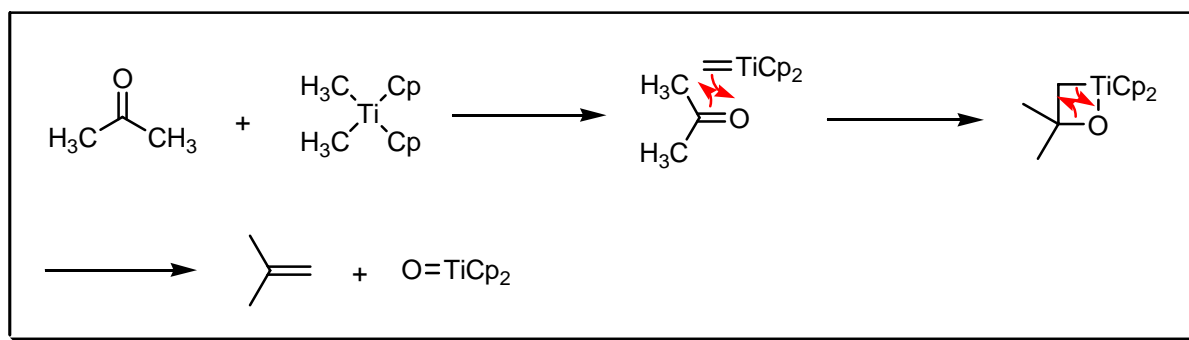
MECHANISM :



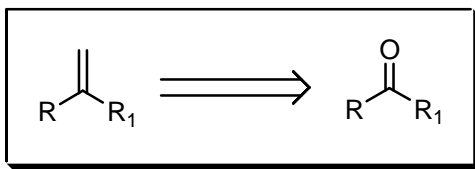
Petasis mechanism :



Hughes mechanism :



## DISCONNECTION :



## NOTES :

The titanium-mediated carbonyl olefination using titanium cyclopentadienide. There are two mechanisms published in the literature the original one by **Petasis** *et al.* and one by **Hughes** *et al.* The latter one is the accepted one. See also **Corey** – Kwiatkowski, **Horner** – Wadsworth – Emmons, **Julia** – Paris – Kocienski – Lythgoe, **Krief** – Reich – Chow, **Nozaki** – Hiyama – Kishi (Takai – Utimoto), **Nysted**, **Paquette**, **Peterson**, **Ramberg** – Bäcklund, **Still** – Gennari, **Takeda**, **Tebbe** and **Wittig** reactions.

## REFERENCES :

**March** : 933

**Smith – March** : 1271

**Smith** : 813

**Smith 2<sup>nd</sup>** : 680

**Org. Synth.** : **69**, 72

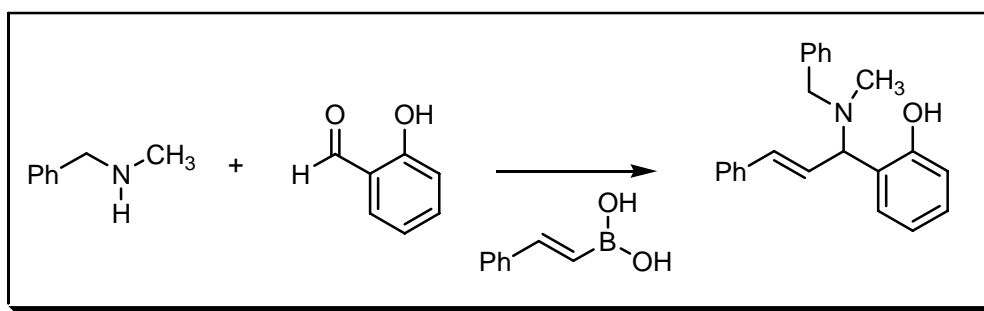
**Org. Synth. Coll. Vol.** : **8**, 512

- 1) N.A. Petasis; E.I. Bzowej, *J. Am. Chem. Soc.*, 1990, **112**, 6392.
- 2) N.A. Petasis; E.I. Bzowej, *J. Org. Chem.*, 1992, **57**, 1327.
- 3) N.A. Petasis; S.-P. Lu, *J. Am. Chem. Soc.*, 1995, **117**, 6394.
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- 5) D.L. Hughes; J.F. Payack; D. Cai; T.R. Verhoeven; P.J. Reider, *Organometallics*, 1996, **15**, 663.
- 6) N.A. Petasis; Y.-H. Hu, *J. Org. Chem.*, 1997, **62**, 782.
- 7) R.C. Hartley; G.J. McKiernan, *J. Chem. Soc., Perkin Trans. 1*, 2002, 2763.
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- 9) M.J. Cook; D.W. Fleming; T. Gallagher, *Tetrahedron Lett.*, 2005, **46**, 297.

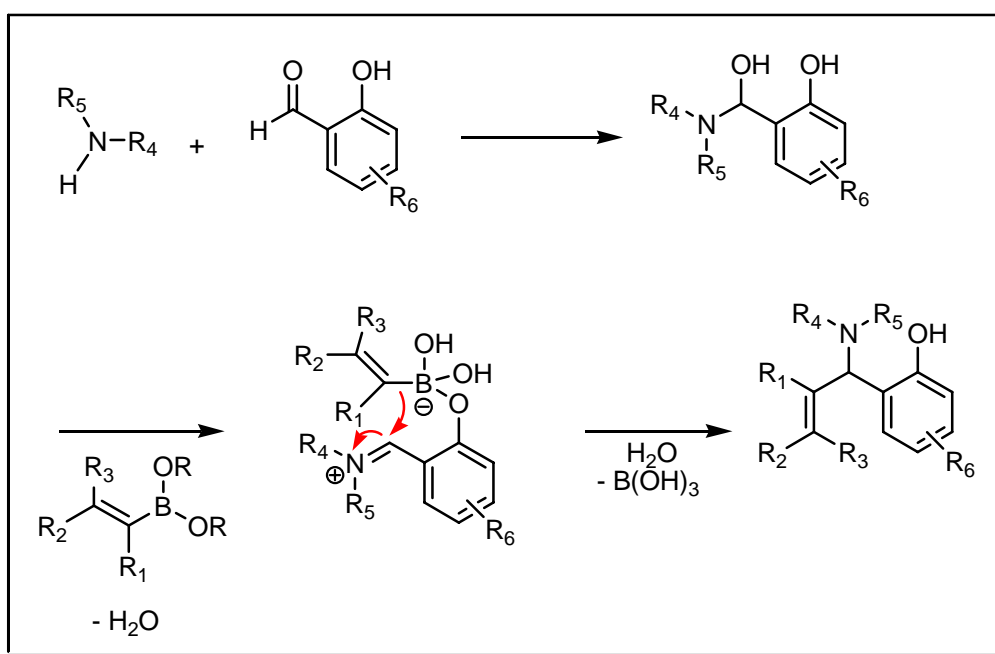
## COMMENTS :

## PETASIS SYNTHESIS

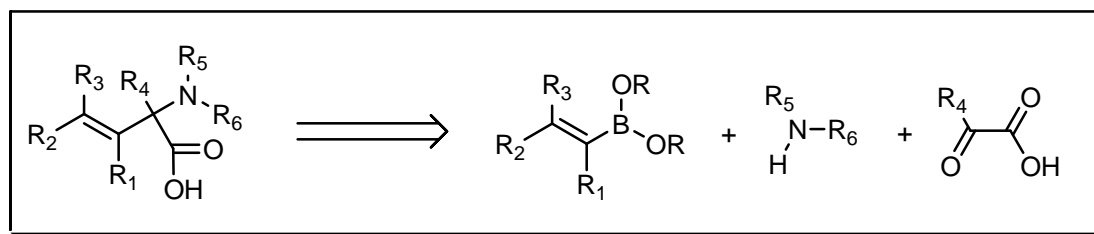
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This is a three-component variant of the **Mannich** reaction involving the condensation of an organoboronic acid or boronate with an amine and an  $\alpha$ -keto acid. Glyoxal and its derivatives have also been used. See also **Mannich** reaction.

## REFERENCES :

- 1) N.A. Petasis; I.A. Zavialov, *Tetrahedron Lett.*, 1996, **37**, 567.
- 2) N.A. Petasis; I.A. Zavialov, *J. Am. Chem. Soc.*, 1997, **119**, 445.
- 3) N.A. Petasis; A.K. Yudin; I.A. Zavialov; G.K.S. Prakash; G.A. Olah, *Synlett*, 1997, 606.
- 4) G.K.S. Prakash; M. Mandal; S. Schweizer; N.A. Petasis; G.A. Olah, *Org. Lett.*, 2000, **2**, 3173.
- 5) N.A. Petasis; S. Boral, *Tetrahedron Lett.*, 2001, **42**, 539.
- 6) F. Berrée; A. Debache; Y. Marsae; B. Carboni, *Tetrahedron Lett.*, 2001, **42**, 3591.
- 7) T. Koolmeister; M. Södergren; M. Scobic, *Tetrahedron Lett.*, 2002, **43**, 5969.
- 8) D. Naskar; A. Roy; W.L. Seibel, *Tetrahedron Lett.*, 2003, **44**, 8861.
- 9) S. Sugiyama; S. Arai; K. Ishii, *Tetrahedron: Asymmetry*, 2004, **15**, 3149.
- 10) K.K. Nanda; B.W. Trotter, *Tetrahedron Lett.*, 2005, **46**, 2025.

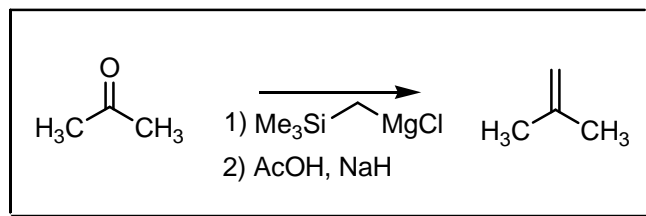
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## COMMENTS :

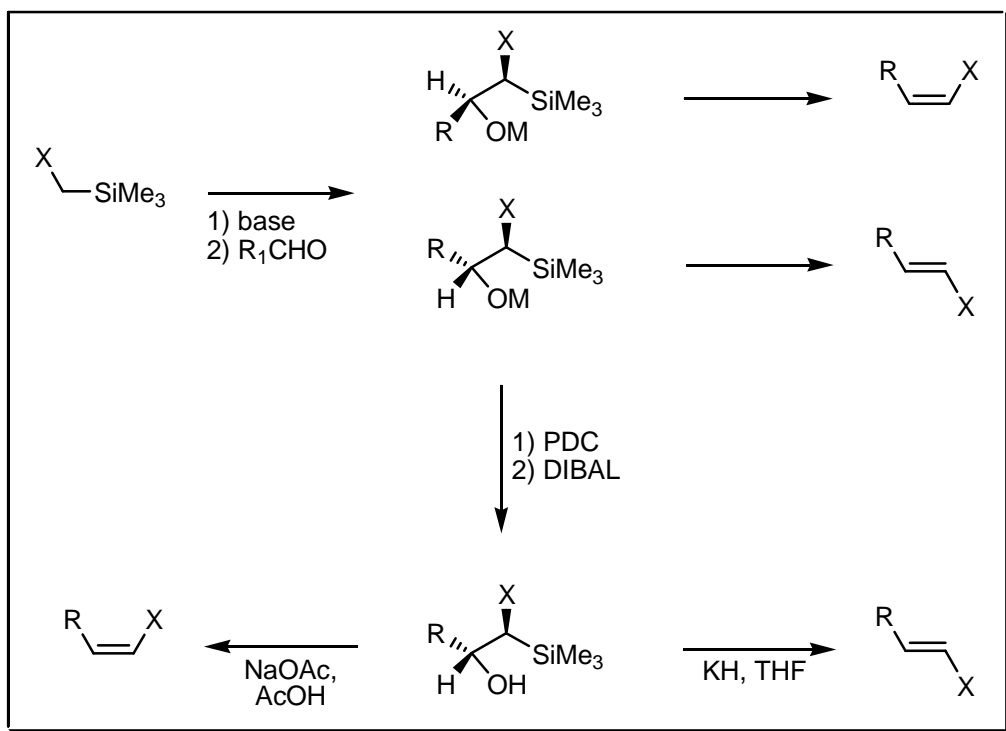
## PETERSON OLEFINATION REACTION

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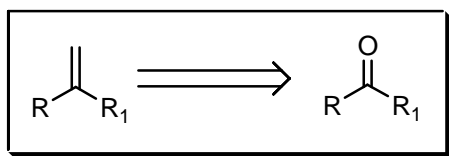
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of alkenes from  $\alpha$ -silyl carbanions (lithium or magnesium salt) and carbonyl compounds. In cases where separation of  $\beta$ -silyl alcohol diastereoisomers can be achieved, pure *Z* or *E* olefins can be isolated. Acidic work-up gives *anti* elimination, while basic conditions gives *syn* elimination. Advantages of this reaction over the **Wittig** reaction include, by-products are more easily removed and the reaction suffers less from steric effects. Both concerted and step-wise mechanisms are possible. There is a **Corey** modification of this reaction. See also **Corey – Kwiatkowski**, **Eastwood**, **Horner – Wadsworth – Emmons**, **Julia – Paris – Kocienski – Lythgoe**, **Krief – Reich – Chow**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Nysted**, **Paquette**, **Petasis** reaction, **Ramberg – Bäcklund**, **Still – Gennari**, **Takeda**, **Tebbe** and **Wittig** reactions.

## REFERENCES :

March : 952

Smith – March : 1228

Smith : 755

Smith 2<sup>nd</sup> : 638

Houben – Weyl : E11, 292, 779, 1236, 1449; E15, 921

Org. React. : 38,1

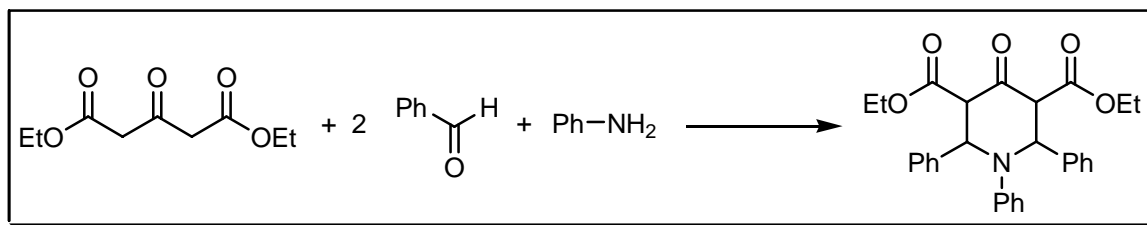
Org. Synth. : 73, 50

- 1) D.J. Peterson, *J. Org. Chem.*, 1968, **33**, 780.
- 2) E.J. Corey; D. Enders; M.G. Bock, *Tetrahedron Lett.*, 1976, **17**, 7.
- 3) D.J.S. Tsai; D.S. Matteson, *Tetrahedron Lett.*, 1981, **22**, 2751.
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- 7) C.-C. Chang; Y.-H. Chen; Y.-T. Hsieh; T.-Y. Luh, *J. Org. Chem.*, 2000, **65**, 4694.
- 8) L.F. van Staden; D. Gravestock; D.J. Ager, *Chem. Soc. Rev.*, 2002, **31**, 195.
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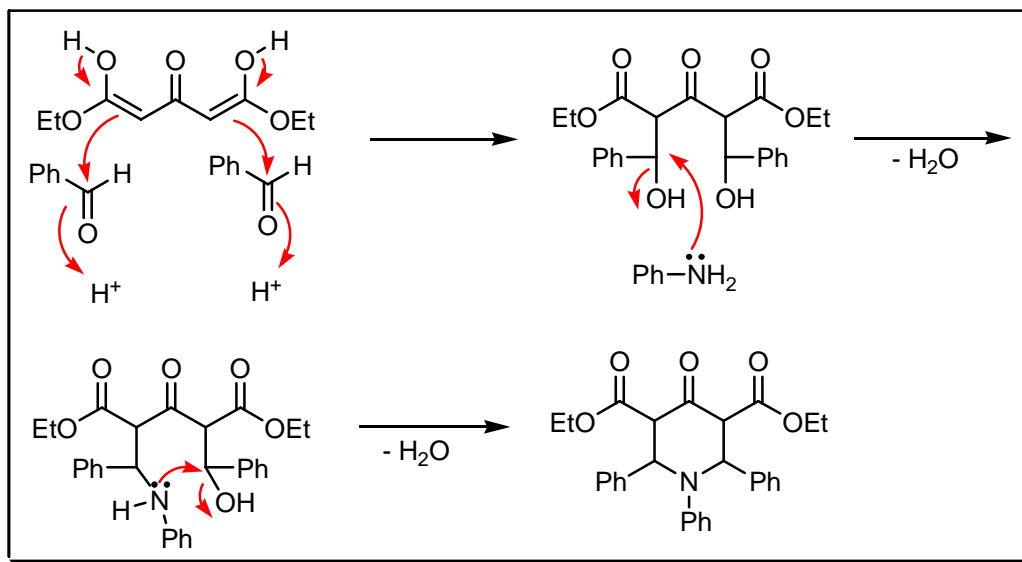
**COMMENTS :**

**PETRENKO–KRITSCHENKO PIPERIDONE SYNTHESIS**

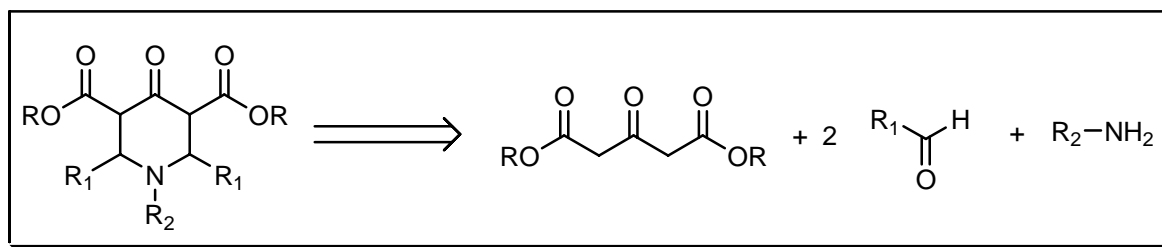
**EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

The ring-closure of two molecules of aldehyde with ammonia or primary amines and dialkyl 3-oxopentanedioates. See also **Bohlmann – Rahtz**, **Chichibabin** pyridine, **Gattermann – Skita**, **Guareschi – Thorpe**, **Hantzsch – Beyer**, **von Meyer – Mohr**, **Riehm** pyridine, **Robinson – Schöpf** and **Wakatsuki – Yamazaki – Bönnemann** reactions.

## REFERENCES :

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- 4) R. Robinson, *J. Chem. Soc.*, 1917, **111**, 876.
- 5) C. Mannich; O. Hieronimus, *Ber. Dtsch. Chem. Ges.*, 1942, **75**, 49.
- 6) H. Leonard, *J. Am. Chem. Soc.*, 1957, **79**, 5279.
- 7) U. Holgrave; B. Piening; R. Kohlmorgen; E. Stoll, *Arch. Pharm. (Weinheim, Ger.)*, 1988, **321**, 917.
- 8) M. Langlois; D. Yang; J.-L. Soulier; C. Florac, *Synth. Commun.*, 1992, **22**, 3115.

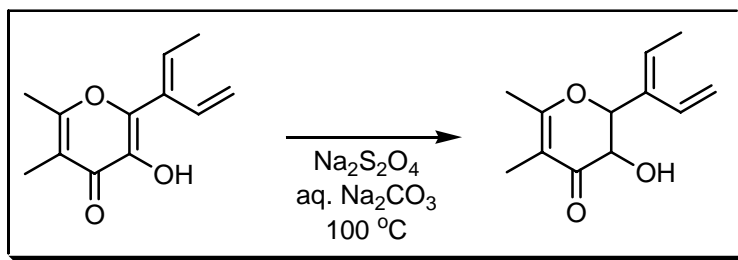
## COMMENTS :



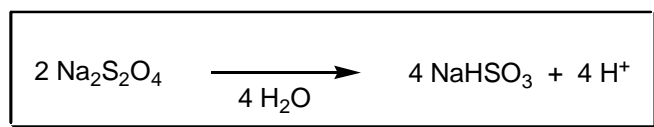
## PEW REDUCTION

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### EXAMPLE :



### MECHANISM :



### NOTES :

This is the classical reduction of flavonols to dihydroflavonols by sodium hydrosulfite (sodium dithionite) at  $100^\circ\text{C}$  in aqueous sodium carbonate solution. This method is generally used for the reductions of nitroso compounds to amines, azo compounds to amines, ketones to alcohols, and quinines to hydroquinones and aldehydes.

### REFERENCES :

**Org. Synth.** : **3**, 7; **17**, 9; **29**, 8; **34**, 1; **37**, 15

**Org. Synth. Coll. Vol.** : **1**, 49; **2**, 39; **3**, 69; **4**, 15, 247

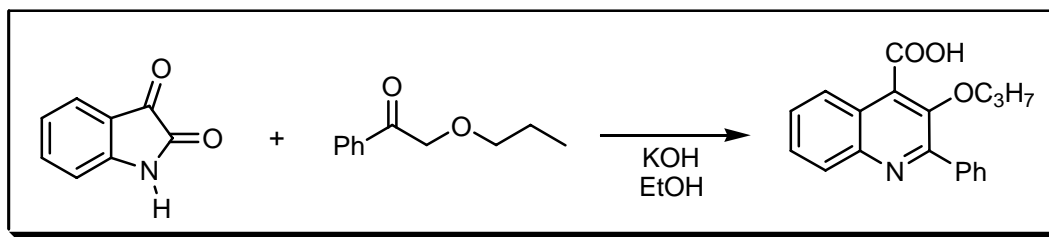
1) J.C. Pew, *J. Am. Chem. Soc.*, 1948, **70**, 3031.

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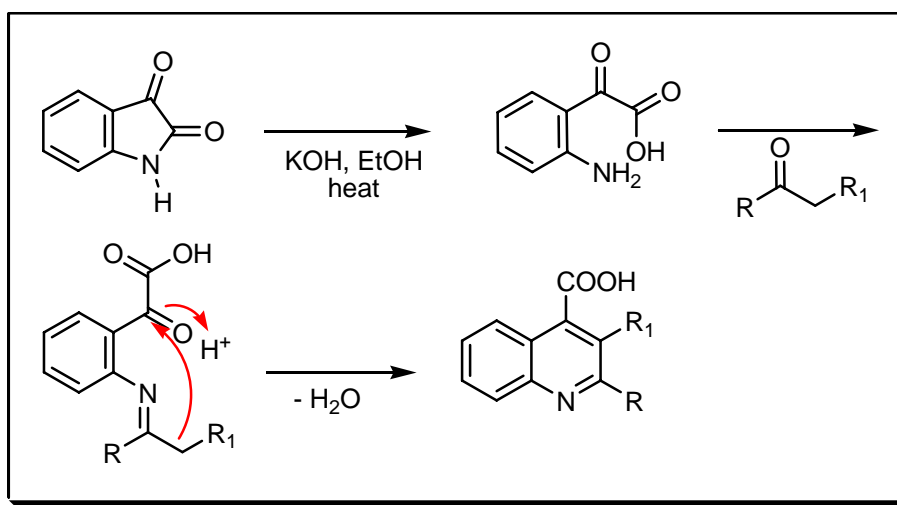
### COMMENTS :

## PFITZINGER – BORSCHÉ REACTION

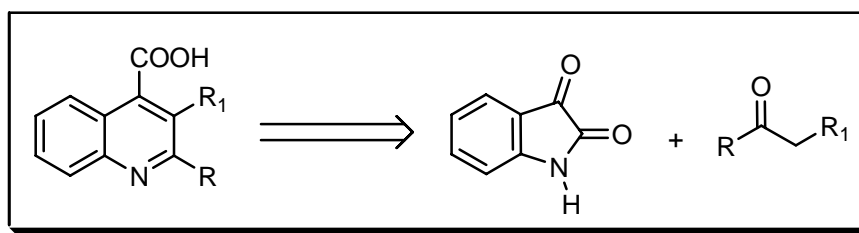
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Quinoline-4-carboxylic acids from isatins and  $\alpha$ -methylene carbonyl compounds. The **Walther** modification uses iminonitrile. The **Halberkann** variant uses *N*-acetyl isatines for the synthesis of quinolinic acids. See also **Allan – Loudon**, **von Baeyer – Drewson** quinoline, **Camps**, **Combes** quinoline, **Conrad – Limpach**, **Doebner** quinoline, **Doebner – von Miller**, **Foulds – Robinson**, **Friedländer**, **Knorr** quinoline, **Meth-Cohn**, **von Niementowski** quinoline, **Riehm** quinoline and **Skraup** quinoline reactions.

## REFERENCES :

Houben – Weyl : **E6a**, 985; **E7a**, 388; **E7b**, 140

Org. Synth. : **40**, 54

Org. Synth. Coll. Vol. : **5**, 635

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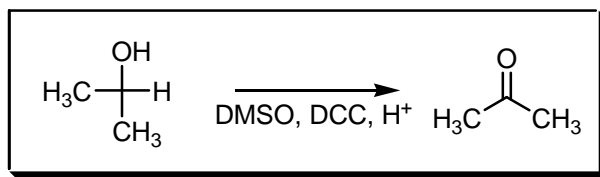
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  - 2) J. Halberkann, *Ber. Dtsch. Chem. Ges.*, 1921, **54**, 3090.
  - 3) R.H. Manske, *Chem. Rev.*, 1942, **30**, 113.
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  - 6) Q.P. Chen; L.W. Deady, *Aust. J. Chem.*, 1993, **46**, 987.
  - 7) K. Lackey; D.D. Sternbach, *Synthesis*, 1993, 993.
  - 8) T.S.T. Wang; R.A. Fawwaz; R.L. van Heertum, *J. Labelled Compd. Radiopharm.*, 1995, **36**, 671.
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## COMMENTS :

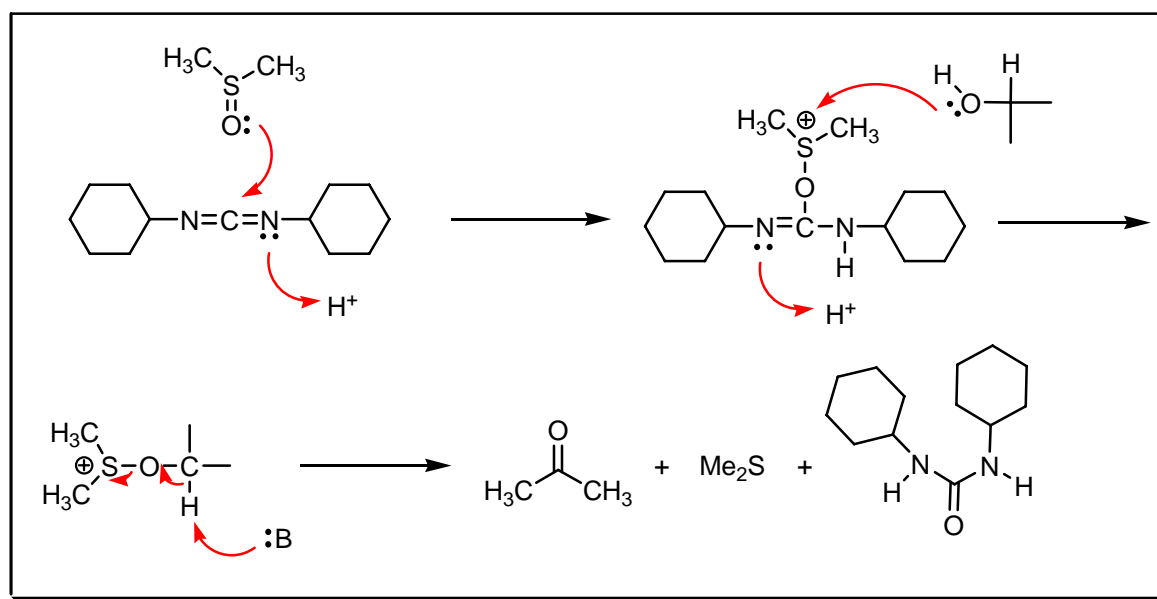
## PFITZNER – MOFFATT OXIDATION

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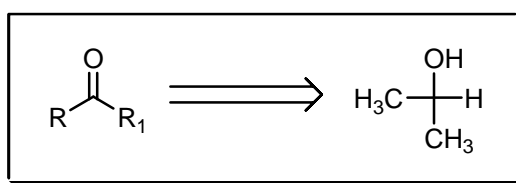
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The mild oxidation of alcohols to ketones or aldehydes using DCC-DMSO. Phenyl dichlorophosphate has been shown to be an efficient DMSO-activating agent in this oxidation. See also **Anelli, Ball – Goodwin – Morton, Collins, Corey – Kim, Corey – Schmidt, Corey – Suggs, David – Thieffry, Delépine, Dess – Martin, Einhorn** oxidation, **Fétizon**, **Jones** oxidation, **Ley, Maurer – Drefahl, Mukaiyama** oxidation, **Nicolaou, Oppenauer, Parikh – von Doering, Pinnick, Sarett, Swern** and **Uemura** reactions.

## REFERENCES :

**March** : 1193

**Smith – March** : 1516

**Smith** : 235

**Smith 2<sup>nd</sup>** : 206

**Houben – Weyl** : E11, 852

**Org. React.** : 39, 297

**Org. Synth.** : 47, 25

**Org. Synth. Coll. Vol.** : 5, 242

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2) W.W. Epstein; F.W. Sweat, *Chem. Rev.*, 1967, **67**, 247.

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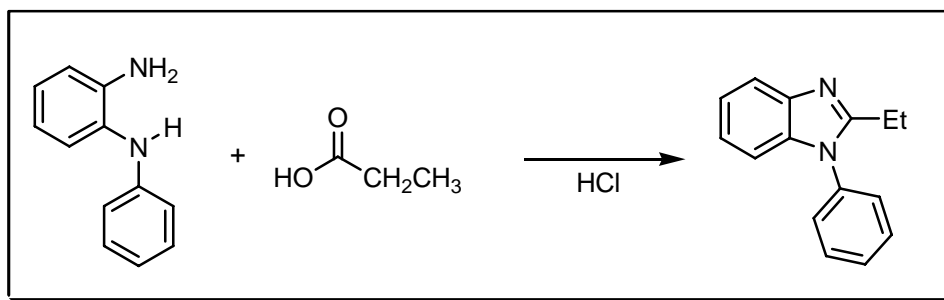
**COMMENTS :**

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## PHILLIPS – LADENBURG RING-CLOSURE

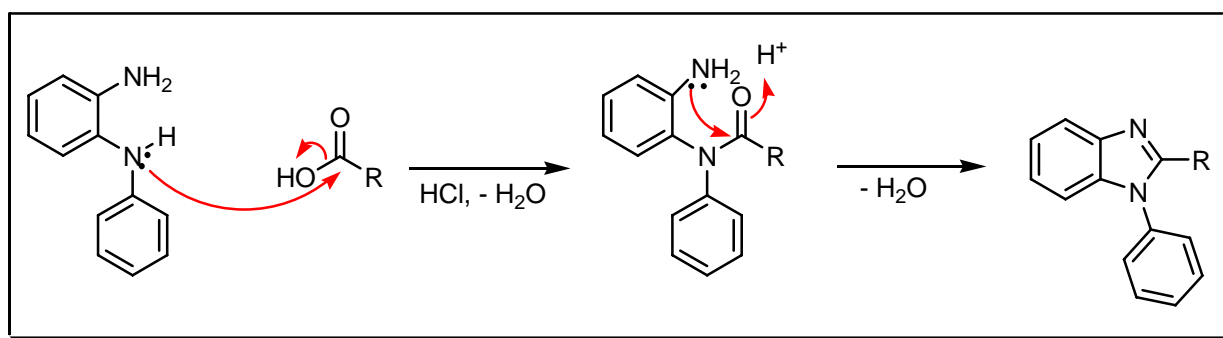
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**EXAMPLE :**

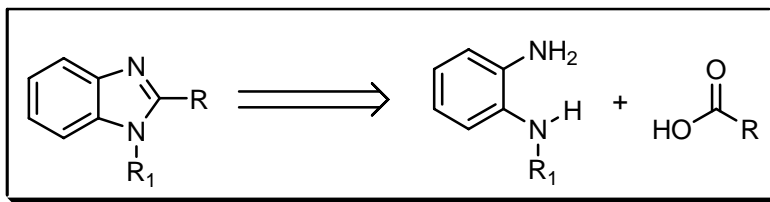


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**MECHANISM :**



## DISCONNECTION :



## NOTES :

The formation of benzimidazole starting from mono- or disubstituted *N*-acyl-*o*-diamine with substituted aliphatic carboxylic acids (no amino acids).

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## REFERENCES :

Houben – Weyl : E8c, 232, 270

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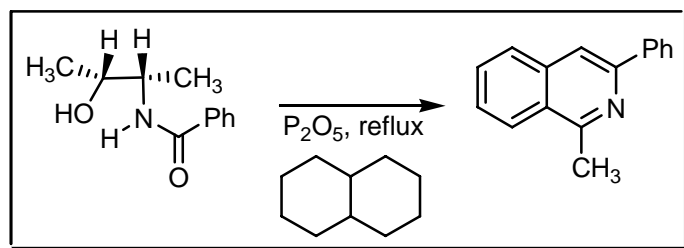
- 1) A. Ladenburg, *Ber. Dtsch. Chem. Ges.*, 1875, **8**, 677.
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  - 6) T. Fonseca; B. Gigante; T.L. Gilchrist, *Tetrahedron*, 2001, **57**, 1793.
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## COMMENTS :

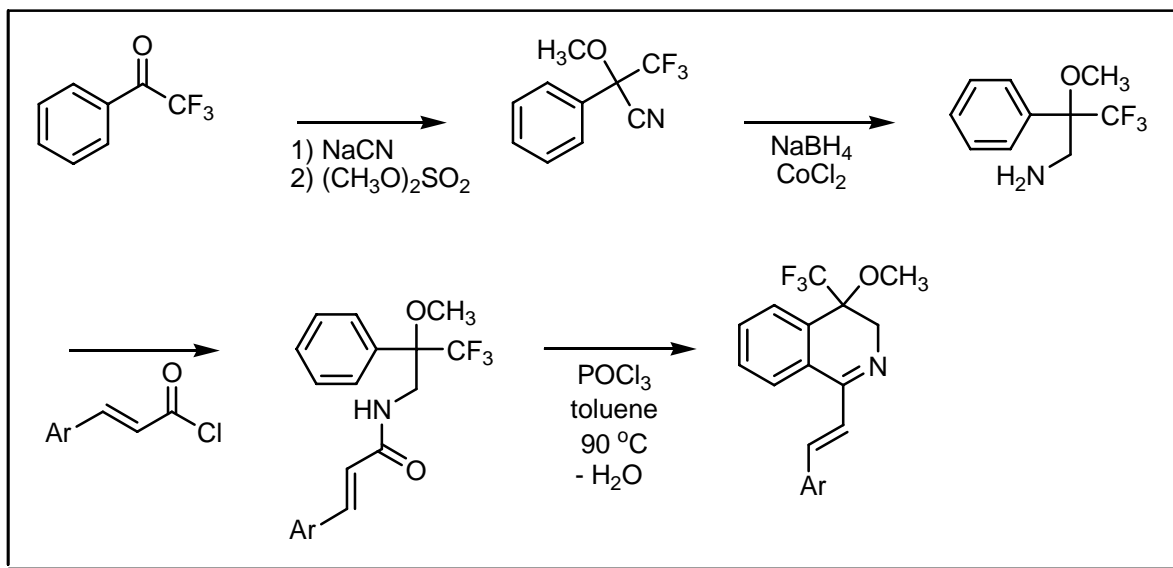
## PICTET – GAMS ISOQUINOLINE SYNTHESIS

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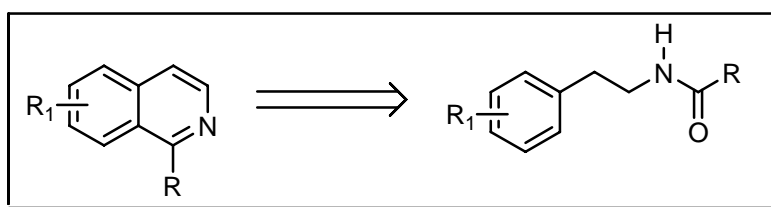
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The isoquinolines synthesis from phenethylamides, phenanthridine from *o*-acylaminobiaryl with POCl<sub>3</sub>, SnCl<sub>4</sub>. Sometimes not the expected product is obtained, as shown in the mechanism scheme. This is a modification of the **Bischler – Napieralski** reaction. See also **Bamberger – Goldschmidt**, **Bischler – Napieralski**, **Bobbit**, **Bruckner**, **Larock** indole, **Pictet – Sprengler**, **Pomeranz – Fritsch**, **Simchen** and **Schlitter – Müller** ring-closure reactions.

## REFERENCES :

Houben – Weyl : E7a, 616, 624, 648

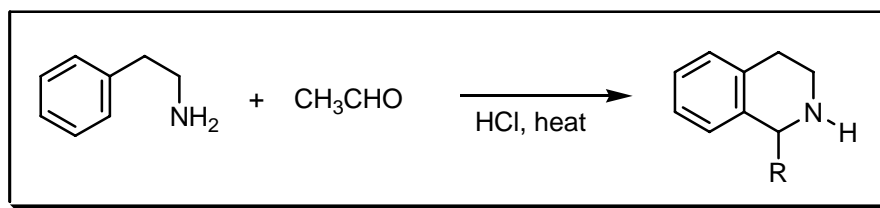
Org. React. : 6, 74

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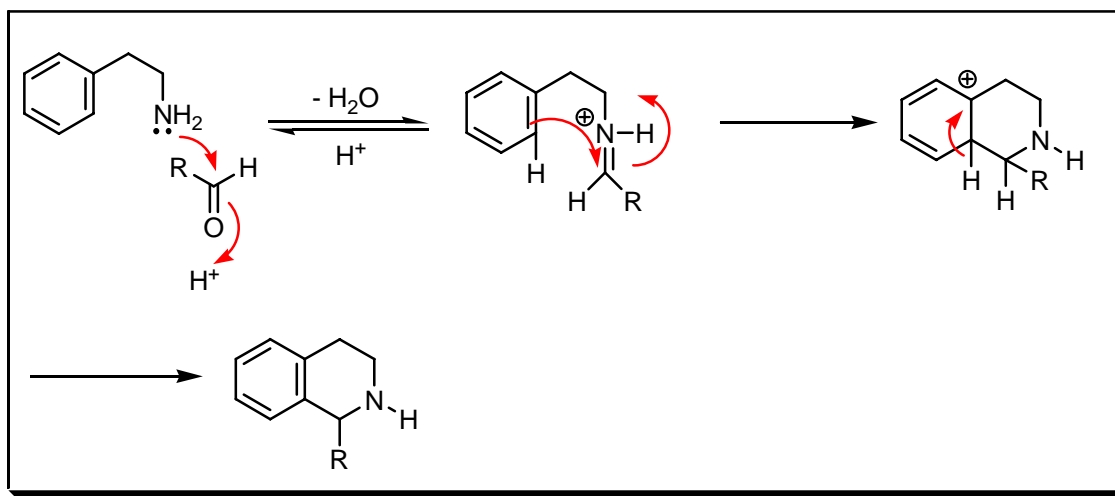
COMMENTS :

PICTET – SPENGLER ISOQUINOLINE SYNTHESIS

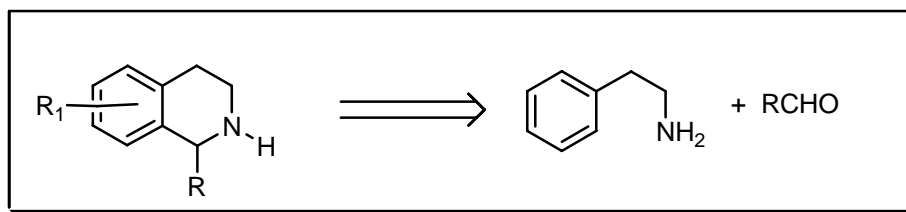
EXAMPLE :



MECHANISM :



DISCONNECTION :





## NOTES :

The condensation of a  $\beta$ -arylethyl amine with a carbonyl compound (*intramolecular* aminomethylation) to yield a 1,2,3,4-tetrahydroisoquinoline. This reaction also works with  $\beta$ -ethyl amine indoles. Asymmetric and superacid-catalysed versions of this reaction have been published, also an oxa-version has been reported. See also **Bamberger – Goldschmidt**, **Betti**, **Bischler – Napieralski**, **Bobbit**, **Bruckner**, **Eschweiler – Clarke**, **Larock** indole, **Mannich**, **Pictet – Gams**, **Pomeranz – Fritsch**, **Simchen** and **Schlitter – Müller** ring-closure reactions.

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## REFERENCES :

**Smith** : 1340

**Smith 2<sup>nd</sup>** : 1073, 1102

**Houben – Weyl** : **4/2**, 33; **E7a**, 612, 624; **E16d**, 1073, 1084

**Org. React.** : **6**, 151

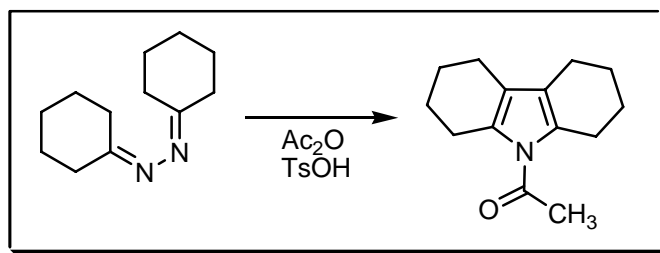
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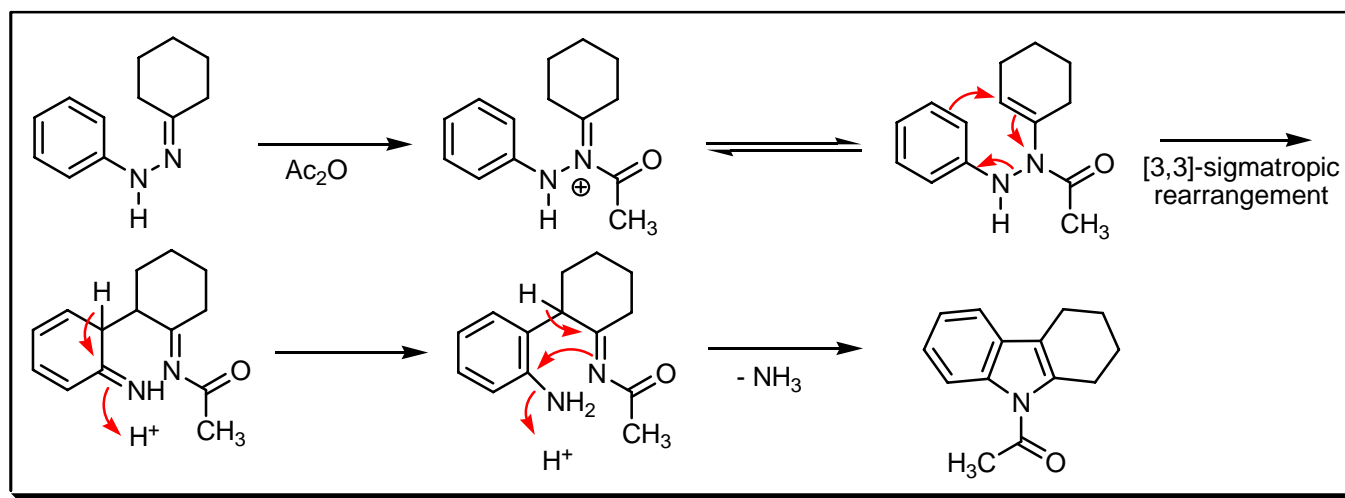
## COMMENTS :

## PILOTY – ROBINSON SYNTHESIS

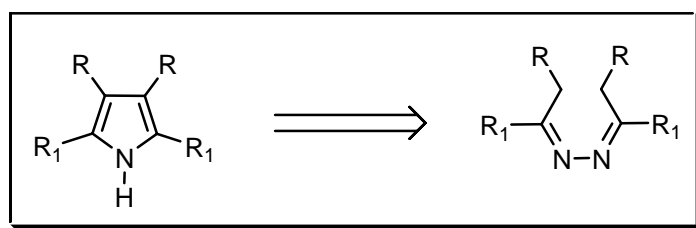
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The indole synthesis from azines of enolisable ketones *via* a [3,3]-sigmatropic rearrangement. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

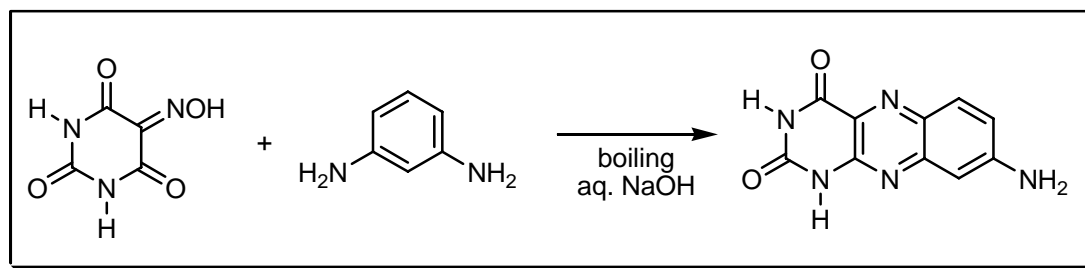
## REFERENCES :

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- 3) G.M. Robinson; R. Robinson, *J. Chem. Soc.*, 1918, **43**, 639.
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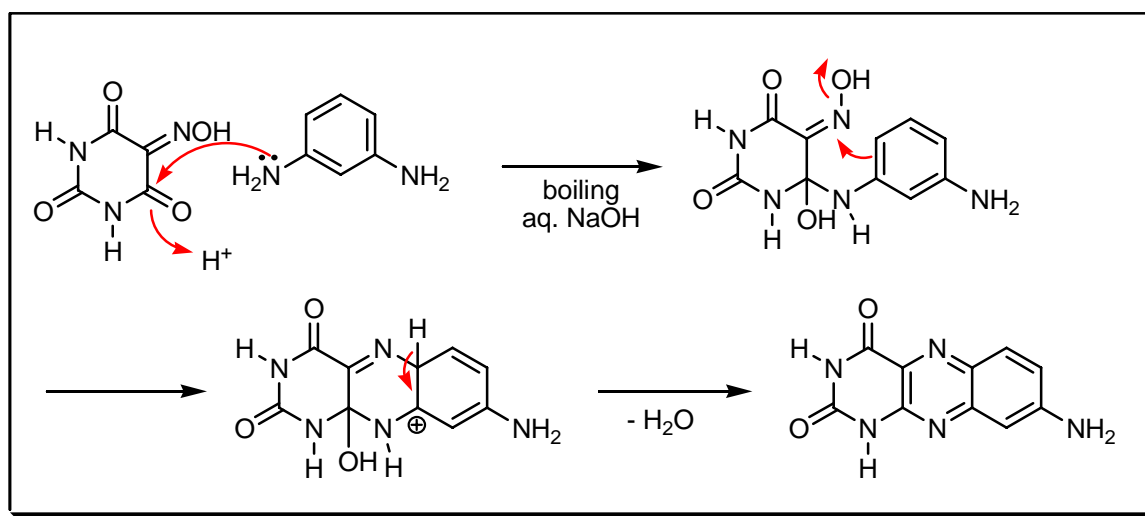
## COMMENTS :

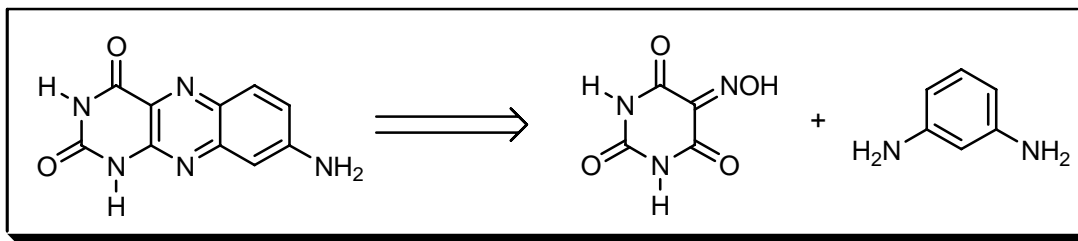
## PILOTY ALLOXAZINE SYNTHESIS

### EXAMPLE :



### MECHANISM :

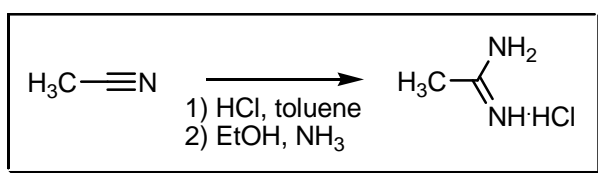


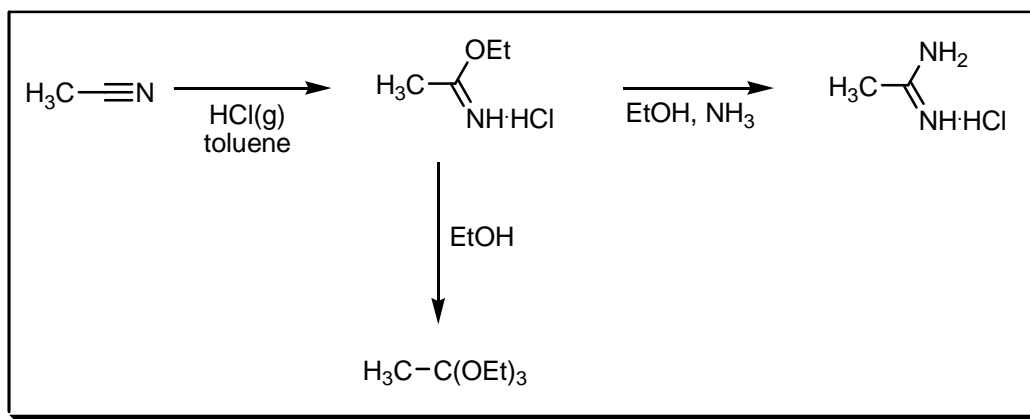
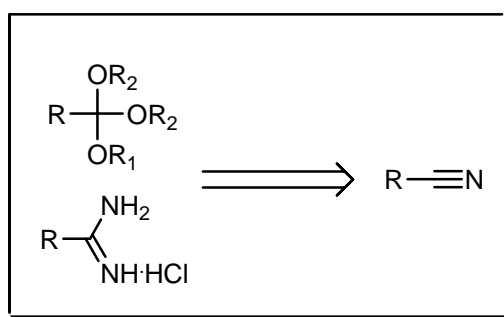
**DISCONNECTION :****NOTES :**

The ring-closure between 5-(hydroxyimino)pyrimidine-2,4,6-(1H, 3H, 5H)trione and benzene-1,3-diamine to afford a 8-aminobenzo[g]pteridine-2,4-(1H, 3H)-dione.

**REFERENCES :**

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**COMMENTS :****PINNER IMINOETHER SYNTHESIS****EXAMPLE :**

**MECHANISM :****DISCONNECTION :****NOTES :**

The synthesis of imino ethers, amidines and ortho esters from nitriles using hydrogen chloride in toluene. In the alcoholysis mixed ortho esters or amides can be obtained by using a different alcohol. See also **Garigipati** reaction.

**REFERENCES :**

**March** : 892

**Smith – March** : 1183

**Houben – Weyl** : **6/3**, 300; **8**, 539, 697

**Org. Synth.** : **8**, 1

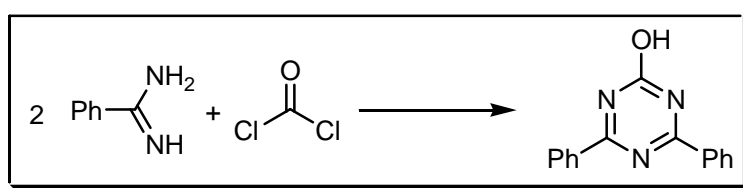
**Org. Synth. Coll. Vol.** : **1**, 5

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- 2) A. Pinner; F. Klein, *Ber. Dtsch. Chem. Ges.*, 1877, **10**, 1889.
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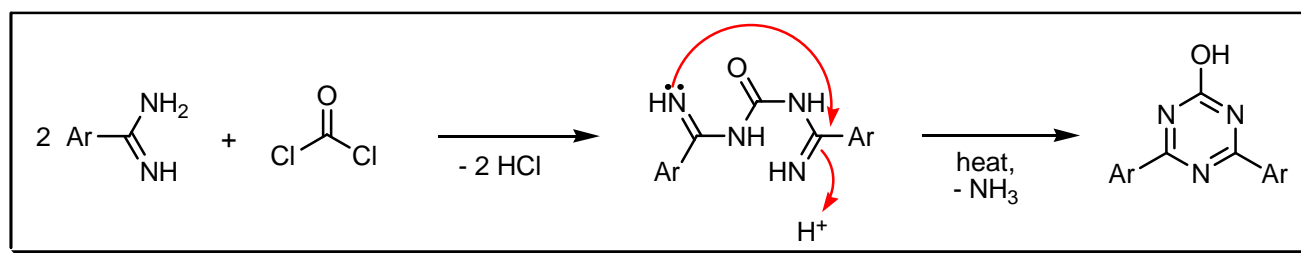
**COMMENTS :**

**PINNER TRIAZINE SYNTHESIS**

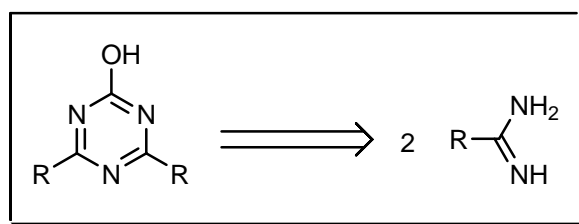
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

The formation of triazines from two arylamidines or  $\alpha$ -chlorinated amidines and phosgene. The intermediate *N,N'*-bisimidylurea cyclises after heating.

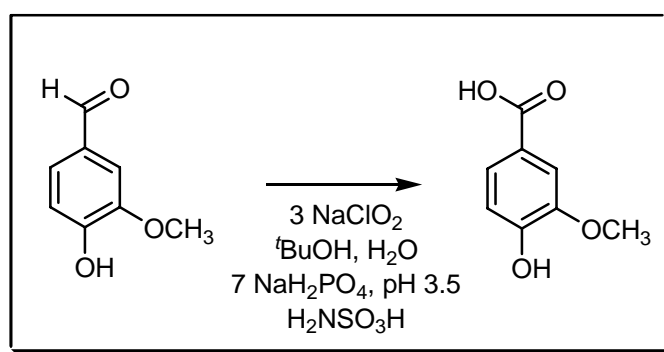
**REFERENCES :**

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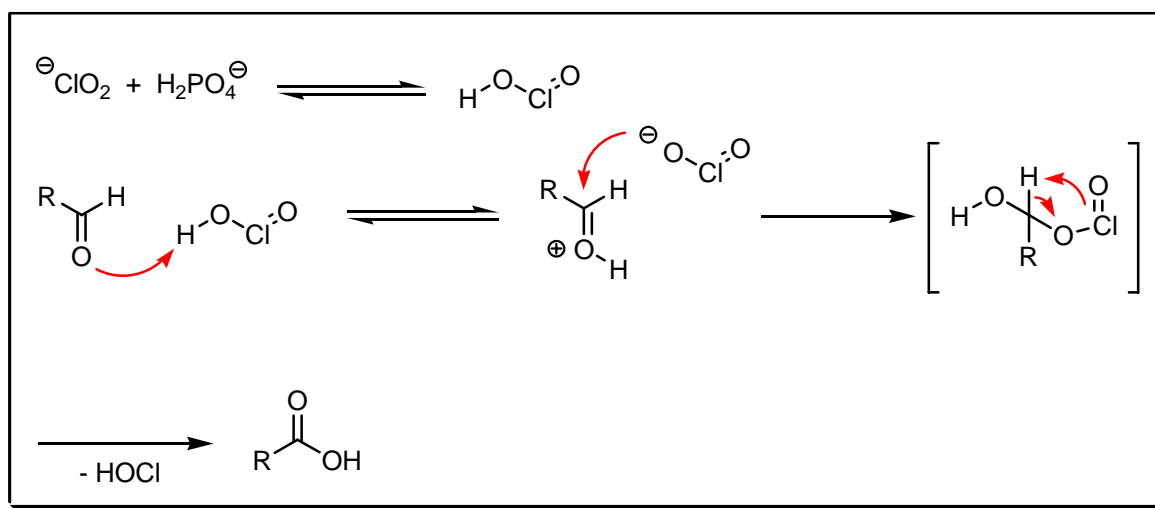
COMMENTS :

PINNICK OXIDATION

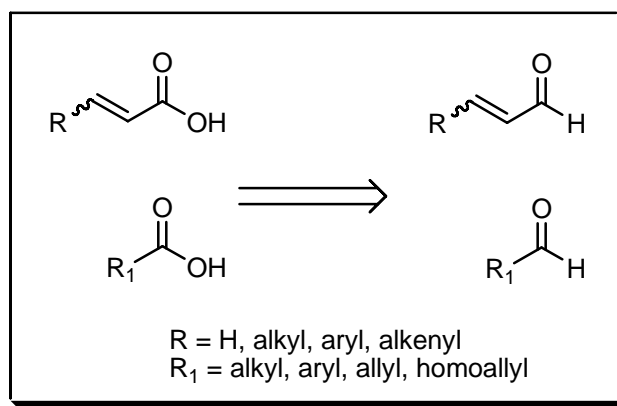
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The transformation of aldehydes (aliphatic, aromatic, saturated or unsaturated) to the corresponding carboxylic acid using sodium chlorite and a scavenger, 2-methyl-2-butene, hydrogen peroxide etc. See also **Anelli**, **Ball – Goodwin** – **Morton**, **Collins**, **Corey – Kim**, **Corey – Schmidt**, **Corey – Suggs**, **David – Thieffry**, **Delépine**, **Dess – Martin**, **Einhorn** oxidation, **Fétizon**, **Jones** oxidation, **Ley**, **Maurer – Drefahl**, **Mukaiyama** oxidation, **Nicolaou**, **Oppenauer**, **Parikh – von Doering**, **Pfitzner – Moffatt**, **Sarett**, **Swern** and **Uemura** reactions.

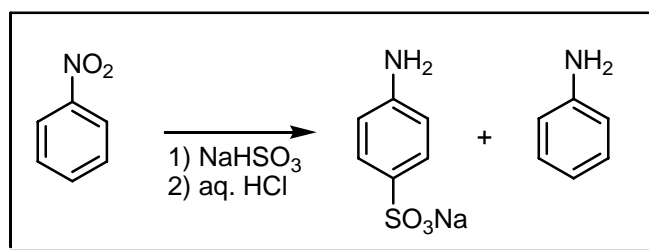
## REFERENCES :

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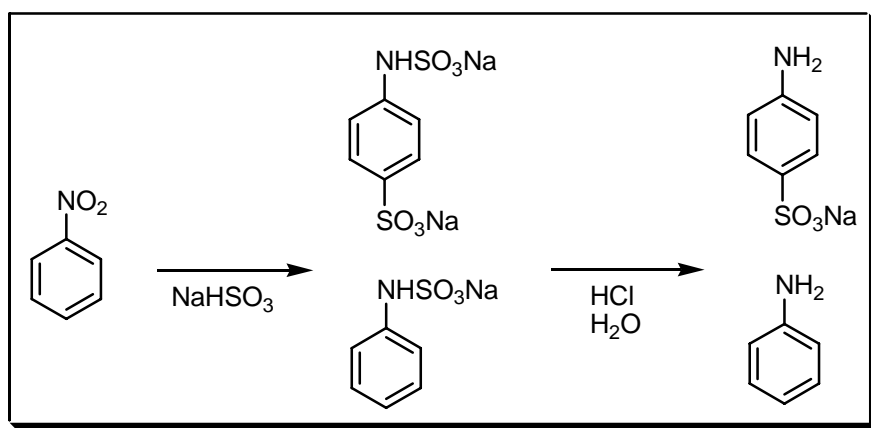
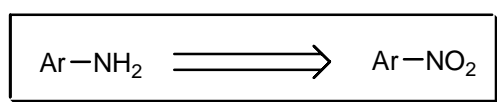
## COMMENTS :

## PIRIA REACTION

### EXAMPLE :





**MECHANISM :****DISCONNECTION :****NOTES :**

The formation of aromatic amines from aromatic nitro compounds *via* aminosulfonic acids using hydrogensulphite.

**REFERENCES :**

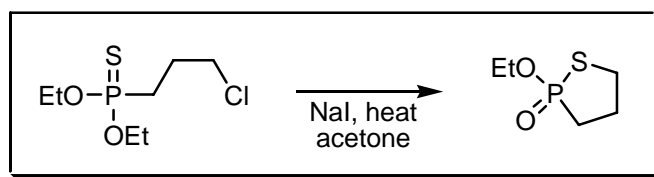
Houben – Weyl : 9, 521; 11/1, 457

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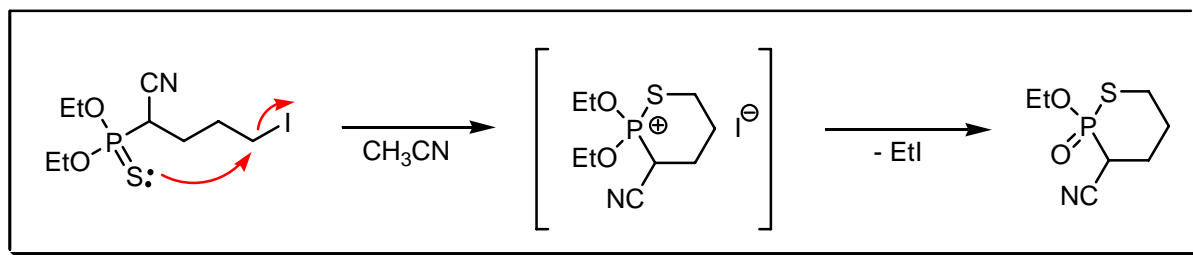
**COMMENTS :**

# PISHCHIMUKA REARRANGEMENT

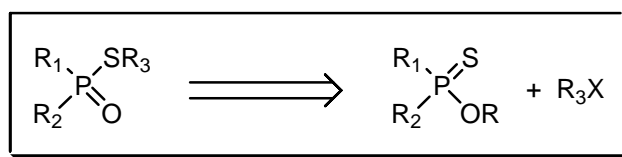
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The *inter*- and *intramolecular* S-alkylation of thiophosphoric acids, followed by dealkylation.

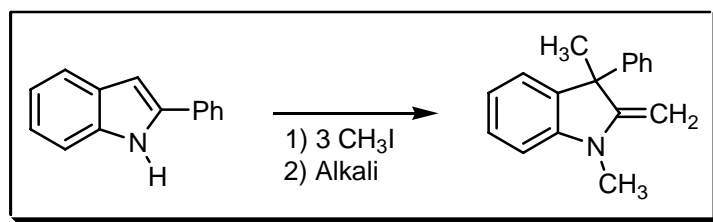
## REFERENCES :

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- 2) A.J. Burn; J.I.G. Cadogan, *J. Chem. Soc.*, 1961, 5532.
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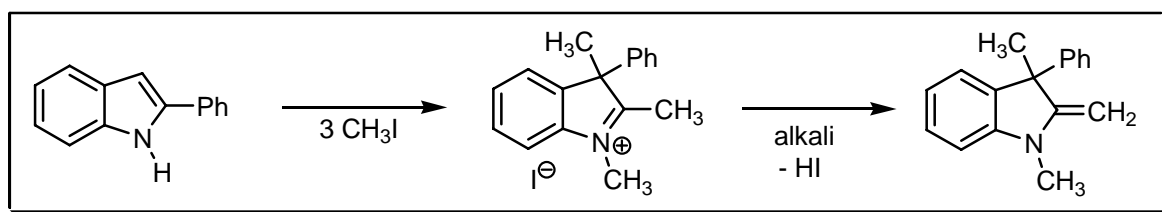
## COMMENTS :

# PLANCHER REARRANGEMENT

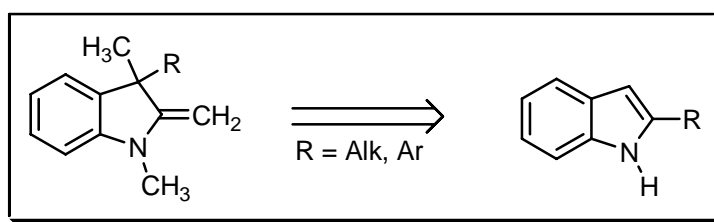
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The migration of an alkyl or phenyl group of indoles from C-2 to C-3 or C-3 to C-2 during methylation with methyl iodide. The reaction is also known as the **Plancher – Brunner** rearrangement. See also **Fischer – Steche** reaction.

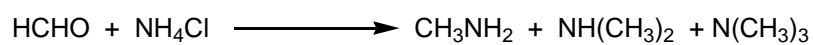
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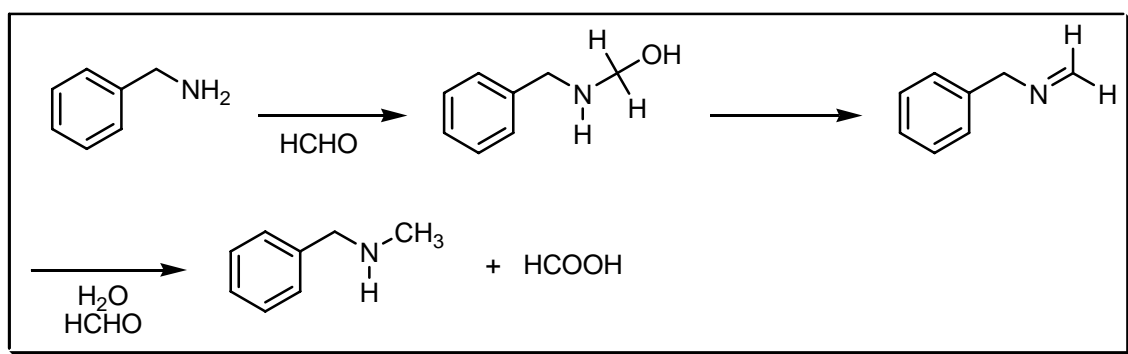
COMMENTS :

## PLÖCHL REACTION

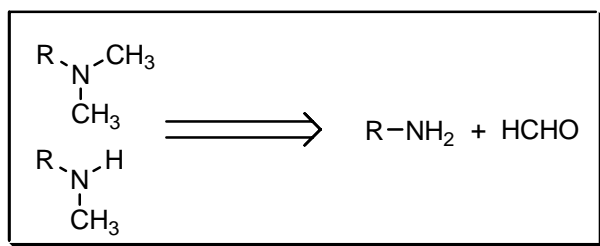
EXAMPLE :



MECHANISM :



DISCONNECTION :

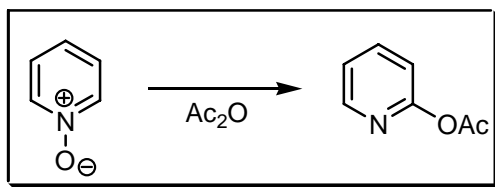


NOTES :

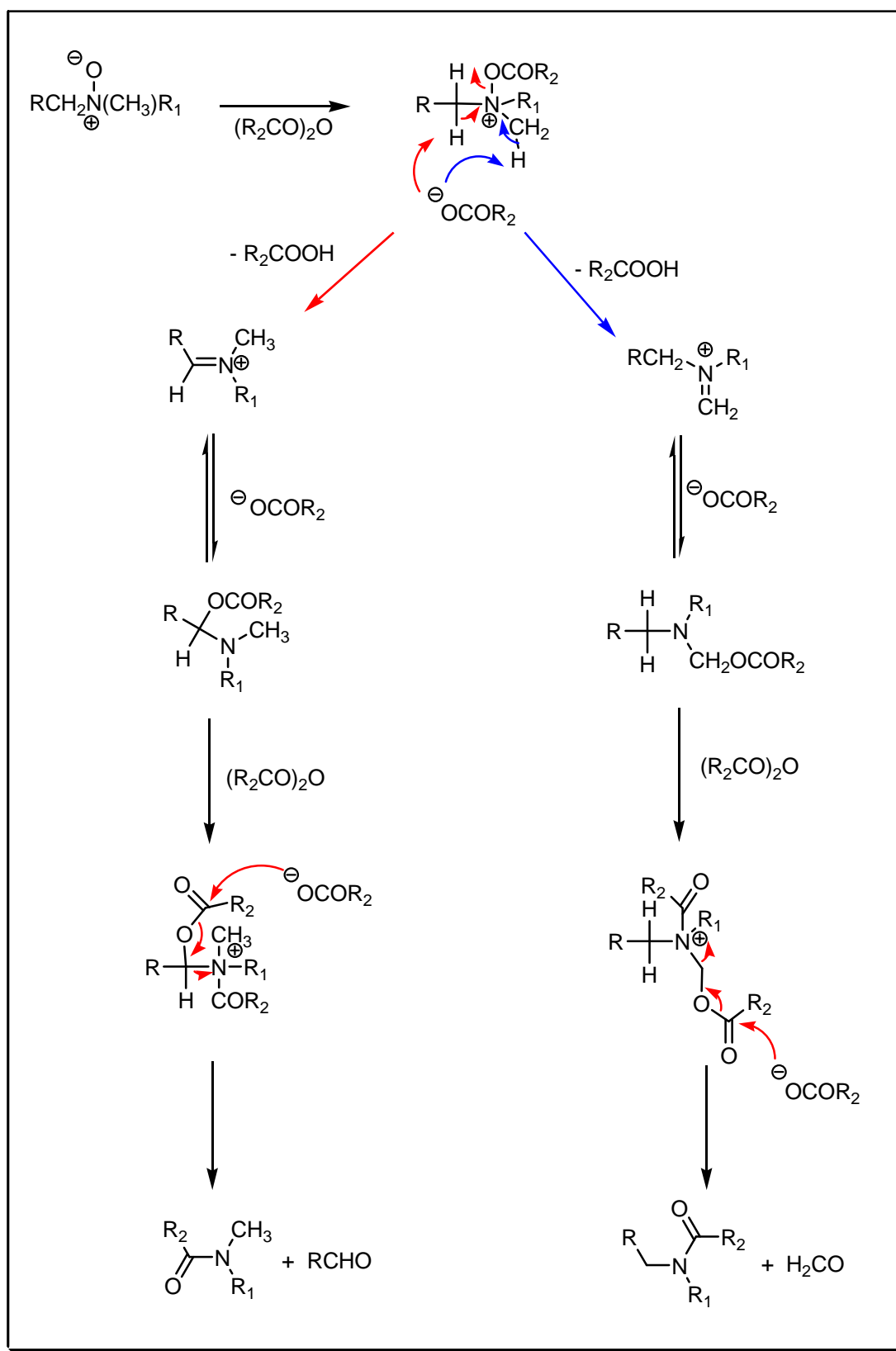
Formaldehyde reacts with amines or ammonium chloride to yield mono-, di-, or trimethylamine and other products. See also **Foster – Decker**, **Leuckart – Wallach**, **Pictet – Spengler** and **Sommelet** reactions.

**REFERENCES :**

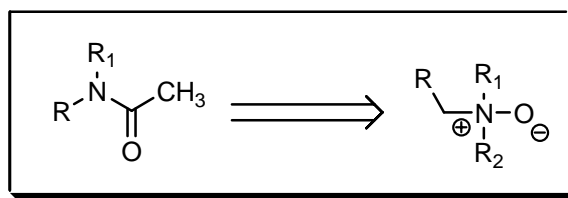
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- 

**COMMENTS :****POLONOVSKI REACTION****EXAMPLE :**

**MECHANISM :**



## DISCONNECTION :



## NOTES :

The conversion of heterocyclic *N*-oxides to  $\alpha$ -acetoxyheterocycles. The reaction proceeds via an iminium ion intermediate which becomes the stable reaction product when trifluoroacetic anhydride is employed. This modified procedure is commonly referred to as the **Potier – Polonovski** reaction. See also **Pummerer** reaction.

## REFERENCES :

Houben – Weyl : **E3**, 333; **E6a**, 691; **E16d**, 875

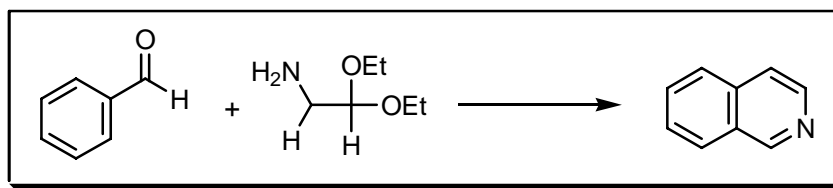
Org. React. : **39**, 85

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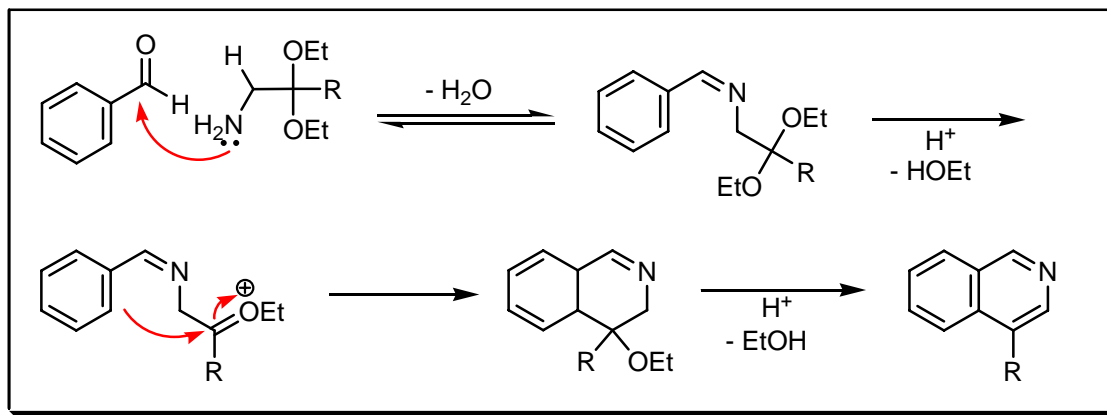
## COMMENTS :

## POMERANZ – FRITSCH REACTION

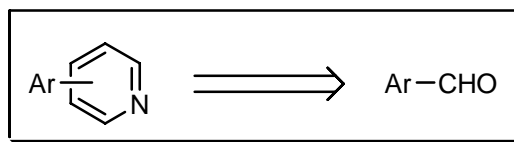
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

An aryl –aldehyde or –ketone is condensed with an aminoacetal to give an iminoacetal, which undergoes cyclisation on treatment with concentrated sulfuric acid or phosphorus oxychloride. The **Bobbitt** modification involves benzylaminoacetaldehyde. Oxazoles can be formed if there is an electron withdrawing group on the aromatic ring and concentrated sulphuric acid is used. See also **Bamberger – Goldschmidt**, **Bischler – Napieralski**, **Bobbitt**, **Bruckner**, **Larock** indole, **Pictet – Gams**, **Pictet – Sprengler**, **Simchen** and **Schlitter – Müller** ring-closure reactions.

### REFERENCES :

Smith : 1342

Smith 2<sup>nd</sup> : 1103

Houben – Weyl : E7a, 616, 624, 635, 638

Org. React. : 6, 191

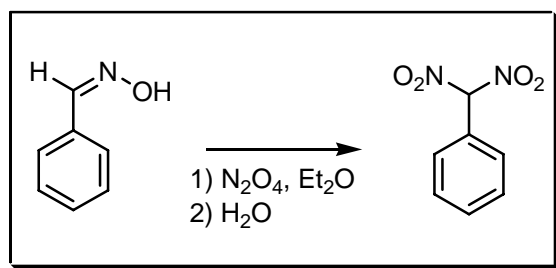


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- 2) P. Fritsch, *Ber. Dtsch. Chem. Ges.*, 1893, **26**, 419.
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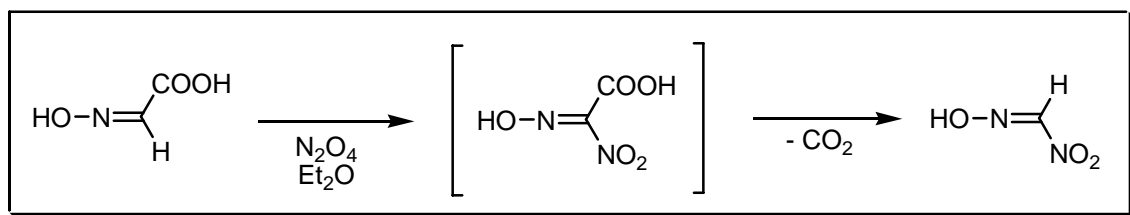
**COMMENTS :**

**PONZIO REACTION**

**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

Benzaldoximes react with nitrogen tetroxide in diethyl ether to yield mainly dinitrophenylmethanes. Other arylaldoximes and ketoximes react similarly. **Suzuki** *et al.* improved the **Ponzio** reaction.

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## REFERENCES :

Houben – Weyl : **10/1**, 113; **E14b**, 395

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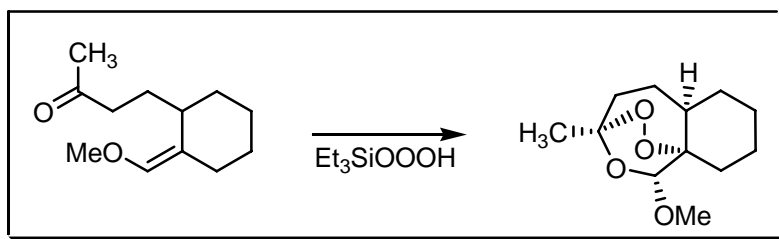
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## COMMENTS :

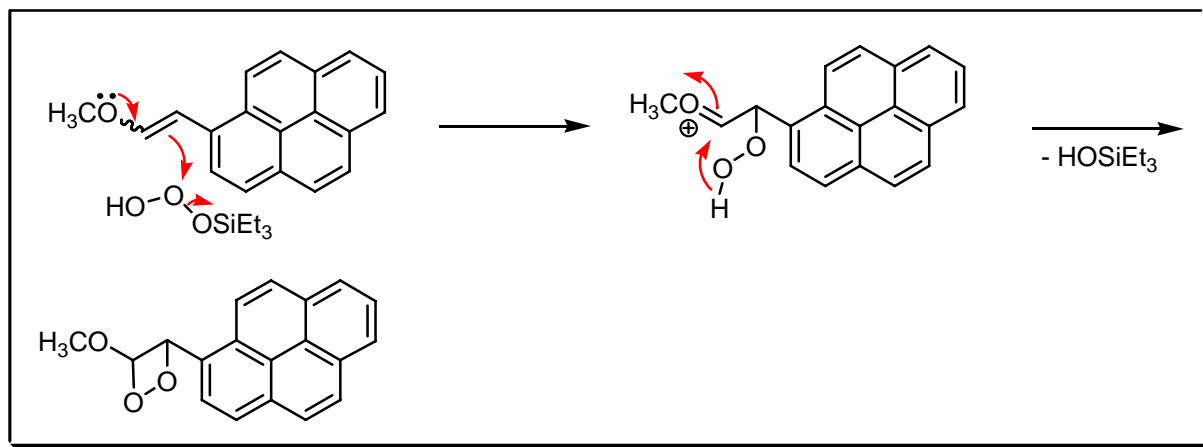
## POSNER TRIOXANE SYNTHESIS

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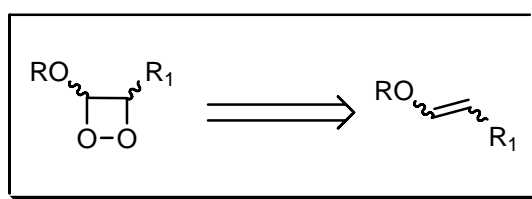
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Triethylsilyl hydrotrioxide reacts with electron-rich olefins to give dioxetanes that react *intramolecularly* with a keto group in the presence of *tert*-butyldimethyl silyl triflate to afford 1,2,4-trioxanes.

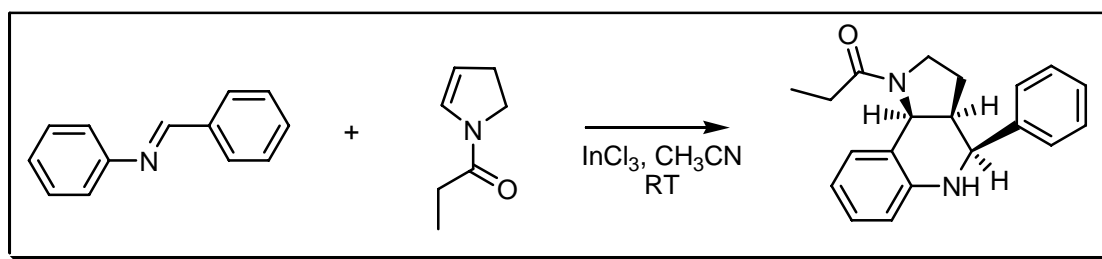
### REFERENCES :

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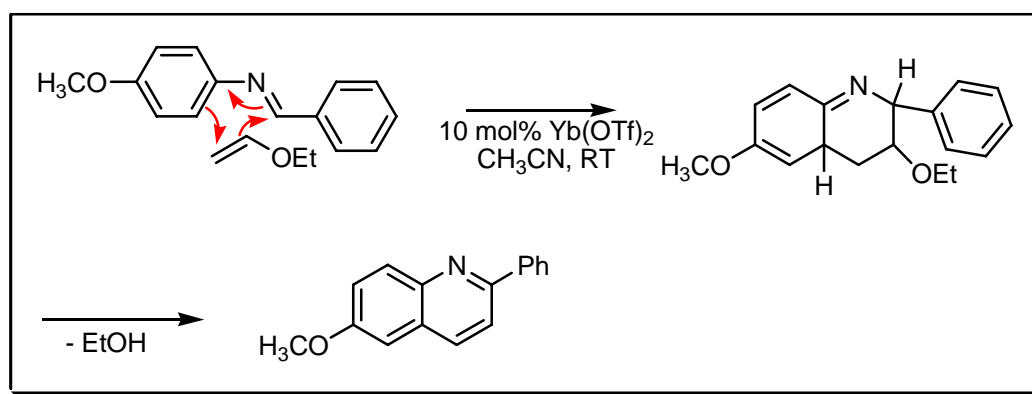
### COMMENTS :

# POVAROV REACTION

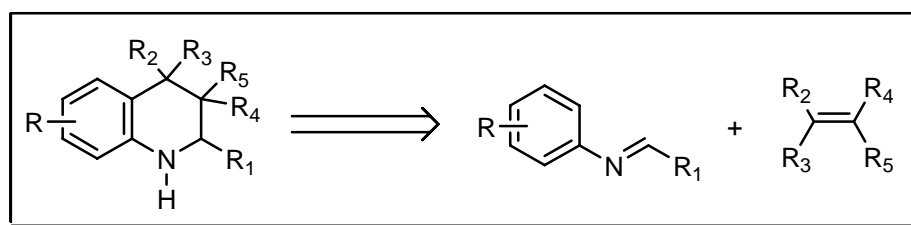
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The imino **Diels – Alder** reaction of imines derived from aromatic amines with electron-rich alkenes. Initially, boron trifluoride etherate was used as a catalyst but more recent developments are using milder Lewis acid catalysts. See also **Diels – Alder** reaction.

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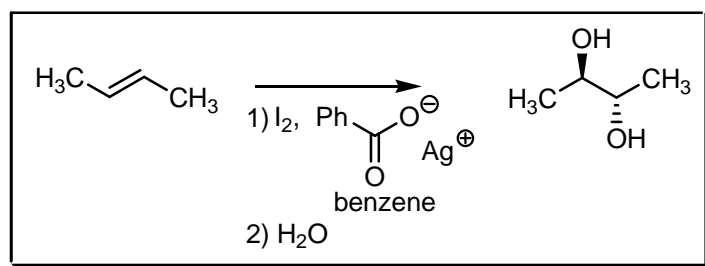
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**COMMENTS :**

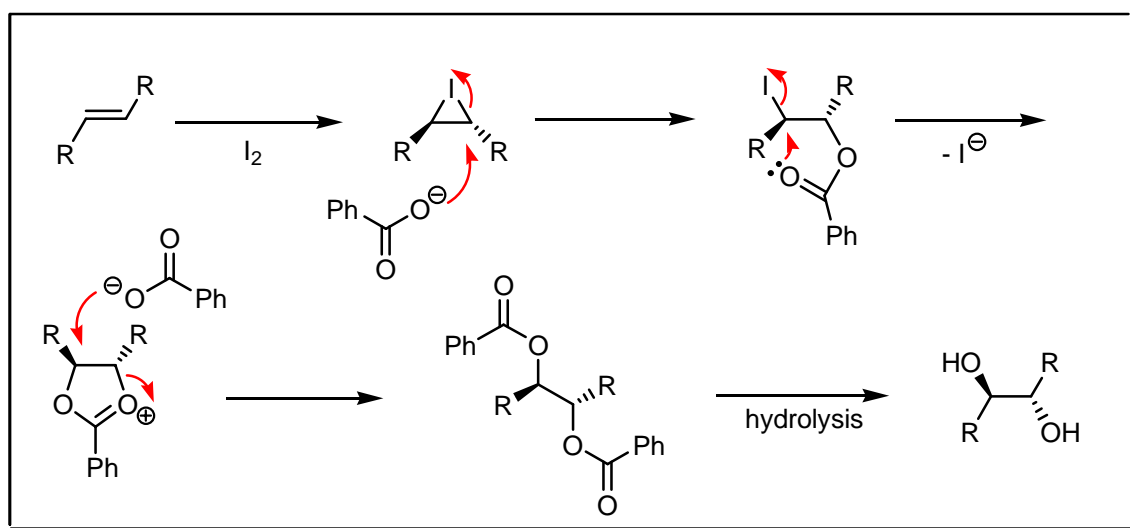
## PRÉVOST REACTION

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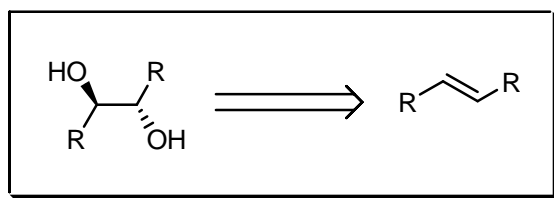
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

An olefinic compound on treatment with silver iodine dibenzoate or diacetate in a dry solvent (benzene), yields by overall *trans*-addition the di-ester of the corresponding glycol. See also **Birnbaum – Simonini**, **Borodine – Hunsdiecker**, **Milas**, **Sharpless** dihydroxylation and **Woodward** *cis*-hydroxylation reactions.

## REFERENCES :

**March** : 823

**Smith – March** : 1049

**Smith** : 289

**Smith 2<sup>nd</sup>** : 254

**Org. React.** : **9**, 350

**Houben – Weyl** : **5/4**, 543

**Org. Synth.** : **59**, 169

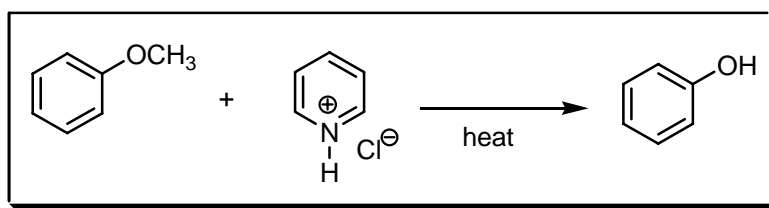
**Org. Synth. Coll. Vol.** : **6**, 348

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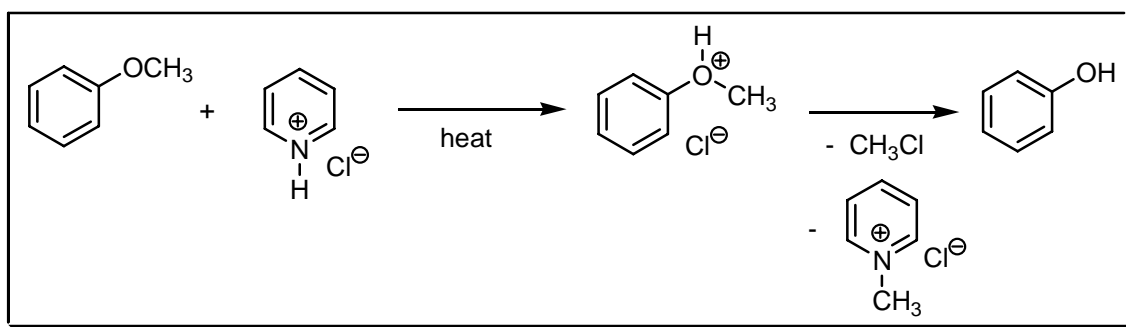
## COMMENTS :

## PREY REACTION

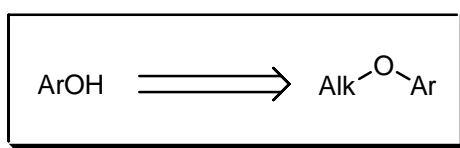
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The arylalkylether bond break due to prolonged heating ( $180 - 200^\circ\text{C}$ ) with water-free pyridine hydrogen chloride. See also **Gustus** cleavage, **Mann** dealkylation and **Stoermer** dealkylation.

### REFERENCES :

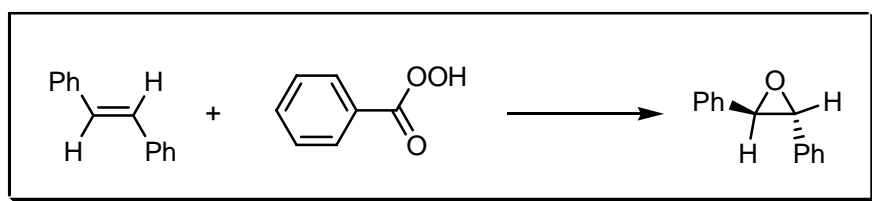
Houben – Weyl : 6/3, 151

- 1) A. Klemenc, *Ber. Dtsch. Chem. Ges.*, 1916, **49**, 1371.
- 2) A. Klemenc, *Ber. Dtsch. Chem. Ges.*, 1916, **49**, 1703.
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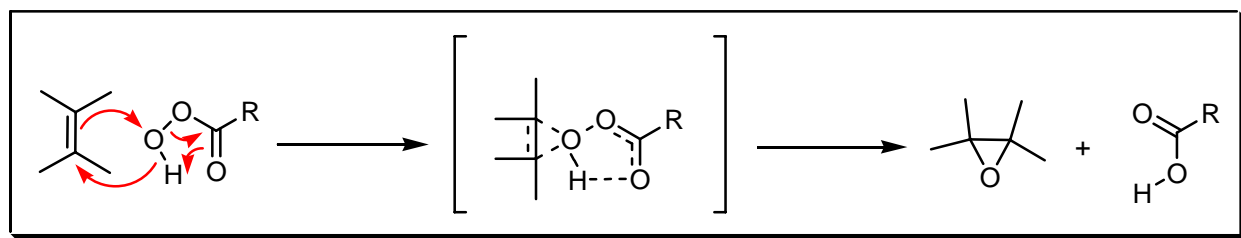
### COMMENTS :

# PRILESCHAJEW REACTION

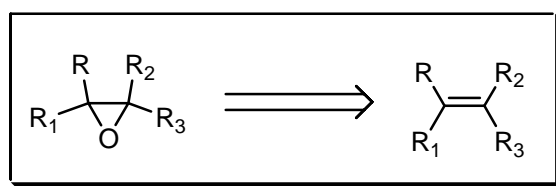
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The epoxidation of olefins with organic peracids. Allenes can give spiro dioxides. See also **von Baeyer – Villiger**, **Buchner – Curtius – Schlotterbeck**, **Corey – Chaykovsky**, **Jacobsen – Katsuki**, **Juliá – Colonna**, **Katsuki – Sharpless**, **Mukaiyama – Yamada**, **Shi** and **Weitz – Scheffer** reactions.

## REFERENCES :

**March** : 826

**Smith – March** : 1052

**Smith** : 220

**Smith 2<sup>nd</sup>** : 234

**Houben – Weyl** : 6/3, 385

**Org. React.** : 7, 378; 9, 332

**Org. Synth.** : 8, 102; 38, 83; 49, 13

**Org. Synth. Coll. Vol.** : 1, 494; 4, 860; 5, 191

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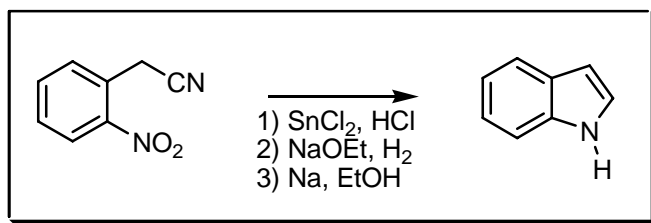
- 3) G.B. Payne, *J. Org. Chem.*, 1961, **26**, 250.  
4) I. Kaneti, *Tetrahedron*, 1986, **42**, 4017.  
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**COMMENTS :**

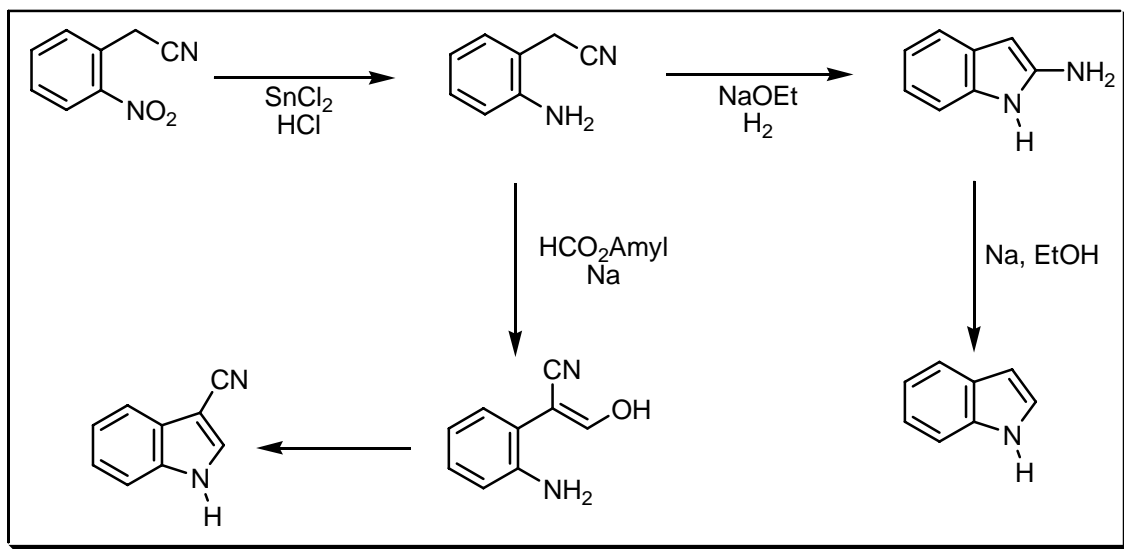
## PSCHORR – HOPPE SYNTHESIS

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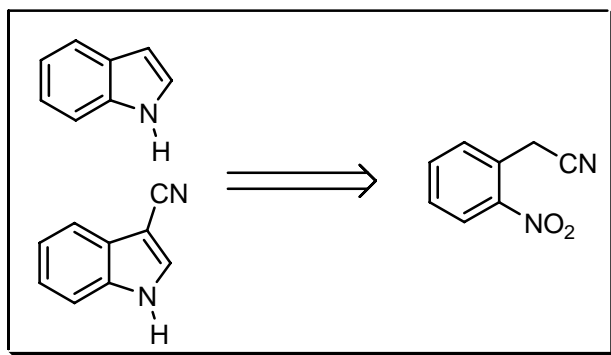
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

o-Nitrophenylacetonitrile is reduced by stannous chloride and hydrochloric acid to the corresponding amine, which when treated with boiling ethanolic sodium ethoxide in an atmosphere of hydrogen yields 2-aminoindole. The latter on treatment with sodium in ethanol yields an indole. Alternatively, the amine may be treated with sodium in amyl formate to give 3-cyanoindole and hence the indole acid. See also **von Baeyer – Emmerling, von Baeyer – Jackson, Bailey – Liebeskind, Bartoli, Bischler – Möhlau, Cadogan – Sundberg, Couture, Engler, Feldman indole, Fischer indole, Foulds – Robinson, Fukuyama, Fürstner, Gassman indole, Grandberg, Hegedus, Hemetsberger – Knittel, Inanaga, Iwao, Japp – Murray, Julia, Kihara, Larock indole, Leimgruber – Batcho, Lipp, Madelung indole, Magnus, Martin, Montevicchi, Mori – Ban, Murphy, Naito, Natsume, Nenitzescu indole, Piloty – Robinson, Reissert indole, Saegusa indole, Schmid, Smith, Sugasawa indole, Sundberg, Thiele – Dimroth, Thyagarajan, Watanabe heterocyclisation, Watanabe indole, Weerman indole, Wender, Widman, Yamamoto indole-1, Yamamoto indole-2 and Yurovskaya reactions.**

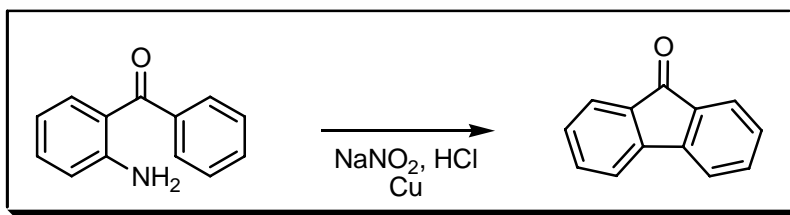
## REFERENCES :

- 1) R. Pschorr; G. Hoppe, *Ber. Dtsch. Chem. Ges.*, 1910, **43**, 2543.
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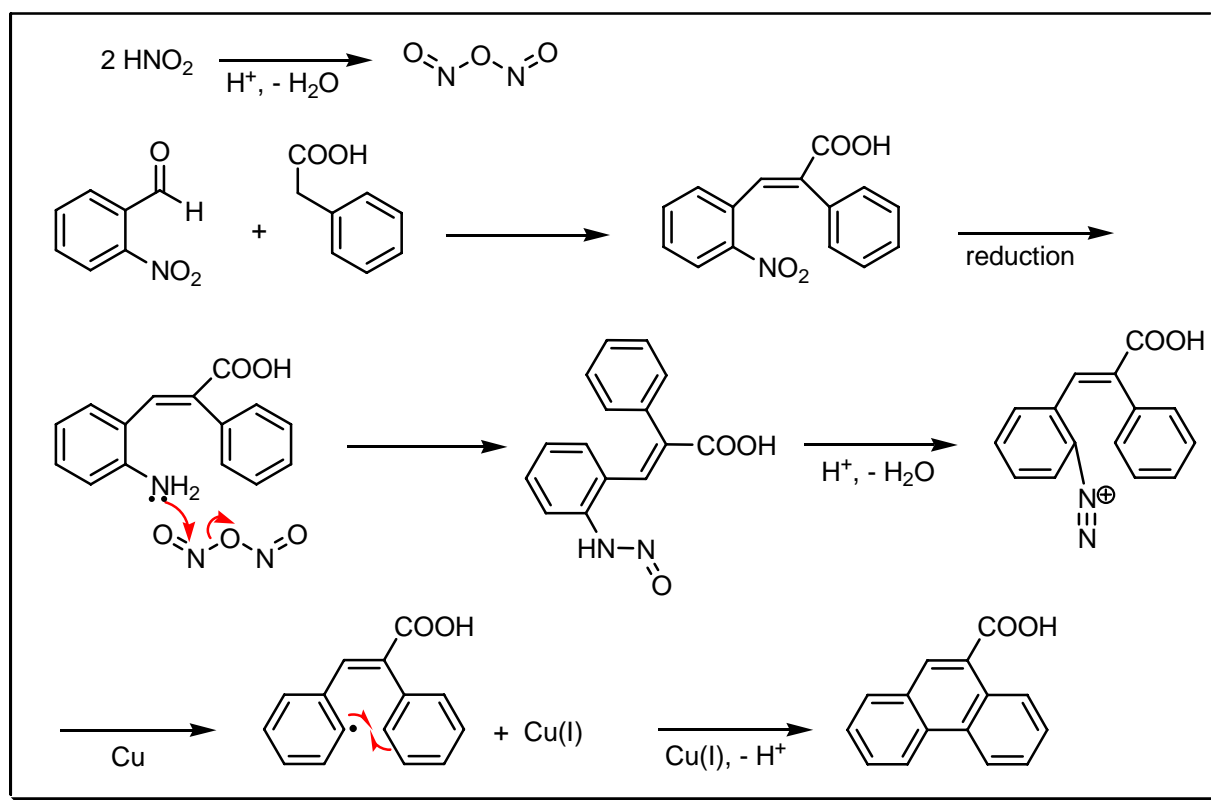
## COMMENTS :

## PSCHORR SYNTHESIS

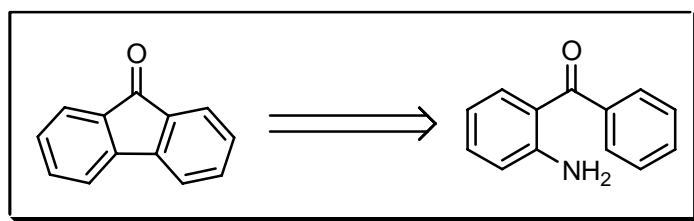
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The formation of polycyclics from diazonium salt. *Intramolecular* copper-catalysed arylation of diazonium salts. See also **Borsche – Koelsch**, **Gomberg – Bachmann – Hey**, **Graebe – Ullmann** fluorene, **von Richter** cinnoline, **Ullmann** fluorene and **Widman – Stoermer** reactions.

## REFERENCES :

March : 715

Smith – March : 929

Smith : 1436

Smith 2<sup>nd</sup> : 1185

Houben – Weyl : E7b, 106

Org. React. : 2, 224; 9, 409

Science of Synthesis : 10, 140, 214, 225

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4) R.I. Duclos, jr.; J.S. Tung; H. Rapoport, *J. Org. Chem.*, 1984, **49**, 5243.

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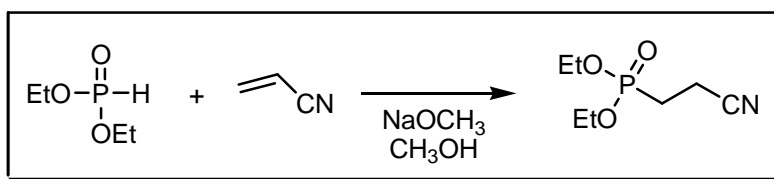
7) S. Karady; J.M. Cummins; J.J. Dannenberg; E. del Rio; P.G. Dormer; B.F. Marune; R.A. Reamer; T.L. Sordo, *Org. Lett.*, 2003, **5**, 1175.

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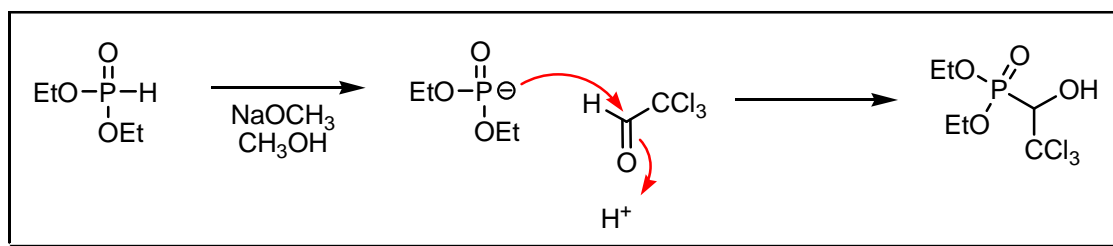
## COMMENTS :

## PUDOVIK REACTION

### EXAMPLE :



### MECHANISM :



## NOTES :

The addition of esters of organophosphorous compounds containing a labile P-H bond with alkenes, alkynes, activated carbonyls, imines, isocyanates, isothiocyanates, cyanides and isocyanides. The reaction progresses *via* a radical or (and) ionic mechanism. See also **Kabachnik – Fields** reaction.

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## REFERENCES :

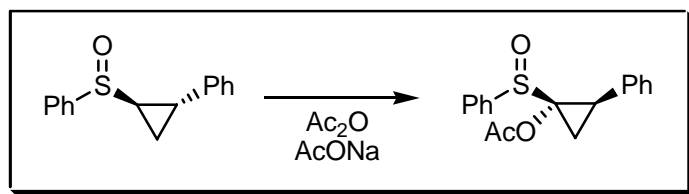
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  - 10) L. Tedeschi; D. Enders, *Org. Lett.*, 2001, **3**, 3515.
  - 11) K. Vercruysse-Moreira; C. Déjugnat; G. Etemad-Moghadam, *Tetrahedron*, 2002, **58**, 5651.
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## COMMENTS :

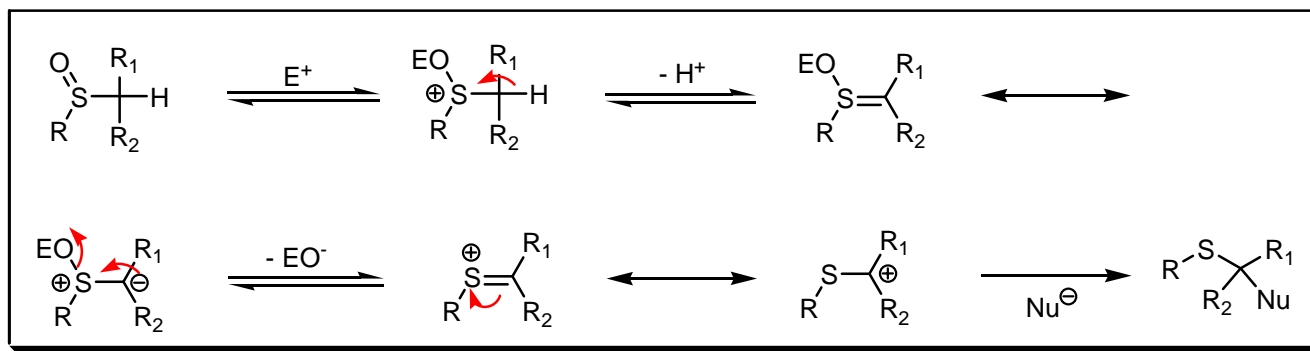
## PUMMERER REARRANGEMENT

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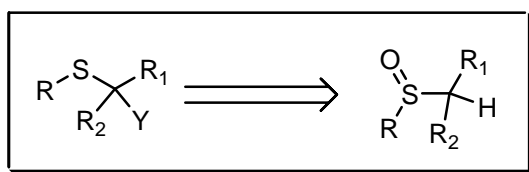
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

There is a similarity to the **Nef** reaction in that there is an internal oxidation – reduction process. There are several types of **Pummerer** reactions, an ‘interrupted’ **Pummerer**, the ‘non-oxidative’ **Pummerer** (NOPR), which allows for a one-pot replacement of a sulfinyl group with a hydroxyl in a stereospecific S<sub>N</sub>2-manner and the ‘non-oxidative’ chloro-**Pummerer** reaction (NOCPR). Seleno- and sila-**Pummerer** rearrangements are also known. See also **Nef**, **Polonovski**, **Sommelet – Hauser**, **Stevens** rearrangement and **Vilsmeier – Haack – Viehe** reactions.

## REFERENCES :

**March** : 1236

**Smith – March** : 1566

**Smith** : 239

**Smith 2<sup>nd</sup>** : 203

**Houben – Weyl** : **E3**, 313, 583; **E6a**, 581; **E8c**, 159; **E7a**, 232, 237; **E11**, 323, 1189; **E15**, 889; **E16b**, 879

**Org. React.** : **40**, 157

**Science of Synthesis** : **10**, 102, 523, 612

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**COMMENTS :**

**R**



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## H

HENKEL PROCESS · 1413  
HOCKET – HUDSON OXIDATION · 1489

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## R

RADZISZEWSKI AMIDE SYNTHESIS · 1409  
RAECKE PROCESS · 1410  
RAMBERG – BÄCKLUND REACTION · 1413  
RANJORWA SYNTHESIS · 1415  
RAPHAEL SYNTHESIS · 1416  
RAPP – STOERMER CONDENSATION · 1418  
RAPSON TRIPHENYLENE REACTION · 1420  
RASCHIG PHENOL PROCESS · 1421  
RASODA SYNTHESIS · 1422  
RATHKE ESTER SYNTHESIS · 1423  
RAUHUT – CURRIER REACTION · 1424  
RAUTENSTRAUCH REARRANGEMENT · 1426  
REED REACTION · 1428  
REETZ TITANIUM ALKYLATION · 1429  
REEVE SYNTHESIS · 1431  
REFORMATSKY REACTION · 1432  
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REISSERT – HENZE REACTION · 1440  
REISSERT INDOLE REACTION · 1442  
REMFY – HULL SYNTHESIS · 1443  
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ROSENMUND REACTION · 1481  
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ROWE REARRANGEMENT · 1487  
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RUPE REARRANGEMENT · 1492  
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RUŽIČKA REARRANGEMENT · 1498  
RYCHNOVSKY POLYOL SYNTHESIS · 1500

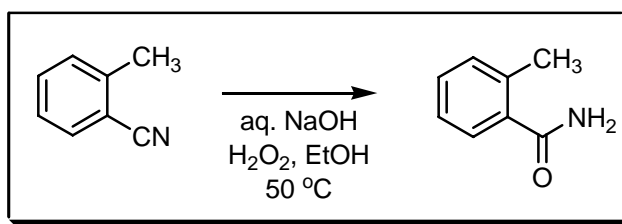
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## S

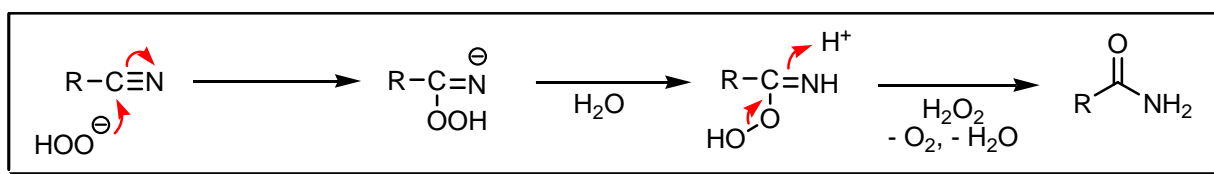
STORK – JUNG – ROBINSON ANNULATION · 1471

# RADZISZEWSKI AMIDE SYNTHESIS

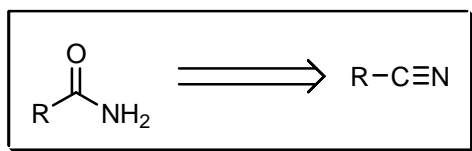
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Hydrogen peroxide in alkaline solution converts nitriles into amides. There are numerous procedures for this type of conversion. See also **Riehmshneider** reaction.

## REFERENCES :

March : 888

Smith – March : 1179

Org. Synth. : 13, 94; 16, 4

Org. Synth. Coll. Vol. : 2, 44, 586

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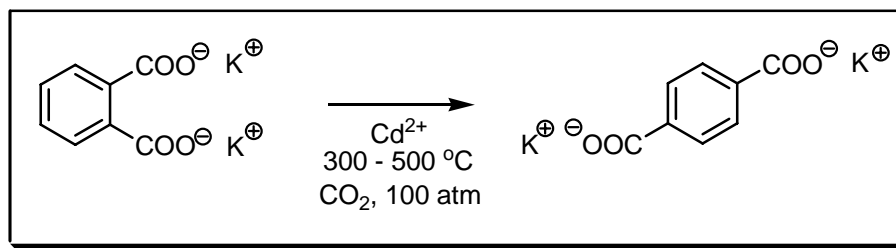
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COMMENTS :

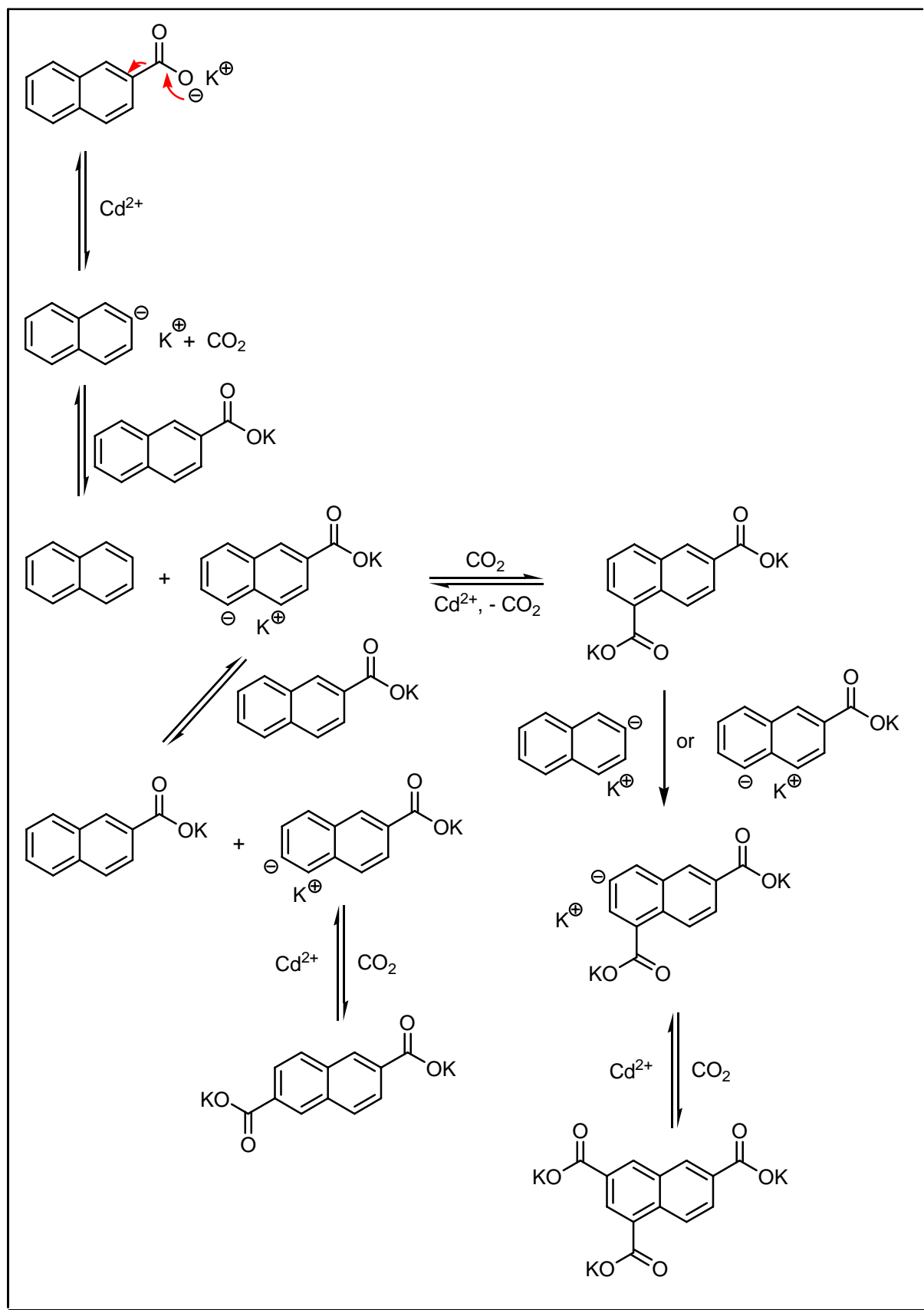
## RAECKE PROCESS

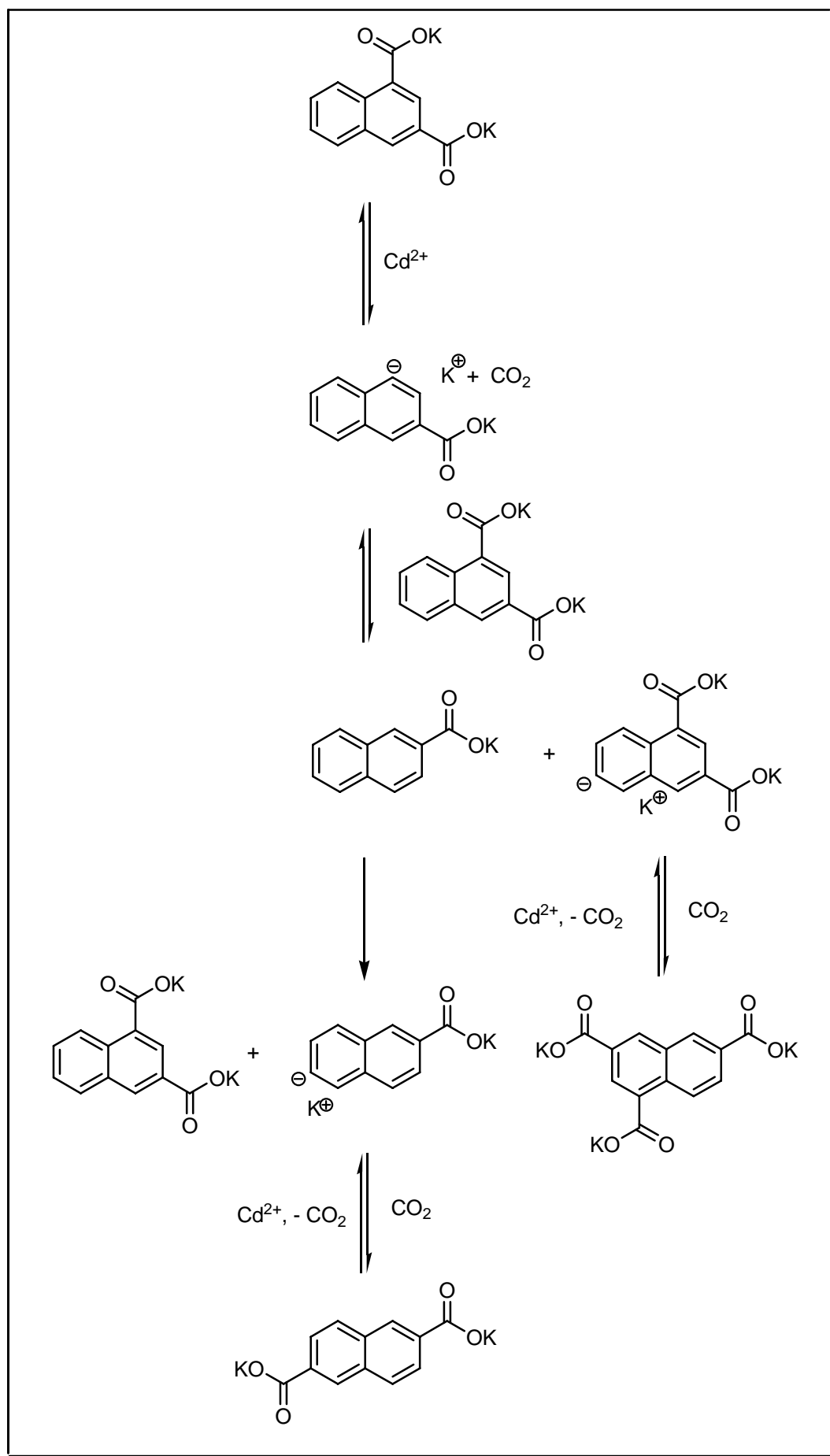
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EXAMPLE :

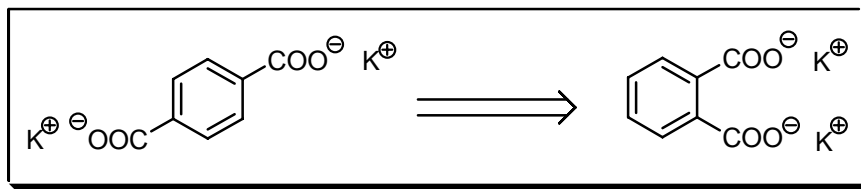


MECHANISM :





## DISCONNECTION :



## NOTES :

Industrial scale thermal rearrangement or disproportionation of alkaline salts of aromatic acids to symmetrical diacids in the presence of cadmium or other metallic salts. This reaction is also known as the **Henkel** process.

## REFERENCES :

**March** : 565

**Smith – March** : 733

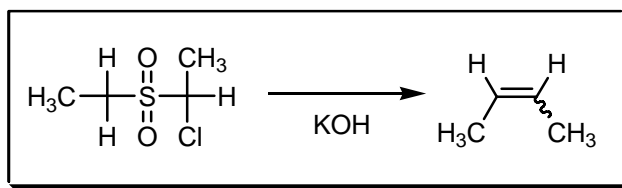
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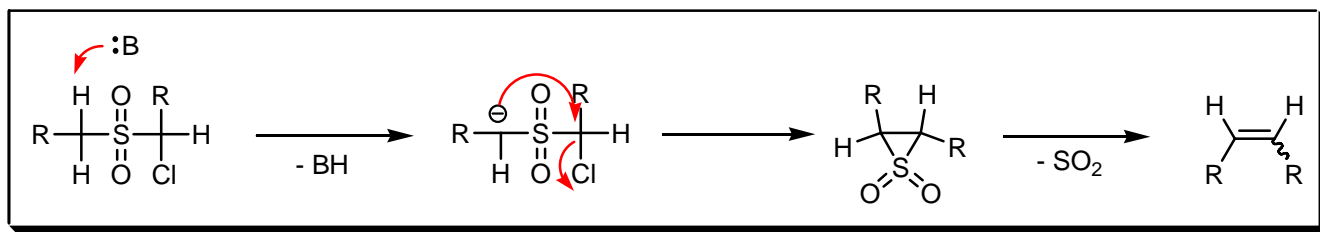
## COMMENTS :

## RAMBERG – BÄCKLUND REACTION

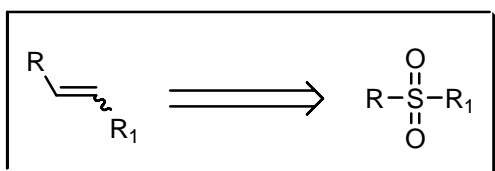
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

This is the conversion of dialkyl sulfones to alkenes by rearrangement of α-halosulfones with base. See also **Corey – Kwiatkowski**, **Horner – Wadsworth – Emmons**, **Julia – Paris – Kocienski – Lythgoe**, **Krief – Reich – Chow**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Nysted**, **Petasis** reaction, **Paquette**, **Peterson**, **Still – Gennari**, **Takeda**, **Tebbe** and **Wittig** reactions.

## REFERENCES :

**March** : 1030

**Smith – March** : 1342

**Smith** : 748

**Smith 2<sup>nd</sup>** : 632

**Houben – Weyl** : **E5**, 447; **E11**, 1521

**Org. React.** : **25**, 1; **62**, 357

**Org. Synth.** : **49**, 18; **65**, 90

**Org. Synth. Coll. Vol.** : **5**, 231; **8**, 212

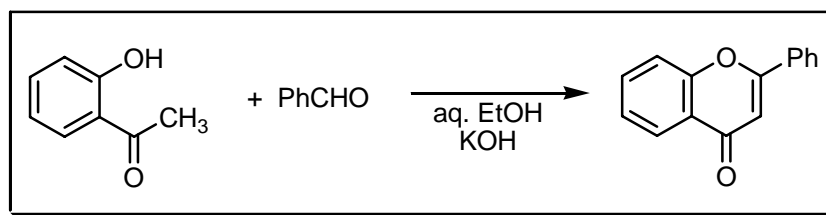
**Science of Synthesis** : **9**, 49

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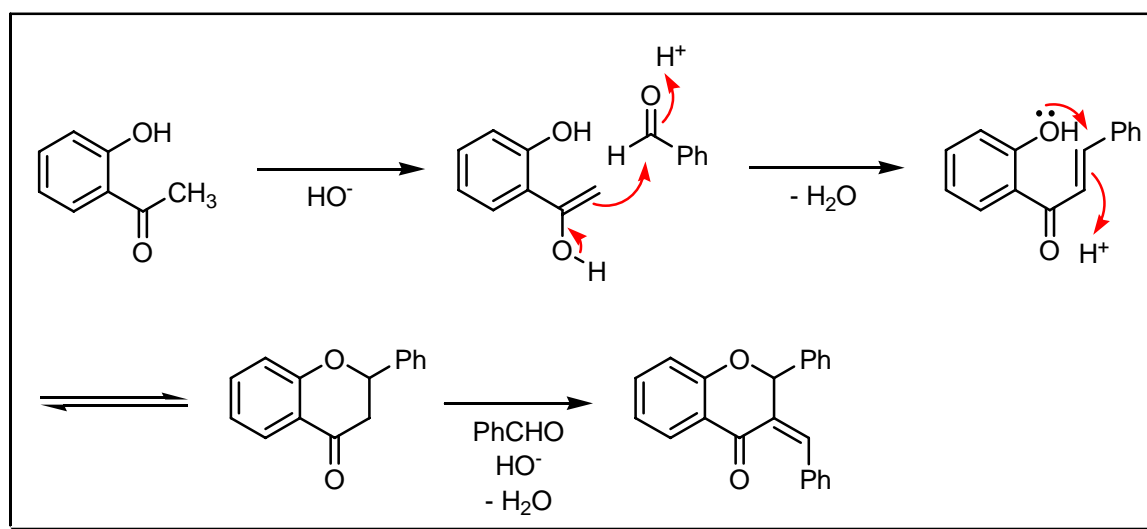
COMMENTS :

## RANJORWA SYNTHESIS

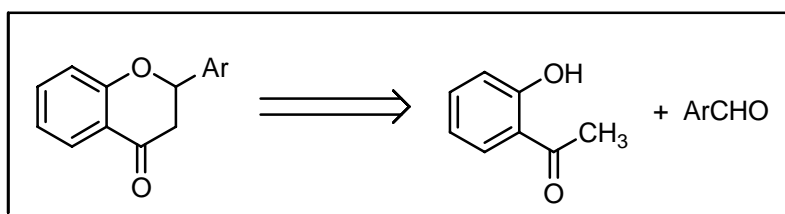
EXAMPLE :



MECHANISM :



DISCONNECTION :





## NOTES :

Flavonols are obtained by treating an o-hydroxyacetophenone with an araldehyde in aqueous ethanolic solution containing alkali. Prolonged agitation and exposure to air are necessary. See also **Algar – Flynn – Oyamada**, **Auwers** flavonol, **Baker – Ollis**, **von Kostanecki (Allan – Robinson)** acylation and **Rasoda** reactions.

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## REFERENCES :

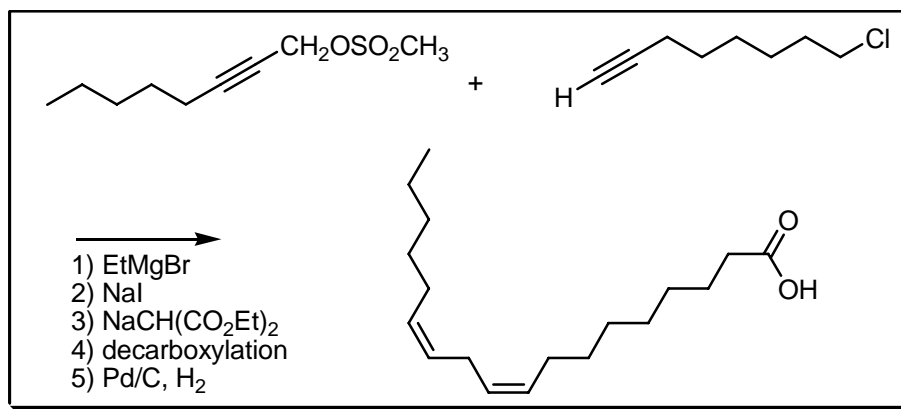
- 1) S.D. Limaye; D.B. Limaye, *Rasáyanam*, 1952, **2**, 41. (*Chem. Abs.*, 1953, **47**, 4879.)
  - 2) F.H. Guidugli; C.E. Ardanaz; J. Kavka; M.E. Garibay; P. Joseph–Nathan, *Org. Mass. Spectrom.*, 1986, **21**, 117.
  - 3) H.M. Chawla; S.K. Sharma, *Indian J. Chem.*, 1987, **26B**, 1075.
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## COMMENTS :

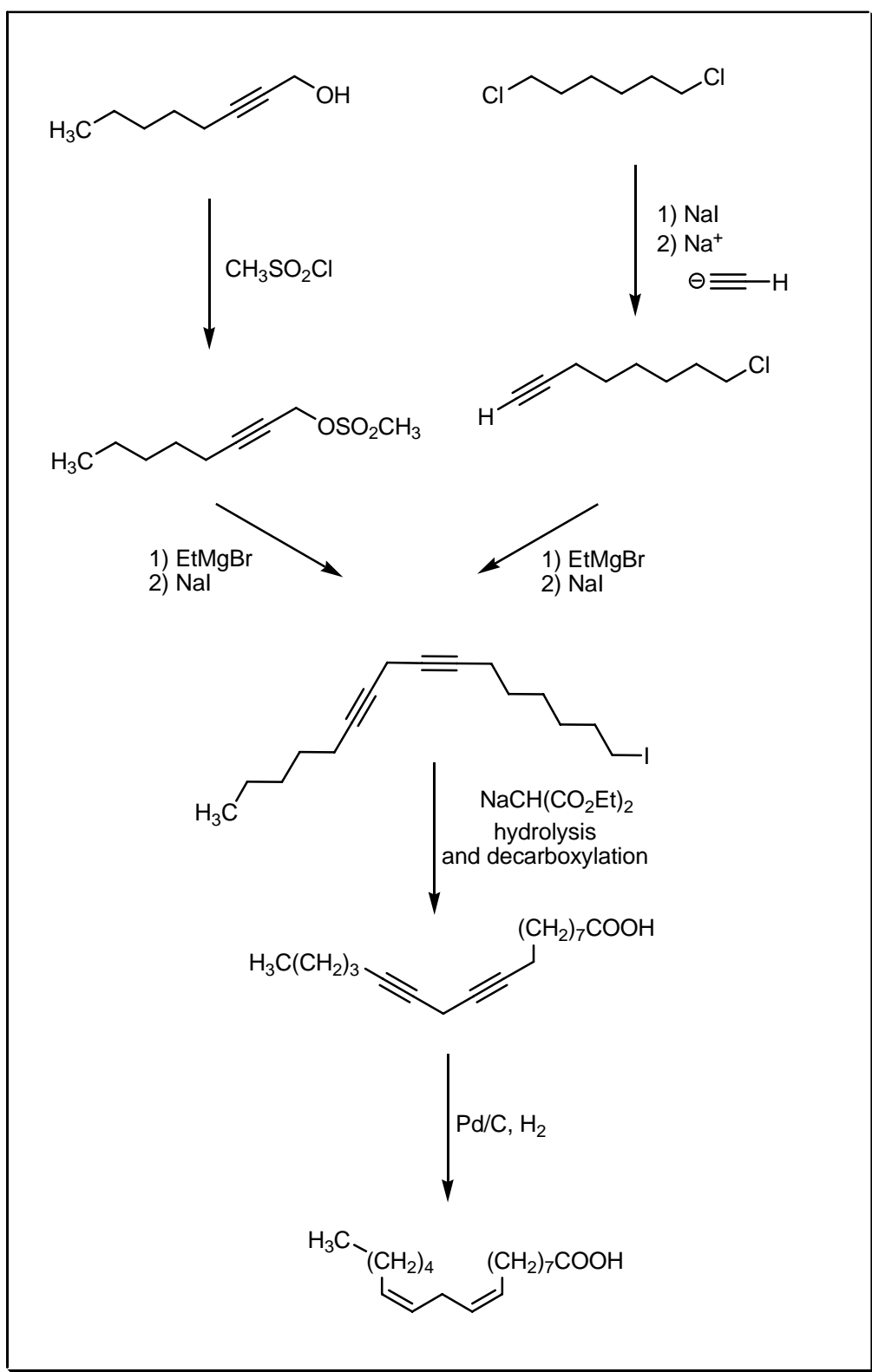
## RAPHAEL SYNTHESIS

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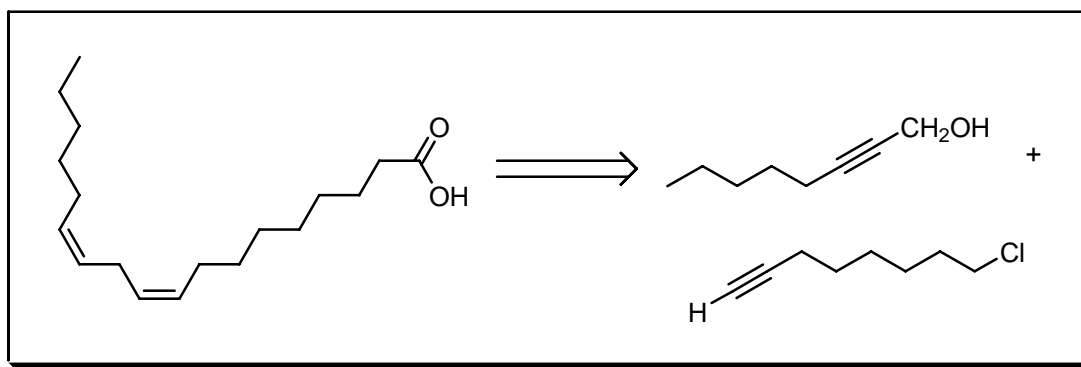
### EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

This synthesis utilises the alkylation of an acetylenic **Grignard** reagent using an alkyl sulfonate. The **Grignard** complex of 8-chloro-oct-1-yne reacts with oct-2-yn-1-yl methanesulfonate to give a diacetylenic chloride. This compound is converted into the iodide and by the malonation process yields heptadeca-8,11-di-yne-1-carboxylic acid. Catalytic (with palladium on calcium carbonate) partial hydrogenation of this acid yields a product consisting of 63% linoleic acid. See also **Ahmed – Strong** reaction.

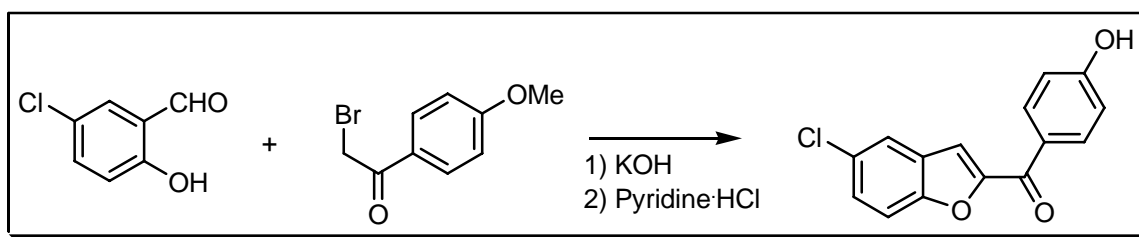
## REFERENCES :

- 1) R.A. Raphael; F. Sondheimer, *J. Chem. Soc.*, 1950, 2100.
- 2) R.A. Raphael; F. Sondheimer, *Nature*, 1950, **165**, 235.

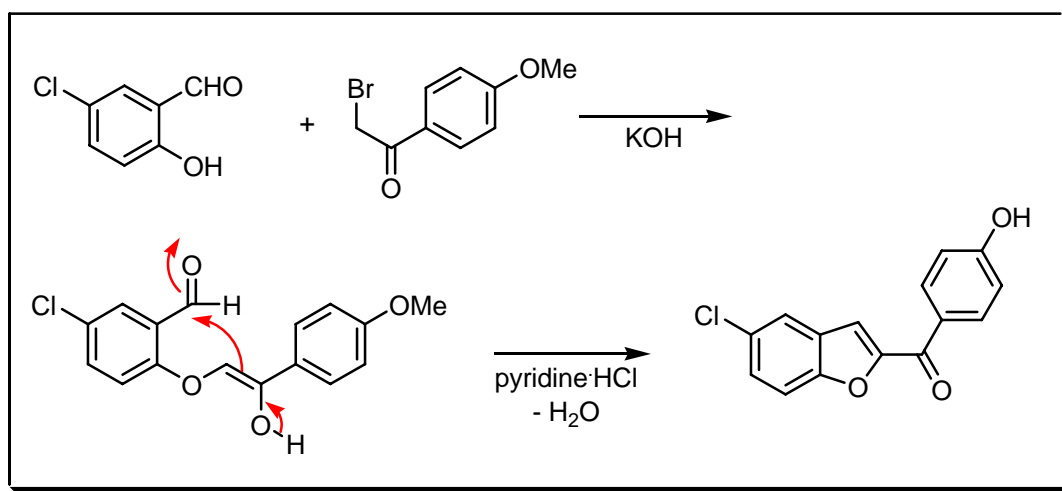
## COMMENTS :

## RAPP – STOERMER CONDENSATION

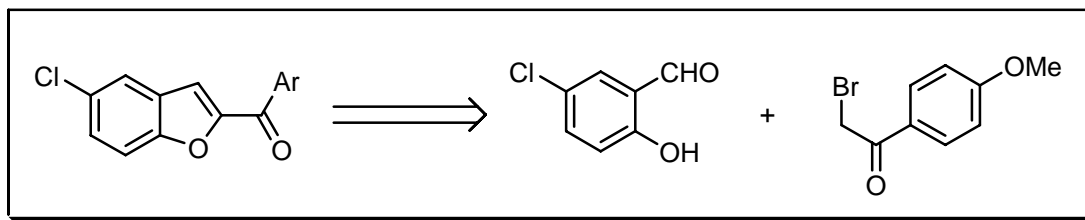
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The 2-acylbenzofuran synthesis from salicylaldehydes and  $\alpha$ -haloketones.

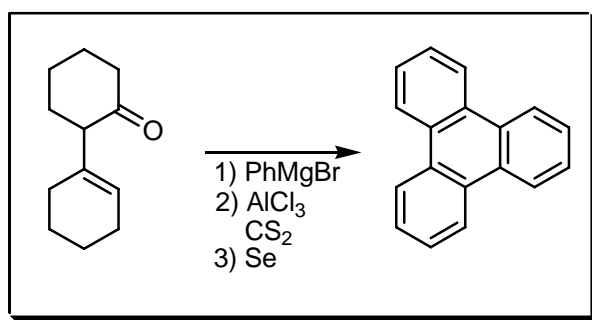
### REFERENCES :

- 1) E. Rapp, *Gazz. Chim. Ital.*, 1895, **25/2**, 285.
- 2) R. Stoermer, *Liebigs Ann. Chem.*, 1900, **312**, 237.
- 3) V.F. Martynoff, *Bull. Soc. Chim. Fr.*, 1952, 1056.
- 4) Ng.Ph. Buu-Hoi; G. Saint-Ruf; T.B. Loc; Ng.D. Xuong, *J. Chem. Soc.*, 1957, 2593.

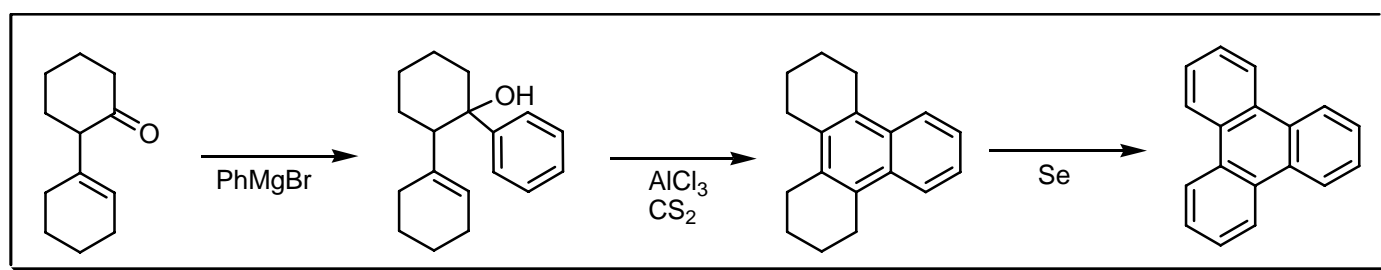
### COMMENTS :

## RAPSON TRIPHENYLENE REACTION

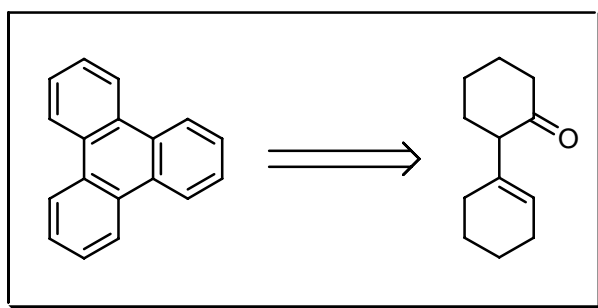
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The triphenylene synthesis by condensation of cyclohexenyl-cyclohexanones with phenylmagnesium bromide, followed by aluminium chloride or stannic chloride and dehydration with selenium.

### REFERENCES :

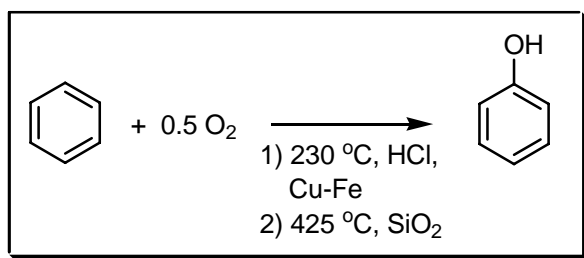
- 1) W.S. Rapson, *J. Chem. Soc.*, 1941, 15.
- 2) P.M.G. Bavin; M.J.S. Dewar, *J. Chem. Soc.*, 1955, 4479.
- 3) C.C. Barker; R.G. Emmerson; J.D. Periam, *J. Chem. Soc.*, 1958, 1077.
- 4) C.M. Buess; D.D. Lawson, *Chem. Rev.*, 1960, **60**, 313.

COMMENTS :

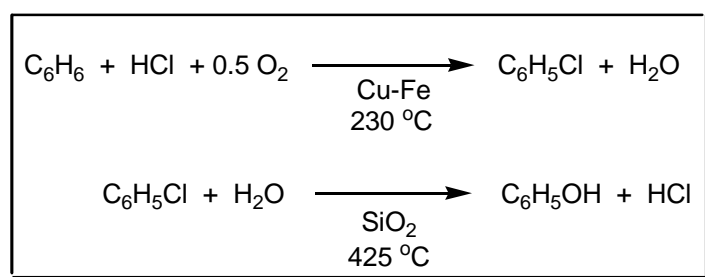
## RASCHIG PHENOL PROCESS

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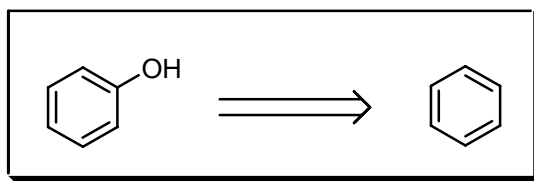
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The synthesis of phenol from chlorobenzene by catalytic vapour phase hydrolysis with water to yield phenol and hydrogen chloride which is regenerated.

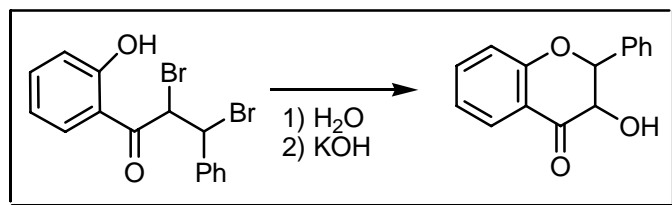
REFERENCES :

- 1) F. Raschig, *French Patent*, 1930, 698341. (*Chem. Abs.*, 1931, **25**, 3012.)
- 2) W.H. Prahl, *U.S. Patent*, 1934, 1963761.
- 3) W. Mathes, *Angew. Chem.*, 1939, **52**, 591.

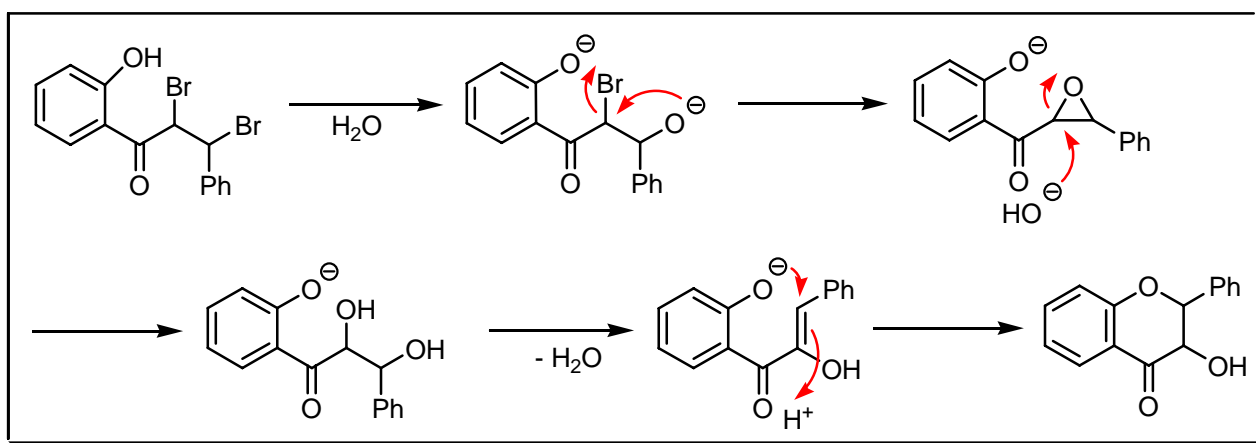
COMMENTS :

## RASODA SYNTHESIS

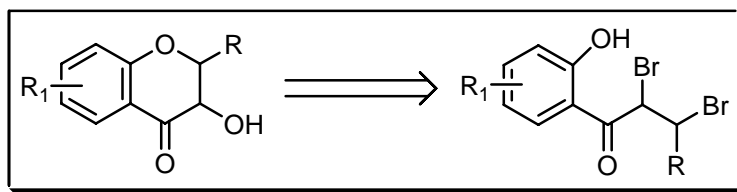
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

2'-Acetoxychalkone dibromides on treatment with water and with alkali yield flavones. See also **Algar – Flynn – Oyamada**, **Auwers** flavonol, **Baker – Ollis**, **von Kostanecki (Allan – Robinson)** acylation and **Ranjorwa** reactions.

REFERENCES :

1) S.D. Limaye, *Rasáyanam*, 1950, **2**, 1.

2) P.M. Hayden; O'Sullivan; Philbin; T.S. Wheeler, *Research*, 1952, **5**, 396.

3) *Science and Culture*, 1954, **20**, 135.

4) J.E. Gowan; P.M. Hayden; T.S. Wheeler, *J. Chem. Soc.*, 1955, 862.

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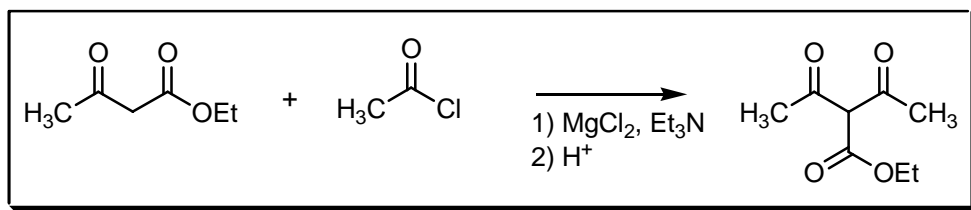
**COMMENTS :**

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**RATHKE ESTER SYNTHESIS**

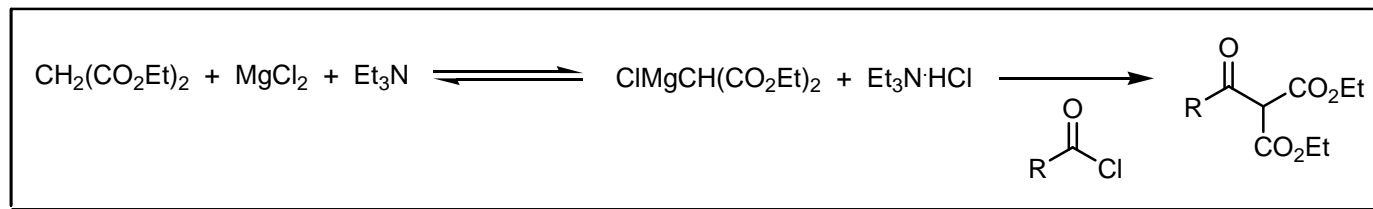
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**EXAMPLE :**



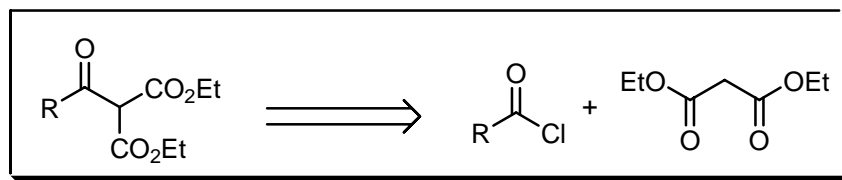
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**MECHANISM :**



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**DISCONNECTION :**



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**NOTES :**

In the presence of magnesium chloride and triethylamine malonates are C-alkylated by acid chlorides to afford  $\beta$ -keto esters.

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**REFERENCES :**

1) M.W. Rathke; P.J. Cowan, *J. Org. Chem.*, 1985, **50**, 2622.

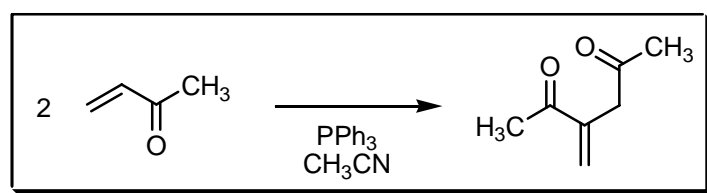
2) R.J. Clay; T.A. Collom; G.L. Karrick; J. Wemple, *Synthesis*, 1993, 290.



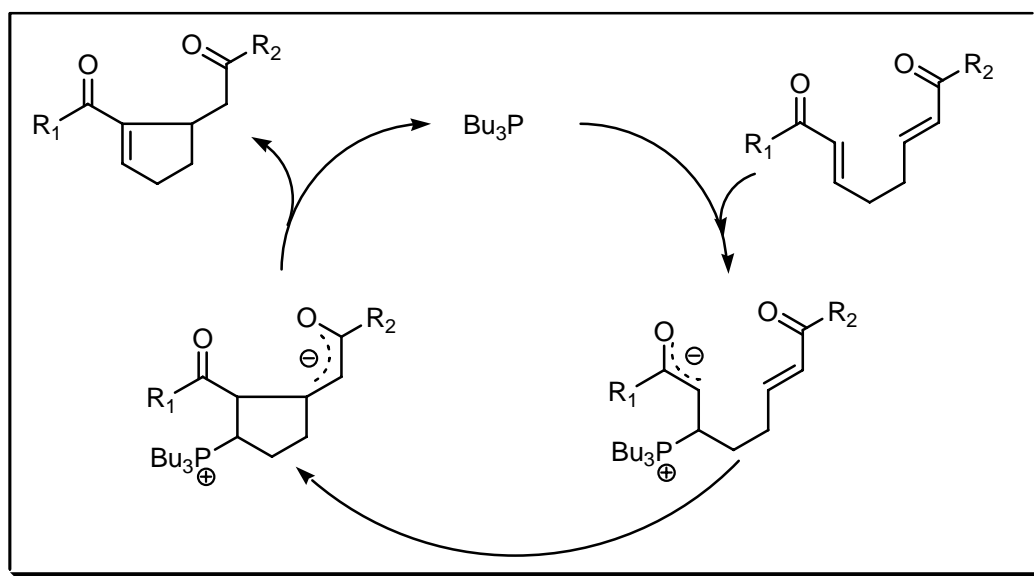
COMMENTS :

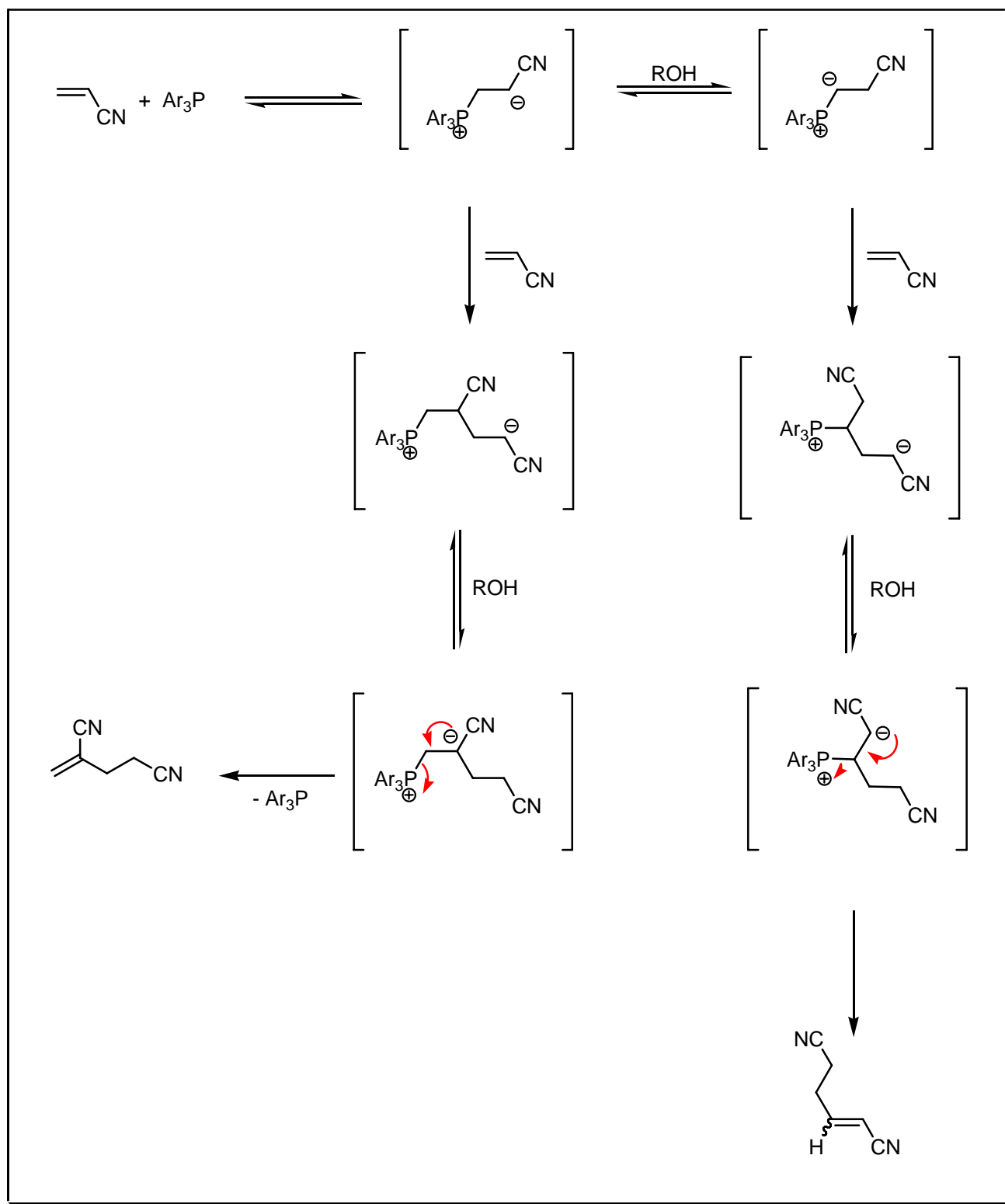
RAUHUT – CURRIER REACTION

EXAMPLE :

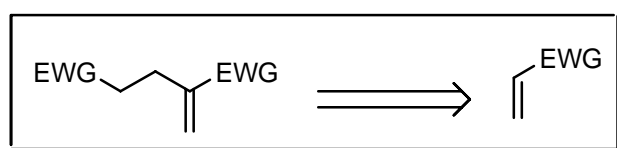


MECHANISM :





DISCONNECTION :



## NOTES :

The phosphine-catalysed dimerisation of electron-deficient alkenes in the presence of a small amount of a protolytic source like *tert*-butyl alcohol. The *intramolecular* variant, an organocatalytic **Michael** cycloisomerisation, has been published by **Krische** *et al.* Both five- and six-membered ring formations occur readily. See also **Bayliss – Hillman – Morita** and **Michael** reactions.

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## REFERENCES :

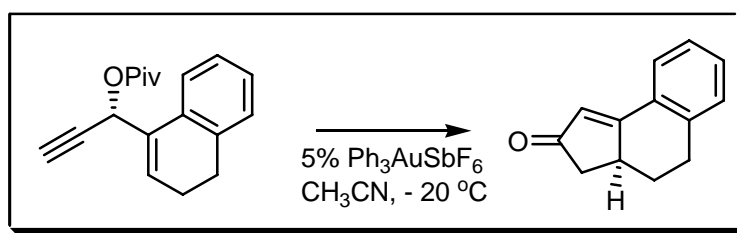
- 1) M.M. Rauhut; H. Currier, *U.S. Patent*, 1963, 3074999.
  - 2) J.D. McClure, *J. Org. Chem.*, 1970, **35**, 3045.
  - 3) D. Basavaiah; V.V.L. Gowriswari; T.K. Bharathi, *Tetrahedron Lett.*, 1987, **28**, 4591.
  - 4) S.E. Drewes; N.D. Emslie; N. Karodia, *Synth. Commun.*, 1990, **20**, 1915.
  - 5) C.D. Hall; N. Lowther; B.R. Tweedy; A.C. Hall; G. Shaw, *J. Chem. Soc., Perkin Trans. 2*, 1998, 2047.
  - 6) L.-C. Wang; A.L. Luis; K. Agapiou; H.-Y. Jang; M.J. Krische, *J. Am. Chem. Soc.*, 2002, **124**, 2402.
- 

## COMMENTS :

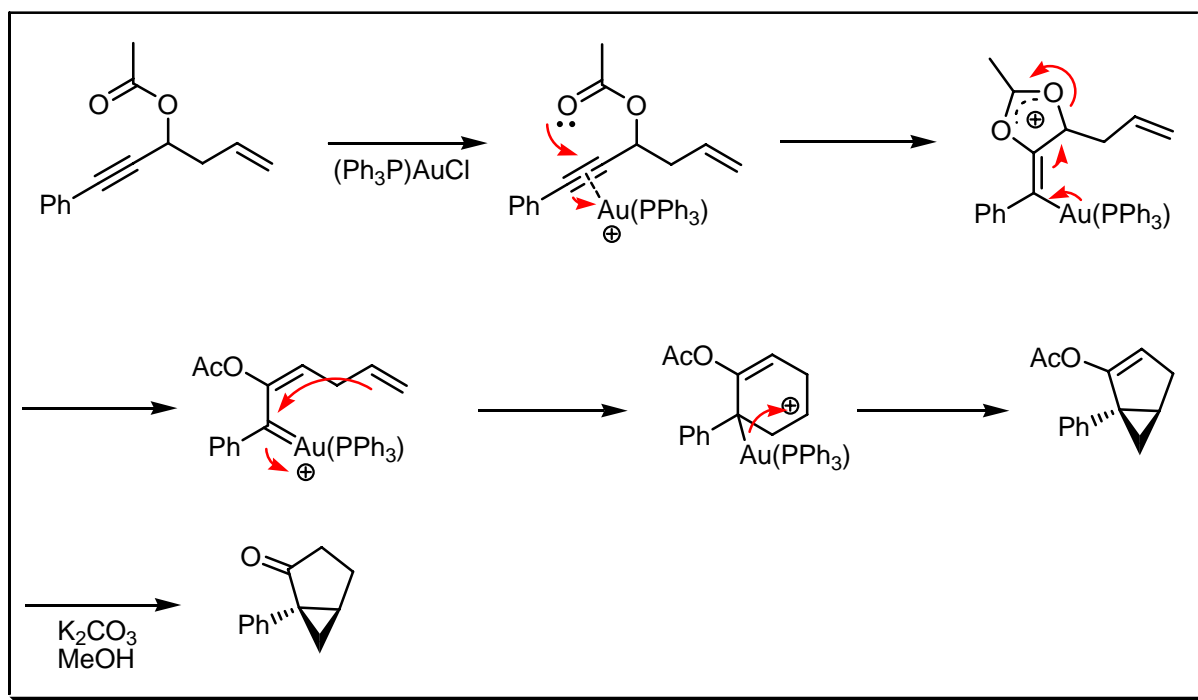
## RAUTENSTRAUCH REARRANGEMENT

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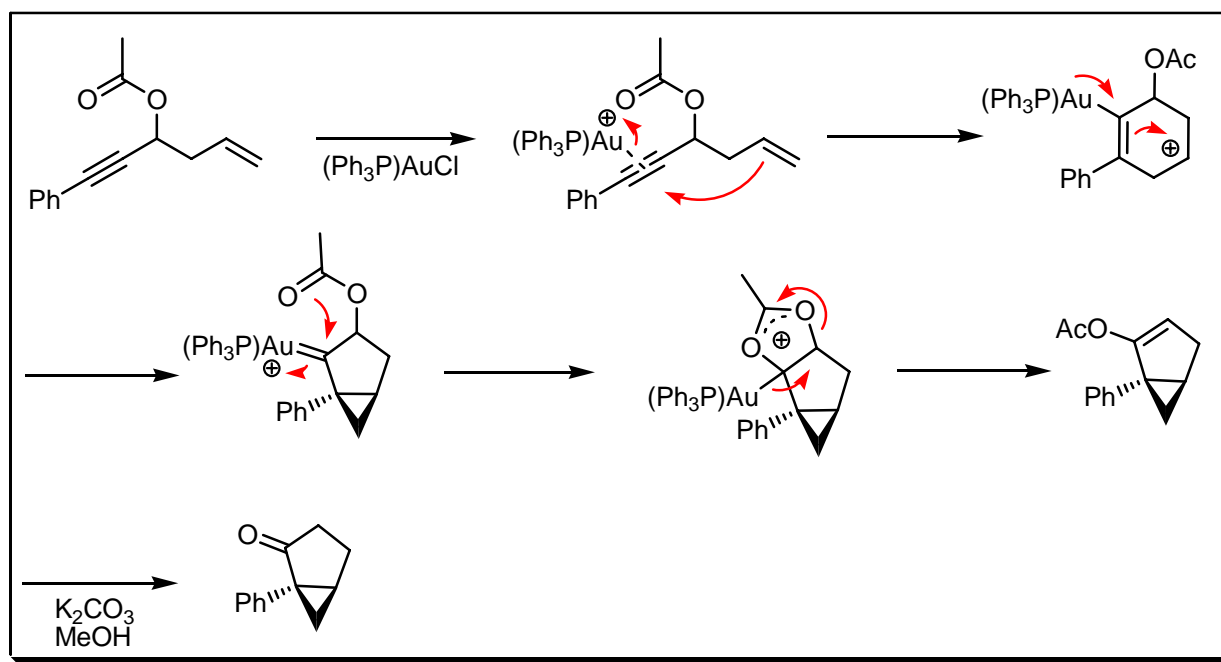
### EXAMPLE :



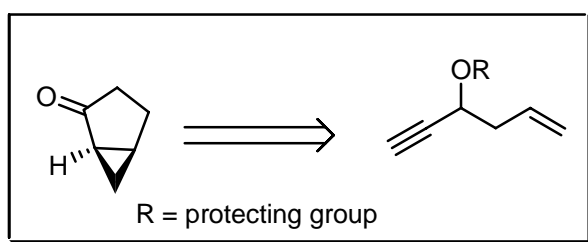
## MECHANISM :



## Also possible :



## DISCONNECTION :



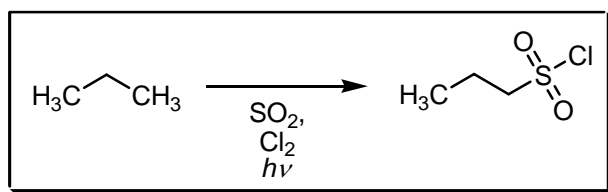
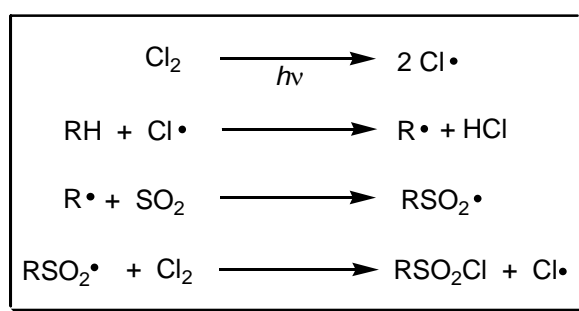
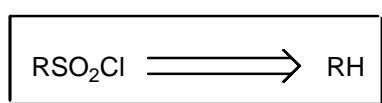
**NOTES :**

2-Cyclopentenones are prepared from 1-ethynyl-2-propenyl derivatives catalysed by gold, platinum or palladium complexes.

---

**REFERENCES :**

- 1) V. Rautenstrauch, *J. Org. Chem.*, 1984, **49**, 950.
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  - 3) X. Shi; D.J. Gorin; F.D. Toste, *J. Am. Chem. Soc.*, 2005, **127**, 5802.
- 

**COMMENTS :****REED REACTION****EXAMPLE :****MECHANISM :****DISCONNECTION :**

## NOTES :

This reaction is the photochemical sulfochlorination of alkanes and cycloalkanes using sulfur dioxide and chlorine under UV radiation. The reaction is radical induced and the side products are usually alkyl chlorides and disulfo chlorides. See also **Hinsberg** sulfone synthesis.

---

## REFERENCES :

**March** : 711

**Smith – March** : 924

**Houben – Weyl** : **9**, 407

- 
- 1) C.F. Reed, *U.S. Patent*, 1936, 2046090.
  - 2) H.J. Schumacher; J. Stauff, *Angew. Chem.*, 1942, **55**, 341.
  - 3) J.H. Helberger; G. Manecka; H.M. Fischer, *Liebigs Ann. Chem.*, 1949, **562**, 23.
  - 4) F. Asinger; B. Fell; H. Scherb, *Chem. Ber.*, 1963, **96**, 3068.
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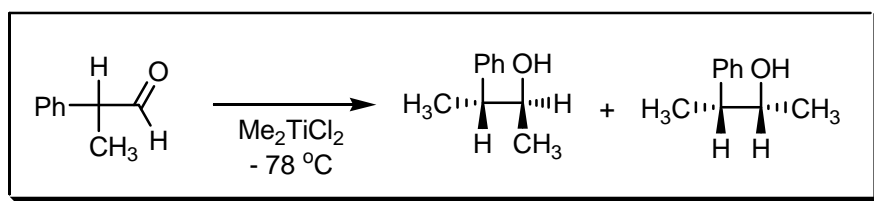
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## COMMENTS :

## REETZ TITANIUM ALKYLATION

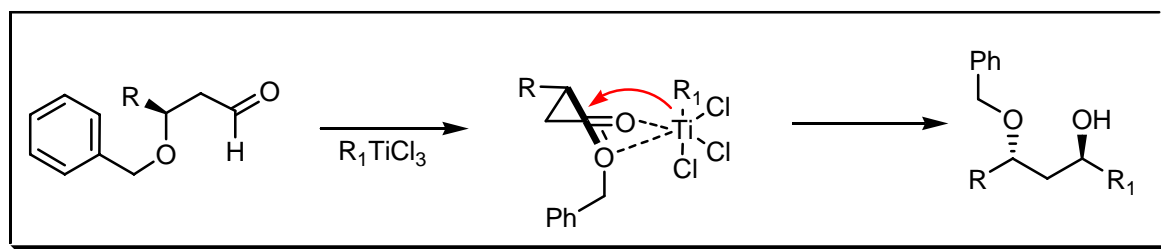
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### EXAMPLE :

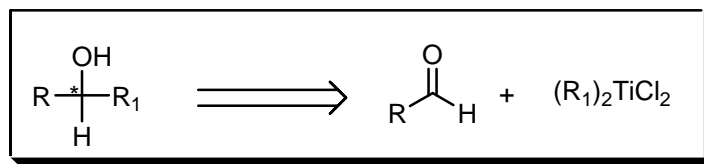


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### MECHANISM :



## DISCONNECTION :



## NOTES :

Alkyltitanium reagents are used in the chemo and diastereoselective addition from the less hindered side to aldehydes. This chelation control can be used for 1,2-, 1,3-, and 1,4-asymmetric inductions.

## REFERENCES :

Smith : 1375

Org. Synth. : **67**, 180

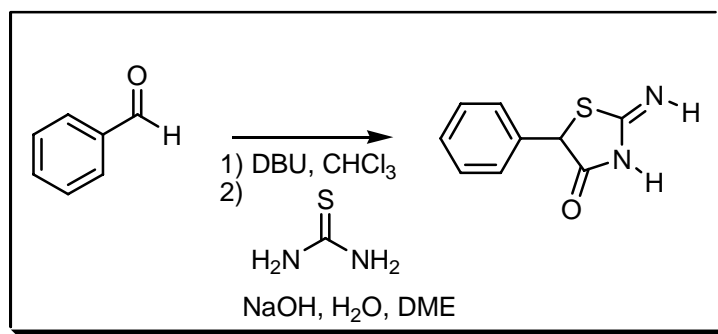
Org. Synth. Coll. Vol. : **8**, 495

- 1) M.T. Reetz; R. Steinback; J. Westermann; R. Peter, *Angew. Chem., Int. Ed. Engl.*, 1980, **19**, 1011.
- 2) G.H. Posner; L.L. Frye; M. Hulce, *Tetrahedron*, 1984, **40**, 1401.
- 3) M.T. Reetz, *Angew. Chem., Int. Ed. Engl.*, 1984, **23**, 556.
- 4) M.T. Reetz, *Acc. Chem. Res.*, 1993, **26**, 462.
- 5) T. Poon; C.A. Goudreau; F.G. Favaloro; B.P. Mundy; A. Greenberg; R. Sullivan, *Synthesis*, 1998, 832.
- 6) F.G. Favaloro; C.A. Goudreau; B.P. Mundy; T. Poon; S.V. Slobodzian; B.L. Jensen, *Synth. Commun.*, 2001, **31**, 1847.

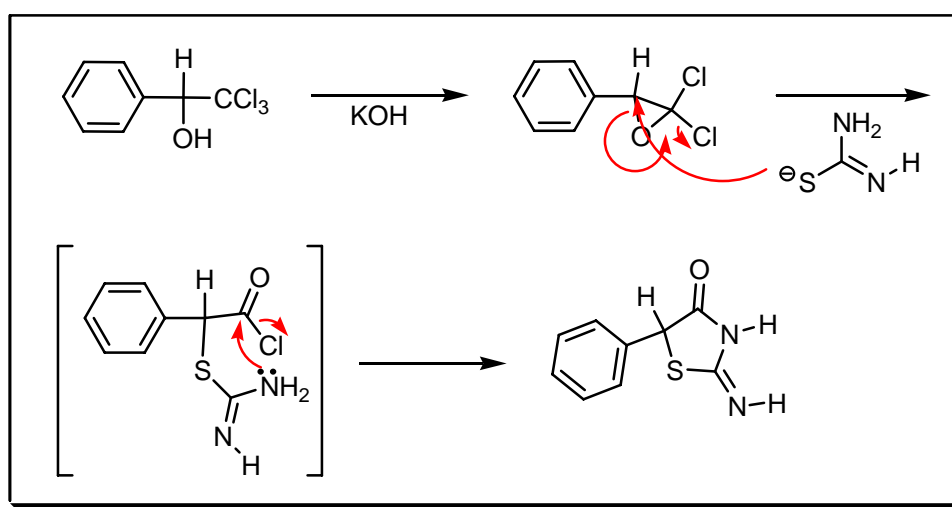
## COMMENTS :

# REEVE SYNTHESIS

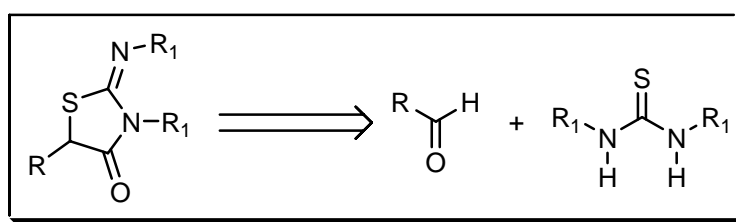
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

2-Imino-4-thiazolidinones are prepared from readily accessible alkyl or aryl trichloromethylcarbinols and thioureas under mild conditions. See also **Corey – Link** reaction.

## REFERENCES :

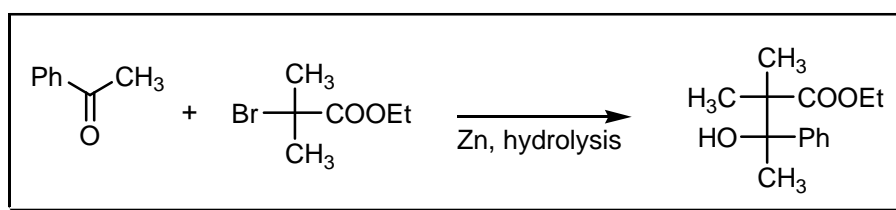
- 1) W. Reeve; C.W. Woods, *J. Am. Chem. Soc.*, 1960, **82**, 4062.
- 2) W. Reeve; M. Nees, *J. Am. Chem. Soc.*, 1967, **89**, 647.
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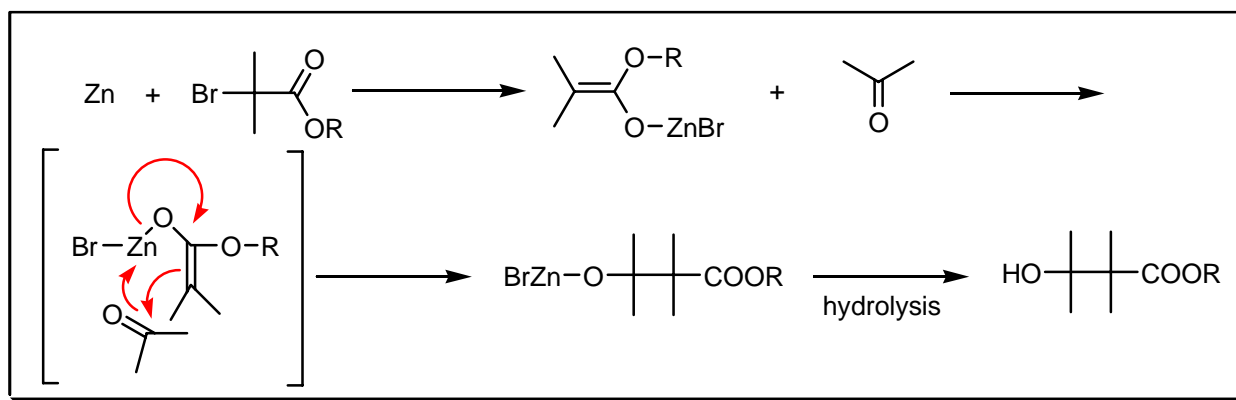
COMMENTS :

REFORMATSKY REACTION

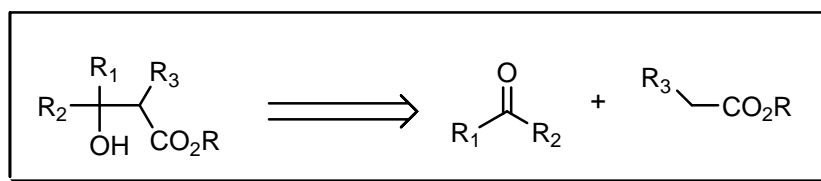
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

This reaction involves the condensation of a carbonyl compound, e.g. an aldehyde, ketone or ester, with a halogeno-ester in the presence of usually zinc to produce a hydroxy ester. This may be readily dehydrated to the unsaturated acid. The reaction, of which there are many variations, see **Blaise** reaction, is of value in extending the carbon chain of the aldehyde. Some reactions are germanium, chromium, rhodium or samarium promoted. Diastereoselectivity can

be obtained with the use of ligands containing free-hydroxyl groups. **Bartsch et al.** reported on high-intensity ultrasound promoted **Reformatsky** reaction. Aza-type variations have been reported. See also **Blaise** ketoester, **Dreiding – Schmidt**, **Frankland – Duppa**, **Gilman – Speeter**, **Grignard** and **Ivanov** reactions.

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#### REFERENCES :

**March** : 930

**Smith – March** : 1212

**Smith** : 962

**Smith 2<sup>nd</sup>** : 800

**Org. React.** : **1**, 1; **22**, 423; **28**, 203

**Houben – Weyl** : **6/2**, 627; **8**, 511; **13/2a**, 809; **E3**, 640; **E5**, 708, 1092; **E6b**, 854, 1212; **E7a**, 109, 600; **E7b**, 44; **E16b**, 901

**Org. Synth.** : **21**, 51; **37**, 37

**Org. Synth. Coll. Vol.** : **3**, 408; **4**, 444

**Science of Synthesis** : **1**, 493

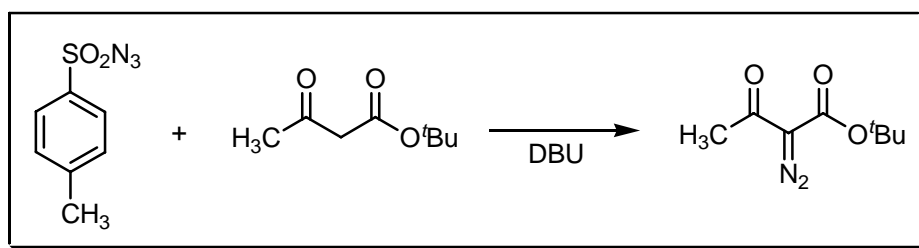
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- 1) S. Reformatsky, *Ber. Dtsch. Chem. Ges.*, 1887, **20**, 1210.
  - 2) W.J. Gensler, *Chem. Rev.*, 1957, **57**, 191.
  - 3) Y.S. Rao, *Chem. Rev.*, 1964, **64**, 353.
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  - 5) H. Mattes; C. Benezra, *Tetrahedron Lett.*, 1985, **26**, 5697.
  - 6) A. Fürstner, *Synthesis*, 1989, 571.
  - 7) A. Fürstner, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 164.
  - 8) L.W. Bieber; I. Malvestiti; E.C. Storch, *J. Org. Chem.*, 1997, **62**, 9061.
  - 9) H. Kagoshima; Y. Hashimoto; D. Oguro; K. Saijo, *J. Org. Chem.*, 1998, **63**, 691.
  - 10) K. Kanai; H. Wakabayashi; T. Honda, *Org. Lett.*, 2000, **2**, 2549.
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  - 16) J.D. Clark; G.A. Weisenburger; D.K. Anderson; P.-J. Colson; A.D. Edney; D.J. Gallagher; H.P. Kleine; C.M. Knable; M.K. Lantz; C.M.V. Moore; J.B. Murphy; T.E. Rogers; P.G. Ruminski; A.S. Shah; N. Storer; B.E. Wise, *Org. Proc. Res. Dev.*, 2004, **8**, 51.
  - 17) R. Ocampo; W.R. Dolbier, jr., *Tetrahedron*, 2004, **60**, 9325.
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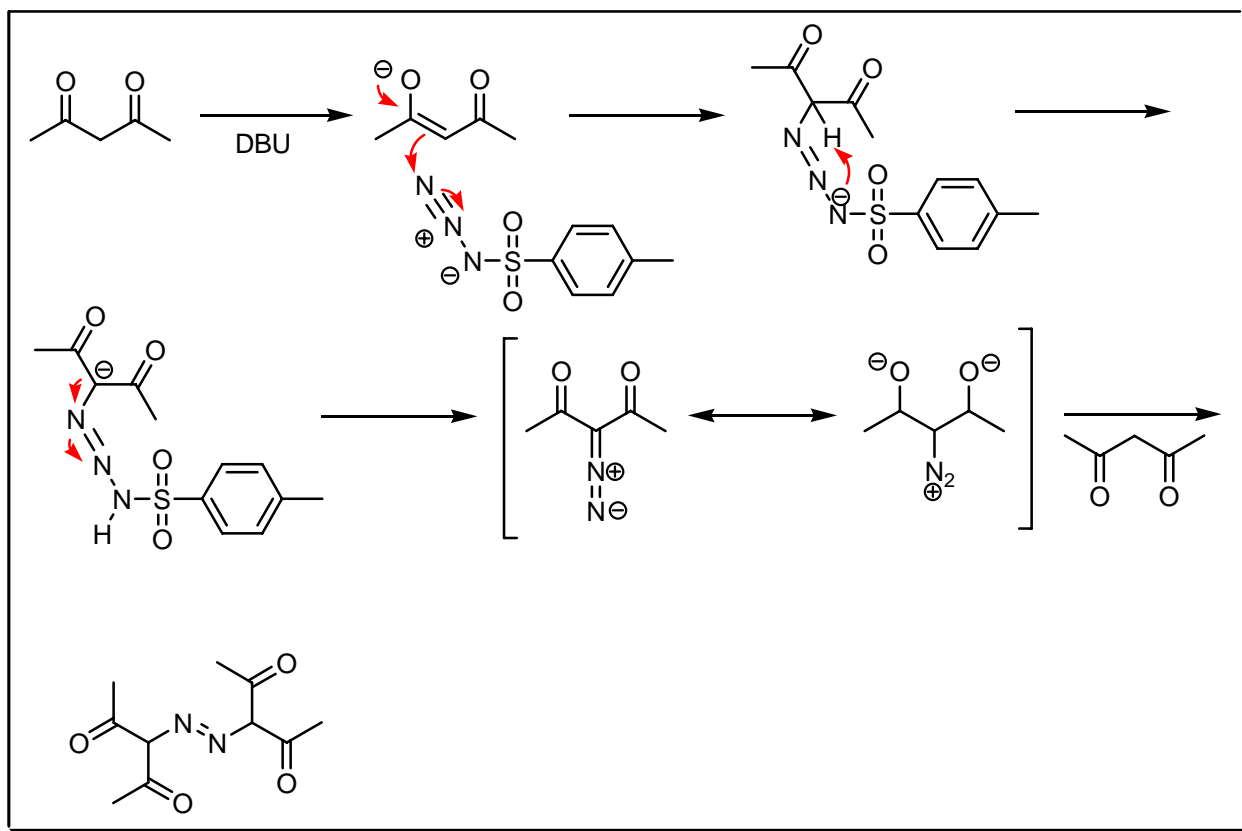
#### COMMENTS :

## REGITZ DIAZO TRANSFER

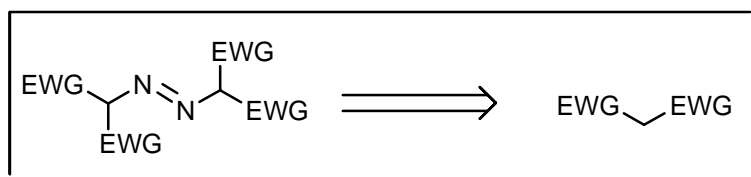
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The simple synthesis of diazo compounds from active methylenes with tosyl azide in the presence of a base. A modification has been introduced by **Ledon** using a two phase system, organic and water layer containing base and a quaternary ammonium salt.

## REFERENCES :

March : 593

Smith – March : 780

Houben – Weyl : 10/4, 557

Org. Synth. : 48, 36; 51, 86; 59, 66; 70, 93; 73, 134

Org. Synth. Coll. Vol. : 5, 179; 6, 389, 414; 9, 197, 422

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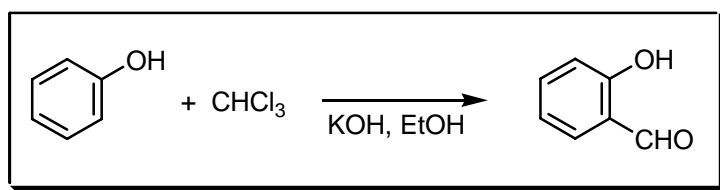
7) A.B. Charette; R.P. Wurcz; T. Ollevier, *J. Org. Chem.*, 2000, **65**, 9252.

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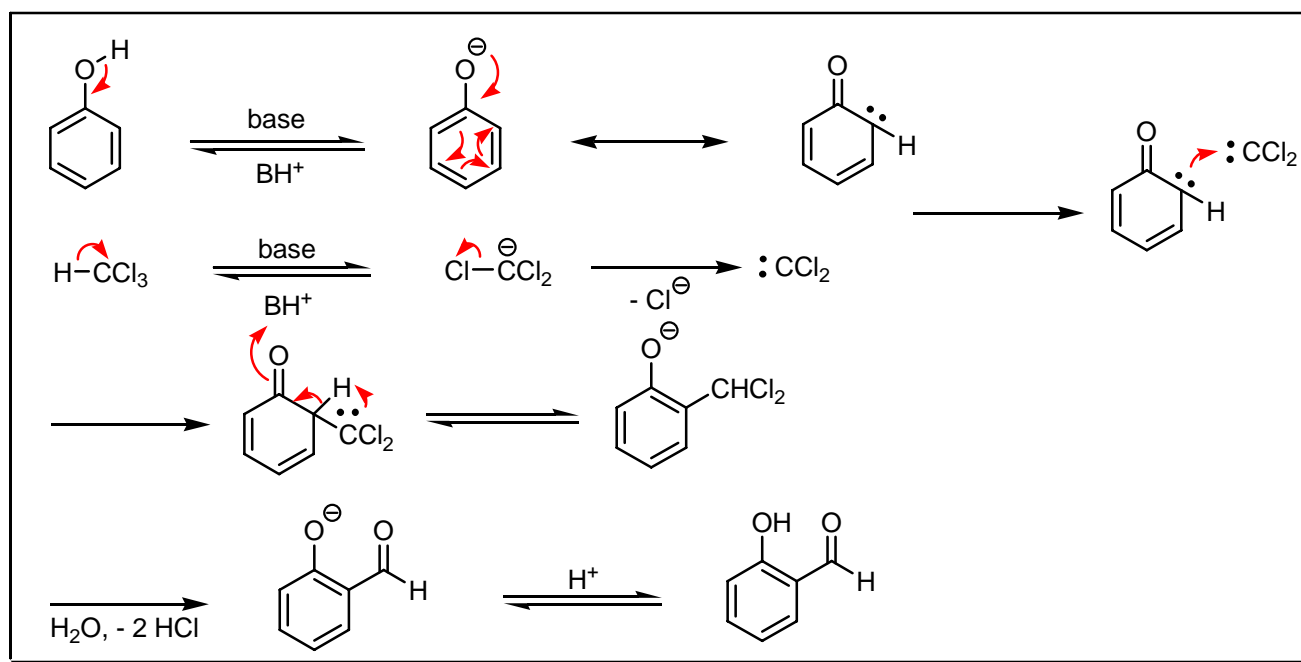
## COMMENTS :

## REIMER – TIEMANN REACTION

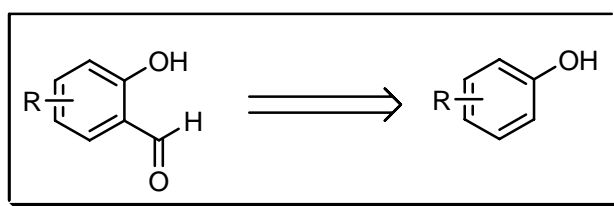
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The preparation of hydroxyaldehydes from phenols, chloroform and a base (alkali, hydroxide, carbonate, pyridine). Hydroxybenzoic acids are obtained if carbon tetrachloride is used. Bromoform and iodoform and trichloroacetic acid have been employed in the reaction. See also **Ciamician – Dennstedt**, **Duff – Bills**, **Gattermann**, **Gattermann – Koch** and **Vilsmeier – Haack – Viehe** reactions.

## REFERENCES :

March : 544

Smith – March : 716

Houben – Weyl : 7/1, 36; E3, 16; E6b, 1053; E7b, 146; E8a, 303

Org. React. : 9, 37; 13, 55; 28, 1

Org. Synth. : 22, 63

Org. Synth. Coll. Vol. : 3, 463

- 1) K. Reimer, *Ber. Dtsch. Chem. Ges.*, 1876, **9**, 423.
- 2) K. Reimer; F. Tiemann, *Ber. Dtsch. Chem. Ges.*, 1876, **9**, 824.
- 3) K. Reimer; F. Tiemann, *Ber. Dtsch. Chem. Ges.*, 1876, **9**, 1285.

- 4) L.N. Ferguson, *Chem. Rev.*, 1946, **38**, 227.
- 5) H. Wynberg, *Chem. Rev.*, 1960, **60**, 169.
- 6) C.W. Bird; A.L. Brown, *Chem. Ind. (London)*, 1983, 827.
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- 8) J.C. Cochran; M.G. Melville, *Synth. Commun.*, 1990, **20**, 609.
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- 12) B.S. Jursic; D.M. Neumann, *Tetrahedron Lett.*, 2001, **42**, 8435.

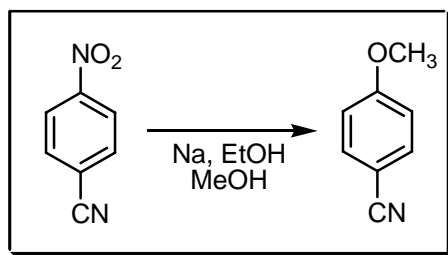
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**COMMENTS :**

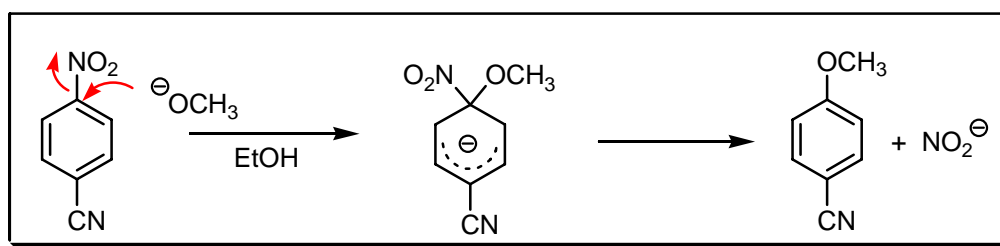
## REINDERS – RINGER DISPLACEMENT

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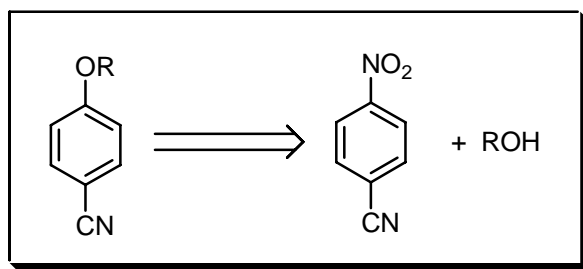
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

The nitro group in a nitro-aryl cyanide is displaced by alkoxy on treatment with sodium dissolved in alcohol.

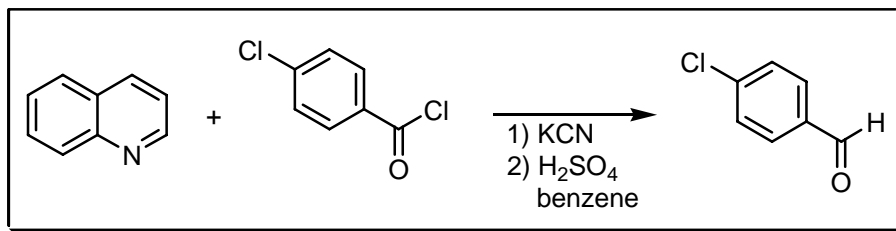
## REFERENCES :

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- 2) C.K. Bradsher; F.C. Brown; H.K. Porter, *J. Am. Chem. Soc.*, 1954, **76**, 2357.
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- 4) N. Kornblum; L. Cheng; R.C. Kerber; M.M. Kerstner; B.N. Newton; H.W. Pinnick; R.G. Smith; P.A. Wade, *J. Org. Chem.*, 1976, **41**, 1560.

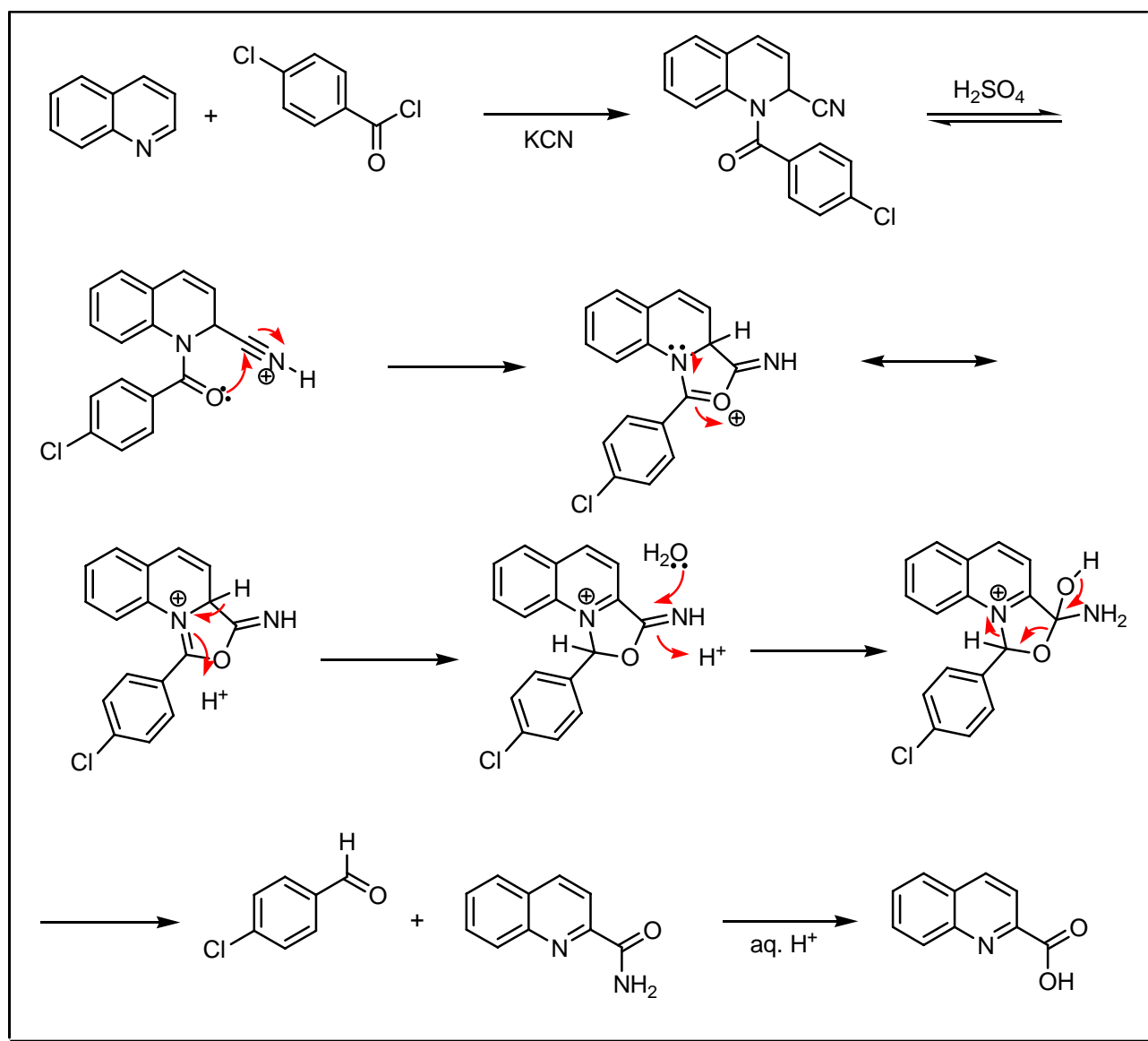
## COMMENTS :

## REISSERT – GROSHEINTZ – FISCHER SYNTHESIS

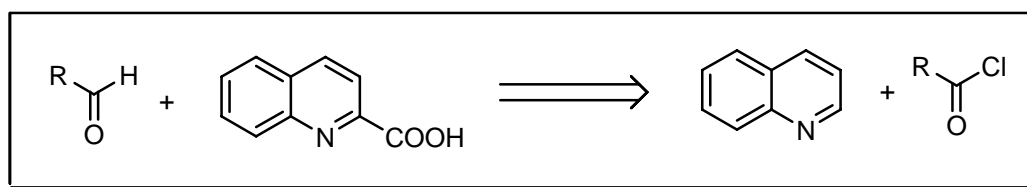
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of aldehydes or alkaloids from aliphatic or aromatic acid chlorides *via* 1-cyano-2-acylisoquinoline or 2-cyanoquinoline intermediates. This reaction is very similar to the **Reissert – Henze** reaction. See also **Padbury – Lindwall** and **Reissert – Henze** reactions.

## REFERENCES :

March : 448

Smith – March : 533



Houben – Weyl : 7/1, 291

Org. React. : 7, 99; 8, 218

Org. Synth. : 38, 58; 56, 19

Org. Synth. Coll. Vol. : 4, 641; 6, 115

1) A. Reissert, *Ber. Dtsch. Chem. Ges.*, 1905, **38**, 1603.

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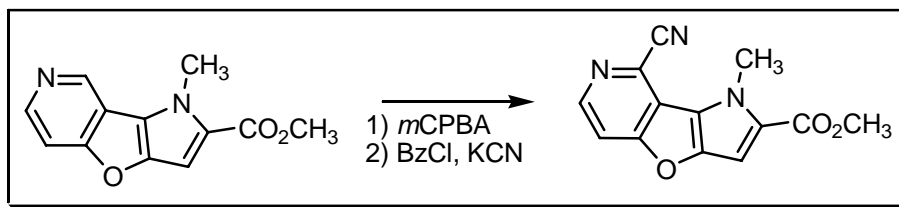
5) H. Suzuki; H. Gyoutoku; H. Yokoo; M. Shinba; Y. Sato; H. Yamada; Y. Murakami, *Synlett*, 2000, 1196.

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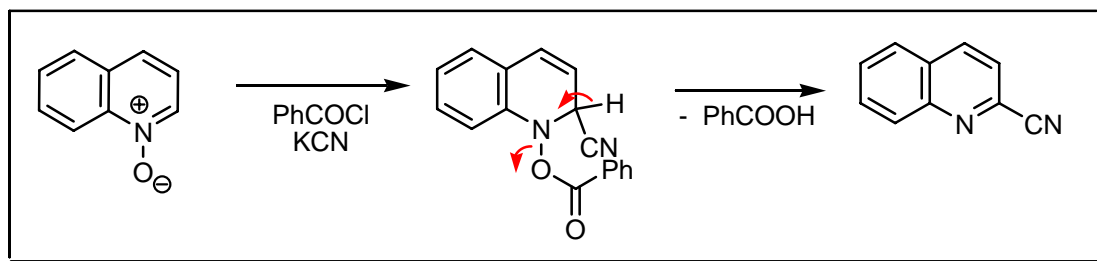
## COMMENTS :

## REISSERT – HENZE REACTION

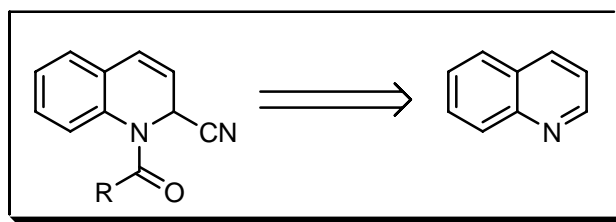
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

This reaction serves to introduce a cyano group into an  $\alpha$  (or occasionally  $\gamma$ ) position to the heteronitrogen atom of an azine ring. The pyridine *N*-oxides can be made by oxidation with hydrogen peroxide or *m*-chloroperbenzoic acid. The term **Reissert** compounds comes from the formal addition of an acyl group and a cyano group to a nitrogen atom and carbon atom, respectively of a nitrogen-carbon bond in quinolines, isoquinolines, and related nitrogen heterocycles. See also **Reissert – Grosheintz – Fischer** reaction.

## REFERENCES :

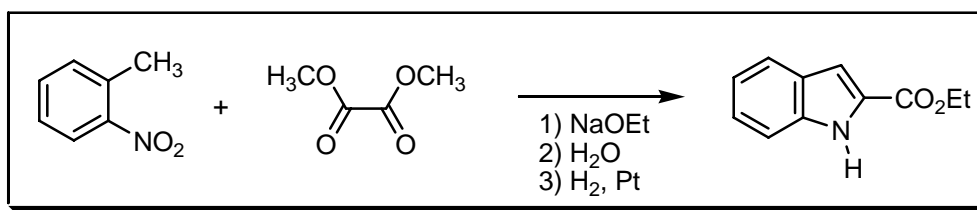
Houben – Weyl : E7a, 662

- 1) A. Reissert, *Ber. Dtsch. Chem. Ges.*, 1905, **38**, 1603.
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- 8) E. Ichikawa; M. Suzuki; K. Yabu; M. Albert; M. Kanai; M. Shibasaki, *J. Am. Chem. Soc.*, 2004, **126**, 11808.

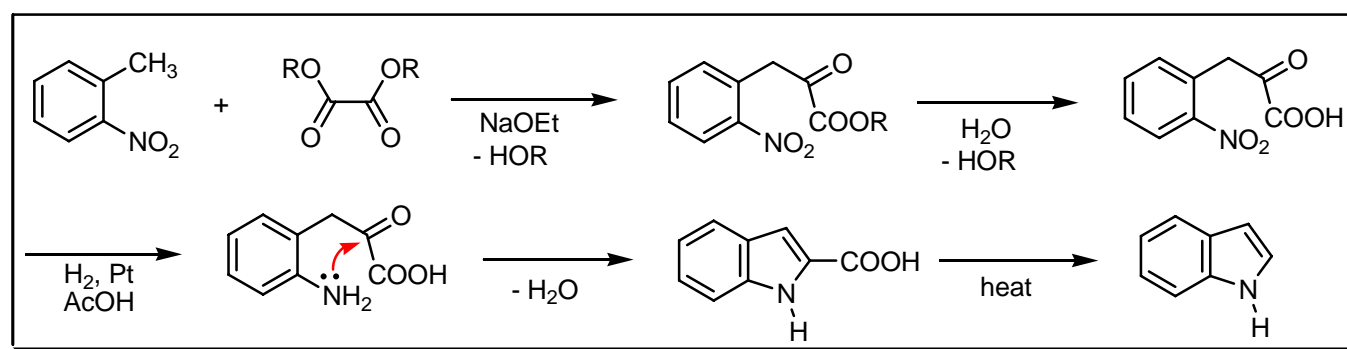
## COMMENTS :

# REISSERT INDOLE REACTION

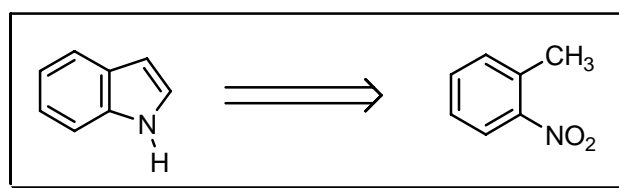
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The indole synthesis from o-nitrotoluene and oxalic acid diethyl ester. An important variation of this route was developed by **Batcho** and **Leimgruber** at Hofmann-LaRoche, see **Org. Synth.** 63, 214 or **Leimgruber – Batcho** reaction for details. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

## REFERENCES :

Houben – Weyl : E7a, 662, 719

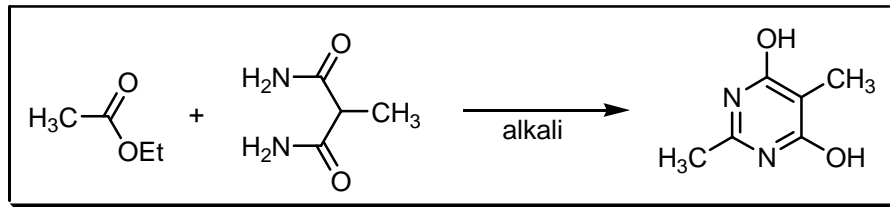
Org. Synth. : 43, 40

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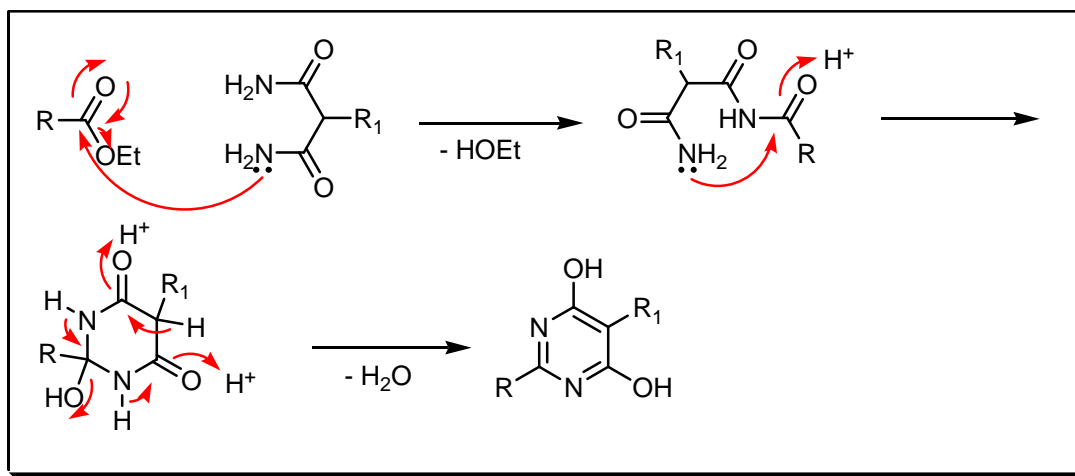
**COMMENTS :**

**REMFRY – HULL SYNTHESIS**

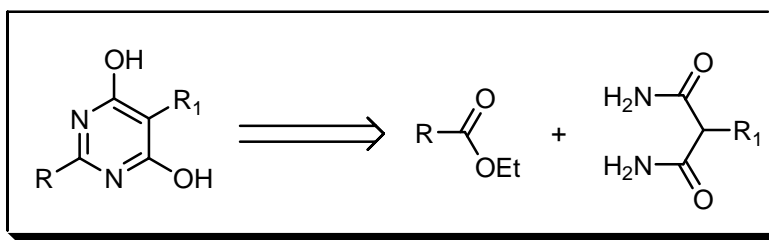
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

A malondiamide is condensed in alkaline solution with an ester to yield a 2,5- or 4,6-dihydroxypyrimidine. See also **Biginelli** reaction.

## REFERENCES :

- 1) F.G.P. Remfry, *J. Chem. Soc.*, 1911, **99**, 610.
- 2) R. Hull, *J. Chem. Soc.*, 1951, 2214.
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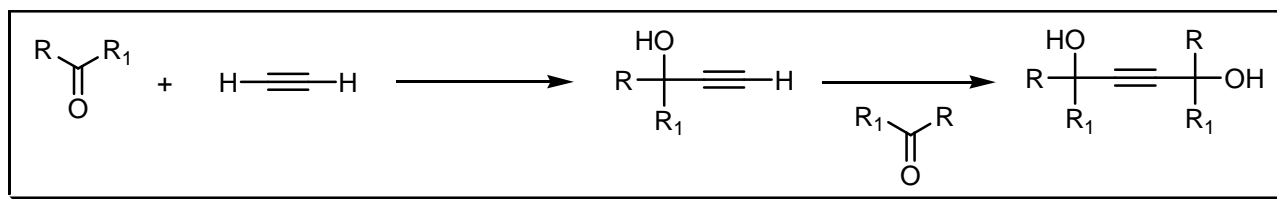
## COMMENTS :

## REPPE ACETYLENE SYNTHESIS

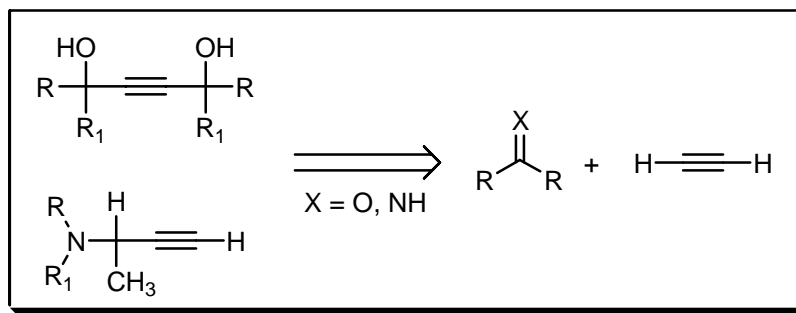
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The reaction between aldehydes, ketones, amines and alkylolamines with acetylenes, under pressure and high temperature using copper, silver, mercury or gold acetylides as catalysts. See also **Arens – van Dorp**, **Favorskii – Babayan** and **Nef** reactions.

## REFERENCES :

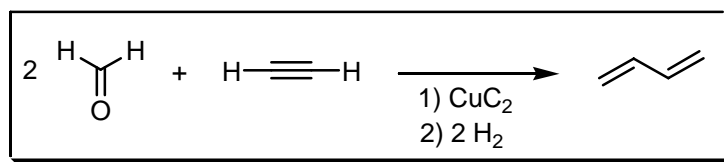
**Houben – Weyl** : 4/2, 413

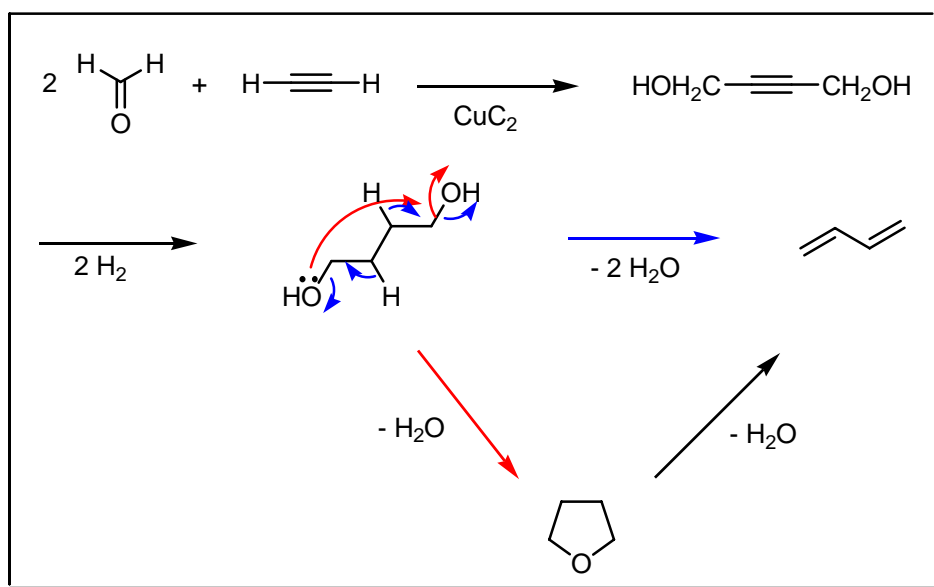
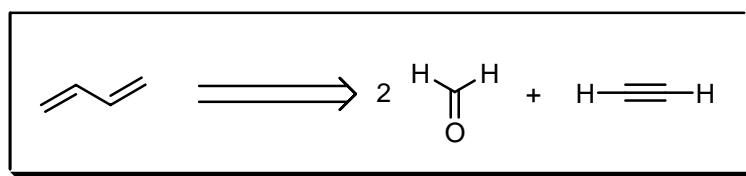
- 1) W. Reppe, *Experientia*, 1949, **5**, 98.
- 2) W. Reppe, *Liebigs Ann. Chem.*, 1955, **596**, 1.

## COMMENTS :

## REPPE BUTADIENE SYNTHESIS

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

The reaction between formaldehyde and acetylene in the presence of copper acetylide to afford butadiene. But-2-yn-1,4-diol is initially formed and then hydrogenated to butane-1,4-diol which either directly is dehydrated to butadiene or in a two stages via tetrahydrofuran.

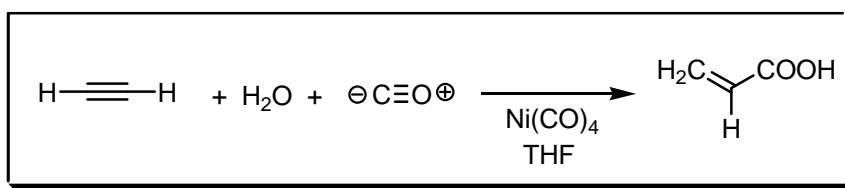
**REFERENCES :**

- 1) W. Reppe; E. Keyssner, *German Patent*, 1937, 725326.
- 2) W. Reppe, *Experientia*, 1949, **5**, 98.
- 3) W. Reppe, *Liebigs Ann. Chem.*, 1955, **596**, 1.

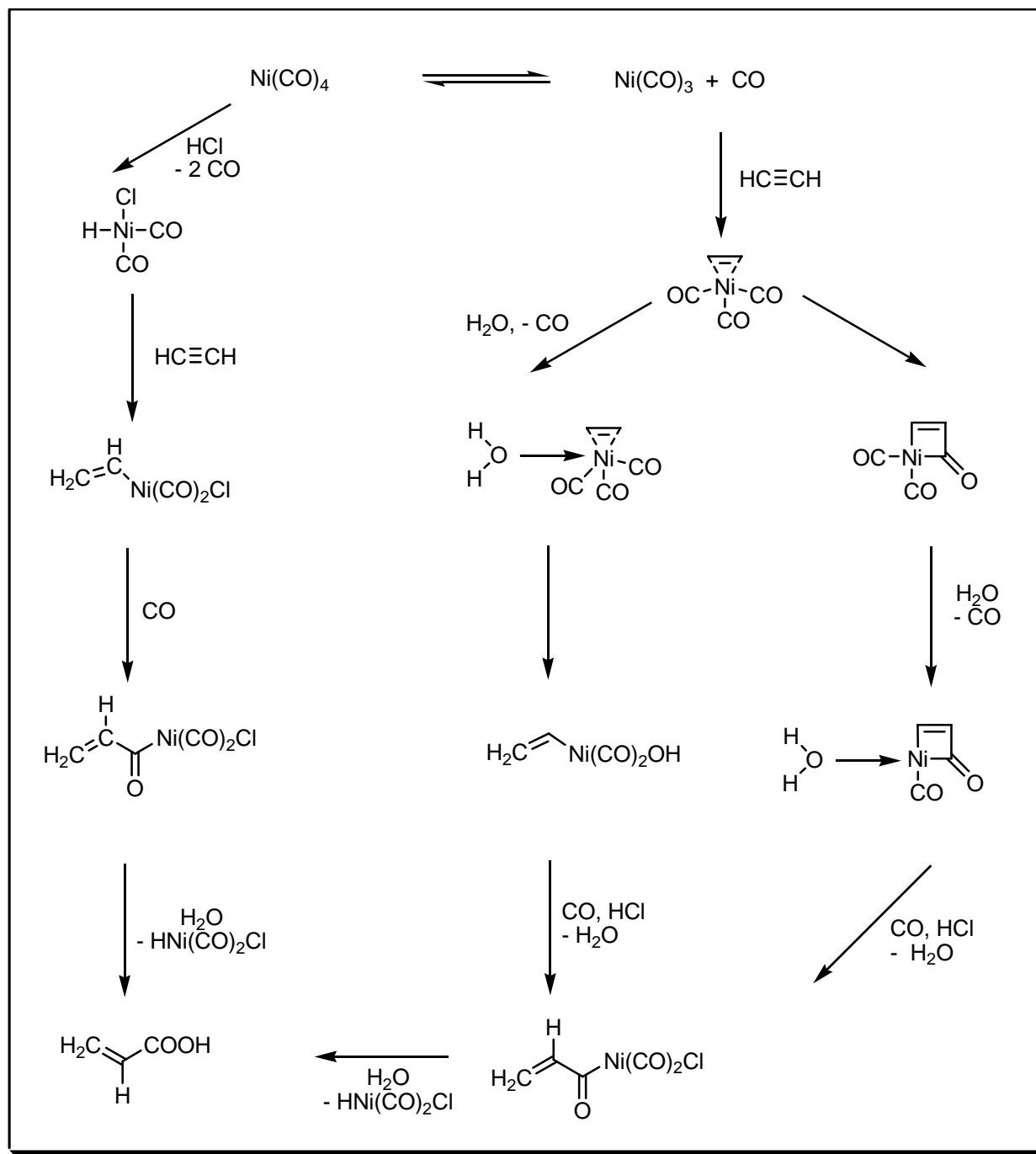
**COMMENTS :**

# REPPE CARBONYLATION

## EXAMPLE :

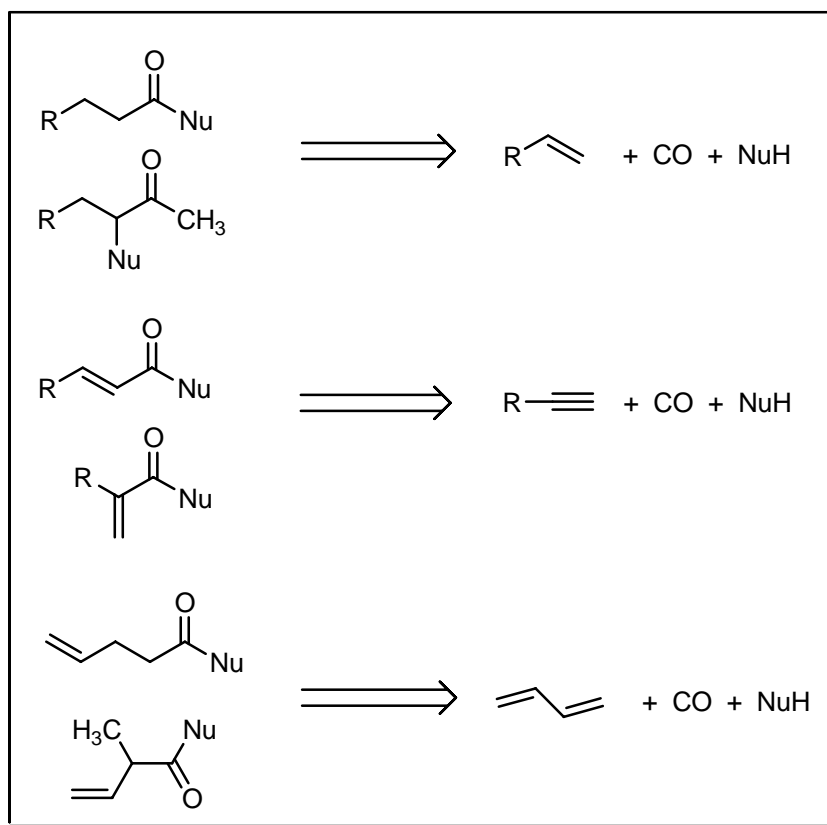


## MECHANISM :





## DISCONNECTION :



## NOTES :

This reaction is related to a number of reactions of acetylene, alkenes and conjugated dienes at high temperatures and pressures. It tolerates a wide variety of functional groups. The co-reagents are carbon monoxide and a nucleophile, water, alcohol, or acid. Nowadays most of the **Reppe** carbonylation processes are based on palladium as the catalyst. See also **Kutscheroff – Denigès** reaction.

## REFERENCES :

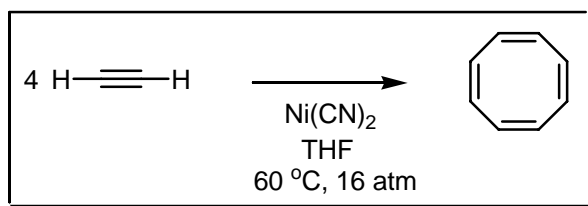
Houben – Weyl : 6/2, 664; E18, 757

- 1) W. Reppe, *Chem. Ing. Tech.*, 1950, **22**, 361.
- 2) W. Reppe, *Liebigs Ann. Chem.*, 1953, **582**, 1.
- 3) C.W. Bird, *Chem. Rev.*, 1962, **62**, 283.
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- 8) G. Kiss, *Chem. Rev.*, 2001, **101**, 3435.

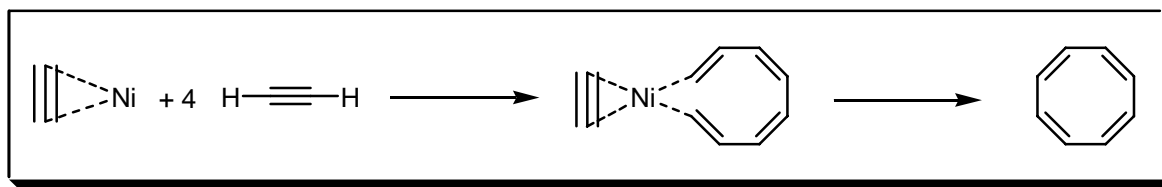
COMMENTS :

## REPPE POLYMERISATION

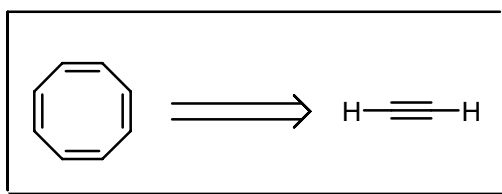
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The [2+2+2+2] cyclomerisation of acetylenes with or without olefins by nickel complexes to afford eight-membered rings. The use of a phosphine ligand increases the yield. The reaction fails using di-substituted alkynes.

REFERENCES :

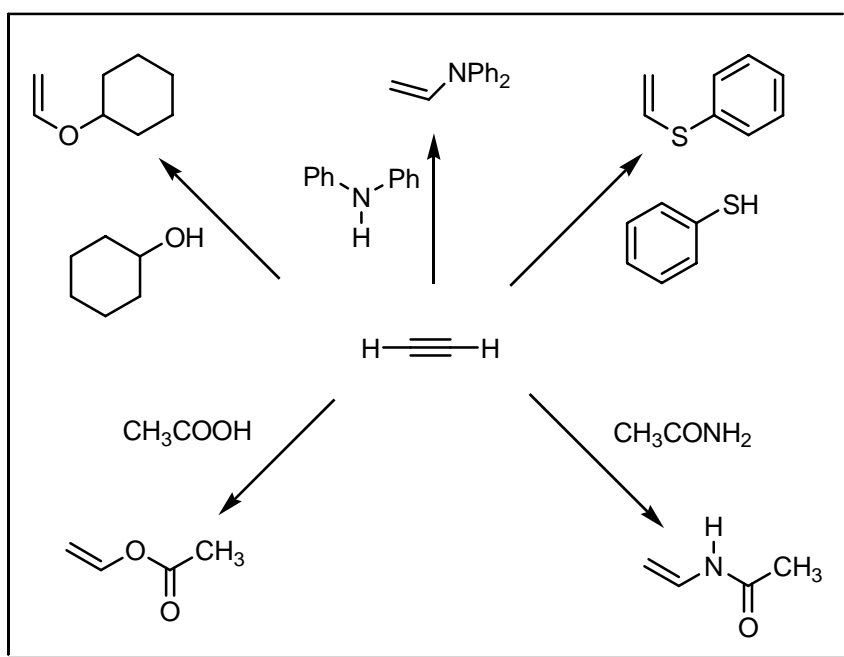
Houben – Weyl : 5/1d, 425

- 1) W. Reppe; O. Schlichting; K. Klager; T. Toepel, *Liebigs Ann. Chem.*, 1948, **560**, 1.
- 2) W. Reppe; W. Toepel, *German Patent.*, 1950, 68579.
- 3) W. Reppe, *Chem. Ing. Technik*, 1950, **22**, 369.
- 4) A.J. Chalk, *J. Am. Chem. Soc.*, 1972, **94**, 5928.

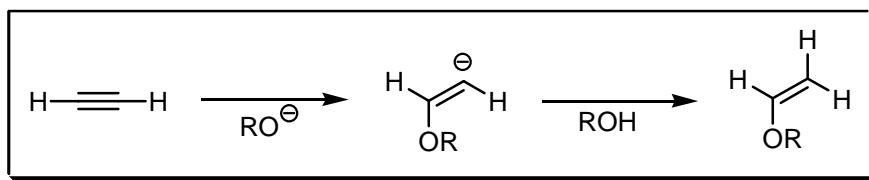
**COMMENTS :**

**REPPE VINYLATION**

**EXAMPLE :**



**MECHANISM :**



**NOTES :**

The vinylation of organic hydroxyl, sulfhydryl, amino, imino, carbonyl and carboxamide compounds having an active hydrogen atom attached to a heteroatom with mono substituted acetylenes or with acetylene itself under base catalysis. Sodium or potassium alkoxides are used as catalysts at high temperature and under pressure.

## REFERENCES :

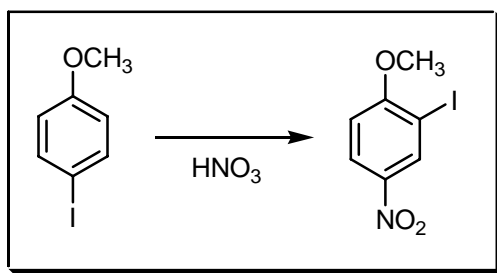
Houben – Weyl : 4/2, 407; 6/3, 90

- 1) W. Reppe, *Experientia*, 1949, **5**, 93.
- 2) W. Reppe, *Liebigs Ann. Chem.*, 1956, **601**, 81.
- 3) M. Seefelder, *Liebigs Ann. Chem.*, 1962, **652**, 107.

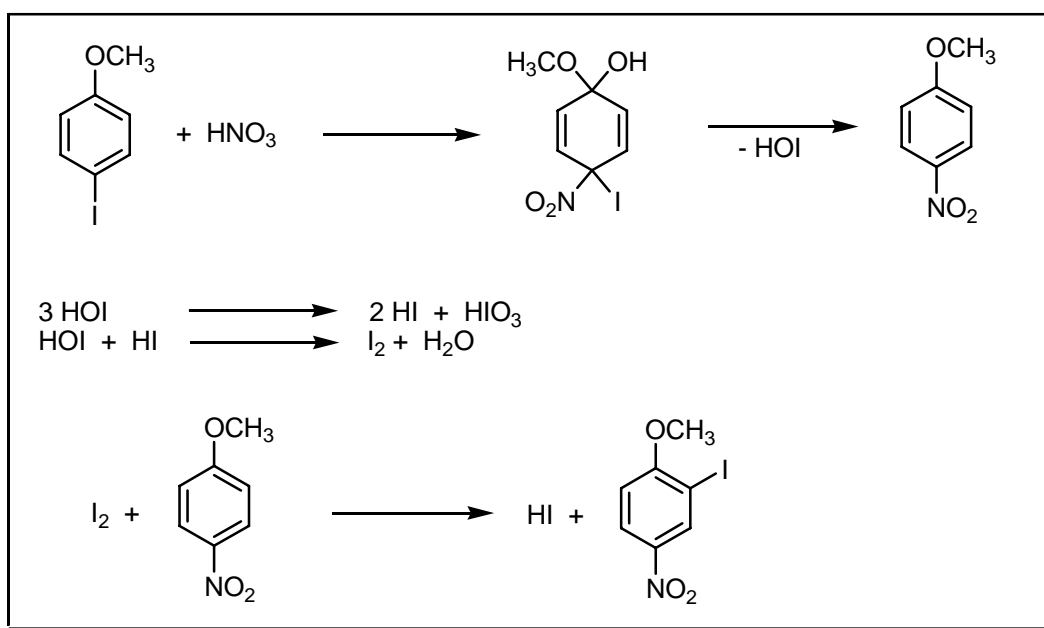
## COMMENTS :

## REVERDIN REACTION

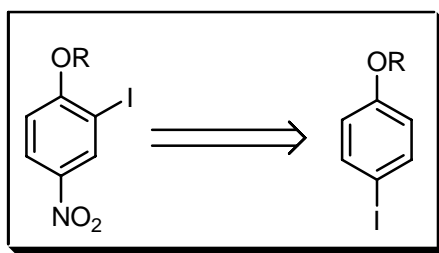
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

During nitration of iodophenoether the iodine atom rearranges from *para* to the *ortho* position.

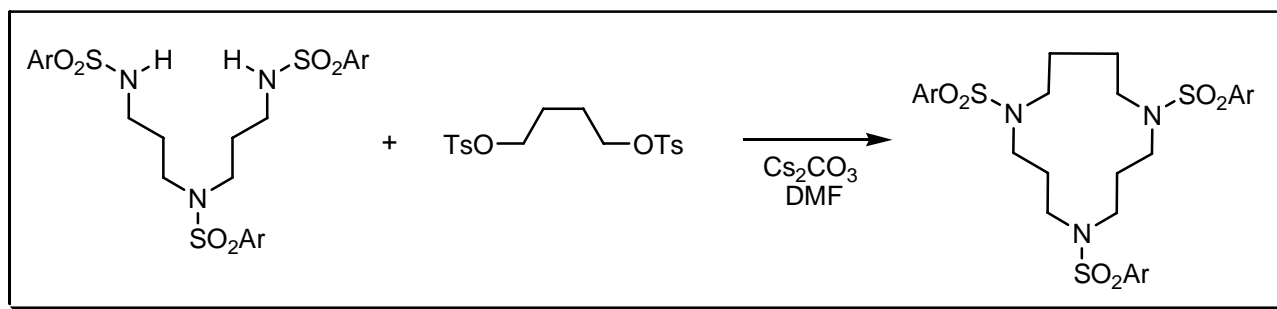
## REFERENCES :

- 1) F. Reverdin, *Ber. Dtsch. Chem. Ges.*, 1896, **29**, 997.
- 2) G.M. Robinson, *J. Chem. Soc.*, 1916, **109**, 1078.
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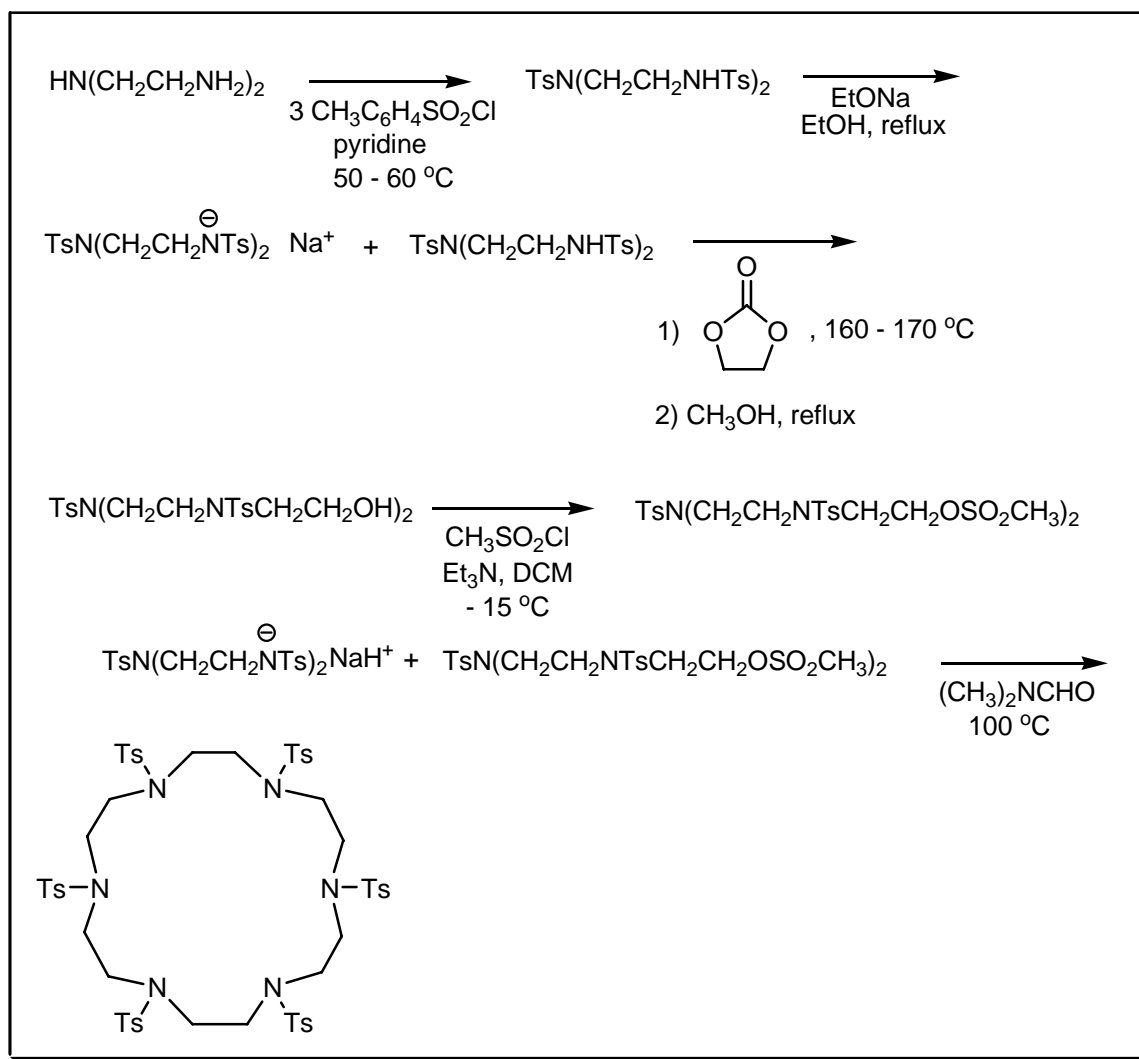
## COMMENTS :

## RICHMAN – ATKINS SYNTHESIS

### EXAMPLE :



## MECHANISM :



## NOTES :

The **Richman – Atkins** cyclisation remains one of the most widely used methods for the preparation of macrocyclic polyamines (polyazamacrocycles). This general procedure is best effected by the reaction of a bis-*para*-toluenesulfonamide salt with a bis-tosylate or mesylate in anhydrous DMF. See also **Moedritzer – Irani** reaction.

## REFERENCES :

**Org. Synth.** : **58**, 86

**Org. Synth. Coll. Vol.** : **6**, 652

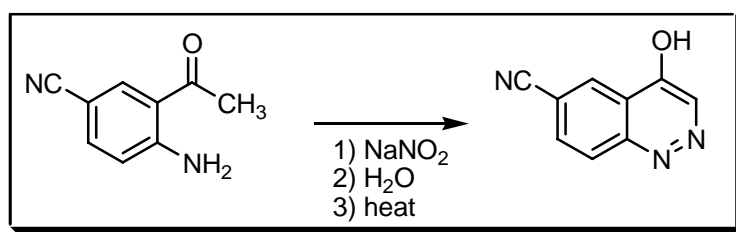
- 1) H. Stetter; E.E. Roos, *Chem. Ber.*, 1955, **88**, 1390.
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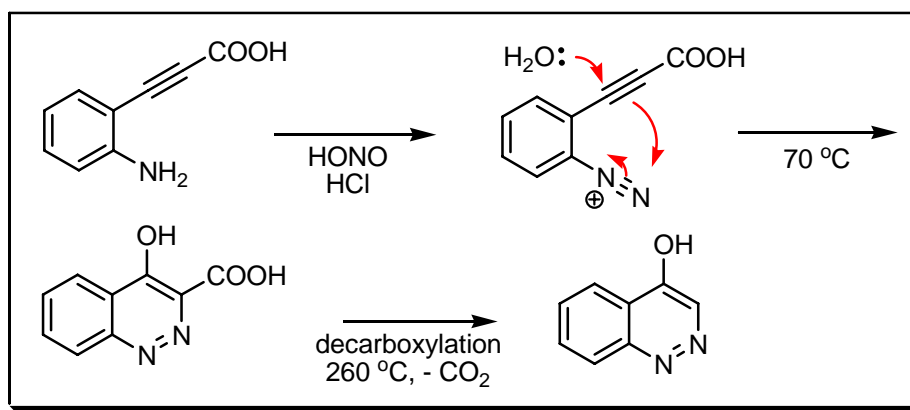
**COMMENTS :**

**von RICHTER CINNOLINE SYNTHESIS**

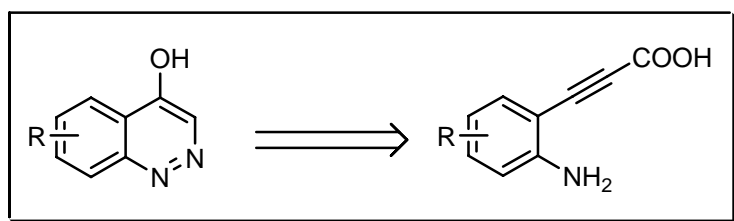
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

The synthesis of cinnolines from substituted anilines *via* diazonium salts. See also **Borsche – Koelsch**, **Neber – Bosset** and **Widman – Stoermer** reactions.

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## REFERENCES :

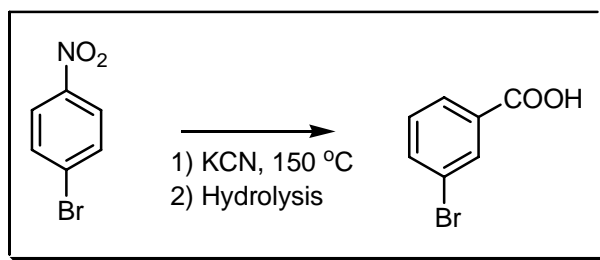
- 1) V. von Richter, *Ber. Dtsch. Chem. Ges.*, 1883, **16**, 677.
  - 2) M. Busch; M. Klett, *Ber. Dtsch. Chem. Ges.*, 1892, **25**, 2847.
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  - 5) C.M. Atkinson; J.C.E. Simpson, *J. Chem. Soc.*, 1947, 808.
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- 

## COMMENTS :

## von RICHTER REACTION

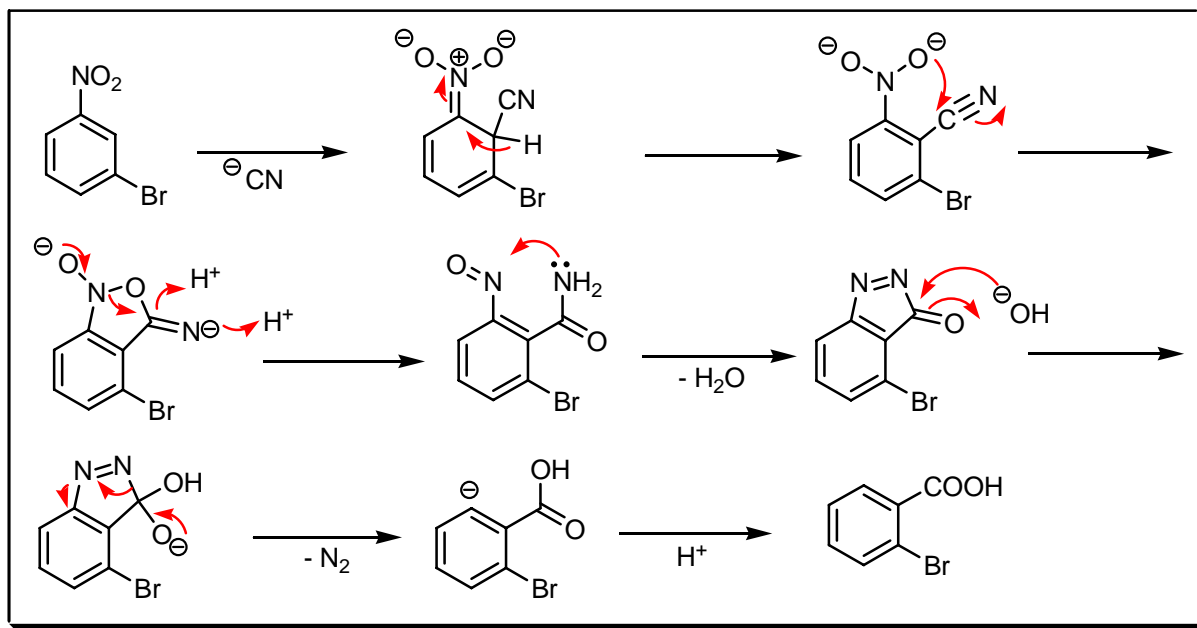
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### EXAMPLE :

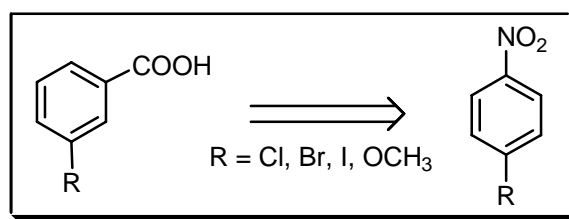




## MECHANISM :



## DISCONNECTION :



## NOTES :

The reaction of *m*- and *p*-nitrohalobenzenes with potassium cyanide leading to *o*- and *m*-halobenzoic acids with loss of the  $\text{NO}_2$ -group as nitrogen.

## REFERENCES :

March : 672

Smith – March : 876

Houben – Weyl : E8a, 399

Org. Synth. : 38, 11

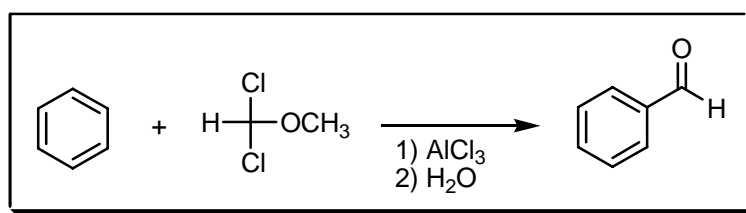
Org. Synth. Coll. Vol. : 4, 114

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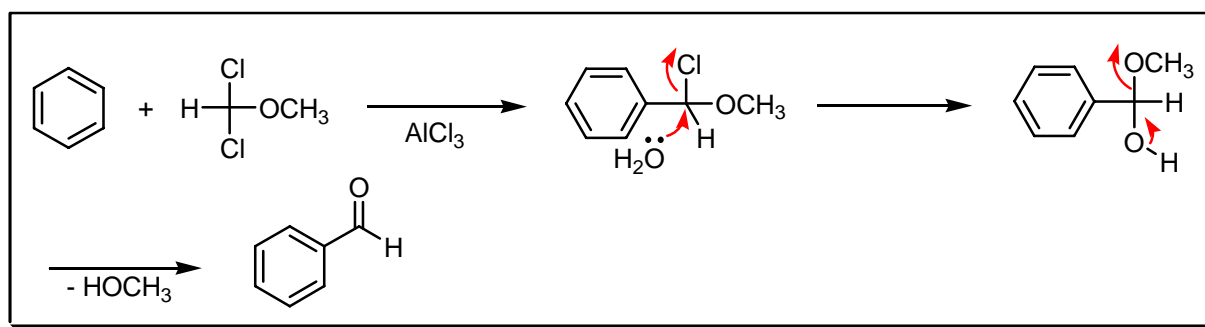
COMMENTS :

RIECHE FORMYLATION

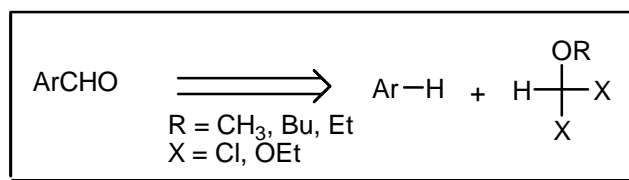
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

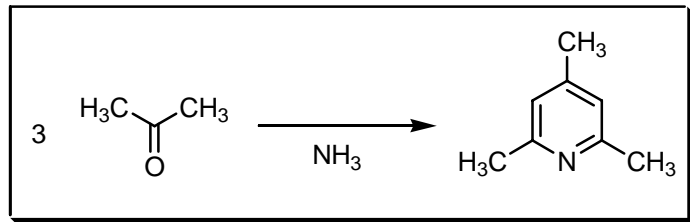
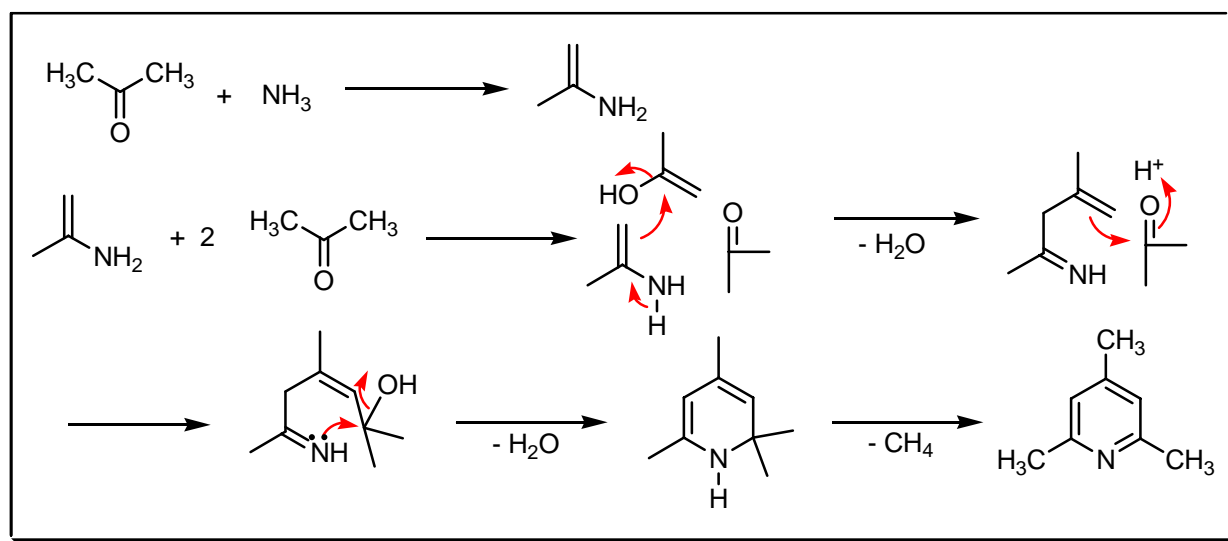
Dichloromethyl methyl ether formylate reacts with an aromatic under **Friedel – Crafts** catalysis (TiCl<sub>4</sub>, SnCl<sub>4</sub>, AlCl<sub>3</sub>). *Ortho* formates can also be used. See also **Friedel – Crafts** and **Gattermann – Koch** reactions.

**REFERENCES :**

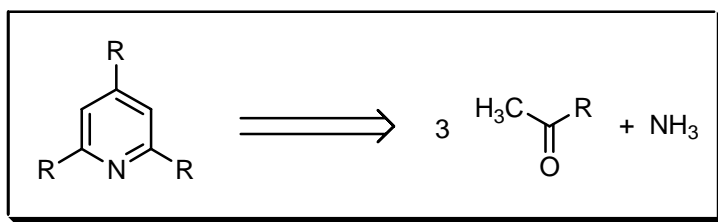
**Org. Synth. :** **47**, 51

**Org. Synth. Coll. Vol. :** **5**, 49, 365

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- 1) A. Rieche; H. Gross; E. Höft, *Chem. Ber.*, 1960, **93**, 88.
  - 2) H. Gross; A. Rieche; G. Matthey, *Chem. Ber.*, 1963, **96**, 308.
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  - 5) S. Mayer; G. Guillaumet; J.Y. Merour, *Heterocycles*, 2001, **55**, 1873.
- 

**COMMENTS :****RIEHM PYRIDINE SYNTHESIS****EXAMPLE :****MECHANISM :**

## DISCONNECTION :



## NOTES :

Pyridine is synthesised from 3 equivalents of acetone and one equivalent of ammonia. See also **Bohlmann – Rahtz**, **Chichibabin** pyridine, **Gattermann – Skita**, **Guareschi – Thorpe**, **Hantzsch**, **Hantzsch – Beyer**, **von Meyer – Mohr**, **Petrenko–Kritschenko** and **Wakatsuki – Yamazaki – Bönnemann** reactions.

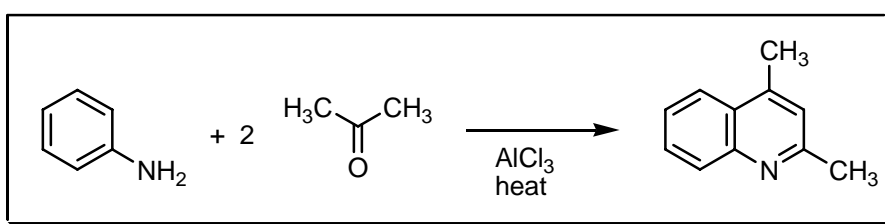
## REFERENCES :

P. Riehm, *Liebigs Ann. Chem.*, 1887, **238**, 1.

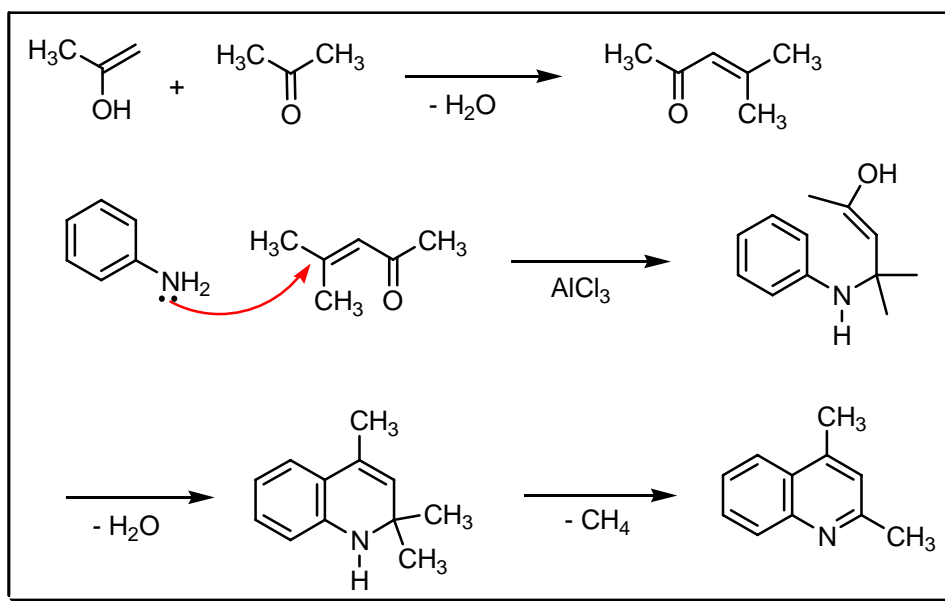
## COMMENTS :

## RIEHM QUINOLINE SYNTHESIS

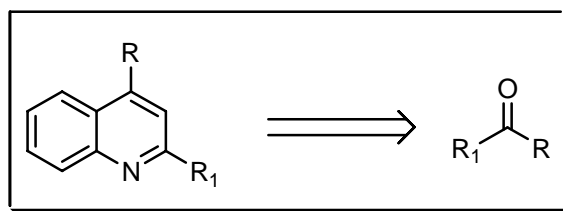
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Quinoline is synthesised from arylaminehydrochlorides and ketones in the presence of phosphorus pentachloride or aluminium chloride. See also **Allan – Loudon**, **von Baeyer – Drewson** quinoline, **Camps, Combes** quinoline, **Conrad – Limpach**, **Doebner** quinoline, **Doebner – von Miller**, **Foulds – Robinson**, **Friedländer**, **Knorr** quinoline, **Meth–Cohn**, **von Niementowski** quinoline, **Pfitzinger – Borsche** and **Skraup** quinoline reactions.

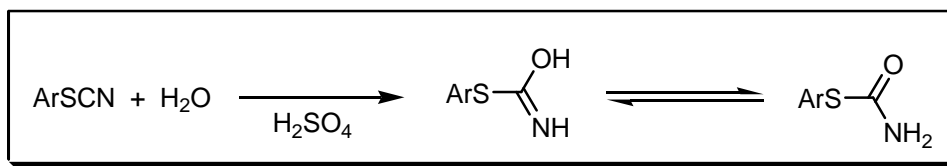
## REFERENCES :

- 1) C. Engler; P. Riehm, *Ber. Dtsch. Chem. Ges.*, 1885, **18**, 2245.
- 2) J. Levin; P. Riehm, *Ber. Dtsch. Chem. Ges.*, 1886, **19**, 1394.
- 3) P. Riehm, *Liebigs Ann. Chem.*, 1887, **238**, 9.
- 4) D.J. Craig, *J. Am. Chem. Soc.*, 1938, **60**, 1458.
- 5) R.C. Elderfield; J.R. McCarthy, *J. Am. Chem. Soc.*, 1951, **73**, 975.

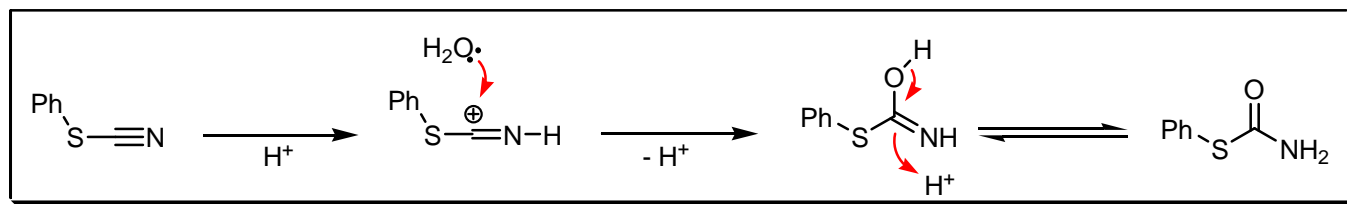
## COMMENTS :

# RIEMSCHNEIDER THIOCARBAMATE SYNTHESIS

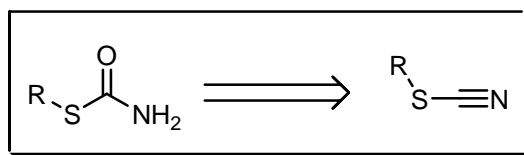
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Thiocarbamates are formed from thiocyanates and 95% sulfuric acid, followed by hydrolysis with ice-water. See also **Radziszewski** reaction.

## REFERENCES :

**March** : 888

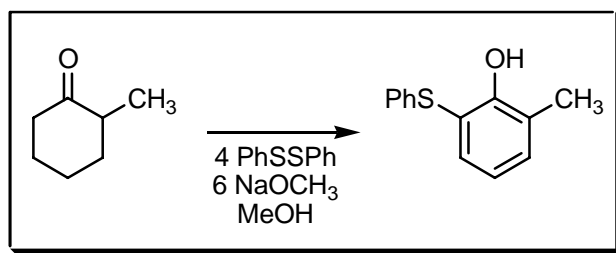
**Smith – March** : 1179

- 1) R. Riemschneider; F. Wojahn, *Pharmazie*, 1949, **4**, 460.
- 2) R. Riemschneider; F. Wojahn; G. Orlick, *J. Am. Chem. Soc.*, 1951, **73**, 5905.
- 3) K. Schmidt; P. Kollek-Bös, *J. Am. Chem. Soc.*, 1953, **75**, 6067.
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- 7) J. Fetter; H. Vásárhelyi; M. Kajtár-Peredy; K. Lempert; J. Tamás; G. Czira, *Tetrahedron*, 1995, **51**, 4763.
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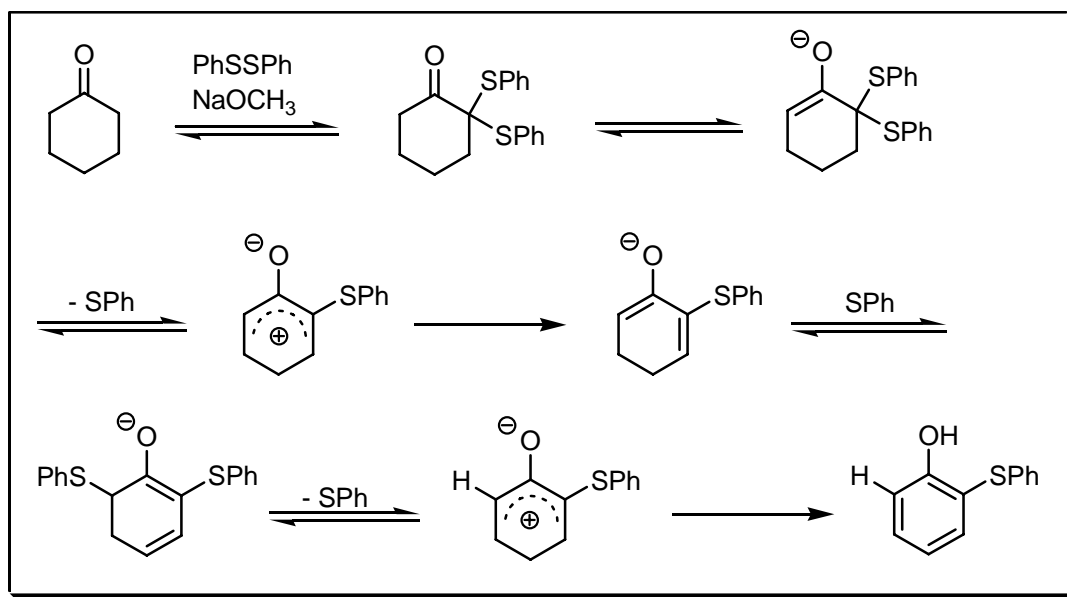
**COMMENTS :**

## RIGBY – TROST DEHYDROGENATIVE SULFENYLATION

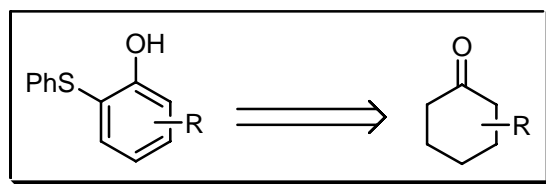
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



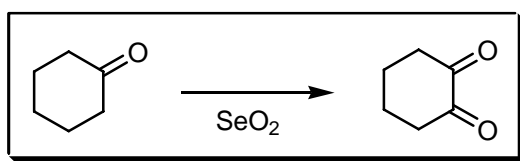
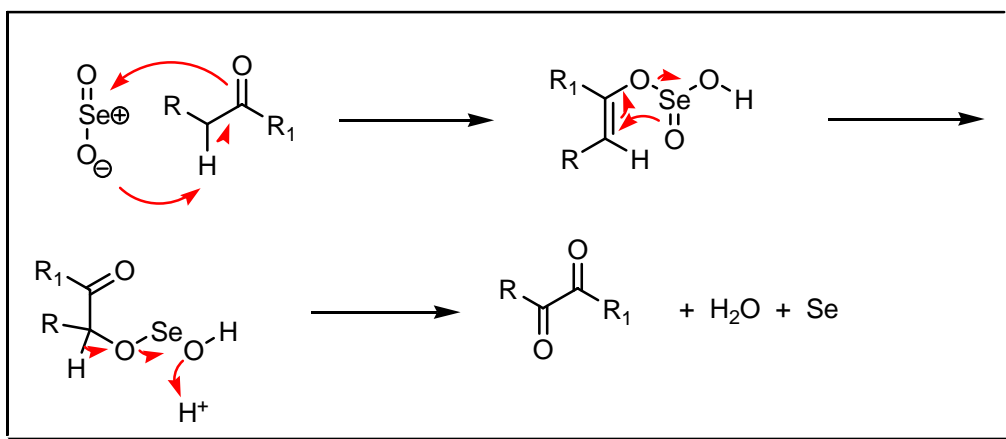
**NOTES :**

Cyclohexanones undergo a remarkably mild aromatisation accompanying sulfenylation to give o-phenylthio phenols. See also **Cohen – Daniewski** reaction.

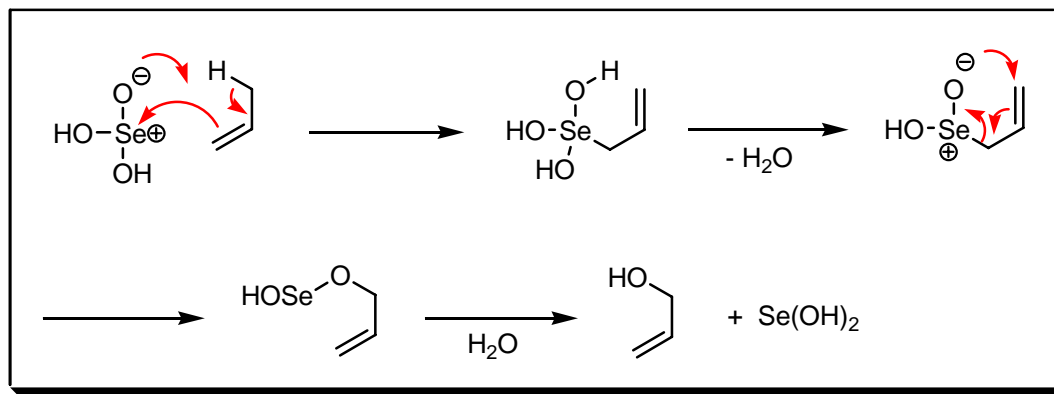
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**REFERENCES :**

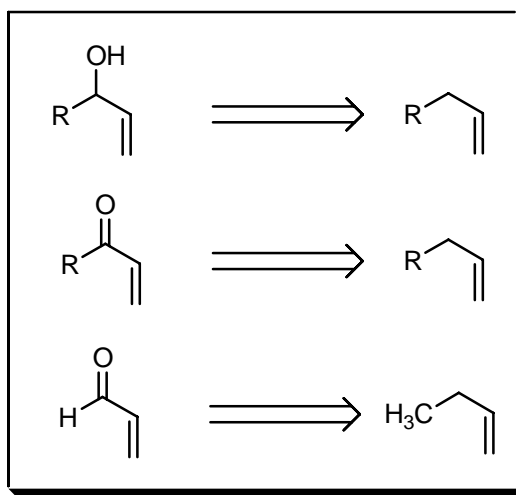
- 1) B.M. Trost; J.H. Rigby, *J. Org. Chem.*, 1976, **41**, 3217.
  - 2) B.M. Trost; J.H. Rigby, *Tetrahedron Lett.*, 1978, **19**, 1667.
- 

**COMMENTS :****RILEY – SHARPLESS OXIDATION****EXAMPLE :****MECHANISM :**





#### DISCONNECTION :



#### NOTES :

The oxidation active methylene groups carbonyl compounds with  $\text{SeO}_2$ . The **Sharpless** method involves the hydroxy dehydrogenation with catalytic amount of selenium dioxide. The reaction involves an **Alder** ene reaction followed by a [2,3]-sigmatropic rearrangement. See also **Alder** ene reaction.

#### REFERENCES :

**March** : 698

**Smith – March** : 915

**Smith** : 313

**Smith 2<sup>nd</sup>** : 273

**Houben – Weyl** : 7/1, 146

**Org. React.** : 5, 331; 24, 261

- 1) H.L. Riley; J.F. Morley; N.A.C. Friend, *J. Chem. Soc.*, 1932, 1875.
- 2) G.R. Waitkins; C.W. Clark, *Chem. Rev.*, 1945, **36**, 235.
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- 6) N.M. Goudgaon; U.R. Nayak, *Indian J. Chem.*, 1985, **24B**, 589.  
 7) V.S. Dalavoy; V.B. Deodhar; U.R. Nayak, *Indian J. Chem.*, 1987, **26B**, 1.  
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 9) A. Thalén; L.I. Wicksöm, *Steroids*, 2000, **65**, 16.

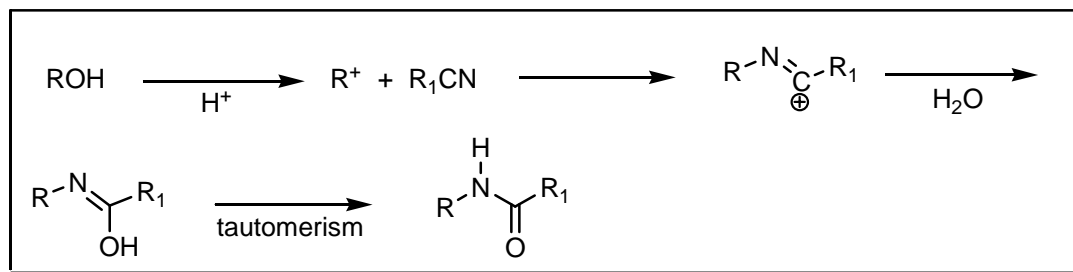
**COMMENTS :**

## RITTER REACTION

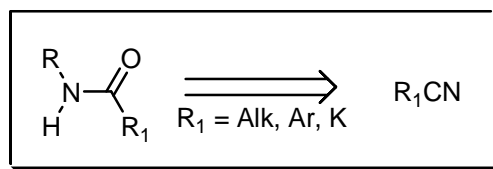
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

Nitriles or aldehyde cyanohydrins react with a variety of alkenes, unsaturated carboxylic acids, esters, hydroxy esters or secondary or tertiary alcohols in concentrated sulphuric acid to yield amines. Acetic acid or dibutyl ether may be employed as a solvent. See also **Kriewitz – Prins** reaction.

## REFERENCES :

March : 970

Smith – March : 1244

Smith : 1068

Smith 2<sup>nd</sup> : 892, 1074

Houben – Weyl : **11/2**, 561; **E5**, 1032, 1554; **E7a**, 652; **E7b**, 335; **E10a**, 771; **E16d**, 650, 733, 1165

Org. React. : **17**, 213

Org. Synth. : **42**, 16; **44**, 44

Org. Synth. Coll. Vol. : **5**, 73, 471

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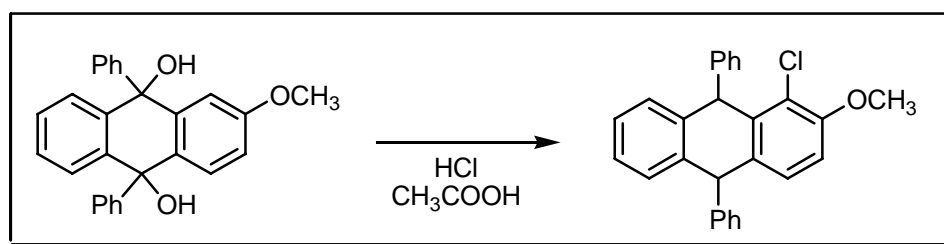
- 1) J.J. Ritter; P.P. Minieri, *J. Am. Chem. Soc.*, 1948, **70**, 4045.
  - 2) J.J. Ritter; J. Kalish, *J. Am. Chem. Soc.*, 1948, **70**, 4048.
  - 3) T. Gajda; A. Kuziara; S. Zawadski; A. Zwierzak, *Synthesis*, 1979, 549.
  - 4) G. Fodor; S. Nagubandi, *Tetrahedron*, 1980, **36**, 1279.
  - 5) S. Top; G. Jaoven, *J. Org. Chem.*, 1981, **46**, 78.
  - 6) Y.D. Vanka; C.T. Rao, *Tetrahedron*, 1985, **41**, 3405.
  - 7) G.A. Olah; Q. Wang, *Synthesis*, 1992, 1090.
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  - 13) J.M. Concellón; E. Riego; J.R. Suárez; S. García-Granada; M.R. Díaz, *Org. Lett.*, 2004, **6**, 4499.
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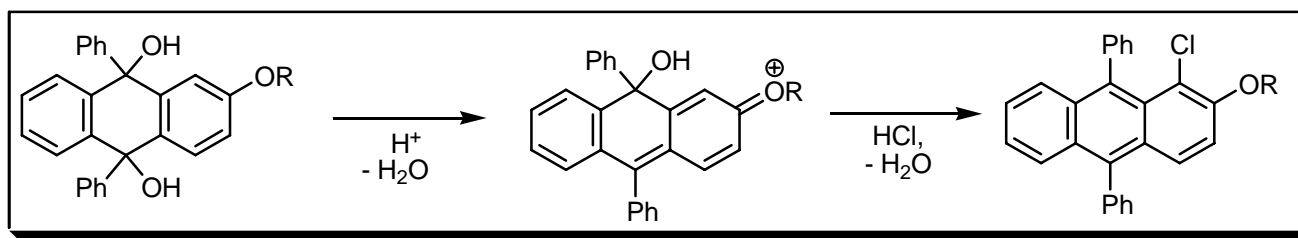
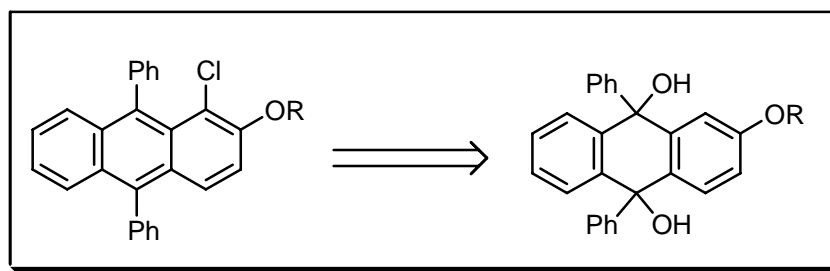
## COMMENTS :

## ROBERT CHLORINATION

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### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

This reaction is illustrated by the fact that 9,10-dihydro-9,10-dihydroxy-2-alkoxy-9,10-diphenylanthracene on treatment with hydrochloric acid in acetic acid yields the corresponding 1-chloro compound. See also **Bergmann** anthracene reaction.

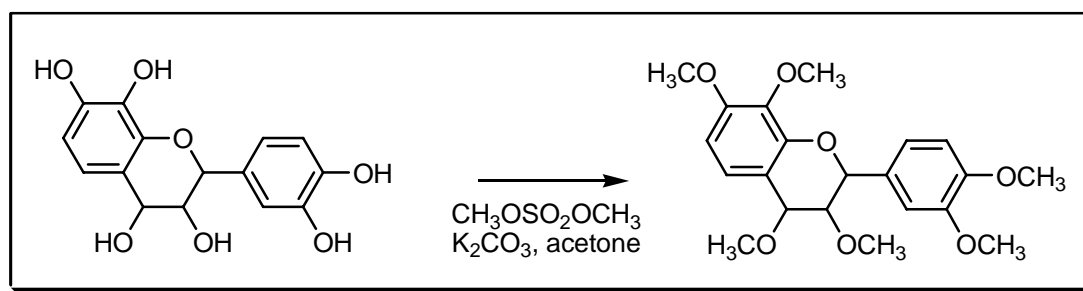
**REFERENCES :**

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- 2) C. Dufraisse; A. Étienne; J. Salmon, *Bull. Soc. Chim. Belg.*, 1953, **62**, 21.

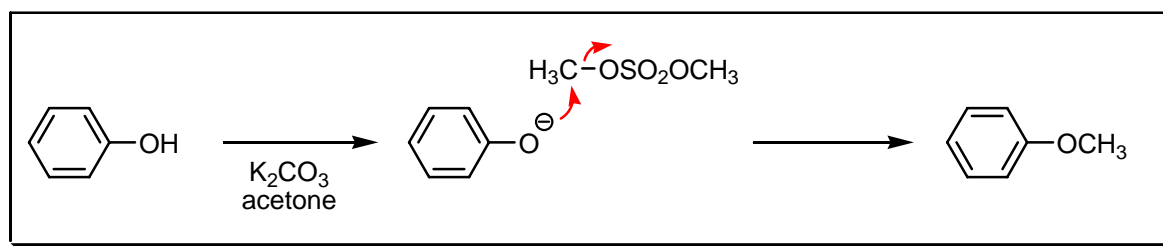
**COMMENTS :**

## ROBERTSON – ROBINSON METHYLATION

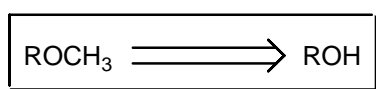
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The use of methyl sulfate and potassium carbonate in acetone in the methylation of hydroxy groups. See also **Claisen** carbonate alkylation, **Fischer** glycosidation, **Hakomori**, **Haworth** methylation, **Irvine – Purdie**, **Meerwein** methylation and **Williamson** reactions.

### REFERENCES :

**March** : 388

**Smith – March** : 478

**Org. Synth.** : **6**, 96; **9**, 12; **13**, 56, 102; **20**, 97; **29**, 63; **31**, 90

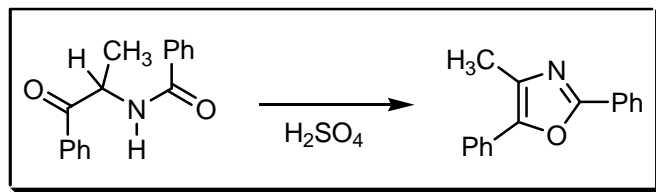
**Org. Synth. Coll. Vol.** : **1**, 387, 619; **2**, 387, 619; **3**, 564, 800; **4**, 836

- 1) S.W. George; A. Robertson, *J. Chem. Soc.*, 1937, 1535.
- 2) F.E. King; W. Bottomly, *J. Chem. Soc.*, 1954, 1399.
- 3) A. Merz, *Angew. Chem., Int. Ed. Engl.*, 1973, **12**, 846.
- 4) M.E. Jung; S.M. Kaas, *Tetrahedron Lett.*, 1989, **30**, 641.

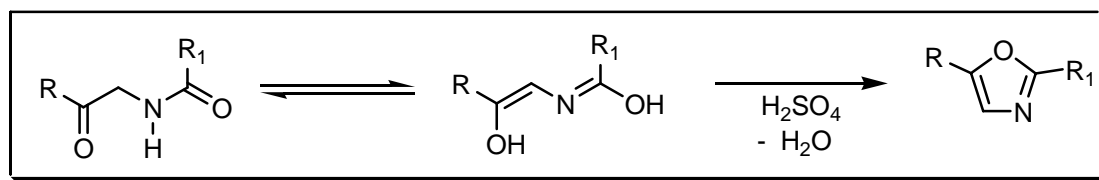
## COMMENTS :

## ROBINSON – GABRIEL SYNTHESIS

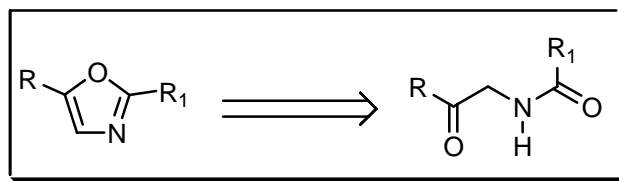
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The oxazole synthesis from amides derived from  $\alpha$ -aminoketones. Also trisubstituted oxazoles can be synthesised by this method. See also **Davidson**, **Fischer** oxazole and **Japp** reactions.

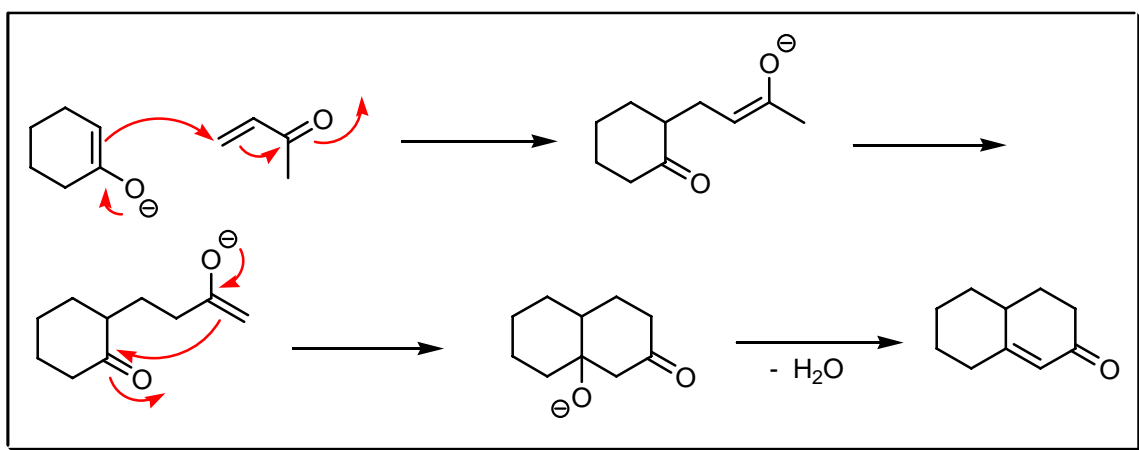
### REFERENCES :

Houben – Weyl : E8a, 935, 972

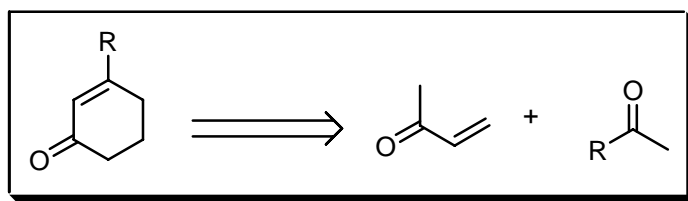
- 1) Laurent, *J. Prakt. Chem.*, 1845, **35**, 461.
- 2) R. Robinson, *J. Chem. Soc.*, 1909, **95**, 2167.
- 3) S. Gabriel, *Ber. Dtsch. Chem. Ges.*, 1910, **43**, 1283.
- 4) R.H. Wiley, *Chem. Rev.*, 1945, **37**, 401.
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## ROBINSON – MANNICH ANNULATION REACTION

C1CCCCC1=O.CC(=O)C=C>>C1CCC2C(C1)C(=O)C=C2CC1=CCCCC1=O.CC(C)C(=O)CC[N+](C)(C)CC.[I-]>>CC1=CCCCC1=O.CC(C)C(=O)CC1(C)CCCC1=O

## DISCONNECTION :



## NOTES :

The fusion of six-membered rings by reaction of cyclanones with vinyl ketones (base- or acid-catalysed), a tandem **Michael** addition – aldol condensation. Cyclohexanones and their  $\beta$ -carboxylic esters react also with quaternary salts of **Mannich** bases of the type  $\text{CH}_3\text{COCH}_2\text{CH}_2\text{N}^+\text{R}_2\text{CH}_3$  in the presence of bases, e.g. sodamide or sodium alkoxide, to yield bicyclic unsaturated ketones. An aza-**Robinson** reaction has been published by **Danishefsky et al.** The **Stork – Jung – Robinson** annulation uses 1-iodo-3-trimethylsilyl-2-butene and derivatives to introduce a 3-oxobutyl group. See also **Hajos – Parrish – Eder – Sauer – Wiechert**, **Mannich** and **Wichterle** reactions.

## REFERENCES :

**March** : 943

**Smith – March** : 1222

**Smith** : 956

**Smith 2<sup>nd</sup>** : 98, 795, 845

**Houben – Weyl** : **E7b**, 675

**Org. React.** : **7**, 113

**Org. Synth.** : **41**, 38; **45**, 80; **63**, 37

**Org. Synth. Coll. Vol.** : **5**, 486, 869; **7**, 368

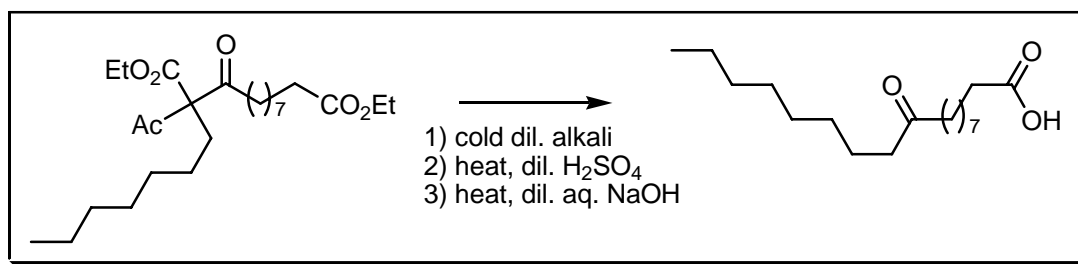
- 1) W.S. Rapson; R. Robinson, *J. Chem. Soc.*, 1935, 1285.
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- 11) B.B. Snider; B. Shi, *Tetrahedron Lett.*, 2001, **42**, 9123.
- 12) M.E. Jung; G. Piizzi, *Org. Lett.*, 2003, **5**, 137.



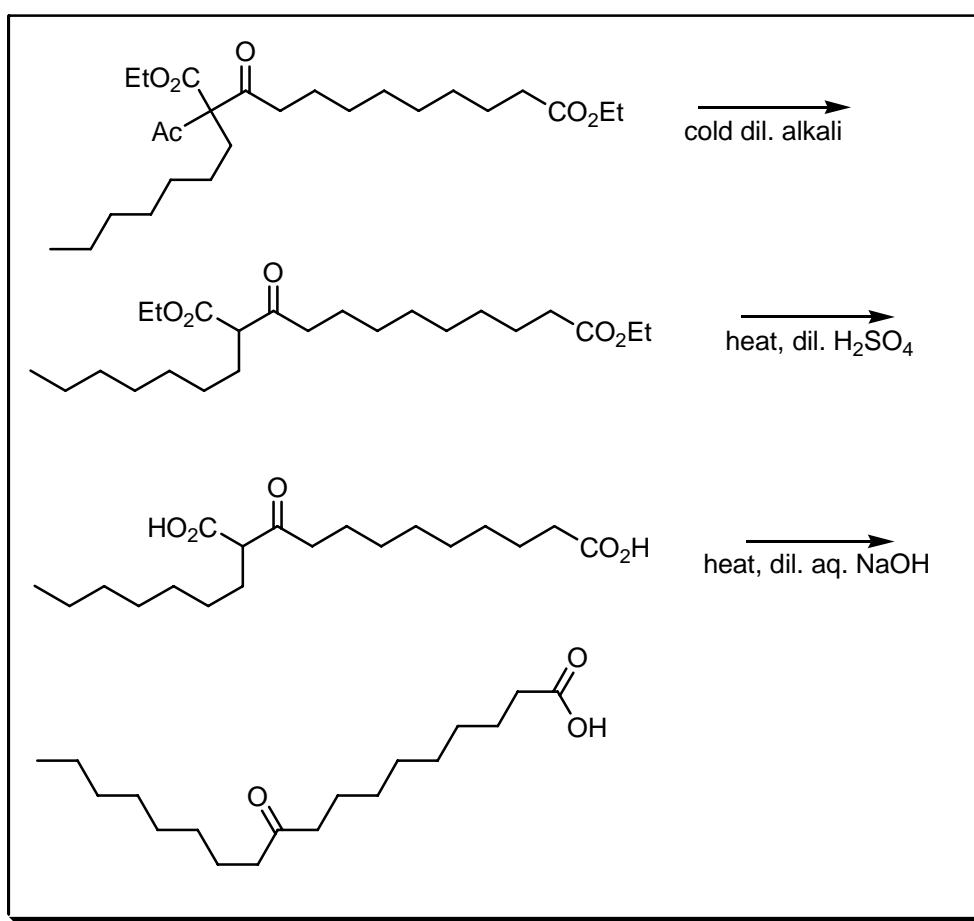
COMMENTS :

## ROBINSON – ROBINSON KETO-ESTER METHOD

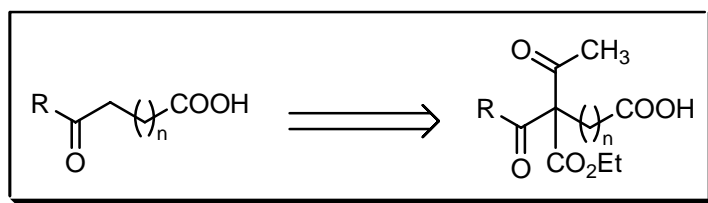
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

This is the graded hydrolysis of an acylalkylacetoacetic ester to a keto-acid. See also **Baudart**, **Bowman**, **Kapp – Knoll** and **Noller** reactions.

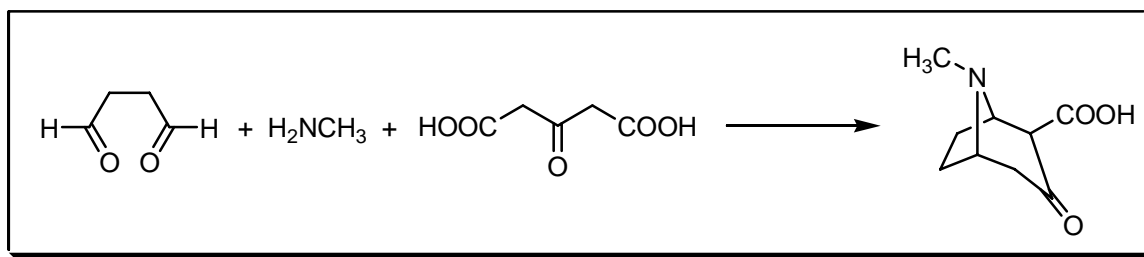
## REFERENCES :

- 1) G.M. Robinson; R. Robinson, *J. Chem. Soc.*, 1925, **127**, 175.
- 2) D.E. Ames; R.E. Bowman; R.G. Mason, *J. Chem. Soc.*, 1950, 174.

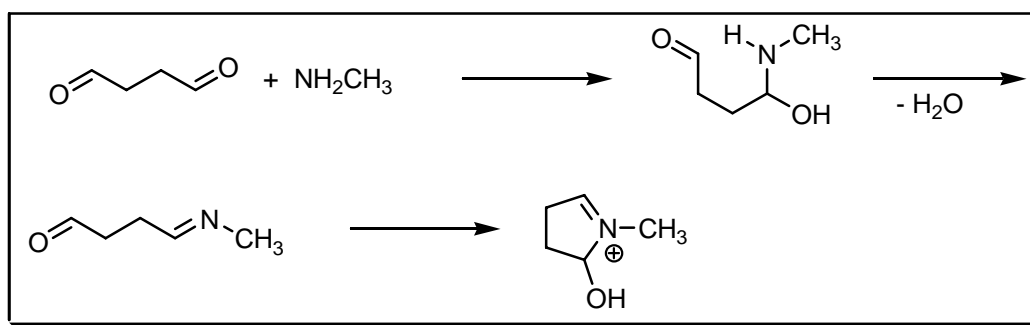
## COMMENTS :

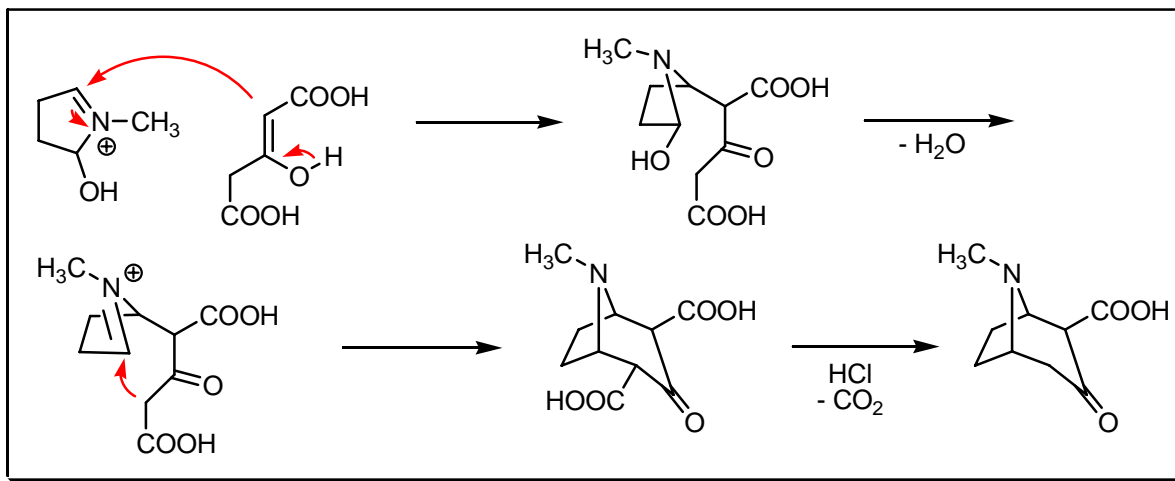
## ROBINSON – SCHÖPF REACTION

### EXAMPLE :

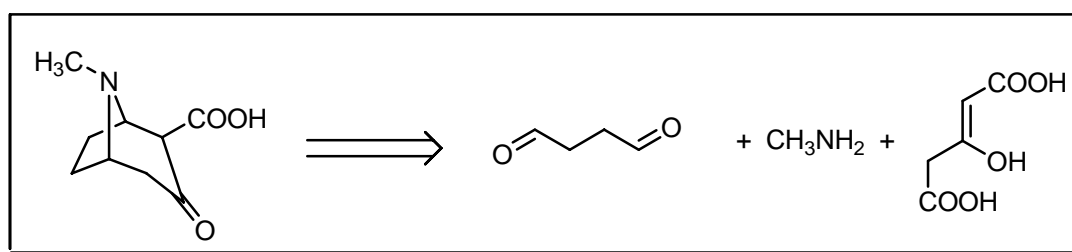


### MECHANISM :





#### DISCONNECTION :



#### NOTES :

This is the tropinone synthesis from succinic dialdehyde, methylamine and acetonedicarboxylic acid. See also **Mannich** and **Petrenko–Kritschenko** reactions.

#### REFERENCES :

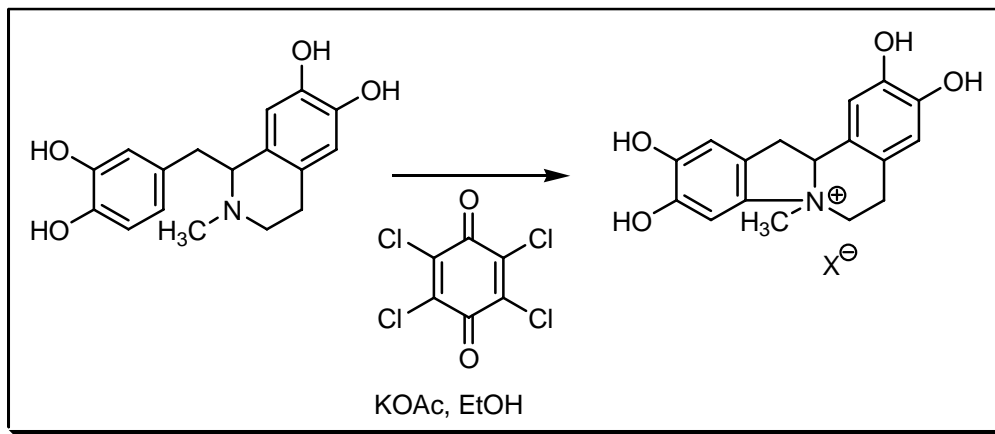
**March** : 900

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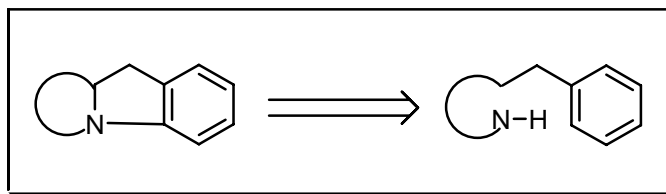
**COMMENTS :**

**ROBINSON DEHYDROGENATION**

**EXAMPLE :**



**DISCONNECTION :**



**NOTES :**

This reaction relates to the cyclisation of methyl tetrahydroisoquinolines to aromatic rings by chloranil in ethanolic solution containing potassium acetate.

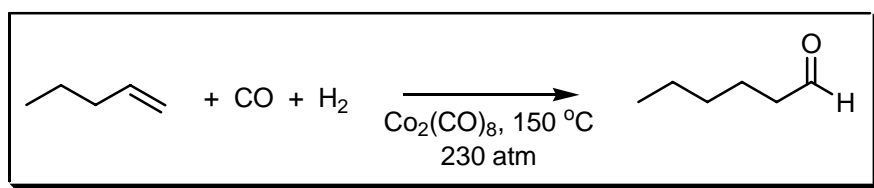
**REFERENCES :**

- 1) R. Robinson: S. Sugawara, *J. Chem. Soc.*, 1932, 789.
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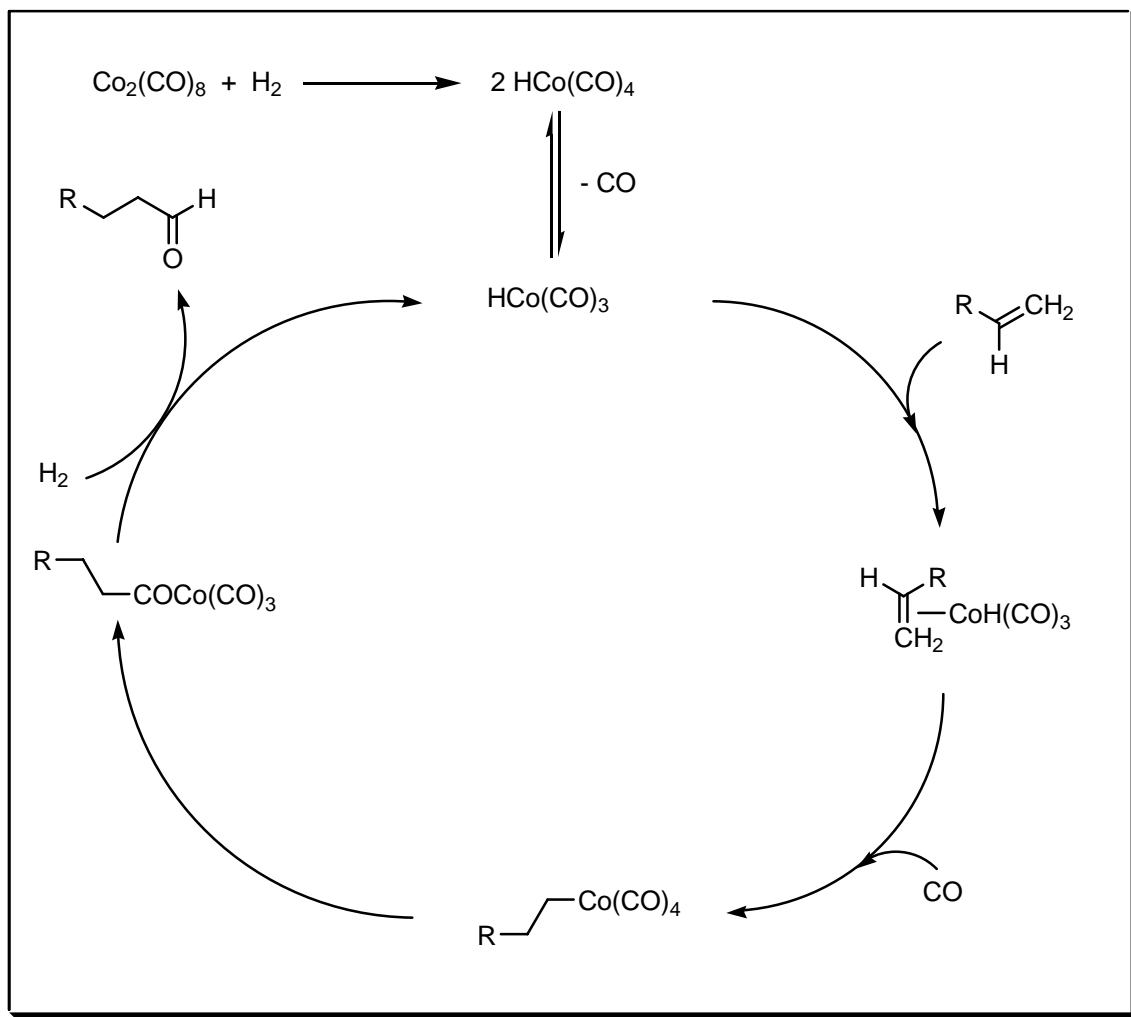
**COMMENTS :**

## ROELEN CARBONYLATION

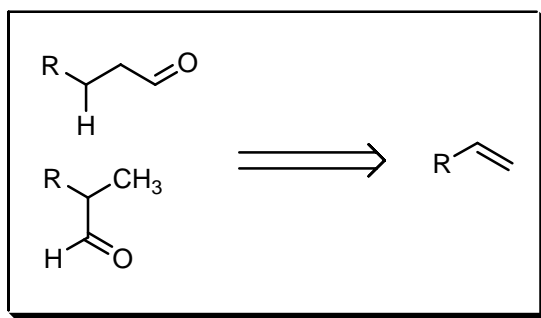
EXAMPLE :



MECHANISM :



## DISCONNECTION :



---

## NOTES :

The cobalt-catalysed addition of  $\text{CO}$ ,  $\text{H}_2$  to olefins. See also **Koch** carbonylation, **Reppe** and **Tsuji – Wacker** reactions.

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**Houben – Weyl** : 7/1, 55; **E3**, 180, 224; **E18**, 759

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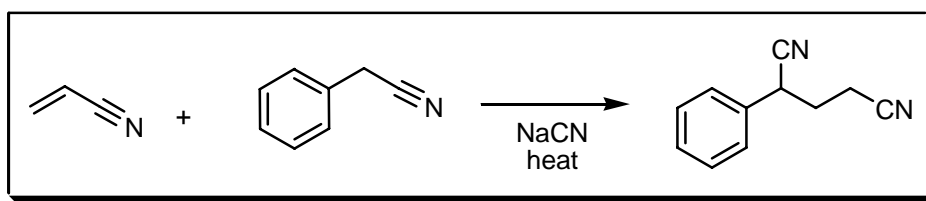
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## COMMENTS :

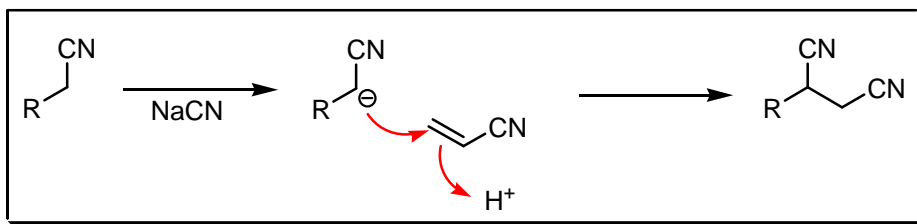
## ROGER SYNTHESIS

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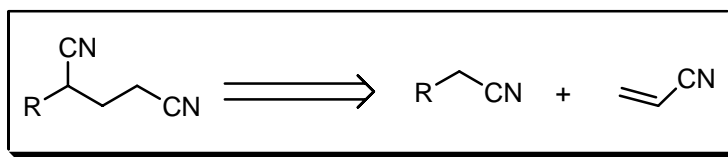
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

These compounds are obtained by the addition of acrylonitrile to an excess of a boiling substituted acetonitrile in the presence of sodium cyanide. See also **Knoevenagel** condensation and **Michael** reaction.

### REFERENCES :

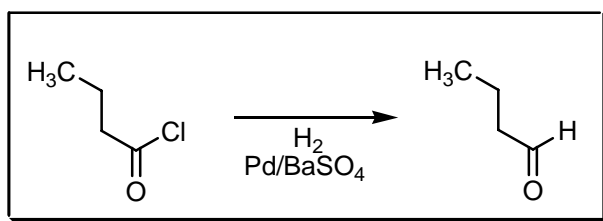
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### COMMENTS :

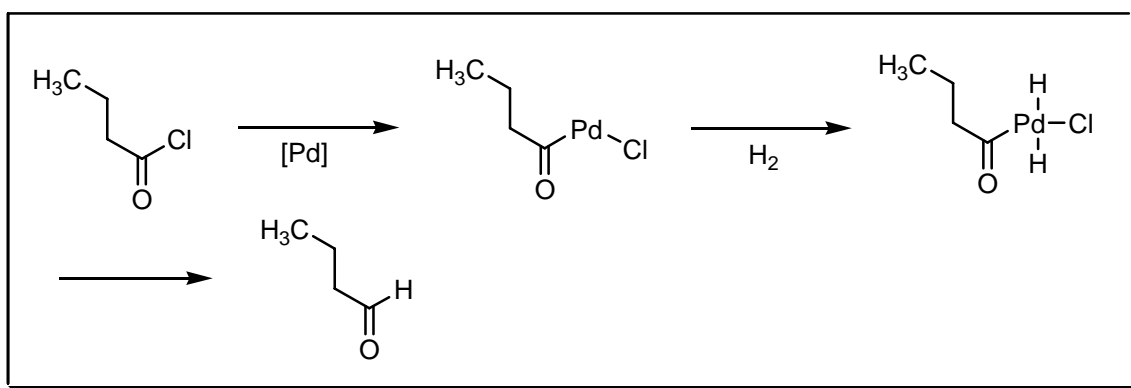
## ROSENMUND – SAYTZEFF REDUCTION

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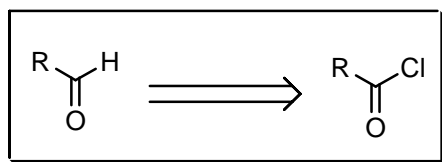
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The hydrogenation of acyl chlorides to aldehydes in the presence of a poisoned palladium catalyst. Carbonyl groups and nitro groups will not be reduced under these conditions. See also **Brandt** and **Grundmann** reactions.

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### REFERENCES :

March : 447

Smith – March : 532

Houben – Weyl : 7/1, 285

Org. React. : 4, 362

Org. Synth. : 26, 77; 51, 8

Org. Synth. Coll. Vol. : 3, 685; 6, 1007

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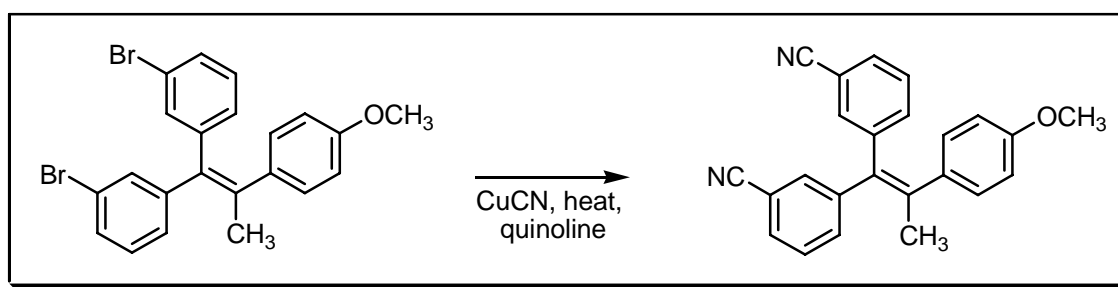


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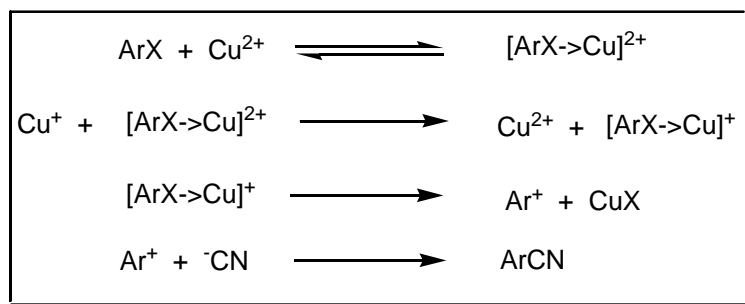
**COMMENTS :**

**ROSENMUND – von BRAUN SYNTHESIS**

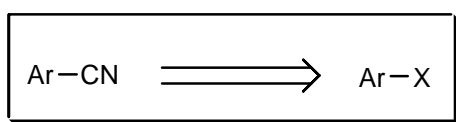
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

The copper catalysed nucleophilic substitution of aromatic halogen by copper cyanide. The reactivity order is (I > Br > Cl > F). The presence of amines promotes the reaction. See also **Hoesch – Fischer** reaction.

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## REFERENCES :

March : 660

Smith – March : 867

Smith : 677

Smith 2<sup>nd</sup> : 574

Houben – Weyl : **8**, 302; **E5**, 1460; **E6a**, 465

Org. Synth. : **21**, 89; **28**, 34

Org. Synth. Coll. Vol. : **3**, 212, 631

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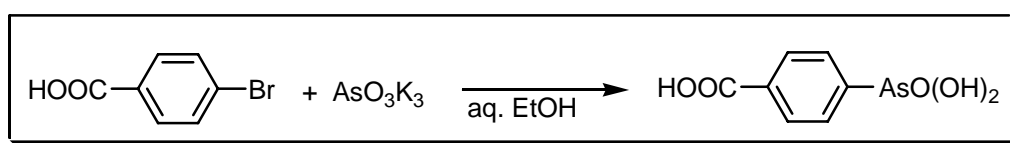
- 1) K.W. Rosenmund; E. Struck, *Ber. Dtsch. Chem. Ges.*, 1919, **52**, 1749.
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  - 3) D.T. Mowry, *Chem. Rev.*, 1948, **42**, 189.
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## COMMENTS :

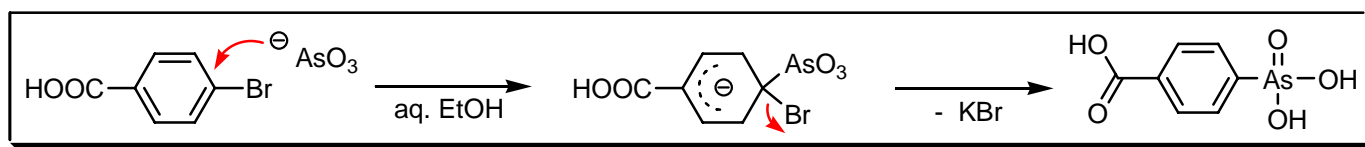
## ROSENMUND REACTION

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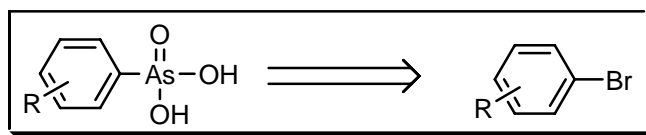
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The arsonylation by substitution of aromatic halides. The reaction has a very limited scope. See also **Bart**, **Béchamp** and **Scheller** reactions.

## REFERENCES :

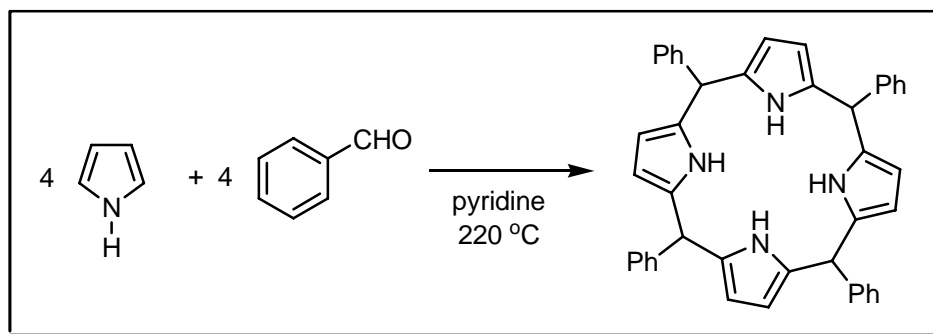
**Org. React.** : **2**, 415

- 1) G. Meyer, *Ber. Dtsch. Chem. Ges.*, 1883, **16**, 1439.
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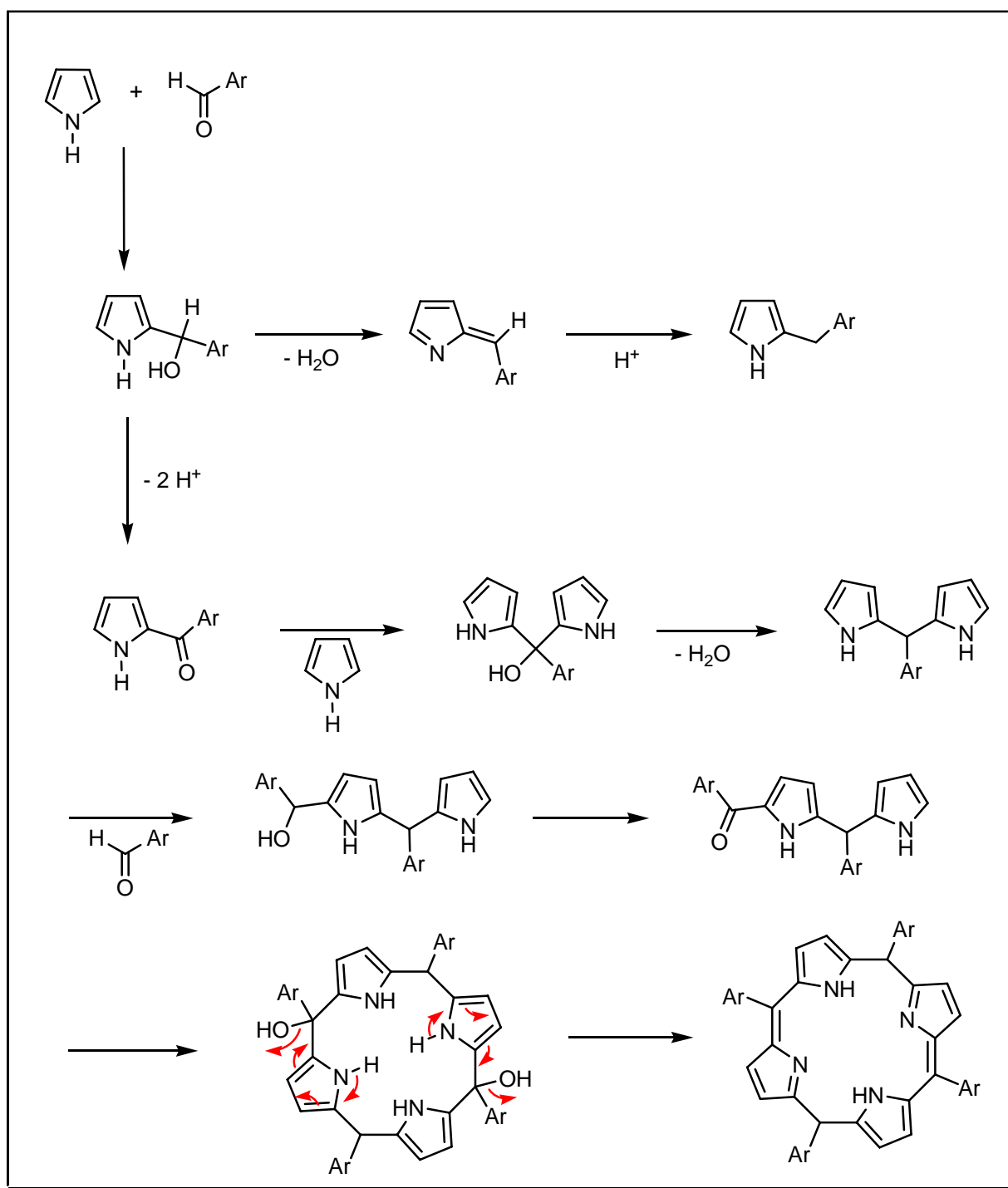
## COMMENTS :

## ROTHEMUND REACTION

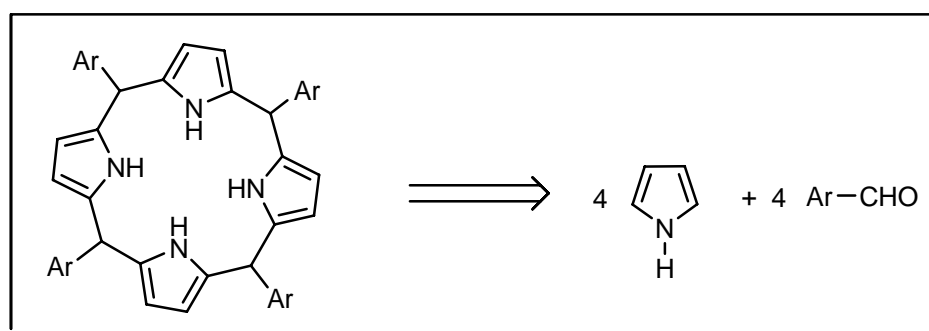
### EXAMPLE :



# MECHANISM :



# DISCONNECTION :



## NOTES :

The porphyrin synthesis from pyrroles and aldehydes. See also **Adler – Longo, Lindsey, MacDonald and Taniguchi** reactions.

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## REFERENCES :

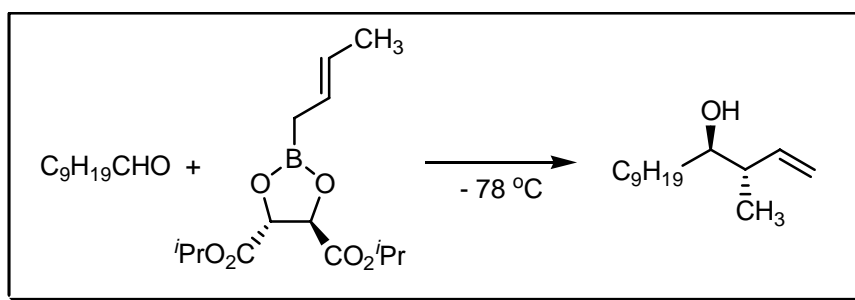
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- 

## COMMENTS :

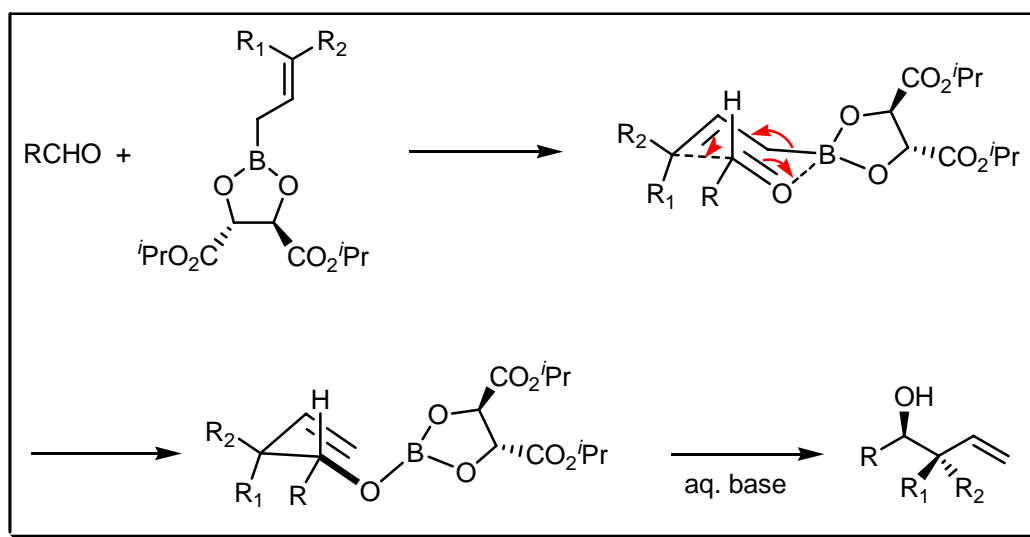
## ROUSH – HOFFMANN – YAMAMOTO STEREOSELECTIVE ALLYLATIONS

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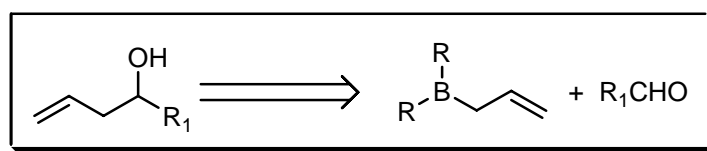
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of *syn* or *anti* homoallylic alcohols from *Z* or *E* crotylboronate camphor derived auxiliary and aldehydes (**Hoffmann**) or of *syn* homoallylic alcohols from crotylboronate tartrate esters, BF<sub>3</sub>, and aldehydes (**Yamamoto**). While **Roush** used isopropyl tartrate as a chiral auxiliary. The favoured transition state is believed to minimise lone-pair lone-pair interactions between aldehyde and carbonyl of the ester group. See also **Duthaler – Hafner**, **Ibuka – Yamamoto**, **Matteson** and **Thomas** reactions.

## REFERENCES :

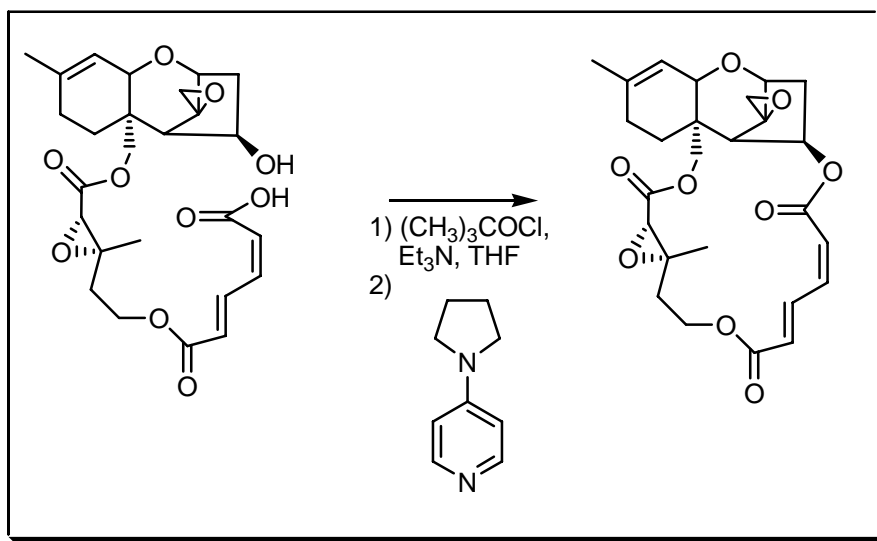
Org. React. : 51, 1

- 1) T. Gasparis; H. Nöth; W. Storch, *Angew. Chem., Int. Ed. Engl.*, 1979, **18**, 326.
- 2) Y. Yamamoto; H. Yatagai; Y. Naruta; K. Maruyama, *J. Am. Chem. Soc.*, 1980, **102**, 7107.
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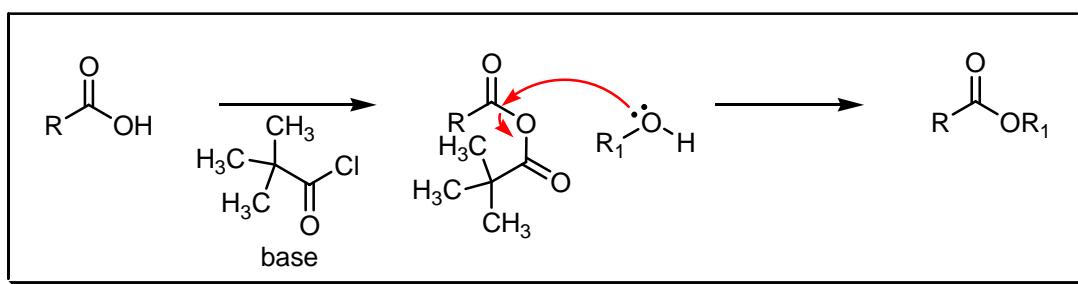
COMMENTS :

## ROUSH MACROLACTONISATION

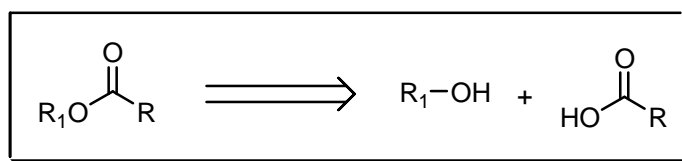
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

Pivaloyl chloride and 4-pyrrolidino pyridine are used as coupling reagents between a carboxylic acid and an alcohol. These reagents were first used by **Roush** in the synthesis of Verrucaric B. See also **Corey – Kwiatkowski**, **Corey – Nicolaou**, **Diels – Alder**, **Eastwood**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Hunsdiecker** ring-

closure, **Julia – Paris – Kocienski – Lythgoe, Keck** macrolactonisation, **Kita, Krief – Reich – Chow, Masamune, McMurry, Michael** condensation, **Mitsunobu, Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao, Nozaki – Hiyama – Kishi (Takai – Utimoto), Petasis reaction, Peterson, Raphael, Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow, Staab, Stacey, Steglich – Hassner, Still – Gennari, Stille – Migita – Kosugi, Story, Suzuki – Miyaura, Takeda, Tebbe, Thorpe – Ziegler, Venkataraman – Wagle, Vorbrüggen – Krolakiewicz, Wittig, Yamaguchi** and **Yamamoto** macrolactonisation reactions.

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#### REFERENCES :

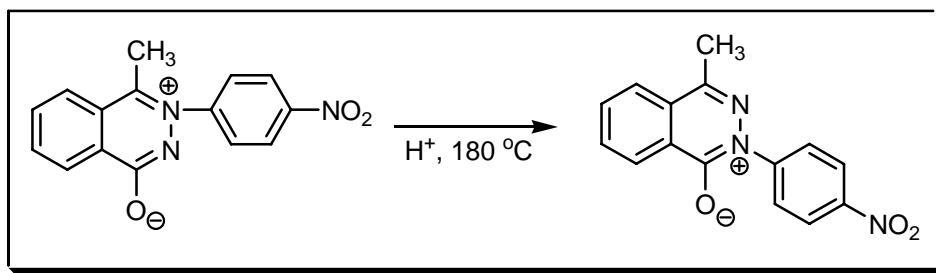
- 1) W.R. Roush; T.A. Blizzard, *J. Org. Chem.*, 1983, **48**, 758.
  - 2) W.R. Roush; T.A. Blizzard, *J. Org. Chem.*, 1984, **49**, 1772.
  - 3) W.R. Roush; T.A. Blizzard, *J. Org. Chem.*, 1984, **49**, 4332.
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#### COMMENTS :

### ROWE REARRANGEMENT

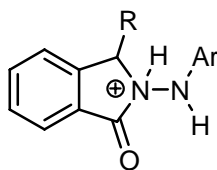
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#### EXAMPLE :



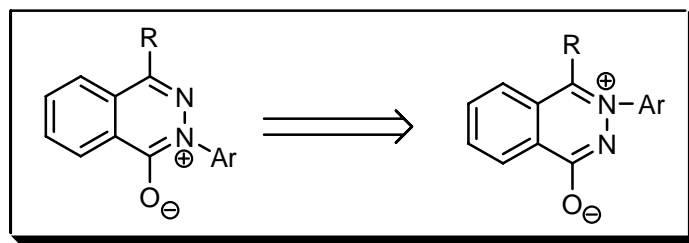
#### MECHANISM :

It is assumed that this is the intermediate :





## DISCONNECTION :



## NOTES :

The  $\psi$ -phthalazone – phthalazone rearrangement in the presence of acid at 180 °C.

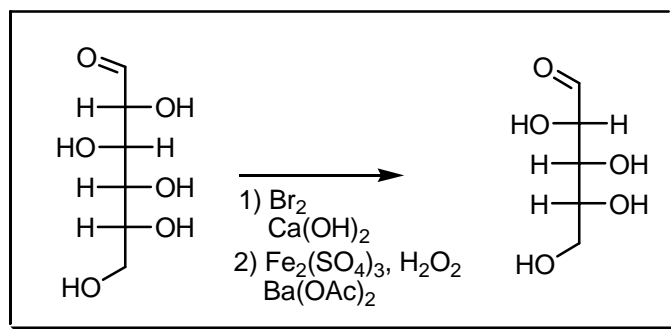
## REFERENCES :

- 1) F.M. Rowe; E. Levin; A.C. Burns; J.S.H. Davies; W. Tepper, *J. Chem. Soc.*, 1926, 690.
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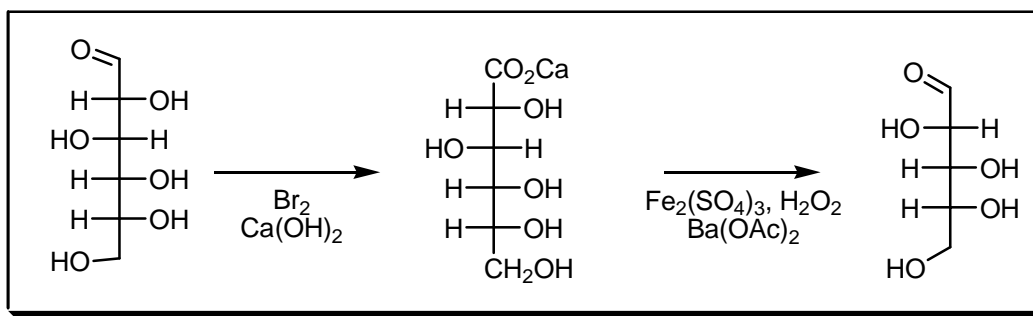
## COMMENTS :

## RUFF – FENTON DEGRADATION

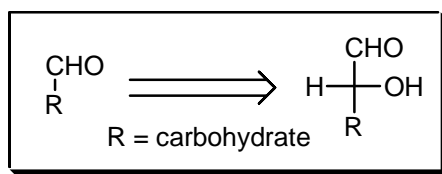
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The oxidative degradation of aldoses *via*  $\alpha$ -hydroxy acids to lower chain aldoses. The use of ferric chloride as a catalyst is called the **Hockett – Hudson** oxidation. A variant of the **Ruff – Fenton** reaction is the chain-shortening of aldonyl chlorides with peroxides. In this case there are two different intermediates possible depending the use of base. See also **Haber – Weiss**, **MacDonald – Fischer** and **Wohl** reactions.

## REFERENCES :

Smith 2<sup>nd</sup> : 225, 1182

Houben – Weyl : E3, 527, 639

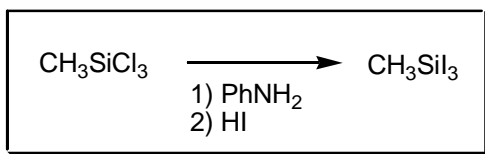
- 1) H.J.H. Fenton, *Proc. Chem. Soc.*, 1893, **9**, 113.
- 2) O. Ruff, *Ber. Dtsch. Chem. Ges.*, 1898, **31**, 1573.
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## COMMENTS :

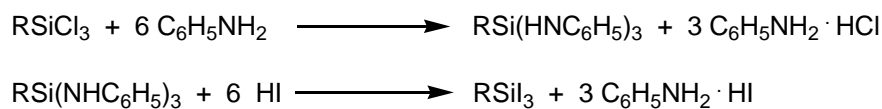
## RUFF REACTION

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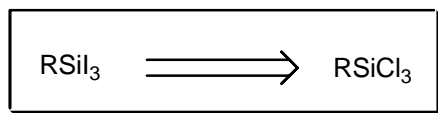
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The transhalogenation of alkyl chlorosilanes to alkyl iodosilanes. See also **Eaborn** reaction.

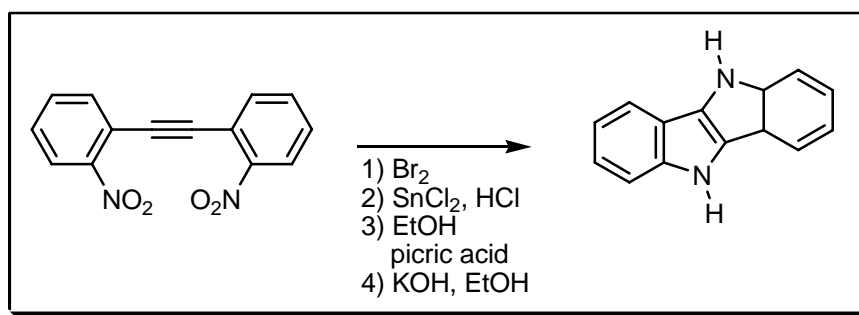
### REFERENCES :

- 1) O. Ruff, *Ber. Dtsch. Chem. Ges.*, 1908, **41**, 3738.
- 2) H.H. Anderson; D.L. Séaton; R.P.T. Rudnicki, *J. Am. Chem. Soc.*, 1951, **73**, 2144.
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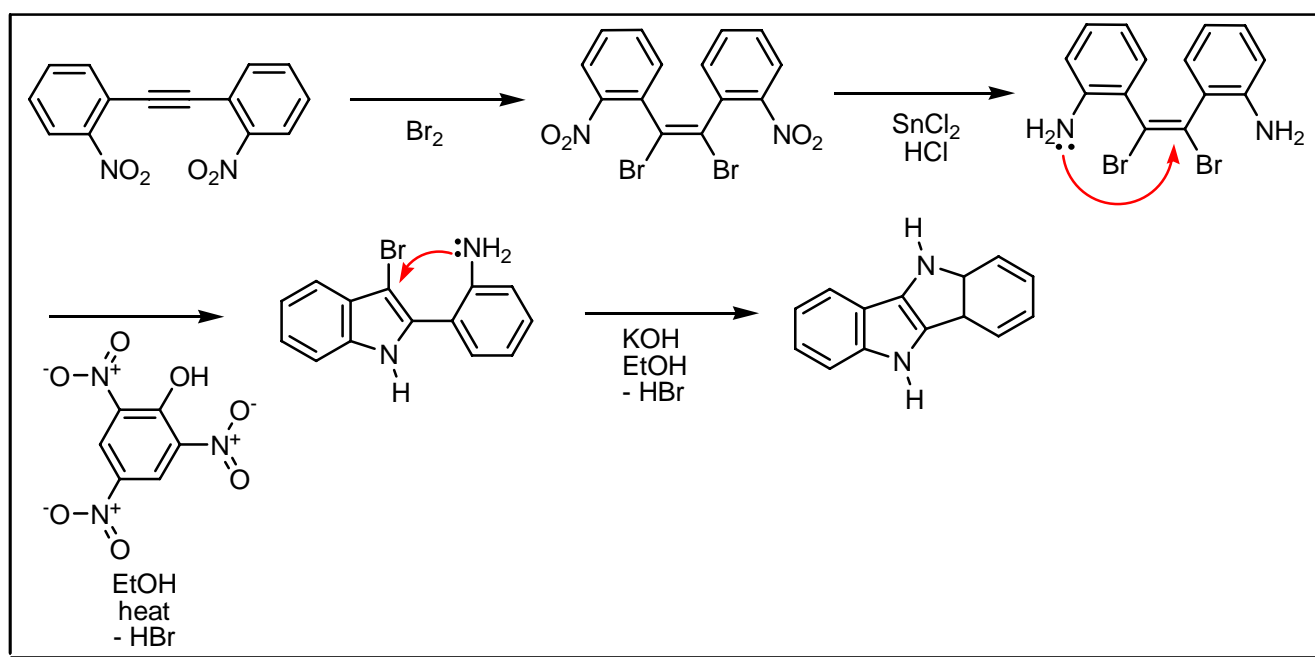
### COMMENTS :

## RUGGLI SYNTHESIS

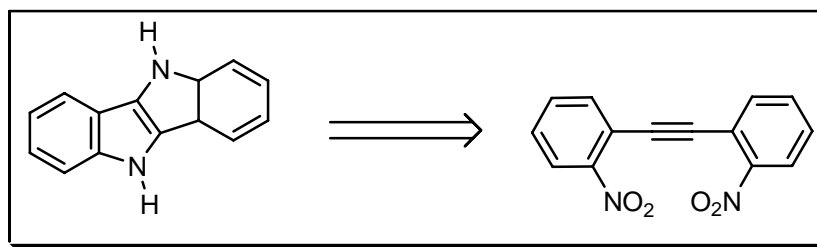
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

1-Nitro-2-[2-(2-nitrophenyl)ethynyl]benzene is brominated to yield  $o,o'$ -dinitrostilbene dibromide which is reduced to the diamino-compound. This on boiling with ethanolic picric acid gives 2-( $o$ -aminophenyl)-3-bromoindole which with ethanolic potassium hydroxide yields the di-indole. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger**

– Knittel, Inanaga, Iwao, Japp – Murray, Julia, Kihara, Larock indole, Leimgruber – Batcho, Lipp, Madelung indole, Magnus, Martin, Montecvecchi, Mori – Ban, Murphy, Naito, Natsume, Nenitzescu indole, Piloty – Robinson, Pschorr – Hoppe, Reissert indole, Saegusa indole, Schmid, Smith, Sugawara indole, Sundberg, Thiele – Dimroth, Thyagarajan, Watanabe heterocyclisation, Watanabe indole, Weerman indole, Wender, Widman, Yamamoto indole-1, Yamamoto indole-2 and Yurovskaya reactions.

## REFERENCES :

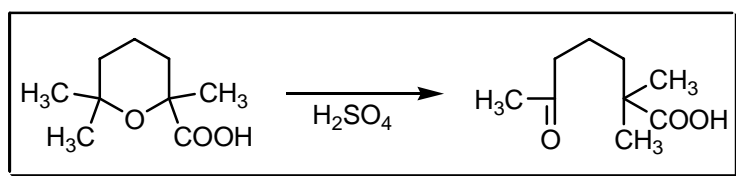
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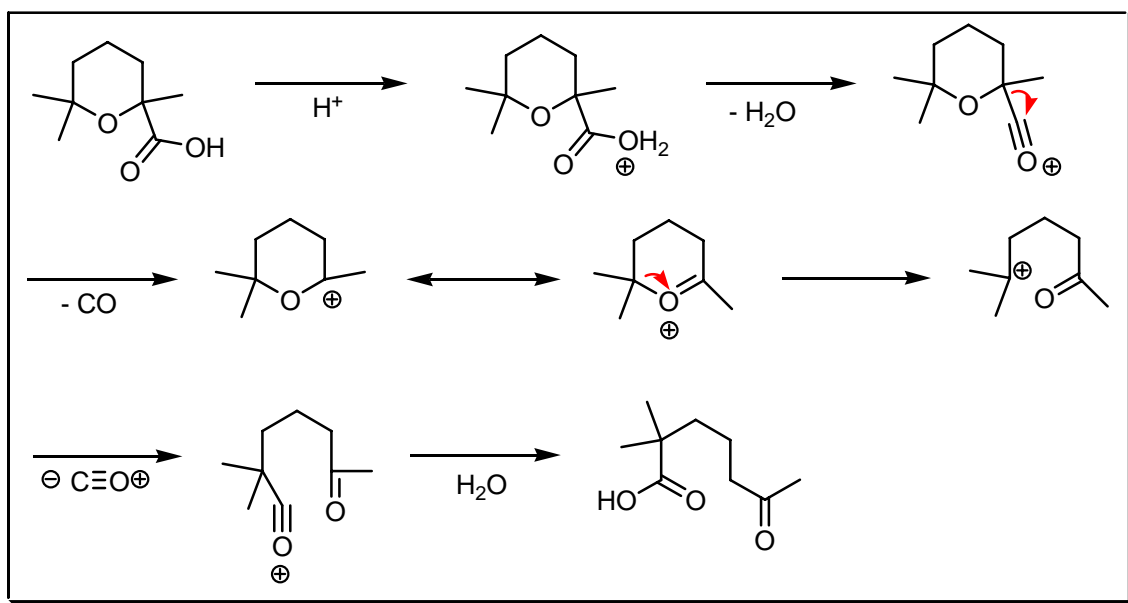
## COMMENTS :

## RUPE REARRANGEMENT

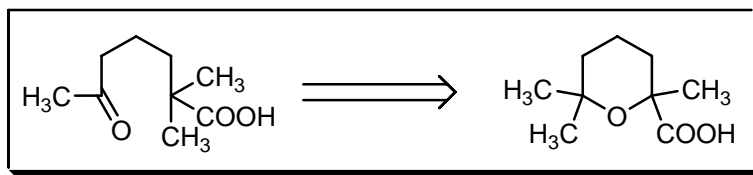
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The acid-catalysed rearrangement of cinenic acid. The loss and subsequent recapture of carbon monoxide is suggested for the carbonyl transfer in this rearrangement. See also **Koch – Haaf** reaction.

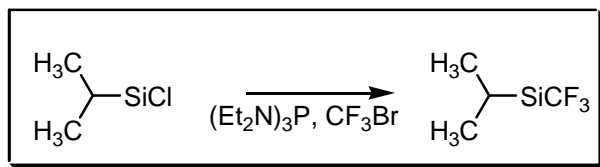
## REFERENCES :

- 1) H. Rupe; C. Liechtenhan, *Ber. Dtsch. Chem. Ges.*, 1908, **41**, 1278.
- 2) H. Rupe; H. Hirschmann, *Helv. Chim. Acta*, 1933, **16**, 505.
- 3) H. Dahn; T. Riechstein, *Helv. Chim. Acta*, 1952, **35**, 1.
- 4) J. Meinwald, *J. Am. Chem. Soc.*, 1955, **77**, 1617.
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- 6) J. Meinwald; H.C. Hwang; D. Christman; A.P. Wolf, *J. Am. Chem. Soc.*, 1960, **82**, 483.

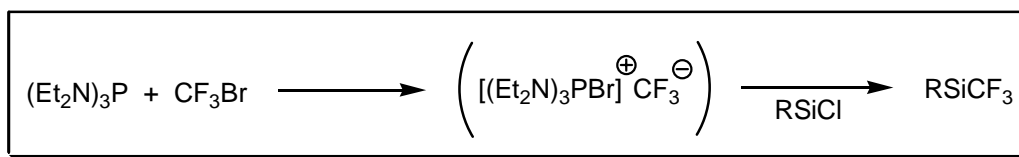
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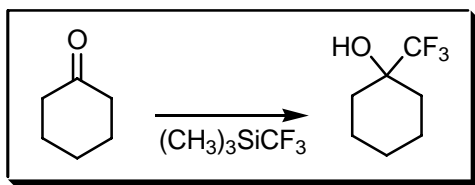
## RUPPERT FLUOROALKYLATION

### EXAMPLE :

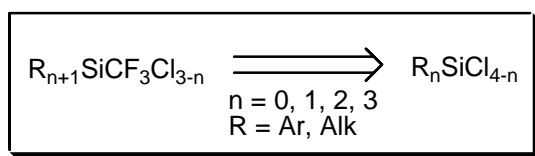


### MECHANISM :





#### DISCONNECTION :



#### NOTES :

Carbon trifluoride substituted organylchlorosilanes (**Ruppert reagent**) are synthesised from alkyl or aryl chlorosilanes using  $(\text{Et}_2\text{N})_3\text{P}$ , and  $\text{CF}_3\text{Br}$ .

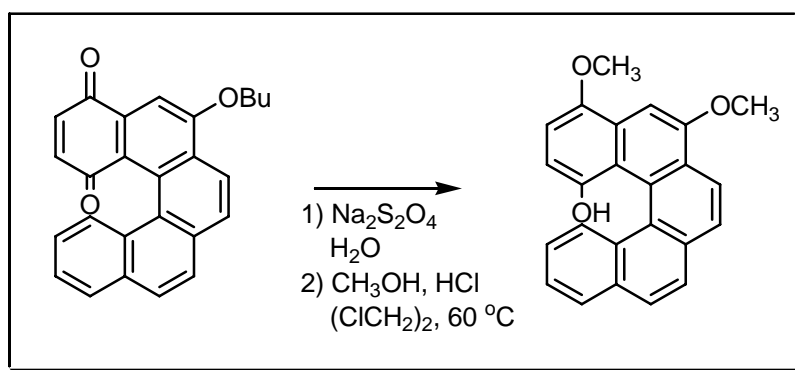
#### REFERENCES :

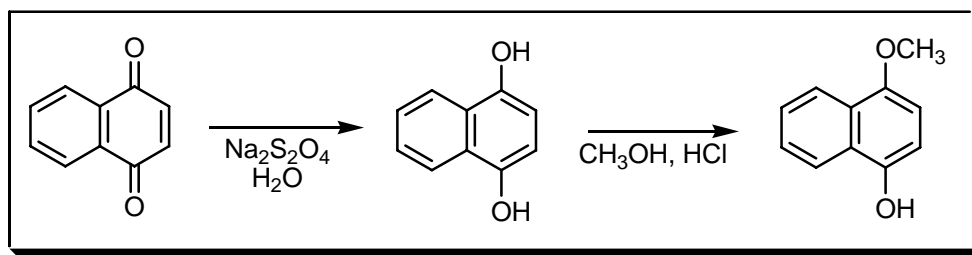
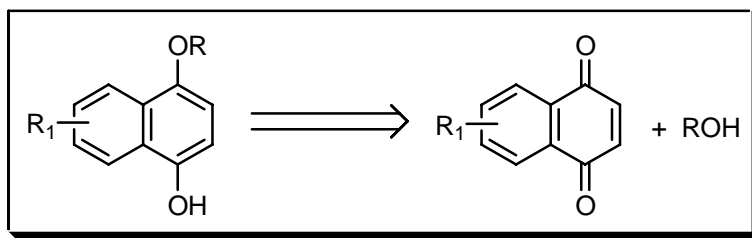
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#### COMMENTS :

### RUSSIG – LAATSCH REACTION

#### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

Naphthalene-1,4-diols are converted regioselectively to monoalkyl ethers using alcohols containing hydrogen chloride. The starting hydrogenquinone is first reduced by sodium thionite to the 1,4-diol.

**REFERENCES :**

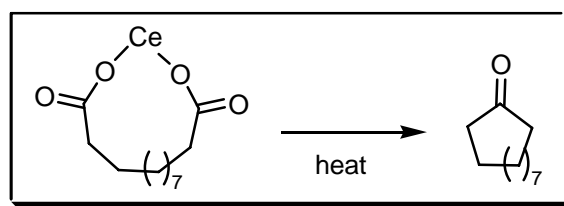
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- 5) S.D. Dreher; T.J. Katz; K.-C. Lam; A.L. Rheingold, *J. Org. Chem.*, 2000, **65**, 815.

**COMMENTS :**

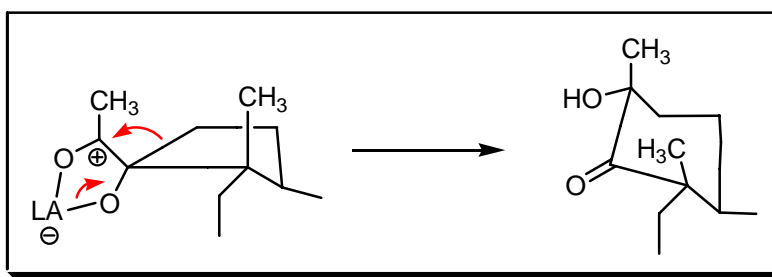


## RUŽIČKA LARGE RING SYNTHESIS

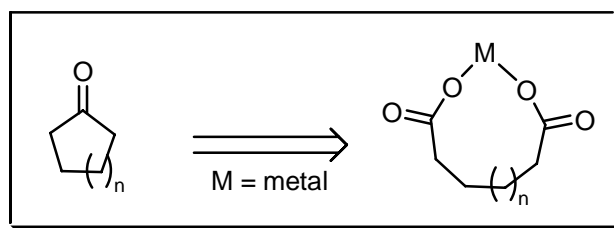
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The formation of large ring alicyclic ketones from dicarboxylic acids by thermal decomposition of salts with metals of the second and fourth groups of the periodic table (Ca, Th, Ce). It is good for the preparation of  $C_5$ ,  $C_6$ ,  $C_8$ ,  $C_{10}$  to  $C_{30}$  cyclic ketones. The reaction is of little use nowadays. See also **Corey – Kwiatkowski**, **Corey – Nicolaou**, **Diels – Alder**, **Eastwood**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Hunsdiecker** ring-closure, **Julia – Paris – Kocienski – Lythgoe**, **Keck** macrolactonisation, **Kita**, **Krief – Reich – Chow**, **Masamune**, **McMurry**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Petasis** reaction, **Peterson**, **Raphael**, **Roush**, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Still – Gennari**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Takeda**, **Tebbe**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolakiewicz**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

## REFERENCES :

March : 496

Smith – March : 574

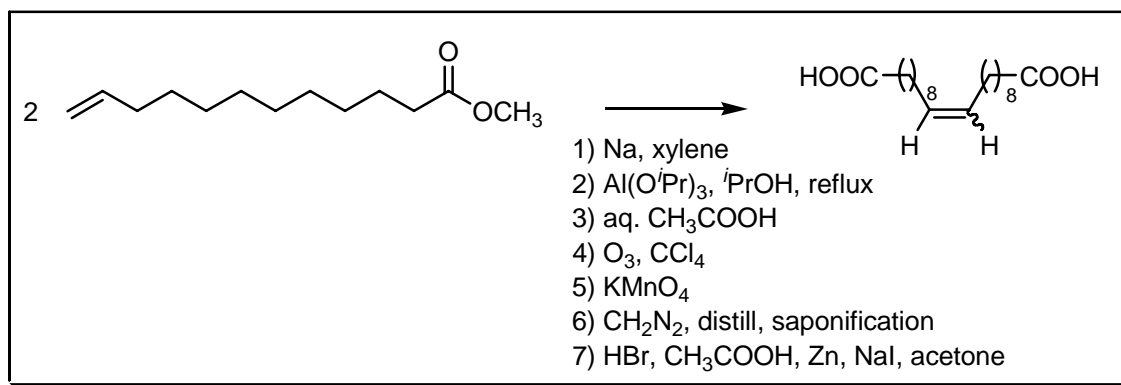
Houben – Weyl : 4/2, 754

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- 1) L. Ružička; M. Stoll; H. Schinz, *Helv. Chim. Acta*, 1926, **9**, 249.
  - 2) L. Ružička; W. Brugger; C.F. Seidel; H. Schinz, *Helv. Chim. Acta*, 1928, **11**, 496.
  - 3) L. Ružička, *Chem. Ind. (London)*, 1935, **54**, 2.
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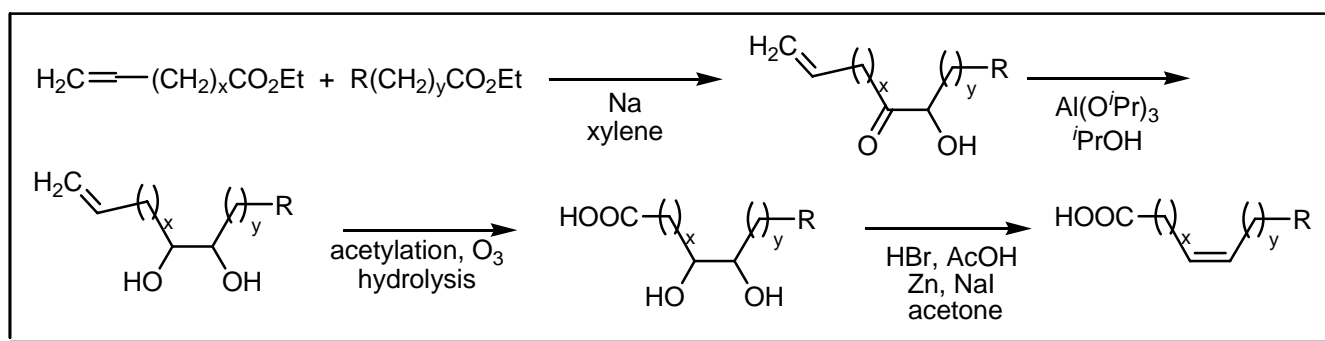
## COMMENTS :

## RUŽIČKA OLEFINIC ACID SYNTHESIS

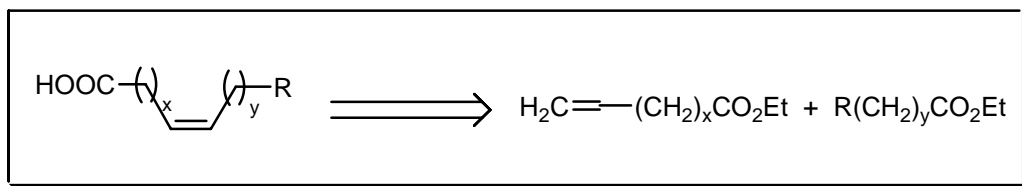
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

A mixed acyloin condensation of an unsaturated ester with a saturated ester to yield an unsaturated acyloin, which when submitted to the **Meerwein – Ponndorf – Verley** reduction, gives an unsaturated glycol. The latter after acetylation of the free hydroxyls is oxidised with ozone to convert the terminal vinyl group into a carboxyl. The dihydroxy acid so obtained is treated with hydrogen bromide in acetic acid to give the dibromo acid, which with zinc yields the mono-olefinic acid.

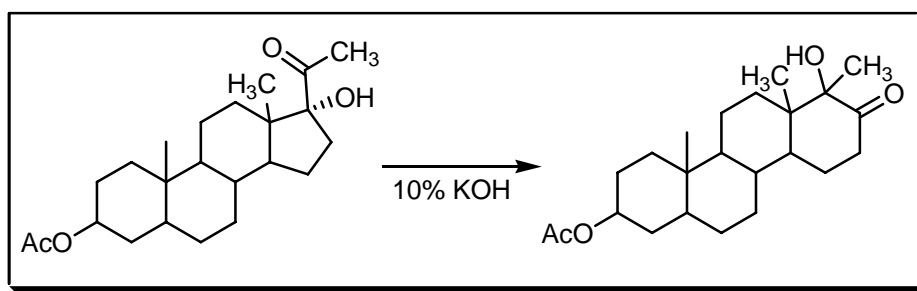
## REFERENCES :

L. Ružička; Pl.A. Plattner; W. Widmer, *Helv. Chim. Acta*, 1942, **25**, 604.

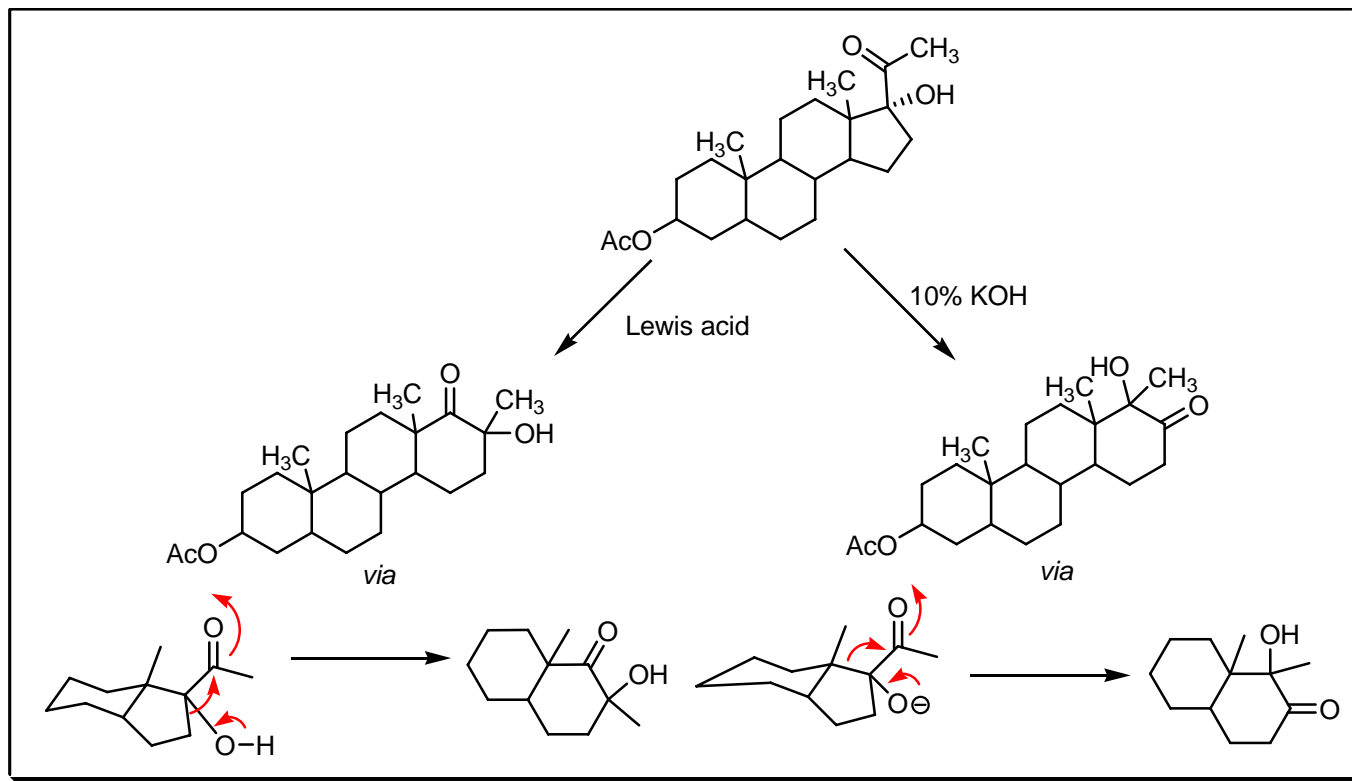
## COMMENTS :

## RUŽIČKA REARRANGEMENT

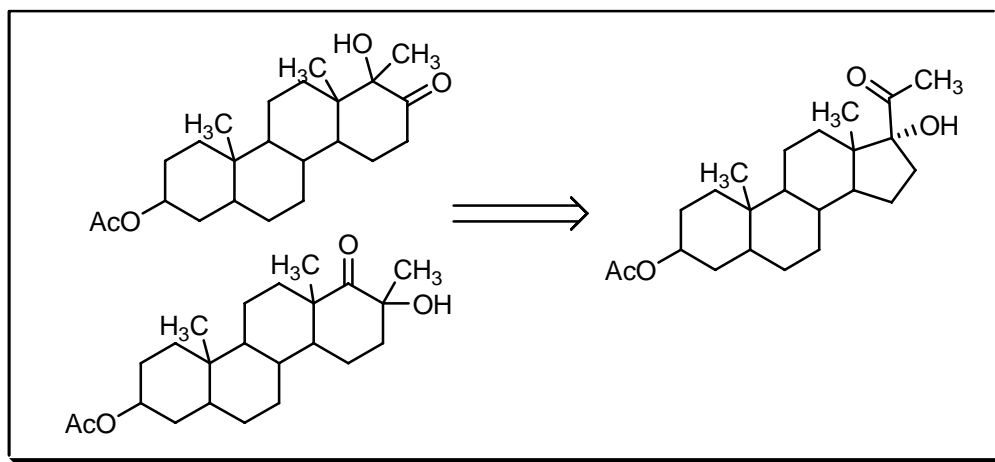
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The base- or acid-catalysed rearrangement of 17 $\alpha$ -hydroxy-20-keto steroids to D-homo steroids.

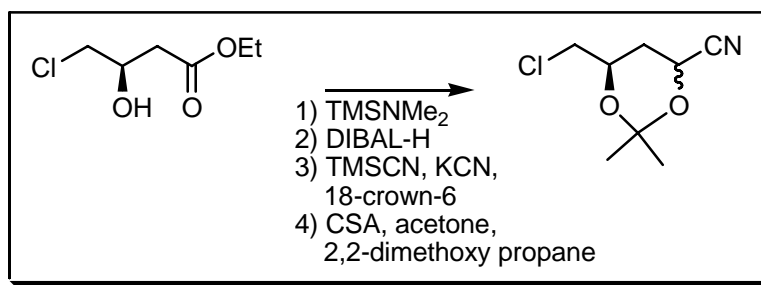
## REFERENCES :

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- 4) N.L. Wender; D. Taub; R.W. Walker, *Tetrahedron*, 1960, **11**, 163.
- 5) N.G. Steinberg; G.H. Rasmusson; G.F. Reynolds; J.H. Hirshfield; B.H. Arison, *J. Org. Chem.*, 1984, **49**, 4731.
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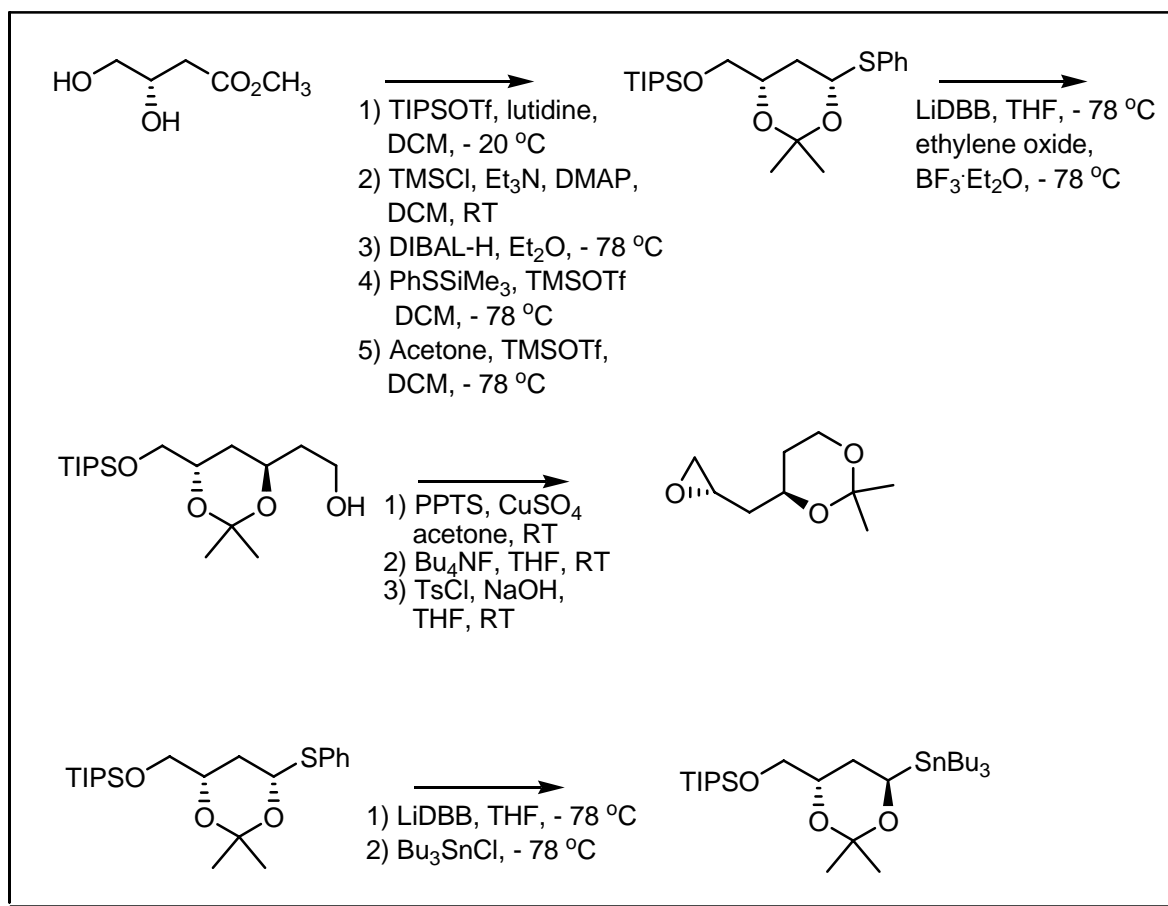
COMMENTS :

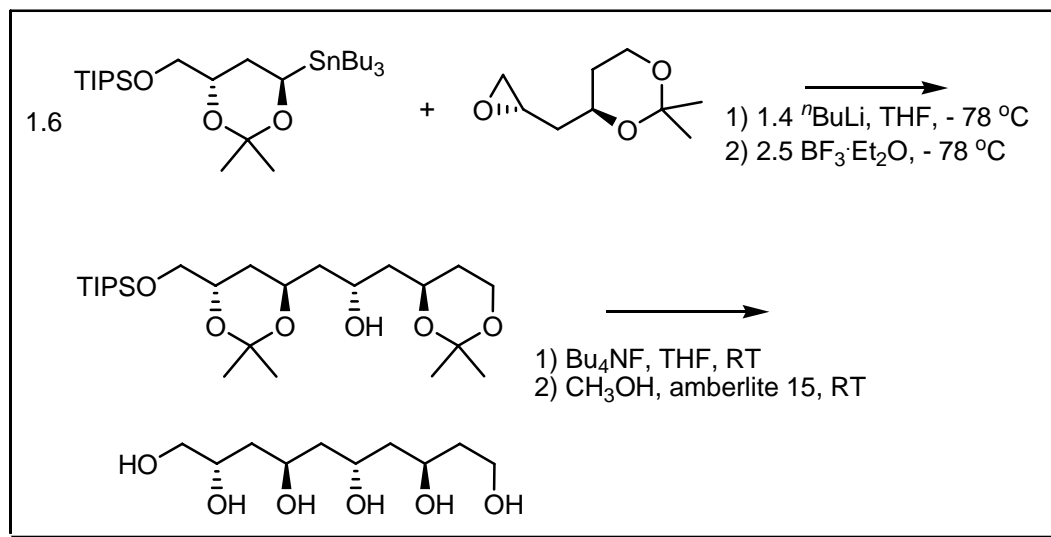
## RYCHNOVSKY POLYOL SYNTHESIS

EXAMPLE :



MECHANISM :





#### NOTES :

The convergent synthesis of polyol chains in which 2 chains are coupled with control of the newly formed stereogenic centre.

#### REFERENCES :

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- 4) S.D. Rychnovsky, *Chem. Rev.*, 1995, **95**, 2022.
- 5) C.J. Sinz; S.D. Rychnovsky, *Top. Cur. Chem.*, 2001, **216**, 51.

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**B**

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**C**

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**O**

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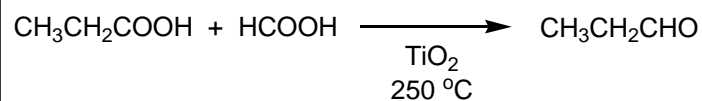
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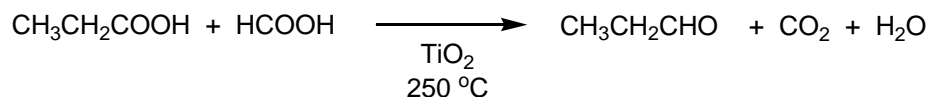
## SABATIER – MAILHE SYNTHESIS

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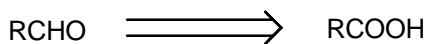
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Aliphatic acids when mixed with vapours of formic acid and passed over a titanium dioxide catalyst at 250 – 300 °C yield aldehydes, water and carbon dioxide. See also **Akabori – Neuberg – Fischer** reaction.

### REFERENCES :

Houben – Weyl : 7/1, 278

1) P. Sabatier; A. Mailhe, *C.R. Séances Acad. Sci.*, 1912, **154**, 561.

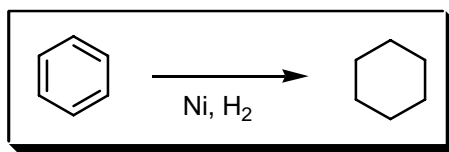
2) P. Sabatier; A. Mailhe, *C.R. Séances Acad. Sci.*, 1914, **158**, 985.

### COMMENTS :

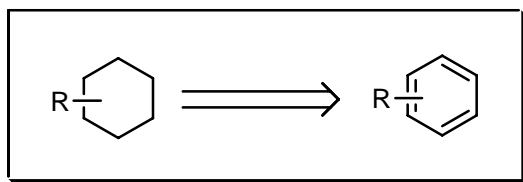
## SABATIER – SENDERENS REACTION

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### EXAMPLE :



### DISCONNECTION :



### NOTES :

Catalytic hydrogenation of unsaturated compounds with hydrogen and finely divided nickel.

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### REFERENCES :

Houben – Weyl : 2, 288; 4/2, 284

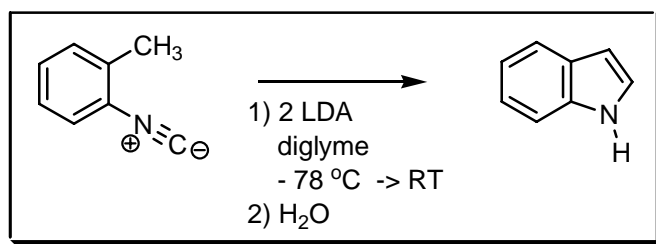
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- 1) P. Sabatier; J.B. Senderens, *C.R. Séances Acad. Sci.*, 1897, **124**, 1360.
  - 2) P. Sabatier; J.B. Senderens, *C.R. Séances Acad. Sci.*, 1899, **128**, 1173.
  - 3) P. Sabatier, *Ber. Dtsch. Chem. Ges.*, 1911, **44**, 1984.
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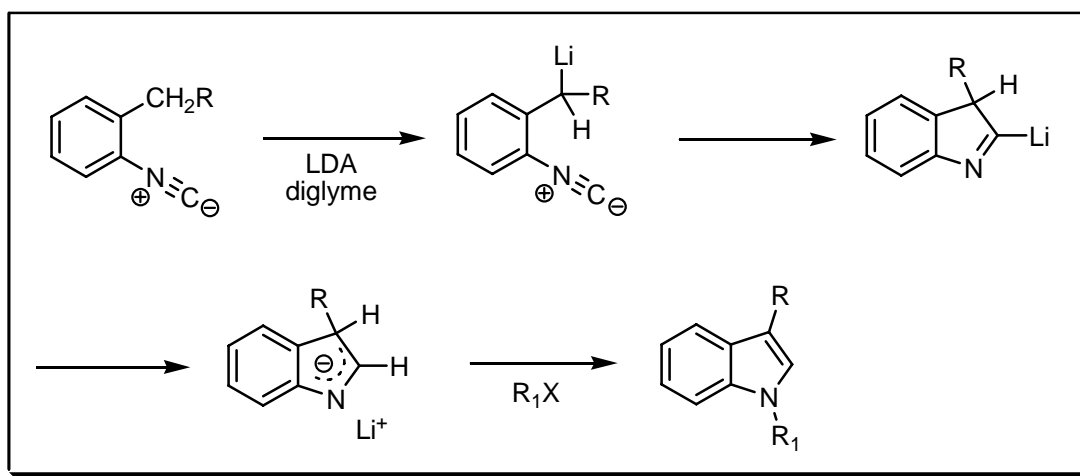
### COMMENTS :

## SAEGUSA INDOLE SYNTHESIS

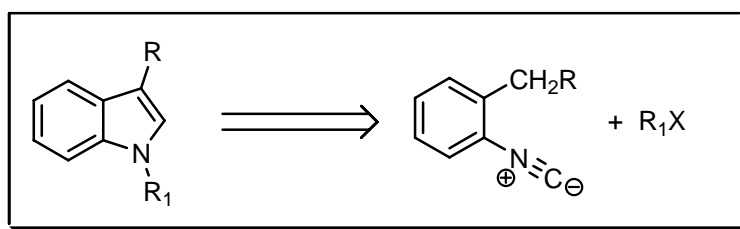
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The cyclisation of *ortho*-lithiated *o*-tolylisocyanides in a 5-*endo*-dig fashion. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

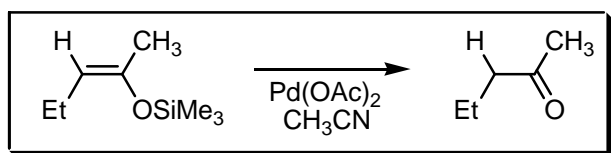
## REFERENCES :

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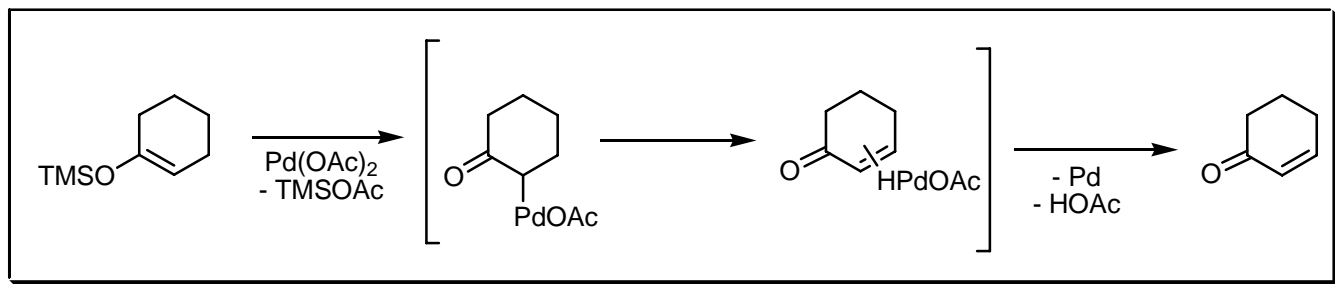
## COMMENTS :

## SAEGUSA REACTION

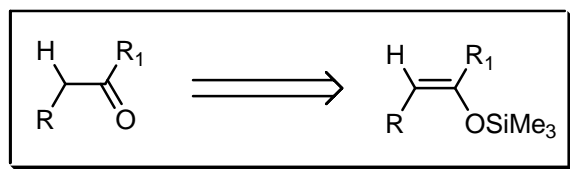
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The **Saegusa** oxidation is a standard method for the conversion of a silyl enol ether into the corresponding  $\alpha,\beta$ -enone. The oxidising agent palladium(II) acetate is added in stoichiometric amounts. The mechanism is analogous to the **Tsuji – Wacker** oxidation, see **Porth et al.**

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## REFERENCES :

**Science of Synthesis** : 1, 113

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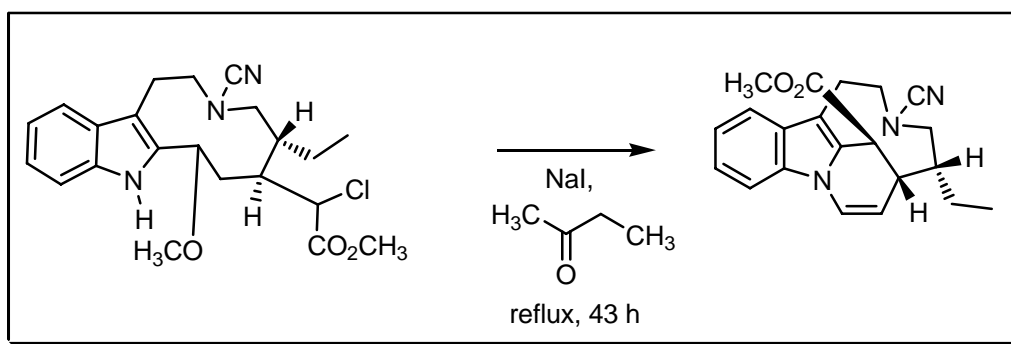
- 1) Y. Ito; T. Konoike; T. Saegusa, *J. Am. Chem. Soc.*, 1975, **97**, 649.
  - 2) Y. Ito; T. Hirao; T. Saegusa, *J. Org. Chem.*, 1978, **43**, 1011.
  - 3) S. Porth; J.W. Bats; D. Trauner; G. Giester; J. Mulzer, *Angew. Chem., Int. Ed.*, 1999, **38**, 2015.
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## COMMENTS :

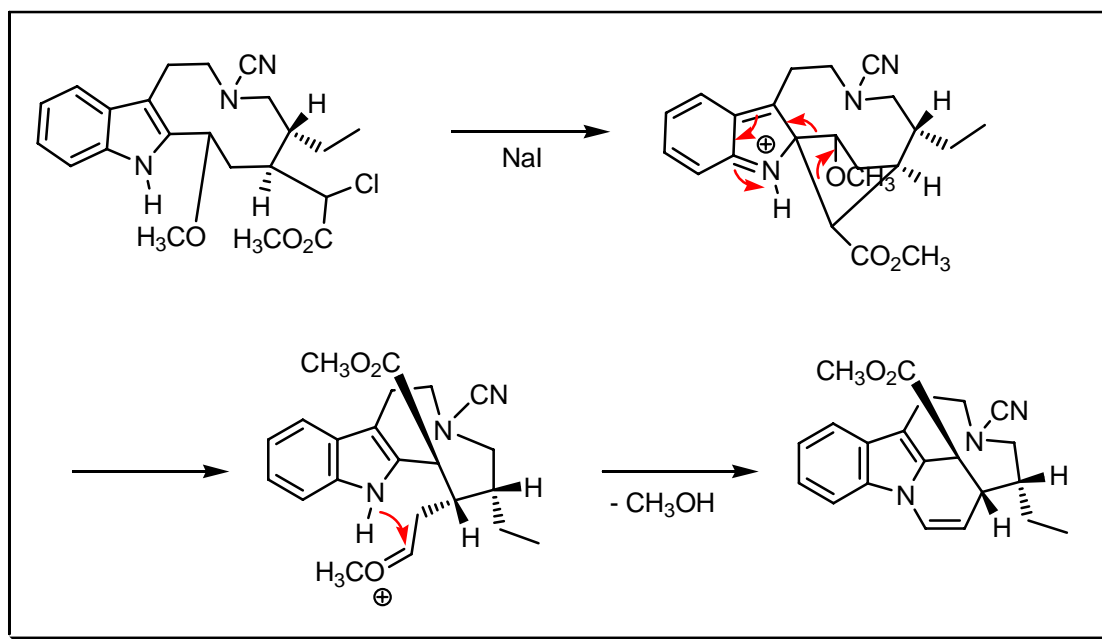
## SAKAI REACTION

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### EXAMPLE :



### MECHANISM :



### NOTES :

The skeletal rearrangement of a Corynanthe-type derivative.

### REFERENCES :

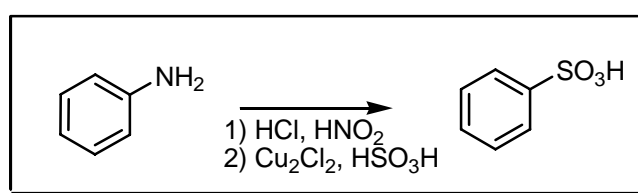
Smith 2<sup>nd</sup> : 1250

T. Koike; H. Takayama; S-i. Sakai, *Chem. Pharm. Bull.*, 1991, **39**, 1677.

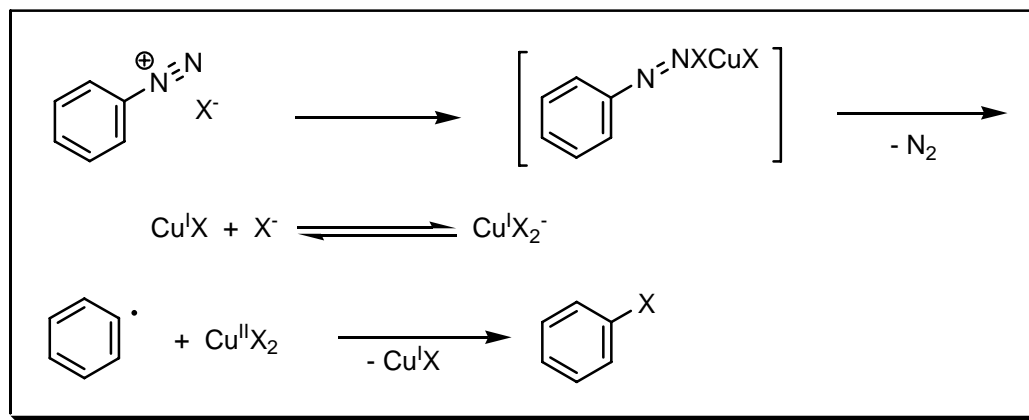
### COMMENTS :

## SANDMEYER DIAZONIUM REACTION

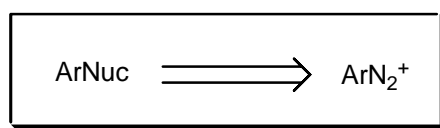
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The formation of aromatic halogeno-, nitro- or cyano-compounds from diazonium salts under the catalytic action of cuprous halide or cyanide. The **Angeli** modification uses copper(I) salts from copper(I) sodium hypophosphite and copper(I) sulfate. The **Brackman – Smith** modification uses copper(II) chloride hydrate in acetone. See also **Balz – Schiemann**, **Cadogan** arylation, **Craig** exchange, **Demjanov** rearrangement, **Gattermann** diazo, **Gattermann** sulphinic acid, **Griess** deamination, **Knoevenagel** diazotation, **Körner – Contardi**, **Meerwein** arylation, **Schwechten** and **Witt** diazotation reactions.

## REFERENCES :

**March** : 532, 723

**Smith – March** : 874, 936

**Smith** : 197

**Smith 2<sup>nd</sup>** : 168, 1247

**Houben – Weyl** : 5/4, 438

**Org. React.** : 2, 262

**Org. Synth.** : 3, 33, 79; 4, 69; 24, 22; 28, 52; 32, 23

**Org. Synth. Coll. Vol.** : 1, 162, 170, 514; 3, 185, 341; 4, 160

**Science of Synthesis** : 10, 257, 736

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- 3) A. Angeli, *Gazz. Chim. Ital.*, 1891, **21**, 258.
- 4) H.H. Hodgson, *Chem. Rev.*, 1947, **40**, 251.
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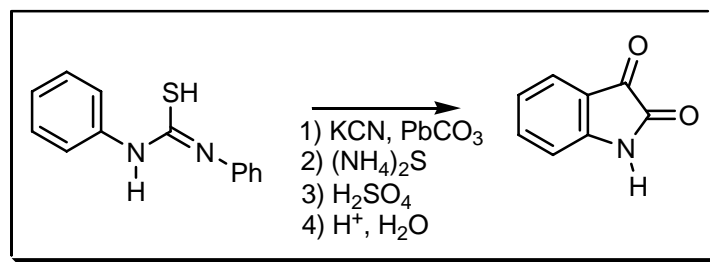
- 6) W. Brackman; P.J. Smith, *Recl. Trav. Chim. Pays-Bas*, 1966, **85**, 857.  
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11) P. Hanson; J.R. Jones; A.B. Taylor; P.H. Walton; A.W. Timms, *J. Chem. Soc., Perkin Trans. 2*, 2002, 1135.  
12) P. Hanson; S.C. Rowell; P.H. Walton; A.W. Timms, *Org. Biomol. Chem.*, 2004, **2**, 1838.
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**COMMENTS :**

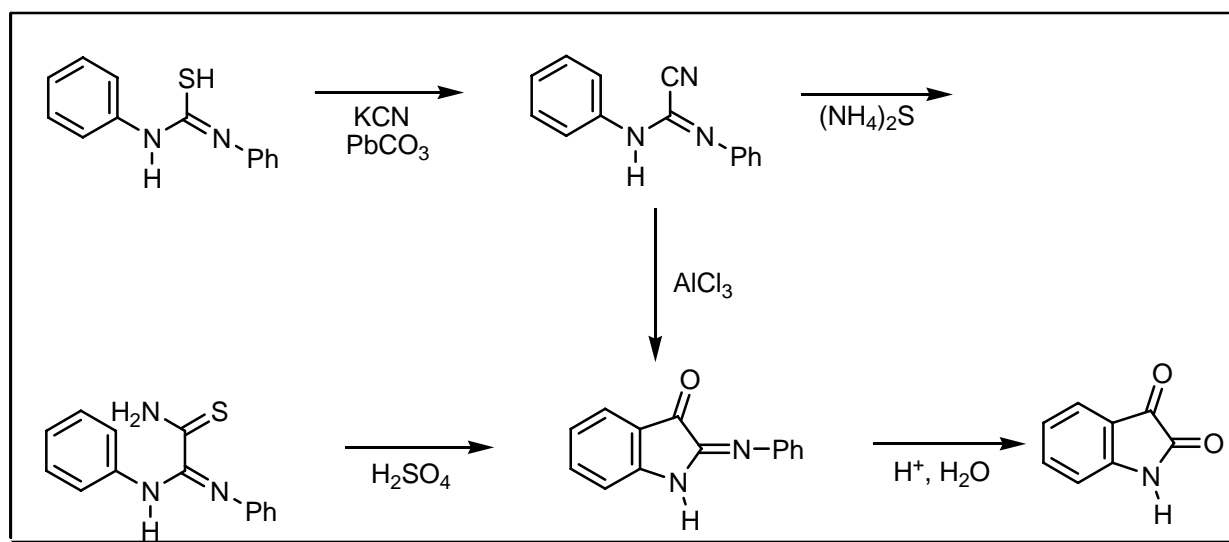
## SANDMEYER DIPHENYLUREA ISATIN SYNTHESIS

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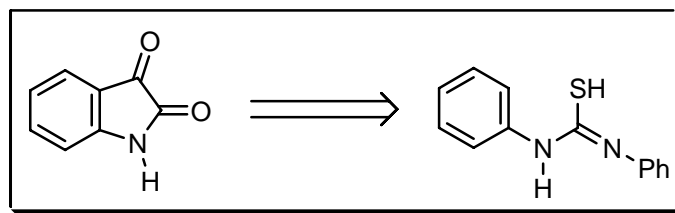
**EXAMPLE :**



### MECHANISM :



### DISCONNECTION :



### NOTES :

A symmetrical diarylthiourea is converted into a cyanoformamidine by the action of potassium cyanide and basic lead carbonate. This amidine with ammonium sulfide gives a thioamide, which yields an isatin-2-anil with concentrated sulfuric acid. The anil can be hydrolysed to the isatin. Alternatively, the cyanoformamidine may be treated with aluminium chloride in benzene to give the isatin-2-anil. See also **Claisen – Shadwell**, **Sandmeyer** isonitrosoacetanilide isatin and **Stollé** reactions.

### REFERENCES :

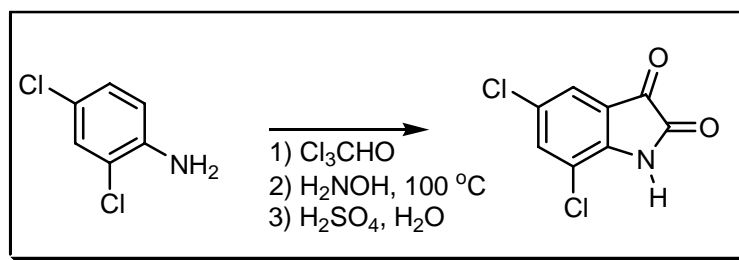
Houben – Weyl : 7/4, 11

- 1) T. Sandmeyer, *Z. Farb. Textil. Chem.*, 1903, **2**, 129.
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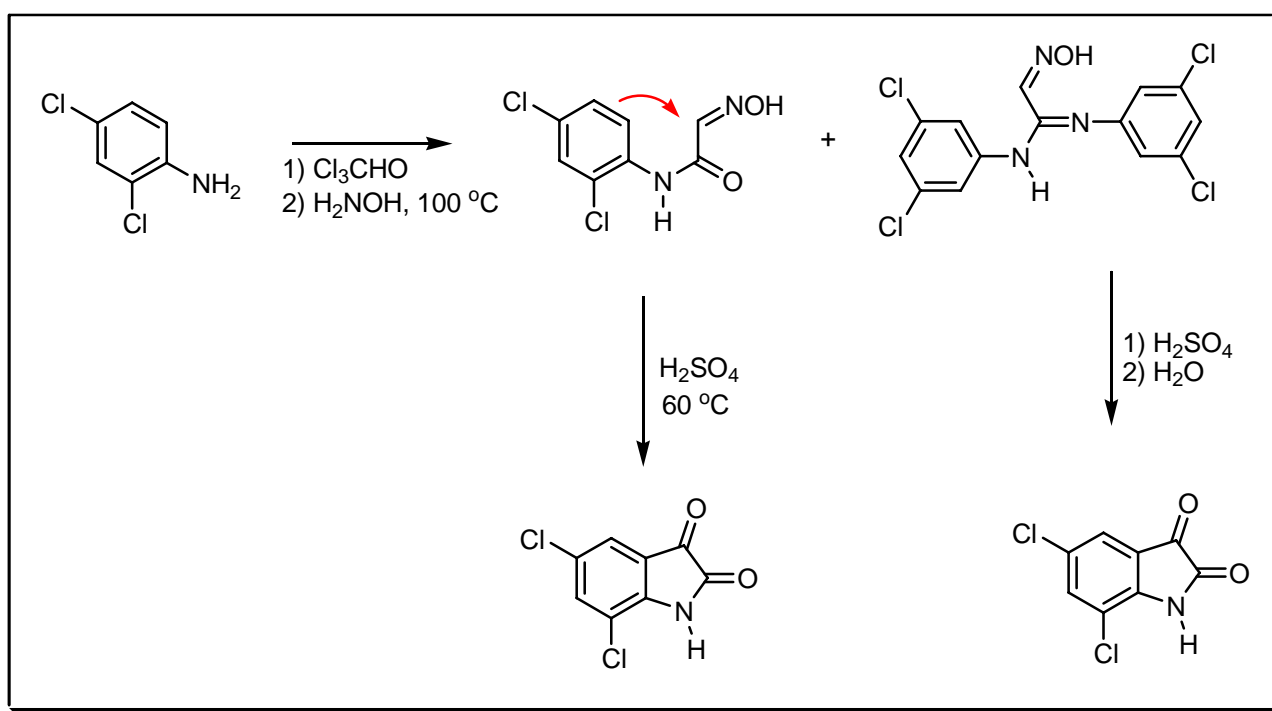
COMMENTS :

## SANDMEYER ISONITROSOACETANILIDE ISATIN SYNTHESIS

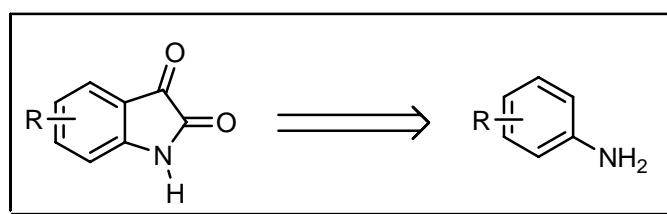
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

Chloral hydrate, hydroxylamine and an aryl amine condense in acid solution to give an isonitrosoacetanilide, which with concentrated sulfuric acid yields isatin. In neutral solution the chloral oxime reacts with the aromatic amine to yield a diphenylisonitrosoacetamidine. Recently, a modification by **Garden et al.** uses ethanol a co-solvent. See also **Claisen – Shadwell**, **Sandmeyer** diphenylurea isatin and **Stollé** reactions.

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## REFERENCES :

Houben – Weyl : 7/4, 14

Org. Synth. : 5, 71

Org. Synth. Coll. Vol. : 1, 327

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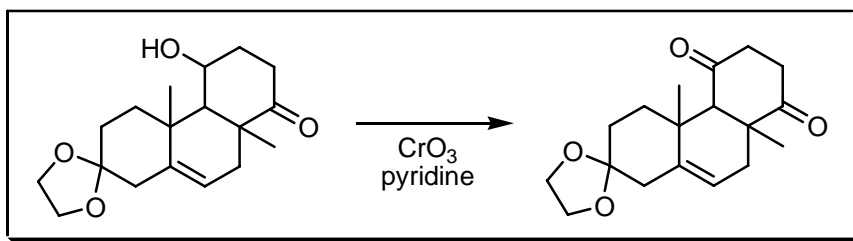
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## COMMENTS :

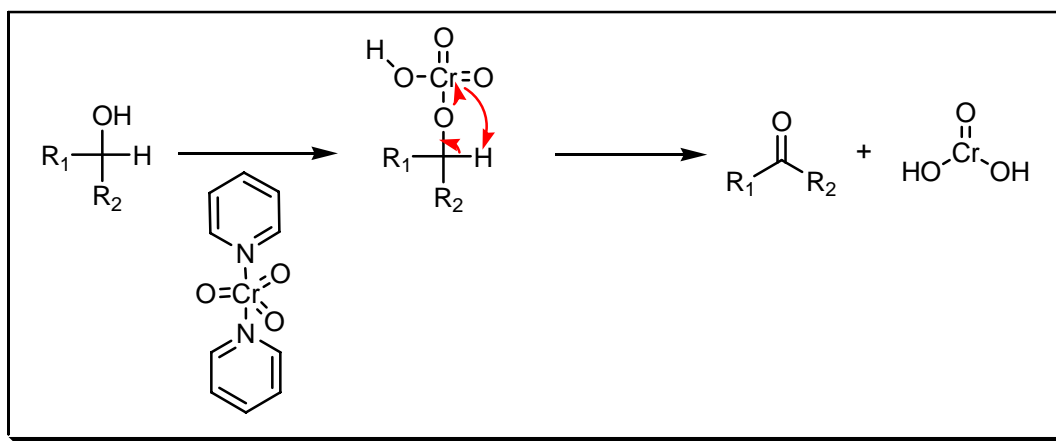
## SARETT OXIDATION

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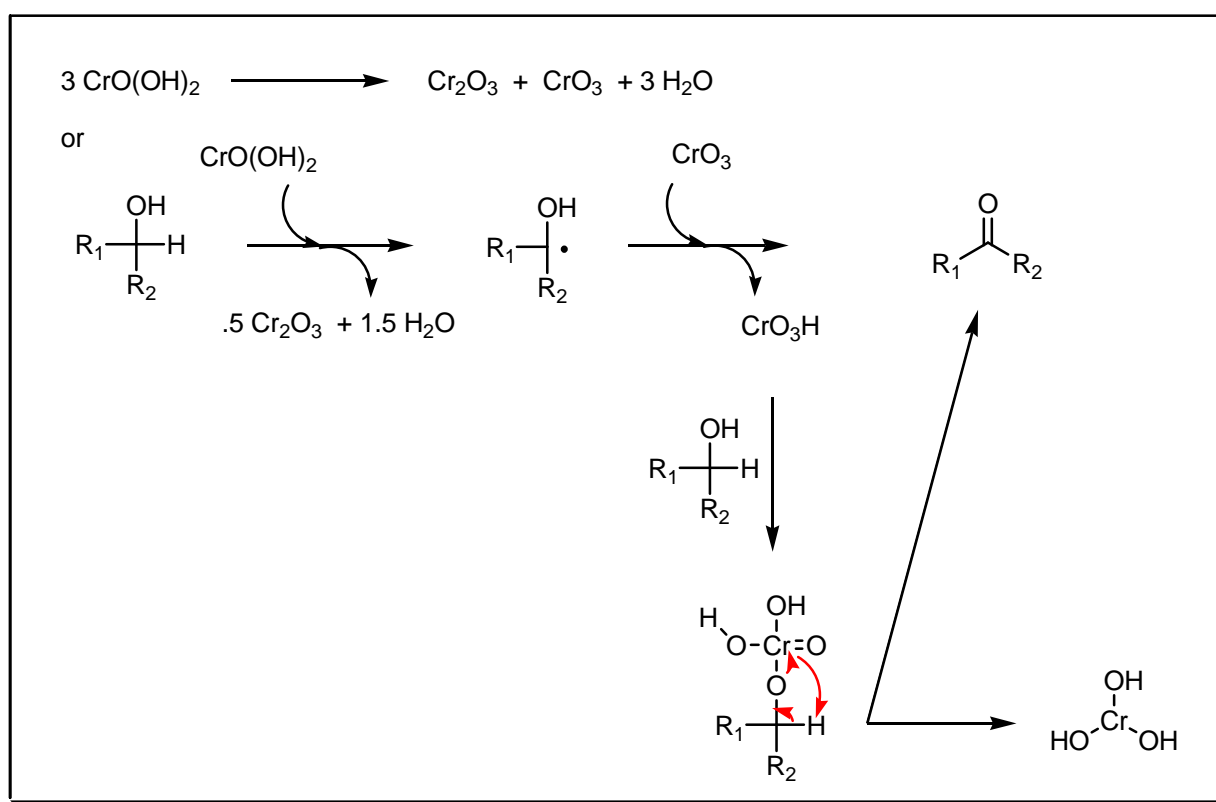
### EXAMPLE :



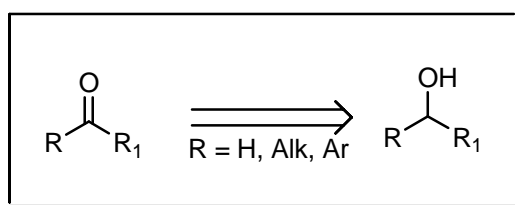
### MECHANISM :



### Follow-up chemistry of Cr(IV) :



### DISCONNECTION :



### NOTES :

This is a useful general method for the oxidation of primary and secondary alcohols even in the presence of double bonds and thioethers. The main problem is the isolation of the products from the pyridine solution. This oxidation reaction is superseded by the **Collins** oxidation, which is originally a modification of the **Sarett** oxidation. Chromium-

mediated oxidations have a competing pathway involving free-radical intermediates. See also **Anelli**, **Ball – Goodwin – Morton**, **Collins**, **Corey – Kim**, **Corey – Schmidt**, **Corey – Suggs**, **David – Thieffry**, **Delépine**, **Dess – Martin**, **Einhorn** oxidation, **Fétizon**, **Jones** oxidation, **Ley**, **Maurer – Drefahl**, **Mukaiyama** oxidation, **Nicolaou**, **Oppenauer**, **Parikh – von Doering**, **Pfizzner – Moffatt**, **Pinnick**, **Swern** and **Uemura** reactions.

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## REFERENCES :

**March** : 1167

**Smith – March** : 1514, 1531

**Smith** : 228

**Smith 2<sup>nd</sup>** : 199

**Org. React.** : **53**, 1

**Org. Synth.** : **52**, 5; **55**, 84

**Org. Synth. Coll. Vol.** : **6**, 373, 644

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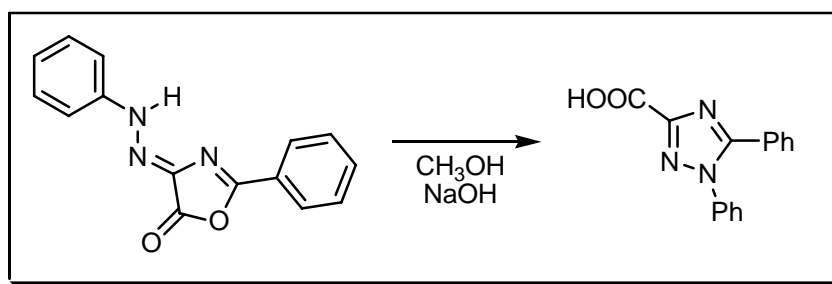
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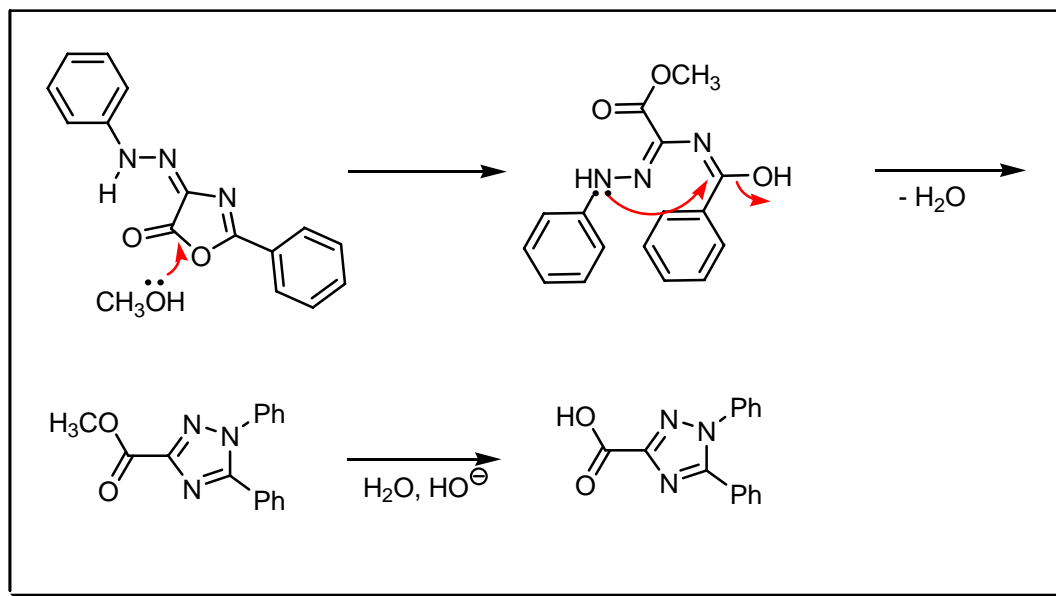
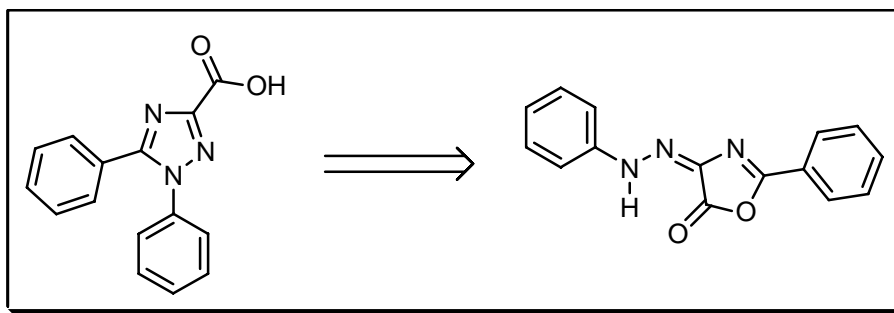
## COMMENTS :

## SAWDEY REARRANGEMENT

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### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

4-Phenylazo-2-phenyloxazolin-5-one is rapidly attacked by methanolic potassium hydroxide or methanolic ammonia with the formation of 1,5-diphenyl-3-carboxy-1H-1,2,4-triazole and 1,5-diphenyl-3-carbamido-1H-1,2,4-triazole, respectively.

**REFERENCES :**

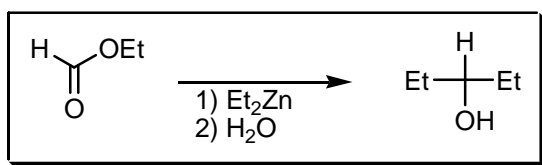
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**COMMENTS :**

## SAYTZEFF SYNTHESIS

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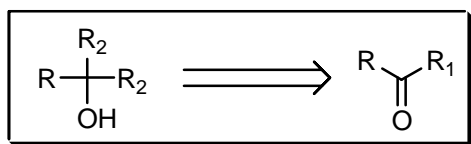
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This method involves the use of zinc, an alkyl halide and a suitable carbonyl compound. See also **Frankland – Duppa**, **Grignard** and **Schorigin – Wanklyn** reactions.

### REFERENCES :

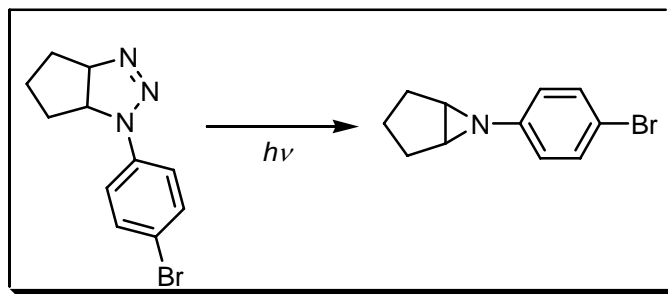
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### COMMENTS :

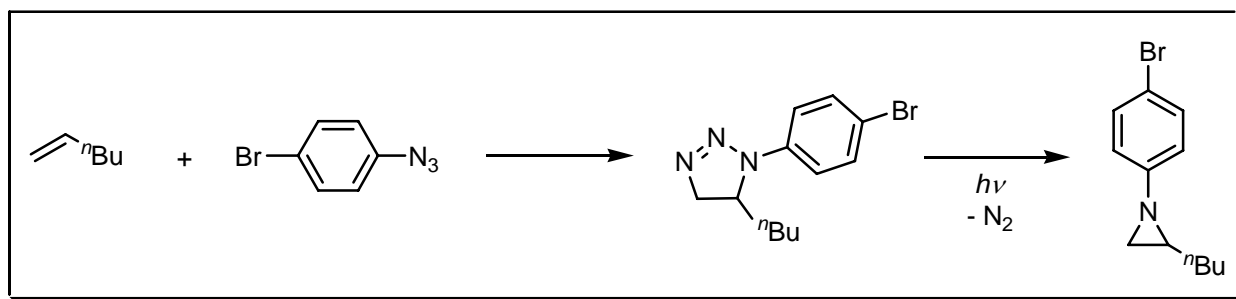


## SCHEINER AZIRIDINE SYNTHESIS

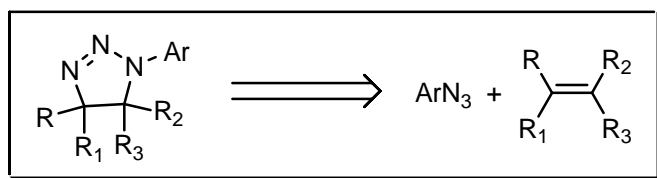
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Arylazides react with unactivated olefins to give 1,2,3- $\Delta^2$ -triazoles. Photodecomposition leads to aziridines. See also **Blum** aziridine, **Hassner**, **Hoch – Campbell**, **Huisgen**, **Mansuy – Evans** and **Wenker** ring-closure reactions.

### REFERENCES :

**March** : 202

**Smith – March** : 1057

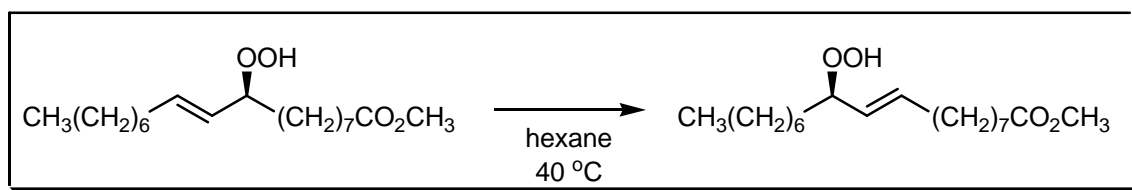
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## COMMENTS :

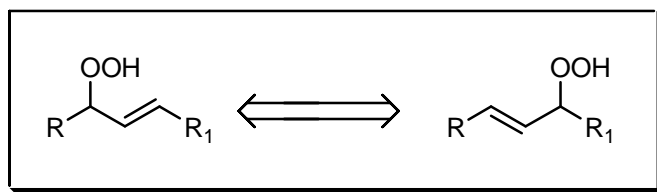
## SCHENCK REARRANGEMENT

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### EXAMPLE :



### DISCONNECTION :



### NOTES :

The [2,3]-allylic hydroperoxide rearrangement in both acyclic and cyclic systems. Initially discovered in steroidal allylic hydroperoxides. Over the years several reaction mechanisms have been proposed, these are discussed in the review by **Beckwith et al.**

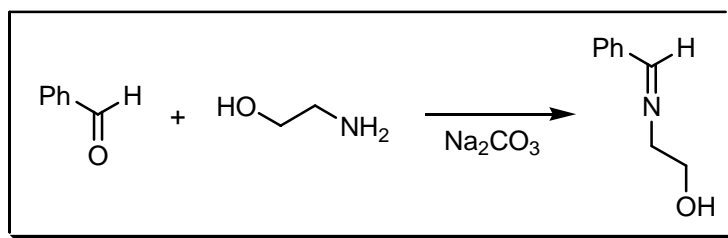
### REFERENCES :

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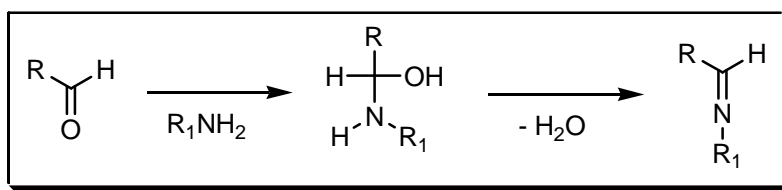
COMMENTS :

## SCHIFF REACTION

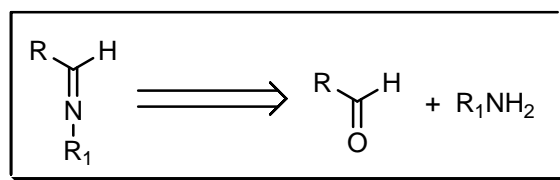
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The formation of imines from aldehydes and primary amines in the presence of alkali. See also **Decker – Forster** and **Grignard** reactions.

## REFERENCES :

March : 896

Smith – March : 1186

Smith : 904

Smith 2<sup>nd</sup> : 764

Houben – Weyl : 7/1, 453

Org. Synth. : 21, 108; 50, 66

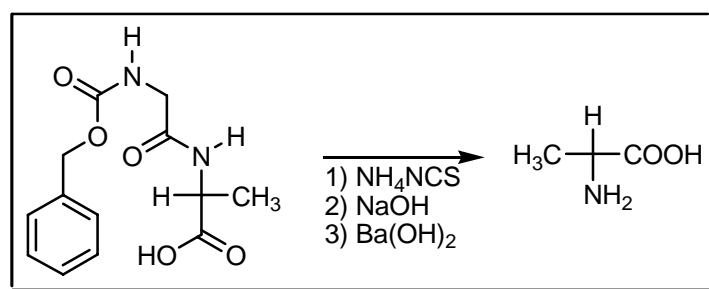
Org. Synth. Coll. Vol. : 3, 827; 6, 901

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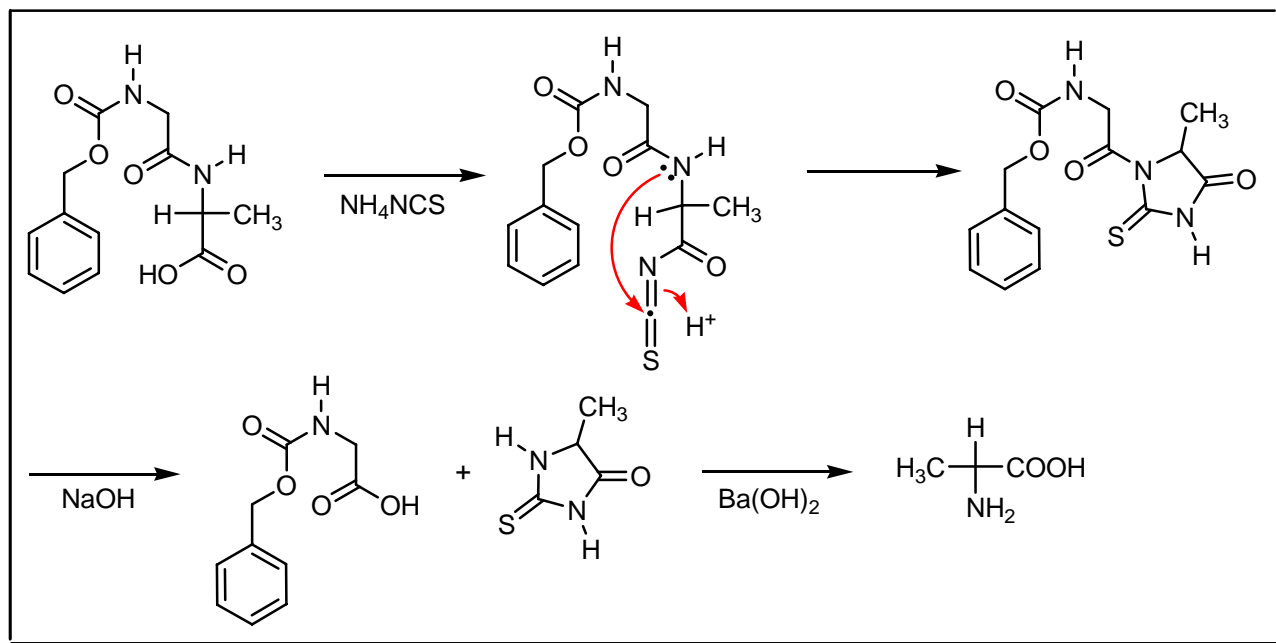
## COMMENTS :

## SCHLACK – KUMPF REACTION

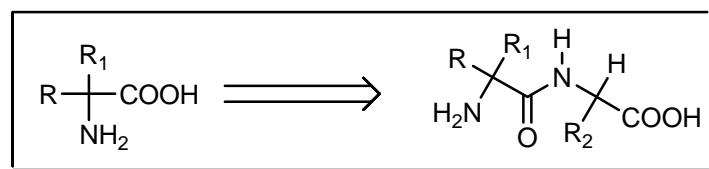
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The degradation of peptides using a hydantoin system. See also **Bergmann** degradation and **Edman** reactions.

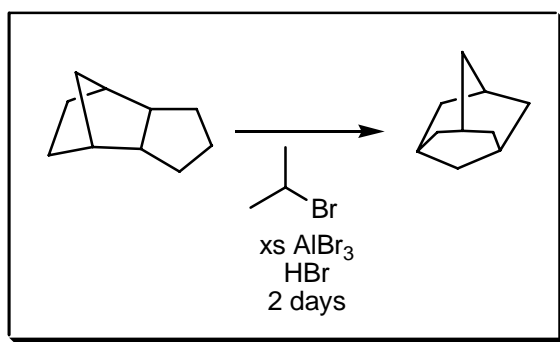
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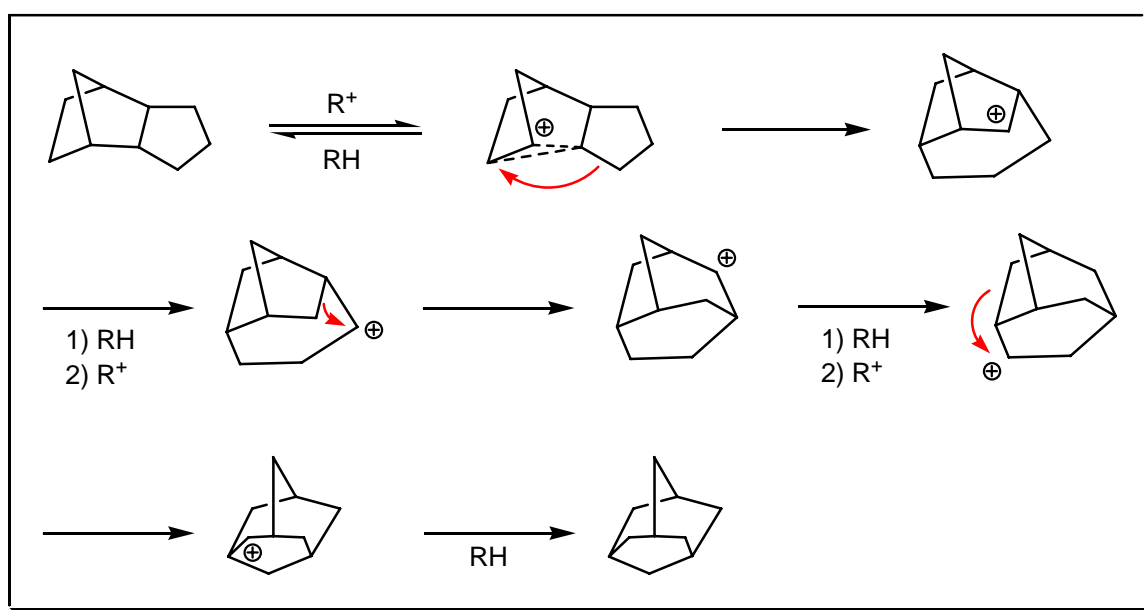
## COMMENTS :

## von RAGUÉ SCHLEYER ADAMANTISATION

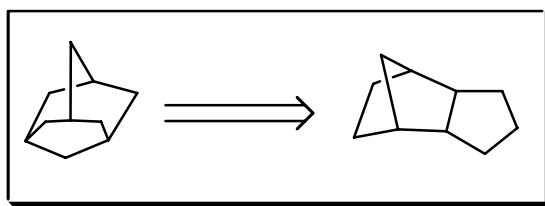
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Tricyclic molecules rearrange in a **Wagner – Meerwein** fashion to adamantane and derivatives if treated with Lewis acids. This is the first synthesis which made adamantane readily available. See also **Wagner – Meerwein** rearrangement.

### REFERENCES :

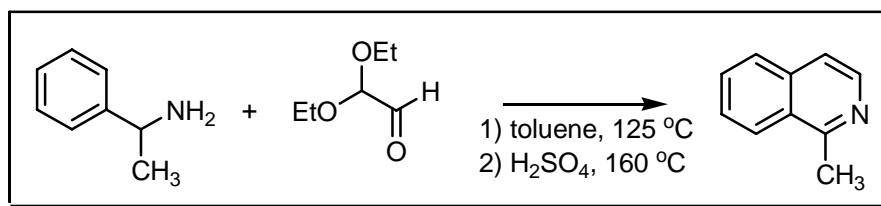
March : 1071

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- 2) V.Z. Williams; P. von Ragué Schleyer; G.J. Gleicher; L.B. Rodewald, *J. Am. Chem. Soc.*, 1966, **88**, 3862.
- 3) Z. Majerski; S.H. Liggers; P. von Ragué Schleyer; A.P. Wolf, *J. Chem. Soc., Chem. Commun.*, 1970, 1596.
- 4) M.A. McKervey, *Tetrahedron*, 1980, **36**, 971.

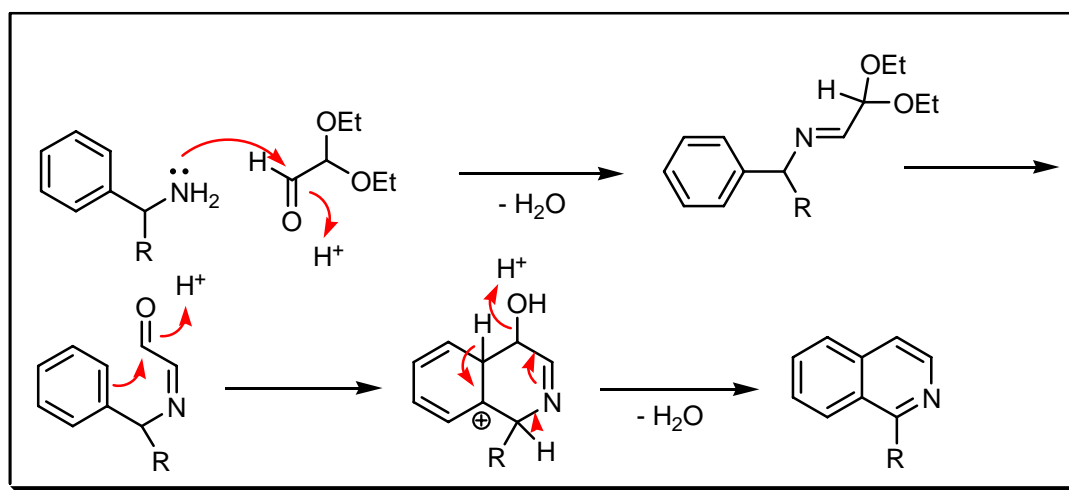
COMMENTS :

## SCHLITTLER – MÜLLER RING-CLOSURE

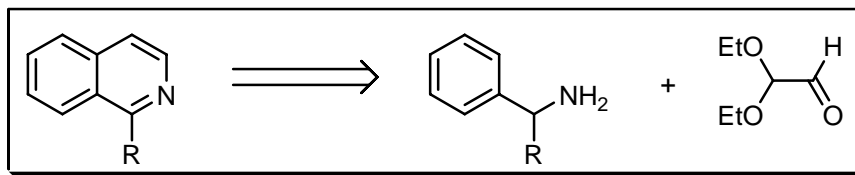
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

This reaction is a modification of the **Pomeranz – Fritsch** reaction using benzylamines and glyoxal semiacetals. The isoquinoline ring-closure of benzylimino acetals using concentrated sulfuric acid at 180 °C. See also **Bamberger – Goldschmidt**, **Bischler – Napieralski**, **Bobbit**, **Bruckner**, **Larock** indole, **Pictet – Gams**, **Pictet – Sprengler**, **Pomeranz – Fritsch** and **Simchen** reactions.

## REFERENCES :

Smith : 1342

Smith 2<sup>nd</sup> : 1104

Houben – Weyl : E7a, 625, 640

Org. React. : 6, 192

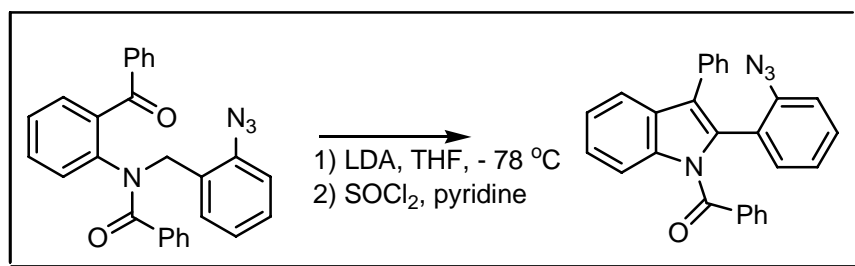
1) C.K. Bradsher, *Chem. Rev.*, 1946, **38**, 447.

2) E. Schlittler; J. Müller, *Helv. Chim. Acta*, 1948, **31**, 914.

## COMMENTS :

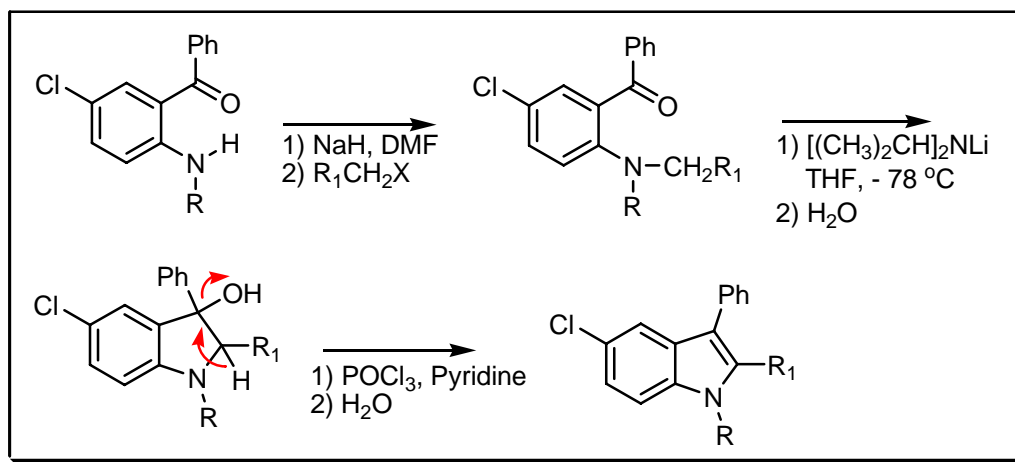
## SCHMID INDOLE SYNTHESIS

### EXAMPLE :

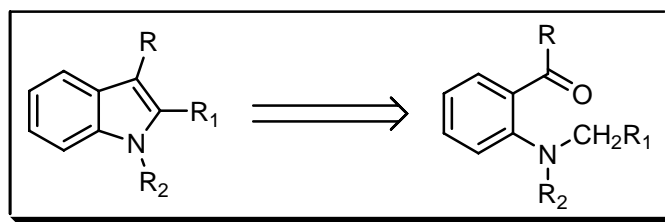




## MECHANISM :



## DISCONNECTION :



## NOTES :

In principle this is a 'reverse-Madelung' reaction to afford an indole. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

## REFERENCES :

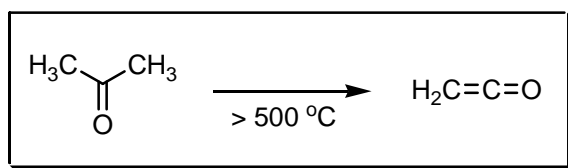
- 1) H. Greuter; H. Schmid, *Helv. Chim. Acta*, 1974, **57**, 281.
- 2) P. Molina; M. Alajarin; A. Vidal, *Tetrahedron*, 1990, **46**, 1063.

## COMMENTS :

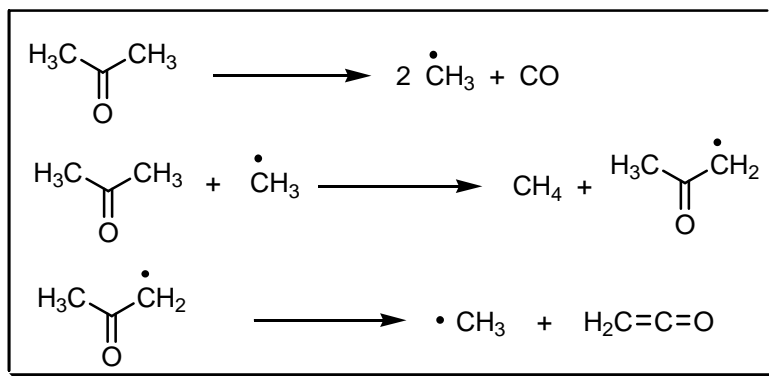
## SCHMIDLIN – BERGMAN – WILSMORE KETENE SYNTHESIS

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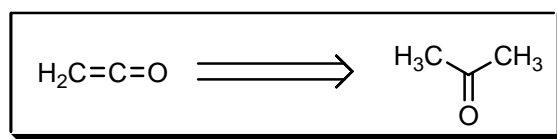
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The pyrolysis of acetone to ketene *via* a radical mechanism.

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### REFERENCES :

Org. React. : 3, 109

Org. Synth. : 4, 39

Org. Synth. Coll. Vol. : 1, 330

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1) N.T.M. Wilsmore; A.W. Stewart, *Proc. Chem. Soc.*, 1907, **23**, 229.

2) J. Schmidlin; M. Bergman, *Ber. Dtsch. Chem. Ges.*, 1910, **43**, 2821.

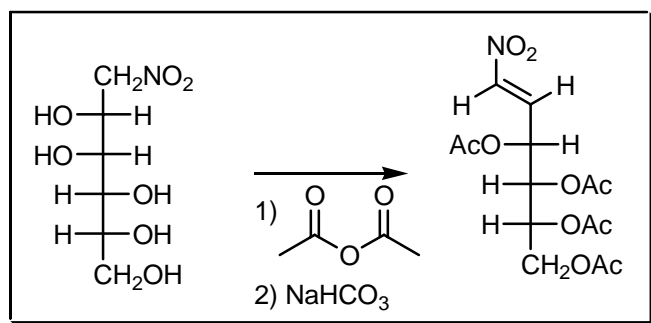
3) G. Quadbeck, *Angew. Chem.*, 1956, **68**, 361.

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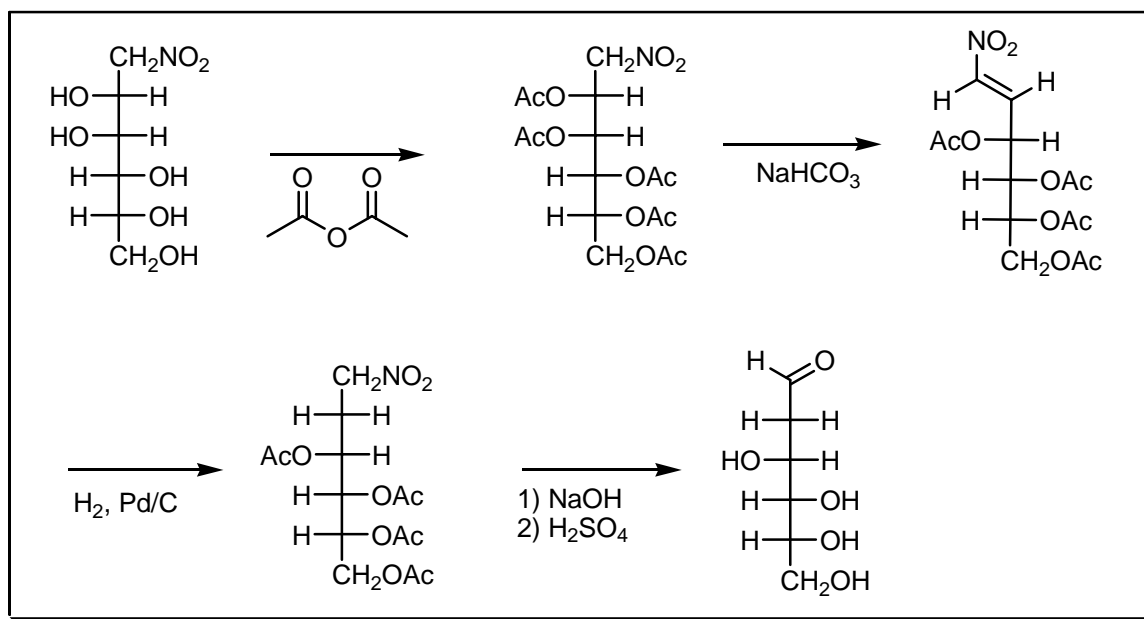
COMMENTS :

## SCHMIDT – RUTZ SYNTHESIS

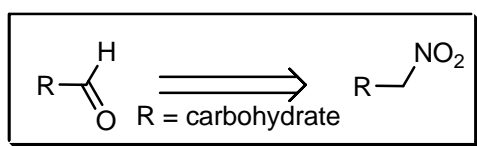
EXAMPLE :



MECHANISM :



DISCONNECTION :

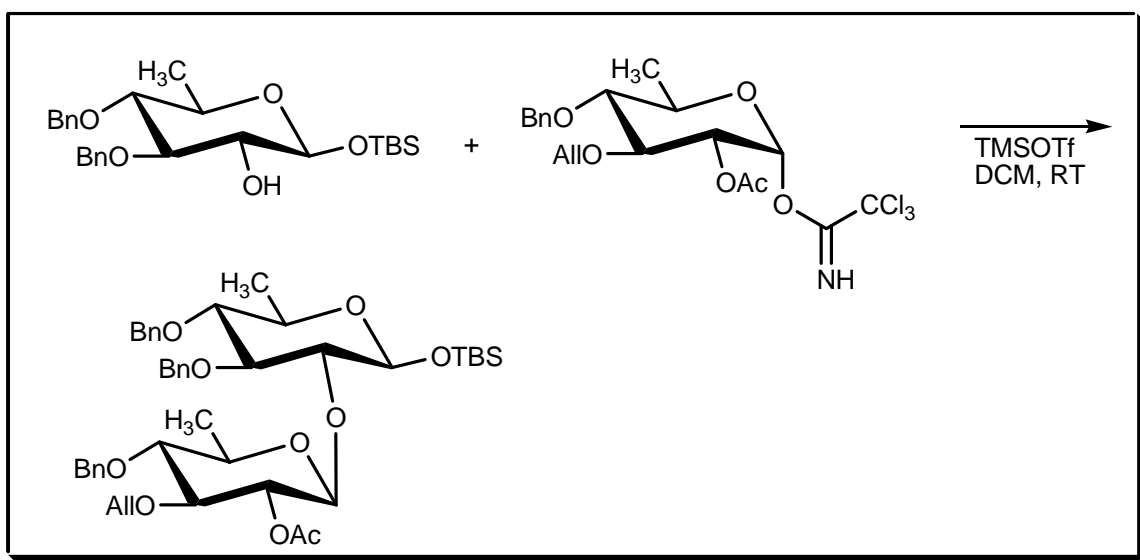


**NOTES :**

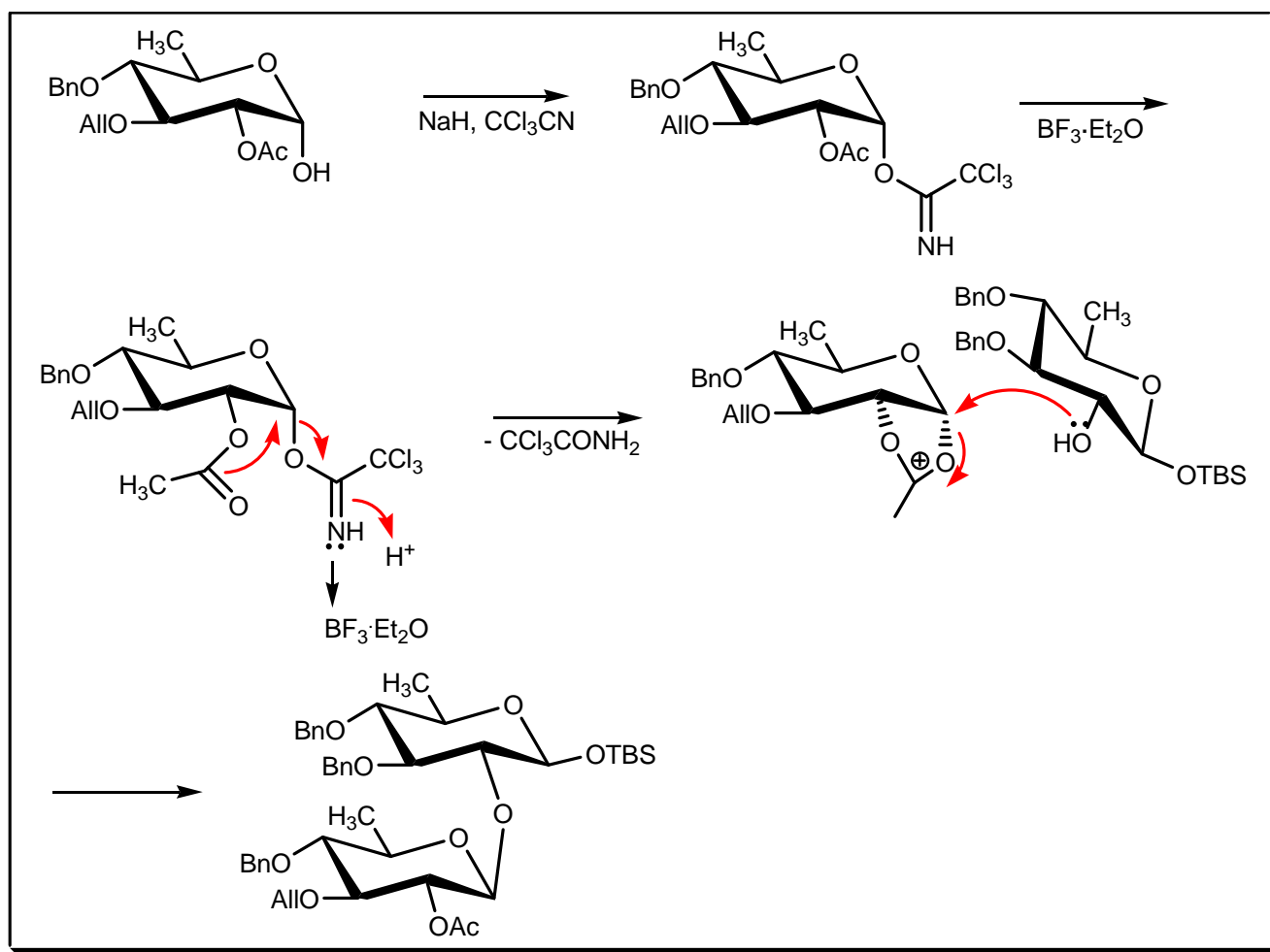
The formation of nitro-olefins from nitro-polyalcohols after acetylation. After this method 2-desoxy-aldoses can be formed.

**REFERENCES :**

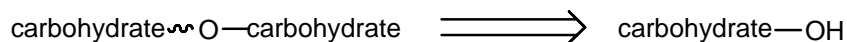
- 1) E. Schmidt; G. Rutz, *Ber. Dtsch. Chem. Ges.*, 1928, **61**, 2142.
- 2) J.C. Sowden, *J. Am. Chem. Soc.*, 1949, **71**, 1897.
- 3) J.C. Sowden; R. Schaffer, *J. Am. Chem. Soc.*, 1951, **73**, 4662.
- 4) A. Matsuda; K.A. Watanabe, *Nucleosides, Nucleotides*, 1996, **15**, 205.

**COMMENTS :****SCHMIDT GLYCOSIDATION****EXAMPLE :**

## MECHANISM :



## DISCONNECTION :



## NOTES :

Electron-deficient nitriles such as trichloroacetonitrile are known to undergo direct and irreversible, base-catalysed addition of alcohols to give O-alkyl trichloroacetimidates. The pioneering work on this reaction was carried out by **Nef**. But it was **Schmidt** who demonstrated that this mild, base-catalysed formation of O-alkyl trichloroacetimidates can be extended to the preparation of O-glycosyl trichloroacetimidates. See also **Fischer** glycosidation, **Kahne** glycosidation, **Koenigs – Knorr** glycosidation and **Michael** glycosidation reactions.

## REFERENCES :

- 1) G. Grundler; R.R. Schmidt, *Carbohydr. Res.*, 1985, **135**, 203.
- 2) R.R. Schmidt, *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 212.
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- 4) K. Toshima; K. Tatsuta, *Chem. Rev.*, 1993, **93**, 1503.
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6) N. Smiljanic; S. Halila; V. Moreau; F. Djedaïni–Pilard, *Tetrahedron Lett.*, 2003, **44**, 8999.

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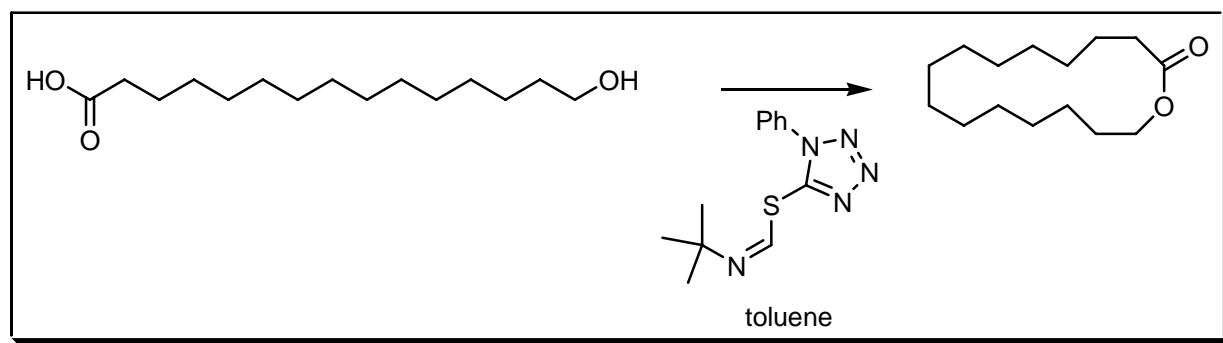
**COMMENTS :**

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**SCHMIDT MACROLACTONISATION**

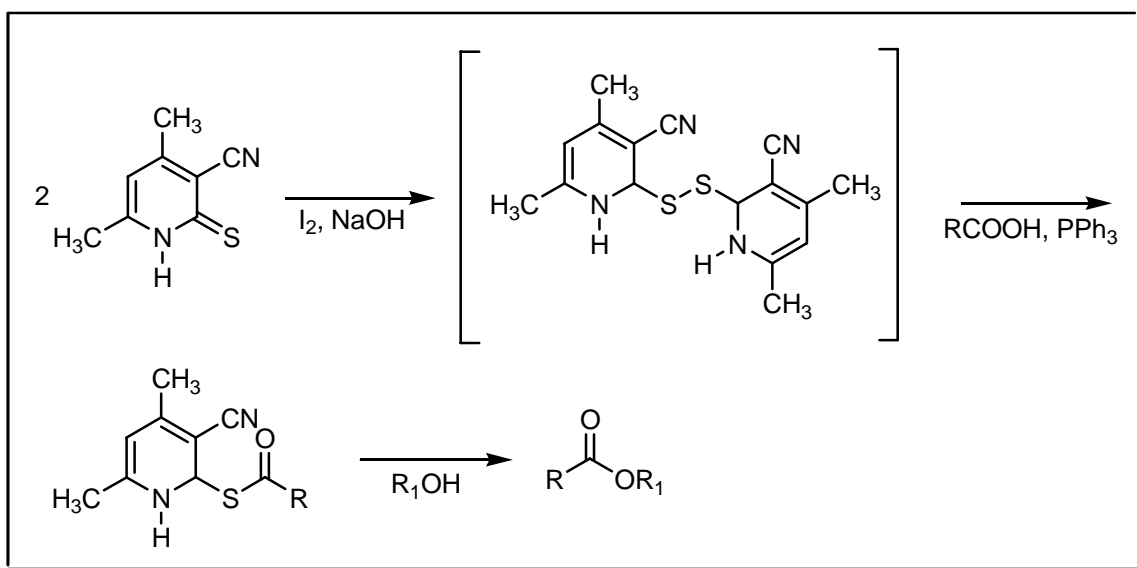
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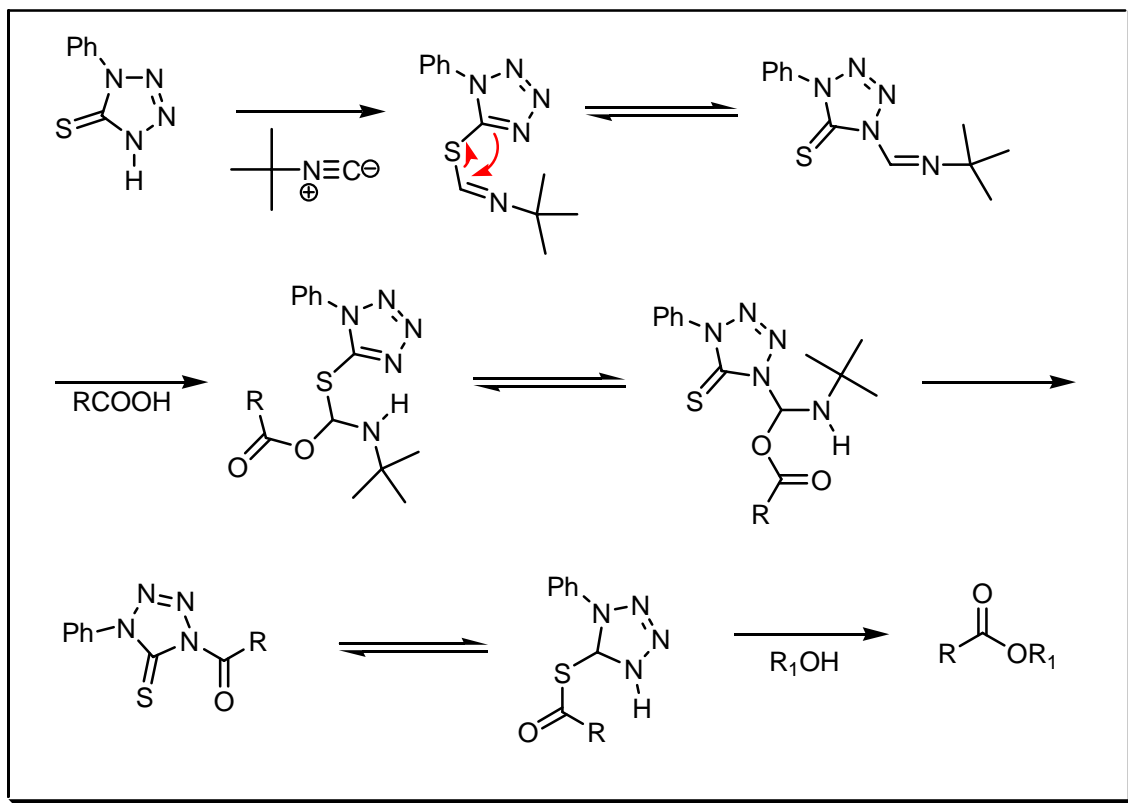
**EXAMPLE :**



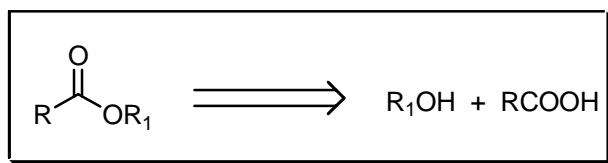
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**MECHANISM :**





#### DISCONNECTION :



#### NOTES :

The ester, lactone and peptide formation with 1,2-dihydro-4,6-dimethyl-2-thioxo-3-pyridinecarbonitrile or 1-phenyl-2-tetrazoline-5-thione. See also **Corey – Nicolaou**, **Diels – Alder**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Kita**, **Masamune**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolkiewicz**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

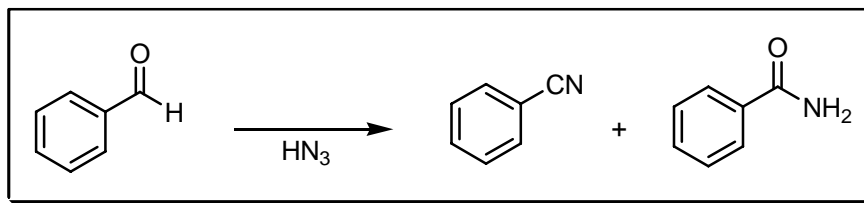
#### REFERENCES :

- 1) U. Schmidt; D. Heermann, *Angew. Chem., Int. Ed. Engl.*, 1979, **18**, 308.
- 2) U. Schmidt; M. Dietsche, *Angew. Chem., Int. Ed. Engl.*, 1981, **20**, 771.
- 3) U. Schmidt; J. Werner, *J. Chem. Soc., Chem. Commun.*, 1986, 996.

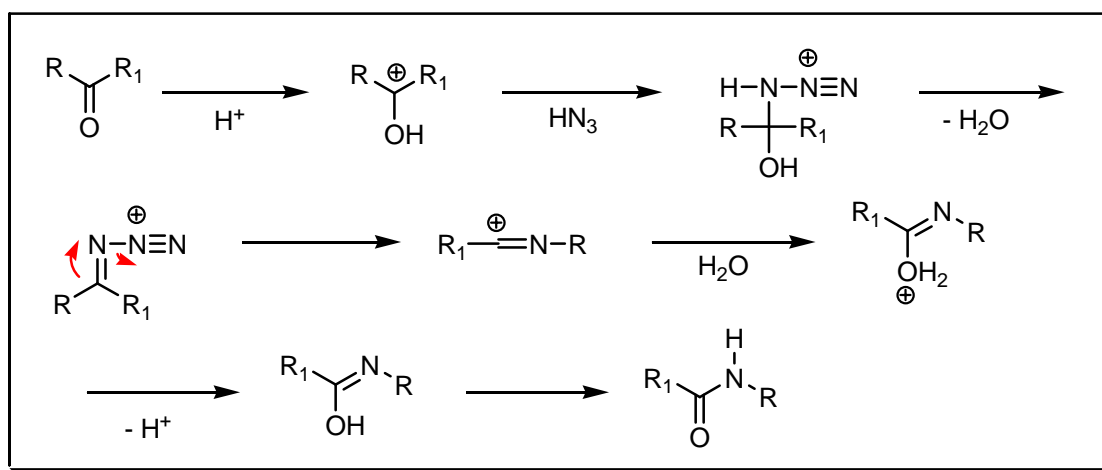
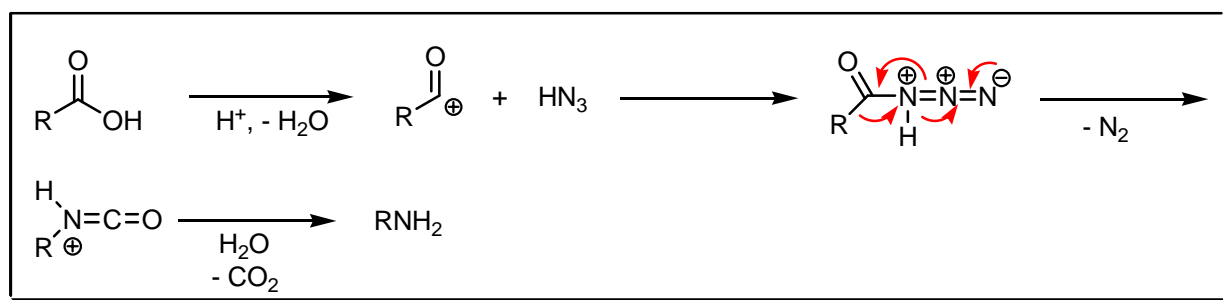
COMMENTS :

## SCHMIDT REARRANGEMENT

EXAMPLE :

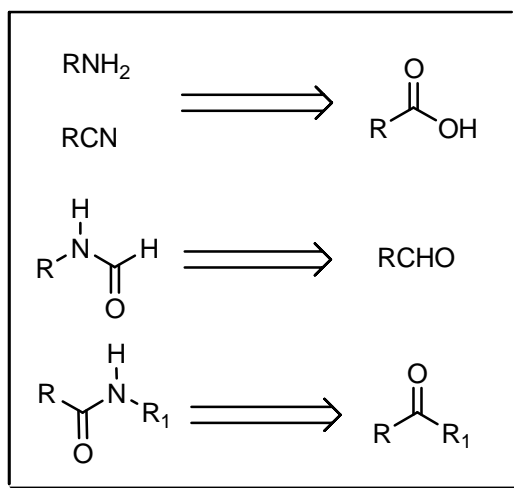


MECHANISM :





## DISCONNECTION :



## NOTES :

Hydrazoic acid in the presence of a strong mineral acid reacts with carbonyl compounds. It converts acids into amines, aldehydes into nitrile and ketones into amides. With a large excess of hydrazoic acid, aldehydes and ketones yield substituted tetrazoles. See also **Curtius** rearrangement, **Hofmann** rearrangement, **Lossen** rearrangement, and **Tiemann** rearrangement.

## REFERENCES :

**March** : 1093

**Smith – March** : 1380, 1413

**Houben – Weyl** : **11/1**, 872; **E5**, 572; **E6b**, 141, 913; **E7b**, 161, 178, 183; **E8a**, 243, 283, 1136

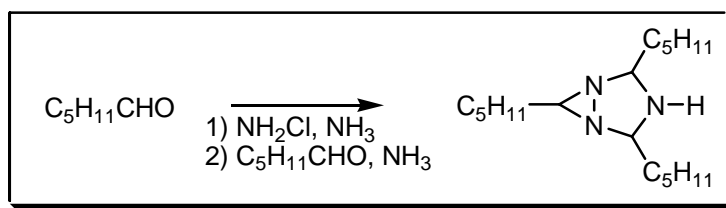
**Org. React.** : **3**, 307

- 1) R.F. Schmidt, *Angew. Chem.*, 1923, **36**, 511.
- 2) R.F. Schmidt, *Ber. Dtsch. Chem. Ges.*, 1924, **57**, 704.
- 3) F.R. Benson, *Chem. Rev.*, 1947, **41**, 1.
- 4) D.E. Applequist; J.D. Roberts, *Chem. Rev.*, 1954, **54**, 1065.
- 5) G. Fodor; S. Nagubandi, *Tetrahedron*, 1980, **36**, 1279.
- 6) A. Hassner; R. Fibiger; A.S. Amarsekara, *J. Org. Chem.*, 1988, **53**, 22.
- 7) N. Gálvez; M. Moreno–Mañas; R.M. Sebastián; A. Vallribera, *Tetrahedron*, 1996, **52**, 1609.
- 8) C.E. Katz; J. Aubé, *J. Am. Chem. Soc.*, 2003, **125**, 13948.
- 9) D.J. Gorin; N.R. Davis; F.D. Toste, *J. Am. Chem. Soc.*, 2005, **127**, 11260.

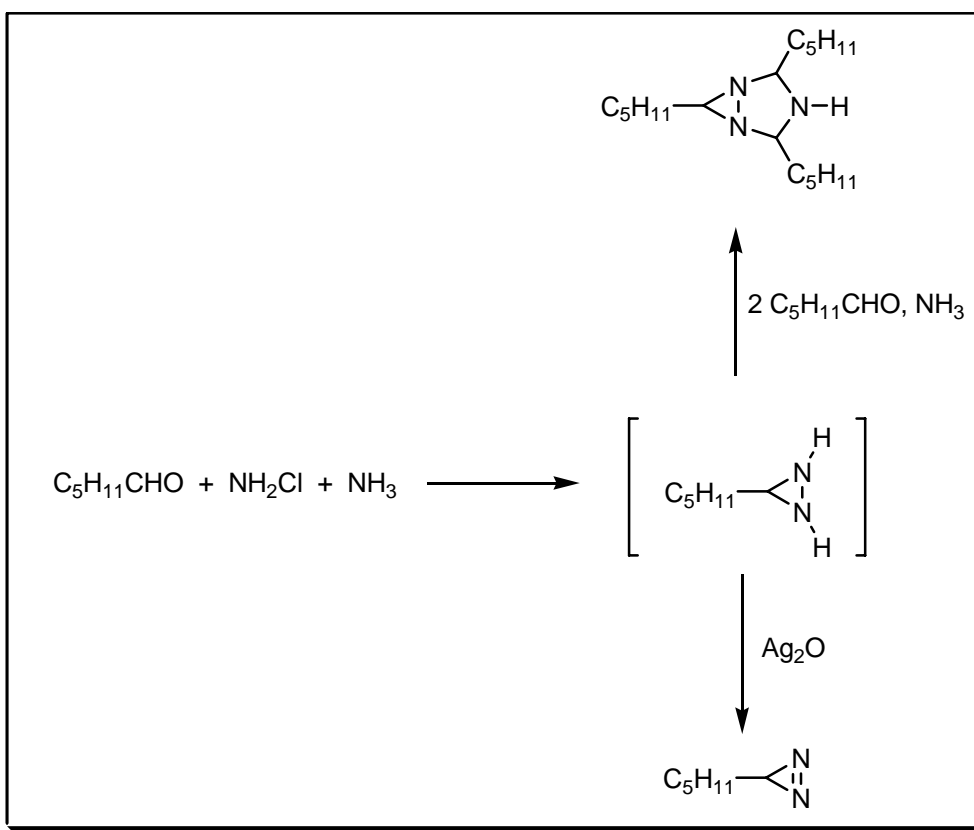
## COMMENTS :

## SCHMITZ DIAZIRIDINE SYNTHESIS

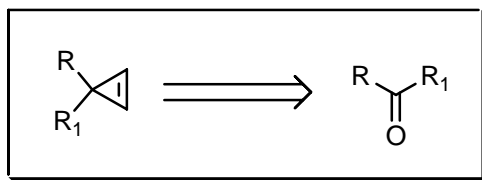
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The diaziridine synthesis from chloramines, ammonia and excess aldehyde. In the presence of excess aldehyde formation of bicyclic triazolidines takes place. See also **Graham** reaction.

## REFERENCES :

Org. Synth. : **45**, 83

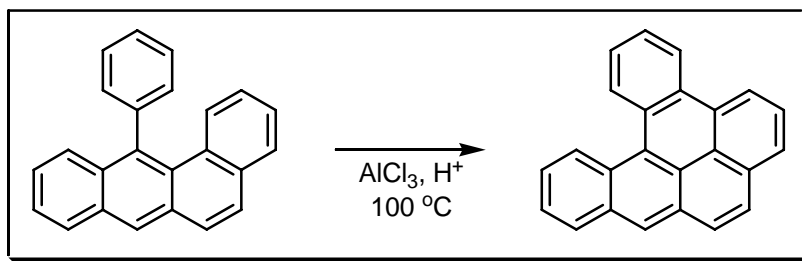
Org. Synth. Coll. Vol. : **5**, 897

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- 1) E. Schmitz, *Angew. Chem.*, 1959, **71**, 127.
  - 2) E. Schmitz, *Angew. Chem., Int. Ed. Engl.*, 1964, **3**, 333.
  - 3) A.T. Nielsen; D.W. Moore; R.L. Atkins; D. Mallory; J. DiPol; J.M. LaBerge, *J. Org. Chem.*, 1976, **41**, 3221.
  - 4) M.T.H. Liu, *Chem. Soc. Rev.*, 1982, **11**, 127.
  - 5) A.N. Mikhailyuk; V.Yu. Petukhova; N.N. Makhova, *Mendeleev Commun.*, 1997, 47.
  - 6) W. Knoll; M.M. Bobek; G. Giester; U.H. Brinker, *Tetrahedron Lett.*, 2001, **42**, 9161.
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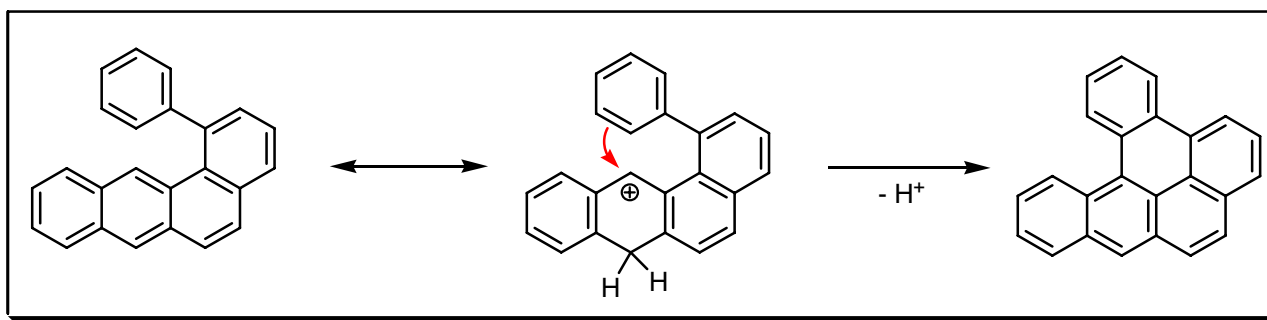
## COMMENTS :

## SCHOLL REACTION

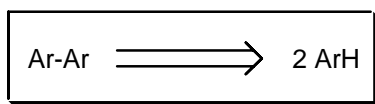
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



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## NOTES :

The preparation of condensed polynuclear aromatics by a Lewis acid catalyst and a protic acid. The reaction requires high temperatures and strong acid catalysts. Both *inter*- and *intramolecular* **Scholl** reactions are possible. See also **Eijkman**, **Elbs** reaction and **Nenitzescu** acylation reactions.

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## REFERENCES :

**March** : 539

**Smith – March** : 711

**Houben – Weyl** : 4/2, 101

**Org. Synth.** : 33, 37

**Org. Synth. Coll Vol.** : 4, 482

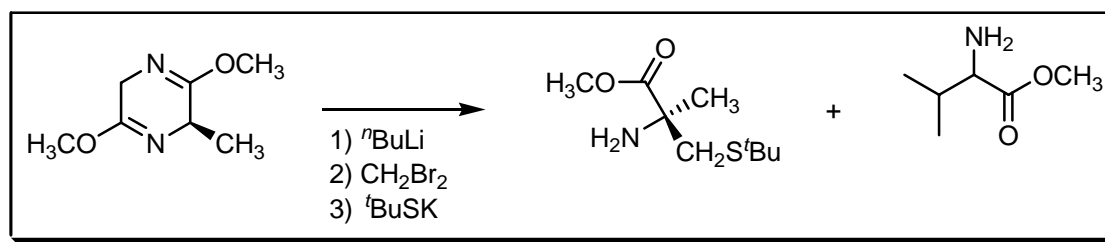
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- 1) R. Scholl; C. Seer; R. Weitzenböck, *Ber. Dtsch. Chem. Ges.*, 1910, **43**, 2202.
  - 2) R. Scholl; C. Seer, *Liebigs Ann. Chem.*, 1912, **394**, 111.
  - 3) C.F.H. Allen, *Chem. Rev.*, 1959, **59**, 983.
  - 4) F.A. Vingiello; J. Yanez; J.A. Campbell, *J. Org. Chem.*, 1971, **36**, 2053.
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  - 7) M.F. Rozas; O.E. Piro; E.E. Castellano; M.V. Mirifico; E.J. Vasini, *Synthesis*, 2002, 2399.
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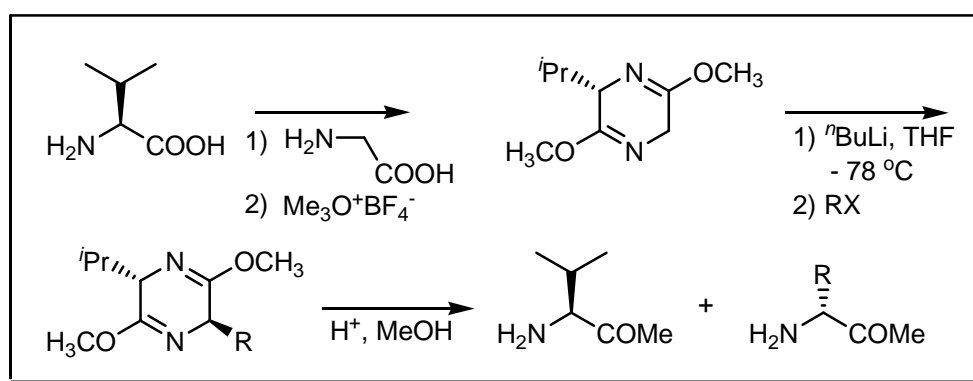
## COMMENTS :

# SCHÖLLKOPF AMINO ACID SYNTHESIS

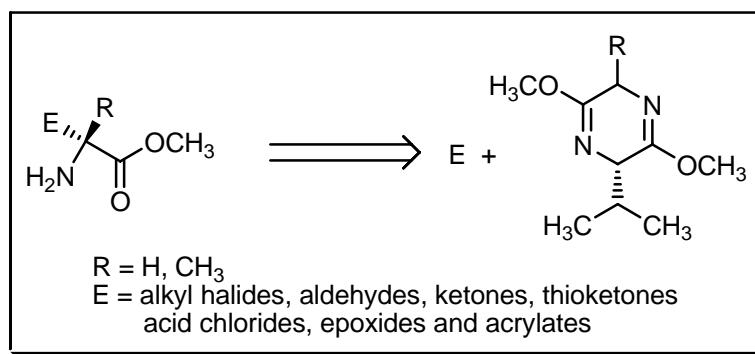
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The essence of this method is the alkylation of a chiral glycine anion. The stereoselectivity is due to the complexation of  $\text{Li}^+$  to the less hindered face of the anion which then guides the approach of the halide electrophile. Major drawback of this approach is the separation of the two amino esters at the end.

## REFERENCES :

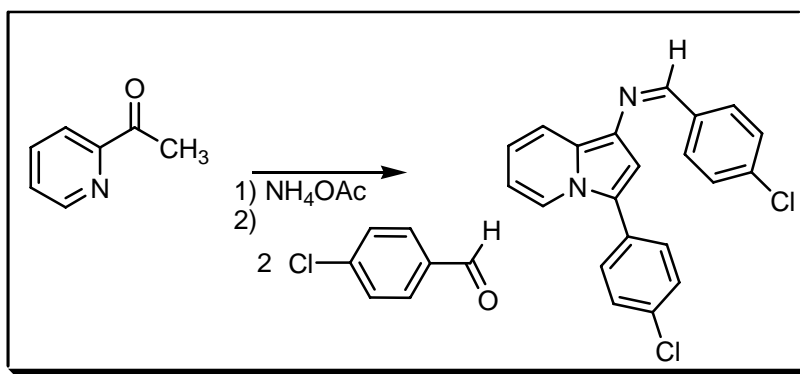
- 1) U. Schöllkopf; U. Groth; K.O. Westphalen; C. Deng, *Synthesis*, 1981, 969.
- 2) U. Schöllkopf, *Pure Appl. Chem.*, 1983, **55**, 1799.
- 3) R. Gull; U. Schöllkopf, *Synthesis*, 1985, 1052.
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- 5) T. Gan; J.M. Cook, *Tetrahedron Lett.*, 1997, **38**, 1301.  
 6) P.D. Croce; C. La Rosa; E. Pizzatti, *Tetrahedron: Asymmetry*, 2000, **11**, 2635.  
 7) H. Zhou; X. Liao; J.M. Cook, *Org. Lett.*, 2004, **6**, 249.  
 8) M. Andrei; C. Römming; K. Undheim, *Tetrahedron: Asymmetry*, 2004, **15**, 1359.

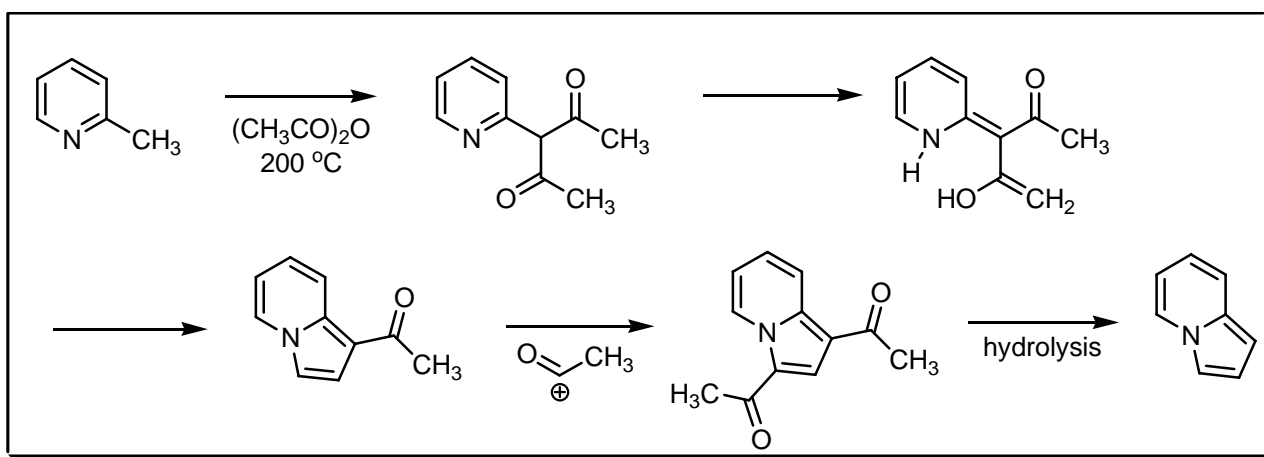
COMMENTS :

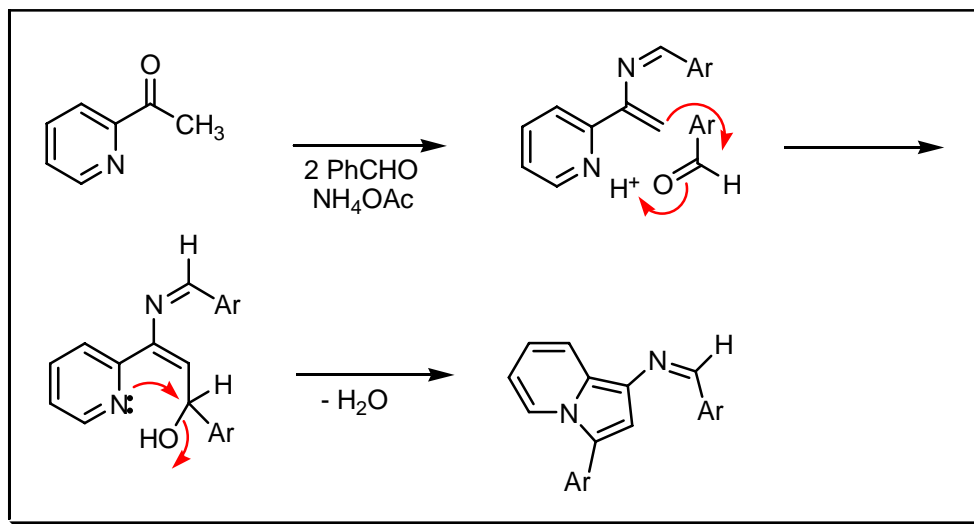
## SCHOLTZ INDOLIZINE SYNTHESIS

EXAMPLE :

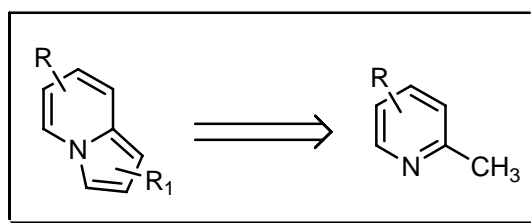


MECHANISM :





#### DISCONNECTION :



#### NOTES :

The indolizine synthesis from reaction of pyridinyl ketones with aldehydes in the presence of ammonium acetate or of 2-methyl pyridine and its derivatives with acid anhydrides. See also **Chichibabin** indolizine reaction.

#### REFERENCES :

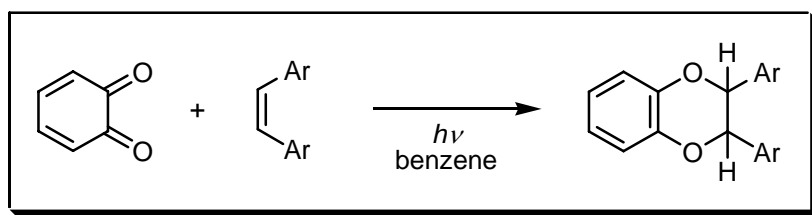
**Science of Synthesis** : 10, 749

- 1) M. Scholtz, *Ber. Dtsch. Chem. Ges.*, 1912, **45**, 734.
- 2) A.E. Chichibabin; E.N. Stepanow, *Ber. Dtsch. Chem. Ges.*, 1929, **62**, 1068.
- 3) E.T. Borrow; D.O. Holland, *Chem. Rev.*, 1948, **42**, 611.
- 4) V. Boekelheide; R.J. Windgassen, jr., *J. Am. Chem. Soc.*, 1959, **81**, 1456.
- 5) T. Uchida; K. Matsumoto, *Synthesis*, 1976, 209.
- 6) R. Sparrapan; M.A. Mendes; M. Carvalho; M.N. Eberlin, *Chem. Eur. J.*, 2000, **6**, 321.

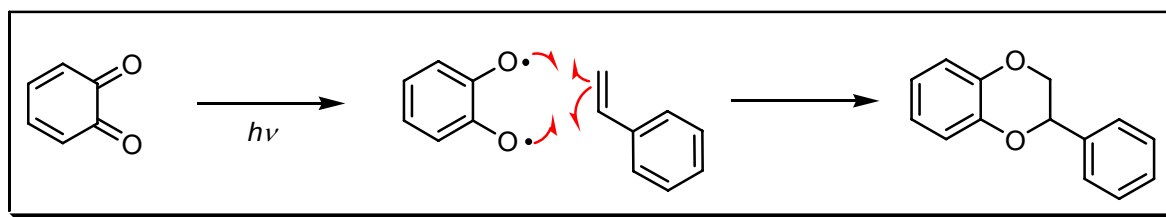
#### COMMENTS :

# SCHÖNBERG ADDITION

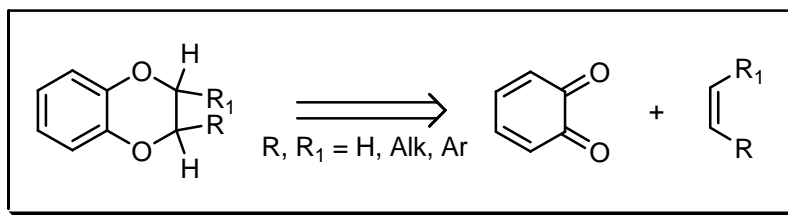
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The quinone addition of olefinic double bonds to dioxanes. Aromatic ethylenes react particularly well, while aliphatic ones lead to side reactions. The mechanism is most probably radical in nature.

## REFERENCES :

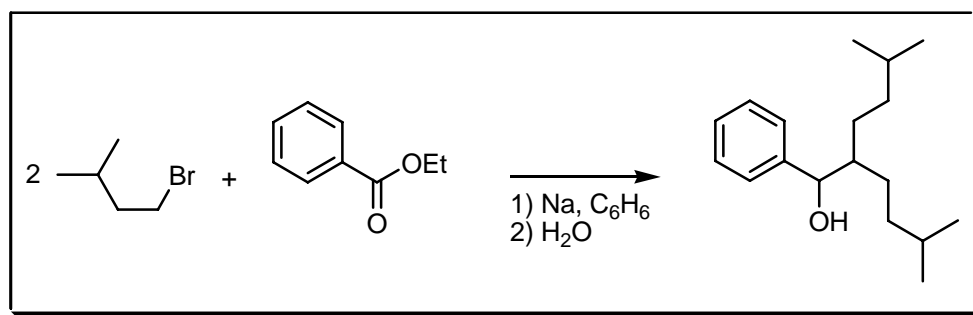
- 1) A. Schönberg; A. Mustafa, *Nature*, 1944, **153**, 195.
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## COMMENTS :

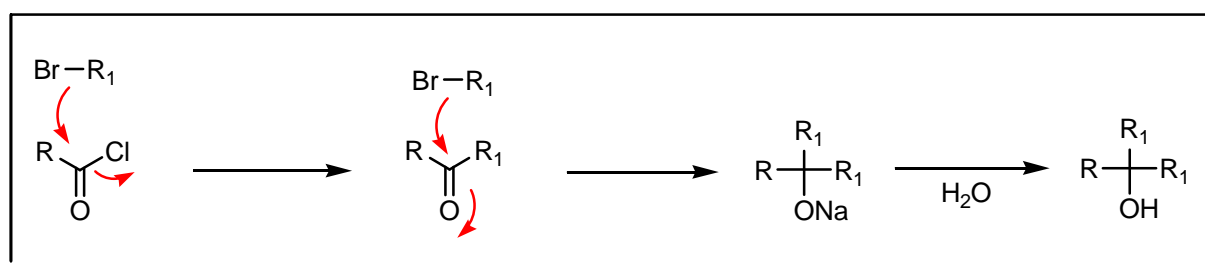


## SCHORIGIN – WANKLYN REACTION

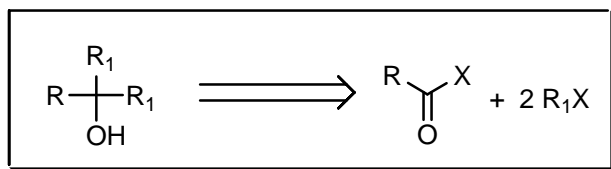
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This reaction is the organo sodium addition to carbonyl moieties in aldehydes, ketones, carboxylic acid esters and carbon dioxide. See also **Grignard** and **Frankland – Duppa** reactions.

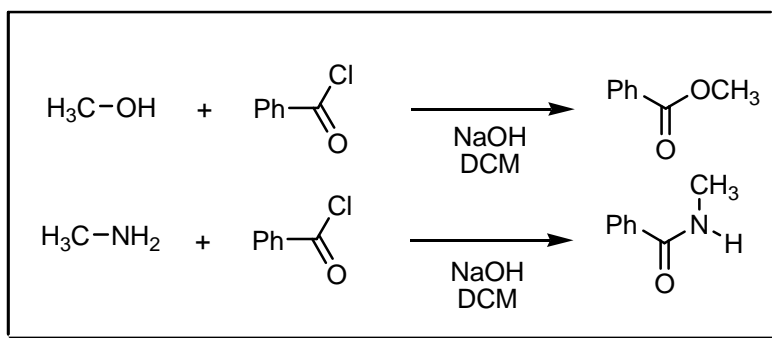
### REFERENCES :

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- 2) P. Schorigin, *Ber. Dtsch. Chem. Ges.*, 1907, **40**, 3111.
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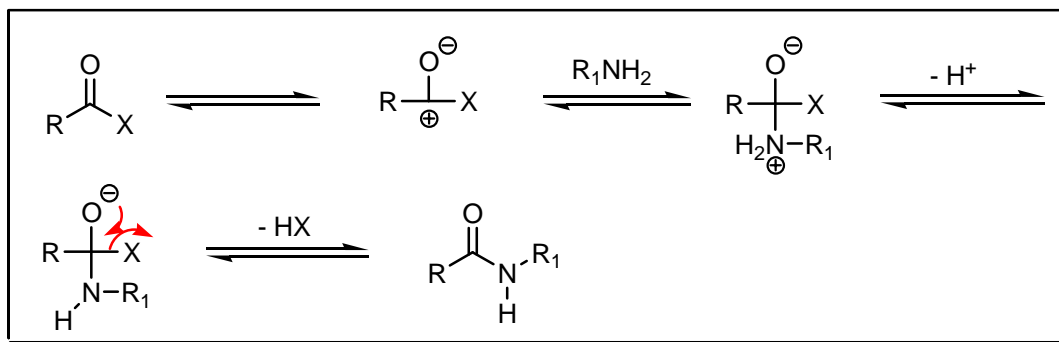
COMMENTS :

## SCHOTTEN – BAUMANN REACTION

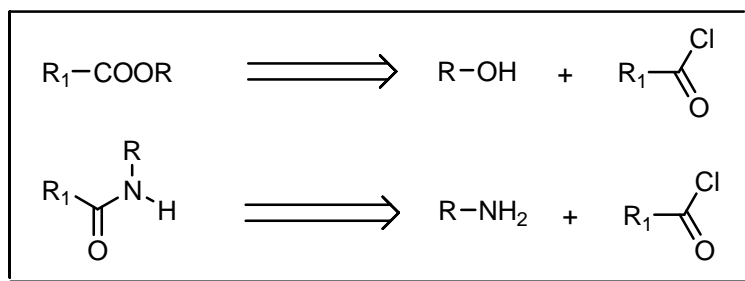
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

The acylation of alcohols, phenols and amino groups with acid chlorides in the presence of dilute alkali. An excess of alkali and acid chloride is necessary. See also **Chattaway** acylation, **Einhorn** acylation, **Galat – Elion**, **Hinsberg** reaction, **Lumière – Barbier**, **Schotten – Baumann** and **Weinreb** acetylation reactions.

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## REFERENCES :

**March** : 392

**Smith – March** : 482, 506

**Houben – Weyl** : **8**, 545; **E6b**, 434; **E8b**, 895

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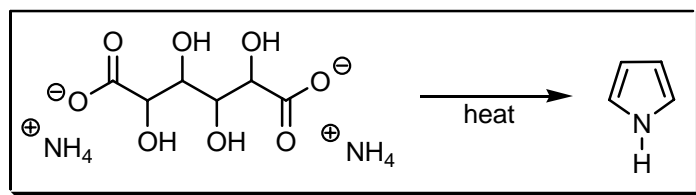
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## COMMENTS :

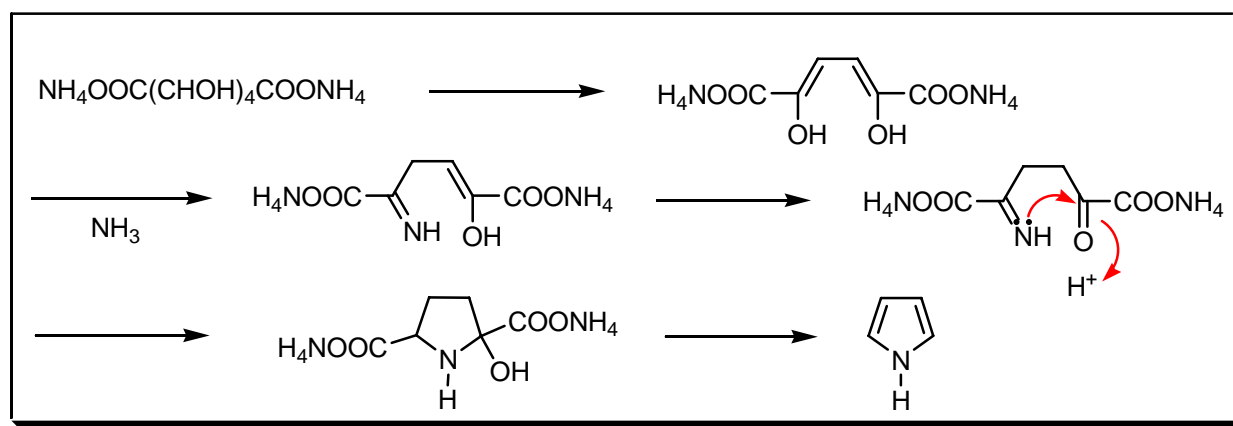
## SCHWANERT SYNTHESIS

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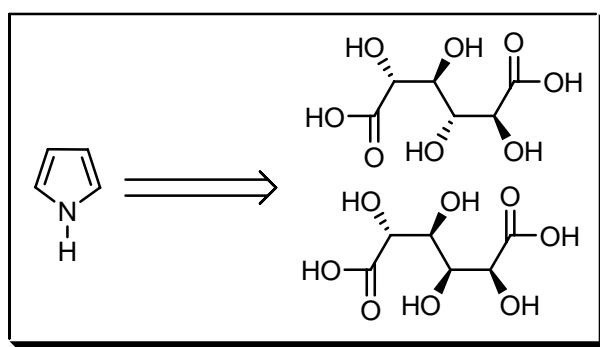
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

This reaction involves the synthesis of pyrroles by heating ammonium mucate or mucic acid and primary amines. Saccharic acid gives the same product as mucic acid. See also **Barton – Zard**, **Clauson-Kaas**, **Fischer – Fink**, **Grob – Camenisch**, **Hantzsch** pyrrole, **Harries** pyrrole, **Kenner**, **Knorr** pyrrole, **Miller – Plöchl**, **Paal – Knorr**, **Padwa**, **Piloty – Robinson**, **Trofimov** and **Zav'yalov** reactions.

## REFERENCES :

Org. Synth. : 9, 78

Org. Synth. Coll. Vol. : 1, 473

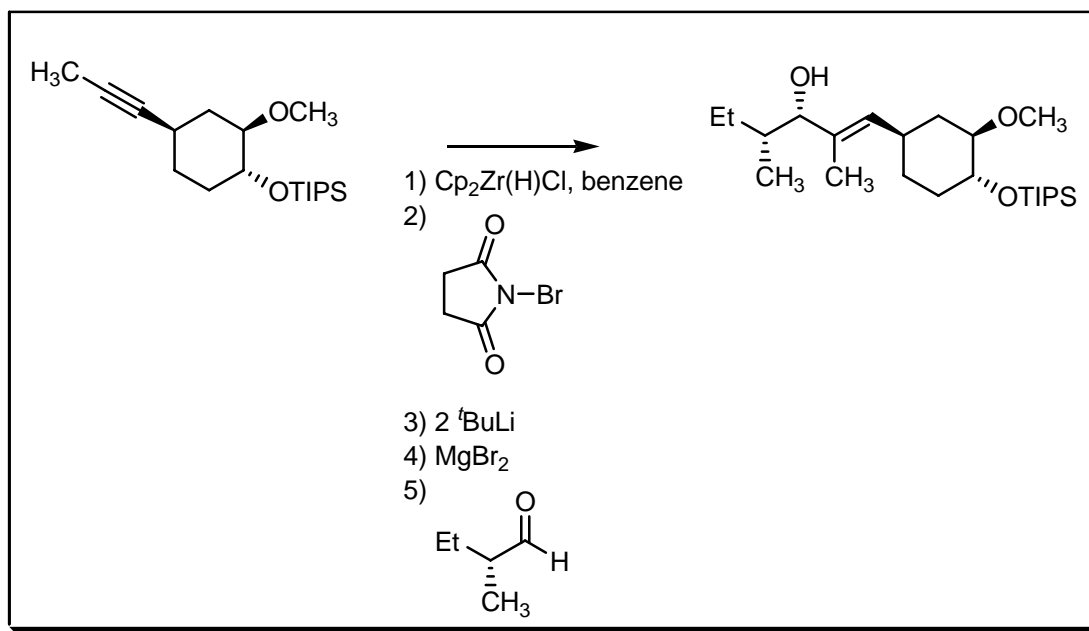
1) H. Schwanert, *Liebigs Ann. Chem.*, 1860, **114**, 63.

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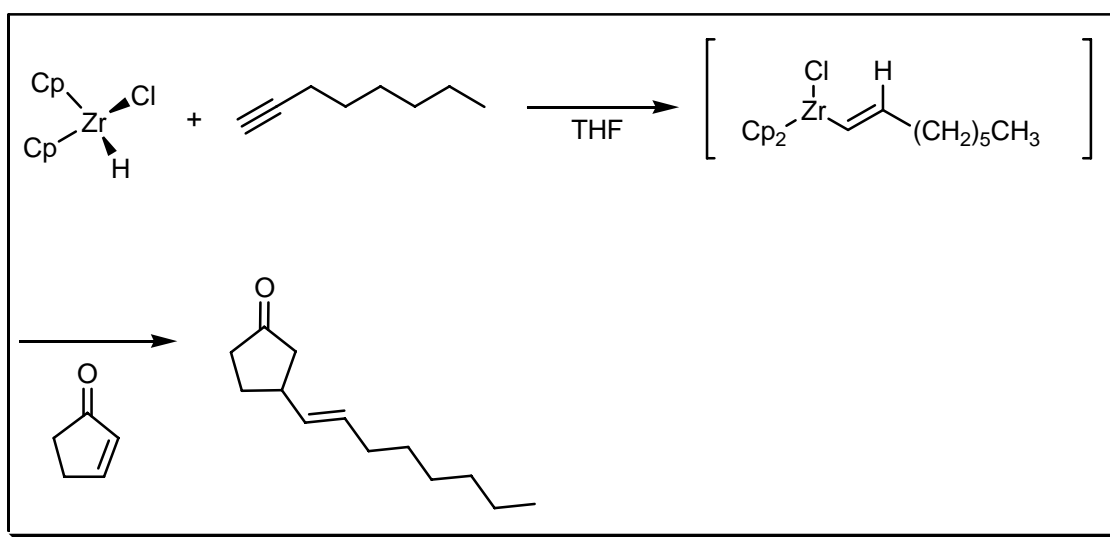
COMMENTS :

## SCHWARTZ HYDROZIRCONATION

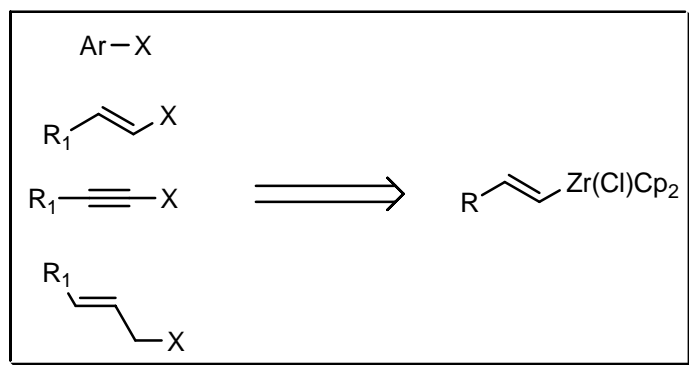
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The hydrozirconation with  $\text{Cp}_2\text{Zr}(\text{Cl})\text{H}$  and **Michael** addition of the Zr reagent. Other reactions involve transmetallation, complexation, oxidative coupling, carbozirconation and oxidative addition. The highly ionic zirconium-hydrogen bond has an hydridic character. The mechanistic details are poorly understood.

## REFERENCES :

**Org. Synth.** : **62**, 31; **71**, 77, 83; **74**, 205

**Org. Synth. Coll. Vol.** : **7**, 245; **9**, 143, 162, 640

**Science of Synthesis** : **2**, 681

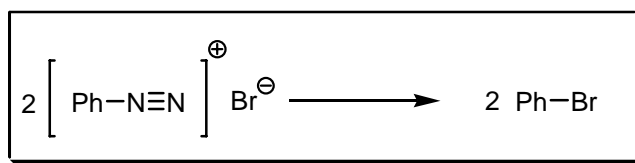
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## COMMENTS :

## SCHWECHTEN REACTION

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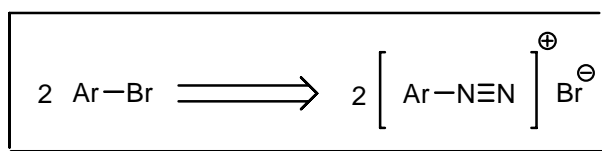
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The diazonium exchange against chlorine or bromine by thermic exchange with mercury halogens. See also **Balz – Schiemann**, **Cadogan** arylation, **Craig** exchange, **Demjanov** rearrangement, **Gattermann** diazo, **Gattermann** sulfinic acid, **Griess** deamination, **Knoevenagel** diazotation, **Körner – Contardi**, **Meerwein** arylation, **Sandmeyer** diazonium and **Witt** diazotation reactions.

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### REFERENCES :

Houben – Weyl : 5/4, 447

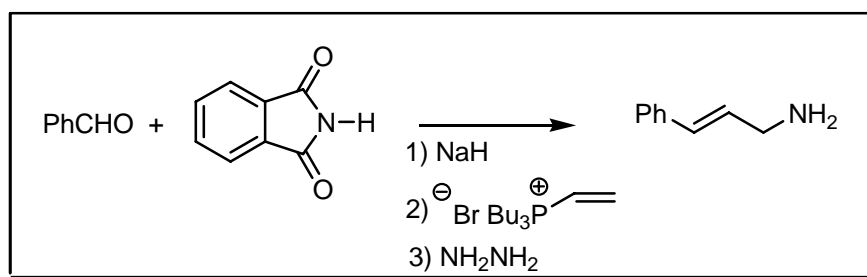
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- 1) H.W. Schwechten, *Ber. Dtsch. Chem. Ges.*, 1932, **65**, 1605.
  - 2) S.W. Fenton; A.E. de Wald; R.T. Arnold, *J. Am. Chem. Soc.*, 1955, **77**, 979.
  - 3) J.A. LaBudde; C. Heidelberger, *J. Am. Chem. Soc.*, 1958, **80**, 1225.
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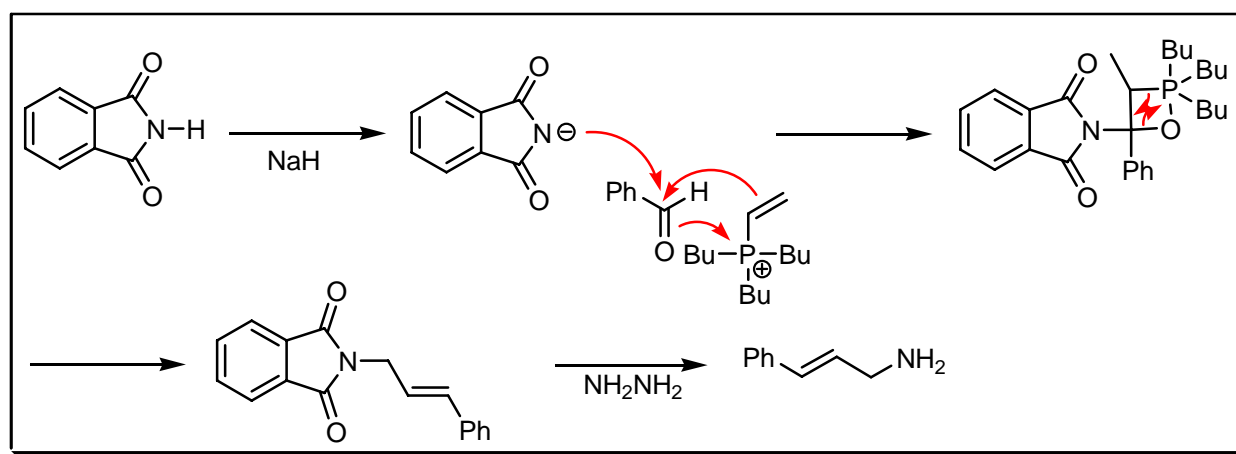
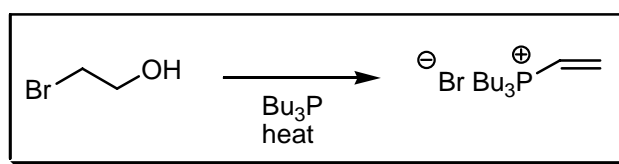
### COMMENTS :

# SCHWEIZER ALLYL AMINE SYNTHESIS

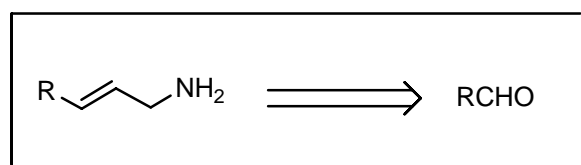
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of *E*-allyl amines from vinylphosphonium salts and aldehydes (via a **Wittig** reaction). See also **Gabriel** synthesis and **Wittig** reactions.

## REFERENCES :

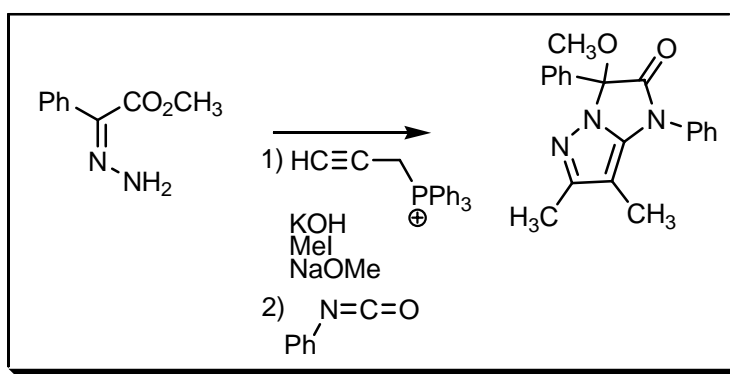
- 1) M.M. Rauhut; G.B. Borswitz; H. Currier Gillham, *J. Org. Chem.*, 1963, **28**, 2565.
- 2) E.E. Schweizer; L.D. Smucker; R.J. Votral, *J. Org. Chem.*, 1966, **31**, 467.
- 3) D.J. Hart; P.A. Cain; D.A. Evans, *J. Am. Chem. Soc.*, 1978, **100**, 1548.



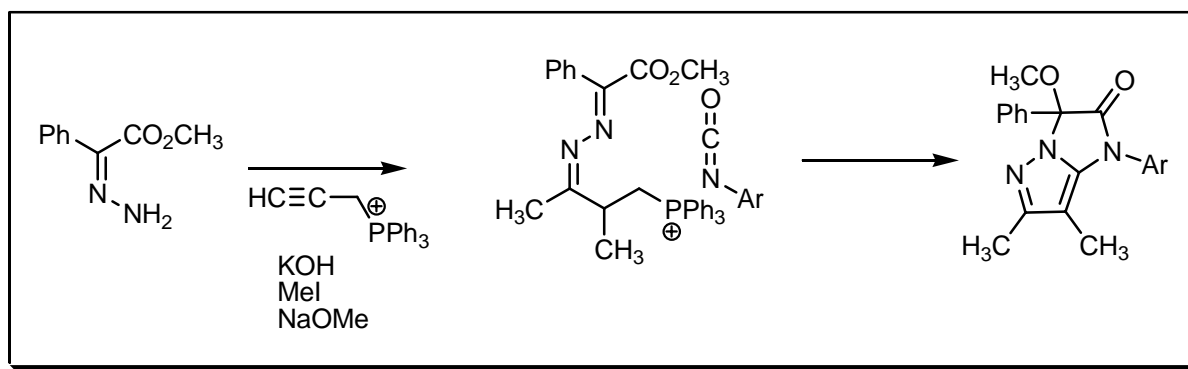
COMMENTS :

SCHWEIZER REARRANGEMENT

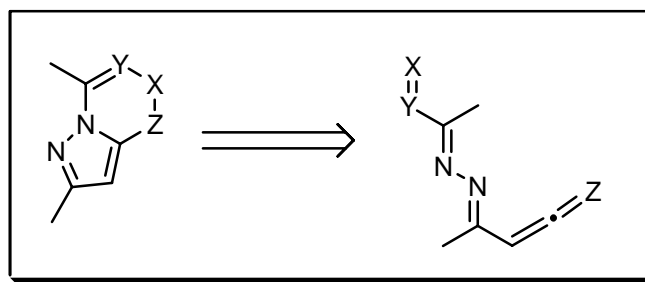
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

The thermal reaction of allenyl azines, derived from propargylphosphonium salts with ketenes, isocyanates, CS<sub>2</sub> or phthalic anhydride to form bi- and tricyclic fused pyrazolo heterocycles.

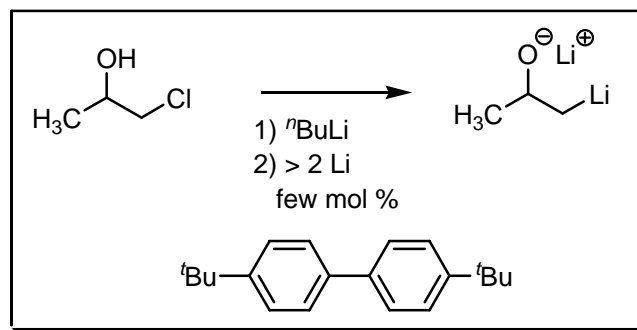
## REFERENCES :

- 1) E.E. Schweizer; S. Evans, *J. Org. Chem.*, 1978, **43**, 4328.
- 2) E.E. Schweizer; K.-J. Lee, *J. Org. Chem.*, 1984, **49**, 1959.
- 3) E.E. Schweizer; J.E. Hayes; A.L. Rheingold; X. Wei, *J. Org. Chem.*, 1987, **52**, 1810.
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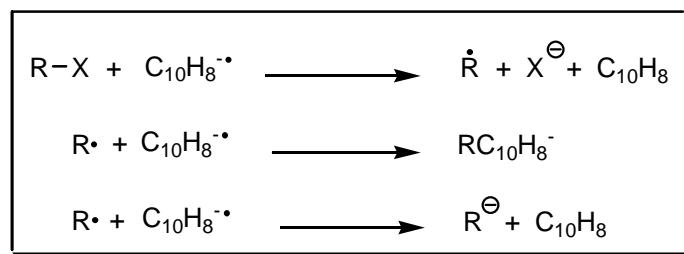
## COMMENTS :

## SCRETTAS – YUS METHOD

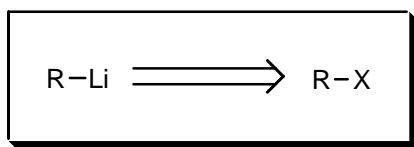
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

Organolithium reagents (RLi) are formed in the reaction of lithium dihydronaphthylide ( $\text{LiC}_{10}\text{H}_8$ ) with alkyl halides. See also **Cohen – Daniewski** process.

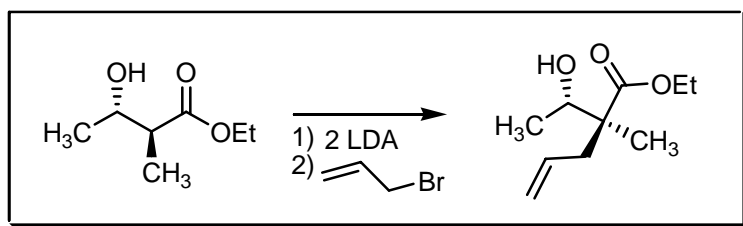
## REFERENCES :

- 1) C.G. Screttas, *J. Chem. Soc., Chem. Commun.*, 1972, 752.
- 2) J.C. Carnahan; W.D. Closson; J.R. Gauson; D.A. Juckett; K.S. Quaal, *J. Am. Chem. Soc.*, 1976, **98**, 2526.
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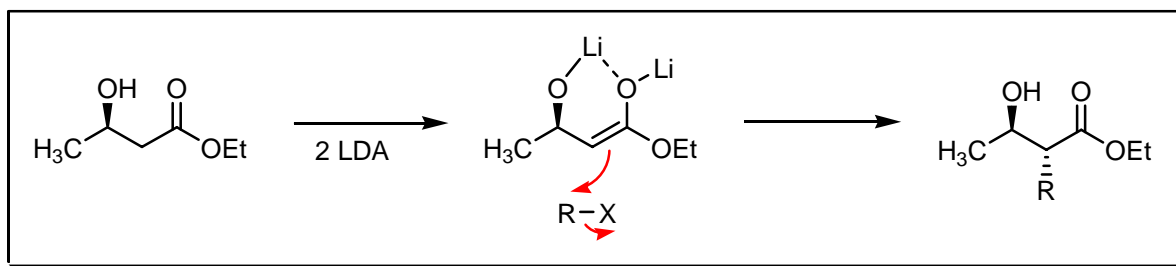
## COMMENTS :

## SEEBACH – FRÁTER ALKYLATION

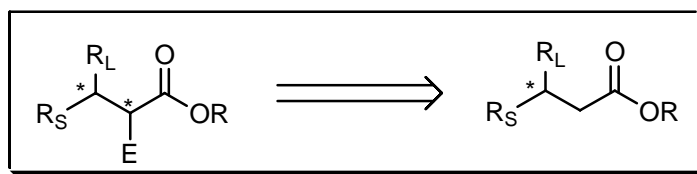
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The diastereoselective alkylation of β-hydroxycarbonyl compounds. See also **Seebach** self-regeneration.

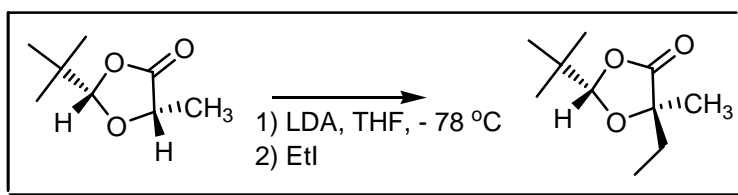
## REFERENCES :

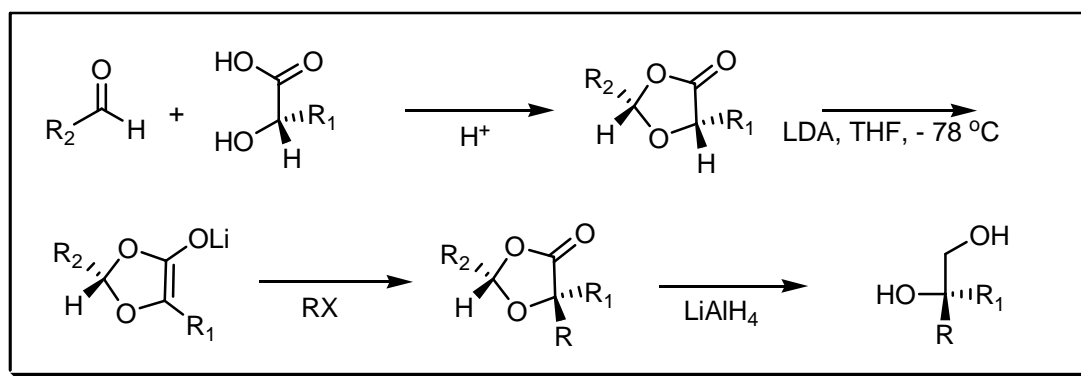
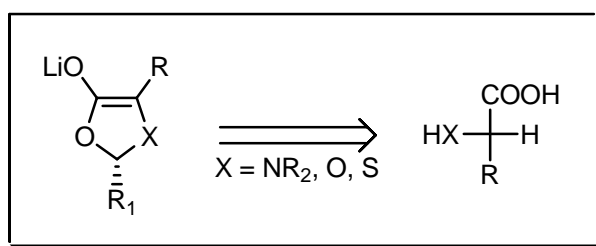
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## COMMENTS :

## SEEBACH SELF-REGENERATION

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

Dioxolanes and oxazolinones derived from pivalaldehyde and lactic acid, mandelic acid, and proline give chiral enolates after deprotonation with LDA. These enolates react in highly diastereoselective fashion with alkyl halides, aldehydes and ketones. The  $R_2$  and  $R_1$  group adopt a 1,3-*syn* relationship on the 5-membered ring. See also **Seebach – Fráter** alkylation.

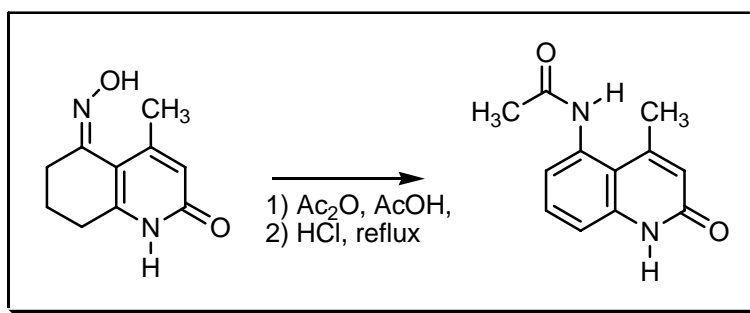
**REFERENCES :**

- 1) D. Seebach; R. Naef, *Helv. Chim. Acta*, 1981, **64**, 2704.
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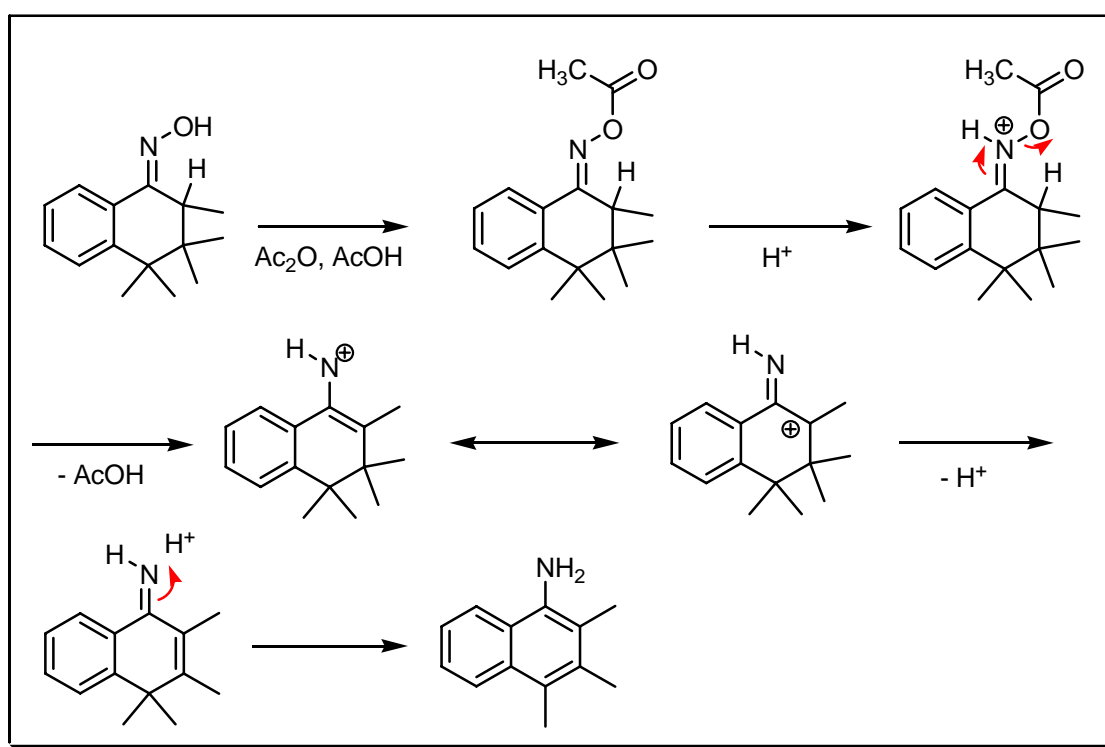
**COMMENTS :**

## SEMMLER – WOLFF – SCHROETER REACTION

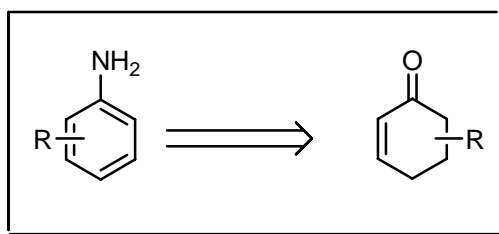
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The aromatisation of an  $\alpha,\beta$ -unsaturated cyclohexanone oximes to anilines. See also **Beckmann** reaction.

## REFERENCES :

Houben – Weyl : **E5**, 1041; **E7a**, 779; **E8a**, 283; **E16d**, 1095

Org. React. : **11**, 30

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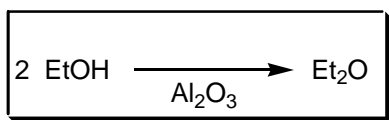
- 1) F.W. Semmler, *Ber. Dtsch. Chem. Ges.*, 1892, **25**, 3352.
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- 

## COMMENTS :

## SENDERENS DIETHYL ETHER SYNTHESIS

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### EXAMPLE :



### NOTES :

This dehydration is effected by passing ethanol vapour over alumina at about 250 °C. There are over 50 reagents known for this dehydration. See also **Ipatiew – Senderens** olefin synthesis.

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## REFERENCES :

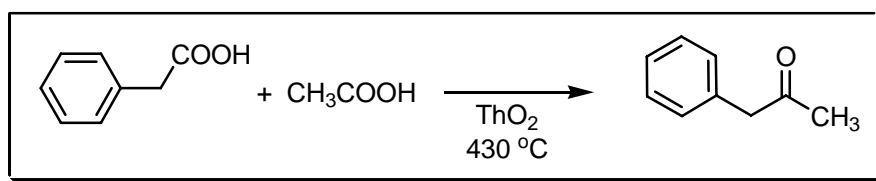
- 1) J.-B. Senderens, *Bull. Soc. Chim. Fr.*, 1909, **5**, 480.
  - 2) R.N. Pease; C.C. Yung, *J. Am. Chem. Soc.*, 1924, **46**, 390.
  - 3) R.H. Clark; W.E. Graham; A.G. Winter, *J. Am. Chem. Soc.*, 1925, **47**, 2748.
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- 

## COMMENTS :

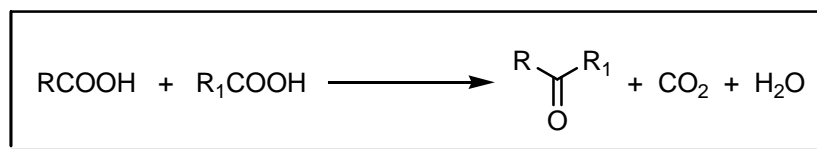
## SENDERENS KETONE SYNTHESIS

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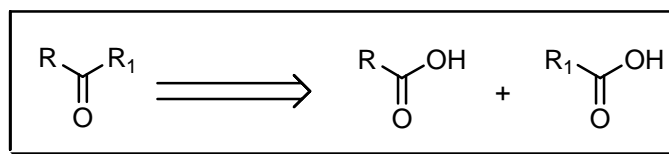
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Ketones are obtained by passing the vapours of fatty acids over catalysts, e.g. heated alumina, thorium oxide. See also **Ružička** reaction.

### REFERENCES :

**Org. Synth.** : **18**, 54

**Org. Synth. Coll. Vol.** : **2**, 389

1) J.-B. Senderens, *C.R. Séances Acad. Sci.*, 1912, **154**, 1518.

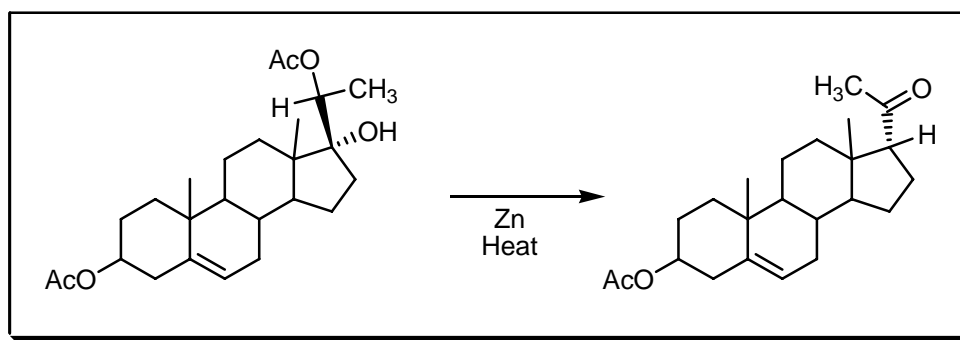
2) J.-B. Senderens, *Ann. Chim. Phys.*, 1913, **28**, 243.

### COMMENTS :

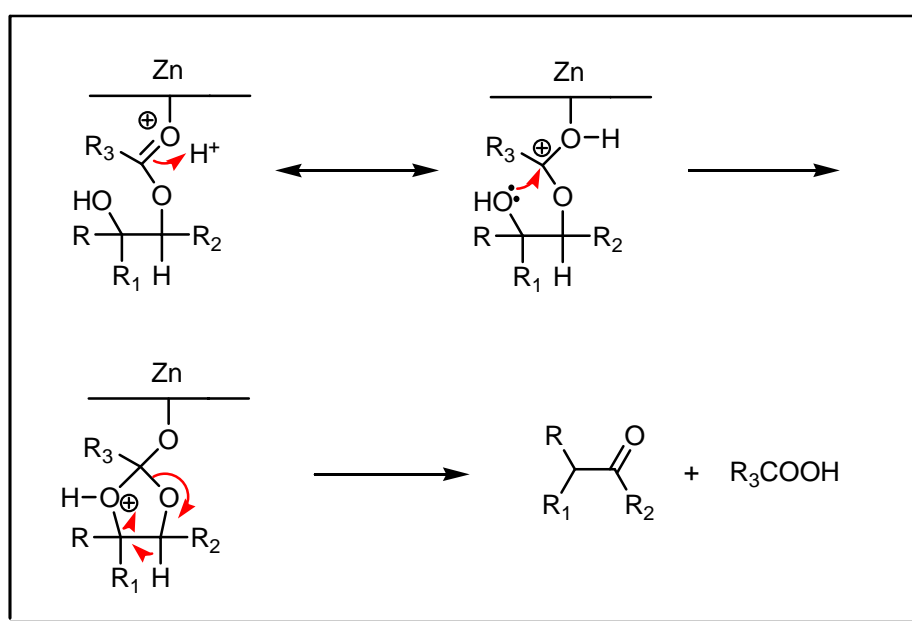


## SERINI REACTION

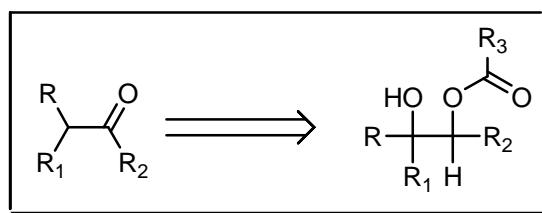
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The glycol desoxyketone configuration changes in a zinc promoted acetic acid elimination. The reaction is also applicable to other cyclic as well as open-chain alcohols. See also **Sarett** reaction.

## REFERENCES :

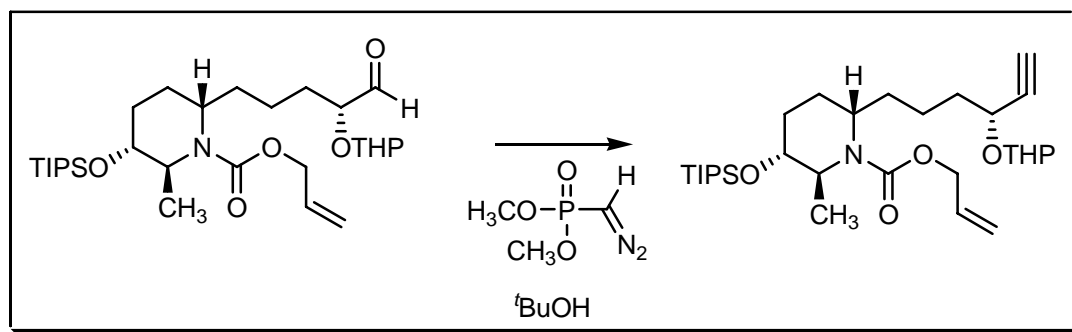
Houben – Weyl : E3, 495

- 1) K.H. Slotta; K. Neisser, *Ber. Dtsch. Chem. Ges.*, 1938, **71**, 2342.
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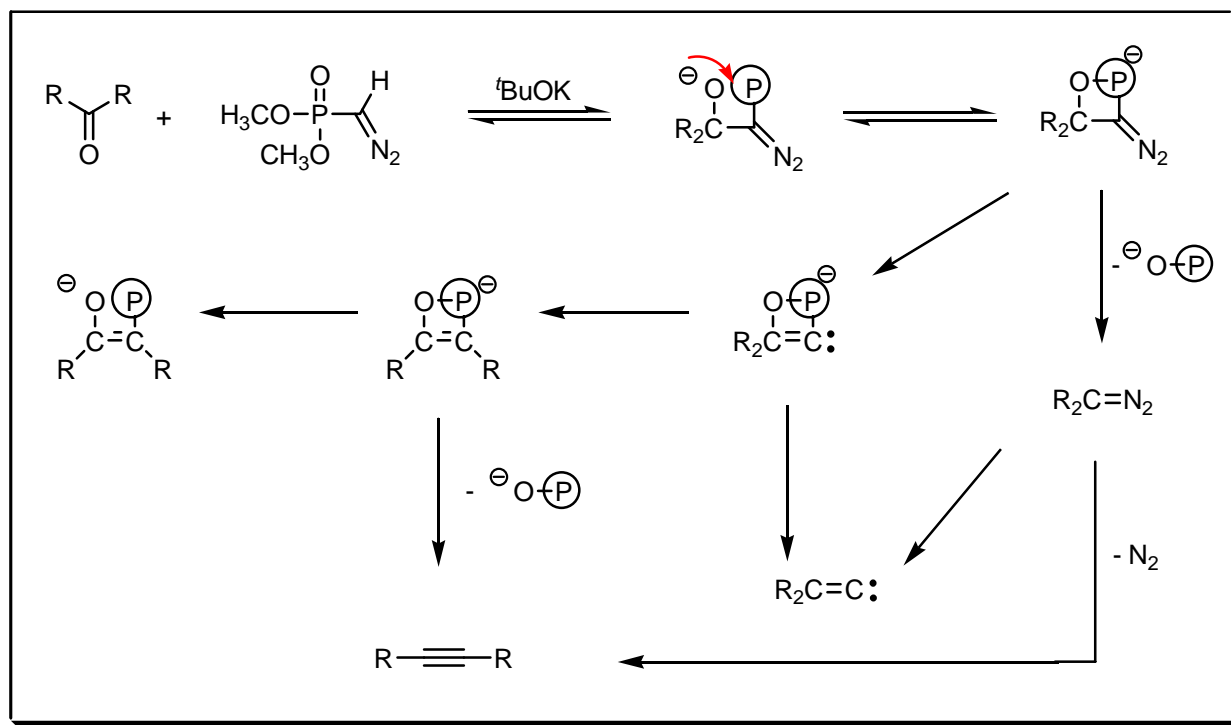
## COMMENTS :

## SEYFERTH – GILBERT HOMOLOGATION

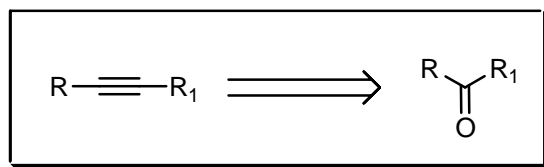
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of alkynes from aldehydes. The resulting alkynes can be easily turned into diazoethenes. The reaction is also known under the name **Seyferth – Hilbert** reaction. Milder reaction conditions have been reported in the **Ohira – Bestmann** procedure. See also **Corey – Fuchs** and **Kowalski** reactions.

## REFERENCES :

Org. Synth. : 65, 119; 74, 108

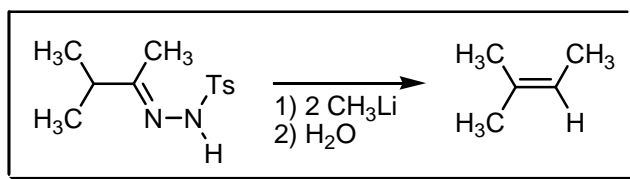
Org. Synth. Coll. Vol. : 8, 451; 9, 230

- 1) D. Seyferth; R.S. Marmor; P. Hilbert, *J. Org. Chem.*, 1971, **36**, 1379.
- 2) J.C. Gilbert; U. Weerasooriya, *J. Org. Chem.*, 1982, **47**, 1837.
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- 4) S. Ohira, *Synth. Commun.*, 1989, **19**, 561.
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- 6) J.D. Ha; D. Lee; J.K. Cha, *J. Org. Chem.*, 1997, **62**, 4550.
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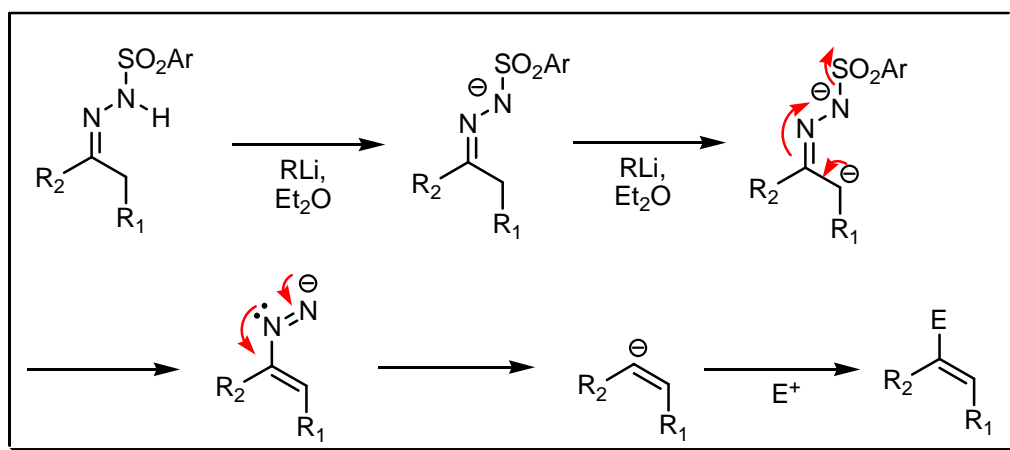
COMMENTS :

## SHAPIRO REACTION

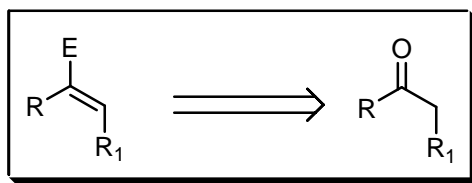
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The formation of unrearranged alkenes, generally the less substituted isomers, by treatment of ketone derived *p*-toluenesulfonylhydrazones with alkyl lithium reagents. For silicon directing effect see the review by **Adlington** and **Barrett**. When sodium in ethylene glycol is used the reaction will give the more substituted alkene and is called the **Bamford – Stevens** reaction. See also **Bamford – Stevens** reaction.

## REFERENCES :

March : 1019

Smith – March : 1334

Smith : 1455

Smith 2<sup>nd</sup> : 1201

Houben – Weyl : E14b, 606

Org. React. : 23, 3; 39, 1

Org. Synth. : 51, 66; 61, 141; 74, 101, 217

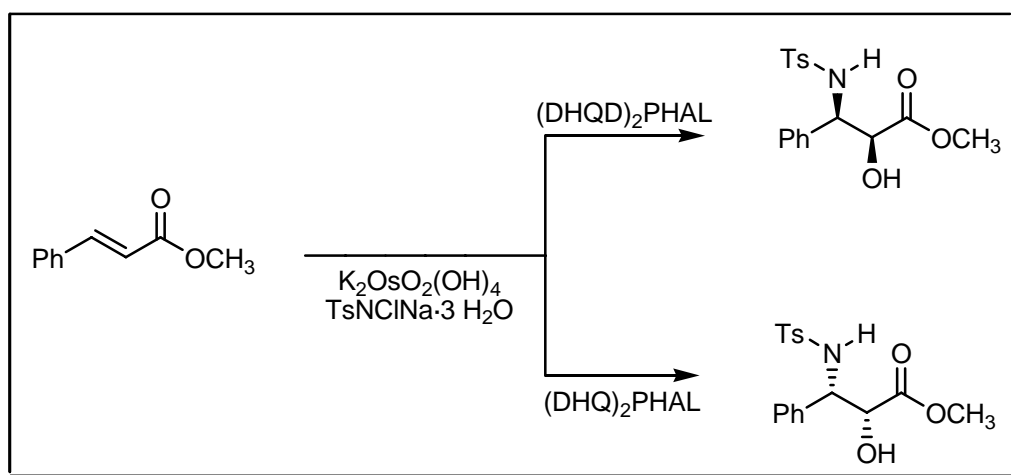
Org. Synth. Coll. Vol. : 6, 172; 7, 77; 9, 147, 281

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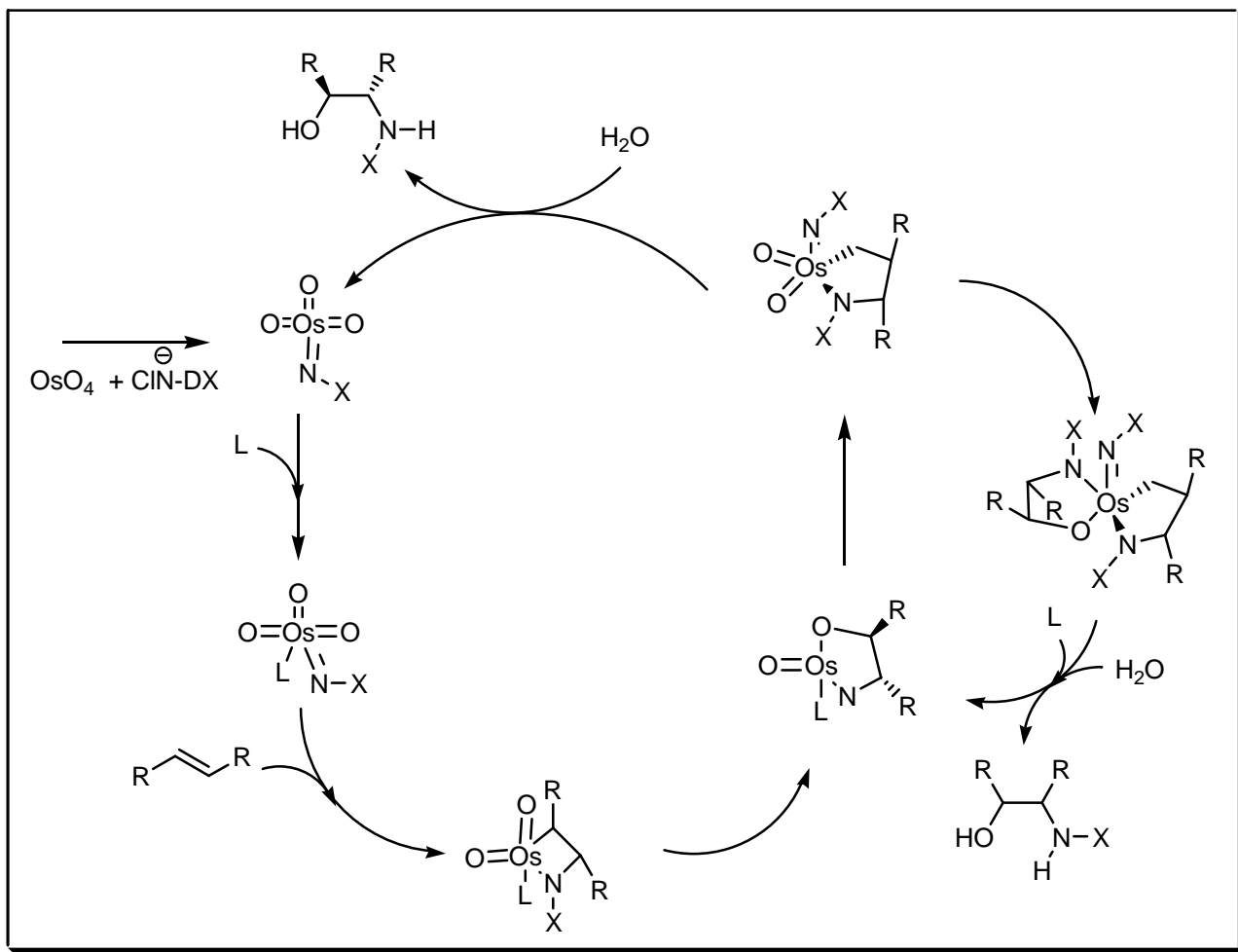
## COMMENTS :

## SHARPLESS ASYMMETRIC AMINOHYDROXYLATION (OXYAMINATION)

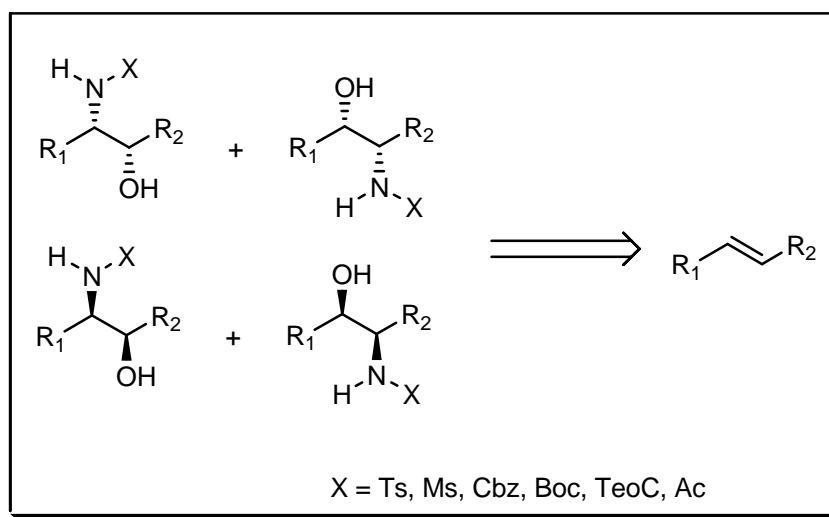
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The catalytic and asymmetric conversion of alkenes into enantiomerically enriched  $N$ -protected amino alcohols. This reaction works particularly well on cinnamate substrates. See also **Bäckvall** and **Sharpless** dihydroxylation reactions.

## REFERENCES :

Smith 2<sup>nd</sup> : 258

Org. Synth. : 61, 85, 93

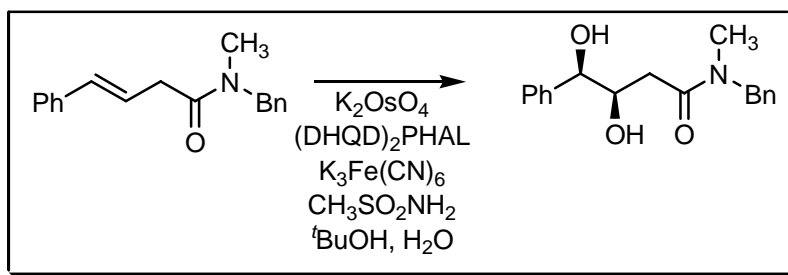
Org. Synth. Coll. Vol. : 7, 223, 375

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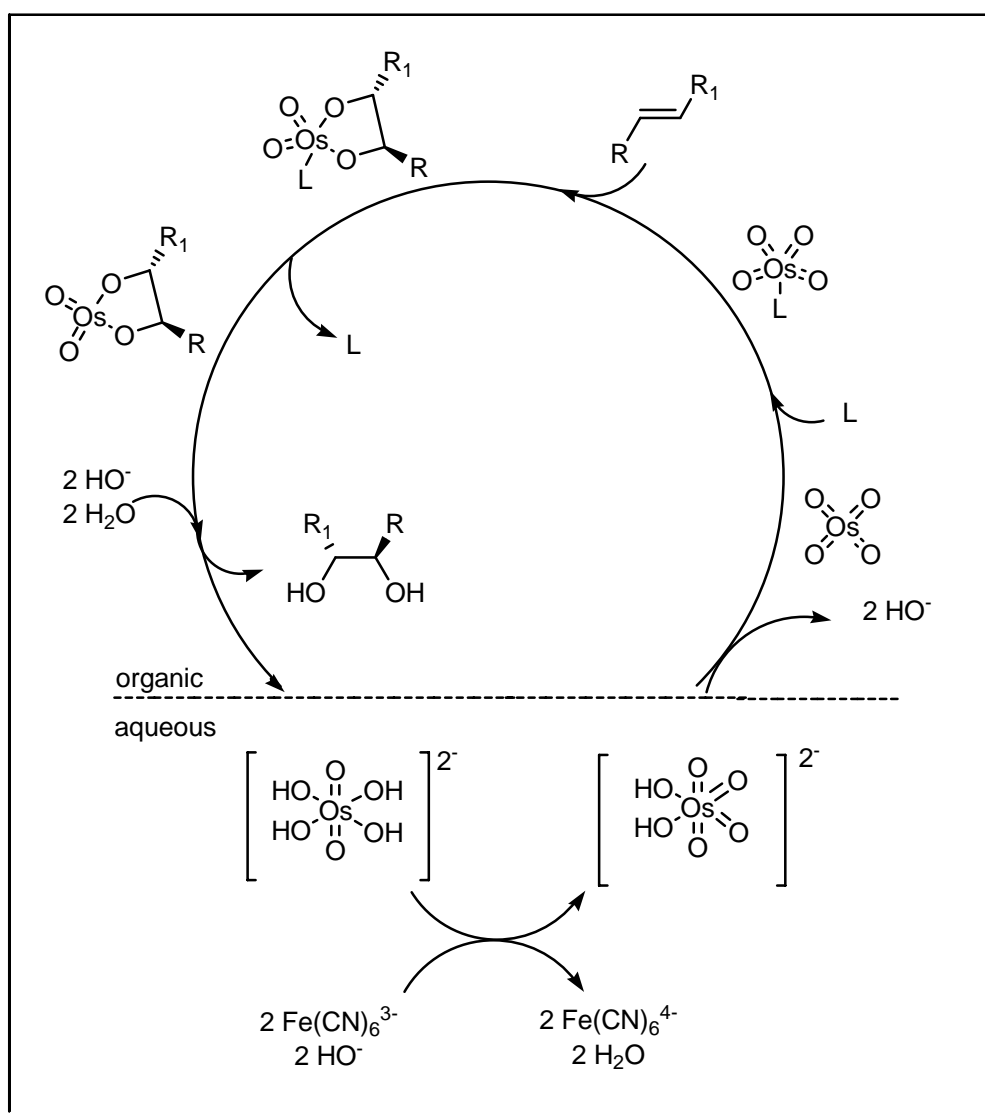
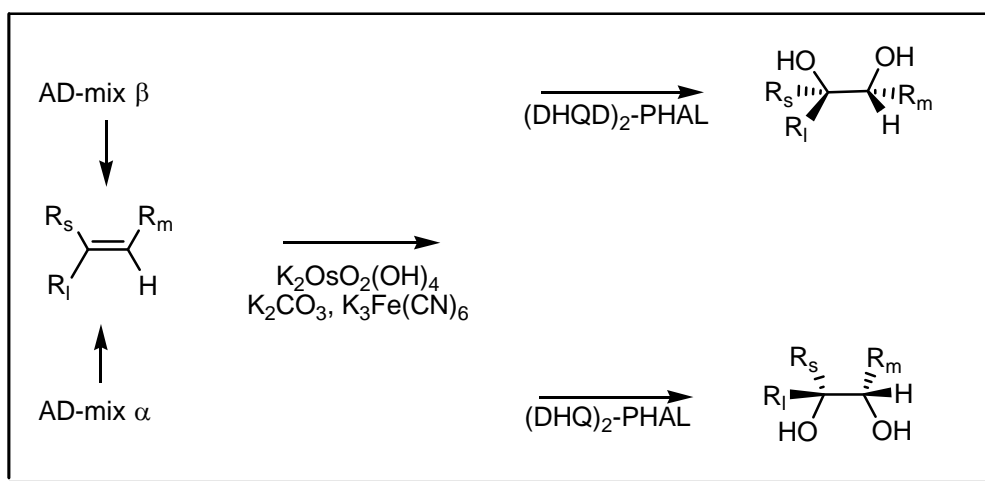
## COMMENTS :

## SHARPLESS DIHYDROXYLATION

### EXAMPLE :

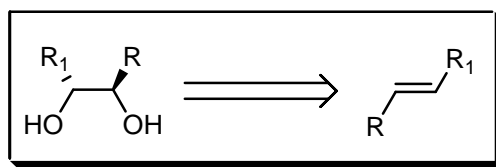


# MECHANISM :





## DISCONNECTION :



## NOTES :

The enantioselective *syn* dihydroxylation of olefins using AD-mix- $\beta$  formed from phthalazinedihydroquinidine or AD-mix- $\alpha$  formed from phthalazine-dihydroquinine and OsO<sub>4</sub>. The key success of this reaction is due to: 1) ligand accelerated catalysis by cinchona alkaloids, 2) potassium ferricyanide as co-oxidant which suppressed non-enantioselective secondary cycle, 3) MeSO<sub>2</sub>NH<sub>2</sub> effect accelerated the hydrolysis of osmium glycolate complex and allowed to perform the reaction at 0 °C boosting enantioselectivity, furthermore it also allows dihydroxylation of tetrasubstituted olefins. The basic conditions favour hydrolysis of the osmium glycolate. The *tert*-butanol water system provides a biphasic system that prevents oxidation from Os(VI) to Os(VIII). An improved version has been published by **Beller** *et al.* The active species is LOsO<sub>4</sub>. **Sharpless** and **Corey** have argued for years about the reaction being a [3+2] or [2+2] mechanism. Although Sharpless is not completely convinced, a [3+2] mechanism is now accepted. See also **Criegee** osmium tetroxide, **Milas**, **Prévost** and **Woodward** *cis*-hydroxylation reactions.

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**Smith – March** : 1050

**Smith** : 286

**Smith 2<sup>nd</sup>** : 250, 345

**Org. Synth.** : **70**, 47; **79**, 93

**Org. Synth. Coll. Vol.** : **9**, 383; **10**, 603

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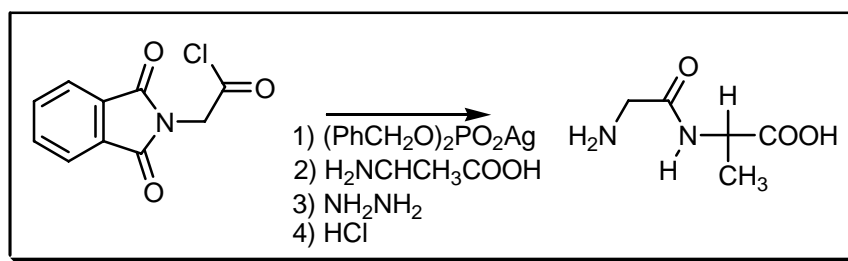
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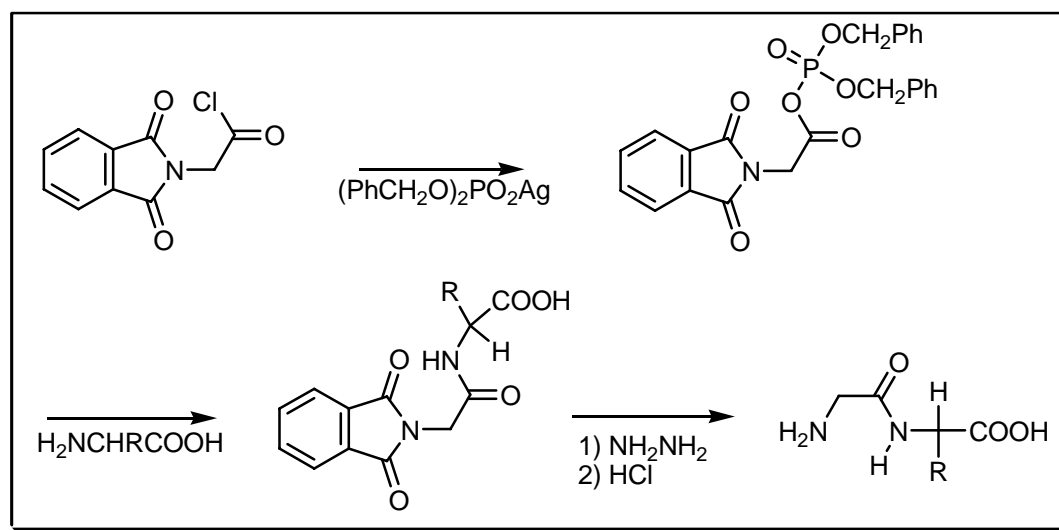
COMMENTS :

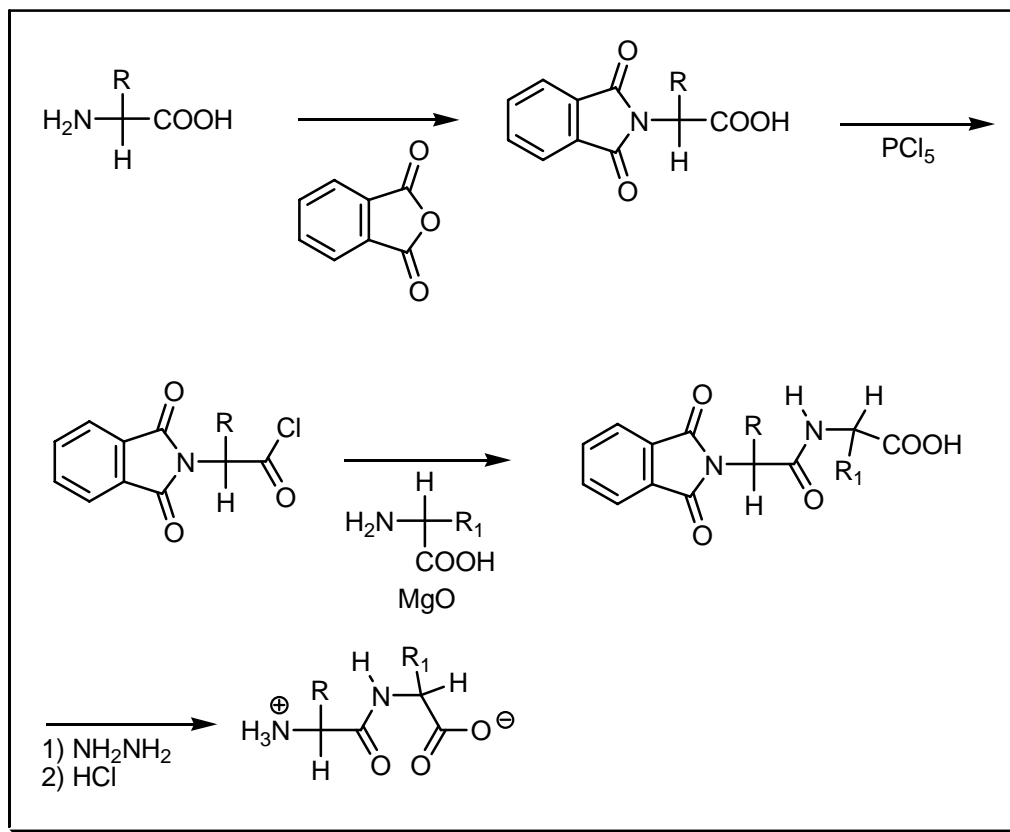
## SHEEHAN – FRANK SYNTHESIS

EXAMPLE :

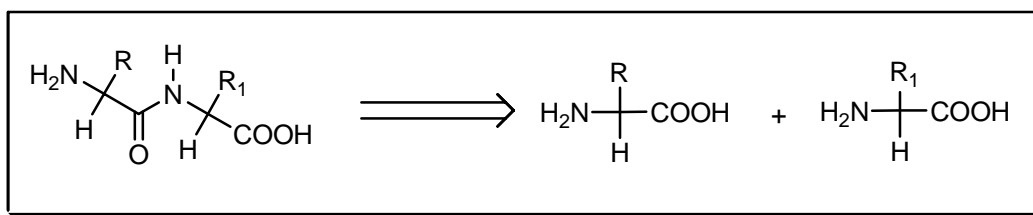


MECHANISM :





#### DISCONNECTION :



#### NOTES :

1. Phthalylglycyl chloride reacts with silver dibenzylphosphate to yield phthalylglycyl dibenzylphosphate. This treated with an amino acid to form a phthalyl peptide which on treatment with hydrazine and subsequently with hydrochloric acid yields a peptide.
2. An amino acid is converted into the phthalimido acid chloride which is condensed with another amino acid molecule in the presence of magnesium oxide. These phthalimido peptides are then converted into the peptide by treatment with hydrazine, followed by hydrochloric acid. See also **Bergmann – Zervas** carbobenzoxy method, **Fischer** peptide, **Gabriel** and **Ing – Manske** reactions.

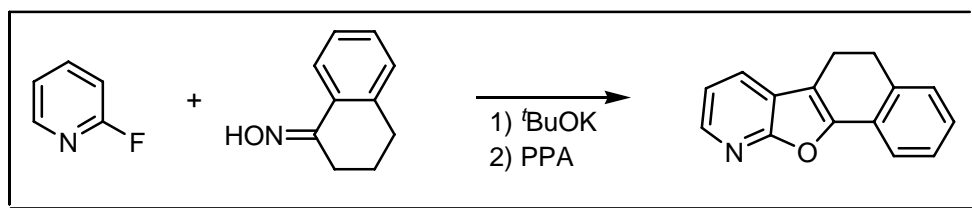
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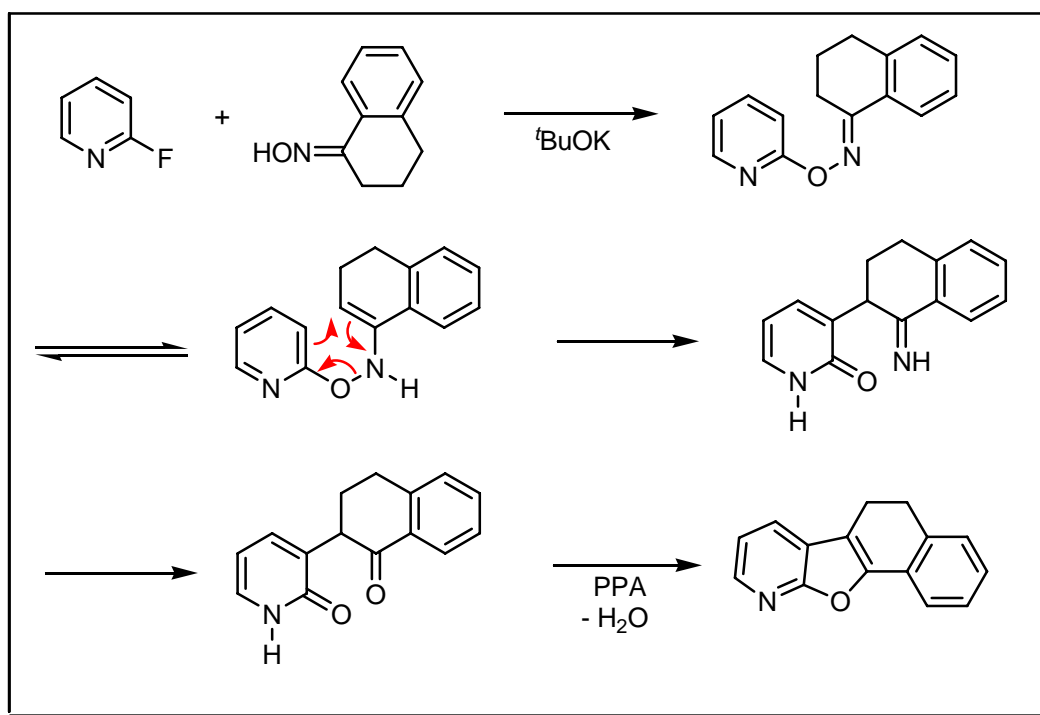
COMMENTS :

## SHERADSKY REARRANGEMENT

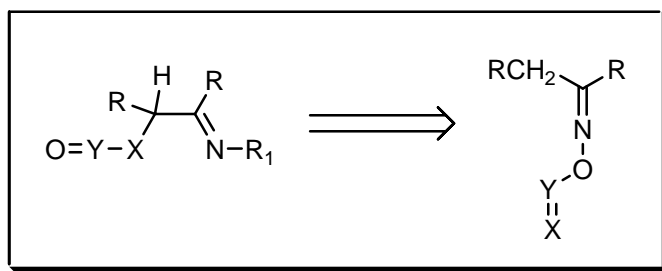
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The rearrangement of O-arylated oximes *via* a hetero-Cope rearrangement using 2-fluoropyridine. Hydroxylamines can undergo a similar acid-catalysed rearrangement (e.g.  $\alpha$ -acetoxyketones derived from ketoxime derivatives). See also Cope rearrangement.

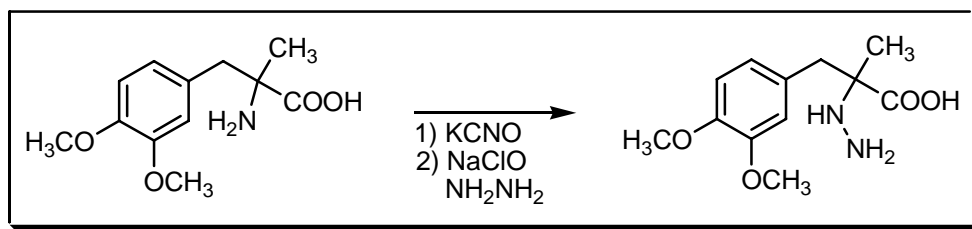
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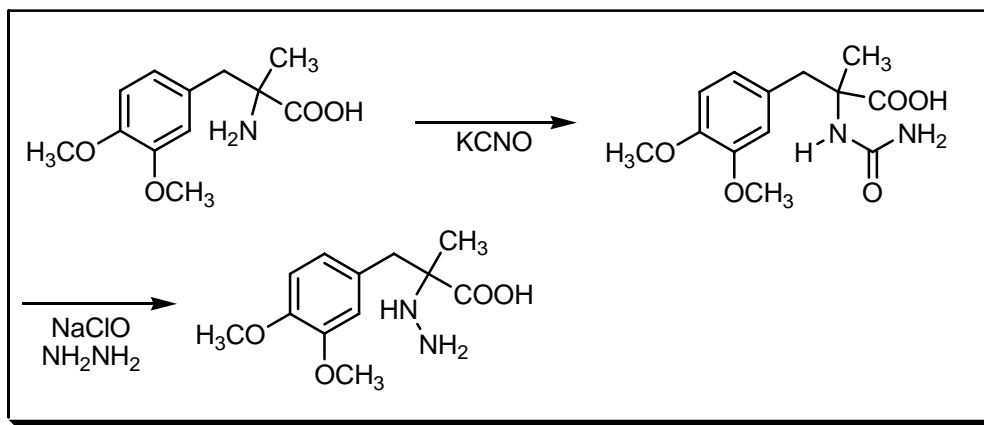
## COMMENTS :

## SHESTAKOV HYDRAZINE SYNTHESIS

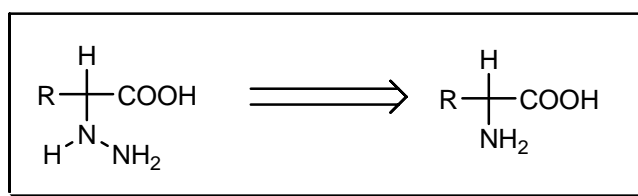
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of  $\alpha$ -hydrazino acids from  $\alpha$ -amino acids *via* ureas using  $\text{KCNO}$  and  $\text{NaOCl}$  or  $\text{KOCl}$ .

## REFERENCES :

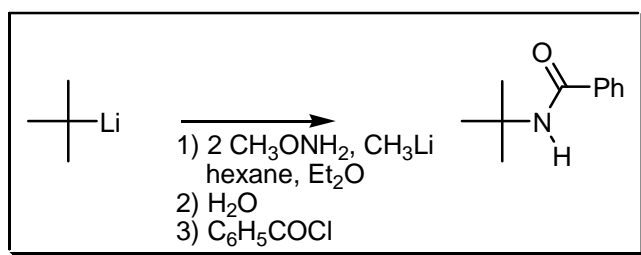
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## COMMENTS :

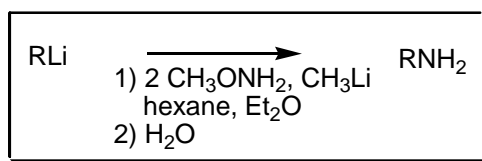
## SHEVERDINA – KOCHESHKOV AMINATION

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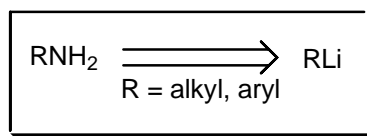
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

**Beak et al.** did modify this reaction to the direct stoichiometric amination of organo lithiums in high yields by methoxyamine and methyl lithium in a mixture of hexane and diethyl ether.

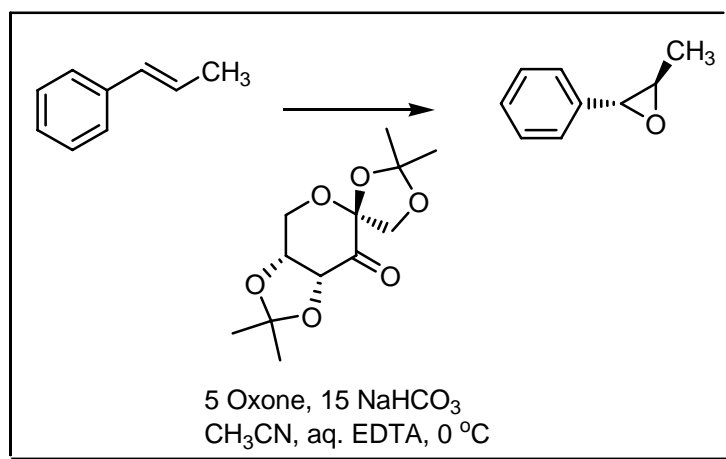
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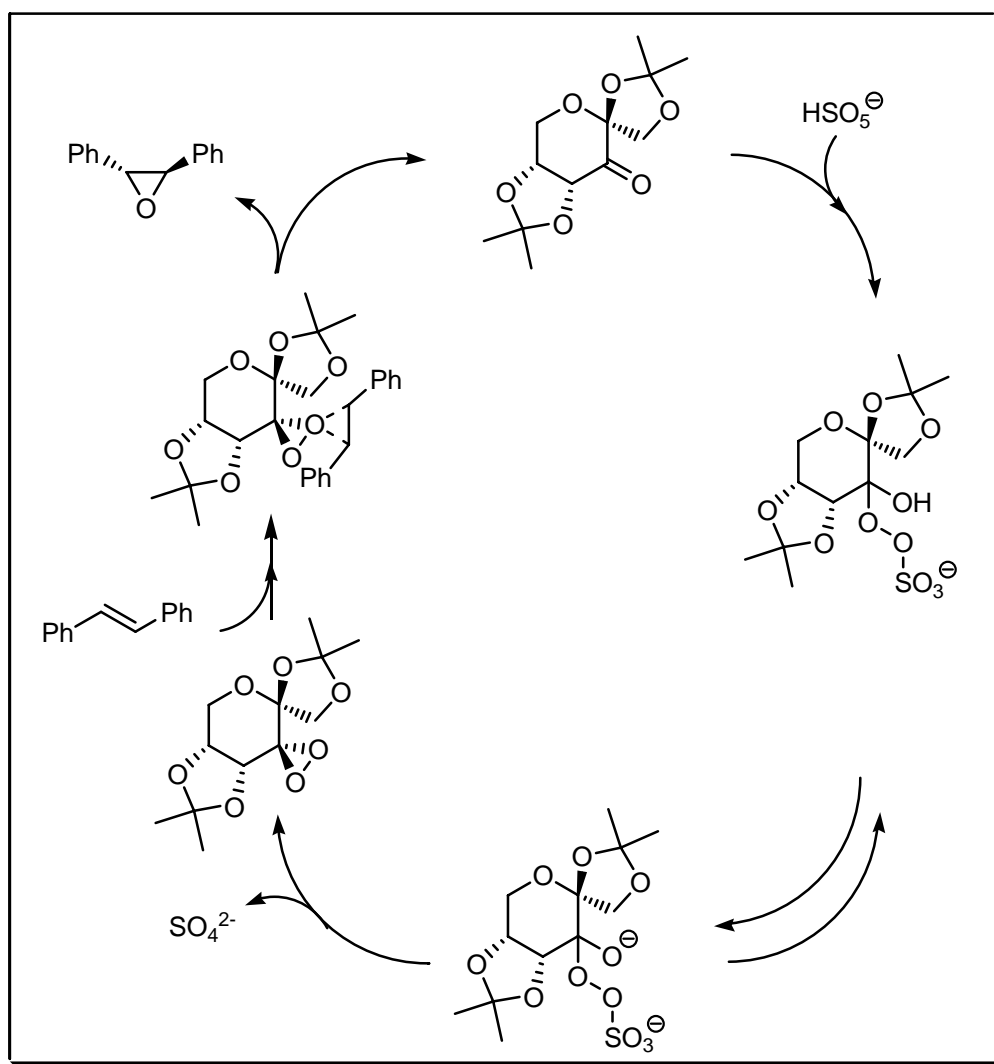
### COMMENTS :

## SHI EPOXIDATION

### EXAMPLE :

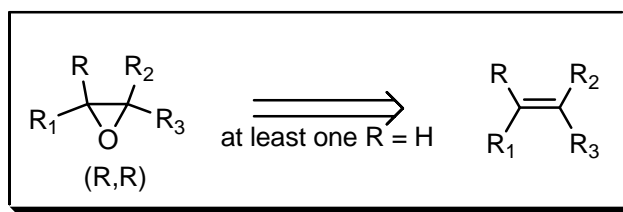


### MECHANISM :





## DISCONNECTION :



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## NOTES :

The asymmetric epoxidation of alkenes bearing a wide range of functional groups using a chiral dioxirane readily prepared from Oxone and *D*-fructose or *D*-glucose. The glucose derived nitrogen analog is also effective for *cis* olefins and terminal olefins. See also **Buchner – Curtius – Schlotterbeck**, **Corey – Chaykovsky**, **Jacobsen – Katsuki**, **Juliá – Colonna**, **Katsuki – Sharpless**, **Mukaiyama – Yamada**, **Prileschajew** and **Weitz – Scheffer** reactions.

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## REFERENCES :

**Org. Synth.** : **80**, 1, 9

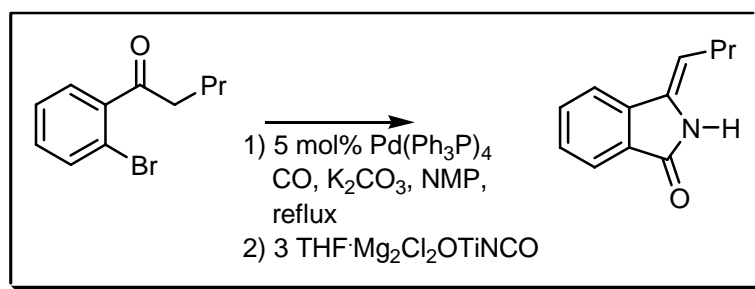
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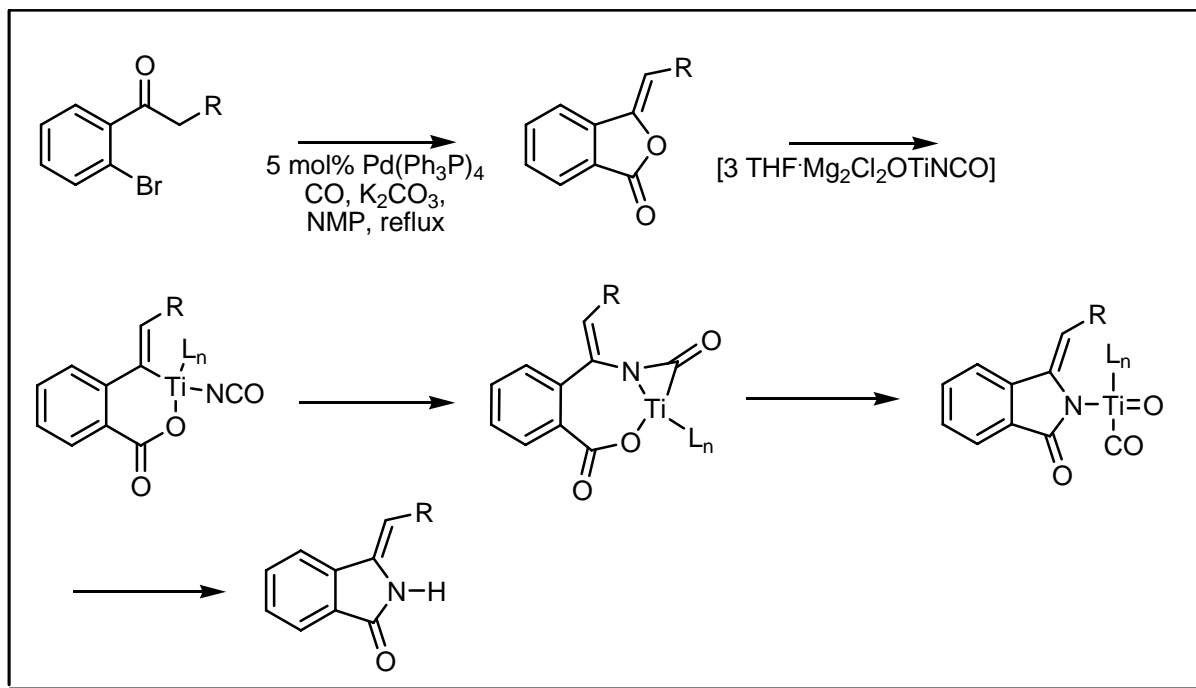
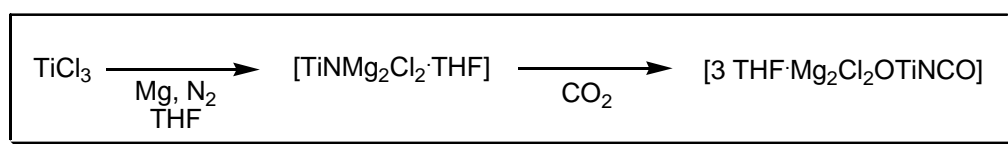
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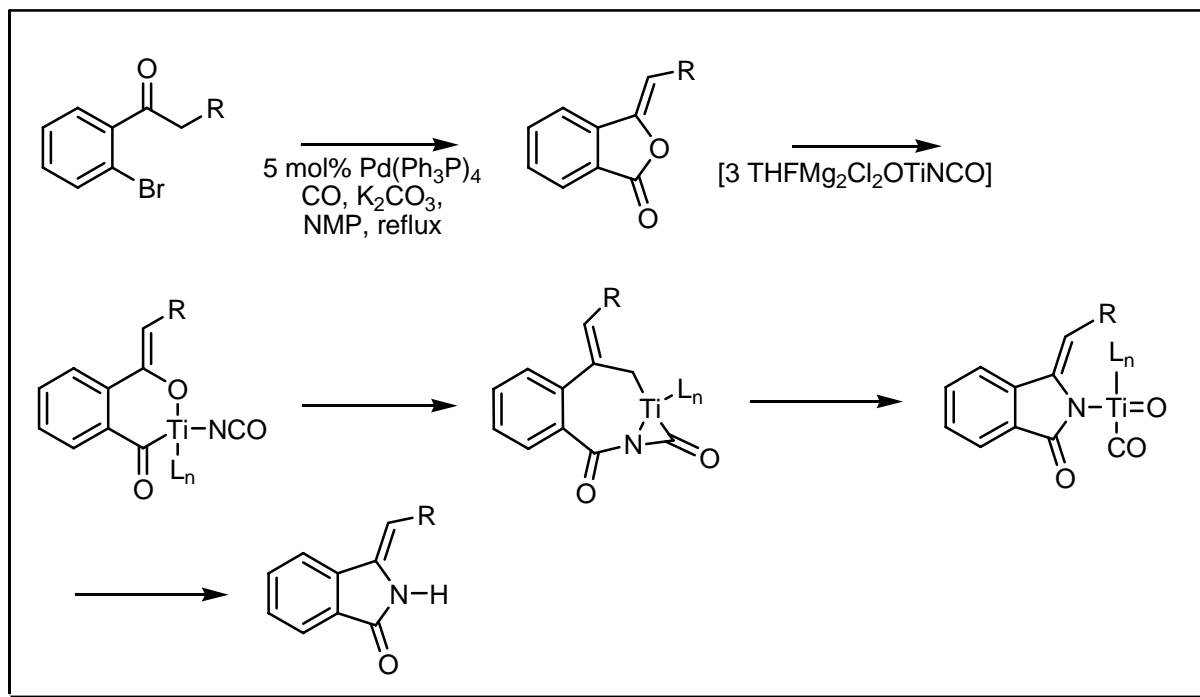
## SHIBASAKI CYCLISATION

### EXAMPLE :

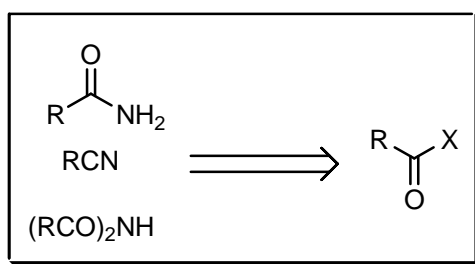


### MECHANISM :





#### DISCONNECTION :



#### NOTES :

The incorporation of molecular nitrogen into amides and imides using titanium-nitrogen complexes.

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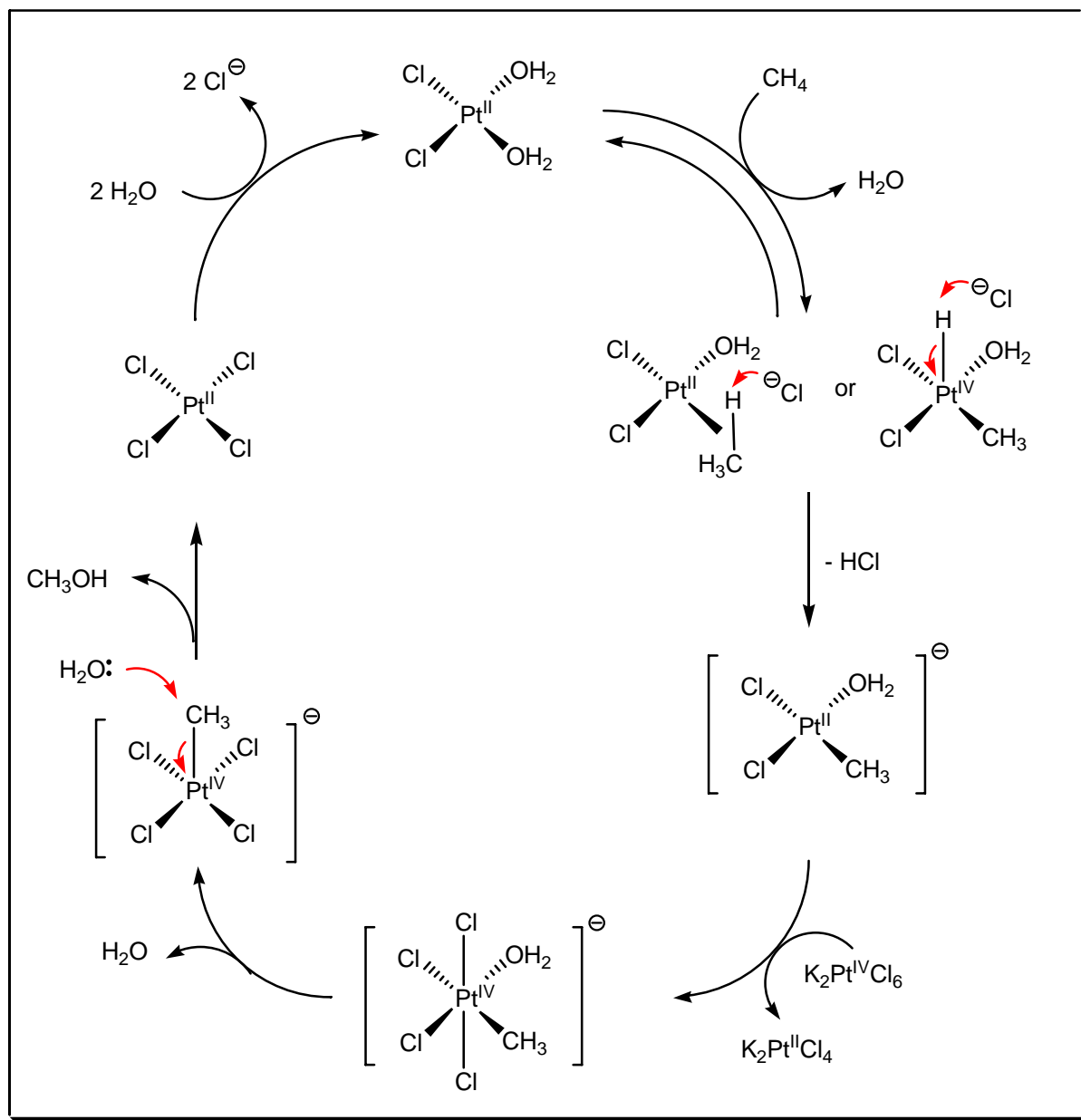
#### COMMENTS :

# SHILOV REACTION

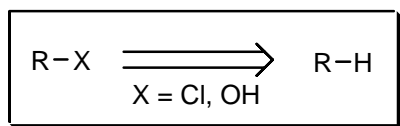
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

The platinum-catalysed alkane oxidation consisting of activation of the alkane by platinum(II), two-electron oxidation to create a platinum(IV) species, followed by reductive elimination. Several mechanistic studies on each individual step has been reported in the literature.

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## REFERENCES :

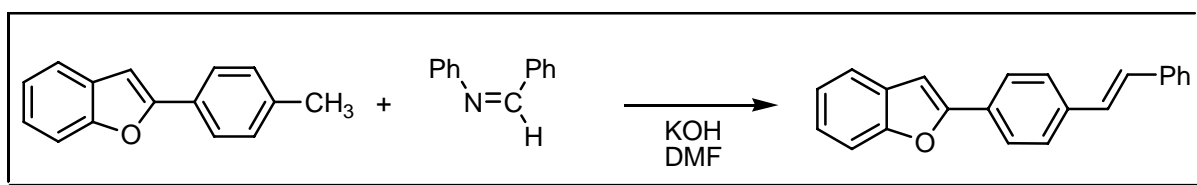
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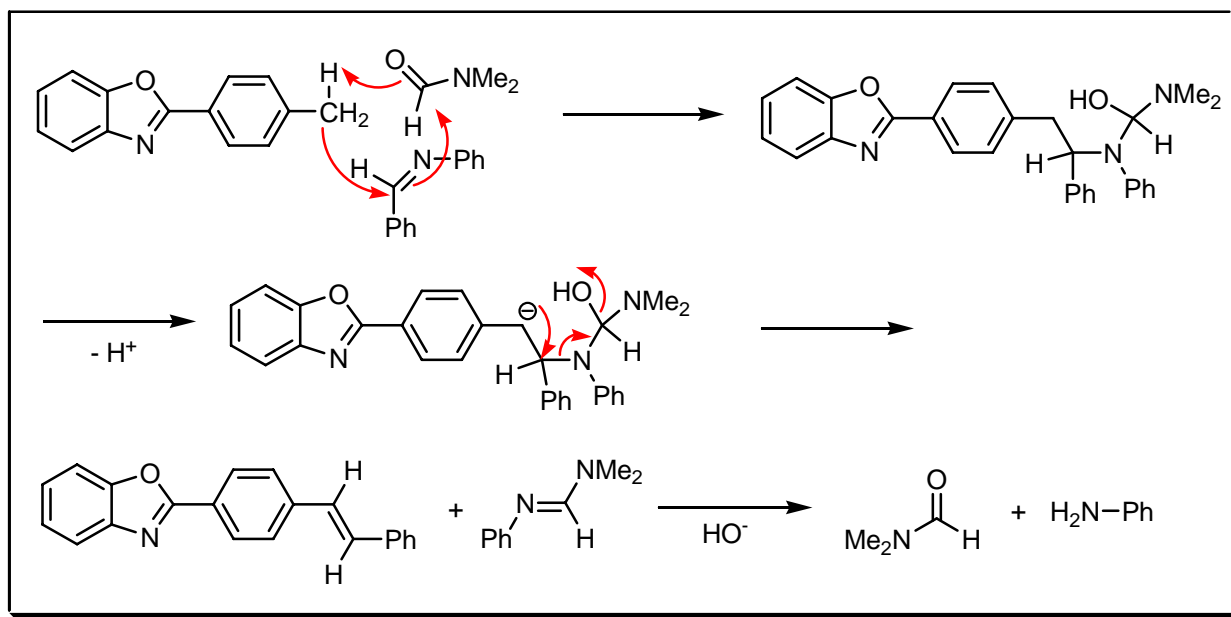
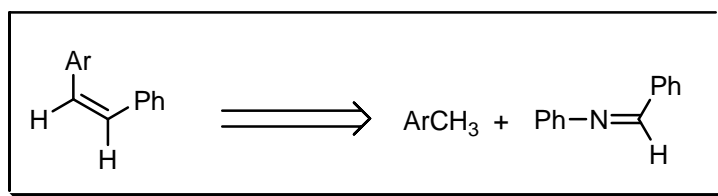
## COMMENTS :

## SIEGRIST STILBENE SYNTHESIS

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### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

The synthesis of stilbenes by base-catalysed condensation of reactive toluenes or naphthalenes with benzalanilines.

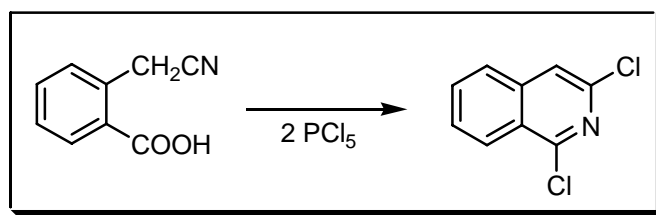
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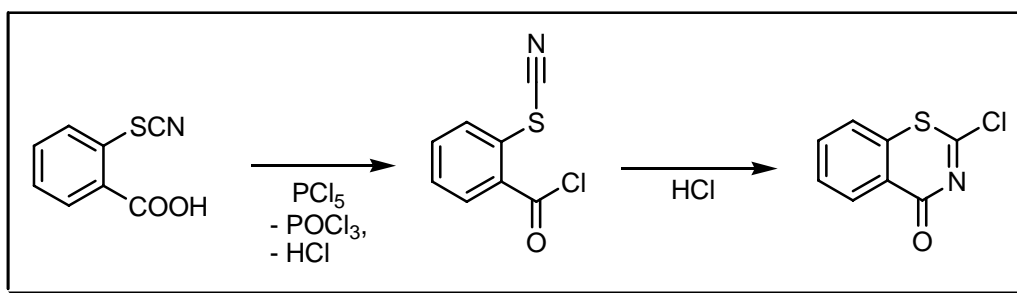
**COMMENTS :**

## SIMCHEN SYNTHESIS

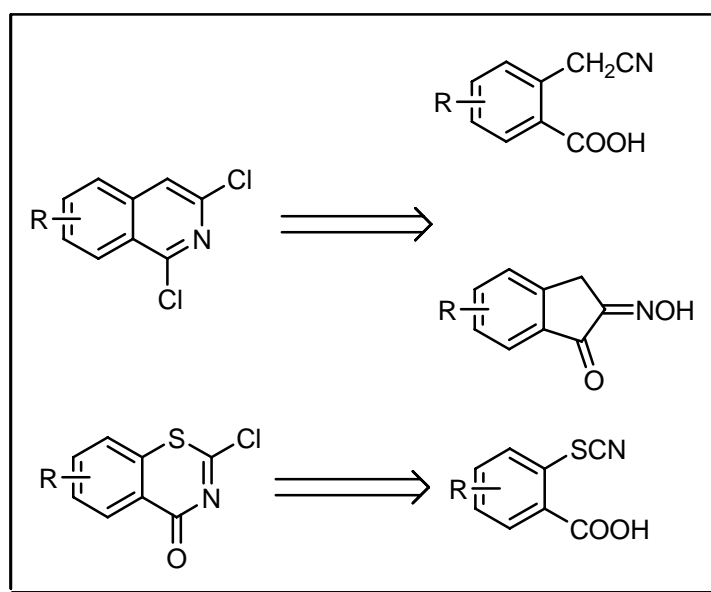
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The synthesis of isoquinolines and its derivatives starting from *ortho*-cyanomethylbenzoic acid compounds using phosphorous pentachloride, hydrogen bromide or iodide. See also **Bamberger – Goldschmidt**, **Bischler – Napieralski**, **Bobbit**, **Bruckner**, **Larock** indole, **Pictet – Gams**, **Pictet – Sprengler**, **Pomeranz – Fritsch** and **Schlitter – Müller** ring-closure reactions.

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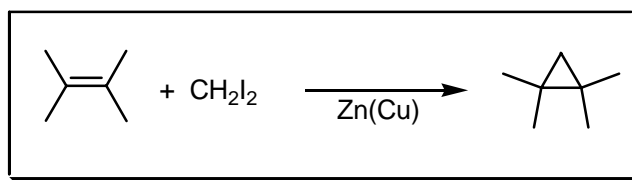
## COMMENTS :

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## SIMMONS – SMITH REACTION

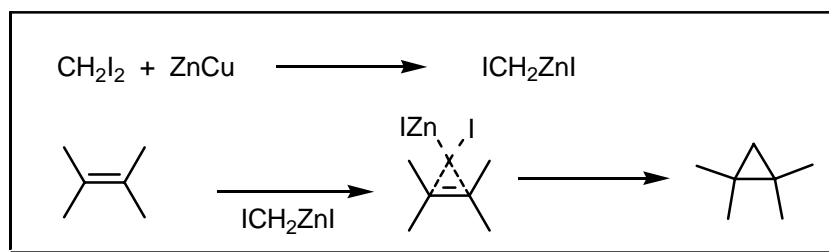
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### EXAMPLE :



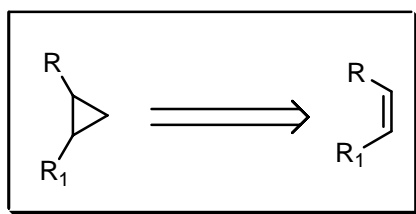
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### MECHANISM :



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### DISCONNECTION :



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### NOTES :

Steric effects play an important role. The cyclopropanation generally takes place from the less-hindered side. A neighbouring hydroxyl group speeds up the reaction and places the cyclopropane ring *syn* to the hydroxyl group. A one-step mechanism has been proposed. The intermediate can be isolated. Also enantioselective **Simmons – Smith** reaction are known. Sometimes even low-valent samarium can be used. The **Furugawa** modification uses diethylzinc



instead of Zn(Cu) couple. See also **Charette**, **Freund**, **Gustavson**, **Hass** cyclopropane, **Ipatiew**, **Kishner**, **Mousseron – Fraisse – McCoy** and **Nerdel** reactions.

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#### REFERENCES :

**March** : 870

**Smith – March** : 1088

**Smith** : 1471

**Smith 2<sup>nd</sup>** : 1207, 1212

**Houben – Weyl** : **E19b**, 195

**Org. React.** : **20**, 1; **58**, 1

**Org. Synth.** : **41**, 72; **59**, 113; **67**, 176; **76**, 86

**Org. Synth. Coll. Vol.** : **5**, 855; **6**, 327; **8**, 321; **10**, 2341

**Science of Synthesis** : **9**, 305

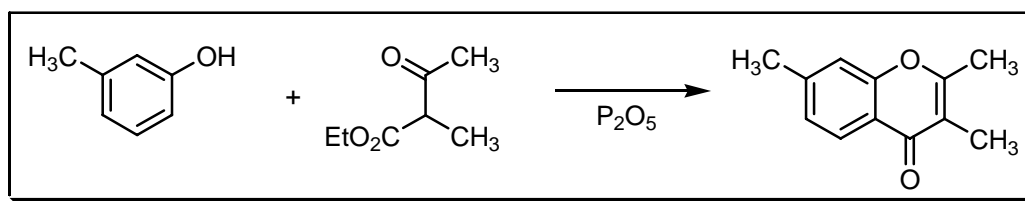
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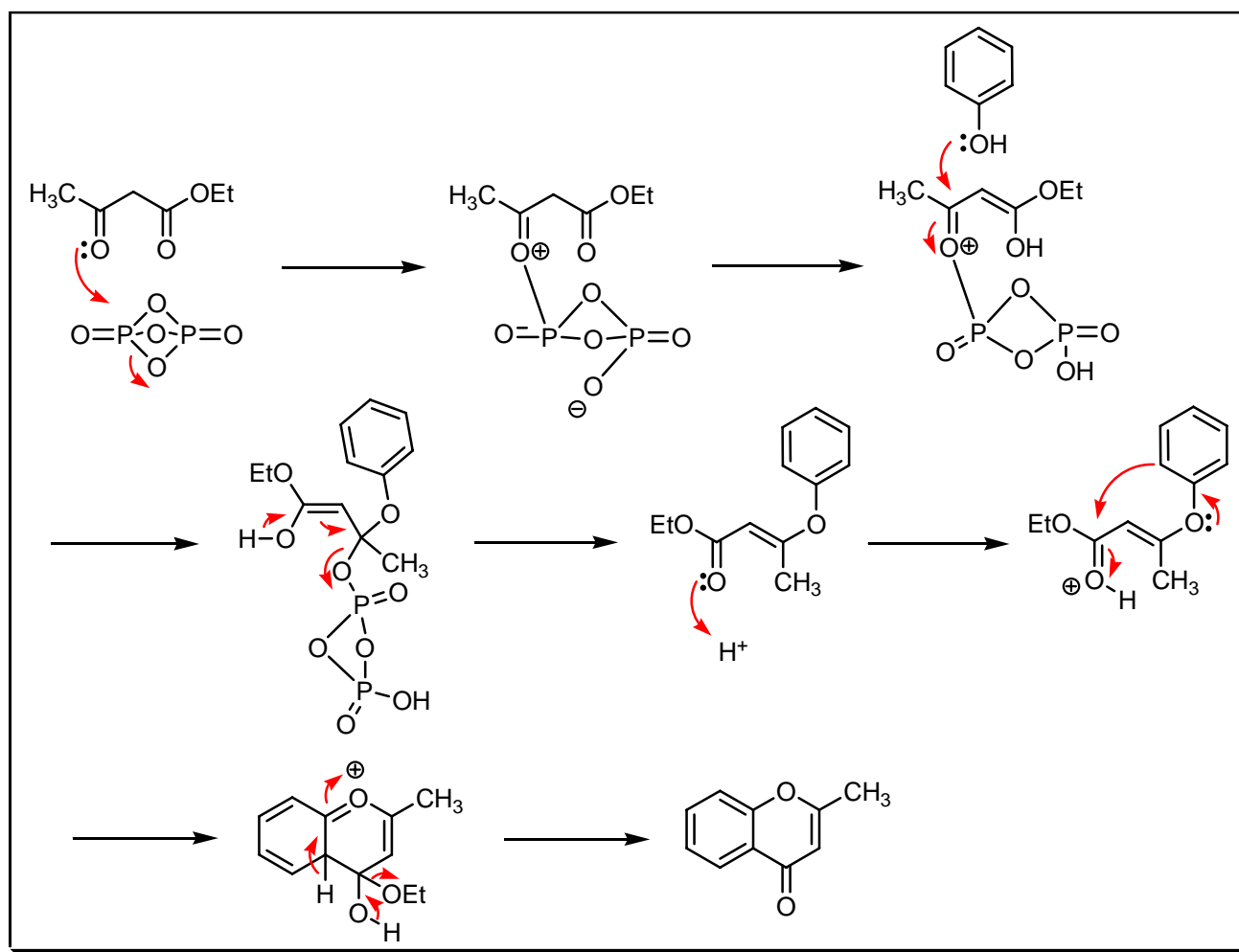
#### COMMENTS :

## SIMONIS CHROMONE CYCLISATION

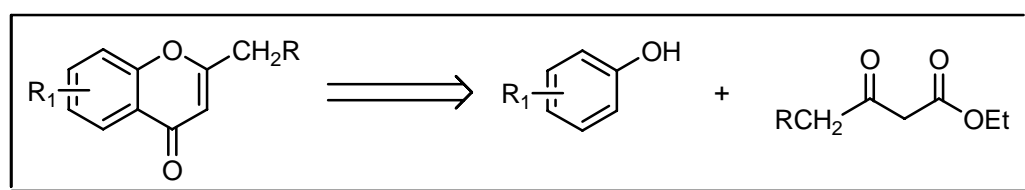
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The benzopyrone synthesis from phenols and  $\beta$ -ketoesters using phosphorous pentoxide. Coumarins may also be formed. See also **Anschütz** hydroxycoumarin, **Bargellini**, **Boyd – Robinson**, **Knoevenagel** coumarin, **Pauly – Lockemann**, **von Pechmann – Duisberg** and **Perkin** coumarin reactions.

## REFERENCES :

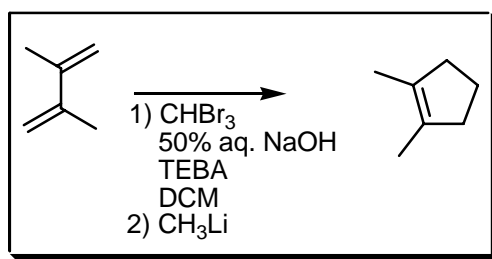
Org. React. : 7, 2

- 1) E. Petschek; H. Simonis, *Ber. Dtsch. Chem. Ges.*, 1913, **46**, 2014.
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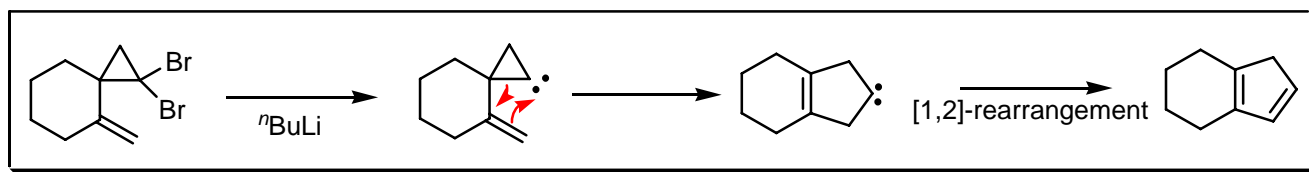
## COMMENTS :

## SKATTEBØL DIHALOCYCLOPROPANE REARRANGEMENT

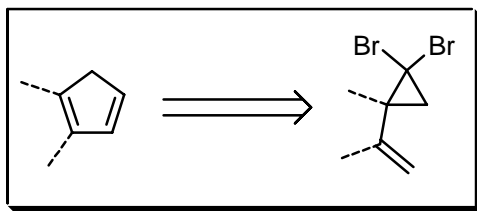
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

This is the rearrangement of *gem*-dihalocyclopropanes to allenes or of vinyl dihalocyclopropanes to cyclopentadienes and fulvenes by alkyl lithium reagents. See also **von Doering – la Flamme – Moore** allene synthesis.

## REFERENCES :

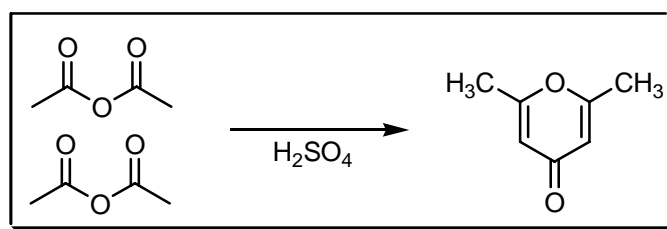
Houben – Weyl : **E19b**, 403, 449, 500, 607

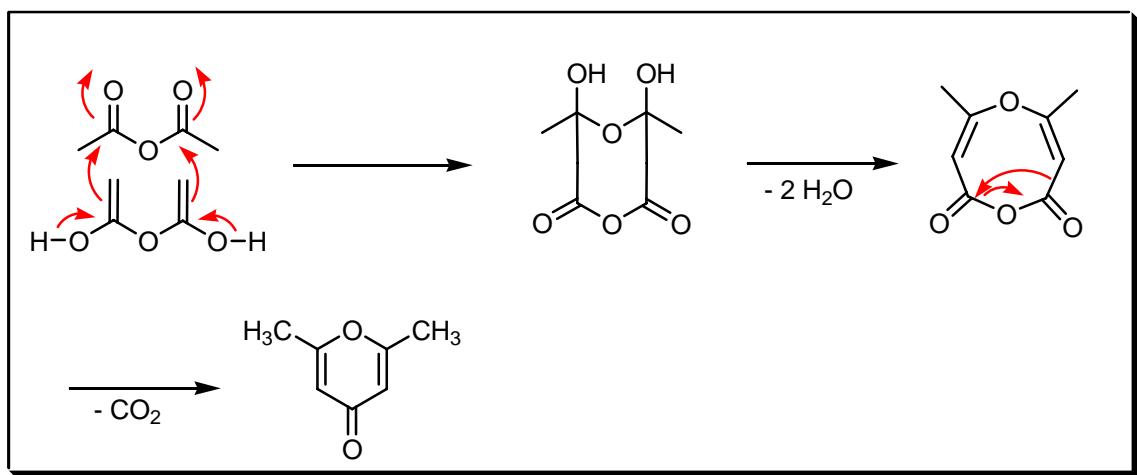
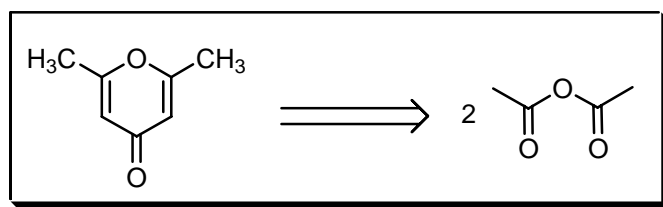
- 1) L. Skattebøl, *J. Org. Chem.*, 1966, **31**, 2789.
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## COMMENTS :

## SKRAUP – PRIGLINGER SYNTHESIS

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

Dimethylpyrone is obtained by the action of sulfuric acid on acetic anhydride. The mechanism involves a double dehydration followed by decarboxylation to afford dimethylpyrone.

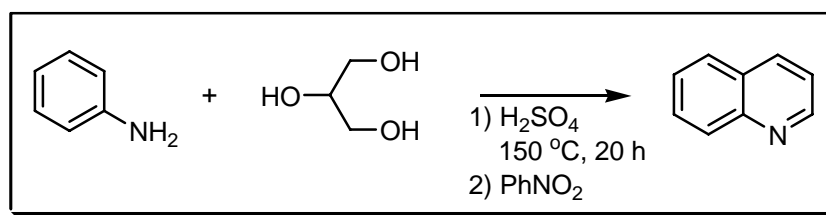
**REFERENCES :**

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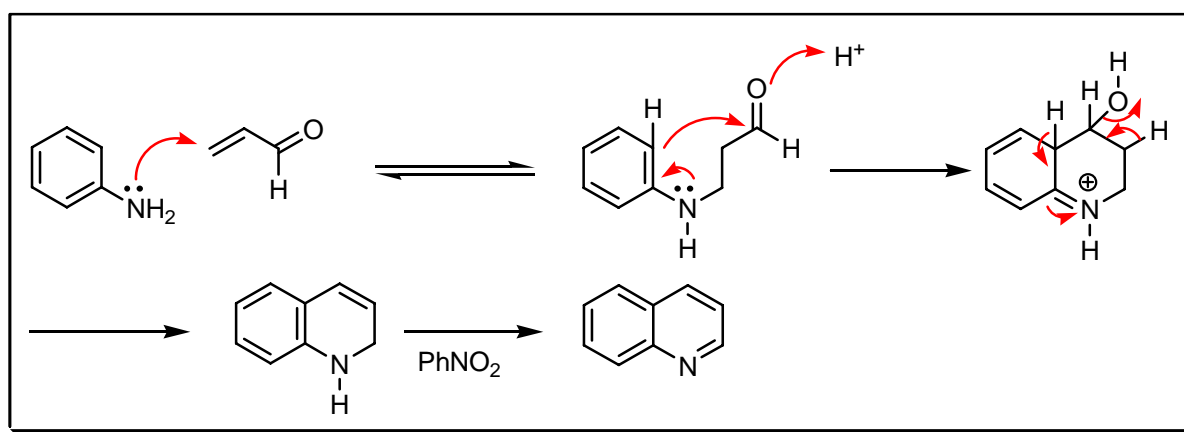
**COMMENTS :**

# SKRAUP QUINOLINE SYNTHESIS

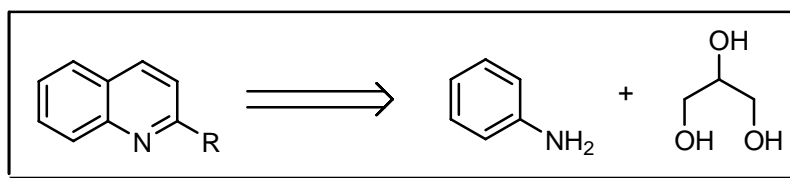
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

This synthesis of quinolines involves the interaction of a primary aromatic amine with at least one position *ortho* to the amino group unsubstituted, glycerol, sulfuric acid or a sulfonic acid, and an oxidising agent, *e.g.* nitrobenzene, or the nitro compound corresponding to the amine, or arsenic pentoxide. A moderator such as ferrous sulfate, boric acid, or water may be added. See also **Allan – Loudon**, **von Baeyer – Drewson** quinoline, **Camps, Combes** quinoline, **Conrad – Limpach**, **Doebner** quinoline, **Doebner – von Miller**, **Foulds – Robinson**, **Friedländer**, **Knorr** quinoline, **Meth-Cohn**, **von Niementowski** quinoline, **Pfitzinger – Borsche** and **Riehm** quinoline reactions.

## REFERENCES :

Smith : 1338

Smith 2<sup>nd</sup> : 1100

Houben – Weyl : E7a, 362; E7b, 684; E8b, 849

Org. React. : 7, 59; 28, 37

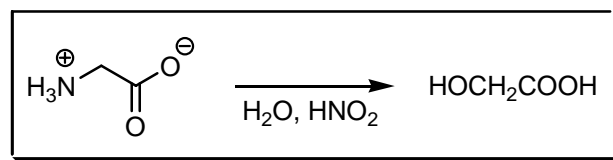
Org. Synth. : 2, 79; 27, 48

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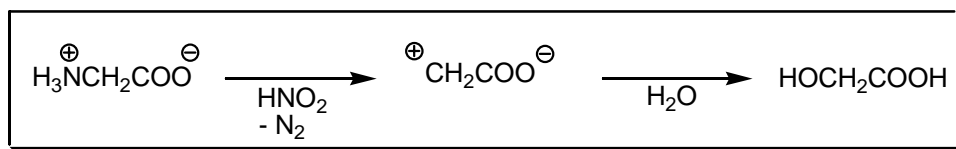
**COMMENTS :**

van SLYKE DETERMINATION

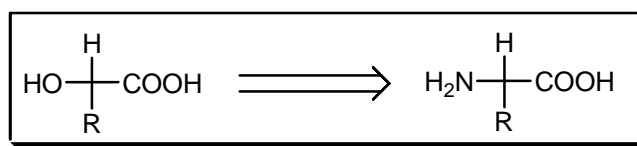
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



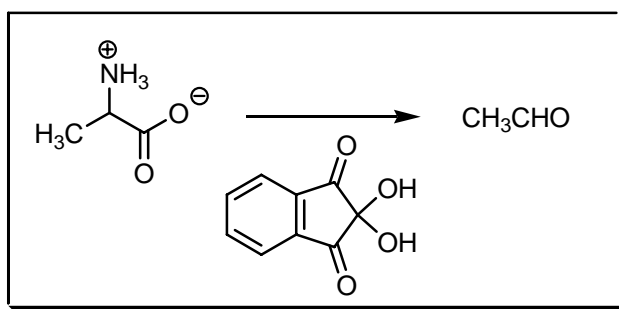
**NOTES :**

Nitrous acid reacts generally quantitatively with  $\alpha$ -amino acids to yield nitrogen and  $\alpha$ -hydroxy-acids. The general scheme does not accurately describe the whole process. The whole process for glycine is described by **Austin**. See also **Strecker** reaction.

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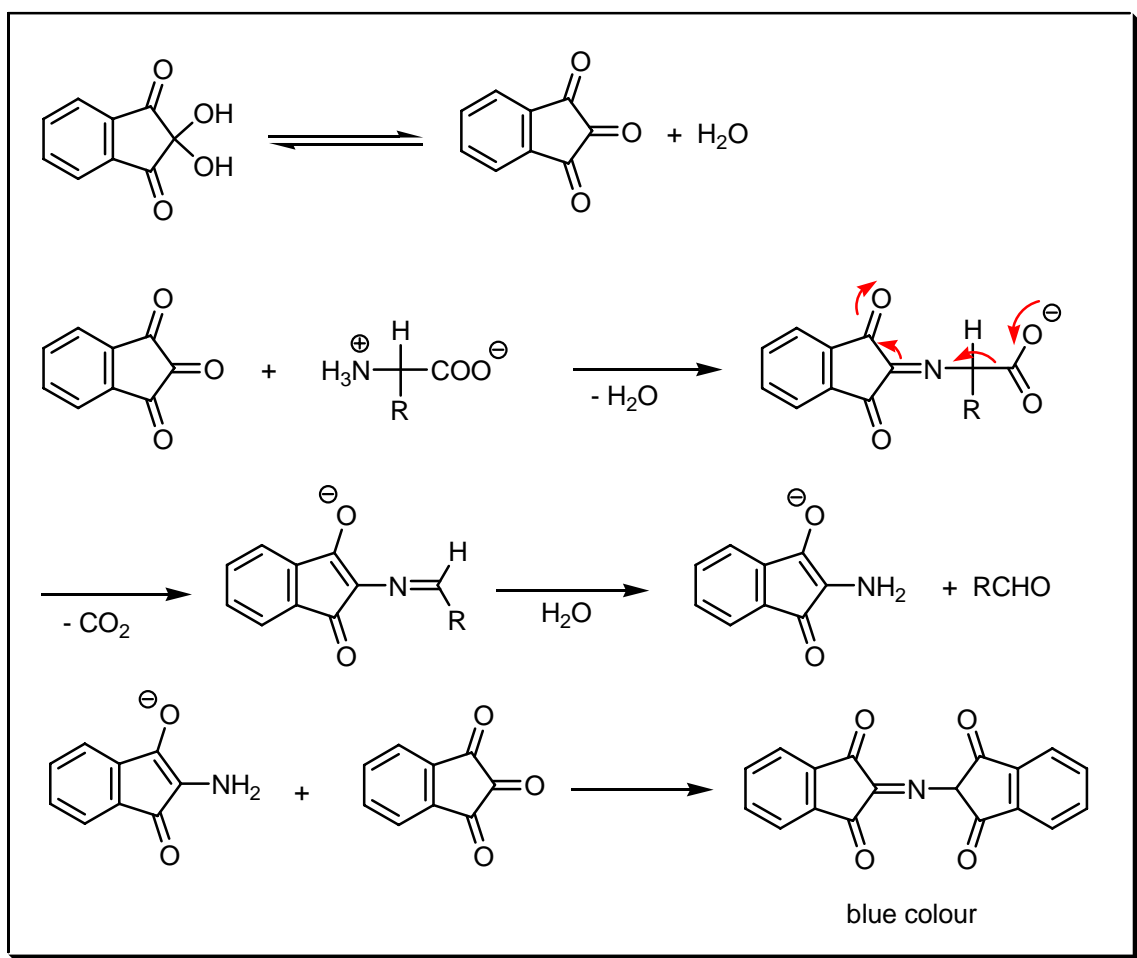
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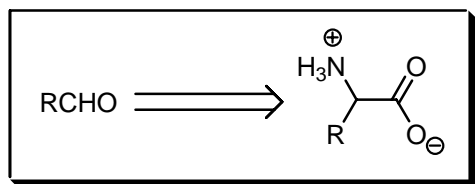
**COMMENTS :**van SLYKE OXIDATIVE DECARBOXYLATION**EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

α-Amino acids can be estimated by the oxidative decarboxylation which they undergo when boiled at pH 1-5 in aqueous solution with ninhydrin (triketohydrindene hydrate). The blue colour is formed due to the reaction between the ninhydrin and ammonia.

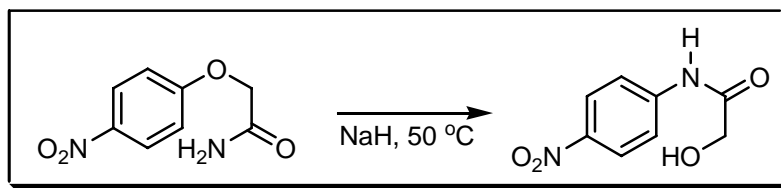
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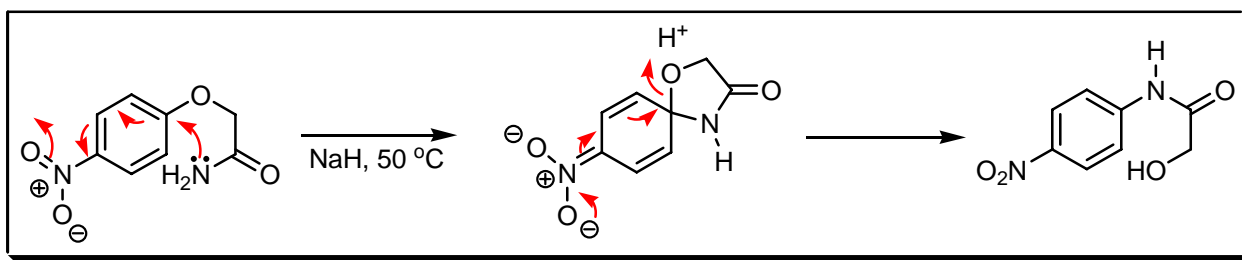
COMMENTS :

## SMILES REARRANGEMENT

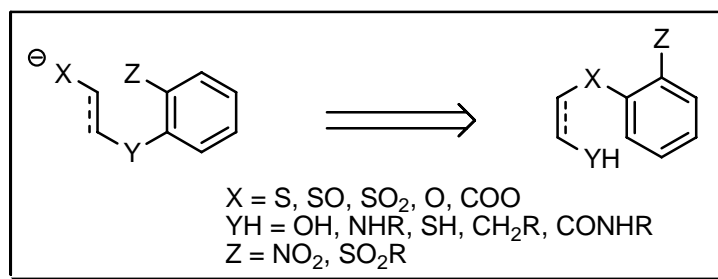
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The *intramolecular* rearrangement by nucleophilic aromatic substitution and aromatic migration (sometimes aliphatic) from one hetero atom to another. The conversion of *o*-methyldiarylsulfones to *o*-benzylbenzenesulfinic acids is referred to as the **Truce – Smiles** rearrangement. See also **Chapman** rearrangement, **Freudenberg – Schönberg** rearrangement, **Hayashi** rearrangement and **Newman – Karnes – Kwart** reactions.

REFERENCES :

March : 675

Smith – March : 879

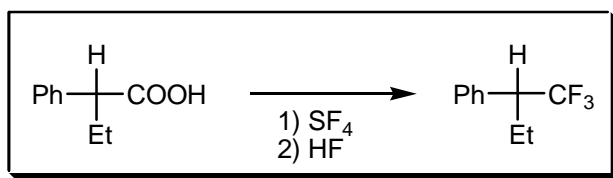
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COMMENTS :

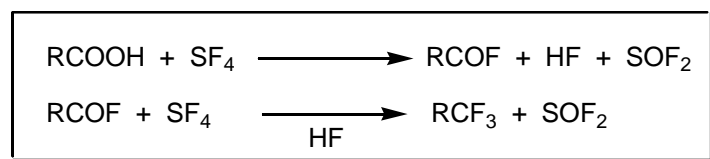
## SMITH – MIDDLETON – ROZEN FLUORINATION

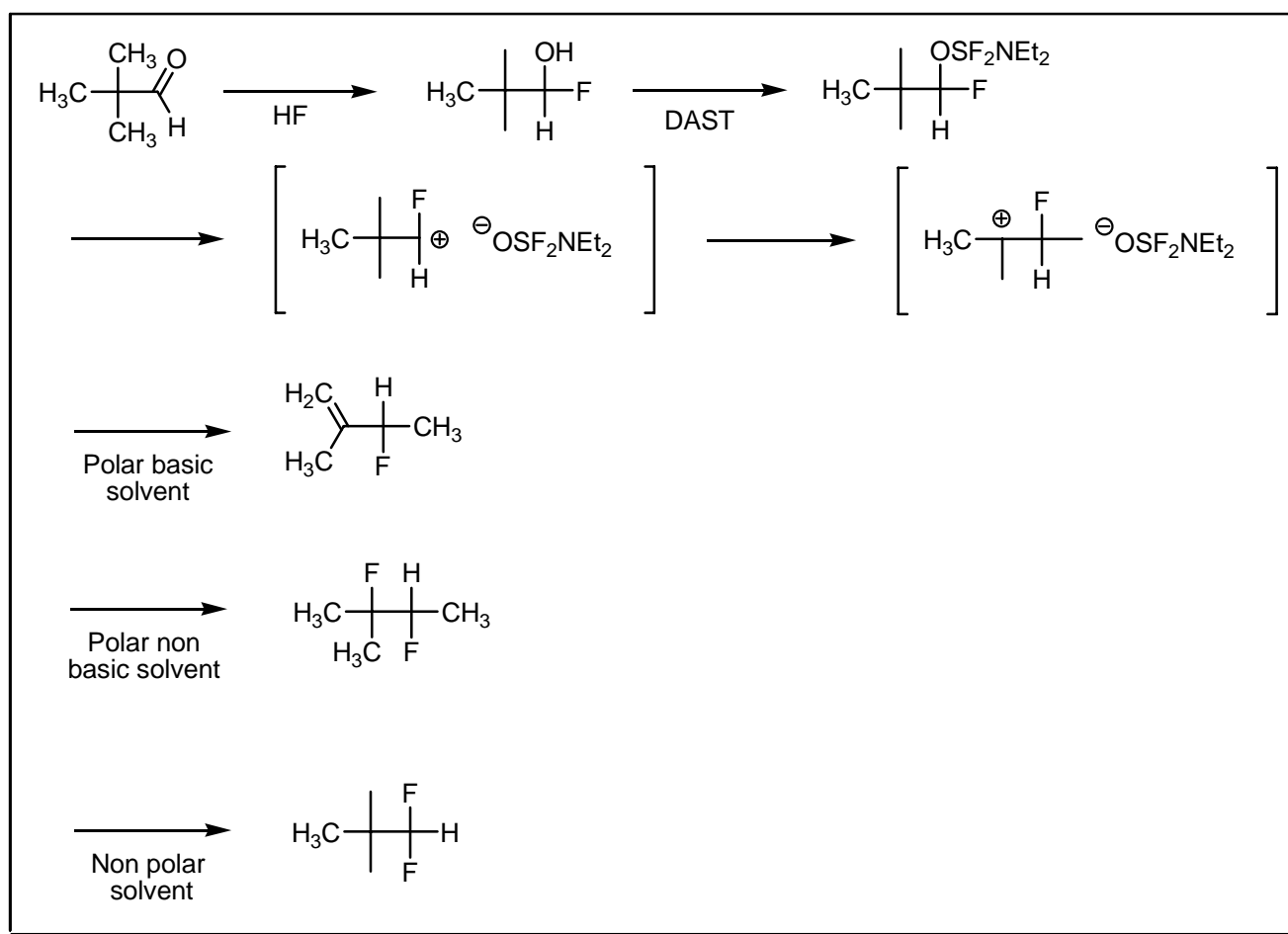
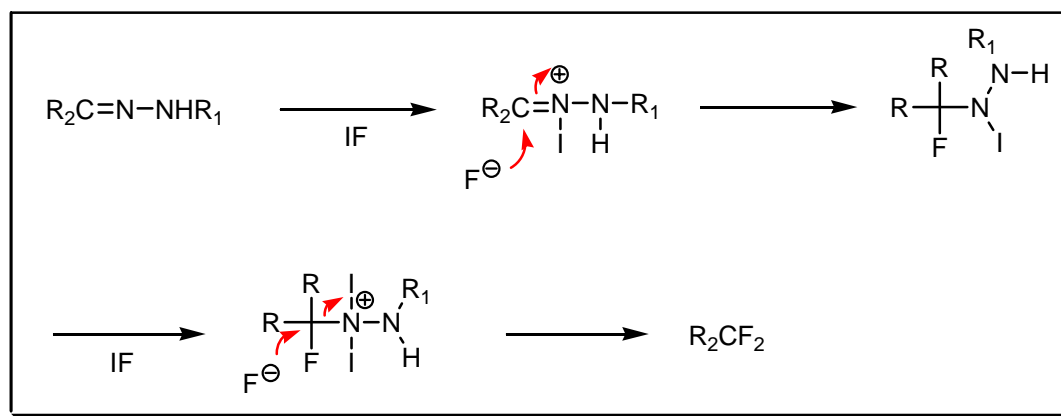
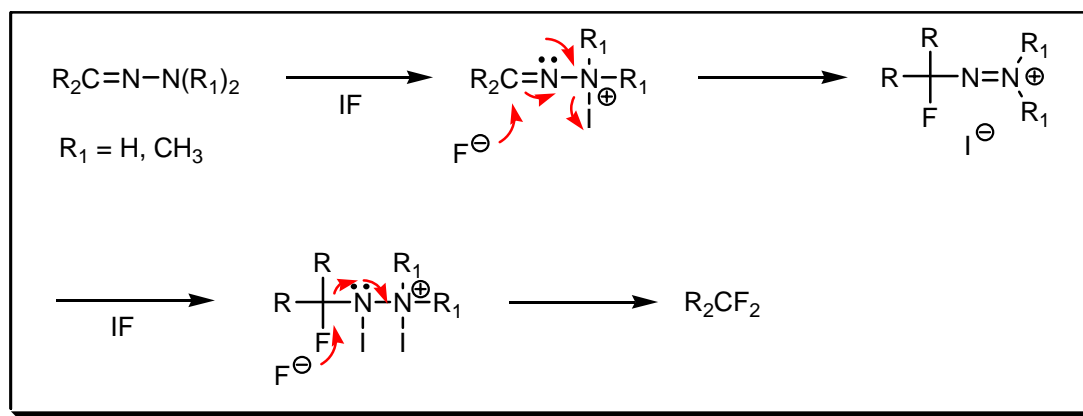
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EXAMPLE :

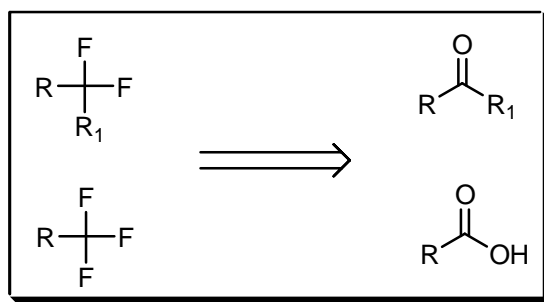


MECHANISM :





## DISCONNECTION :



## NOTES :

Carbonyls are converted to  $\text{CF}_2$  compounds by  $\text{SF}_4$  (**Smith**) or diethylaminosulfur trifluoride (DAST) (**Middleton**) or by IF on hydrazones (**Rozen**).

## REFERENCES :

**Org. React.** : 21, 1

**Org. Synth.** : 64, 221

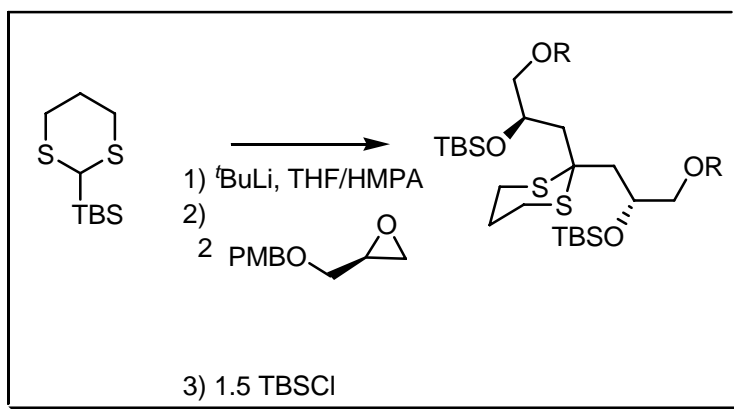
**Org. Synth. Coll. Vol.** : 7, 528

- 1) W.C. Smith; C.W. Tullock; E.L. Muettertis; W.R. Hasek; F.S. Fawcett; V.A. Engelhardt; D.D. Coffman, *J. Am. Chem. Soc.*, 1959, **81**, 3165.
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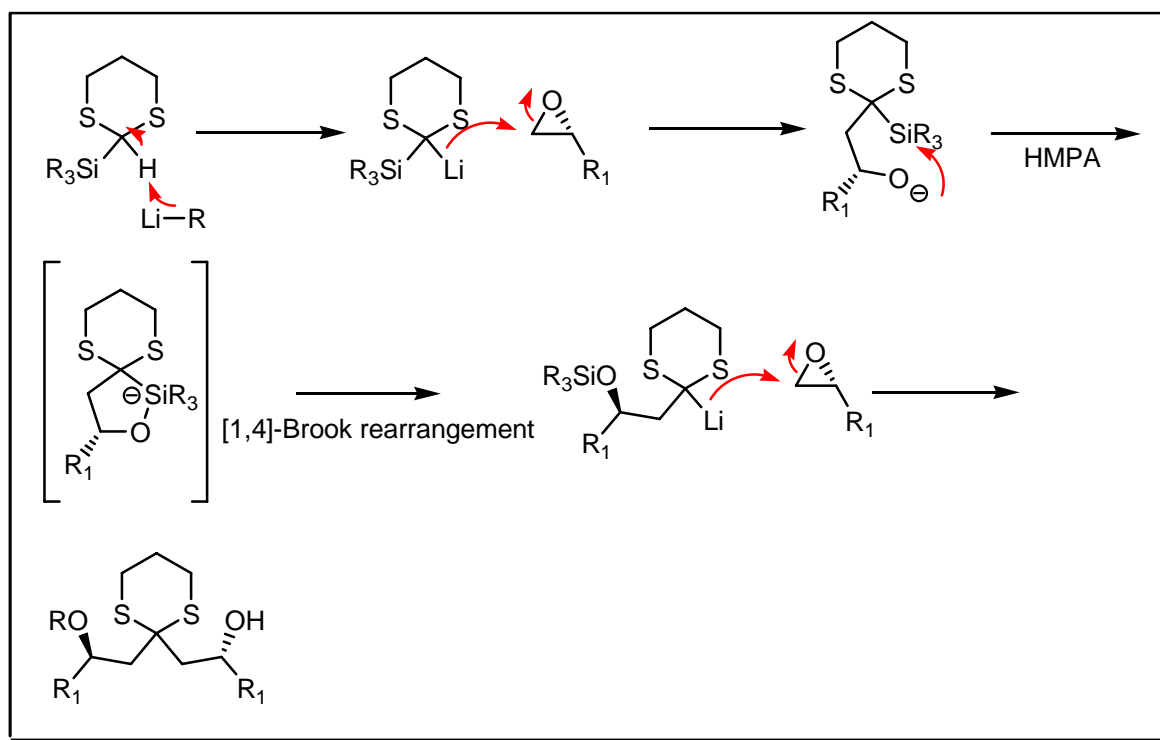
## COMMENTS :

## SMITH – TIETZE COUPLING

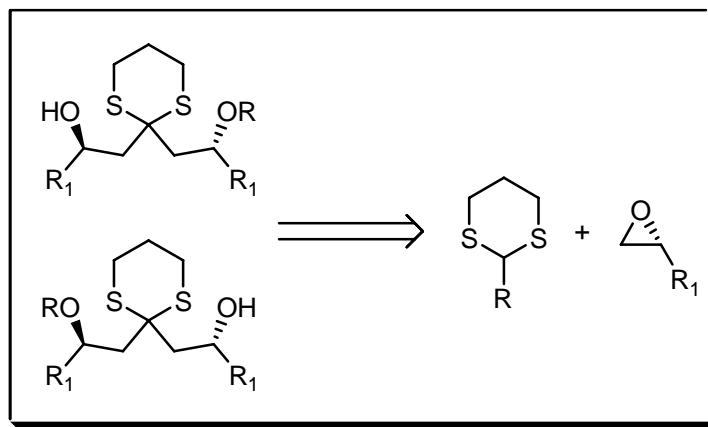
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The one-pot coupling of 2-silylated-1,3-dithianes with epoxides to afford 1,5-polyol fragments. The keystone in the mechanism is the [1,4]-**Brook** rearrangement. This rearrangement only takes place after the addition of the HMPA. See also **Brook** rearrangement, and **Corey – Seebach** reaction.

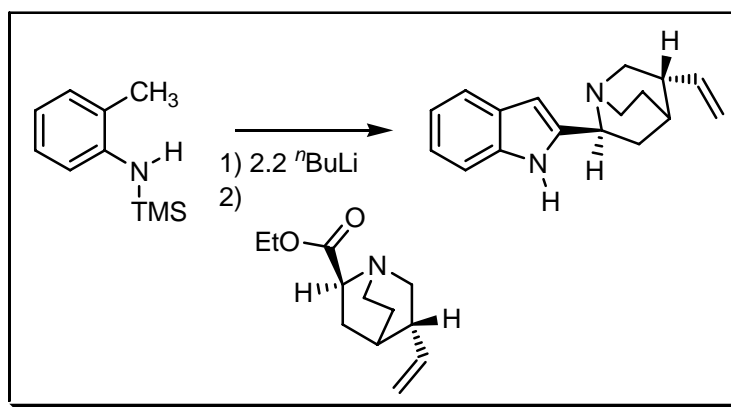
## REFERENCES :

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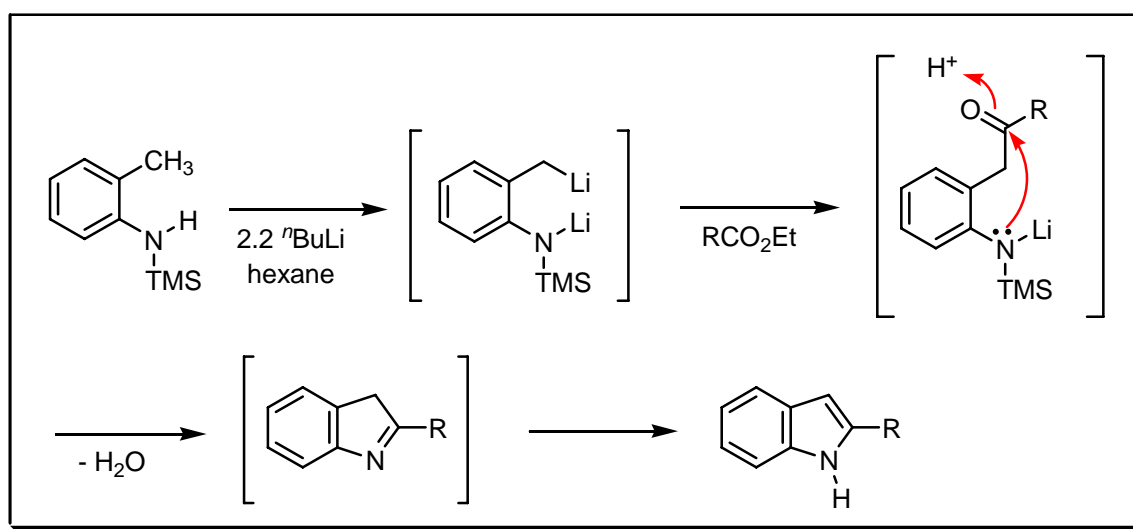
## COMMENTS :

## SMITH INDOLE SYNTHESIS

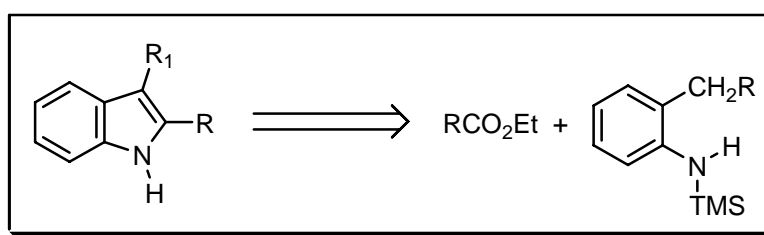
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Dilithium reagents derived from 2-alkyl-N-trimethylsilyl anilines undergo condensation with esters of carboxylic acids to afford substituted indoles. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**,



**Reissert** indole, **Saegusa** indole, **Schmid**, **Sugasawa** indole, **Sundberg**, **Thiele** – **Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

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#### REFERENCES :

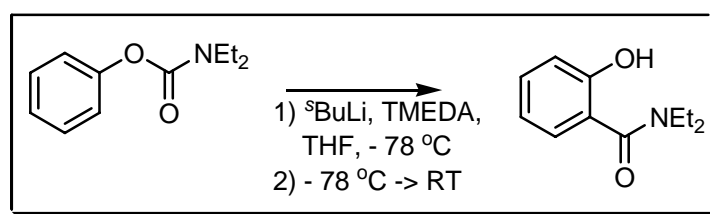
- 1) A.B. Smith III; M. Visneck; J.N. Haseltine; P.A. Sprengeler, *Tetrahedron*, 1986, **42**, 2957.
  - 2) K.E. Henegar; D.A. Hunt, *Heterocycles*, 1996, **43**, 1471.
- 

#### COMMENTS :

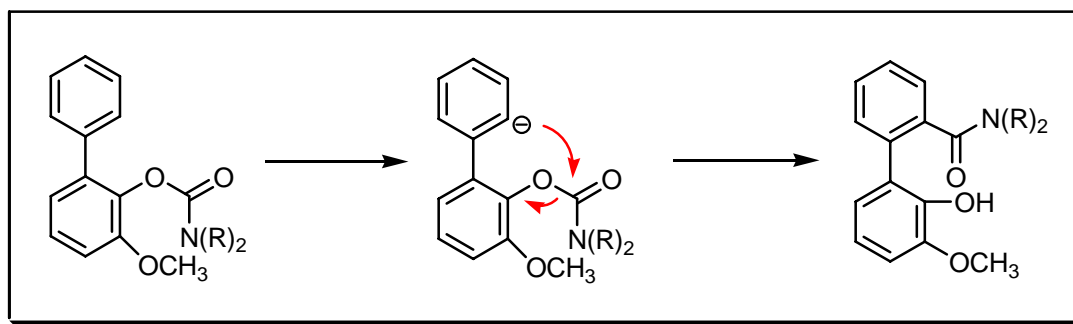
### SNIECKUS REARRANGEMENT

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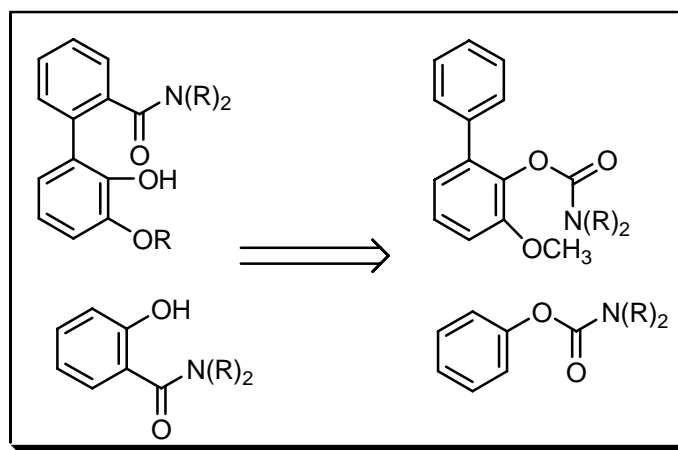
#### EXAMPLE :



#### MECHANISM :



## DISCONNECTION :



## NOTES :

[1,2]- or [1,4]-carbamoyl migration of benzylic carbamates after direct *ortho* lithiation with <sup>s</sup>BuLi or LDA in THF. This is formally an anionic **Fries** rearrangement. See also **Fries** rearrangement.

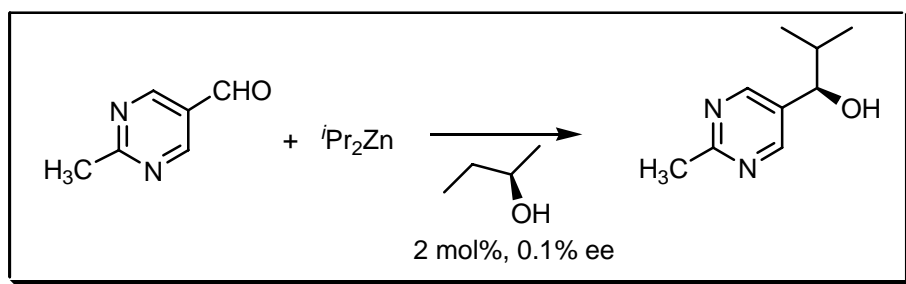
## REFERENCES :

- 1) M.P. Sibi; V. Snieckus, *J. Org. Chem.*, 1983, **48**, 1935.
- 2) M.P. Sibi; S. Chattopadhyay; J.W. Dankwardt; V. Snieckus, *J. Am. Chem. Soc.*, 1985, **107**, 6312.
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- 5) P. Zhang; R.E. Gawley, *J. Org. Chem.*, 1993, **58**, 3223.
- 6) M. Stratakis, *J. Org. Chem.*, 1997, **62**, 3024.
- 7) C.A. James; V. Snieckus, *Tetrahedron Lett.*, 1997, **38**, 8149.

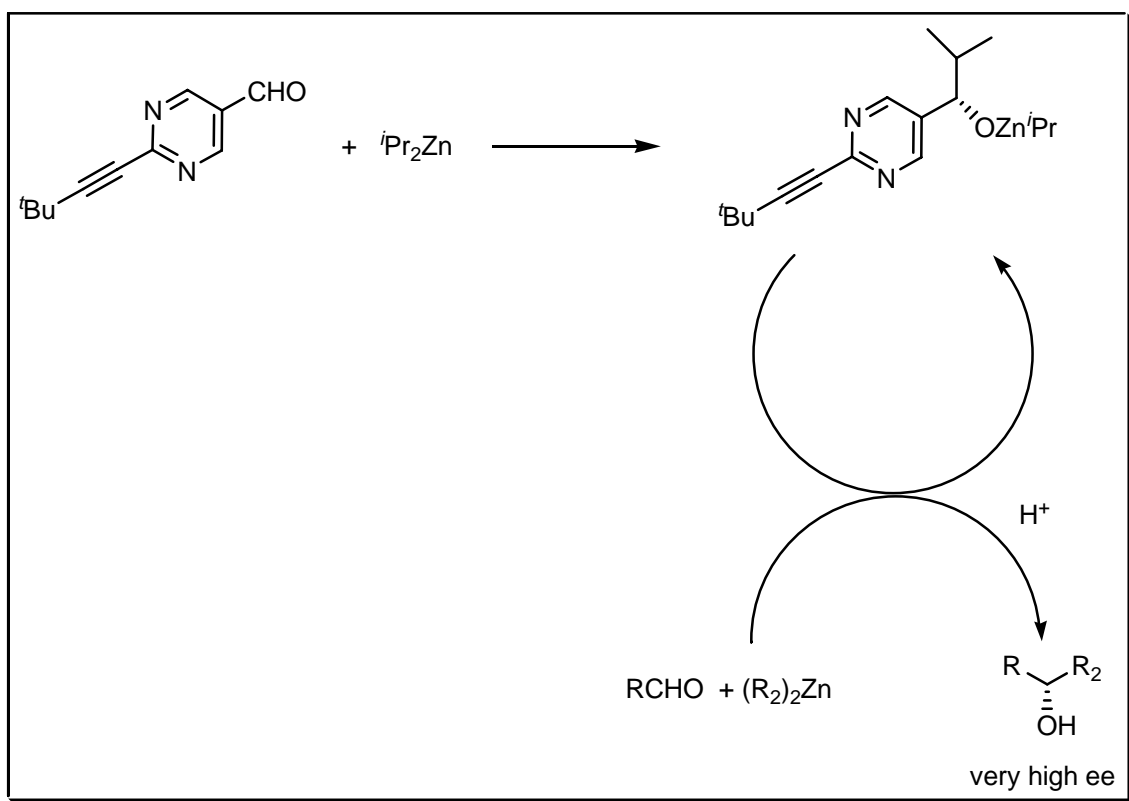
## COMMENTS :

## SOAI AUTOCATALYSIS

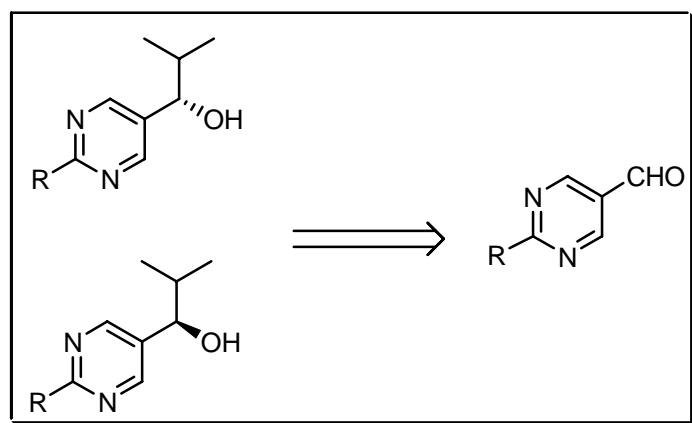
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

This is the asymmetric automultiplication of chiral compounds by asymmetric autocatalysis. Various chiral compounds with very low ee act as chiral initiators in the reaction of pyrimidine-5-carbaldehyde and diisopropylzinc to give 5-pyrimidyl alkanol with high ee. **Blackmond** *et al.* have shown that the transition state exists of a tetrameric species.

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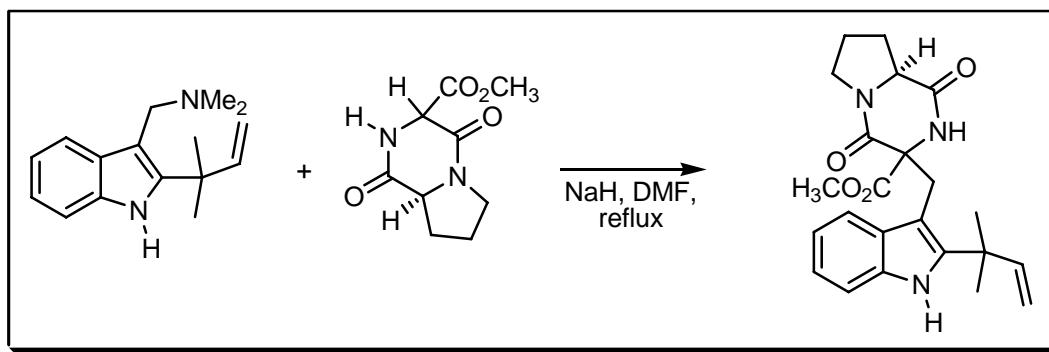
## REFERENCES :

- 1) K. Soai; T. Shibata; H. Morioka; K. Choji, *Nature*, 1995, **378**, 767.
  - 2) T. Shibata; S. Yonekubo; K. Soai, *Angew. Chem., Int. Ed.*, 1999, **38**, 659.
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  - 4) K. Soai, *Enantiomer*, 1999, **4**, 591.
  - 5) K. Soai; T. Shibata; I. Sato, *Acc. Chem. Res.*, 2000, **33**, 382.
  - 6) K. Soai; I. Sato; T. Shibata, *The Chemical Record*, 2001, **1**, 321.
  - 7) I. Sato; H. Urabe; S. Ishii; S. Tanji; K. Soai, *Org. Lett.*, 2001, **3**, 3851.
  - 8) D.G. Blackmond, *Adv. Synth. Catal.*, 2002, **344**, 156.
  - 9) K. Soai; I. Sato, *Chirality*, 2002, **14**, 548.
  - 10) I. Sato; H. Urabe; S. Ishiguro; T. Shibata; K. Soai, *Angew. Chem., Int. Ed.*, 2003, **42**, 315.
  - 11) F.G. Buono; D.G. Blackmond, *J. Am. Chem. Soc.*, 2003, **125**, 8978.
  - 12) T. Buhse, *Tetrahedron: Asymmetry*, 2003, **14**, 1055.
  - 13) K. Soai; T. Shibata; I. Sato, *Bull. Chem. Soc. Jpn.*, 2004, **77**, 1063.
  - 14) I. Sato; M. Shimizu; T. Kawasaki; K. Soai, *Bull. Chem. Soc. Jpn.*, 2004, **77**, 1587.
  - 15) I. Sato; K. Kadowaki; Y. Ohgo; K. Soai, *J. Mol. Catal. A: Chem.*, 2004, **216**, 209.
  - 16) I. Sato; T. Nakao; R. Sugie; T. Kawasaki; K. Soai, *Synthesis*, 2004, 1419.
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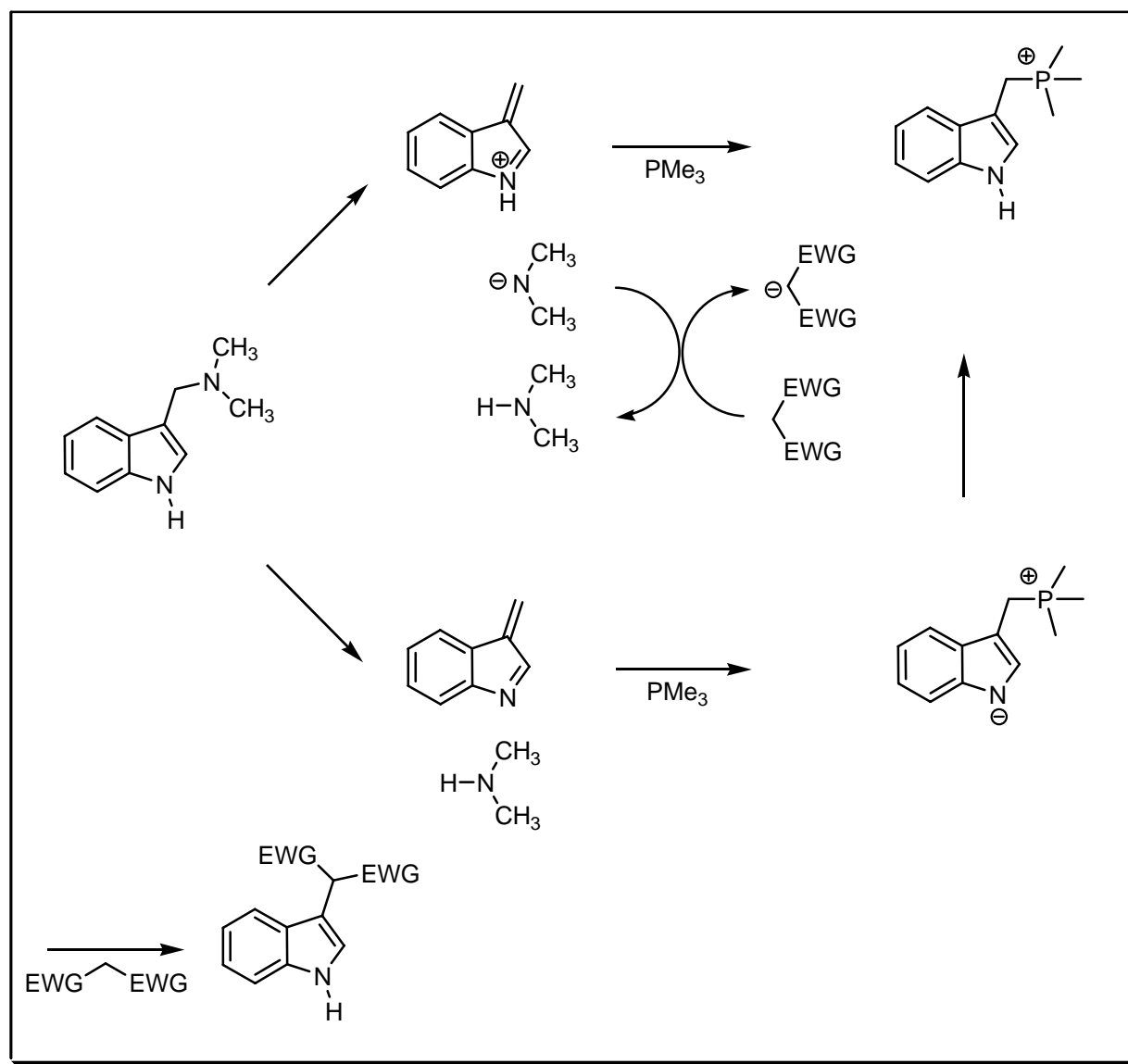
## COMMENTS :

## SOMEI – KAMETANI REACTION

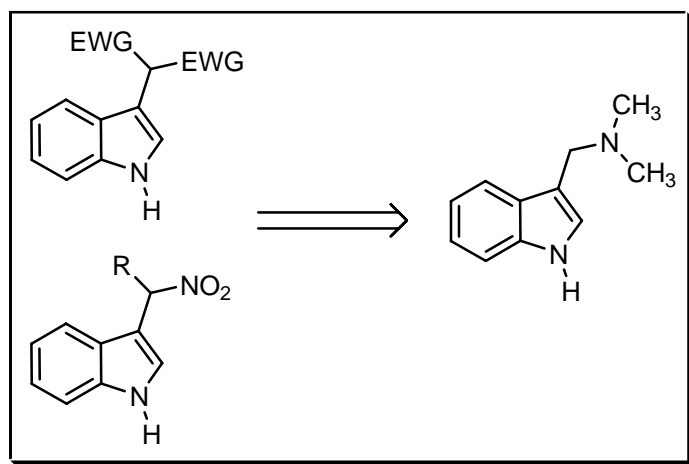
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

Gramine derivatives are mono-alkylated with carbon nucleophiles, especially nitro-alkanes in the presence of tri-*n*-butylphosphine as catalyst.

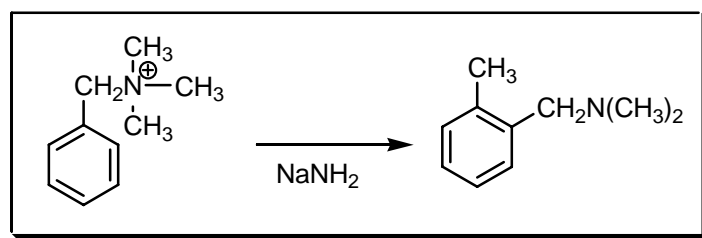
## REFERENCES :

- 1) T. Kametani; N. Kanaya; M. Ihara, *J. Am. Chem. Soc.*, 1980, **102**, 3974.
- 2) M. Somei; Y. Karasawa; C. Kaneko, *Heterocycles*, 1981, **16**, 941.
- 3) T.D. Cushing; J.F. Sanz-Cervera; R.M. Williams, *J. Am. Chem. Soc.*, 1996, **118**, 557.

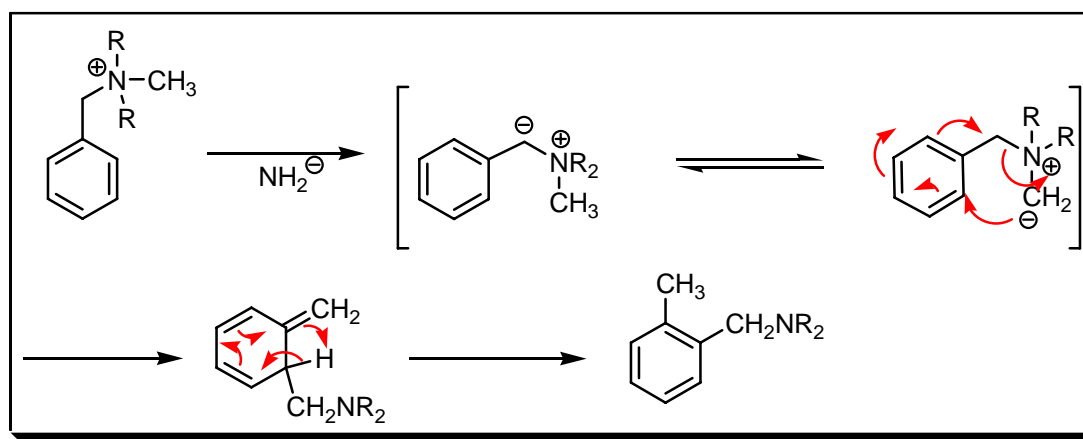
## COMMENTS :

## SOMMELET – HAUSER REACTION

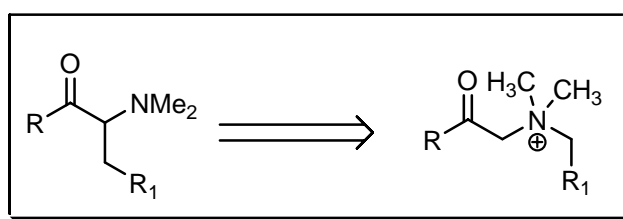
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

In this rearrangement, a trialkylammonium or dialkylsulfonium residue becomes detached from the side-chain carbon atom of a benzyl or substituted benzyl group and reattaches to the *ortho*-position of the benzene ring by way of the  $\alpha$ -carbon atom of one of the alkyl group. The rearrangement has been effected by sulfuric acid, phosphorous pentoxide, phenyl lithium or photochemically. The reaction may take place with sulfonium salts instead of ammonium salts. See also **Stevens** reaction.

## REFERENCES :

March : 673, 1194

Smith – March : 877, 1420, 1455

Smith : 809

Smith 2<sup>nd</sup> : 670, 677

Houben – Weyl : **E6b**, 699; **E7b**, 634; **E11**, 910, 1362, 1381; **E16d**, 1140, 1149

Org. React. : **8**, 197; **18**, 404

Org. Synth. : **34**, 61

Org. Synth. Coll. Vol. : **4**, 585

Science of Synthesis : **10**, 387

- 1) M. Sommelet, *C.R. Séances Acad. Sci.*, 1937, **205**, 56.
- 2) S.W. Kantor; C.R. Hauser, *J. Am. Chem. Soc.*, 1951, **73**, 4122.
- 3) G.C. Jones; C.R. Hauser, *J. Org. Chem.*, 1962, **27**, 3572.
- 4) J. Biellmann; J. Schmitt, *Tetrahedron Lett.*, 1973, **14**, 4615.

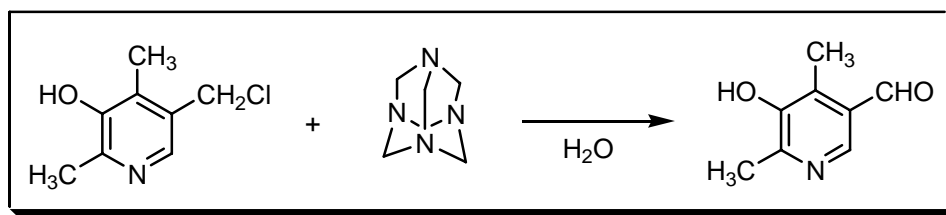
- 5) T.J. Lee; W.J. Holtz, *Tetrahedron Lett.*, 1983, **24**, 2071.  
6) N. Shirai; Y. Sato, *J. Org. Chem.*, 1988, **53**, 194.  
7) J.M. Klunder, *J. Heterocycl. Chem.*, 1995, **32**, 1687.  
8) J. Park, J.H. Shin; C. Lee, *Tetrahedron Lett.*, 1999, **40**, 7485.  
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- 

**COMMENTS :**

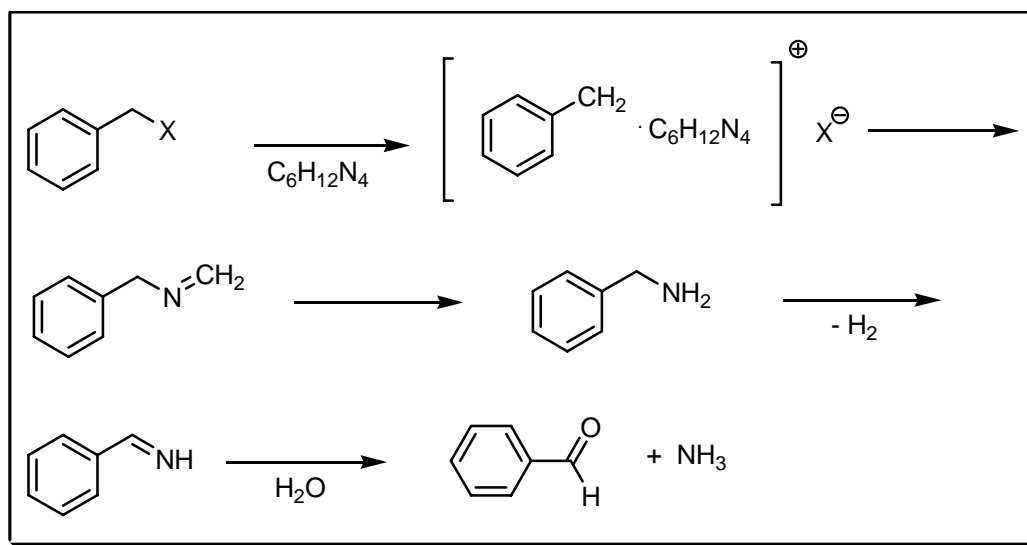
## SOMMELET ALDEHYDE REACTION

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**EXAMPLE :**

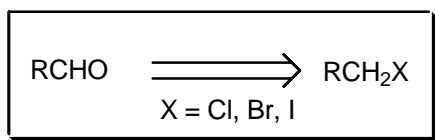


**MECHANISM :**





## DISCONNECTION :



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## NOTES :

Primary alkyl and aryl halides can be oxidised to aldehydes easily by the use of hexamethylenetetramine. See also **Delépine**, **Duff** and **Kröhnke** reactions.

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## REFERENCES :

**March** : 1193

**Smith – March** : 1536

**Houben – Weyl** : 7/1, 194

**Org. React.** : 8, 197; 21, 1

**Org. Synth.** : 33, 93; 47, 76

**Org. Synth. Coll. Vol.** : 4, 690, 918; 5, 668

- 
- 1) M. Sommelet, *Bull. Soc. Chim. Fr.*, 1913, **13**, 1085.
  - 2) C.W. Shoppee, *Nature*, 1948, **162**, 619.
  - 3) V. Franzen, *Liebigs Ann. Chem.*, 1956, **600**, 109.
  - 4) M.-C. Zaluski; M. Robba; M. Bonhomme, *Bull. Soc. Chim. Fr.*, 1970, 1445.
  - 5) S. Miyano; H. Fukushima; H. Inagawa; H. Hashimoto, *Bull. Chem. Soc. Jpn.*, 1986, **59**, 3285.
  - 6) D. Evans; M.P. Serve; B. Ramalingam; L. Barna; W. Feld, *Heterocycles*, 1987, **26**, 1569.
  - 7) I. Simiti; O. Oniga, *Monatsh. Chem.*, 1996, **127**, 733.

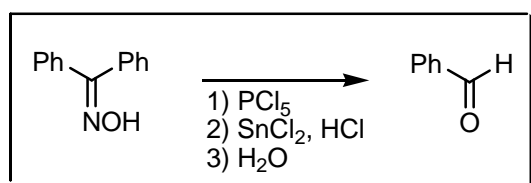
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## COMMENTS :

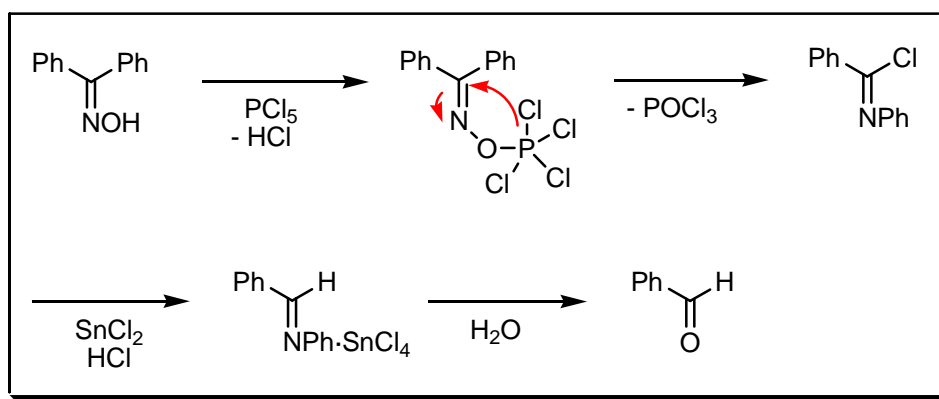
## SONN – MÜLLER ALDEHYDE SYNTHESIS

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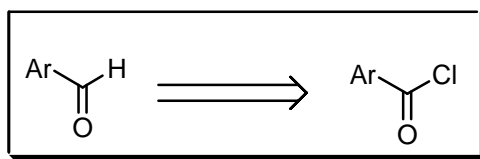
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The aromatic aldehyde synthesis from amides or ketoximes, by reduction of imino chlorides. The **von Braun – Rudolph** modification involves the use of chromous chloride in the reduction of the imido-chlorides. See also **Grundmann** and **Stephen** reactions.

## REFERENCES :

Houben – Weyl : 7/1, 480

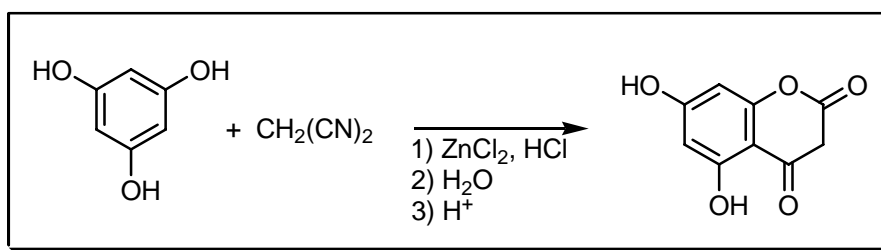
Org. React. : 8, 225, 240

- 1) A. Sonn; E. Müller, *Ber. Dtsch. Chem. Ges.*, 1919, **52**, 1929.
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- 3) L.N. Ferguson, *Chem. Rev.*, 1946, **38**, 227.
- 4) G.H. Coleman; R.E. Pyle, *J. Am. Chem. Soc.*, 1946, **68**, 2007.
- 5) F. Effenberger; R. Gleiter, *Chem. Ber.*, 1964, **97**, 480.

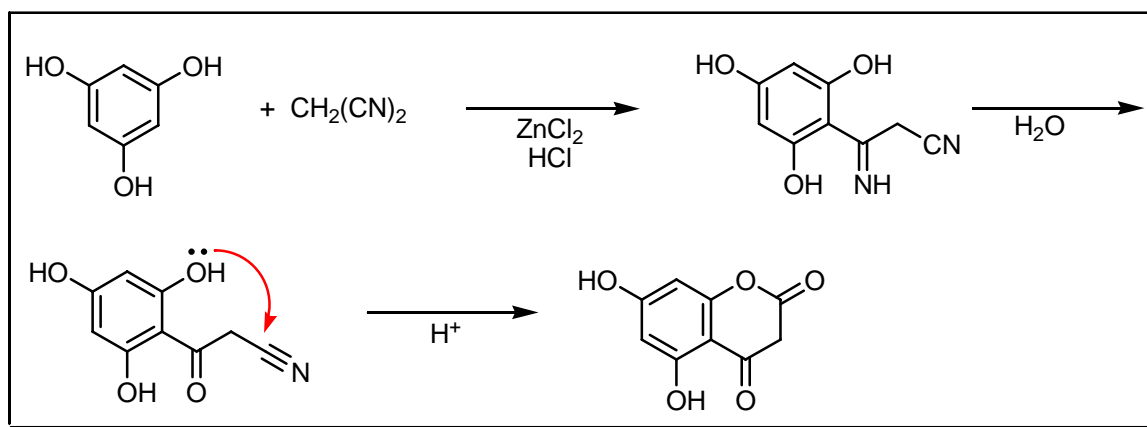
## COMMENTS :

## SONN EXTENSION OF THE HOESCH REACTION

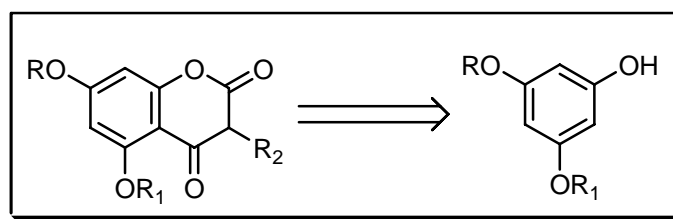
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

In this extension of the **Hoesch** reaction, malononitrile or ethyl cyanoacetate is condensed with resorcinol or phloroglucinol. See also **Hoesch – Houben** reaction.

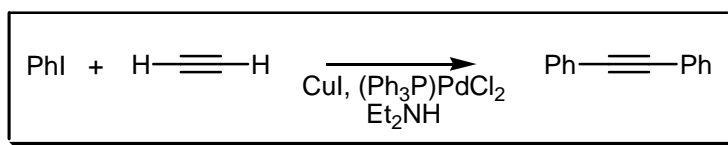
### REFERENCES :

A. Sonn, *Ber. Dtsch. Chem. Ges.*, 1917, **50**, 1292.

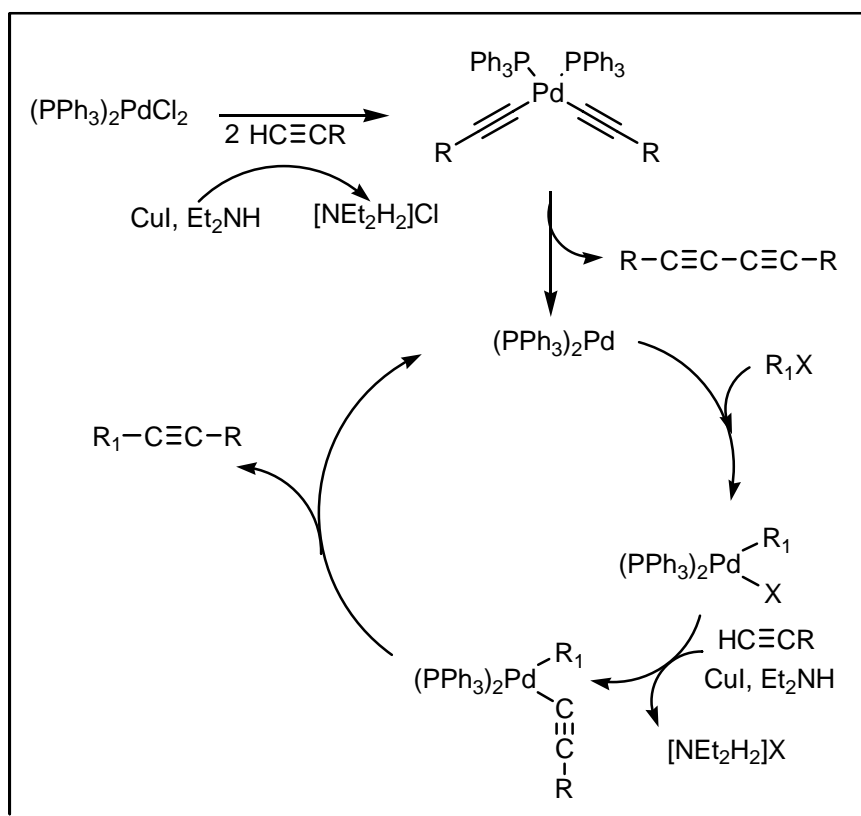
### COMMENTS :

## SONOGASHIRA – HAGIHARA COUPLING

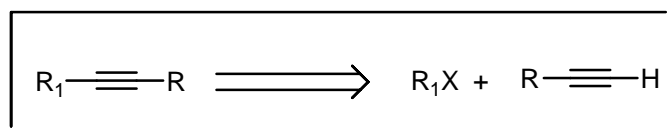
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Terminal alkynes can be alkenylated by alkenyl triflates (bromides, iodides) and arylated by aryl triflates (bromide, iodides). These reactions are called **Cacchi** coupling reactions if the reaction is catalysed by  $\text{Cu(I)}$  and  $\text{Pd(0)}$  and if triflate reagents are employed, **Sonogashira – Hagihara** coupling reactions if the reaction is catalysed by  $\text{Cu(I)}$  and  $\text{Pd(0)}$  and halides are employed as substrates. Nickel-catalysed reactions have been reported by **Beletskaya et al.** **Stephens – Castro** coupling reactions for the non-catalysed coupling of copper acetylides with aryl halides. See also **Liebeskind – Srogl** and **Stephens – Castro** reactions.

## REFERENCES :

March : 718

Smith 2<sup>nd</sup> : 1124

Org. Synth. : **72**, 104; **76**, 263

Org. Synth. Coll. Vol. : **9**, 117; **10**, 2358

Science of Synthesis : **1**, 285, 801; **9**, 266; **10**, 750

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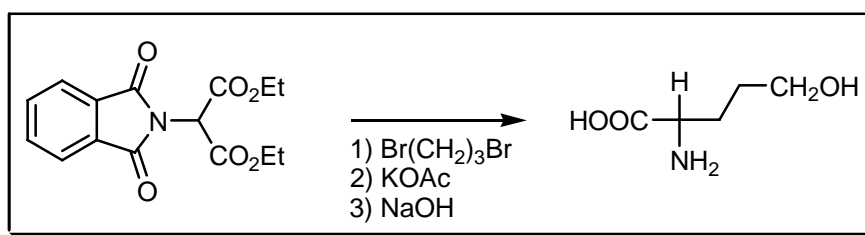
- 1) K. Sonogashira; Y. Tohda; N. Hagihara, *Tetrahedron Lett.*, 1975, **16**, 4467.
  - 2) R. Rossi; A. Carpita; F. Bellina, *Org. Prep. Proced. Int.*, 1995, **27**, 129.
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  - 7) P. Appukkuttan; W. Dehaen; E. van der Eycken, *Eur. J. Org. Chem.*, 2003, 4713.
  - 8) I.P. Beletskaya; G.V. Latyshev; A.V. Tsvetkov; N.V. Lukashev, *Tetrahedron Lett.*, 2003, **44**, 5011.
  - 9) N.E. Leadbeater; M. Marco; B.J. Tominack, *Org. Lett.*, 2003, **5**, 3919.
  - 10) L. Wang; P. Li; Y. Zhang, *Chem. Commun.*, 2004, 514.
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  - 12) G. Zeni; D. Alves; J.M. Pena; A.L. Braga; H.A. Stefani; C.W. Nogueira, *Org. Biomol. Chem.*, 2004, **2**, 803.
  - 13) M. Amjad; D.W. Knight, *Tetrahedron Lett.*, 2004, **45**, 539.
  - 14) A. Köllhofer; H. Plenio, *Adv. Synth. Catal.*, 2005, **347**, 1295.
- 

## COMMENTS :

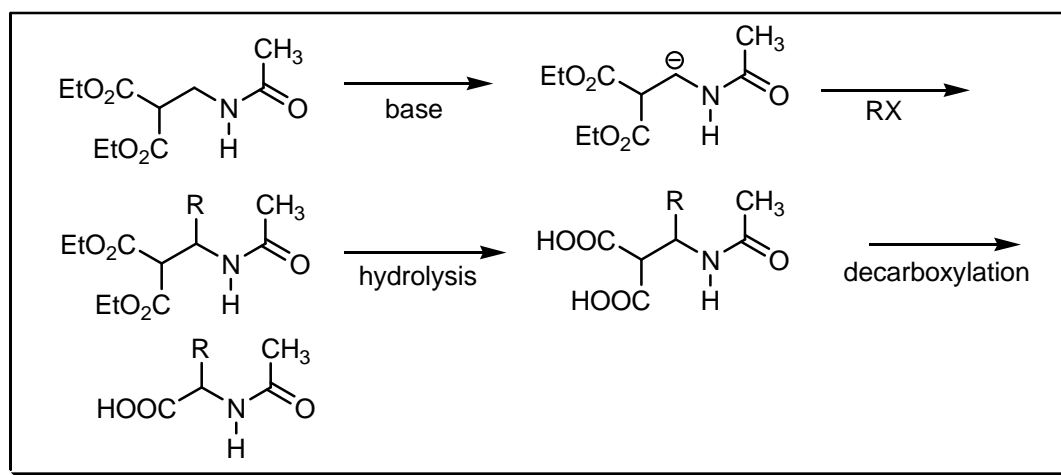
## SORENSEN AMINO ACID SYNTHESIS

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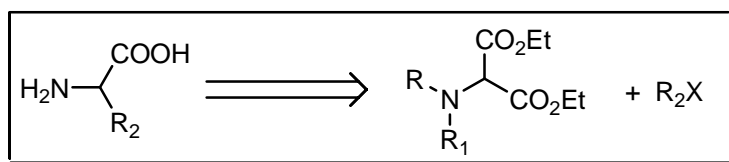
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The alkylation at a carbon bearing an active hydrogen atom in this case *N*-acetylaminomalonic ester. As in the malonic or cyanoacetic ester synthesis, the product can be hydrolysed and decarboxylated to give an  $\alpha$ -amino acid. Other acidic CH hydrogens can be hydrolysed too. See also **Gabriel** synthesis.

## REFERENCES :

**March** : 465

**Smith – March** : 549

**Houben – Weyl** : 4, 759

- 1) Z. Sorenson, *Bull. Soc. Chim. Fr.*, 1905, **33**, 1042.
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- 3) E.J. Corey; D.E. Cane, *J. Org. Chem.*, 1970, **35**, 3405.
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- 6) R.D.A. Hudson; S.A. Osborne; G.R. Stephenson, *Synlett*, 1996, 845.

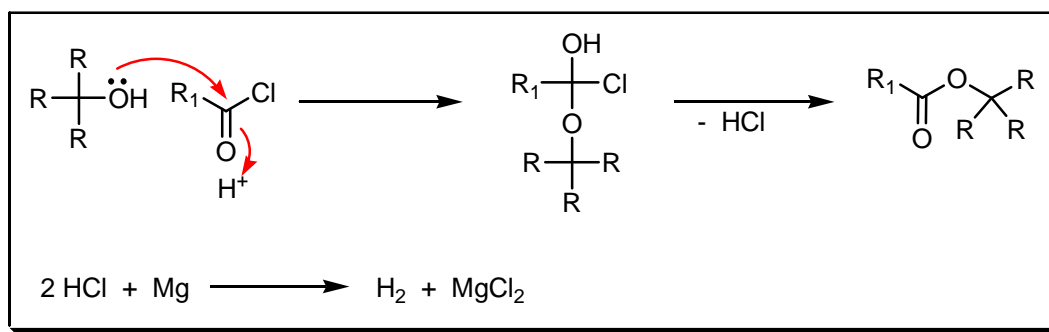
COMMENTS :

## SPASSOW ESTERIFICATION

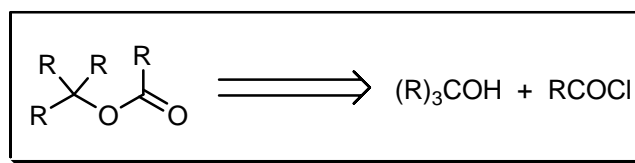
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

A method for the preparation of esters by the reaction of acid chloride with alcohols in benzene or diethyl ether in the presence of magnesium. With ethyl acetoacetate C-acyl derivatives are obtained. See also **Corey – Nicolaou**, **Diels – Alder**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Kita**, **Masamune**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Staab**, **Stacey**, **Steglich – Hassner**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolikiewicz**, **Wittig**, **Yamaguchi**, and **Yamamoto** macrolactonisation reactions.

## REFERENCES :

Org. Synth. : **21**, 46; **24**, 18

Org. Synth. Coll. Vol. : **3**, 141, 390

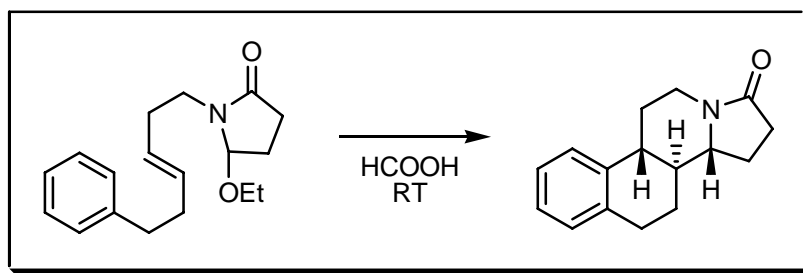
1) A. Spassow, *Ber. Dtsch. Chem. Ges.*, 1937, **70**, 1926.

2) A. Spassow, *Ber. Dtsch. Chem. Ges.*, 1937, **70**, 2381.

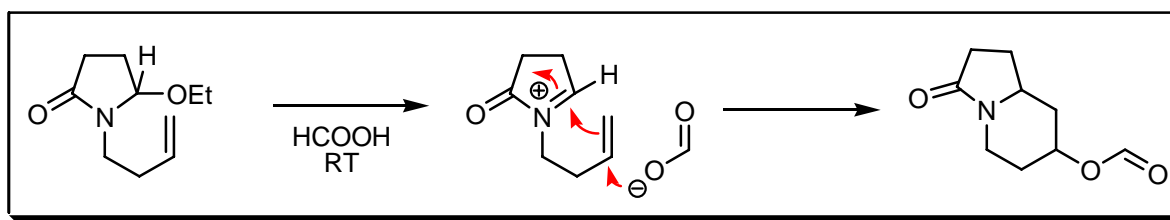
## COMMENTS :

## SPECKAMP RING-CLOSURE

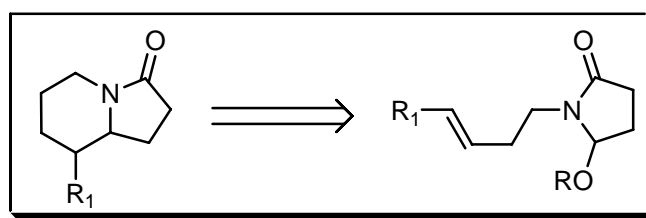
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :





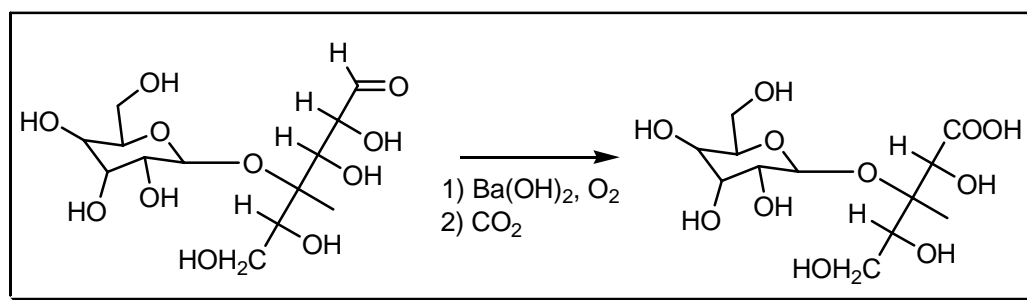
**NOTES :**

The cyclisation of olefinic  $\omega$ -ethoxy lactams which leads to ring-closed products *via* an  $\alpha$ -acyliminium ion. Acetylene derivatives undergo a similar cyclisation.

---

**REFERENCES :**

- 1) H.E. Schoemaker; J. Dijkink; W.N. Speckamp, *Tetrahedron*, 1978, **34**, 163.
  - 2) H.E. Schoemaker; Tj. Boer-Terpstra; J. Dijkink; W.N. Speckamp, *Tetrahedron*, 1980, **36**, 143.
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- 

**COMMENTS :****SPENGLER – PFANNENSTIEL OXIDATION****EXAMPLE :****NOTES :**

The oxidation of reductive sugars in alkaline solution with molecular oxygen.

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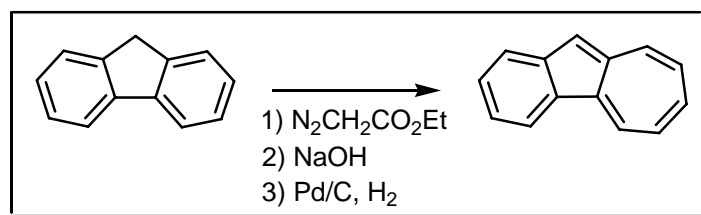
**REFERENCES :**

- 1) O. Spengler; A. Pfannenstiel, *Z. Wirtschaftsgruppe Zuckind.*, 1935, **85**, Techtl. 547.
  - 2) N.K. Richtmyer; R.M. Hann; C.S. Hudson, *J. Am. Chem. Soc.*, 1939, **61**, 340.
  - 3) E. Hardegger; K. Kreis; H. El Khadem, *Helv. Chim. Acta*, 1951, **34**, 2343.
  - 4) E. Hardegger; K. Kreis; H. El Khadem, *Helv. Chim. Acta*, 1952, **35**, 618.
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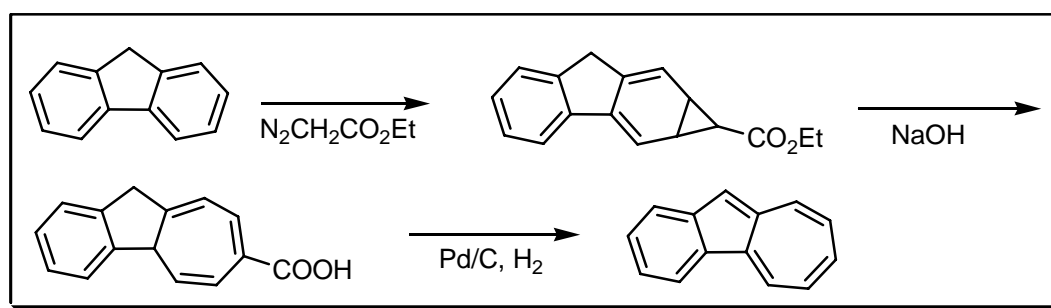
COMMENTS :

ST. PFAU – PLATTNER SYNTHESIS

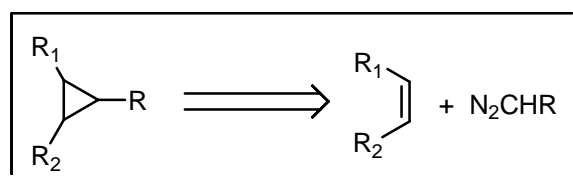
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

This method of synthesis involves ring enlargement of olefins by addition of ethyl diazoacetate followed by hydrolysis. The resulting acid is dehydrogenated and decarboxylated, generally by distillation *in vacuo* over palladium on charcoal. See also **Buchner** and **Ciamician – Dennstedt** reactions.

REFERENCES :

- 1) A. St. Pfauf; P.A. Plattner, *Helv. Chim. Acta*, 1939, **22**, 202.
- 2) J.R. Nunn; W.S. Rapson, *J. Chem. Soc.*, 1949, 825.
- 3) K. Hafner, *Angew. Chem.*, 1958, **70**, 419.

4) H.-J. Hansen, *Chimia*, 1996, **50**, 489.

5) H.-J. Hansen, *Chimia*, 1997, **51**, 147.

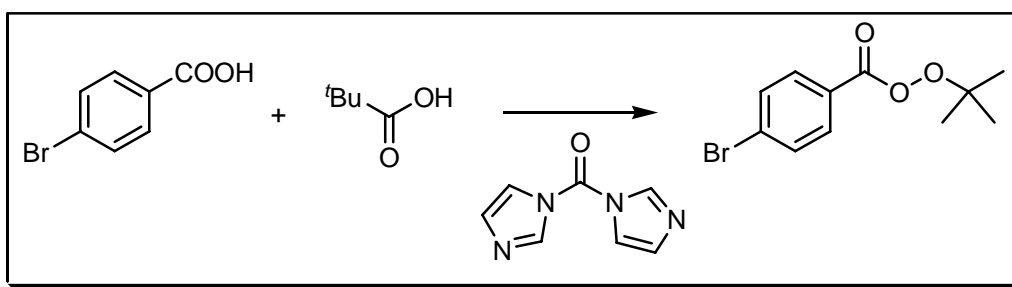
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COMMENTS :

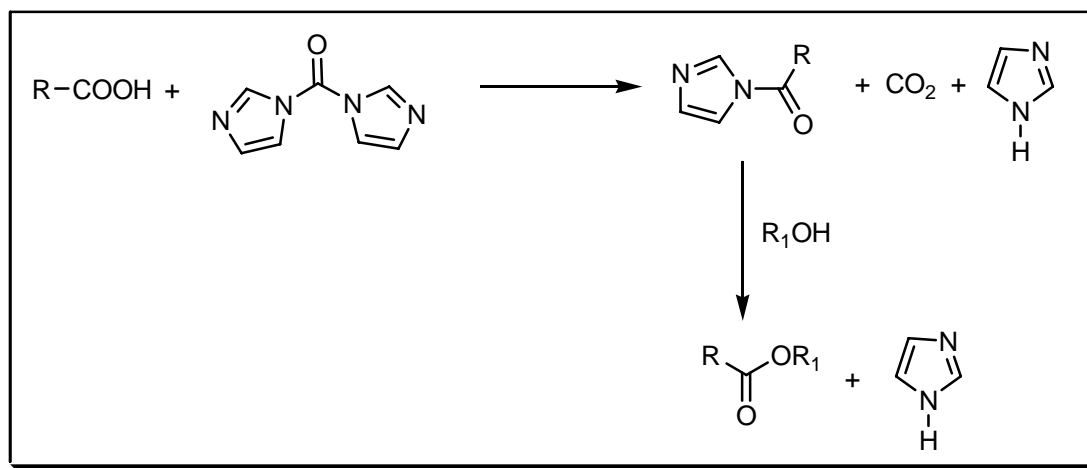
## STAAB ACYLATION

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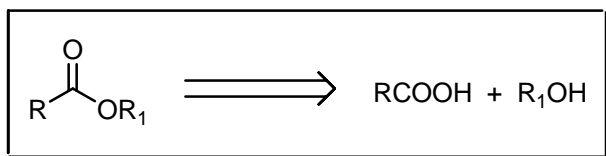
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

The *trans* acylation of alcohols to esters with *N*-acyl imidazoles. An easier route using benzotriazole has been published by **Katritzky**. The macrolactonisation version of this reaction is sometimes called **Raphael** macrolactonisation. See also **Corey – Nicolaou**, **Diels – Alder**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Kita**, **Masamune**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Stacey**, **Steglich – Hassner**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolikiewicz**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

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## REFERENCES :

Org. Synth. : **48**, 44

Org. Synth. Coll. Vol. : **5**, 201

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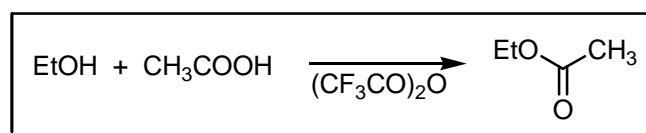
- 1) H.A. Staab, *Chem. Ber.*, 1956, **89**, 1927.
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  - 4) E.W. Colvin; T.A. Purcell; R.A. Raphael, *J. Chem. Soc., Perkin Trans. 1*, 1976, 1718.
  - 5) T. Kömives, *Org. Prep. Proced. Int.*, 1989, **21**, 251.
  - 6) M.J. Ford; S.V. Ley, *Synlett*, 1990, 255.
- 

## COMMENTS :

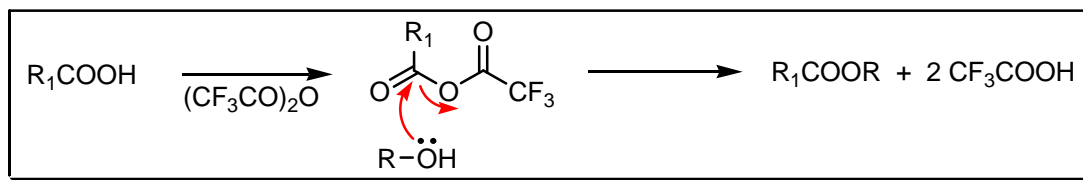
## STACEY ESTERIFICATION

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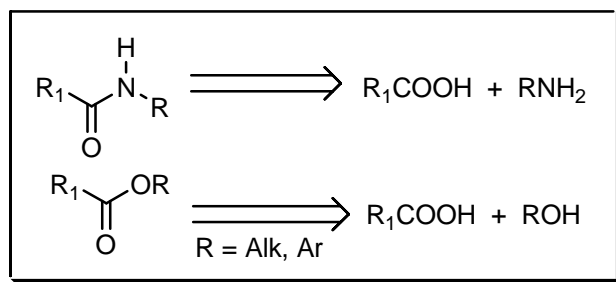
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Esters or amides are formed from alcohols and phenols or amines by treatment with carboxylic acids in the presence of trifluoroacetic anhydride. See also **Corey – Nicolaou**, **Diels – Alder**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Kita**, **Masamune**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Steglich – Hassner**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolikiewicz**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

### REFERENCES :

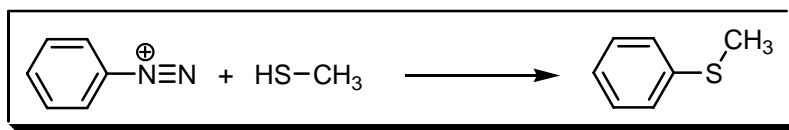
- 1) M. Stacey; E.J. Bourne; J.C. Tatlow; J.M. Tedder, *Nature*, 1949, **164**, 705.
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- 4) F. Wüst; C.S. Dence; T.J. McCarthy; M.J. Welch, *J. Labelled Compd. Radiopharm.*, 2000, **43**, 1289.
- 5) N.M. Khvoinova; D.V. Muslin; S.Ya. Khorshev, *Russ. J. Gen. Chem. (Engl. Transl.)*, 2001, **71**, 1799.

### COMMENTS :

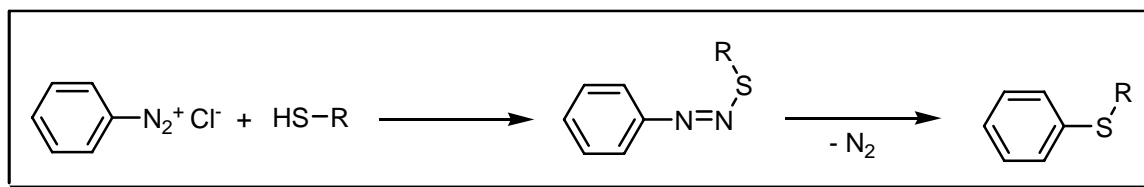
## STADLER – ZIEGLER REACTION

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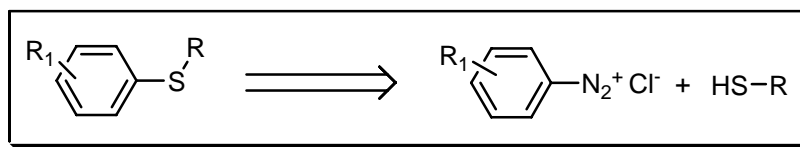
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The alkylthiodediazoniation is a **very dangerous** reaction to carry out due to the formation of diazosulfides. The reaction has been used extensively in industry to produce arylthioglycolic acids. Safer laboratory routes have been prepared by **Degani** and **Fochi**.

### REFERENCES :

Org. Synth. : 12, 76

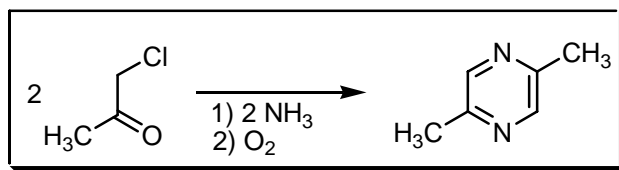
Org. Synth. Coll. Vol. : 2, 580

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- 3) J.D. Baleja, *Synth. Commun.*, 1984, **14**, 215.
- 4) T. Schaefer; J.D. Baleja, *Can. J. Chem.*, 1986, **64**, 1376.
- 5) M. Barbero; I. Degani; N. Diulgheroff; S. Dughera; R. Fochi; M. Migliaccio, *J. Org. Chem.*, 2000, **65**, 5600.

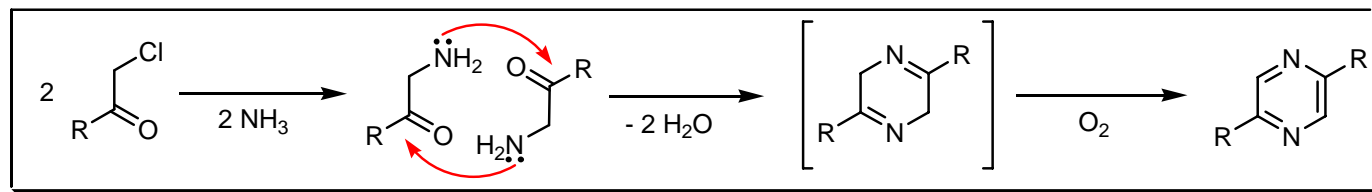
### COMMENTS :

# STADEL – RÜGHEIMER PYRAZINE SYNTHESIS

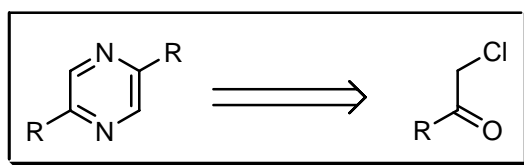
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The reaction between  $\alpha$ -halogenketones and ammonia to afford pyrazine. See also **Gastaldi** and **Gutknecht** reactions.

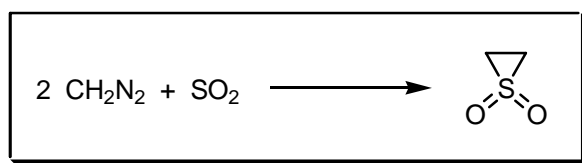
## REFERENCES :

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- 3) F. Tutin, *J. Chem. Soc.*, 1910, **97**, 2495.
- 4) I.J. Krems; P.E. Spoerri, *Chem. Rev.*, 1947, **40**, 279.

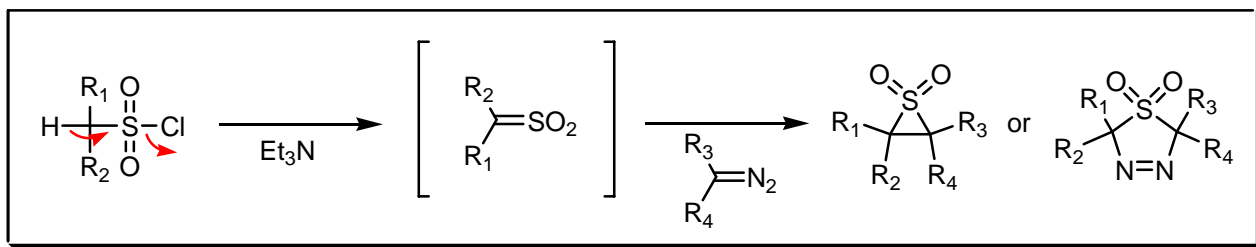
## COMMENTS :

# STAUDINGER – PFENNINGER THIIRANE DIOXIDE SYNTHESIS

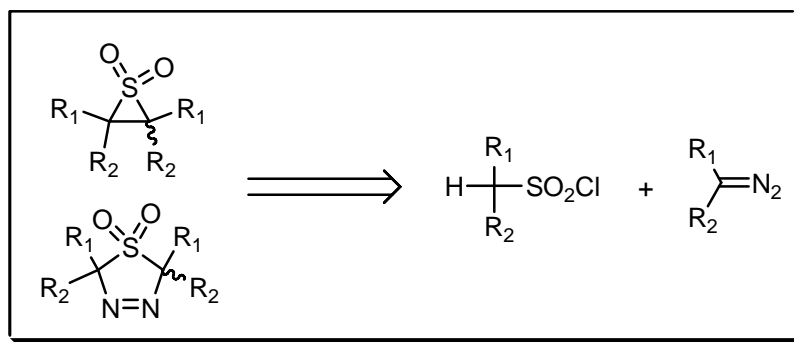
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The thiirane dioxide episulfone synthesis by reaction of diazomethane with sulfenes or  $\text{SO}_2$ .

## REFERENCES :

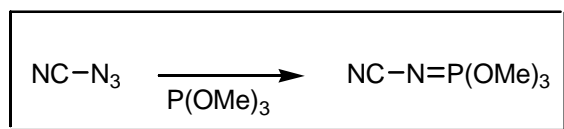
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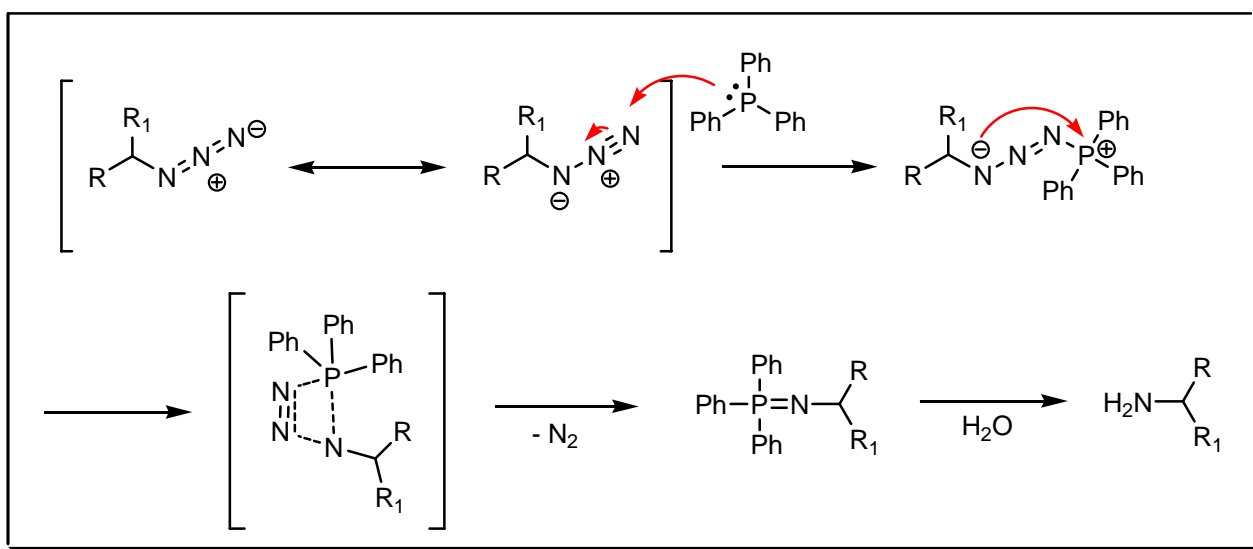
COMMENTS :

## STAUDINGER AZIDE REDUCTION

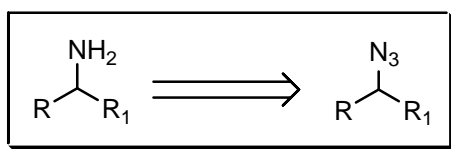
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The conversion of organic azides with phosphines or phosphates to iminophosphoranes and their hydrolysis to amines. **Kosower** *et al.* has published a detailed mechanistic study about how the sequence of reactants alters the course of the reaction.

REFERENCES :

March : 1219

Smith – March : 1555

Houben – Weyl : E8a, 962; E15, 872, 2349; E16a, 1279

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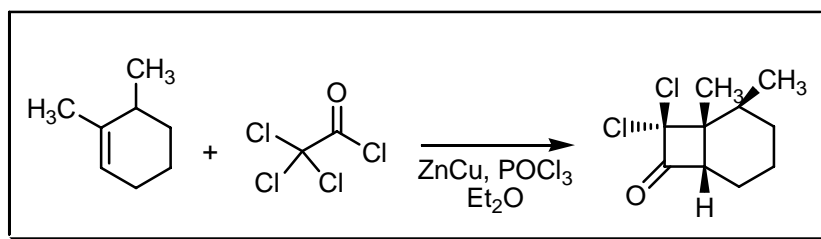
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  - 11) W.Q. Tian; Y.A. Wang, *J. Org. Chem.*, 2004, **69**, 4299.
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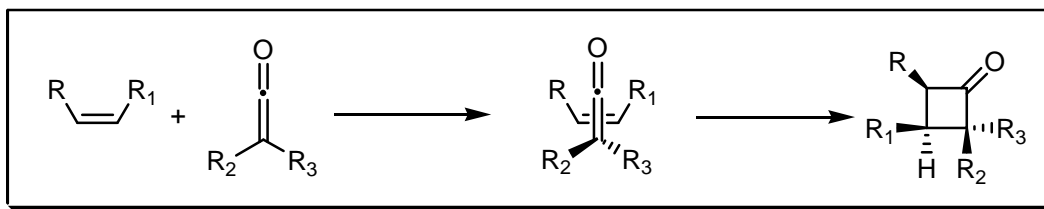
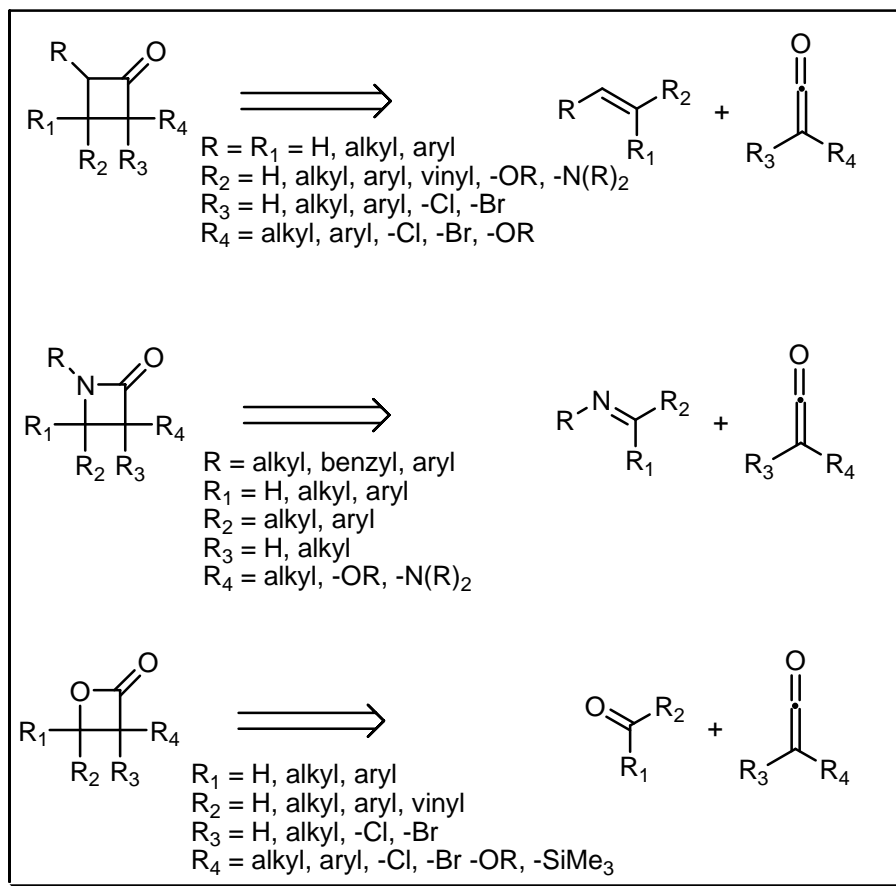
#### COMMENTS :

### STAUDINGER KETENE ADDITION

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#### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

The thermal [2+2] cycloaddition reaction between ketenes and carbon-carbon, carbon-oxygen and carbon-nitrogen double bonds. The reaction of ketenes with alkenes is assumed to occur *via* a concerted mechanism, the path of approach between the reactants is orthogonal.

## REFERENCES :

March : 856, 858

Smith – March : 1077

Smith : 1183

Smith 2<sup>nd</sup> : 979

Org. React. : **45**, 159

Org. Synth. : **4**, 39; **20**, 47; **21**, 13, 64; **33**, 29; **45**, 50; **55**, 32; **68**, 32

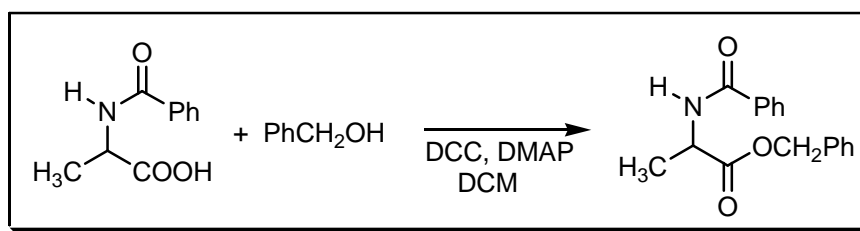
Org. Synth. Coll. Vol. : **1**, 330; **3**, 164, 356, 508; **4**, 348; **5**, 679; **6**, 210; **8**, 82

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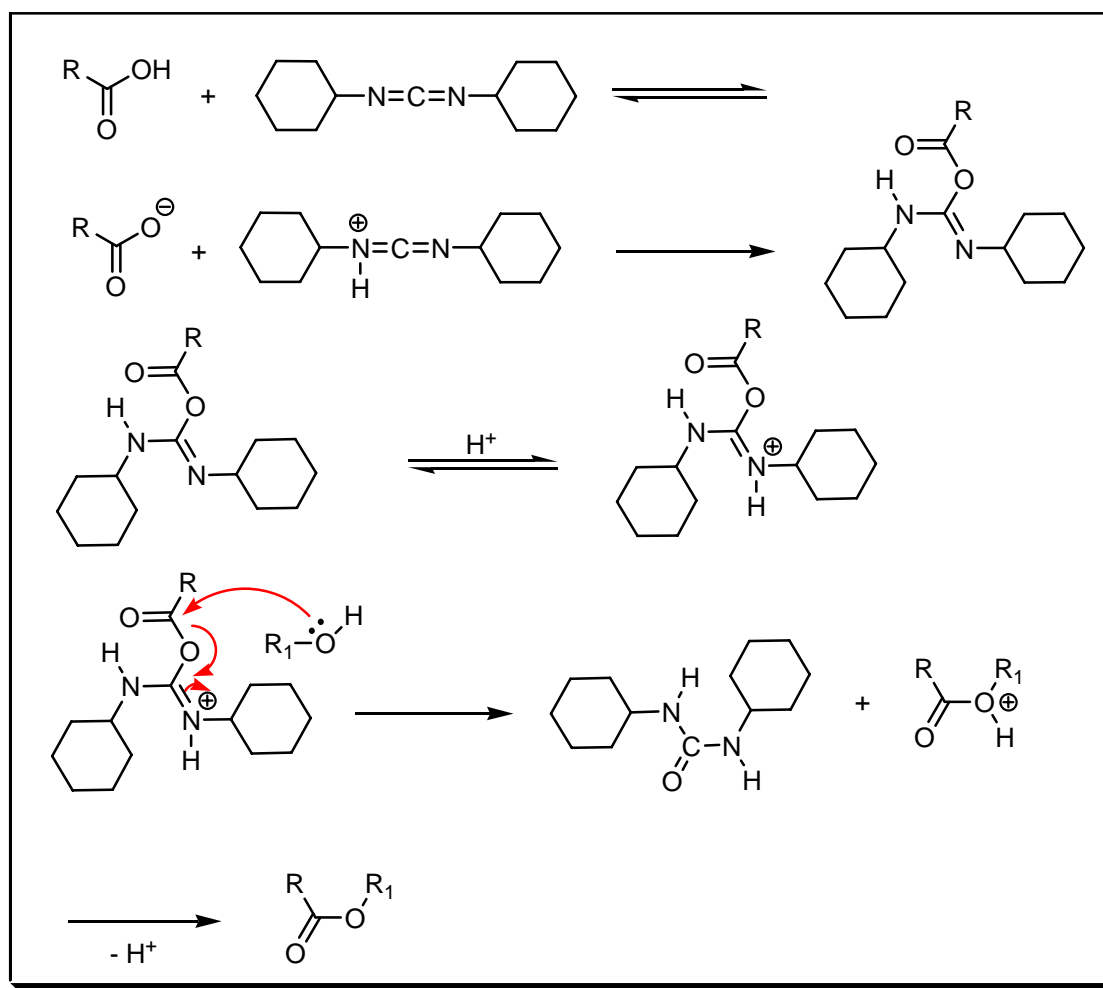
## COMMENTS :

## STEGLICH – HASSNER ESTERIFICATION

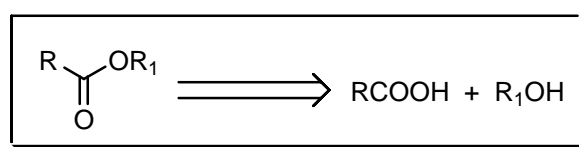
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The direct room temperature esterification of carboxylic acids with alcohols, including *tert*-alcohols with the help of dicyclohexylcarbodiimide (DCC) and 4-dialkylaminopyridine (DMAP) catalysts. The *intramolecular* version uses an additional reagent DMAP·HCl and is called the **Keck** macrolactonisation. See also **Corey – Nicolaou**, **Diels – Alder**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Kita**, **Masamune**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolakiewicz**, **Wittig**, **Yamaguchi**, and **Yamamoto** macrolactonisation reactions.

## REFERENCES :

March : 395

Smith – March : 485

Org. Synth. : 63, 183

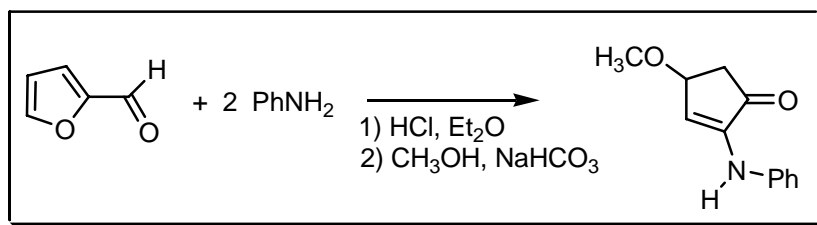
Org. Synth. Coll. Vol. : 7, 93

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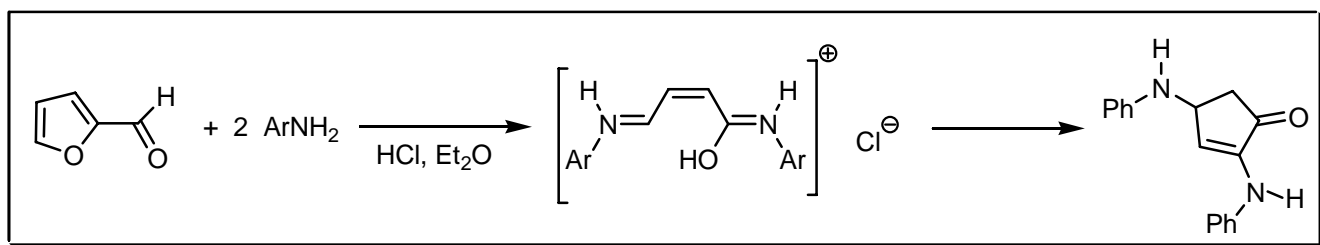
## COMMENTS :

## STENHOUSE CLEAVAGE

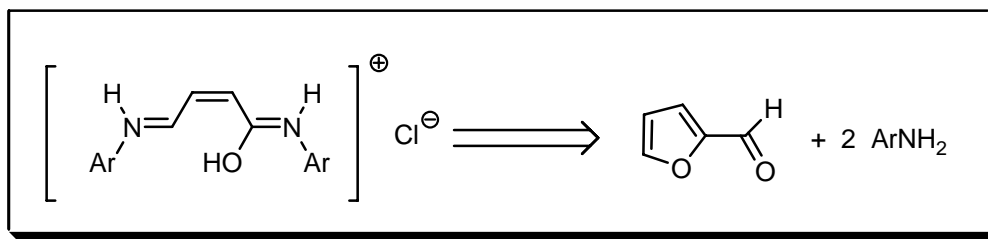
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

This reaction includes the cleavage of 2-furaldehydes (other aldehydes can also be used) in the presence of acid and aromatic amines to yield anils. These salts also react with piperidines, dimethyl malonate anions and methanol. The intermediate salts are called **Stenhouse** salts. Some of the **Stenhouse** salts show reverse photochromism.

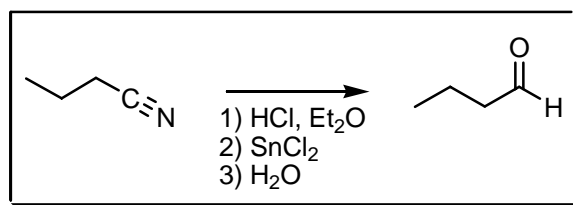
## REFERENCES :

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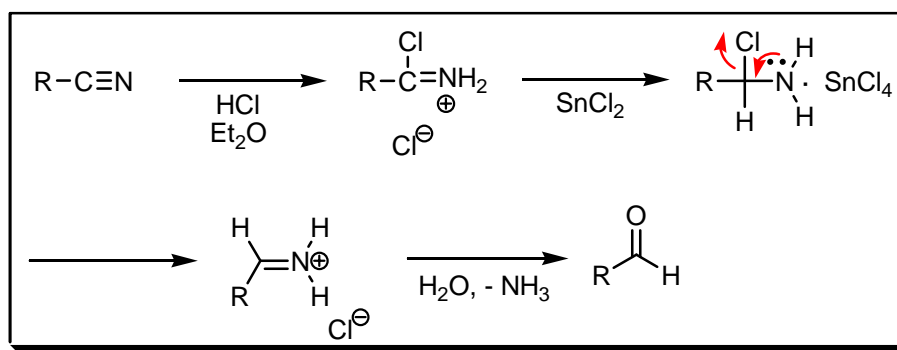
## COMMENTS :

## STEPHEN ALDEHYDE SYNTHESIS

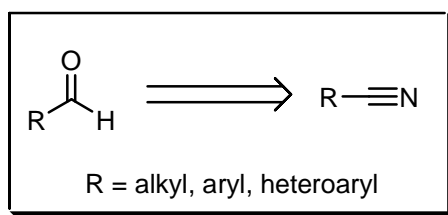
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

This synthesis comprises the production of aldehydes from nitriles by treatment with anhydrous stannous chloride dissolved in diethyl ether saturated with hydrogen chloride. The resulting aldimine –  $SnCl_4$  complex is hydrolysed with warm water. See also **Sonn – Müller** reaction.

## REFERENCES :

March : 919

Smith – March : 1204

Smith : 470

Smith 2<sup>nd</sup> : 406

Houben – Weyl : 7/1, 301; E3, 485

Org. React. : 8, 246

Org. Synth. : 23, 63

Org. Synth. Coll. Vol. : 3, 626

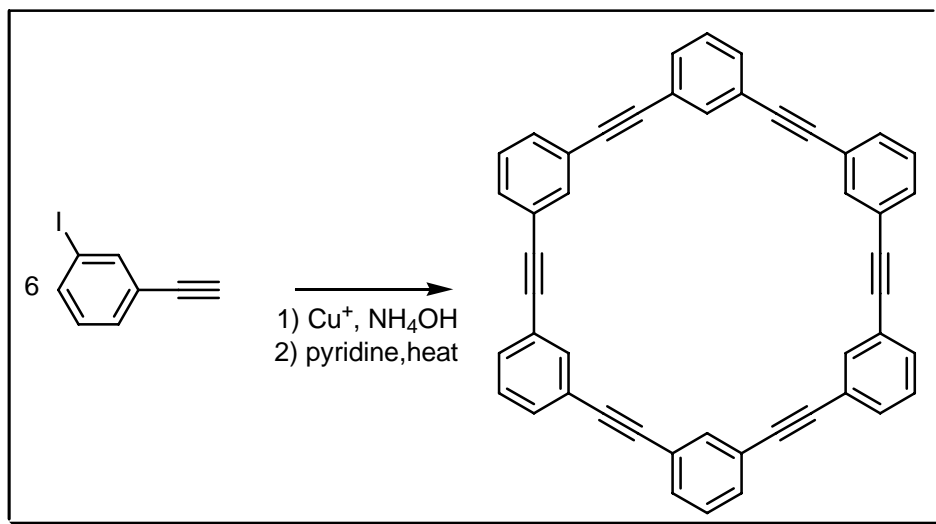
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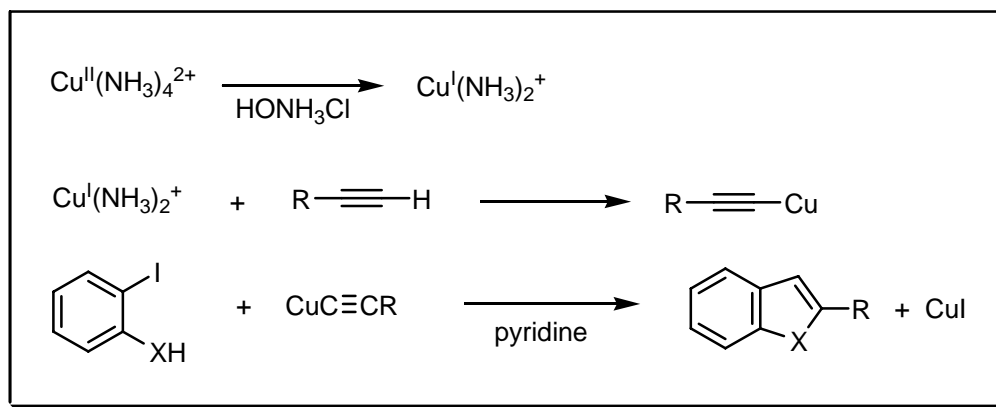
COMMENTS :

## STEPHENS – CASTRO SYNTHESIS

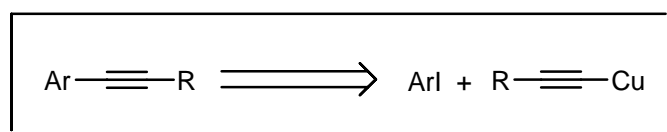
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

The reaction between unactivated cuprous acetylides and aryl halides. See also **Cadiot – Chodkiewicz – Eglington**, **Rosenmund – von Braun** and **Sonogashira – Hagihara** reactions.

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## REFERENCES :

March : 662

Smith – March : 868

Smith 2<sup>nd</sup> : 1124

Org. React. : **22**, 253

Org. Synth. : **52**, 128; **72**, 104

Org. Synth. Coll. Vol. : **6**, 916; **9**, 117

Science of Synthesis : **10**, 20

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1) R.D. Stephens; C.E. Castro, *J. Org. Chem.*, 1963, **28**, 3313.

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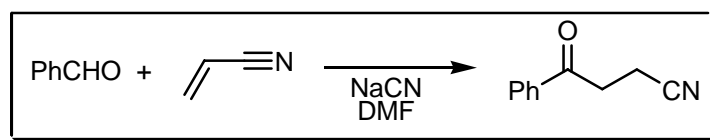
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## COMMENTS :

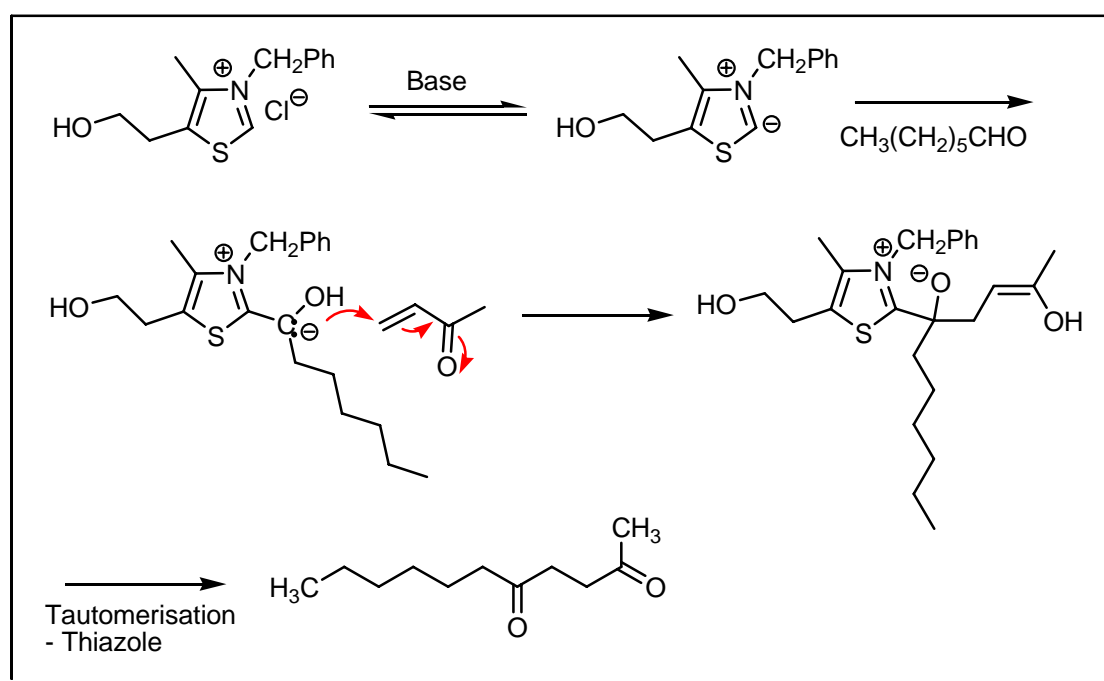
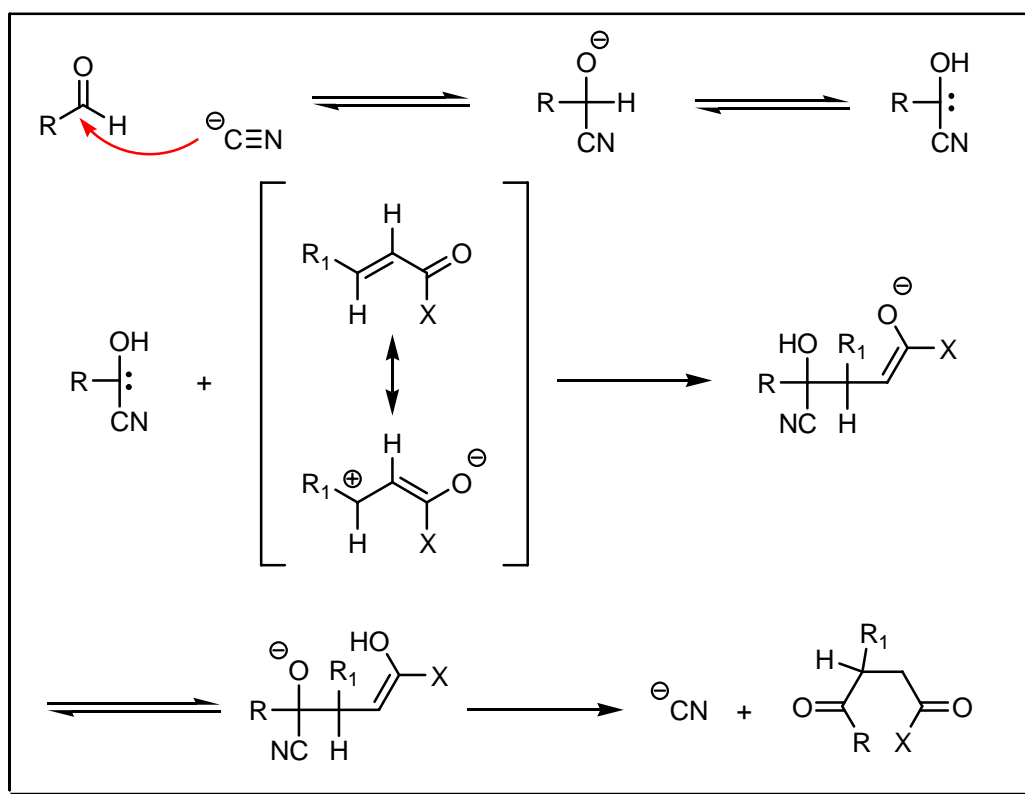
## STETTER 1,4-DICARBONYL SYNTHESIS

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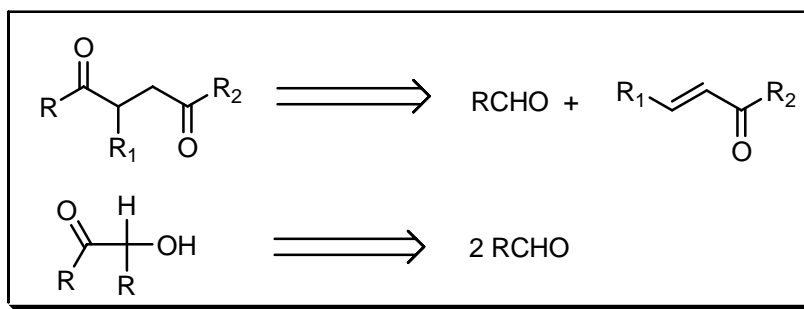
### EXAMPLE :



# MECHANISM :



## DISCONNECTION :



## NOTES :

The **Michael** addition (benzoin condensation) of aromatic or heterocyclic aldehydes (*via* cyanohydrins) to  $\alpha,\beta$ -unsaturated systems in aprotic solvents. Also the addition of aliphatic aldehydes catalysed by thiazolium ylids. Highly enantioselective catalytic *intramolecular Stetter* reactions are reported in the literature.

## REFERENCES :

**March** : 471, 806, 970

**Smith – March** : 1243

**Houben – Weyl** : **E5**, 453

**Org. React.** : **40**, 407

**Org. Synth.** : **62**, 170; **65**, 26

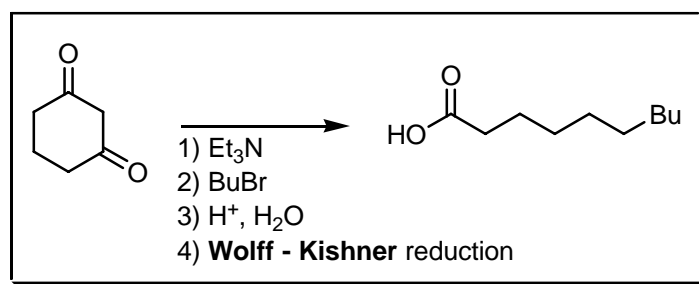
**Org. Synth. Coll. Vol.** : **7**, 95; **8**, 620

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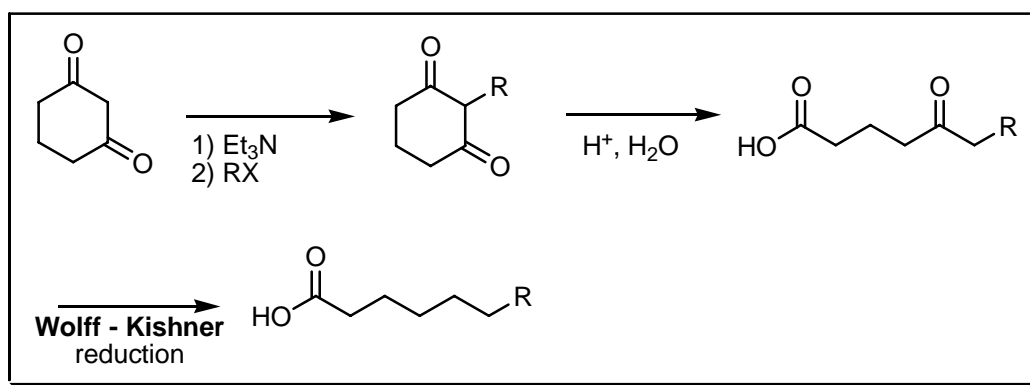
## COMMENTS :

# STETTER CARBOXYLIC ACID SYNTHESIS

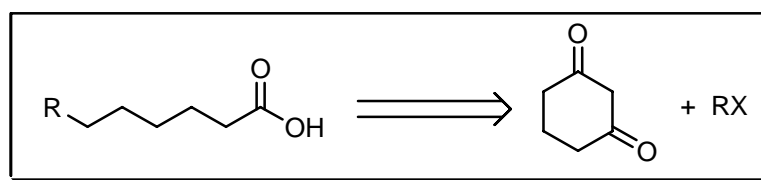
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of carboxylic acids using C-alkylation of 1,3-cyclohexanedione in the 2-position, followed by acidic treatment and reduction of the ketone group to afford the carboxylic acid.

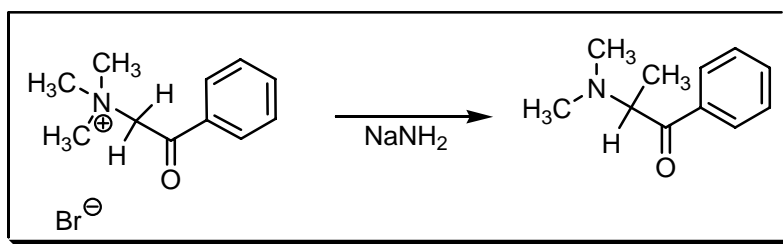
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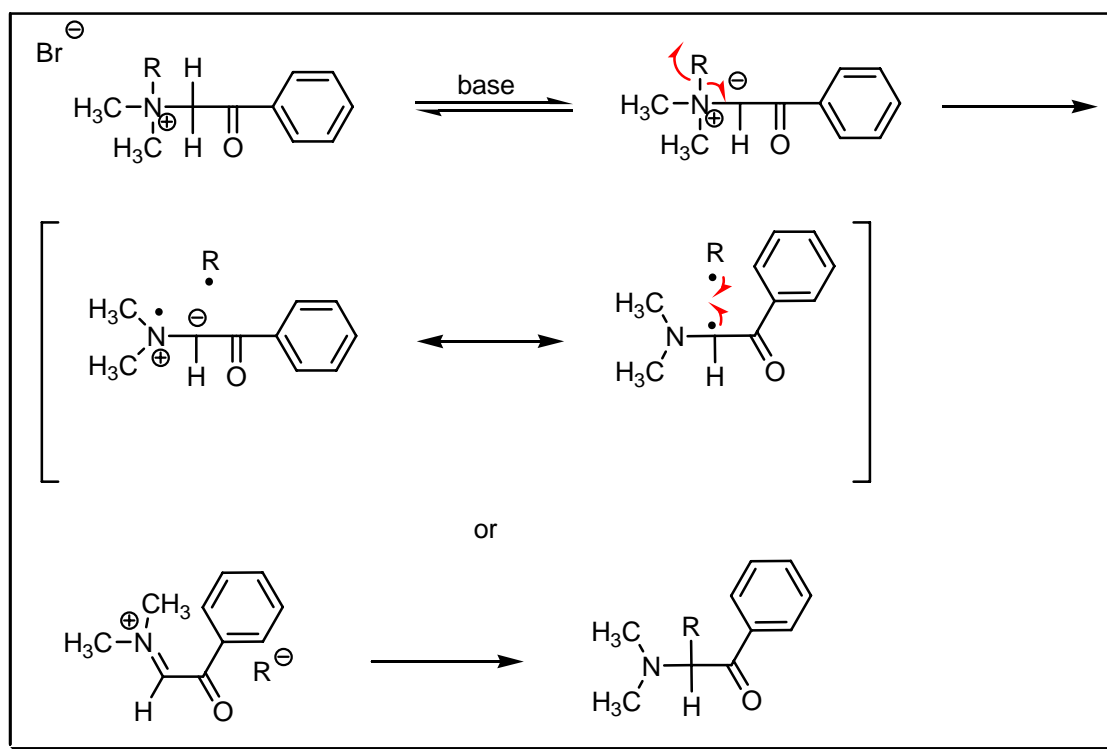
## COMMENTS :

# STEVENS REARRANGEMENT

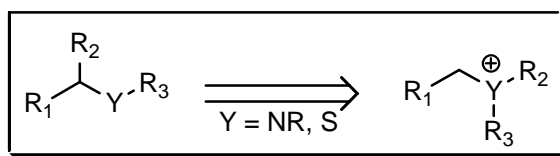
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Quaternary ammonium or sulfonium salts give amino ketones or sulfides on treatment with base. The reaction proceeds through hydrogen abstraction from the ammonium salt to the ylid. A N  $\rightarrow$  C 1,2-benzyl shift occurs *via* a carbanionic intermediate to give the rearranged amine. It is still under debate if the reaction proceeds through a ion pair or radical pair in the solvent cage. A third possibility (a concerted 1,2-shift) is mentioned in Smith – March. See also **Meisenheimer**, **Sommelet – Hauser** and **[1,2]-Wittig** rearrangement reactions.

## REFERENCES :

March : 673

Smith – March : 878, 1419, 1454

Smith : 809

Smith 2<sup>nd</sup> : 324, 677

Houben – Weyl : **13/1**, 230; **E5**, 816; **E7b**, 179, 750; **E8b**, 855; **E11**, 1414, 1457; **E16d**, 1149; **E19b**, 271, 1582

Org. React. : **8**, 271; **18**, 403

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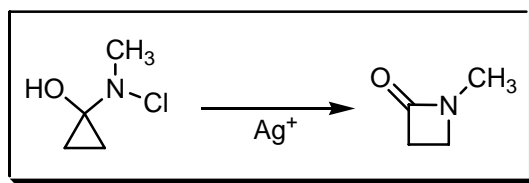
- 1) T.S. Stevens; E.M. Creighton; A.B. Gordon; M. MacNicol, *J. Chem. Soc.*, 1928, 3193.
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## COMMENTS :

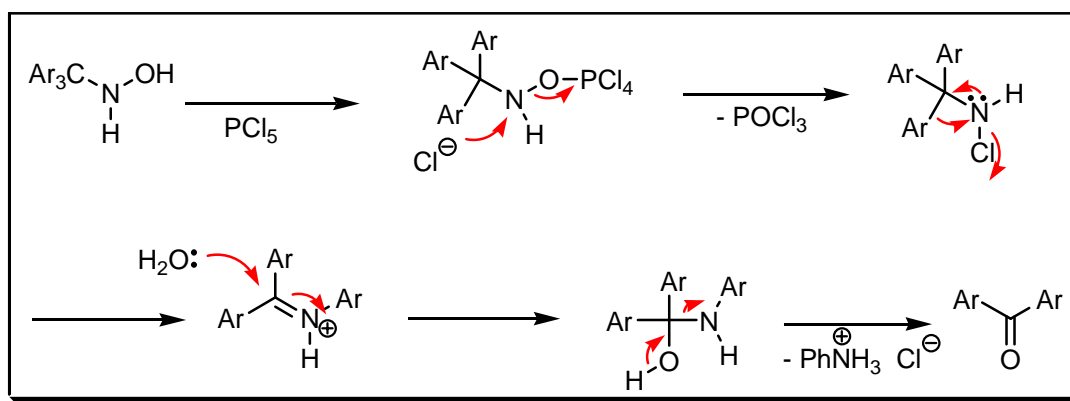
## STIEGLITZ REARRANGEMENT

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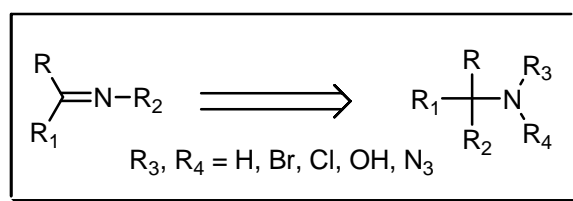
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The rearrangement or ring enlargement of amines, normally containing aromatic residues, *via* nitrenes using phosphorous pentachloride or lead tetraacetate. See also **Beckmann** rearrangement, **Curtius** rearrangement, **Hofmann** rearrangement, **Lossen** rearrangement, **Schmidt** rearrangement, **Tiemann** rearrangement and **Wolff** reaction.

## REFERENCES :

March : 1097

Smith – March : 1416

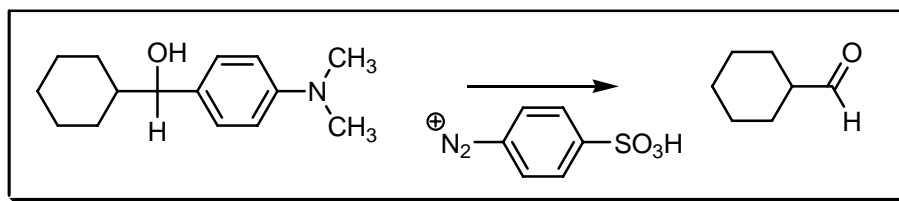
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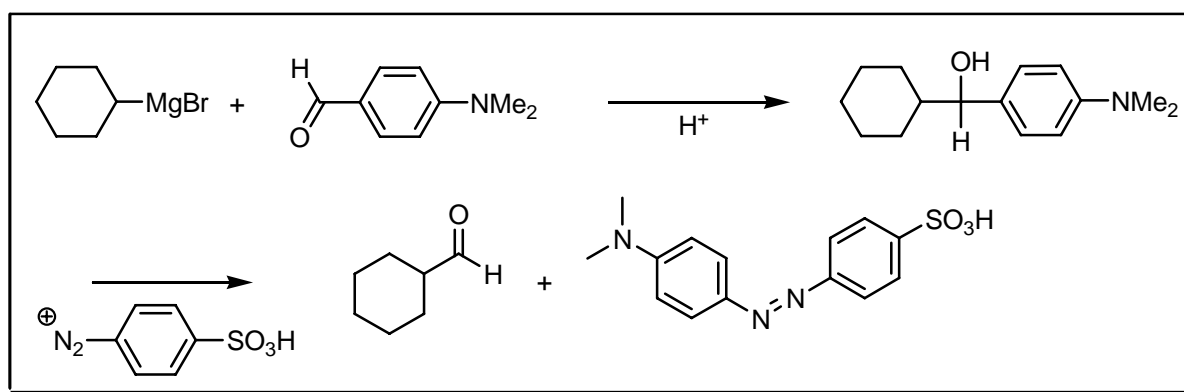
COMMENTS :

## STILES – SISTI FORMYLATION

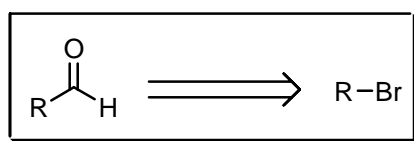
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The synthesis of aldehydes by formylation of **Grignard** reagents with *p*-dimethylaminobenzaldehyde and a diazonium salt.

## REFERENCES :

Org. Synth. : **44**, 4

Org. Synth. Coll. Vol. : **5**, 46

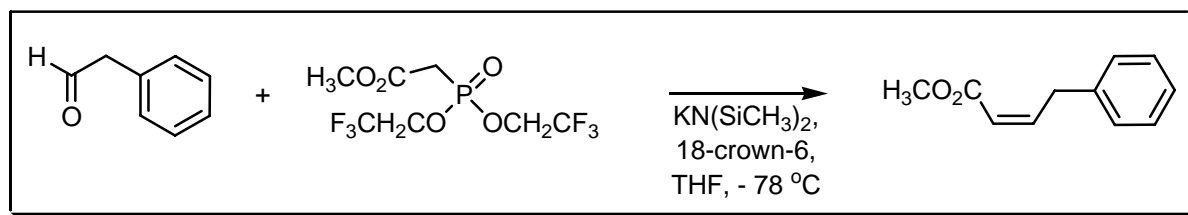
1) M. Stiles; A.J. Sisti, *J. Org. Chem.*, 1960, **25**, 1691.

2) A.J. Sisti; J. Burgmaster; M. Fudim, *J. Org. Chem.*, 1962, **27**, 279.

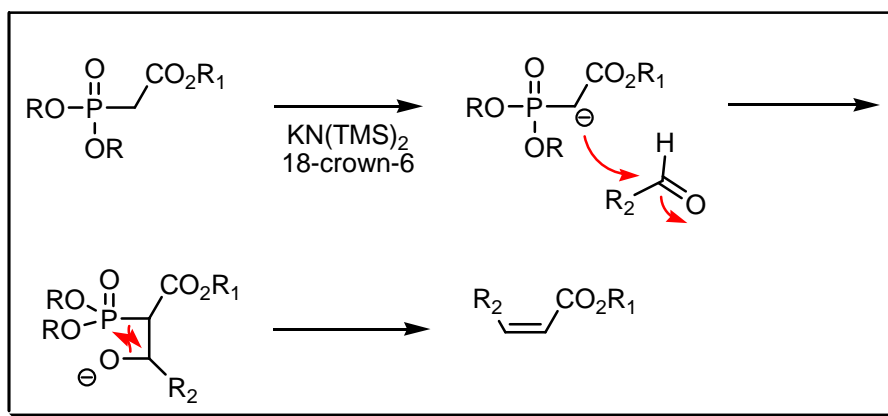
## COMMENTS :

## STILL – GENNARI REACTION

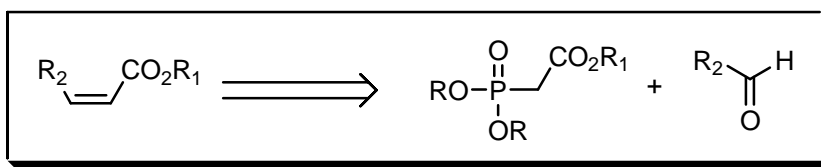
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

This is the structural variant of the **Horner – Wadsworth – Emmons** reaction. It makes *cis*-substituted acrylic esters and *Z*-substituted methacrylic esters accessible. See also **Corey – Kwiatkowski**, **Eastwood**, **Horner – Wadsworth – Emmons**, **Julia – Paris – Kocienski – Lythgoe**, **Krief – Reich – Chow**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Nysted**, **Paquette**, **Petasis** reaction, **Peterson**, **Ramberg – Bäcklund**, **Takeda**, **Tebbe** and **Wittig** reactions.

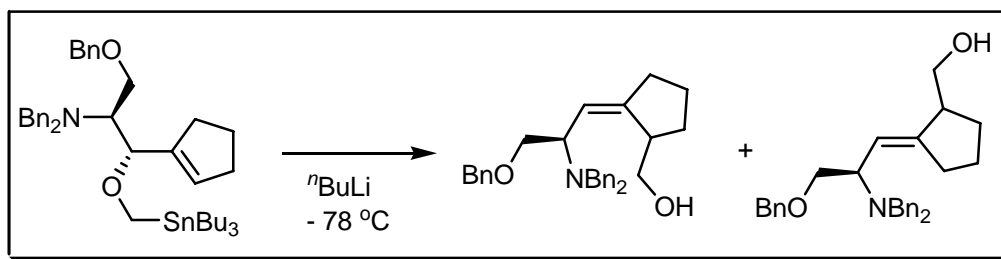
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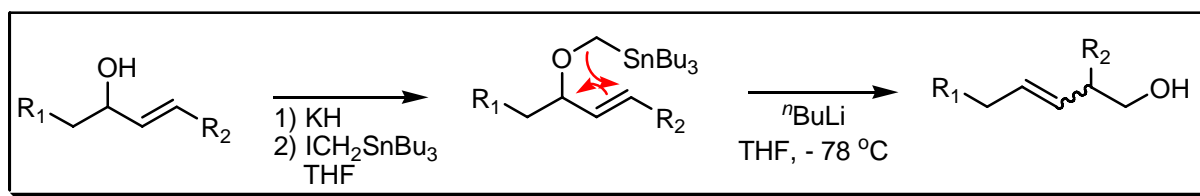
## COMMENTS :

## STILL – WITTIG REARRANGEMENT

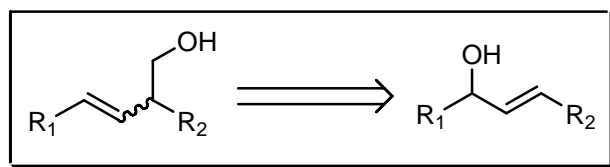
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The general [2,3]-sigmatropic rearrangement has been studied extensively, providing detailed accounts of how substitution of the allylic ether precursor determines the stereochemical outcome of the rearrangement in a predictable way. While (*E*)- or (*Z*)-alkene selectivity of [2,3]-sigmatropic rearrangements can be predicted by conformational analysis of the expected transition state, little has been demonstrated regarding solvent effects. See also [2,3]-Wittig rearrangement.

## REFERENCES :

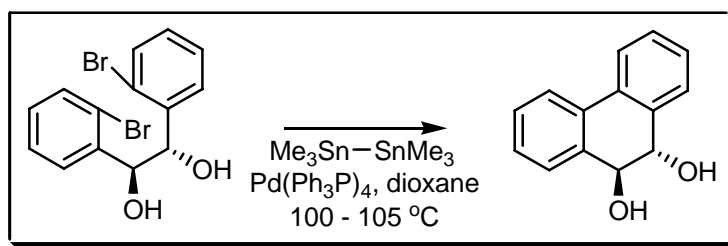
Org. React. : 46, 105

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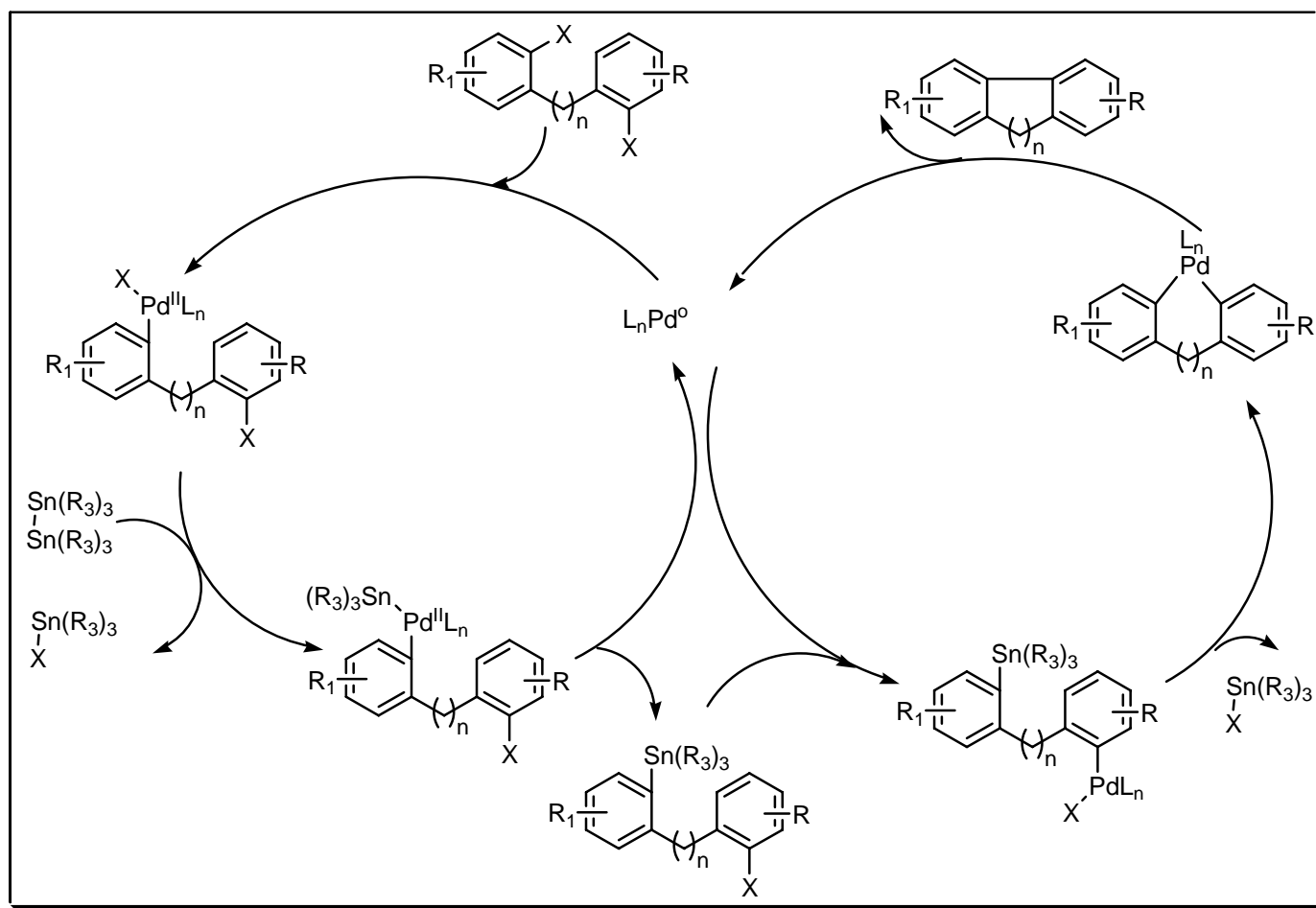
## COMMENTS :

## STILLE – KELLY COUPLING

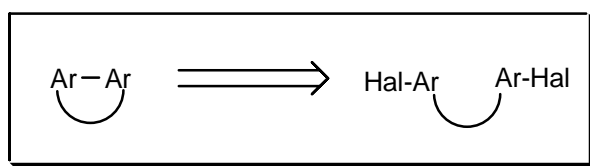
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

This is the palladium-catalysed *intramolecular* aryl dihalide cyclisation (also other aromatic compounds like thiophenes react in a similar way.) using ditin compounds. The mechanism consists of two connected catalytic cycles. See also **Grigg** and **Stille – Migita – Kosugi** reactions.

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## REFERENCES :

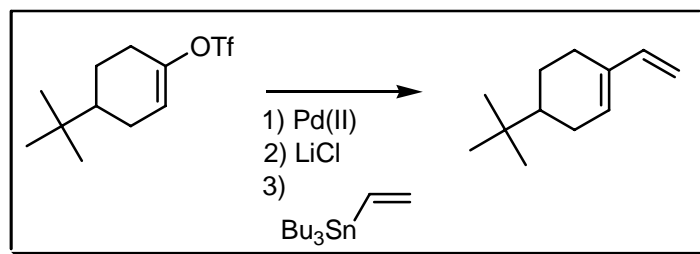
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## COMMENTS :

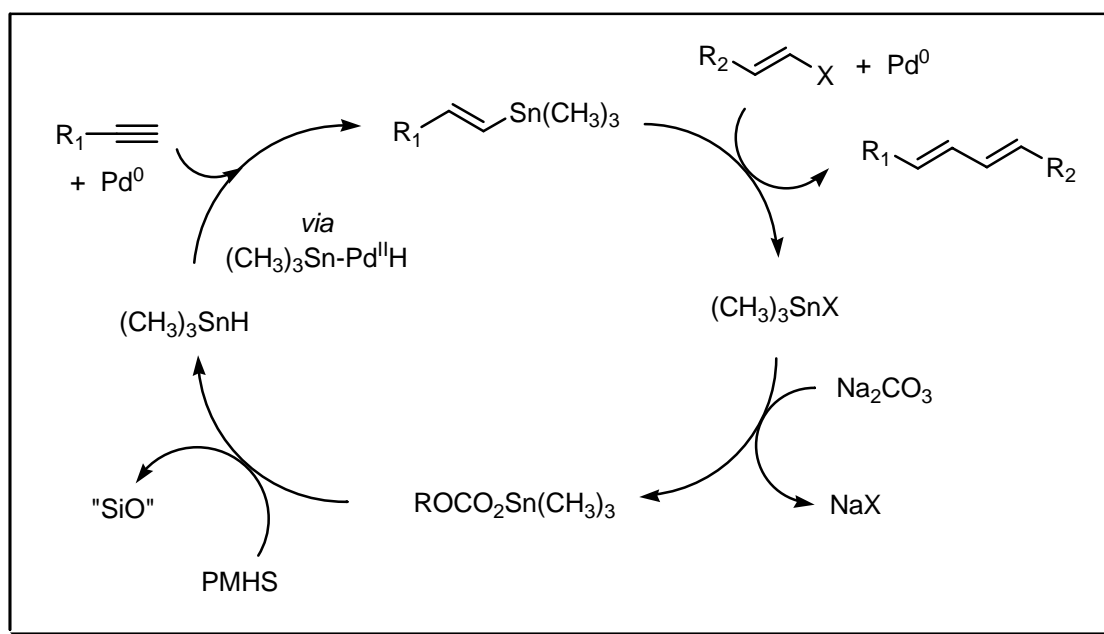
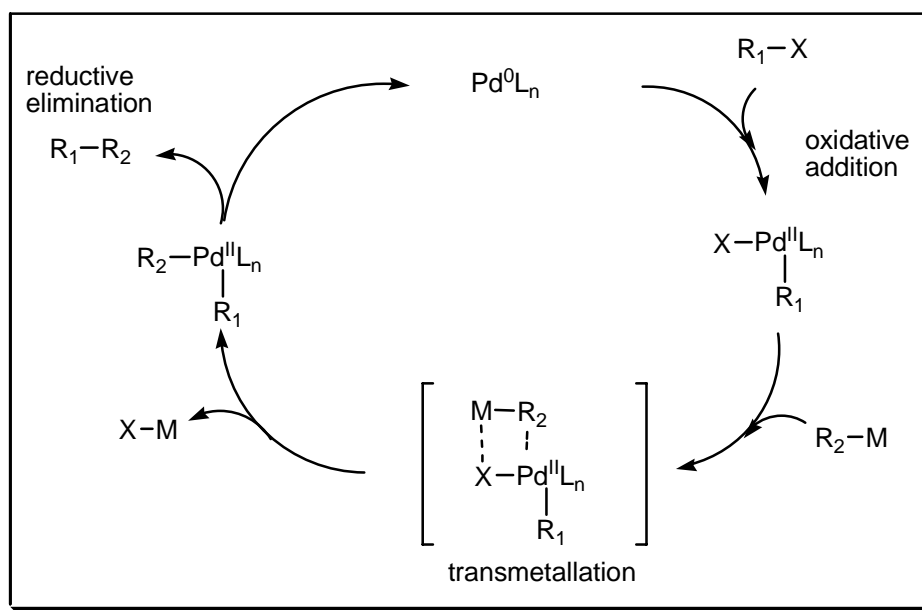
## STILLE – MIGITA – KOSUGI COUPLING

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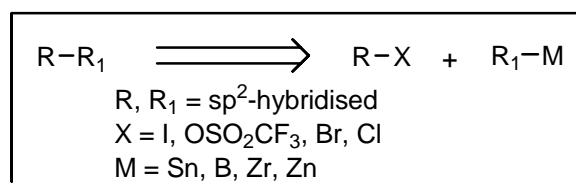
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The coupling of organotin (expensive and highly toxic) reagents (and Pd catalyst) with aryl or vinyl halides or triflates, acyl chlorides or allyl acetates. Tandem hydrostannylation and **Stille** coupling provide a way to make the reaction catalytic in tin. The reaction has an exceptional tolerance of functional groups. The transmetallation step is supposed to be the rate-determining step. Dramatic rate enhancements have been observed with readily dissociable ligands, like  $AsPh_3$  and  $P(furyl)_3$ . **Fu et al.** has developed the use of aryl chlorides in the **Stille – Migata – Kosugi** coupling.

For more on the mechanism see **Espinet** and **Echavarren**. See also **Corey – Nicolaou**, **Diels – Alder**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Kita**, **Masamune**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi** (**Takai – Utimoto**), **Raphael**, **Roush**, **Růžicka** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Stille – Kelly**, **Story**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolkiewicz**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

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#### REFERENCES :

**Smith – March** : 931

**Smith** : 1364

**Smith 2<sup>nd</sup>** : 1122, 1127

**Org. React.** : **50**, 1

**Org. Synth.** : **67**, 86; **71**, 97, 125; **77**, 135

**Org. Synth. Coll. Vol.** : **8**, 268; **9**, 553, 741; **10**, 2376

**Science of Synthesis** : **1**, 801; **9**, 258, 370, 527

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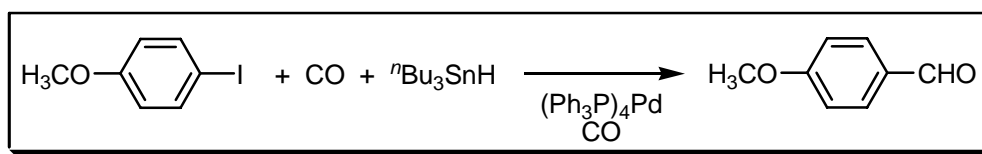
- 1) W.J. Scott; G.T. Crisp; J.K. Stille, *J. Am. Chem. Soc.*, 1984, **106**, 4630.
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#### COMMENTS :

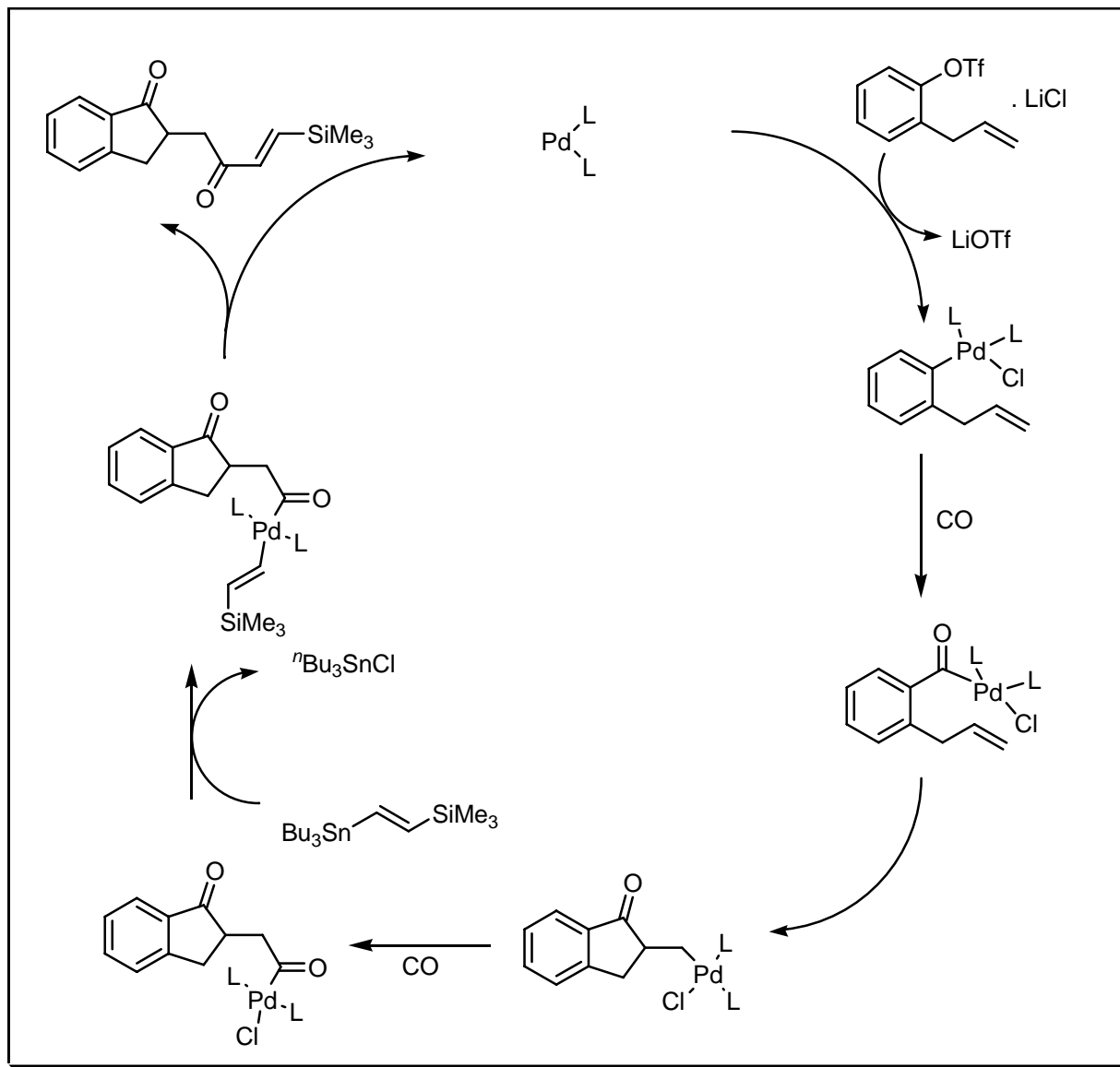


# STILLE CARBONYL SYNTHESIS

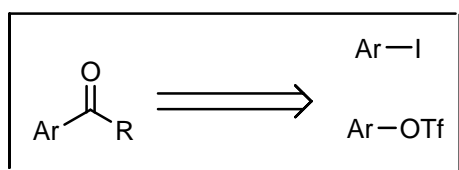
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



**NOTES :**

The synthesis of aryl ketones or aldehydes from aryl triflates or iodides and organo stannanes in the presence of CO and a palladium catalyst. See also **Yamamoto** ketone synthesis.

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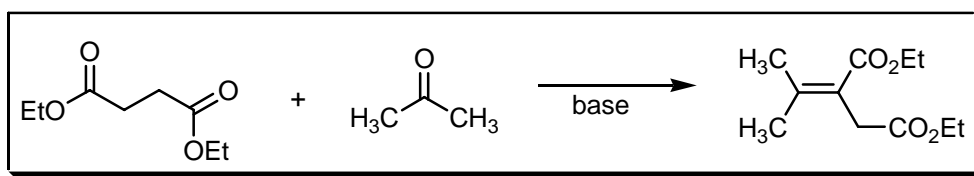
**REFERENCES :**

Org. Synth. : **68**, 116

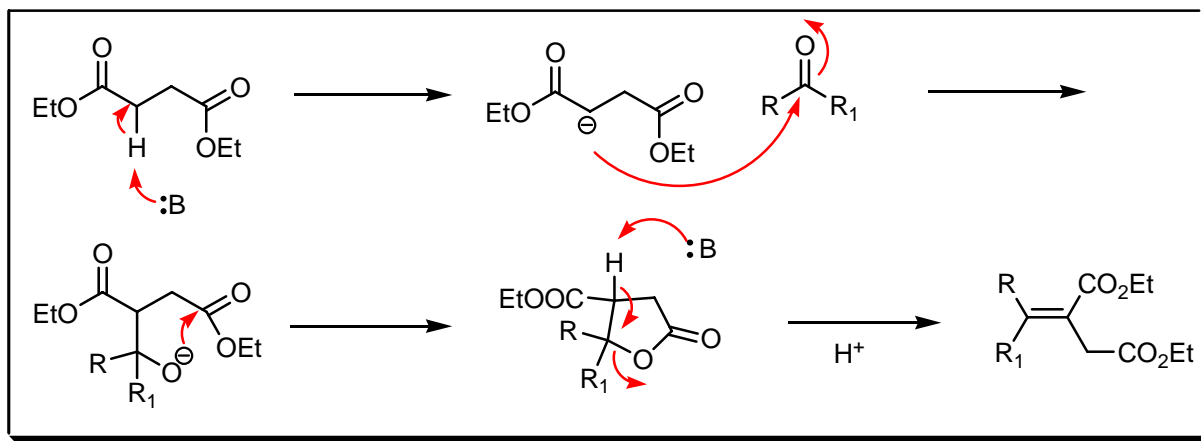
Org. Synth. Coll. Vol. : **8**, 97

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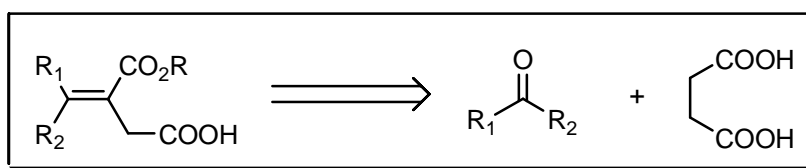
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  - 6) S.R. Dubbaka; P. Steunenbergh; P. Vogel, *Synlett*, 2004, 1235.
- 

**COMMENTS :****STOBBE CONDENSATION****EXAMPLE :**

## MECHANISM :



## DISCONNECTION :



## NOTES :

The base-catalysed condensation of aldehydes or ketones with an ester of succinic acid to give alkylidenesuccinic acids. If the ketone has an  $\alpha$ -hydrogen atom an alkenylsuccinic acid may be obtained. The method enables a propionic acid residue to be introduced at the site of a carbonyl group in a molecule. See also **Claisen – Geuther** and **Haworth** reactions.

## REFERENCES :

March : 944

Smith – March : 1224

Smith : 901

Smith 2<sup>nd</sup> : 753

Houben – Weyl : 5/1b, 865; 5/1c, 536; E3, 645; E5, 412, 726; E6a, 953; E6b, 111

Org. React. : 6, 1; 8, 67

Org. Synth. : 9, 38; 30, 18

Org. Synth. Coll. Vol. : 1, 252; 4, 132

Science of Synthesis : 10, 67, 479, 719

1) H. Stobbe, *Ber. Dtsch. Chem. Ges.*, 1893, **26**, 2312.

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6) A.M.A. Asiri; A. Cleaves; H.G. Heller, *J. Chem. Soc., Perkin Trans. 1*, 2000, 2741.

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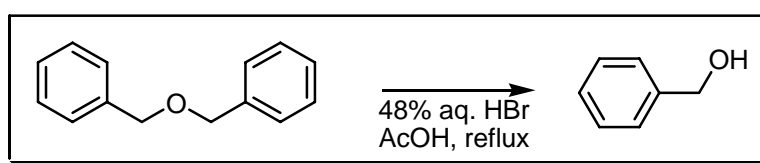
**COMMENTS :**

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**STOERMER DEALKYLATION**

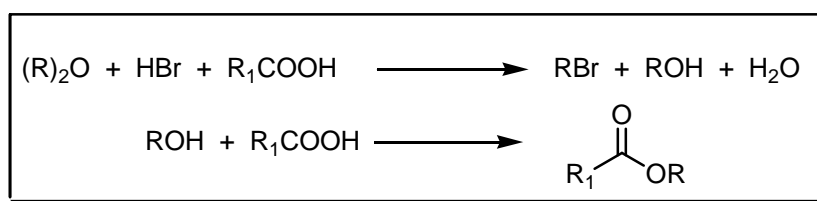
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**EXAMPLE :**



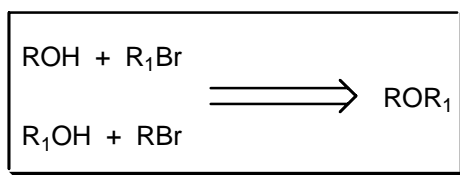
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**MECHANISM :**



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**DISCONNECTION :**



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**NOTES :**

The dealkylation of alkylaromatic and dialkyl ethers is effected by the action of hydrogen bromide in acetic acid. See also **Gustus** cleavage, **Mann** dealkylation and **Prey** reaction.

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**REFERENCES :**

**March** : 433

**Smith – March** : 465, 519

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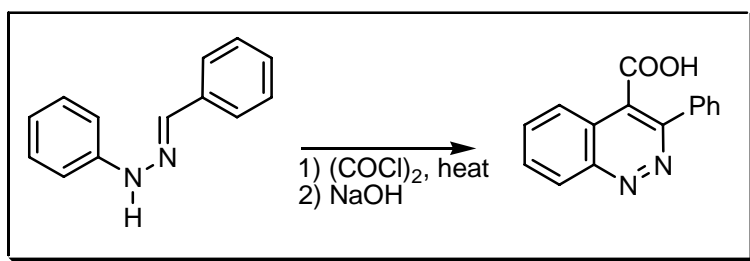
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- 2) R.L. Burwell, jr., *Chem. Rev.*, 1954, **54**, 615.  
3) M.V. Bhatt; S.U. Kulkarni, *Synthesis*, 1983, 249.  
4) M. Tiecco, *Synthesis*, 1988, 749.

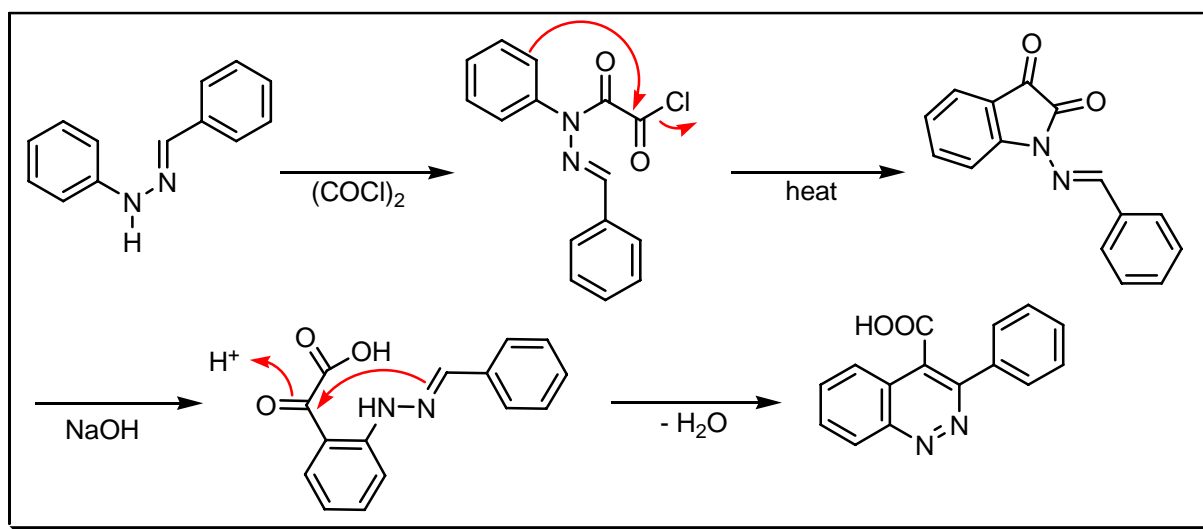
COMMENTS :

## STOLLÉ – BECKER SYNTHESIS

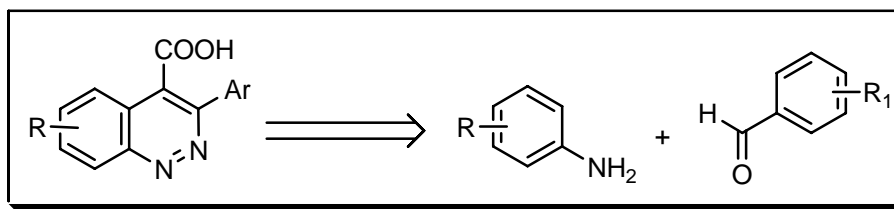
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

Benzaldehyde-phenylhydrazone on treatment with oxalyl chloride yields an oxalylhydrazine which at 150 °C cyclises to *N*-(benzylidene-amino)-isatin. The latter on treatment with aqueous sodium hydroxide yields 3-phenylcinnoline-4-carboxylic acid. See also **Borsche – Koelsch**, **Neber – Bossell**, **von Richter** cinnoline and **Widman – Stoermer** reactions.

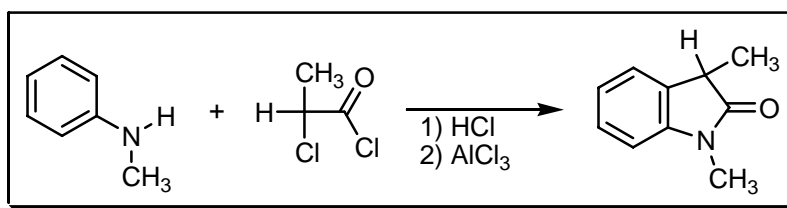
## REFERENCES :

- 1) R. Stollé; W. Becker, *Ber. Dtsch. Chem. Ges.*, 1924, **57**, 1123.
- 2) K. Schofield; J.C.E. Simpson, *J. Chem. Soc.*, 1945, 512.

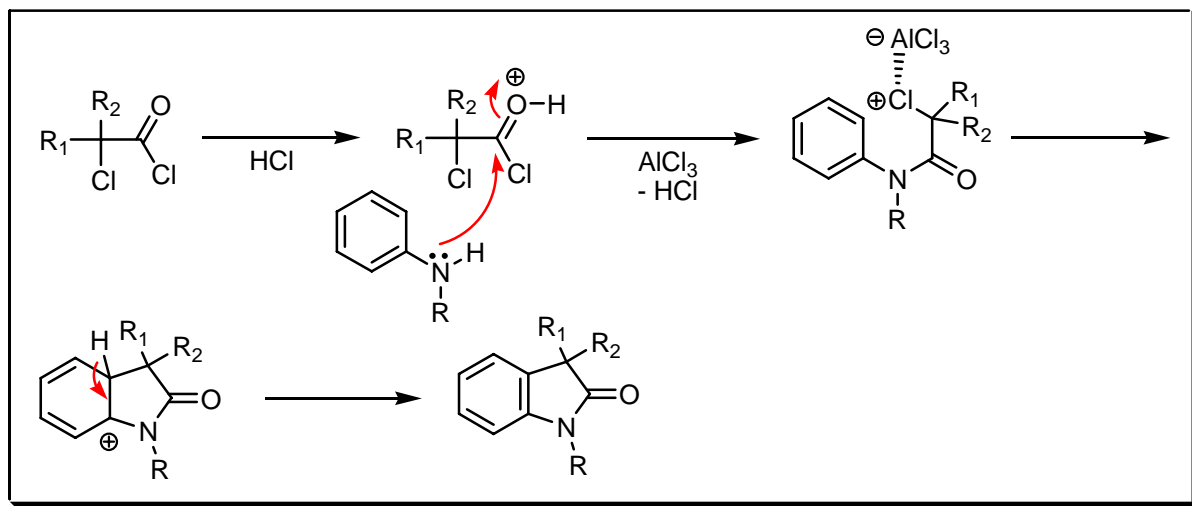
## COMMENTS :

## STOLLÉ SYNTHESIS

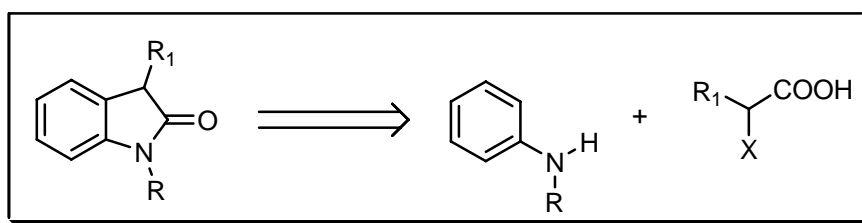
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

In the presence of dry aluminium chloride aniline reacts with  $\alpha$ -halogenocarboxylic acid chlorides to afford oxindoles. If oxalyl chloride is used, the intermediate can be cyclised in the presence of a Lewis acid to afford the isatin. See also **von Baeyer** oxindole, **Brunner**, **Friedel – Crafts** and **Hinsberg** reactions.

## REFERENCES :

Smith : 1346

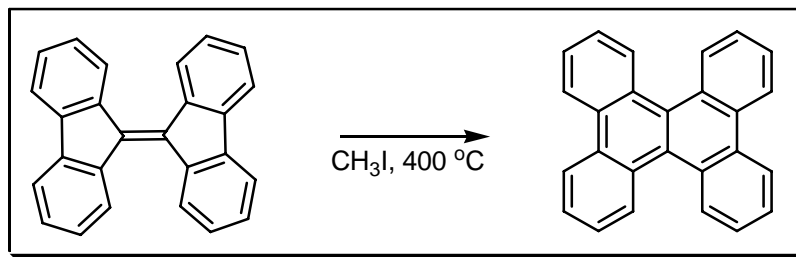
Smith 2<sup>nd</sup> : 1107

- 1) R. Stollé, *Ber. Dtsch. Chem. Ges.*, 1913, **46**, 3915.
- 2) W.C. Stumpter, *Chem. Rev.*, 1944, **34**, 393.
- 3) W.C. Stumpter, *Chem. Rev.*, 1945, **37**, 443.
- 4) A.H. Beckett; R.W. Daisley; J. Walker, *Tetrahedron*, 1968, **24**, 6093.
- 5) G. Loloïu; O. Maior, *Rev. Roum. Chim.*, 1997, **42**, 67.
- 6) J.F.M. da Silva; S.J. Garden; A.C. Pinto, *J. Braz. Chem. Soc.*, 2001, **12**, 273.

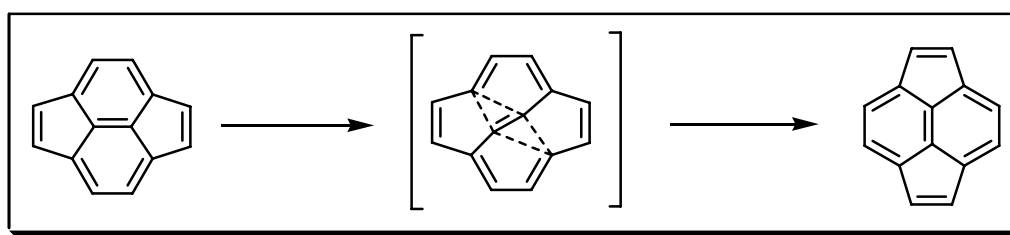
**COMMENTS :**

## STONE – WALES REARRANGEMENT

**EXAMPLE :**



**MECHANISM :**



**NOTES :**

The essence of this rearrangement is the transposition of two sp<sup>2</sup>-hybridised carbon atoms within a framework of other sp<sup>2</sup>-hybridised atoms.

**REFERENCES :**

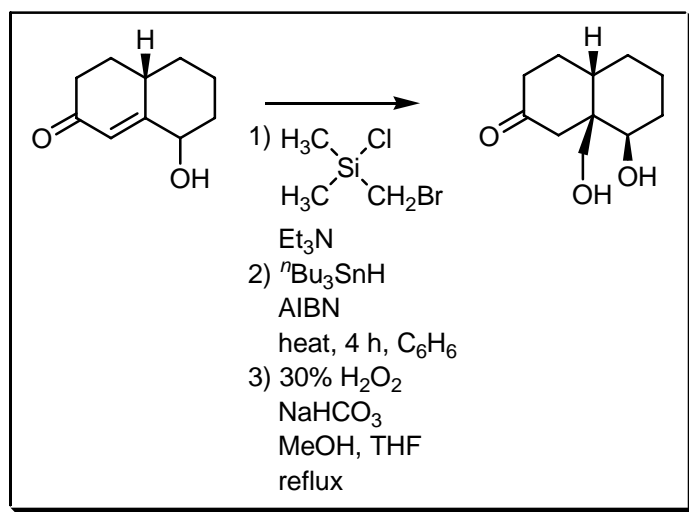
- 1) R.W. Alder; G. Whittaker, *J. Chem. Soc., Perkin Trans. 2*, 1975, 712.
- 2) A.J. Stone; D.J. Wales, *Chem. Phys. Lett.*, 1986, **128**, 501.
- 3) B.R. Eggen; M.I. Heggie; G. Jungnickel; C.D. Latham; R. Jones; P.R. Briddon, *Science*, 1996, **272**, 87.
- 4) P.I. Dosa; A. Schleifenbaum; K.P.C. Vollhardt, *Org. Lett.*, 2001, **3**, 1017.
- 5) Y. Kumeda; D.J. Wales, *Chem. Phys. Lett.*, 2003, **374**, 125.
- 6) R.W. Alder; J.N. Harvey, *J. Am. Chem. Soc.*, 2004, **126**, 2490.

**COMMENTS :**

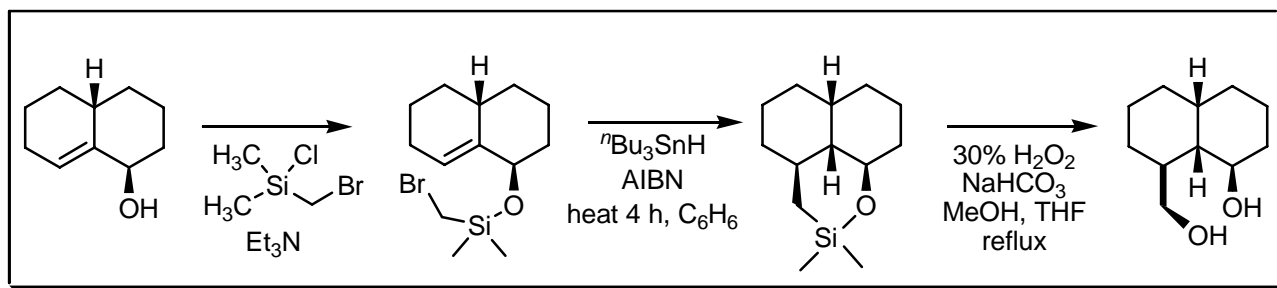


## STORK – NISHIYAMA RADICAL CYCLISATION

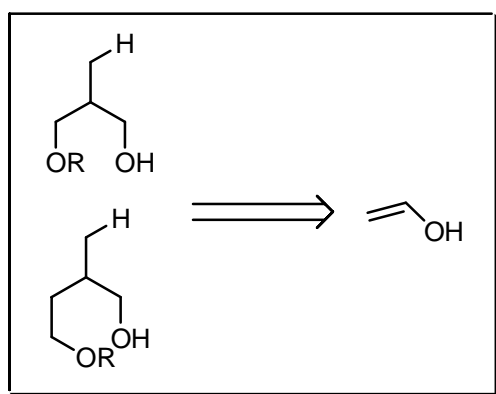
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

(Bromomethyl)dimethylsilyl allylic ethers cyclise by treatment with *n*-tributyltin hydride in a free-radical process. Oxidation with hydrogenperoxide will give 1,2 or 1,3-diols with high stereoselectivity (**Kumada – Tamao – Fleming** oxidation). See also **Kumada – Tamao – Fleming** stereoselective hydroxylation.

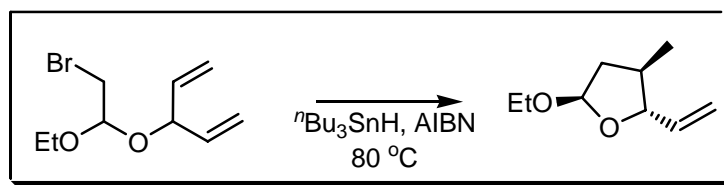
## REFERENCES :

- 1) H. Nishiyama; T. Kitajima; M. Matsumoto; K. Itoh, *J. Org. Chem.*, 1984, **49**, 2298.
- 2) G. Stork; M. Kahn, *J. Am. Chem. Soc.*, 1985, **107**, 500.
- 3) G. Stork; P.M. Sher, *J. Am. Chem. Soc.*, 1986, **108**, 303.
- 4) M. Crimmins; R. O'Mahoney, *J. Org. Chem.*, 1989, **54**, 1157.
- 5) J. Lejeune; J.Y. Lallemand, *Tetrahedron Lett.*, 1992, **33**, 2977.
- 6) V. Pedretti; J.M. Mallet; P. Sinay, *Carbohydr. Res.*, 1993, **244**, 247.
- 7) P.R. Jenkins, *Pure Appl. Chem.*, 1996, **68**, 771.

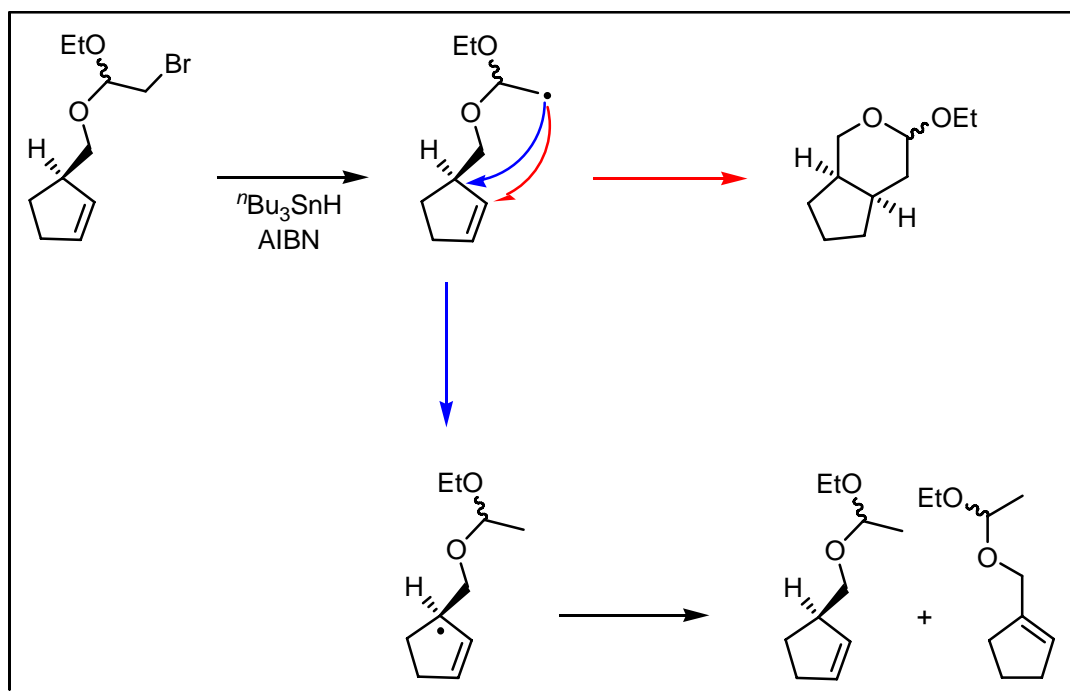
## COMMENTS :

## STORK – UENO REACTION

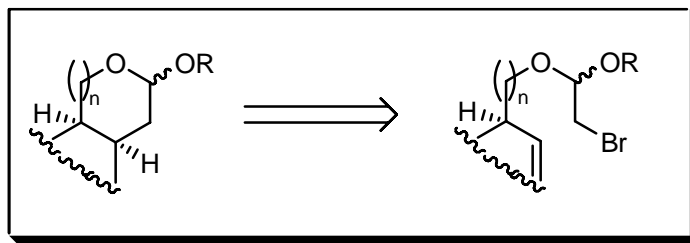
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The free-radical cyclisation of bromoacetals to construct acetals and bicyclic lactones.

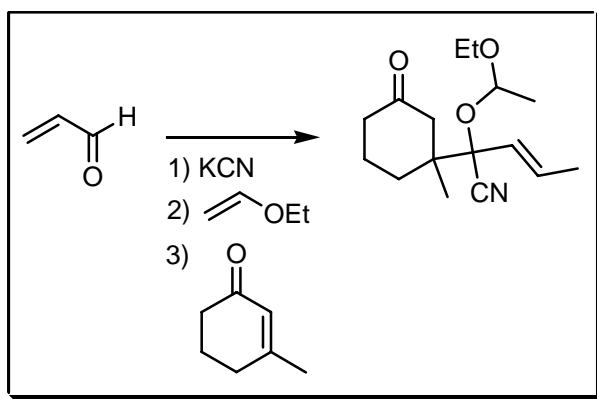
## REFERENCES :

- 1) Y. Ueno; K. Chino; M. Watanabe; O. Moriya; M. Okawara, *J. Am. Chem. Soc.*, 1982, **104**, 5564.
- 2) G. Stork; R. Mook; S.A. Biller; S.D. Rychnovsky, *J. Am. Chem. Soc.*, 1983, **105**, 3741.
- 3) G. Stork; P.M. Sher; H.-L. Chen, *J. Am. Chem. Soc.*, 1986, **108**, 6384.
- 4) Y. Ueno; K. Chino; M. Watanabe; O. Moriya; M. Okawara, *J. Chem. Soc., Perkin Trans. 1*, 1986, 1351.
- 5) G. Stork, *Bull. Chem. Soc. Jpn.*, 1988, **61**, 149.
- 6) G. Stork, *Bull. Soc. Chim. Fr.*, 1990, **127**, 675.
- 7) F. Villar; O. Equey; P. Renaud, *Org. Lett.*, 2000, **2**, 1061.

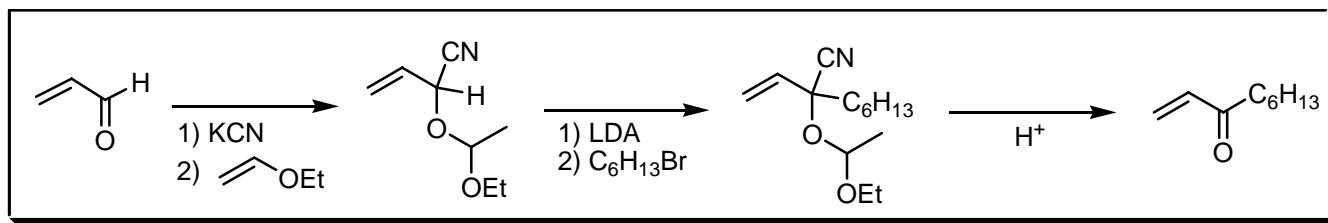
## COMMENTS :

## STORK CYANOHYDRIN ALKYLATION

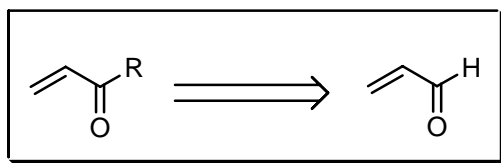
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The conversion of aldehydes to ketones via cyanohydrin derivatives by alkylation or **Michael** addition; also used with silyl ethers, dialkylaminonitriles. See also **Stetter** reaction.

### REFERENCES :

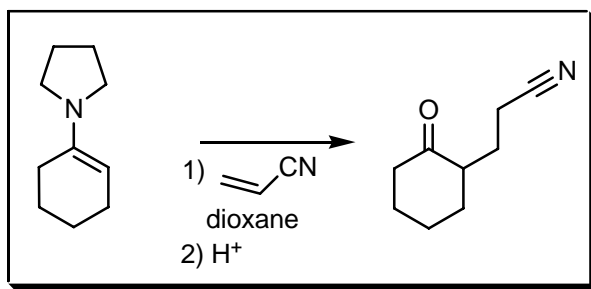
Org. React. : 31, 1

- 1) G. Stork; L. Maldonado, *J. Am. Chem. Soc.*, 1971, **93**, 5286.
- 2) S. Hünig; M. Öller, *Chem. Ber.*, 1981, **114**, 959.
- 3) J.D. Albright, *Tetrahedron*, 1983, **39**, 3207.
- 4) G. Stork, *Med. Res. Rev.*, 1999, **19**, 370.

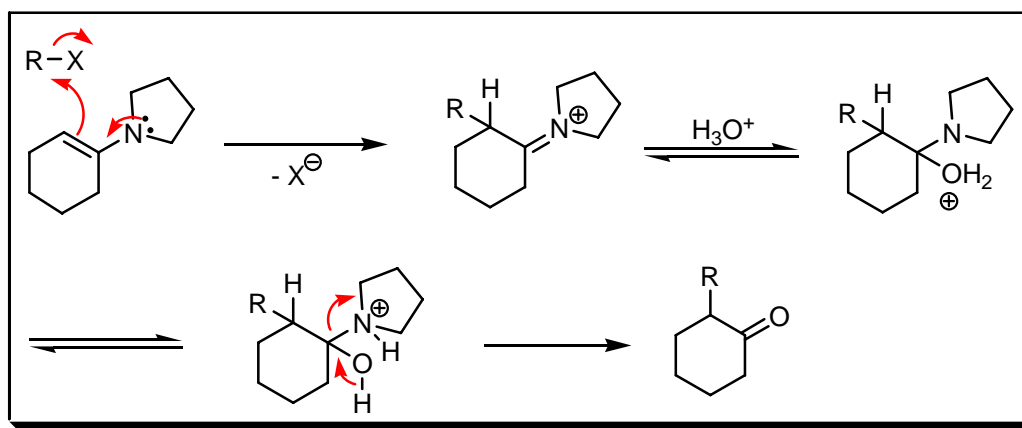
### COMMENTS :

## STORK ENAMINE ALKYLATION AND ACYLATION

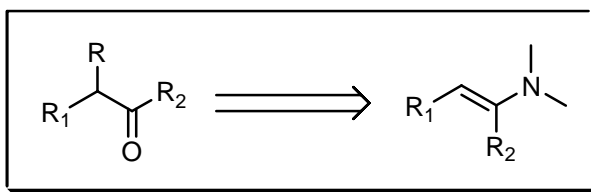
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

$\alpha$ -Alkylation and acylation of ketones *via* enamines or imines and the **Michael** addition *via* enamines.

### REFERENCES :

March : 601

Smith – March : 787

Smith : 951

Smith 2<sup>nd</sup> : 792

Houben – Weyl : 7/2a, 473

Org. Synth. : 53, 59; 54, 39

Org. Synth. Coll. Vol. : 6, 592, 1014

- 1) G. Stork; R. Terrell; J. Szumskovicz, *J. Am. Chem. Soc.*, 1954, **76**, 2029.
- 2) G. Stork; H. Landesman, *J. Am. Chem. Soc.*, 1956, **78**, 5128.
- 3) A. Doutheau; J. Gore, *Tetrahedron Lett.*, 1972, **13**, 4545.
- 4) J.K. Whitesell; M.A. Whitesell, *Synthesis*, 1983, 510.
- 5) J.J. Li; B.K. Trivedi; J.R. Rubin; B.D. Roth, *Tetrahedron Lett.*, 1998, **39**, 6111.
- 6) G. Stork, *Med. Res. Rev.*, 1999, **19**, 370.
- 7) B. Kempf; N. Hampel; A.R. Ofial; H. Mayr, *Chem. Eur. J.*, 2003, **9**, 2209.

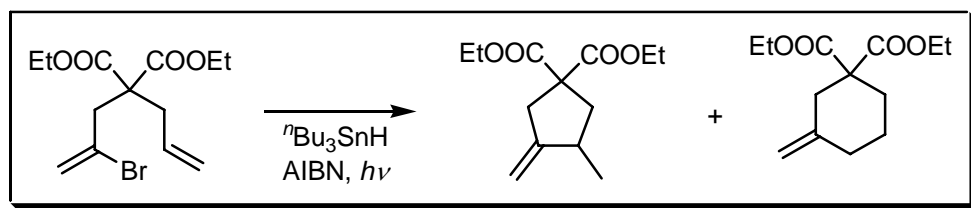
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**COMMENTS :**

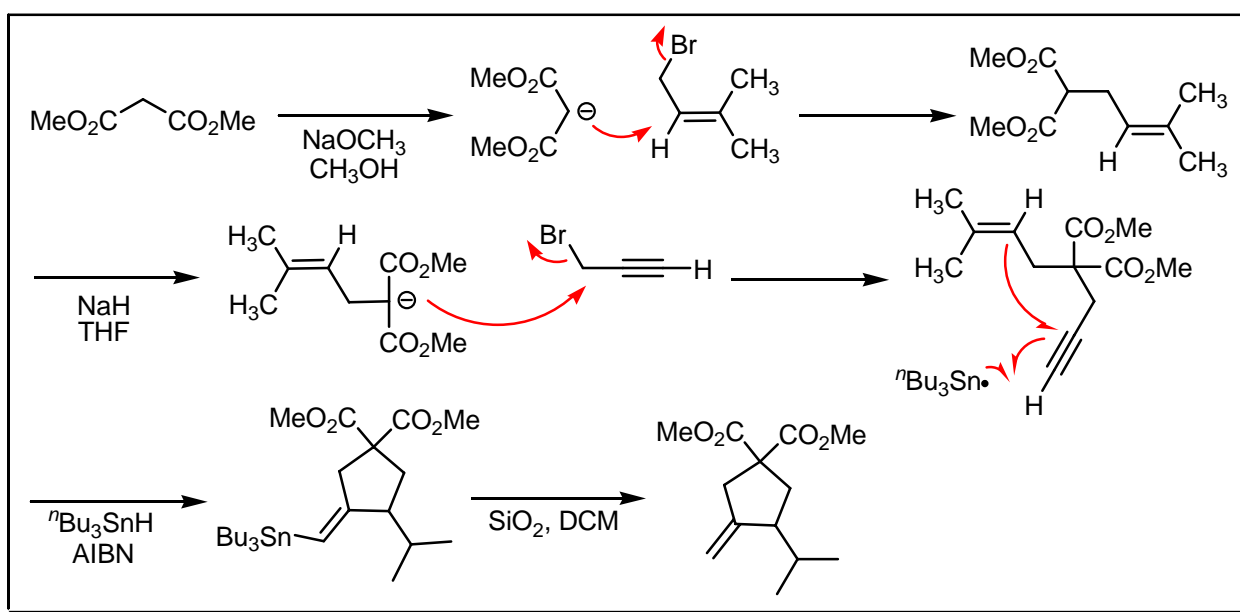
**STORK RADICAL CYCLISATION**

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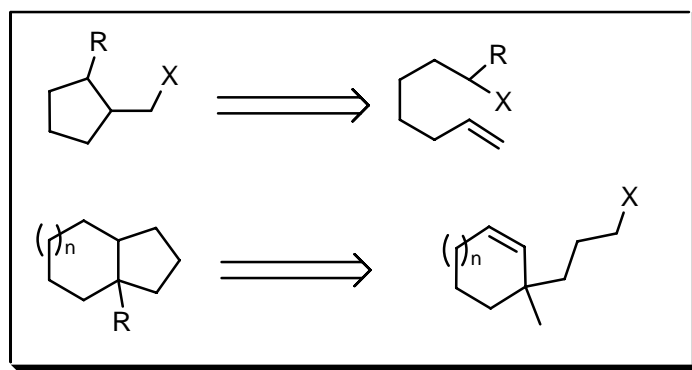
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

The free radical cyclisation with preferential formation of cyclopentanes. The free radical reactions are synthetically useful as alternatives for producing C-C bonds. Vinyl radicals are valuable in the ring forming reactions since they place a double bond in a predictable position. They are compatible with many unprotected functional groups.

## REFERENCES :

Smith 2<sup>nd</sup> : 472

Org. Synth. : 66, 75

Org. Synth. Coll. Vol. : 8, 381

1) G. Stork; N.H. Baine, *J. Am. Chem. Soc.*, 1982, **104**, 2321.

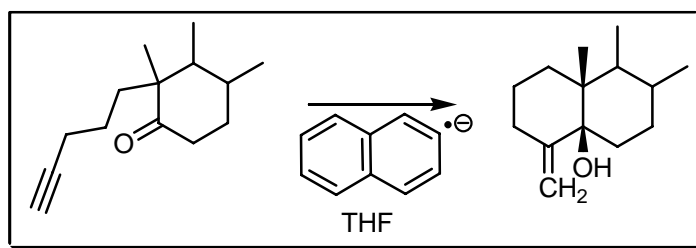
2) G. Stork; R. Mook, jr., *J. Am. Chem. Soc.*, 1987, **109**, 2829.

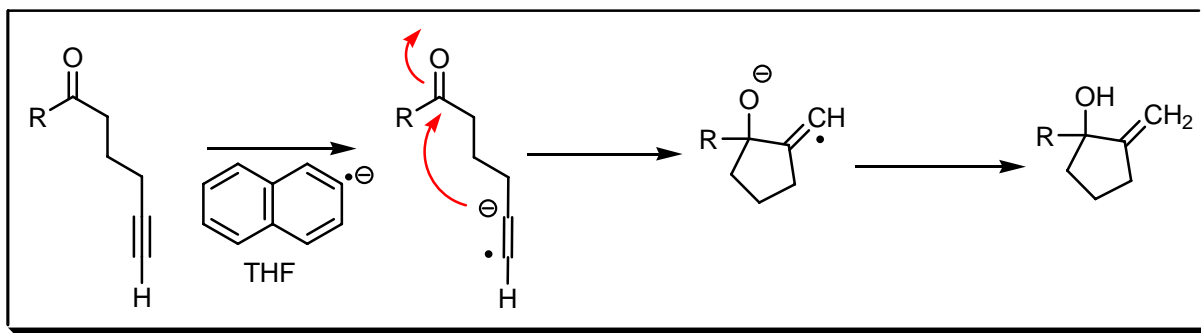
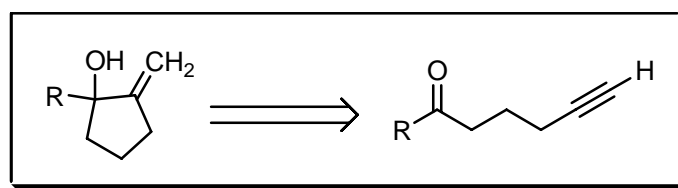
3) G. Stork; F. West; H.Y. Lee; R.C.A. Isaacs; S. Manabe, *J. Am. Chem. Soc.*, 1996, **118**, 10660.

## COMMENTS :

## STORK REDUCTIVE CYCLISATION

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

The cyclisation of acetylenic ketones to allyl alcohols by one electron reduction with Li in ammonia; also electrochemically (**Shono**) or by  $Sml_2$  (**Molander**) or with naphthalene anion radicals (**Pradhan**). See also **Kagan – Molander** reaction.

**REFERENCES :**

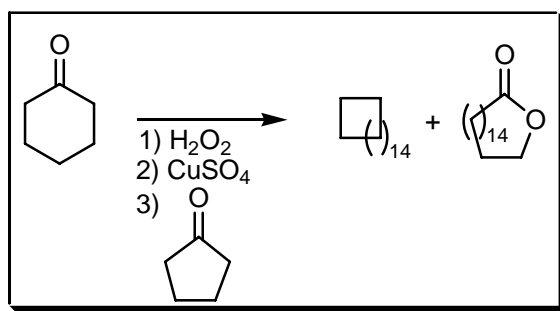
- 1) G. Stork; S. Malhotra; H. Thompson; M. Uchibayashi, *J. Am. Chem. Soc.*, 1965, **87**, 1148.
- 2) S.K. Pradhan; T.V. Radhakrishnan; R. Subramanian, *J. Org. Chem.*, 1976, **41**, 1943.
- 3) G. Stork; R.K. Boeckmann, jr.; D.F. Taber; W.C. Still; J. Singh, *J. Am. Chem. Soc.*, 1979, **101**, 7107.
- 4) G. Molander; C. Kenny, *J. Am. Chem. Soc.*, 1989, **111**, 8236.

**COMMENTS :**

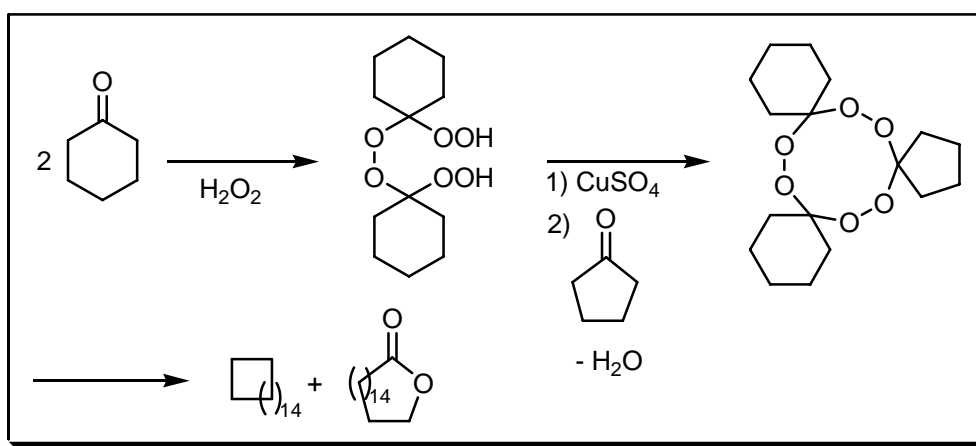


# STORY MACROCYCLE SYNTHESIS

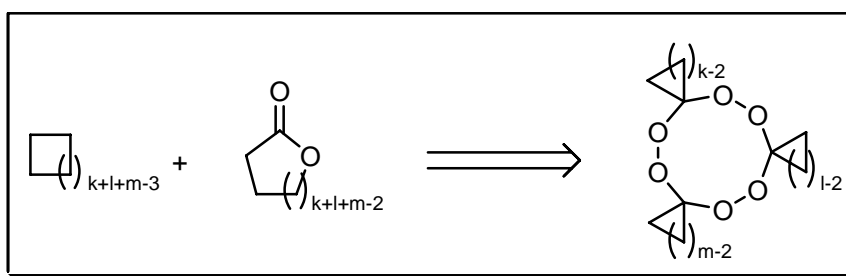
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of large ring alkanes and lactones from smaller ring ketones *via* peroxides. The products have 3 and 2 carbon atoms less than the starting peroxide. See also **Corey – Nicolaou**, **Diels – Alder**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Kita**, **Masamune**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Stille – Migita – Kosugi**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolakiewicz**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

## REFERENCES :

March : 1048

Smith – March : 1355

---

1) P.R. Story; D.D. Denson; C.E. Bishop; B.C. Clark; J.-C. Farine, *J. Am. Chem. Soc.*, 1968, **90**, 817.

2) P.R. Story; P. Bush, *Adv. Org. Chem.*, 1972, **8**, 67.

3) J.R. Sanderson; K. Paul; D.D. Denson; J.A. Alford, *Synthesis*, 1975, 159.

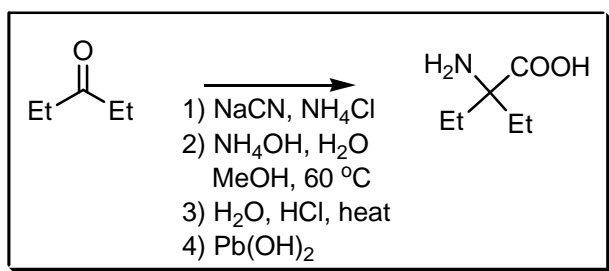
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## COMMENTS :

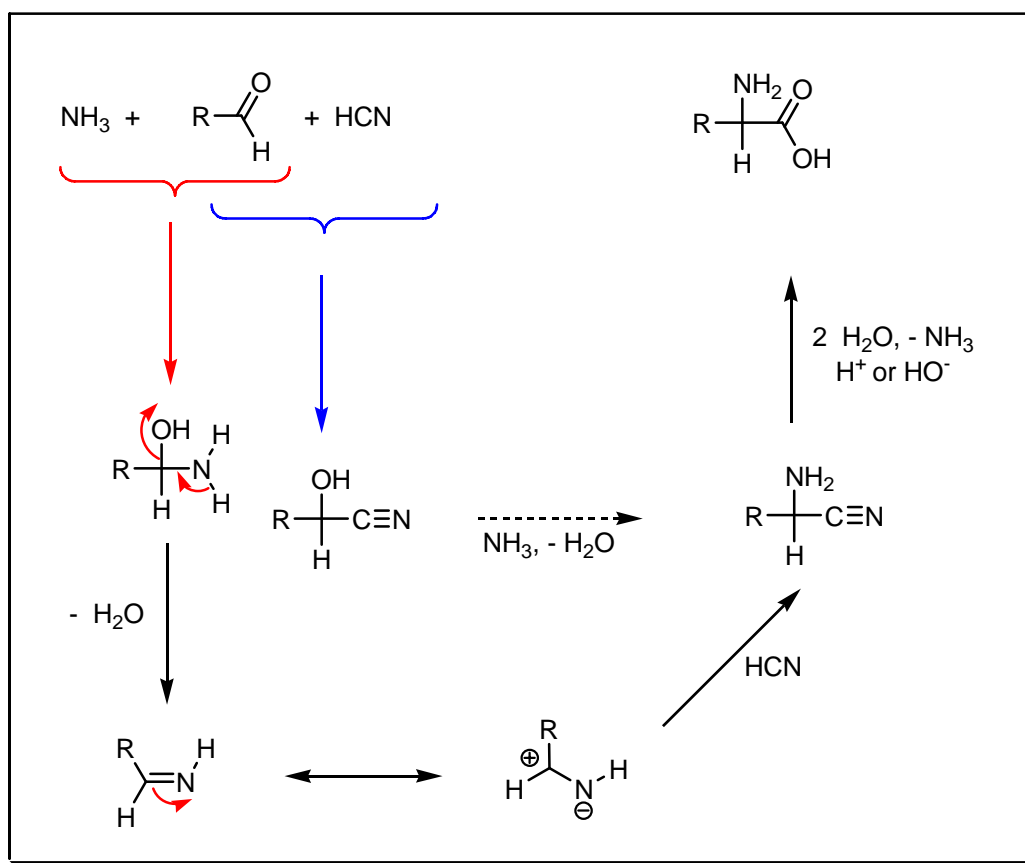
## STRECKER AMINO ACID SYNTHESIS

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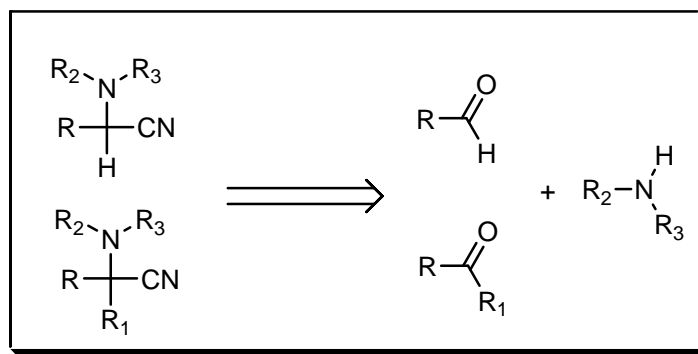
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

This is a special case of the **Mannich** reaction. Aldehyde-ammonia compounds are condensed with hydrogen cyanide and the resulting amino-nitrile is hydrolysed. The synthesis has been applied in a variety of forms to which special names (**Tiemann**) are sometimes applied. The Lewis acid asymmetric hydrocyanation is gaining special reverence since it provides rapid access to a library of valuable chiral building blocks. See also **Bruylants**, **Bucherer**, **Corey – Link**, **Mannich**, **Tiemann**, **Ultee**, **Urech** and **Zelinsky – Stadnikoff** reactions.

## REFERENCES :

March : 965

Smith – March : 1240

Smith : 678

Smith 2<sup>nd</sup> : 575

Houben – Weyl : **E5**, 534, 543, 1425; **E16d**, 550, 1073, 1243

Org. Synth. : **4**, 47; **9**, 4; **11**, 4; **22**, 13, 23; **24**, 9; **32**, 50; **58**, 101

Org. Synth. Coll. Vol. : **1**, 21, 355; **2**, 29; **3**, 66, 84, 88; **4**, 274; **6**, 334

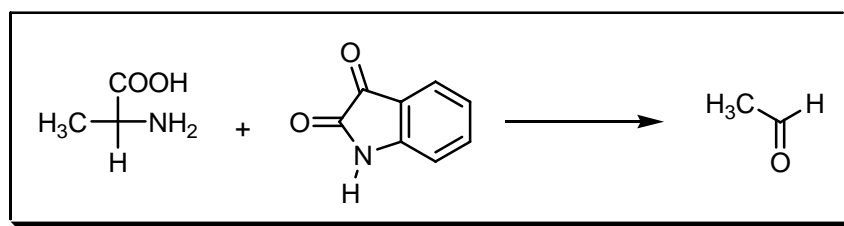
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- 1) A. Strecker, *Liebigs Ann. Chem.*, 1850, **75**, 27.
  - 2) E. Ware, *Chem. Rev.*, 1950, **46**, 403.
  - 3) C. O'Connor, *J. Chem. Soc., Quat. Rev.*, 1970, **24**, 553.
  - 4) F.A. Davis; R.E. Reddy; P.S. Portonovo, *Tetrahedron Lett.*, 1994, **35**, 9351.
  - 5) M.S. Iyer; K.M. Gigstad; N.D. Namdev; M. Lipton, *J. Am. Chem. Soc.*, 1996, **118**, 4910.
  - 6) E.J. Corey; M.J. Grogan, *Org. Lett.*, 1999, **1**, 157.
  - 7) D. Enders; J.P. Shilvock, *Chem. Soc. Rev.*, 2000, **29**, 359.
  - 8) W.H.J. Boesten; J.-P.G. Seerden; B. de Lange; H.J.A. Dielemans; H.L.M. Elsenberg; B. Kaptein; H.M. Moody; R.M. Kellogg; Q.B. Broxterman, *Org. Lett.*, 2001, **3**, 1121.
  - 9) D. Enders; M. Moser, *Tetrahedron Lett.*, 2003, **44**, 8479.
  - 10) U. Meyer; E. Breitling; P. Bisel; A.W. Frahm, *Tetrahedron: Asymmetry*, 2004, **15**, 2029.
  - 11) K. Matsumoto; J.C. Kim; H. Iida; H. Hamana; K. Kumamoto; H. Kotsuki; G. Jenner, *Helv. Chim. Acta*, 2005, **88**, 1734.
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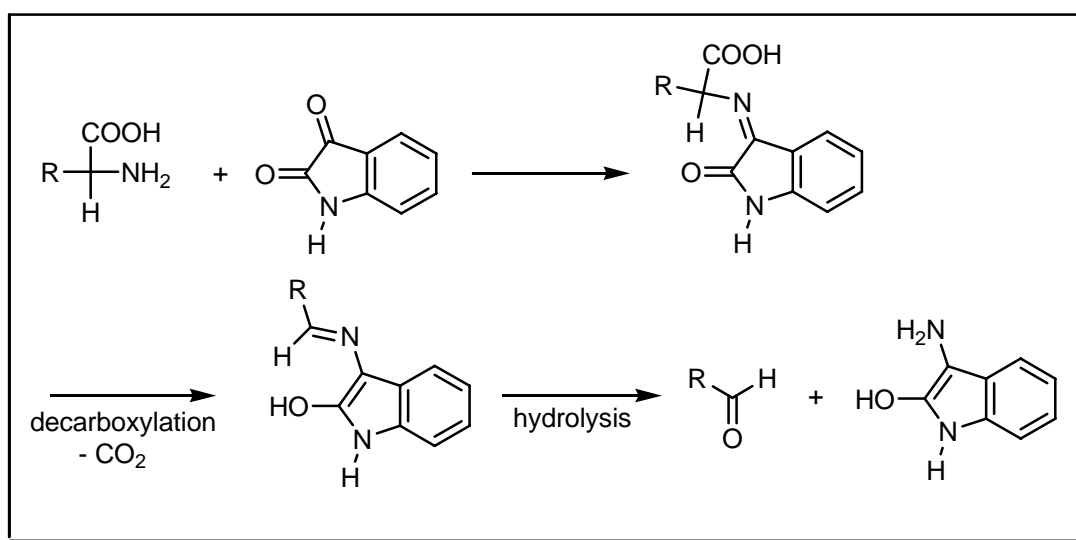
COMMENTS :

# STRECKER DEGRADATION

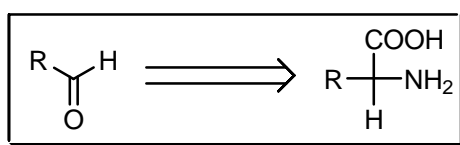
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Interaction of an α-amino acid with a carbonyl compound (**Strecker** used alloxan, an oxidation product of uric acid) in aqueous solution or suspension to give carbon dioxide and an aldehyde or ketone containing one less carbon atom. Inorganic oxidising agents can also be used to bring about the reaction. See also **Herbst – Engels** reaction.

## REFERENCES :

Houben – Weyl : 11/2, 322; E3, 533

- 1) A. Strecker, *Liebigs Ann. Chem.*, 1862, **123**, 363.
- 2) Th. Wieland, *Angew. Chem.*, 1942, **55**, 147.
- 3) A. Schönberg; R. Moubasher, *Chem. Rev.*, 1952, **50**, 261.

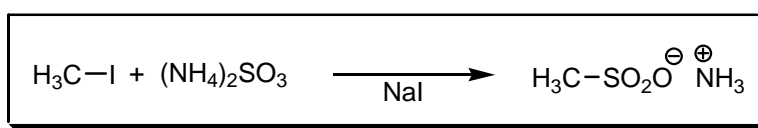
- 4) T. Nyhammar; K. Olsson; P.A. Pernemalm, *Acta Chem. Scand.*, 1983, **B37**, 879.  
5) J. Koch; M. Pischetsrieder; K. Polborn; T. Severin, *Carbohydr. Res.*, 1998, **313**, 117.
- 

COMMENTS :

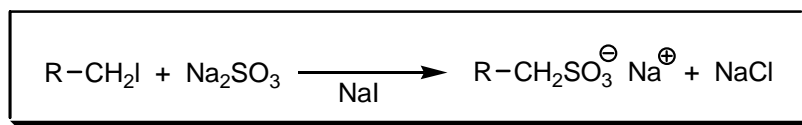
## STRECKER SULFITE ALKYLATION

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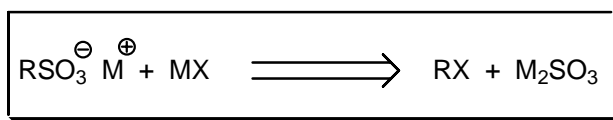
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The sulfite alkylation of primary and sometimes secondary alkyl halogens with alkylsulfonic acids using a catalytic amount of sodium iodide. See also **Kolbe** reaction.

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REFERENCES :

March : 410

Houben – Weyl : **9**, 372

Org. Synth. : **10**, 96; **37**, 55

Org. Synth. Coll. Vol. : **2**, 558; **4**, 529

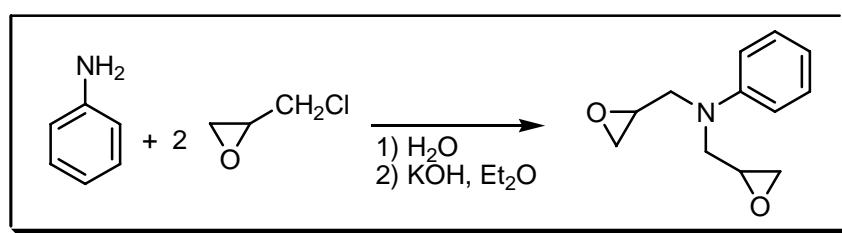
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- 1) A. Strecker, *Liebigs Ann. Chem.*, 1868, **148**, 90.  
2) R.M. Reed; H.V. Tartar, *J. Am. Chem. Soc.*, 1935, **57**, 570.

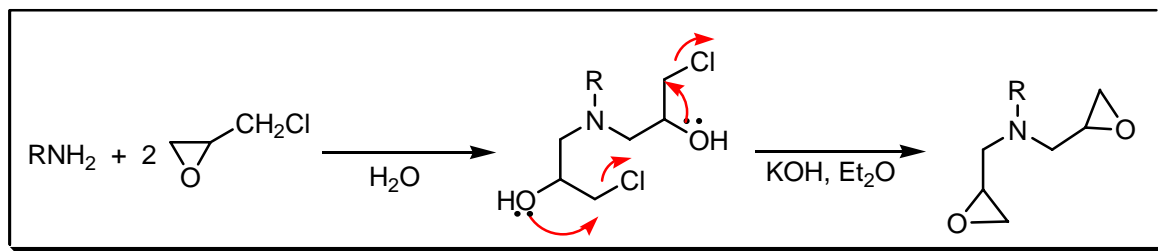
**COMMENTS :**

**STRUKOV SYNTHESIS**

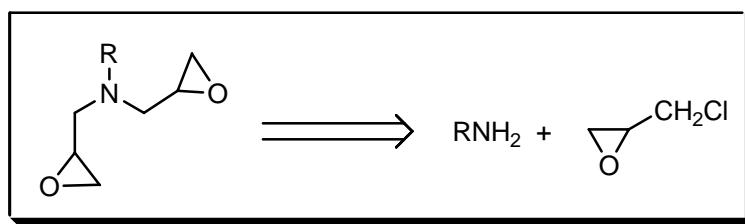
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

Epichlorohydrin reacts with an arylamine hydrochloride in aqueous solution at room temperature to give the di-(chlorohydroxy)amine, which on treatment with powdered alkali hydroxide in diethyl ether yields *N,N*-di-(2,3-epoxy-*n*-propyl)arylamine.

**REFERENCES :**

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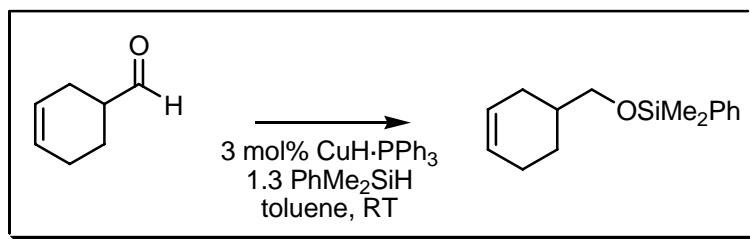
**COMMENTS :**

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**STRYKER REGIOSELECTIVE REDUCTION**

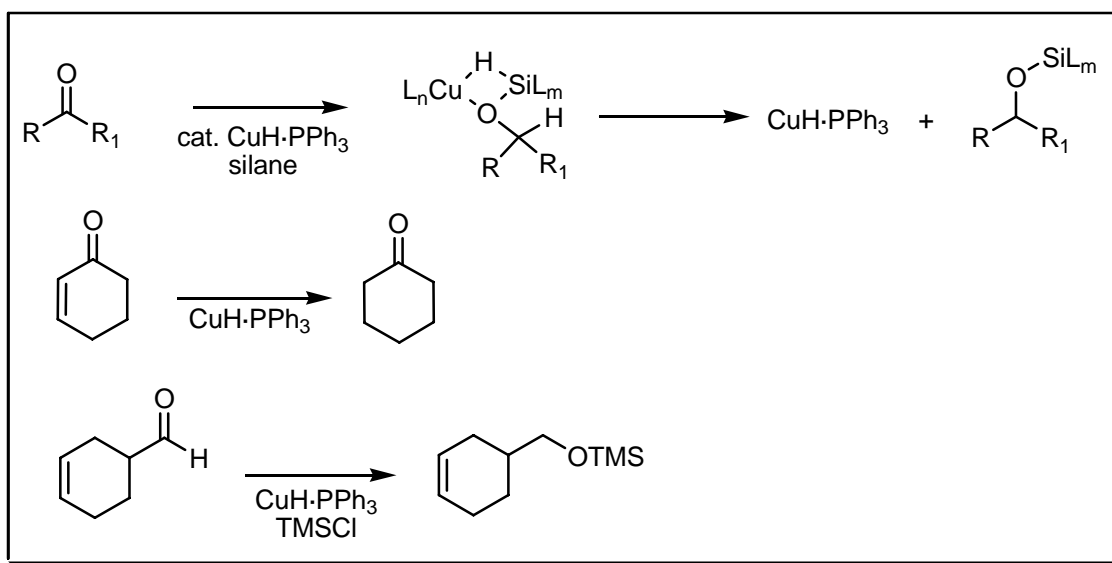
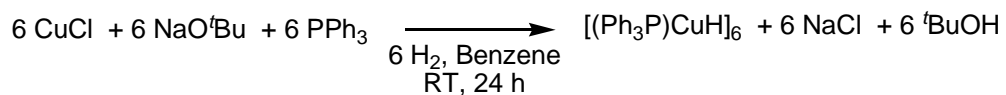
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**EXAMPLE :**



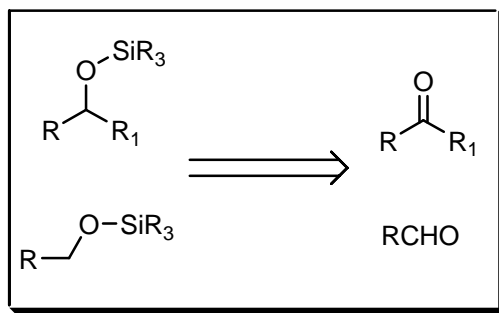
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**MECHANISM :**





## DISCONNECTION :



## NOTES :

The regioselective conjugate reduction and reductive silylation of  $\alpha,\beta$ -unsaturated ketones, esters, and aldehydes using stable copper(I)hydride cluster  $[(\text{Ph}_3\text{P})\text{CuH}]_6$  with or without a silane.

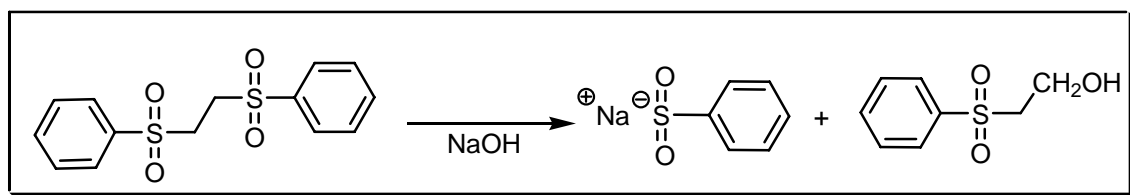
## REFERENCES :

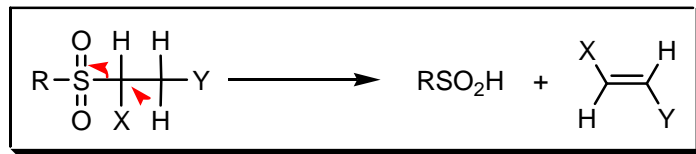
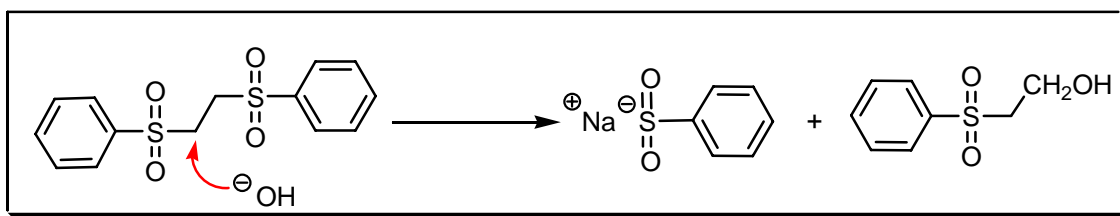
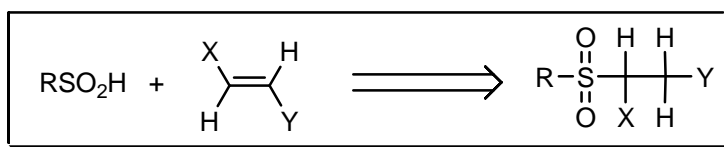
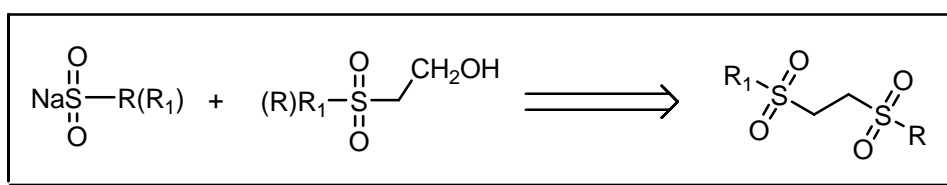
- 1) W.S. Mahoney; D.M. Brestensky; J.M. Stryker, *J. Am. Chem. Soc.*, 1988, **110**, 291.
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## COMMENTS :

## STUFFER – BACKER DISULFONE HYDROLYSIS

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

γ-Disulfones when treated with alkali yield a hydroxysulfone and a sulfinate. If one of the 2 carbon atoms attached to the SO<sub>2</sub> group has an electron withdrawing group on the α-position and the β-carbon atom has acidic hydrogens elimination takes place.

**REFERENCES :**

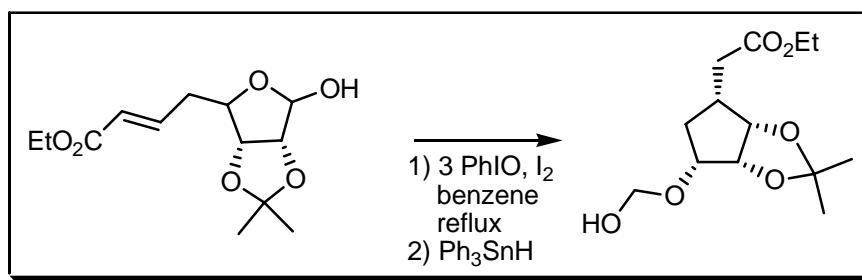
Houben – Weyl : 9, 257

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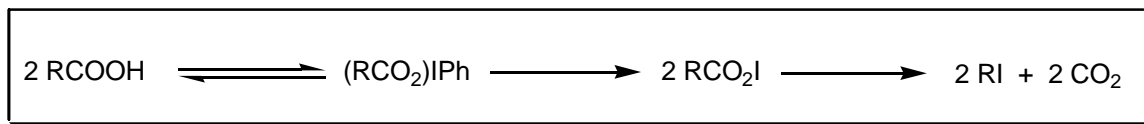
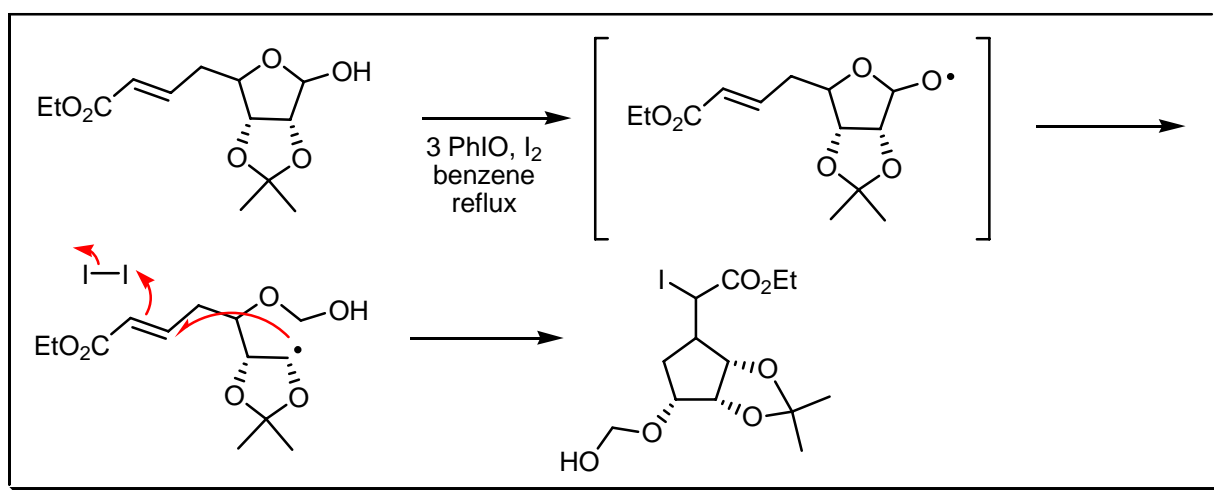
**COMMENTS :**

# SUÁREZ – HEUSLER – KALVODA REACTION

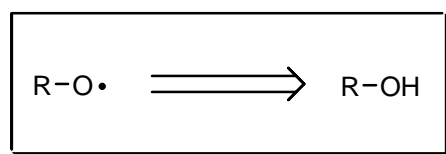
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

This reaction is the photoinduced conversion of hydroxyl-containing substrates with hypervalent iodine to the corresponding oxygen-centered radical. **Heusler – Kalvoda** used Pb(OAc)<sub>4</sub>, I<sub>2</sub>, CaCO<sub>3</sub>, light, while **Suárez** used diacetoxyiodobenzene, I<sub>2</sub> and light. See also **Hunsdiecker** reaction.

## REFERENCES :

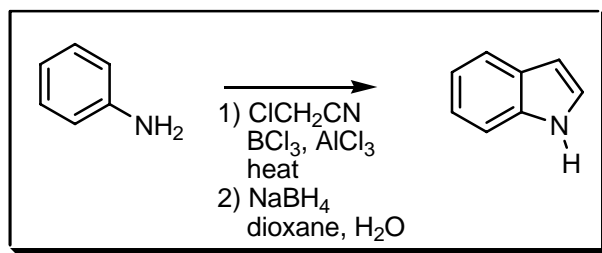
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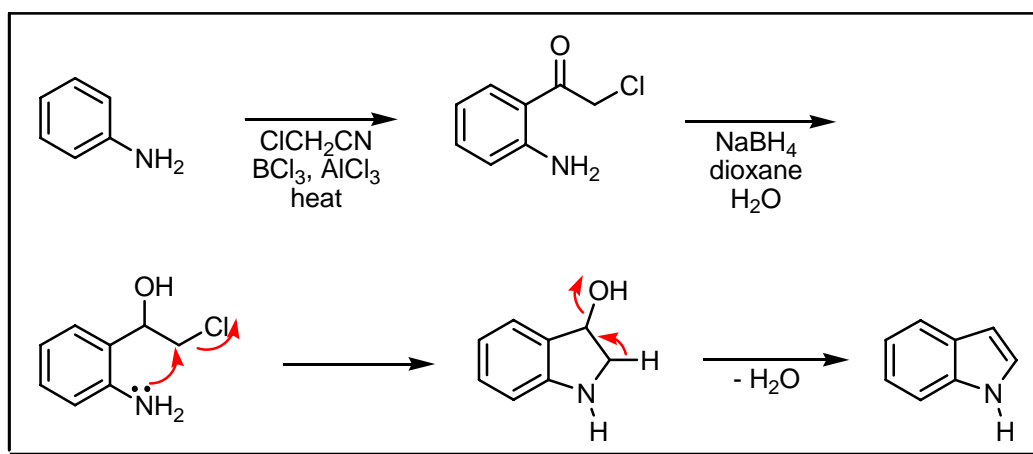
COMMENTS :

## SUGASAWA INDOLE SYNTHESIS

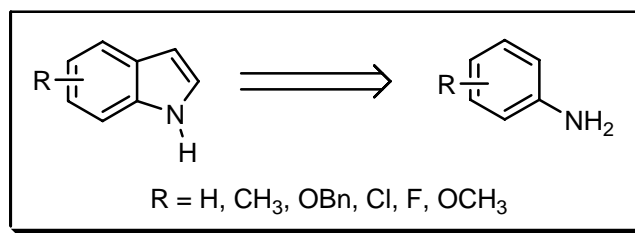
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

Arylamines undergo **Friedel – Crafts** acylation *ortho* to the nitrogen atom. Up to 2 Lewis acids can be used. The ring-closure takes place after reduction of the ketone to a hydroxyl. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

## REFERENCES :

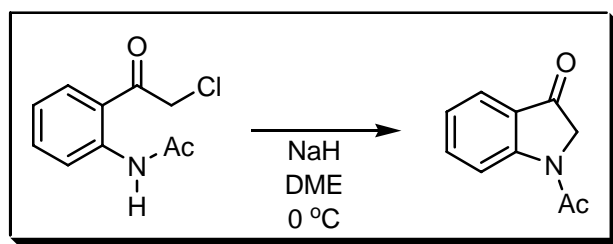
**Science of Synthesis : 10**, 438

- 1) T. Sugasawa; M. Adachi; K. Sasakura; A. Kitagawa, *J. Org. Chem.*, 1979, **44**, 578.
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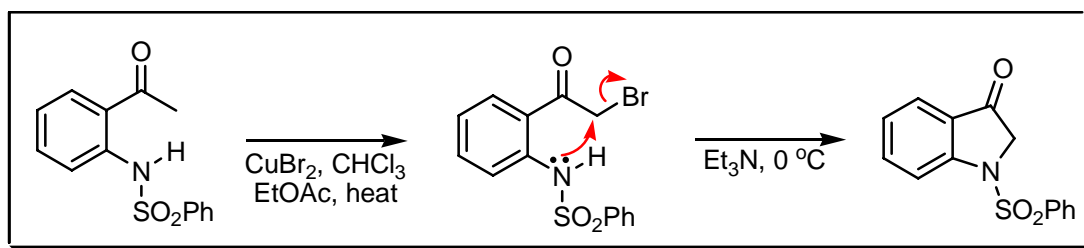
## COMMENTS :

## SUGASAWA INDOXYL SYNTHESIS

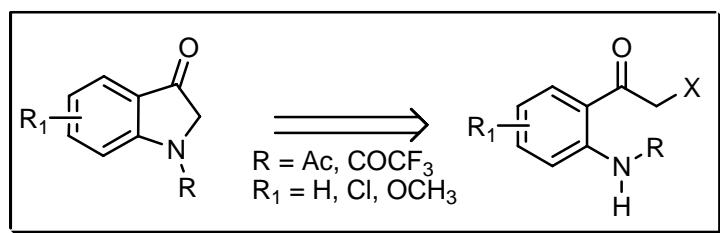
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The simple *intramolecular* displacement of a halide by the amino group will give indoxyls. Base affects the ring-closure.

### REFERENCES :

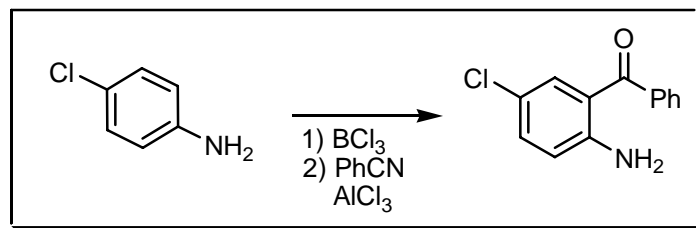
Science of Synthesis : 10, 621

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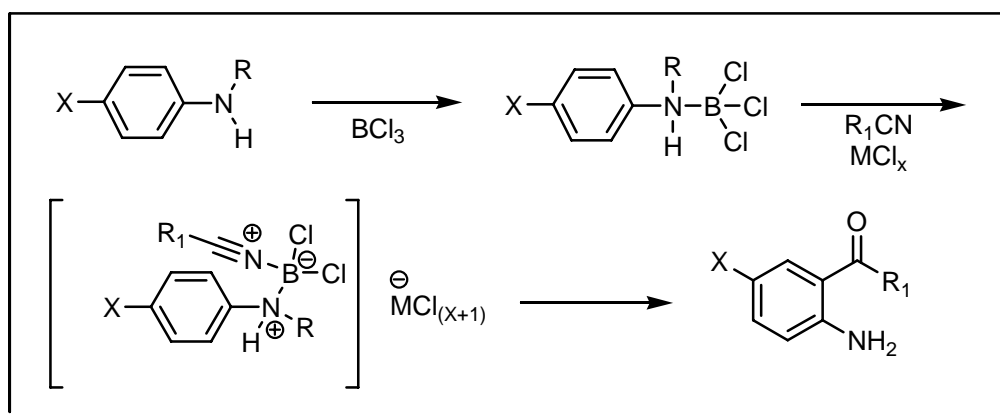
COMMENTS :

## SUGASAWA REACTION

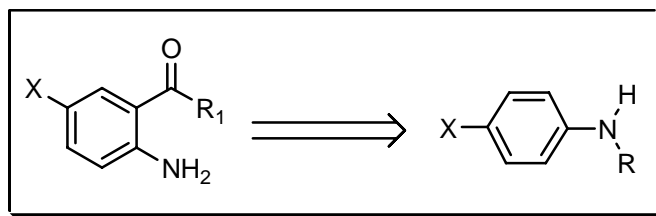
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

*Ortho* acylation of anilines by nitriles in the presence of  $\text{BCl}_3$  and a second Lewis acid appear to proceed through an intermediate "supercomplex" including all four components. Yield improvements were obtained based on recognition that chloride affinity of the second Lewis acid governs supercomplex formation. Aniline protonation was found to be the cause of incomplete reaction.

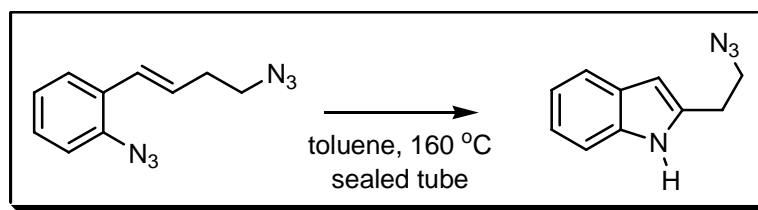
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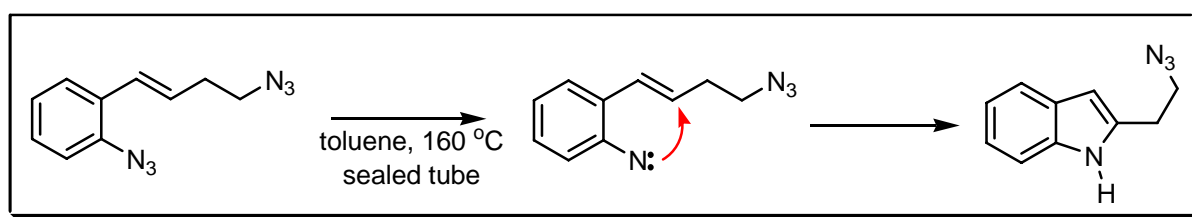
## COMMENTS :

## SUNDBERG INDOLE SYNTHESIS

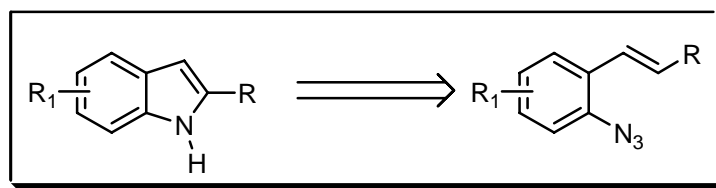
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :





## NOTES :

The thermolysis of *ortho*-azidostyrenes and resulting cyclisation of the nitrene will afford indoles. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

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## REFERENCES :

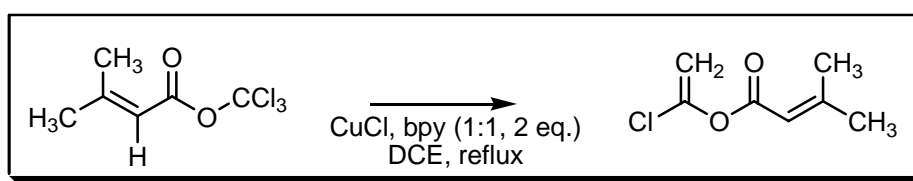
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## COMMENTS :

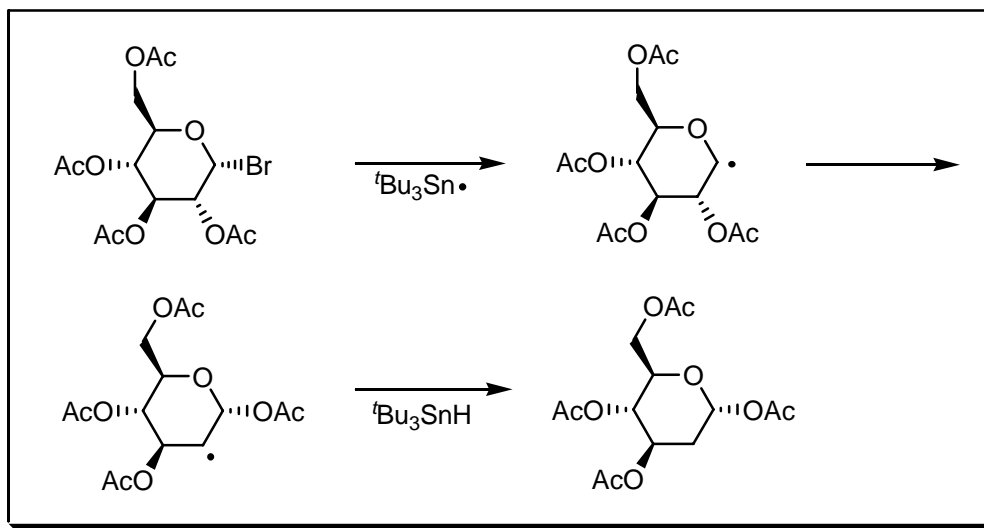
## SURZUR – TANNER REARRANGEMENT

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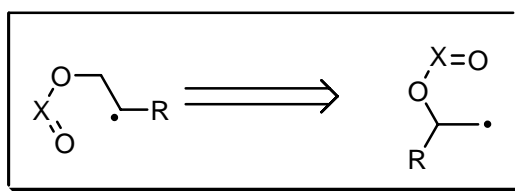
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

This is the *intramolecular* 1,2-suprafacial migration of the acyloxy group in  $\beta$ -acyloxyalkyl radicals. See also **Schenck** rearrangement.

## REFERENCES :

**Org. Synth.** : **69**, 66

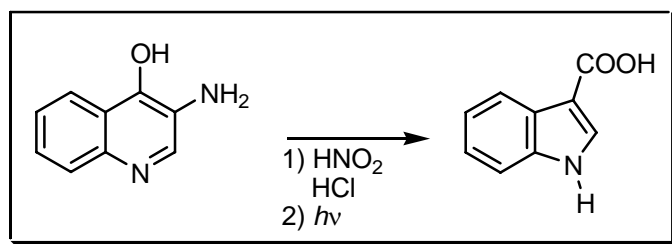
**Org. Synth. Coll. Vol.** : **8**, 583

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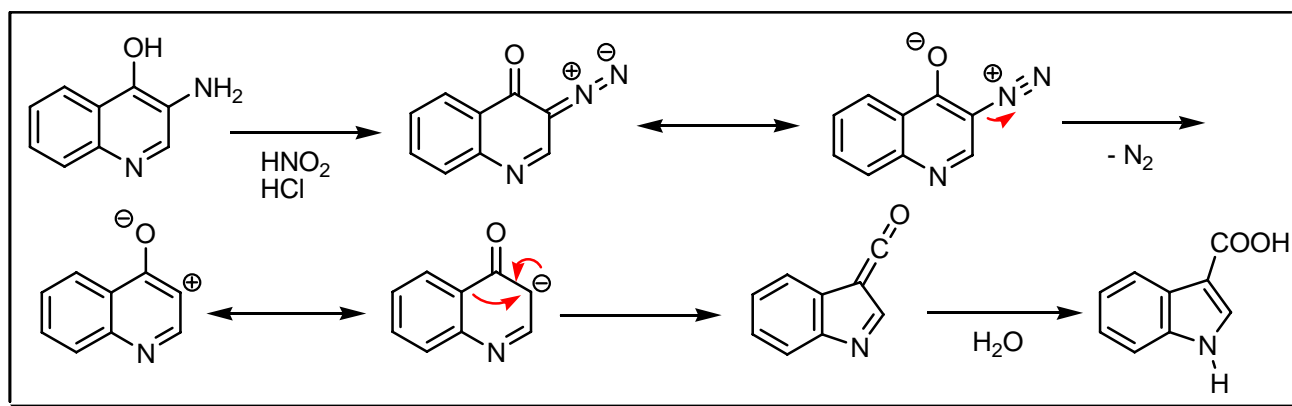
COMMENTS :

## SÜS REACTION

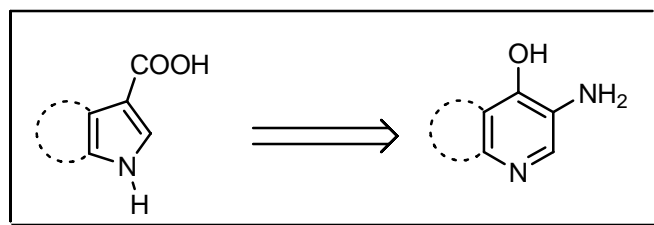
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The ring-contraction of 6-membered 1,2-amino alcohols. See also **Wolff** rearrangement.

REFERENCES :

1) O. Süss, *Liebigs Ann. Chem.*, 1944, **556**, 65.

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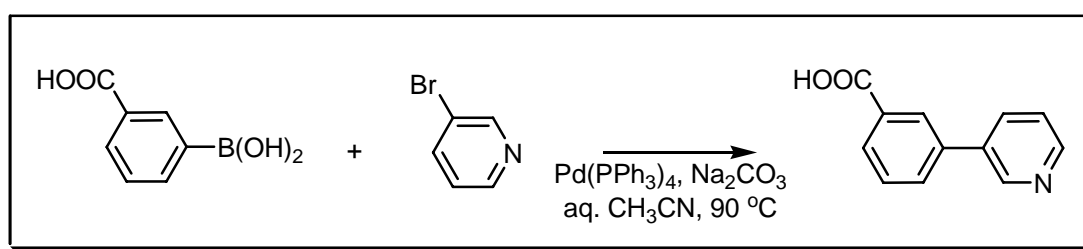
**COMMENTS :**

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**SUZUKI – MIYAUURA VINYL COUPLING**

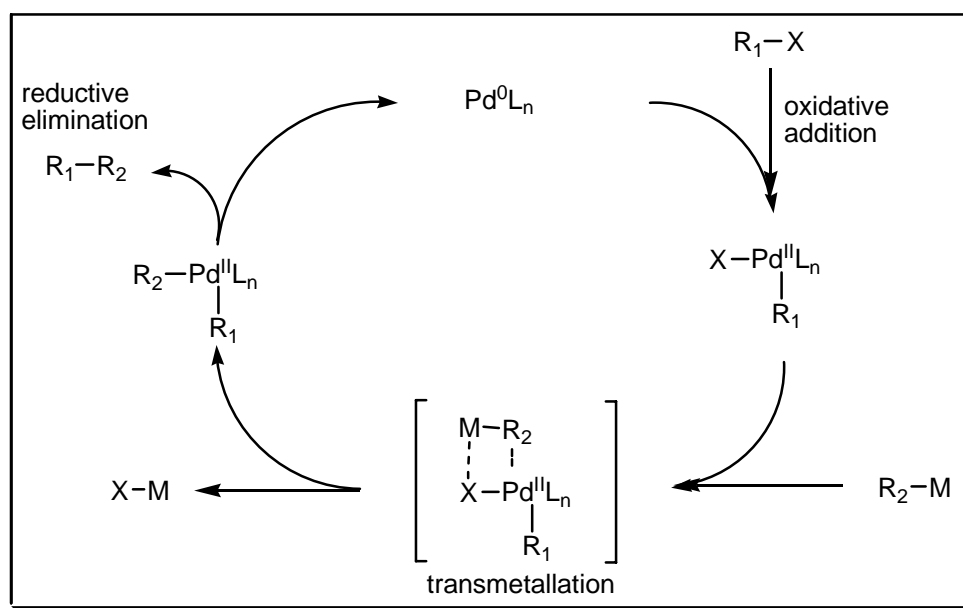
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**EXAMPLE :**

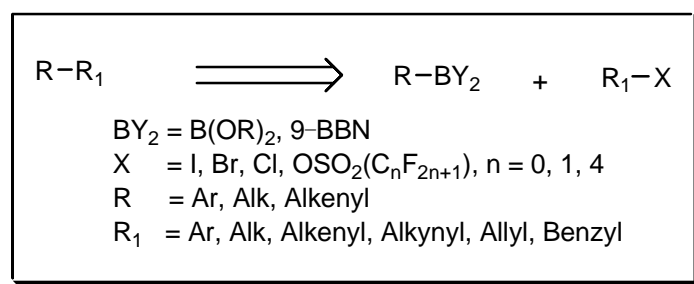


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**MECHANISM :**



## DISCONNECTION :



## NOTES :

Trialkylboranes resulting from the addition of 9-BBN to terminal alkenes or alkynes can be combined with aryl-X or alkenyl-X compounds ( $\text{X} = \text{Br, I, OTf}$ ) *via* palladium catalysed **Suzuki** coupling. This reaction is less expensive and less toxic alternative to the **Stille** coupling. Depending on the leaving group, the oxidative addition can be the rate determining step. The reaction is performed under basic conditions ( $\text{Na}_2\text{CO}_3, \text{NaOEt, Et}_3\text{N, TIOH}$ ). There are water-soluble **Suzuki** catalysts known. Recently palladium has been substituted for nickel. See also **Corey – Nicolaou, Diels – Alder, Hanessian** macrolactonisation, **Hansley – Prelog – Stoll, Horner – Wadsworth – Emmons, Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Kita, Liebeskind – Srogl, Masamune, Michael** condensation, **Mitsunobu, Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao, Nozaki – Hiyama – Kishi (Takai – Utimoto), Raphael, Roush, Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow, Staab, Stacey, Steglich – Hassner, Stille – Migita – Kosugi, Story, Thorpe – Ziegler, Venkataraman – Wagle, Vorbrüggen – Krolikiewicz, Wittig, Yamaguchi, Yamamoto** macrolactonisation and **Yamamoto** ketone reactions.

## REFERENCES :

**Smith – March** : 868

**Smith 2<sup>nd</sup>** : 476, 1123

**Org. Synth.** : **68**, 130; **71**, 89; **75**, 53, 61, 69, 129; **77**, 176

**Org. Synth. Coll. Vol.** : **8**, 532; **9**, 107

**Science of Synthesis** : **9**, 257, 373, 527; **10**, 420, 735

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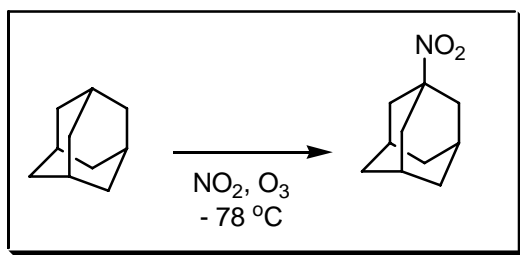
- 13) M.D. Smith; A.F. Stephan; C. Ramarao; P.E. Brennan; S.V. Ley, *Chem. Commun.*, 2003, 2652.  
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- 

**COMMENTS :**

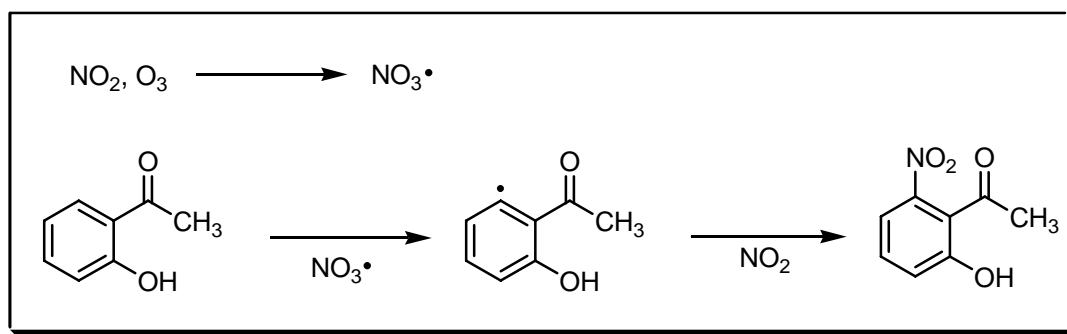
**SUZUKI (KYODAI) REACTION**

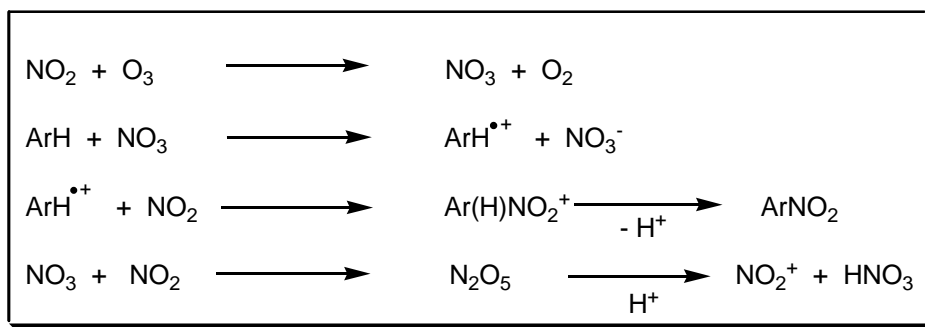
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**EXAMPLE :**



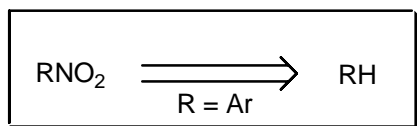
**MECHANISM :**






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**DISCONNECTION :**




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**NOTES :**

Nitrogen dioxide is activated in the presence of ozone and joins mainly aromatic moieties as a nitro group at low temperature.

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**REFERENCES :**

**Smith – March :** 696

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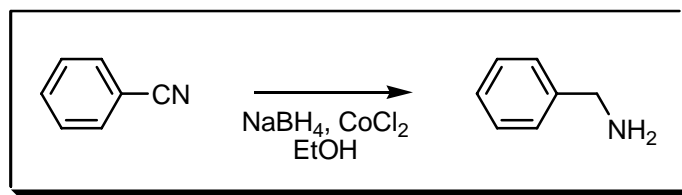
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**COMMENTS :**

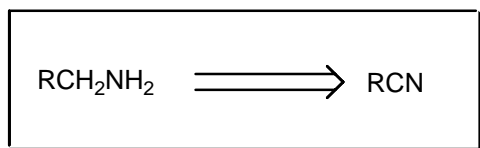
## SUZUKI REDUCTION

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### EXAMPLE :



### DISCONNECTION :



### NOTES :

The reduction of nitriles, amides, nitro compounds by sodium borohydride in the presence of cobalt dichloride to the corresponding primary amines. It is not clear what the exact nature is of the reducing species.

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### REFERENCES :

**March** : 918

**Smith – March** : 1204

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### COMMENTS :



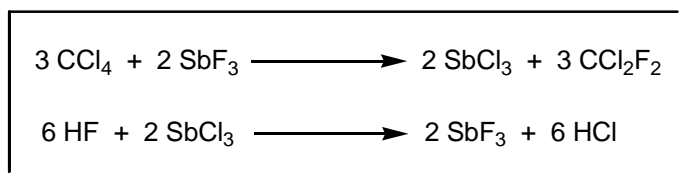
## SWARTS REACTION

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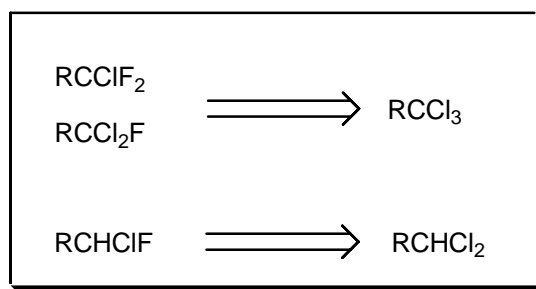
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

C-F bonds can be formed by the stoichiometric reaction of  $\text{SbF}_3$  with activated C-Cl bonds. Trace amounts of  $\text{SbF}_5$  are required. See also **Gryszkiewicz – Trochimowski – McCombie** reaction.

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### REFERENCES :

Org. React. : 2, 49

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1) F. Swarts, *Bull. Acad. Royal Belg.*, 1892, **24**, 309.

2) H.W. Daudt; M.A. Youker, *U.S. Patent*, 1935, 2005705. (*Chem. Abs.*, 1935, **29**, 5123.)

3) T. Midgley, jr.; A.L. Henne; R.R. McNary, *U.S. Patent*, 1935, 2007208. (*Chem. Abs.*, 1935, **29**, 5459.)

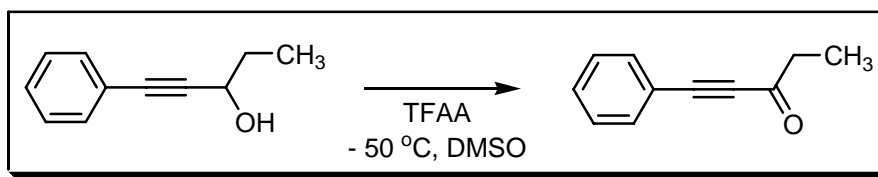
4) A.L. Henne; A.M. Whalley; J.K. Stevenson, *J. Am. Chem. Soc.*, 1941, **63**, 3478.

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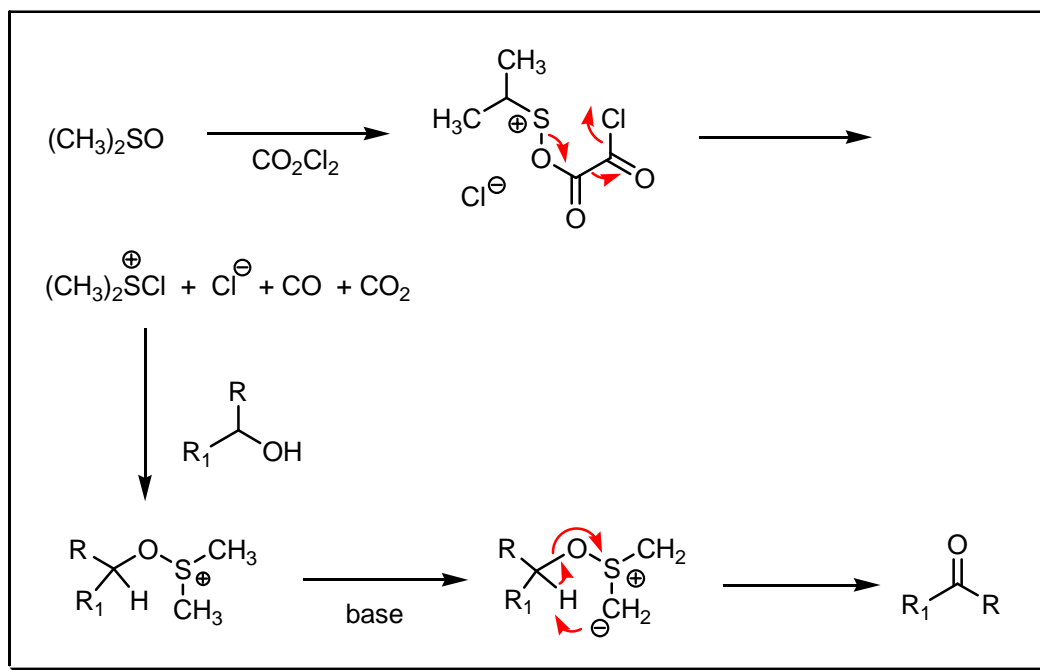
### COMMENTS :

## SWERN OXIDATION

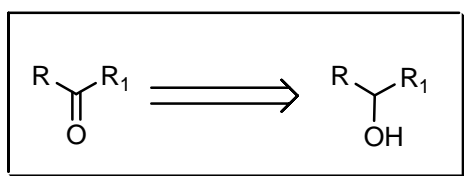
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The oxidation of alcohols using DMSO and oxalyl chloride or trifluoroacetic anhydride to aldehydes or ketones in the presence of other groups. See also **Anelli**, **Ball – Goodwin – Morton**, **Collins**, **Corey – Kim**, **Corey – Schmidt**, **Corey – Suggs**, **David – Thieffry**, **Delépine**, **Dess – Martin**, **Einhorn** oxidation, **Fétizon**, **Jones** oxidation, **Ley**, **Maurer – Drefahl**, **Mukaiyama** oxidation, **Nicolaou**, **Oppenauer**, **Parikh – von Doering**, **Pfitzner – Moffatt**, **Sarett** and **Uemura** reactions.

### REFERENCES :

March : 1194

Smith – March : 1516

Smith : 239

Smith 2<sup>nd</sup> : 204, 540, 550

Houben – Weyl : E6b, 877

Org. React. : 39, 297; 53, 1

Org. Synth. : 64, 164; 66, 14; 70, 120; 76, 110; 77, 64

Org. Synth. Coll. Vol. : 7, 258; 8, 501; 9, 692

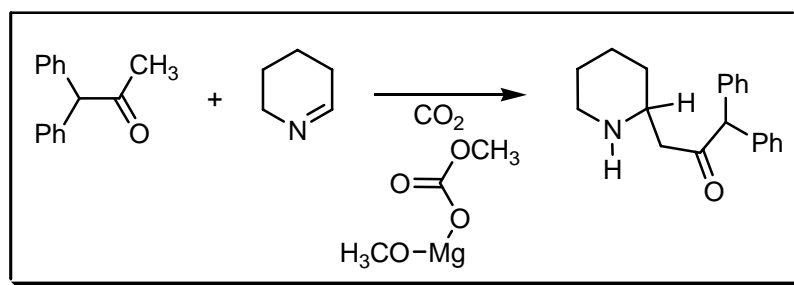
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- 1) K. Omura; D. Swern, *Tetrahedron*, 1978, **34**, 1651.
  - 2) A.J. Manusco; S.-L. Huang; D. Swern, *J. Org. Chem.*, 1978, **43**, 2480.
  - 3) D. Keirs; K. Overton, *Chem. Commun.*, 1987, 1660.
  - 4) T.T. Tidwell, *Synthesis*, 1990, 857.
  - 5) L. Gentilucci; Y. Grijzen; L. Thijs; B. Zwanenburg, *Tetrahedron Lett.*, 1995, **36**, 4665.
  - 6) J.M. Harris; Y. Li; S. Chai; M.D. Andrews; J.C. Vederas, *J. Org. Chem.*, 1998, **63**, 2407.
  - 7) D. Crich; S. Neelamkavil, *J. Am. Chem. Soc.*, 2001, **123**, 7449.
  - 8) D. Crich; S. Neelamkavil, *Tetrahedron*, 2002, **58**, 3865.
  - 9) K. Nishide; S.-I. Ohsugi; M. Fudesaka; S. Kodama; M. Node, *Tetrahedron Lett.*, 2002, **43**, 5177.
- 

#### COMMENTS :

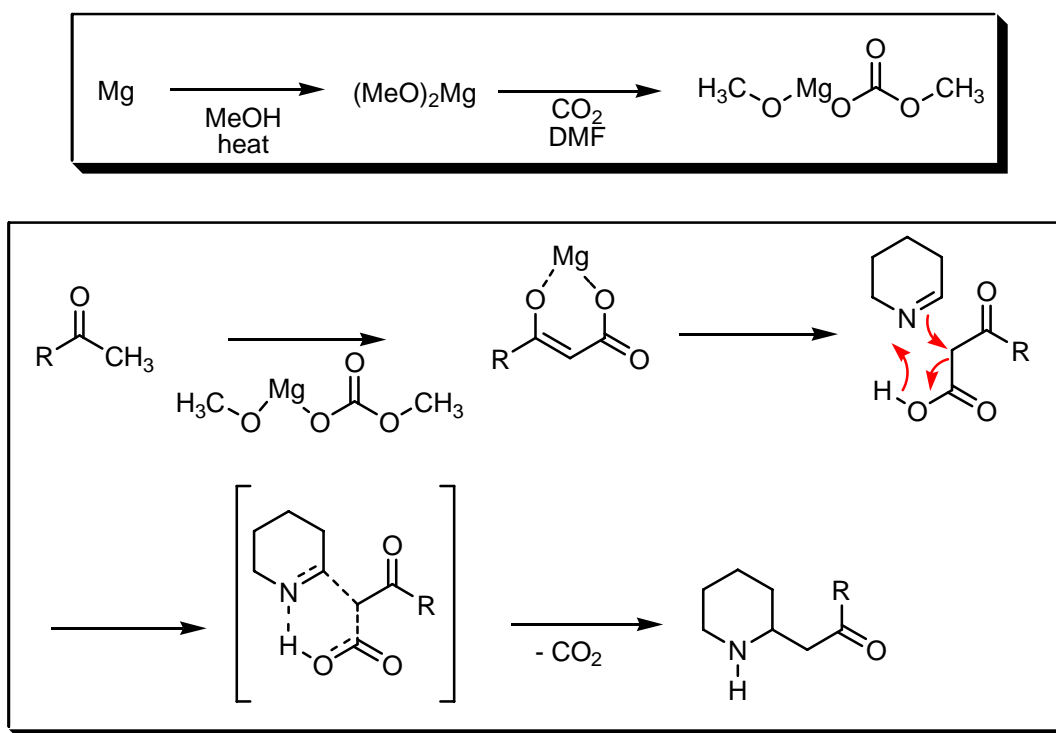
### SZARVASY – SCHÖPF CARBOMETHOXYLATION

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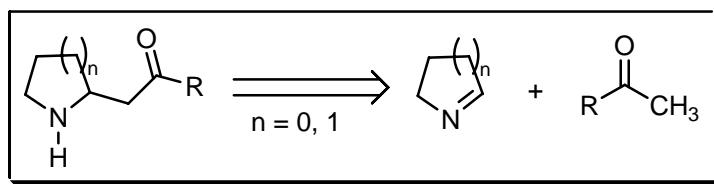
#### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



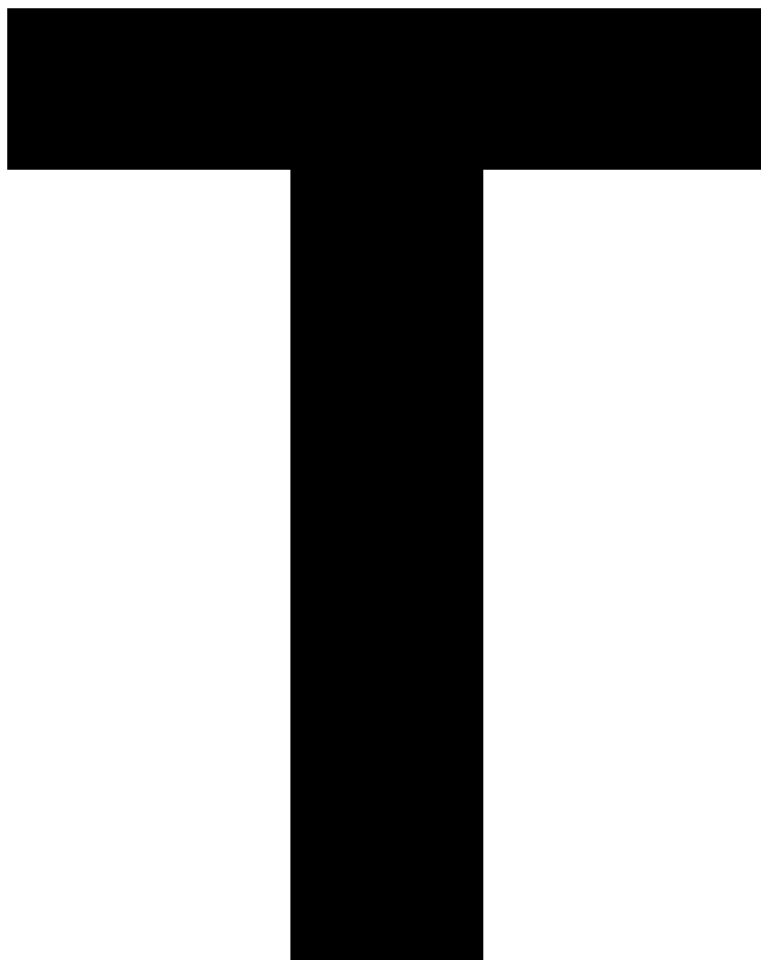
## NOTES :

The carboxylation of activated CH groups with MMC (methoxy magnesium methyl carbonate) (**Szarvasy**) and addition of the resulting activated ketones to C=N bonds (**Schöpf**).

## REFERENCES :

- 1) E. Szarvasy, *Ber. Dtsch. Chem. Ges.*, 1897, **30**, 1836.
- 2) C. Schöpf; A. Komzak; F. Braun; E. Jacobi, *Liebigs Ann. Chem.*, 1948, **559**, 1.
- 3) C. Schöpf, *Angew. Chem.*, 1949, **61**, 31.
- 4) C. Schöpf; H. Arm; H. Krimm, *Chem. Ber.*, 1951, **84**, 690.
- 5) C. Schöpf; F. Braun; K. Burkhardt; G. Dummer; H. Müller, *Liebigs Ann. Chem.*, 1959, **626**, 123.
- 6) J.M. Grisar; G.P. Claxton; K.T. Stewart, *Synthesis*, 1974, 284.
- 7) W.H. Parsons; R.H. Schlessinger; M.L. Quesada, *J. Am. Chem. Soc.*, 1980, **102**, 889.

## COMMENTS :



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**E**

EVANS – TISCHTSCHENKO REDUCTION · 1726

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**T**

TABOURY SYNTHESIS · 1694

TAFEL REARRANGEMENT · 1695

TAKEDA REACTION · 1696

TANIGAWA REACTION · 1698

TANIGUCHI REACTION · 1699

TÄUBER SYNTHESIS · 1700

TAYLOR SYNTHESIS · 1702

TEBBE OLEFINATION · 1703

TEUBER QUINONE SYNTHESIS · 1705

THIELE – DIMROTH SYNTHESIS · 1708

THIELE – WINTER QUINONE ACETOXYLATION · 1709

THIELE FULVENE SYNTHESIS · 1710

THOMAS REACTION · 1712

THORPE – ZIEGLER REACTION · 1713

THYAGARAJAN INDOLE SYNTHESIS · 1715

TIEMANN AMINATION · 1716

TIEMANN REARRANGEMENT · 1718

TIFFENEAU – DEMJANOV RING ENLARGEMENT · 1719

TIFFENEAU SYNTHESIS · 1721

TIMMIS PTERIDINE SYNTHESIS · 1722

TIPSON – COHEN OLEFINATION · 1723

TISHCHENKO – CLAISEN REACTION · 1725

TOLLENS ADDITION · 1726

TORGOV SYNTHESIS · 1728

TRAHANOVSKY ETHER OXIDATION · 1731

TRAUBE PURINE SYNTHESIS · 1732

TREIBS ALLYLIC OXIDATION · 1733

TROFIMOV PYRROLE SYNTHESIS · 1735

TROST – CHEN DECARBOXYLATION · 1737

TROST CYCLOPENTANATION · 1738

TROST DESYMMETRISATION · 1740

TROST OXIDATIVE DECARBOXYLATION · 1741

TSCHUGAEFF (CHUGAEV) OLEFIN SYNTHESIS · 1743

TSUGE REACTION · 1744

TSUJI – TROST ALLYLATION · 1746

TSUJI – WACKER OLEFIN OXIDATION · 1747

TSUJI – WILKINSON REACTION · 1750

TWITCHELL PROCESS · 1751

TYRER SULFONATION PROCESS · 1752

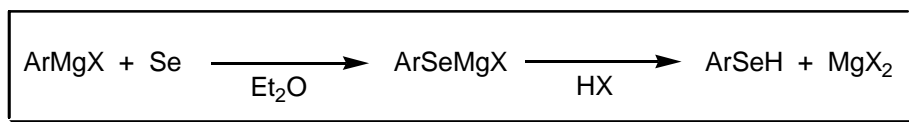
## TABOURY SYNTHESIS

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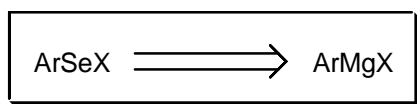
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

An aromatic **Grignard** compound is treated in diethyl ether with selenium to give an aryl selenium magnesium halide, which with a hydrohalic acid yields the selenophenol. See also **Grignard** reaction.

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### REFERENCES :

Houben – Weyl : **9**, 958

Org. Synth. : **24**, 89

Org. Synth. Coll. Vol. : **3**, 771

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1) M. Taboury, *Bull. Soc. Chim. Fr.*, 1903, **29**, 761.

2) H. Wuyts, *Bull. Soc. Chim. Fr.*, 1906, **35**, 166.

3) D.G. Foster; S.F. Brown, *J. Am. Chem. Soc.*, 1928, **50**, 1184.

4) T. Jayachandran; T. Manimaran; V.T. Ramakrishnan, *Indian J. Chem.*, 1984, **23B**, 328.

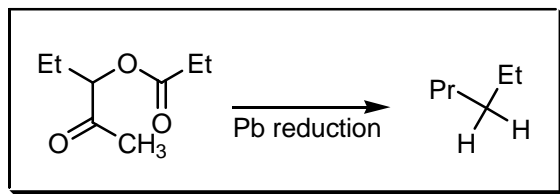
5) R.V. Bonnert; P.R. Jenkins, *J. Chem. Soc., Perkin Trans. 1*, 1989, 413.

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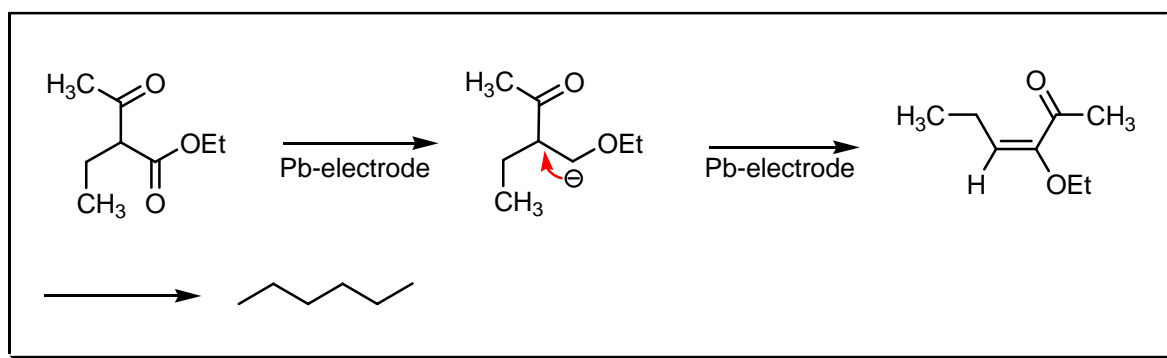
COMMENTS :

## TAFEL REARRANGEMENT

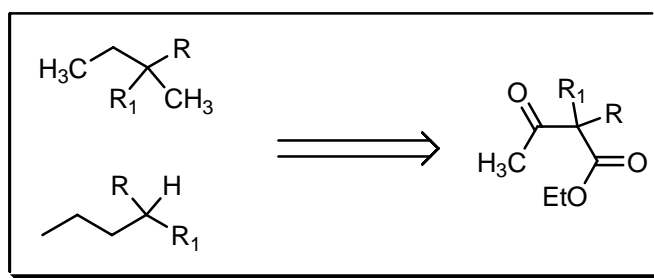
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

Substituted acetoacetic acid and similar ketonic compounds when submitted to cathodic (lead) reduction give hydrocarbons with rearranged carbon skeletons. Both the oxo and carboxyl groups are reduced to methylene and methyl groups.



## REFERENCES :

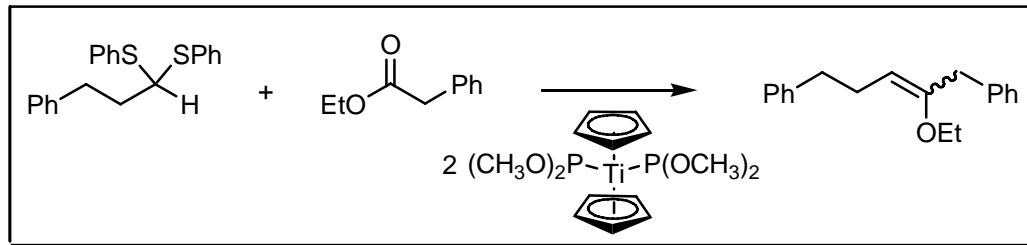
Houben – Weyl : 5/1a, 280, 471

- 1) J. Tafel; H. Hahl, *Ber. Dtsch. Chem. Ges.*, 1907, **40**, 3312.
- 2) J. Tafel; W. Jürgen, *Ber. Dtsch. Chem. Ges.*, 1909, **42**, 2548.
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- 4) H. Stenzl; F. Fichter, *Helv. Chim. Acta*, 1934, **17**, 669.
- 5) H. Stenzl; F. Fichter, *Helv. Chim. Acta*, 1936, **19**, 392.
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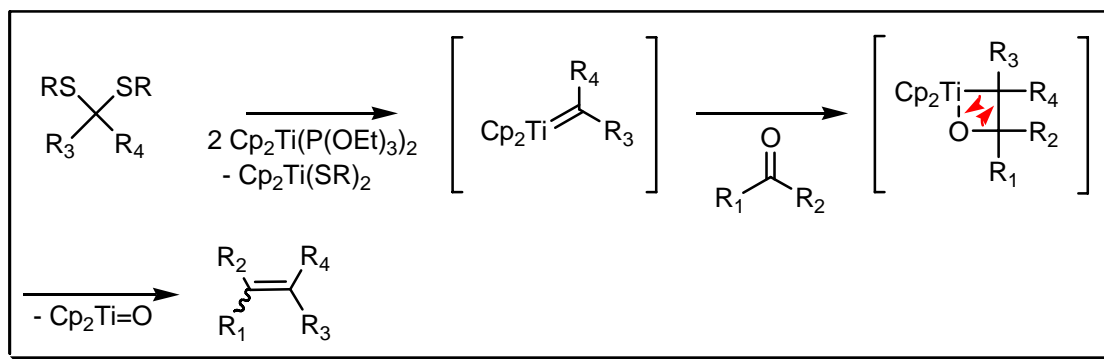
## COMMENTS :

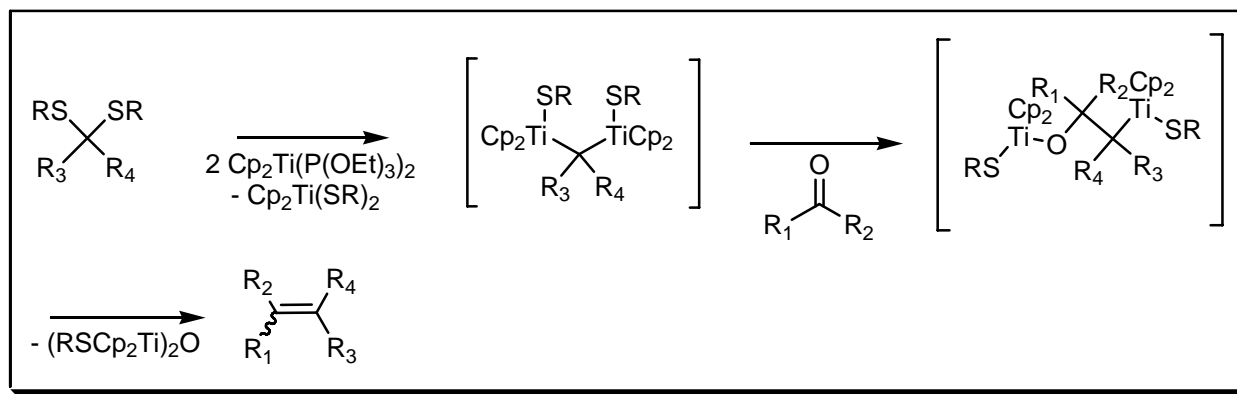
## TAKEDA REACTION

### EXAMPLE :

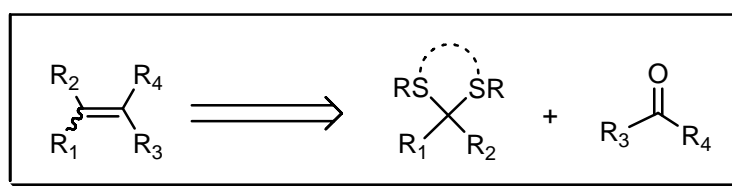


### MECHANISM :





#### DISCONNECTION :



#### NOTES :

The **Takeda** reaction solves the problems of the **Nozaki – Hiyama – Kishi (Takai – Utimoto)** reaction. The major drawback is the difficult access to substituted dihalomethane compounds. Dithioacetals however are very easily accessible. The reaction proceeds smoothly with aldehydes, ketones, esters but also with olefins, which are cyclopropanated and symmetrically disubstituted alkynes to afford trisubstituted 1,3-dienes. See also **Corey – Kwiatkowski, Eastwood, Horner – Wadsworth – Emmons, Julia – Paris – Kocienski – Lythgoe, Krief – Reich – Chow, Nozaki – Hiyama – Kishi (Takai – Utimoto), Nysted, Paquette, Petasis** reaction, **Peterson, Ramberg – Bäcklund, Still – Gennari, Tebbe** and **Wittig** reactions.

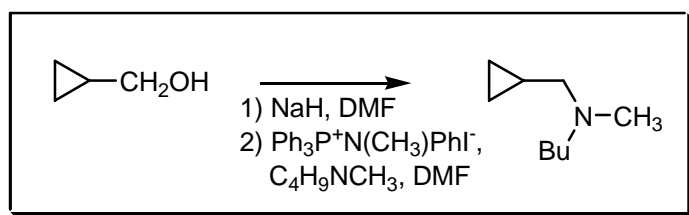
#### REFERENCES :

- 1) T. Takeda; H. Shimokawa; Y. Miyachi; T. Fujiwara, *Chem. Commun.*, 1997, 1055.
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- 4) B. Breit, *Angew. Chem., Int. Ed.*, 1998, **37**, 453.

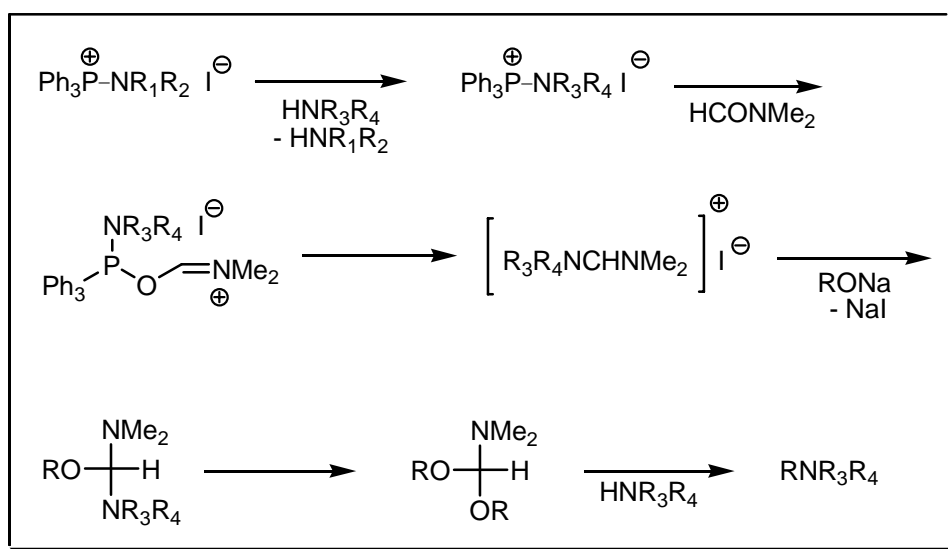
#### COMMENTS :

## TANIGAWA REACTION

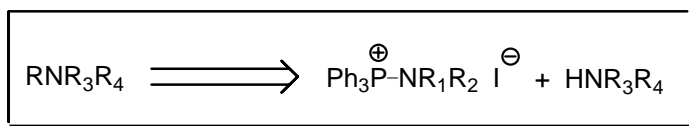
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The **Tanigawa** reaction has been widely cited in numerous reviews and textbooks. Unfortunately, there has been no report by any worker that has made any amine by this method since the originally work was published. This is because this reaction does not work under the reaction conditions reported by **Tanigawa et al.**

### REFERENCES :

March : 414

Smith – March : 502

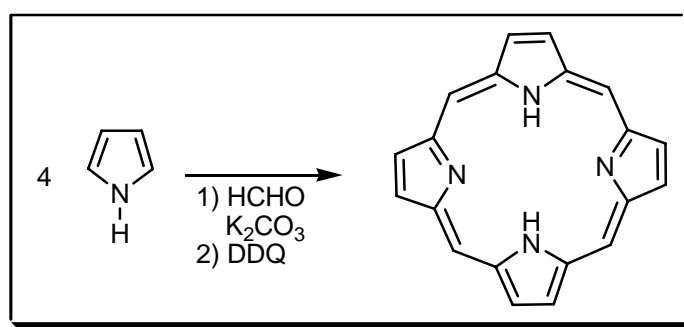
1) Y. Tanigawa; S.L. Murahashi; I. Moritani, *Tetrahedron Lett.*, 1975, **16**, 471.

2) P. Frøyen; J. Skramstad, *Tetrahedron Lett.*, 1998, **39**, 6387.

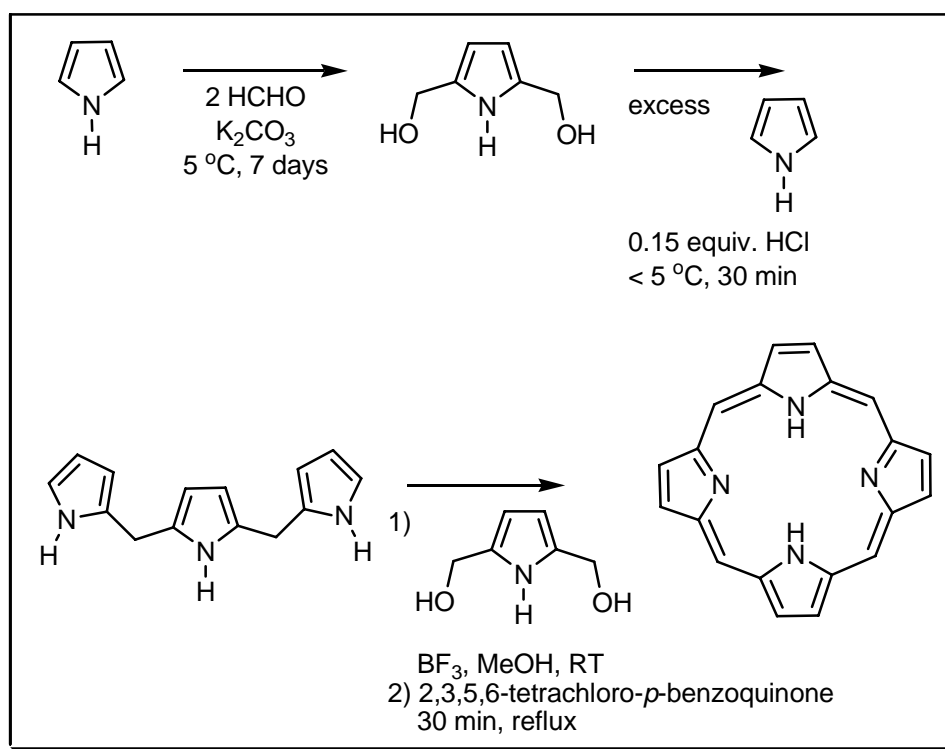
COMMENTS :

## TANIGUCHI REACTION

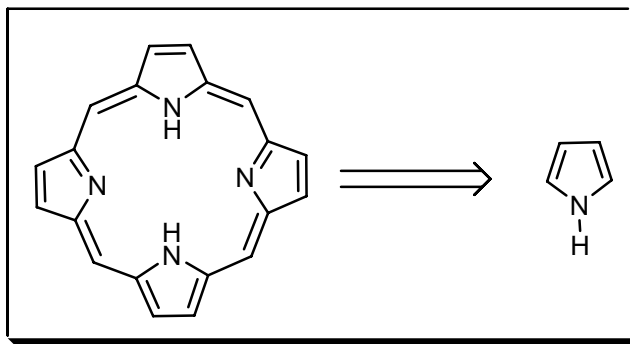
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The reaction between 2,5-bis(hydroxymethyl)pyrrole and pyrrole in the presence of hydrochloric acid affords tripyrrane, which gives porphyrins by the standard [3+1] **MacDonald** condensation. See also **Adler – Longo**, **Lindsey**, **MacDonald**, and **Rothmund** reactions.

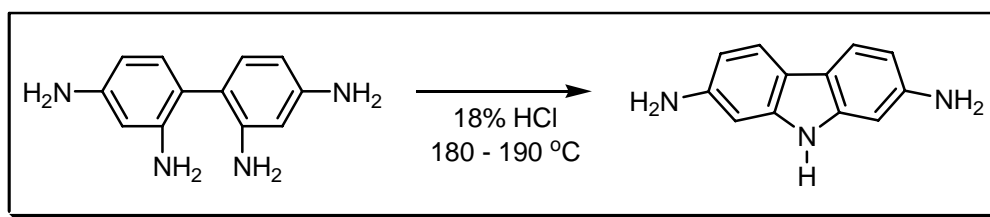
## REFERENCES :

S. Taniguchi; H. Hasegawa; M. Nishimura; M. Takahashi, *Synlett*, 1999, 73.

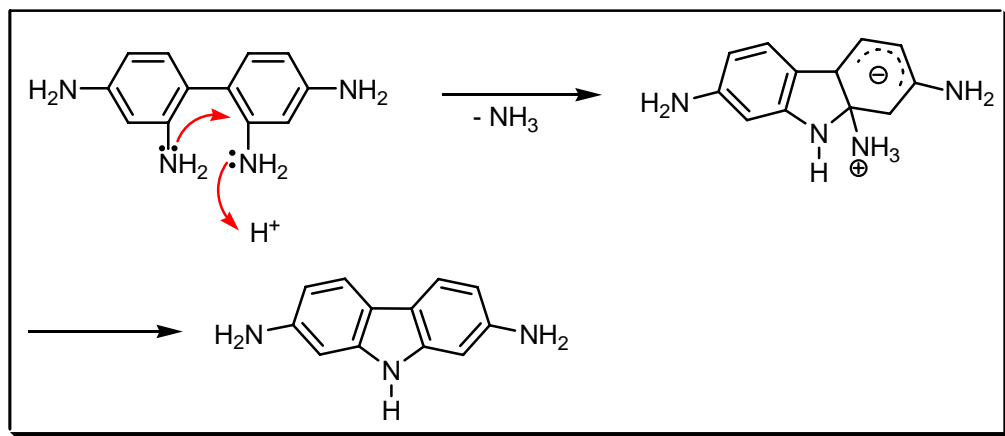
## COMMENTS :

## TÄUBER SYNTHESIS

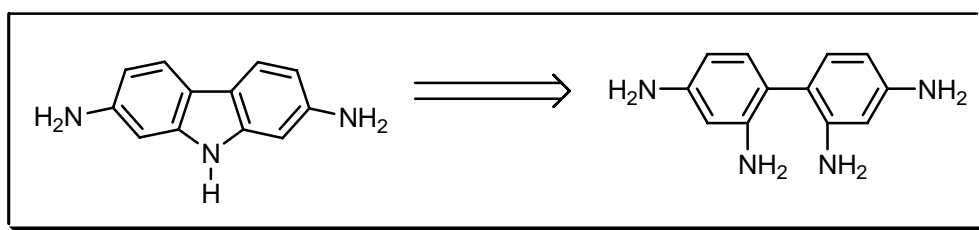
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Carbazoles are obtained by heating 2,2'-diaminodiphenyls with mineral acid or phosphoric acid at 180 – 190 °C. See also **Borsche – Drechsel**, **Bucherer** carbazole and **Graebe – Ullmann** reactions.

### REFERENCES :

Houben – Weyl : E6a, 932

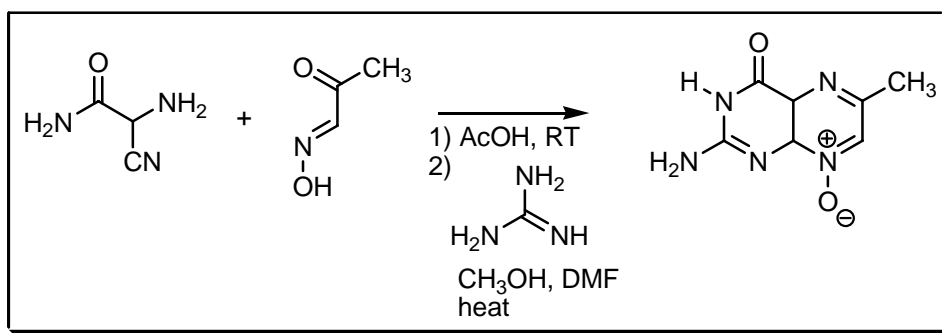
Science of Synthesis : 10, 710

- 1) E. Täuber, *Ber. Dtsch. Chem. Ges.*, 1890, **23**, 3266.
- 2) F.E. King; F.J. King, *J. Chem. Soc.*, 1945, 824.
- 3) H. Leditschke, *Chem. Ber.*, 1953, **86**, 522.
- 4) T. Yamamoto; C. Hideshima; K. Suehiro; M. Tashiro; G.K.S. Prakash; G.A. Olah, *J. Org. Chem.*, 1991, **56**, 6248.

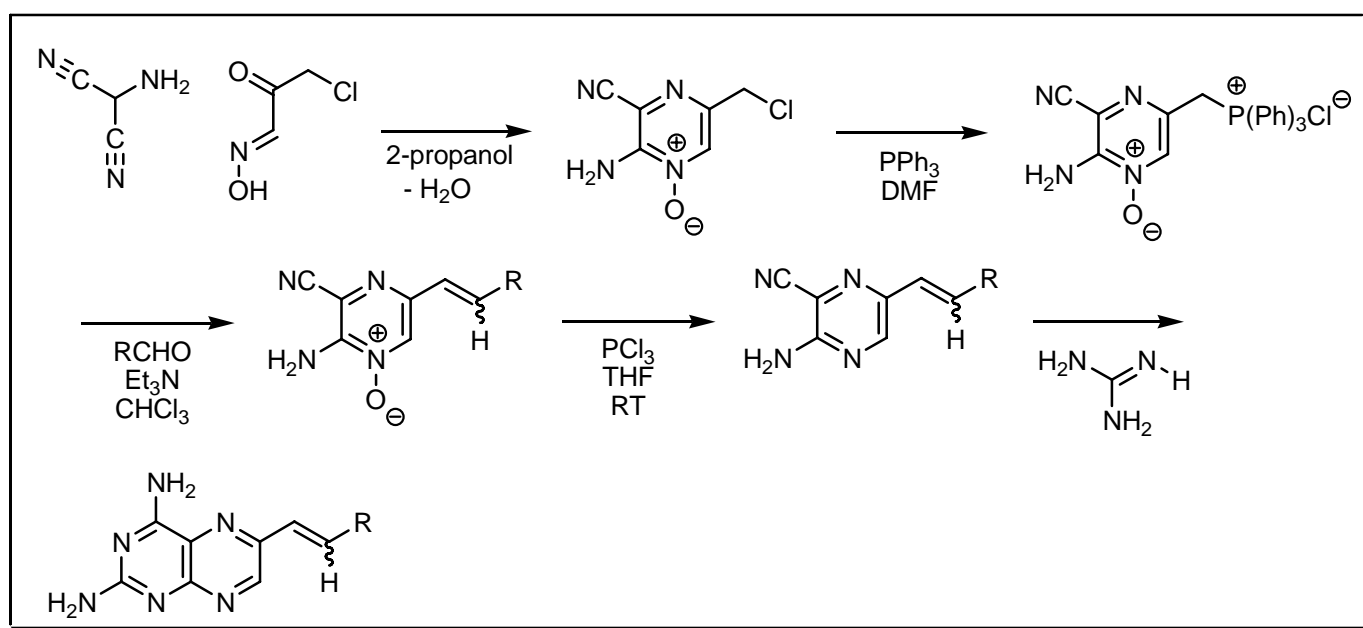
### COMMENTS :

## TAYLOR SYNTHESIS

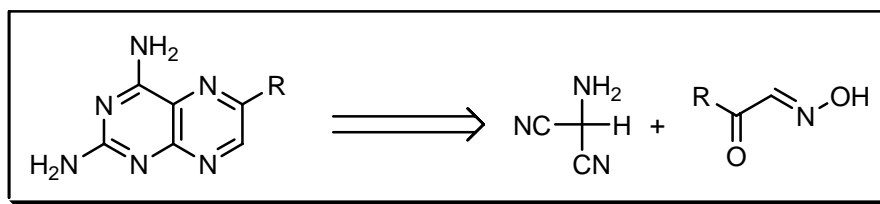
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Another pteridine synthesis using 2-malononitrile and 2-oxoalkanal oximes as reagents. See also **Blicke – Pachter**, **Boon – Polonovski**, **Isay** and **Timmis** reactions.

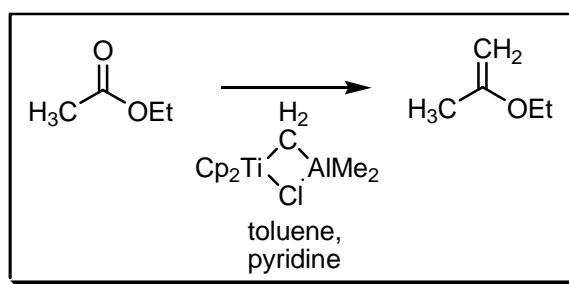
## REFERENCES :

- 1) E.C. Taylor; T. Kobayashi, *J. Org. Chem.*, 1973, **38**, 2817.
- 2) E.C. Taylor; R.F. Abdulla, *Tetrahedron Lett.*, 1973, **14**, 2093.
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- 4) H. Bader; A. Rosowsky, *J. Org. Chem.*, 1991, **56**, 3386.
- 5) A. Rosowsky; R.A. Forsch; V.E. Reich; J.H. Freisheim; R.G. Moran, *J. Med. Chem.*, 1992, **35**, 1578.
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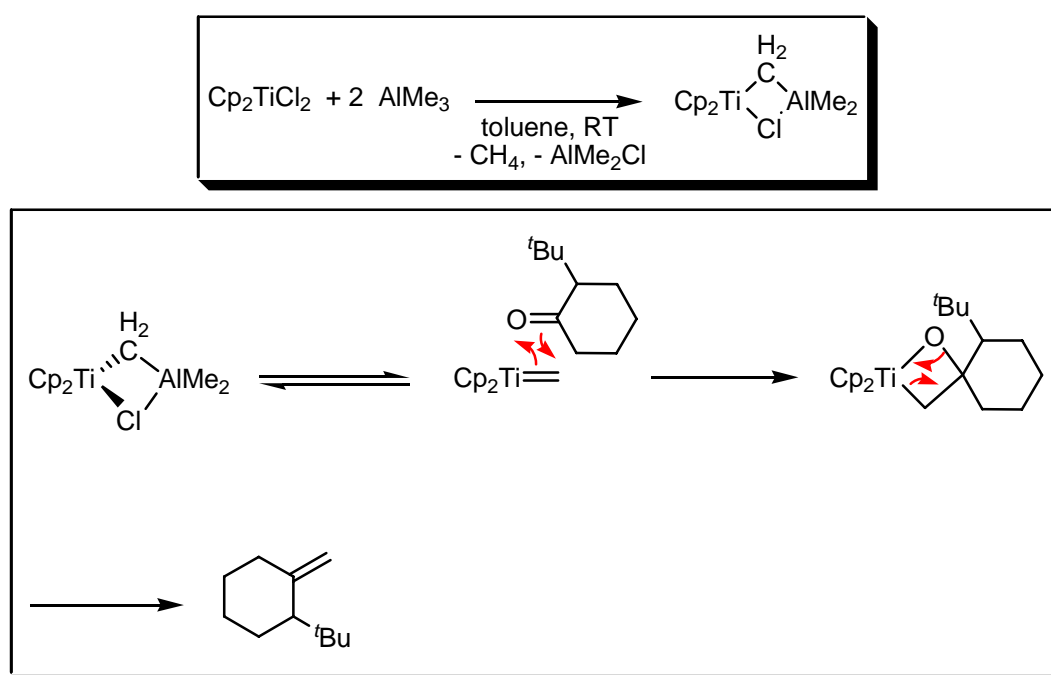
## COMMENTS :

## TEBBE OLEFINATION

### EXAMPLE :

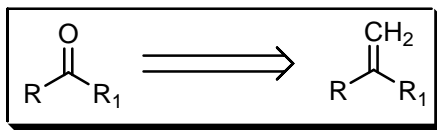


### MECHANISM :





## DISCONNECTION :



## NOTES :

This is the synthesis of terminal olefins from ketones or esters *via* a titanium methylene transfer reagent. **Takai** and **Lombardo** published a still undefined reagent that accomplishes methylation and alkylidenation of carboxylic acid derivatives including silyl esters. The catalyst is also used for olefin metathesis. See also **Corey – Kwiatkowski**, **Eastwood**, **Horner – Wadsworth – Emmons**, **Julia – Paris – Kocienski – Lythgoe**, **Krief – Reich – Chow**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Nysted**, **Paquette**, **Petasis** reaction, **Peterson**, **Ramberg – Bäcklund**, **Still – Gennari**, **Takeda** and **Wittig** reactions.

## REFERENCES :

**March** : 933

**Smith – March** : 1237

**Smith** : 813

**Smith 2<sup>nd</sup>** : 679

**Org. React.** : 43, 1

**Org. Synth.** : 65, 81; 69, 72

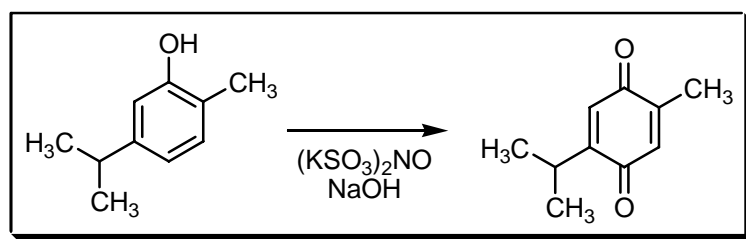
**Org. Synth. Coll. Vol.** : 8, 386, 512

- 1) F.N. Tebbe; G.W. Parshall; G.S. Reddy, *J. Am. Chem. Soc.*, 1978, **100**, 3611.
- 2) K. Takai; Y. Hotta; K. Oshima; H. Nozaki, *Tetrahedron Lett.*, 1978, **19**, 2417.
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- 7) R.C. Hartley; G.J. McKiernan, *J. Chem. Soc., Perkin Trans. 1*, 2002, 2763.
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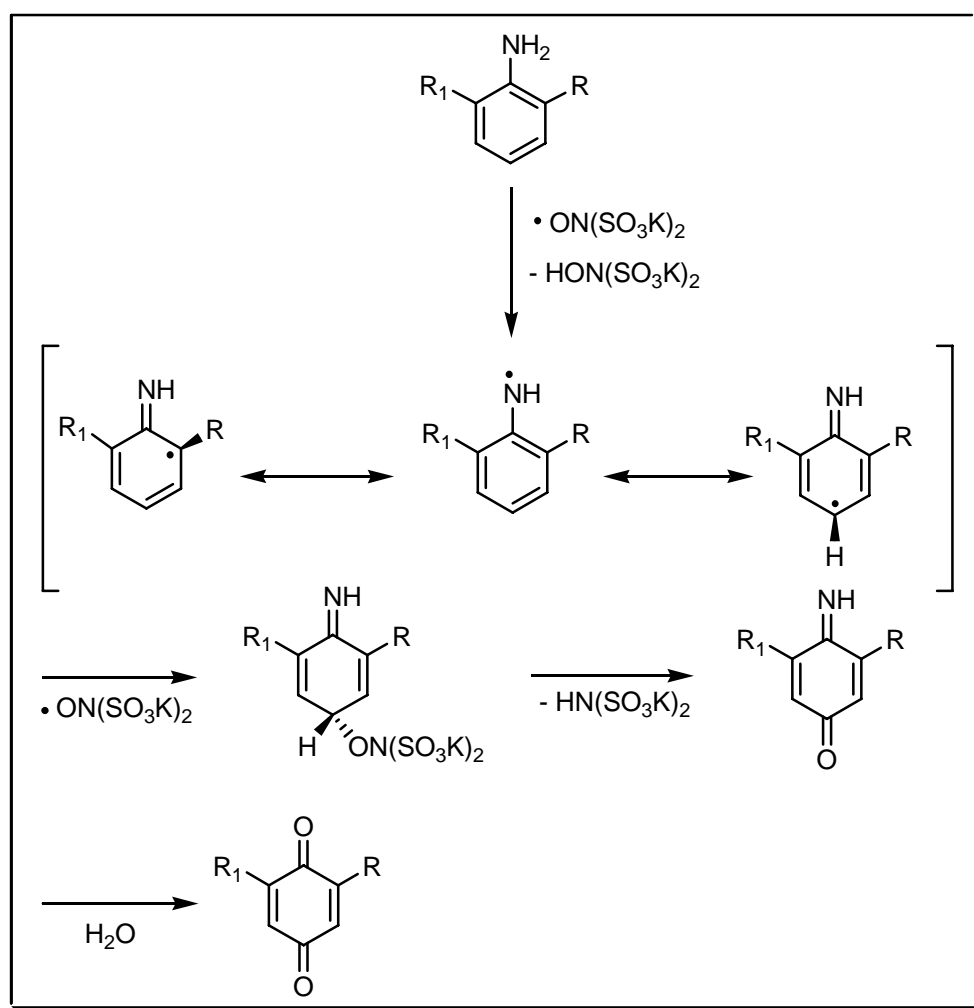
## COMMENTS :

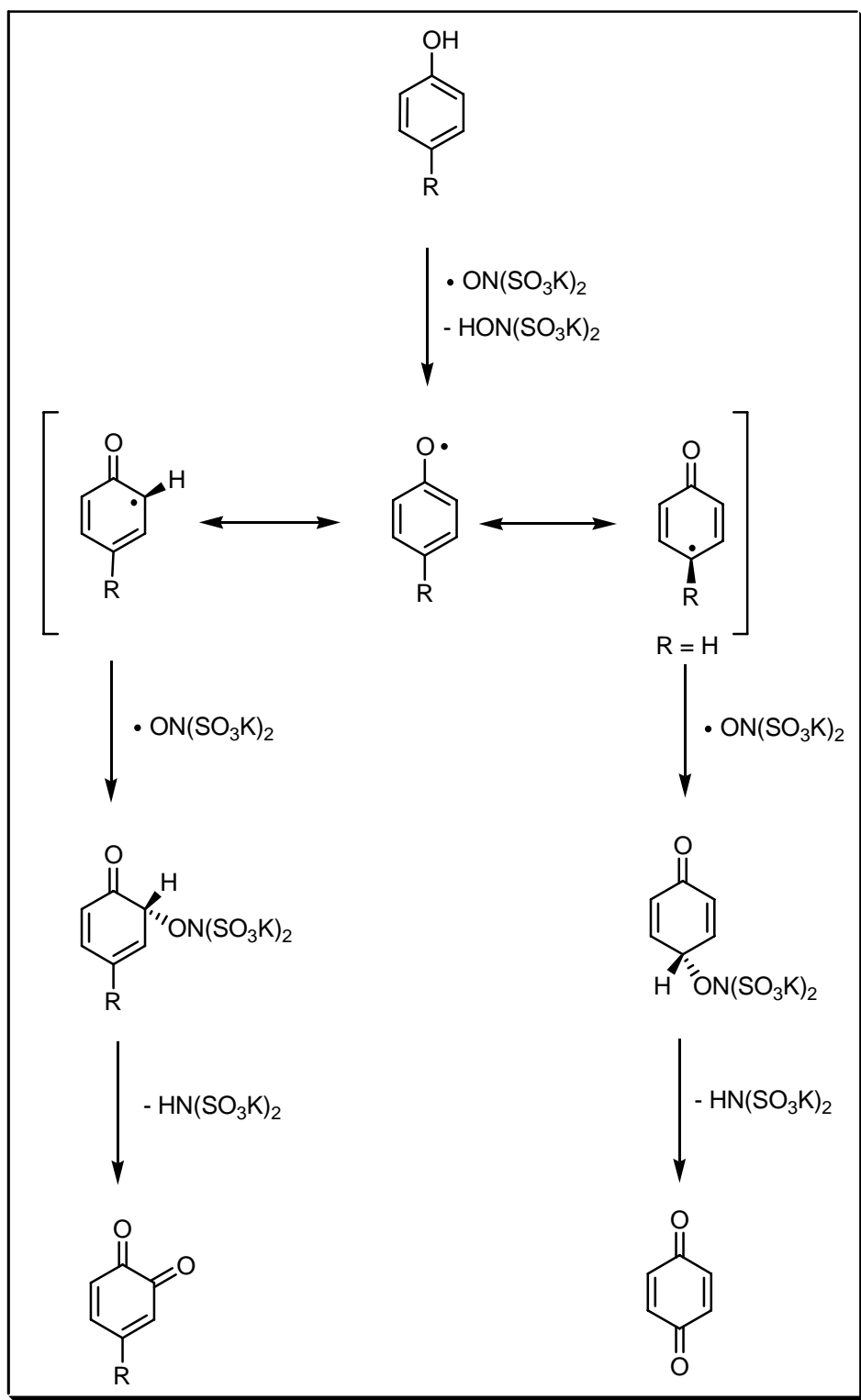
## TEUBER QUINONE SYNTHESIS

### EXAMPLE :

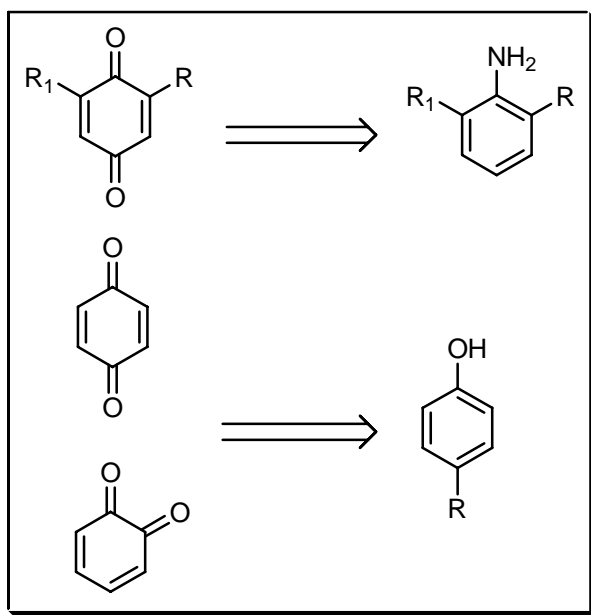


### MECHANISM :





## DISCONNECTION :



## NOTES :

The oxidation of phenols and anilines derivatives to quinones using potassium nitrosodisulfonate (**Fremy's salt**). See also **Adler** phenol oxidation.

## REFERENCES :

**March** : 1171

**Smith – March** : 1518

**Smith** : 256

**Smith 2<sup>nd</sup>** : 221

**Org. Synth.** : **52**, 83, 88

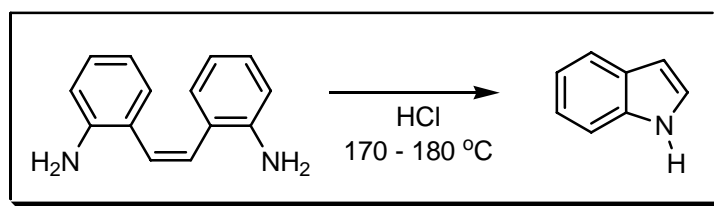
**Org. Synth. Coll. Vol.** : **6**, 480, 1010

- 1) H.-J. Teuber; G. Jellinek, *Chem. Ber.*, 1952, **85**, 95.
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- 4) A.P. Kozikowski; K. Sugiyama; J.P. Springer, *J. Org. Chem.*, 1981, **46**, 2426.
- 5) J.A. Hadfield; A.T. McGown; J. Butler, *Molecules*, 2000, **5**, 82.

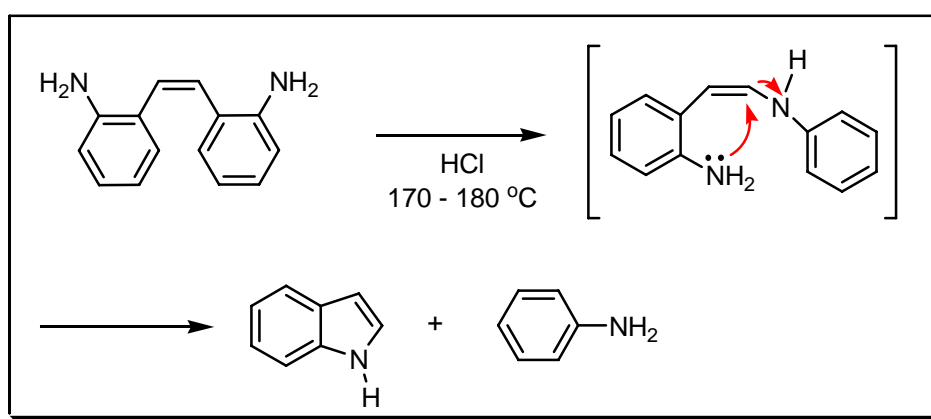
## COMMENTS :

## THIELE – DIMROTH SYNTHESIS

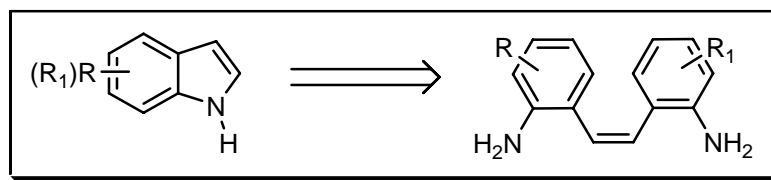
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

A mixture of equimolecular amounts of 2,2'-diaminostilbene and its anhydrous dihydrochloride, when heated at 170 – 185 °C yields indole and aniline. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

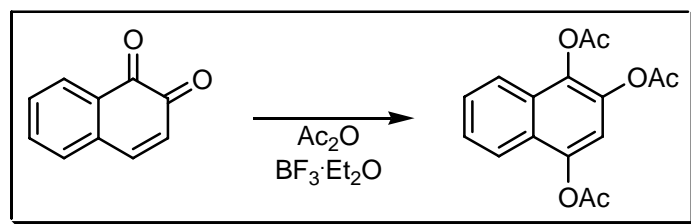
### REFERENCES :

J. Thiele; O. Dimroth, *Ber. Dtsch. Chem. Ges.*, 1895, **28**, 1411.

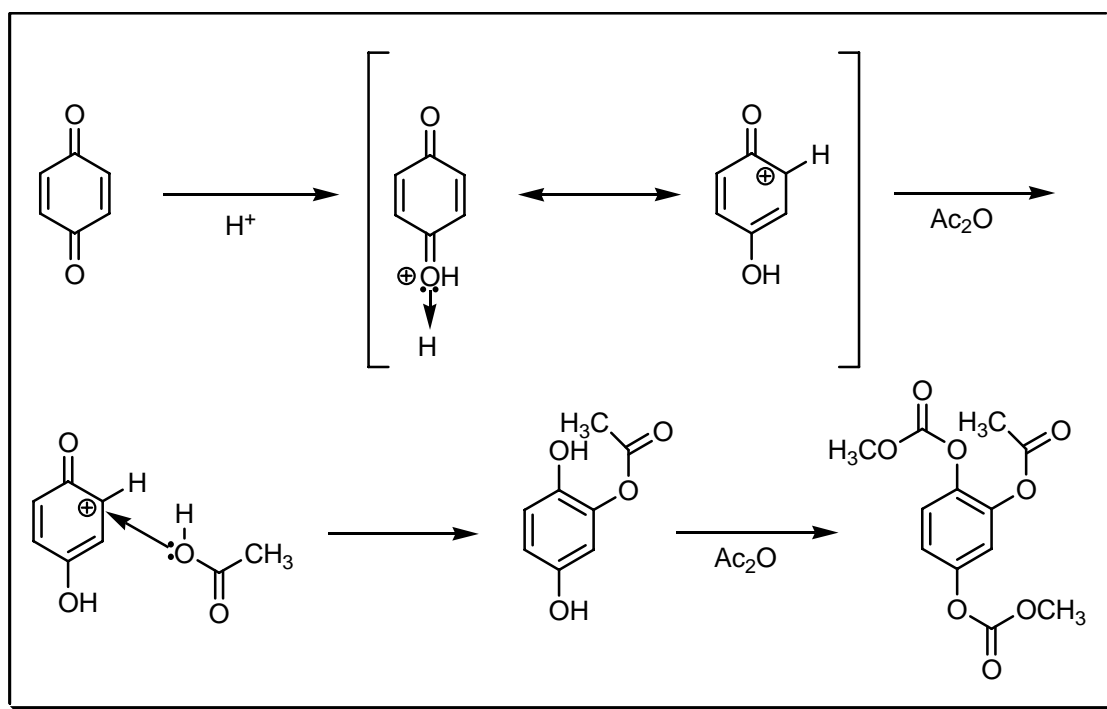
COMMENTS :

## THIELE – WINTER QUINONE ACETOXYLATION

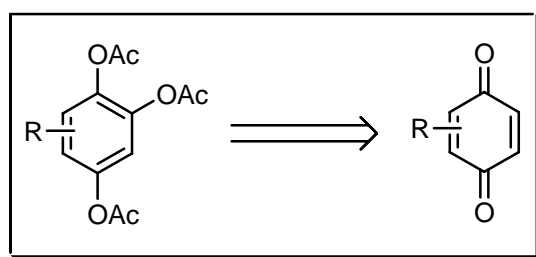
EXAMPLE :



MECHANISM :



DISCONNECTION :



**NOTES :**

The synthesis of triacetoxaryl derivatives from quinones and derivatives catalysed by sulfuric acid or boron trifluoride. See also **Hinsberg** sulfone reaction.

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**REFERENCES :**

Houben – Weyl : **4/2**, 40; **E5**, 55

Org. React. : **19**, 199

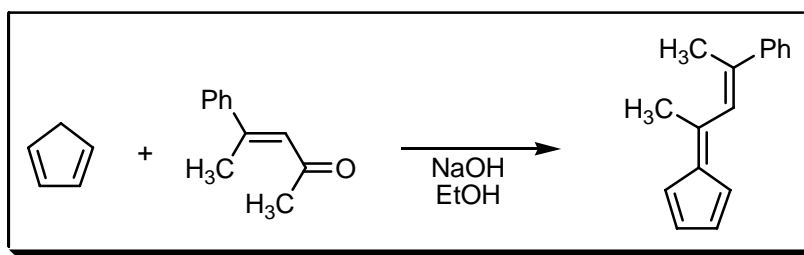
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- 1) J. Thiele, *Ber. Dtsch. Chem. Ges.*, 1898, **31**, 1247.
  - 2) J. Thiele; E. Winter, *Liebigs Ann. Chem.*, 1900, **311**, 341.
  - 3) H. Erdtman, *proc. Roy. Soc., Ser. A*, 1934, **143**, 177.
  - 4) J.M. Blatchly; J.F.W. McOmie, *J. Chem. Soc.*, 1963, 5311.
  - 5) M. Hirama; S. Ito, *Chem. Lett.*, 1977, 627.
  - 6) D. Villemin; N. Bar; M. Hammadi, *Tetrahedron Lett.*, 1997, **38**, 4777.
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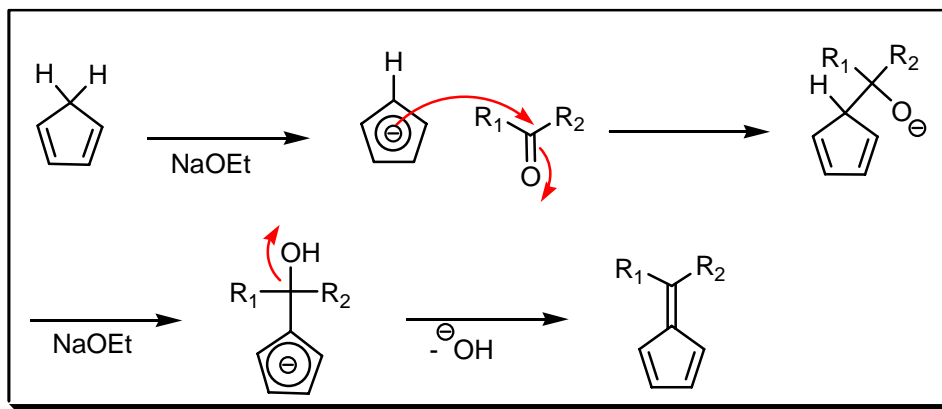
**COMMENTS :**

## THIELE FULVENE SYNTHESIS

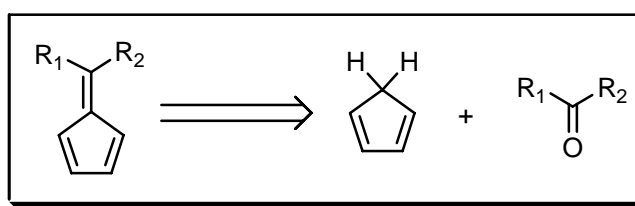
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**EXAMPLE :**

### MECHANISM :



### DISCONNECTION :



### NOTES :

1,3-Cyclopentadiene reacts with aldehydes and ketones in the presence of sodium ethoxide or sodium hydroxide in ethanol. The base not only deprotonates but also catalyses the dehydration of the primary adduct *via* the substituted cyclopentadienide. See also **Nesmanjanov** fulvene reaction.

### REFERENCES :

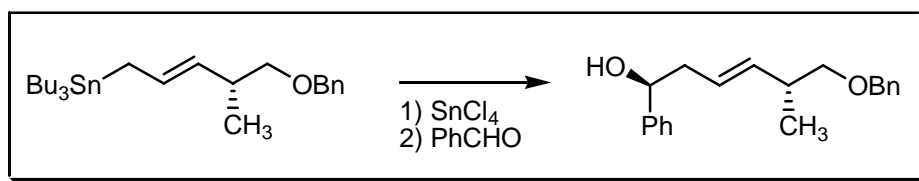
- 1) J. Thiele, *Ber. Dtsch. Chem. Ges.*, 1900, **33**, 666.
- 2) J. Thiele; H. Balhorn, *Liebigs Ann. Chem.*, 1906, **348**, 1.
- 3) J. Thiec; J. Wiemann, *Bull. Soc. Chim. Fr.*, 1956, 177.
- 4) J. Thiec; J. Wiemann, *Bull. Soc. Chim. Fr.*, 1960, 1066.
- 5) R.D. Little; K.J. Stone, *J. Org. Chem.*, 1984, **49**, 1849.
- 6) I. Erden; F.-P. Xu; A. Sadoun; W. Smith; G. Sheff; M. Ossun, *J. Org. Chem.*, 1995, **60**, 813.
- 7) K. Chajara; H. Ottoson, *Tetrahedron Lett.*, 2004, **45**, 6741.

### COMMENTS :

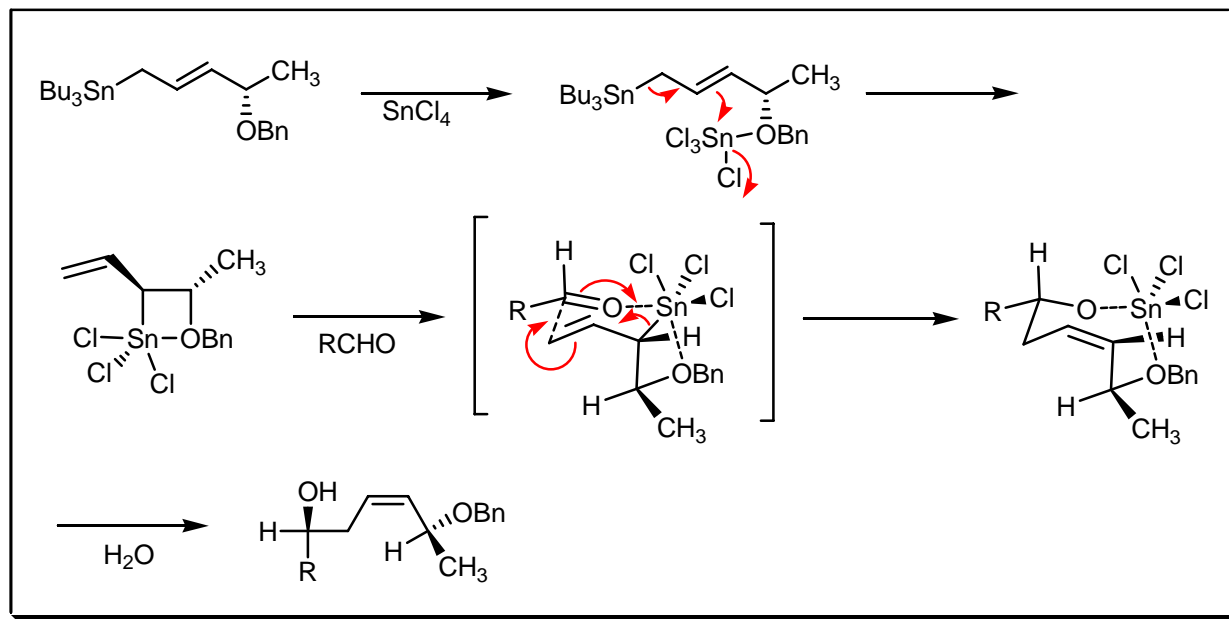


# THOMAS REACTION

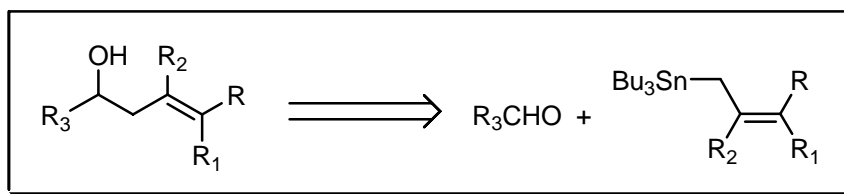
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Alk-2-enylstannanes with heteroatom substituents at the 4-, 5-, and 6-positions undergo stereoselective transmetalation (under kinetic control) on treatment with tin(IV) halides to generate allyltin trihalides which react with aldehydes and imines with useful levels of 1,5-, 1,6- and 1,7-asymmetric induction. 1,8-Asymmetric induction has also been reported by **Thomas**. See also **Duthaler – Hafner**, **Ibuka – Yamamoto**, **Matteson** and **Roush – Hoffmann – Yamamoto** reactions.

## REFERENCES :

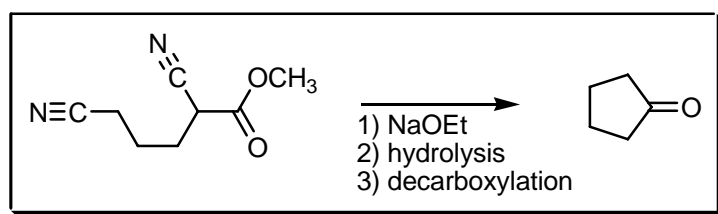
- 1) S.V. Mortlock; E.J. Thomas, *Tetrahedron Lett.*, 1988, **29**, 2479.
- 2) A.H. McNeil; E.J. Thomas, *Tetrahedron Lett.*, 1990, **31**, 6239.

- 3) A.H. McNeil; E.J. Thomas, *Synthesis*, 1994, 322.
- 4) E.J. Thomas, *Chem. Commun.*, 1997, 411.
- 5) E.-M. Moffatt; E.J. Thomas, *Tetrahedron*, 1999, **55**, 3723.
- 6) N.H. Taylor; E.J. Thomas, *Tetrahedron*, 1999, **55**, 8757.
- 7) P. Kumar; E.J. Thomas; D.R. Tray, *J. Braz. Chem. Soc.*, 2001, **12**, 623.
- 8) N. Martin; E.J. Thomas, *Tetrahedron Lett.*, 2001, **42**, 8373.

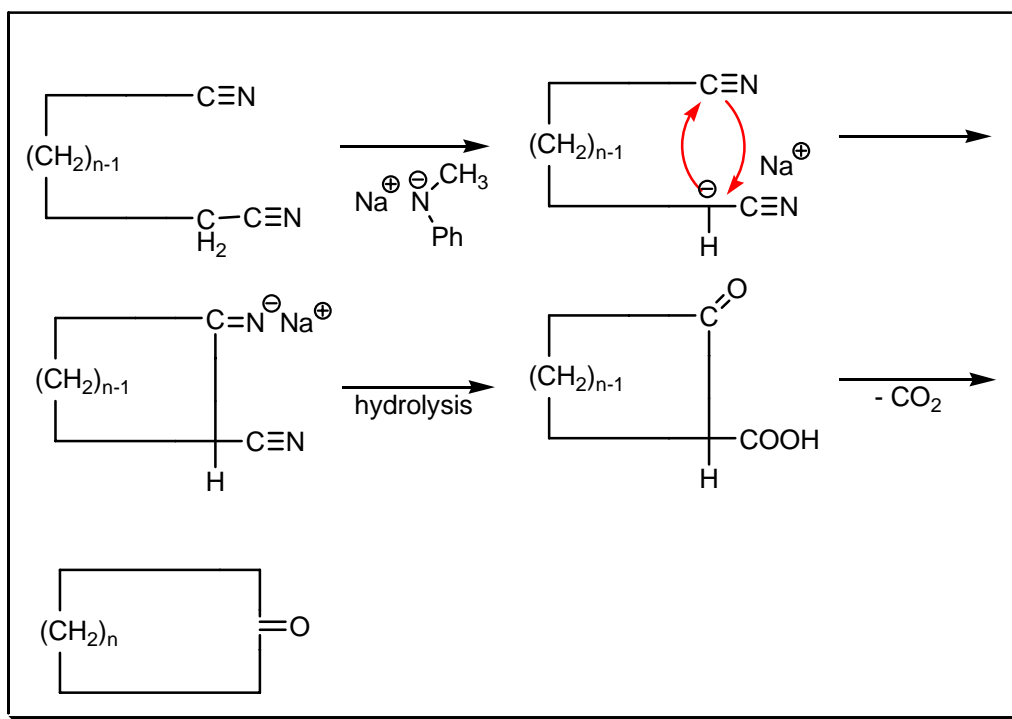
COMMENTS :

## THORPE – ZIEGLER REACTION

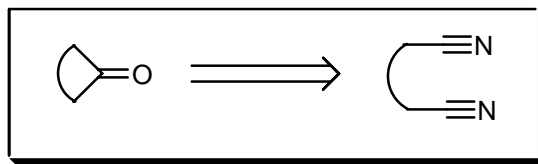
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The *intermolecular* reaction is called the **Thorpe** reaction. The *intramolecular* reaction is called the **Thorpe – Ziegler** reaction. The synthesis involves the cyclisation of  $\alpha,\omega$ -dinitriles with metal amines, in high dilution to yield iminonitriles, which are hydrolysed, and decarboxylated to the ketones. For 5-, 6-, 7-, 8- and 18-membered rings the yields are high. For 9-, 10-, 11-, and 12- membered rings the yields are moderate. It is also possible to make larger oxygen containing rings. See also **Corey – Nicolaou**, **Dieckmann** condensation, **Diels – Alder**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Kita**, **Masamune**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi** (**Takai – Utimoto**), **Raphael**, **Roush**, **Ruggli**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolakiewicz**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

## REFERENCES :

**March** : 963

**Smith – March** : 1219, 1238

**Smith** : 899

**Smith 2<sup>nd</sup>** : 752

**Houben – Weyl** : **4/2**, 758; **E6a**, 335, 618; **E7a**, 321; **E8a**, 674, 723

**Org. React.** : **15**, 1; **31**, 1

**Org. Synth.** : **53**, 98

**Org. Synth. Coll. Vol.** : **6**, 932

1) H. Baron; F.G.P. Remfry; J.F. Thorpe, *J. Chem. Soc.*, 1904, **85**, 1726.

2) K. Ziegler; H. Eberle, H. Ohlinger, *Liebigs Ann. Chem.*, 1933, **504**, 94.

3) K. Ziegler, *Chem. Ber.*, 1934, **67**, 139.

4) H.J. Nitzchke, *Angew. Chem.*, 1951, **63**, 491.

5) H.J. Nitzchke; H. Dudka, *Chem. Ber.*, 1955, **88**, 264.

6) E.C. Taylor; A. McKillop, *Adv. Org. Chem.*, 1970, **7**, 1.

7) D.P. Curran; W.D. Liu, *Synlett*, 1999, 117.

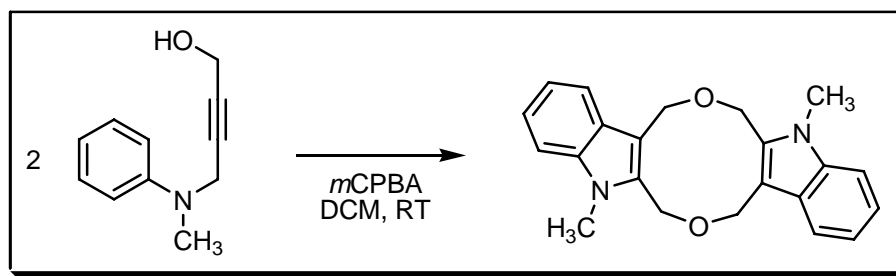
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9) R. Malassene; L. Toupet; J.-P. Hurvois; C. Moinet, *Synlett*, 2002, 895.

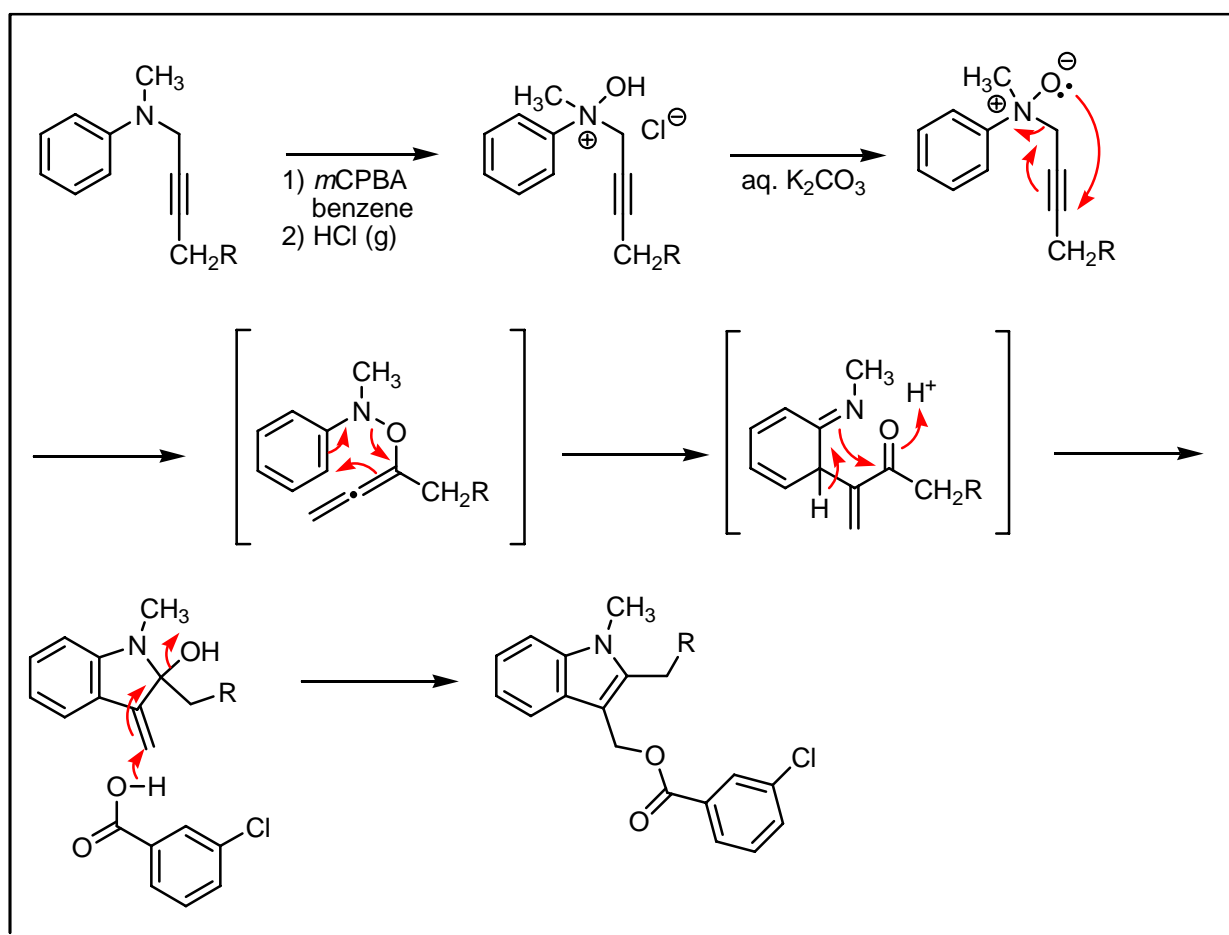
**COMMENTS :**

## THYAGARAJAN INDOLE SYNTHESIS

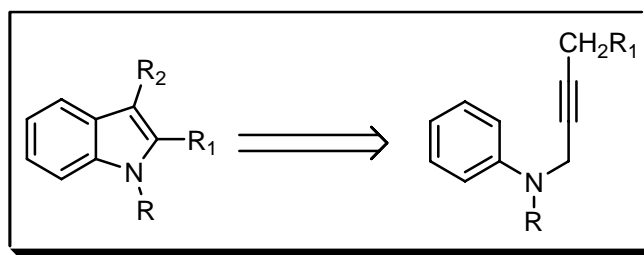
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

The formation of indole by sequential [2,3]- and [3,3]-sigmatropic rearrangements from the *N*-oxide of the aryl propynylamine. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

## REFERENCES :

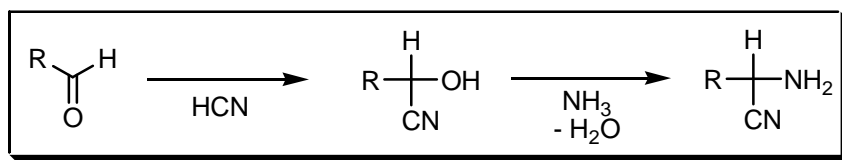
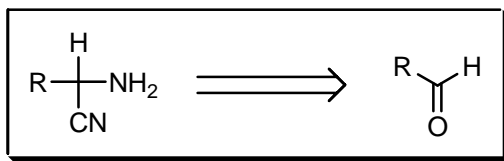
- 1) B.S. Thyagarajan; J.B. Hillard; K.V. Reddy; K.C. Majumdar, *Tetrahedron Lett.*, 1974, **15**, 1999.
- 2) J.B. Hillard; K.V. Reddy; K.C. Majumdar; B.S. Thyagarajan, *J. Heterocycl. Chem.*, 1974, **11**, 369.
- 3) T. Balasubramanian; K.K. Balasubramanian, *J. Chem. Soc., Chem. Commun.*, 1994, 1237.
- 4) K.C. Majumdar; G.H. Dana; U. Das, *Chem. Commun.*, 1996, 517.
- 5) K.C. Majumdar; G.H. Dana; U. Das, *J. Chem. Soc., Perkin Trans. 1*, 1997, 1229.

## COMMENTS :

## TIEMANN AMINATION

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

The cyanohydrin amination of aldehydes. See also **Bucherer – Bergs**, **Corey – Link**, **Strecker** amino acid, **Ultee**, **Urech** and **Zelinsky – Stadnikoff** reactions.

**REFERENCES :**

**March** : 964

**Smith – March** : 1239

**Houben – Weyl** : **8**, 280

**Org. Synth.** : **11**, 4; **22**, 13, 23

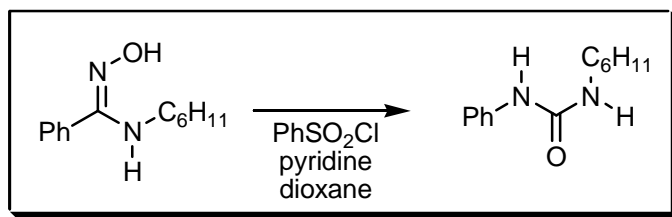
**Org. Synth. Coll. Vol.** : **2**, 29; **3**, 66, 84

- 1) A. Strecker, *Liebigs Ann. Chem.*, 1850, **75**, 27.
- 2) F. Tiemann, *Ber. Dtsch. Chem. Ges.*, 1880, **13**, 381.
- 3) D.T. Mowry, *Chem. Rev.*, 1948, **42**, 189.

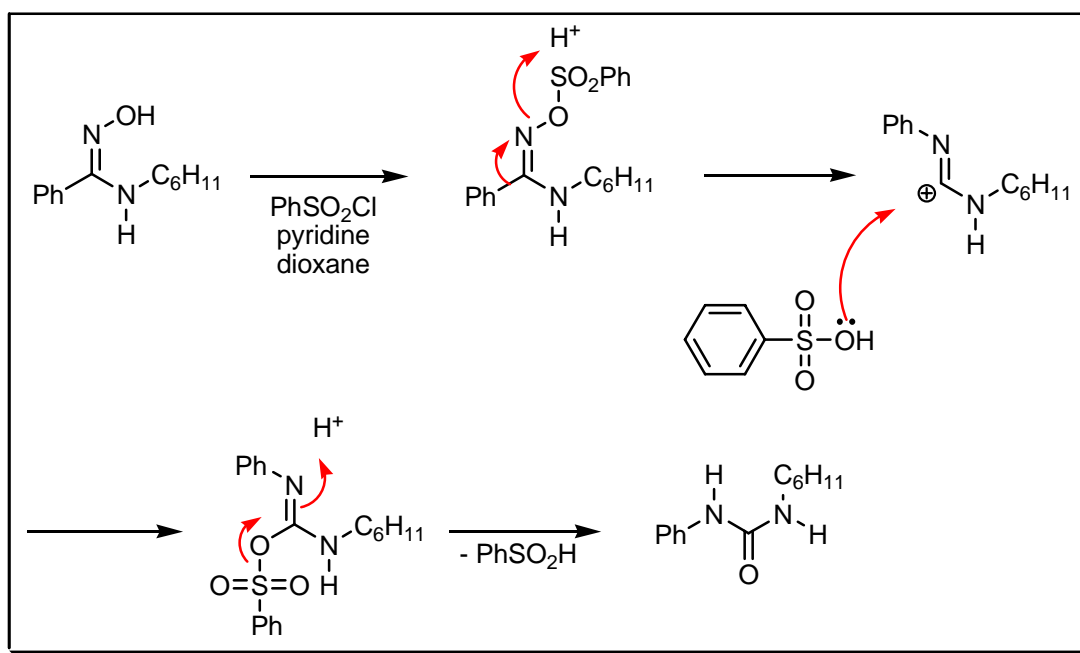
**COMMENTS :**

# TIEMANN REARRANGEMENT

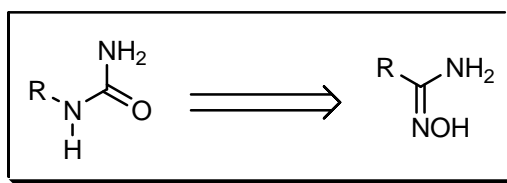
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The **Beckmann** rearrangement of amidoximes to urea derivatives in the presence of acids (benzene sulfonyl chloride). See also **Beckmann** rearrangement, **Curtius** rearrangement, **Hofmann** rearrangement and **Lossen** reactions.

## REFERENCES :

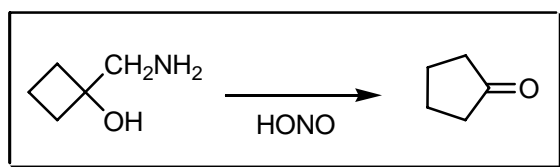
Org. React. : 3, 337

- 1) F. Tiemann, *Ber. Dtsch. Chem. Ges.*, 1891, **24**, 4162.
- 2) L.A. Paquette; J.P. Freeman, *J. Org. Chem.*, 1970, **35**, 2249.
- 3) J. Garapon; B. Sillion; J.M. Bonnier, *Tetrahedron Lett.*, 1970, **11**, 4905.
- 4) R. Richter; B. Tucker; H. Ulrich, *J. Org. Chem.*, 1983, **48**, 1694.
- 5) S.A. Bakunov; A.V. Rukavishnikov; A.V. Tkachev, *Synthesis*, 2000, 1148.

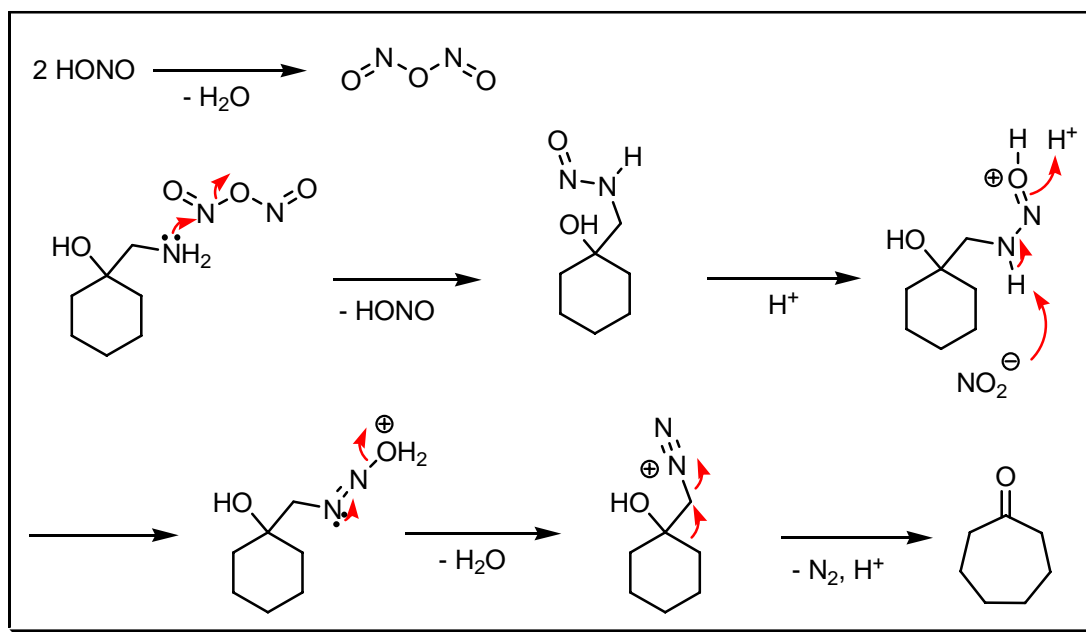
COMMENTS :

## TIFFENEAU – DEMJANOV RING ENLARGEMENT

EXAMPLE :

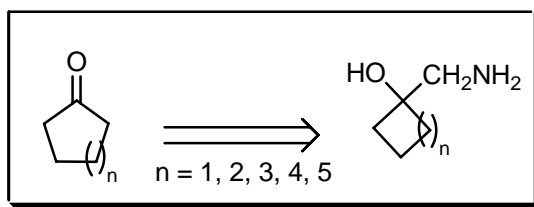


MECHANISM :





## DISCONNECTION :



## NOTES :

Amino alcohols, of the type 1-hydroxy-1-cycloalkylmethanamine obtained, e.g. by the reduction of a cyanohydrin, undergo deamination and rearrangement to cycloalkylones with one more carbon atom in the ring when treated with nitrous acid. There is also a halogenohydrin rearrangement. *Tert*- $\beta$ -iodoalcohols rearrange when treated with silver or mercuric salts to yield carbonyl compounds, *C.R. Séances Acad. Sci.*, 1907, **145**, 593. See also **Demjanov** rearrangement.

## REFERENCES :

**March** : 1074

**Smith – March** : 1399

**Smith** : 1293

**Smith 2<sup>nd</sup>** : 1068

**Houben – Weyl** : 4/2, 793; **E19c**, 400

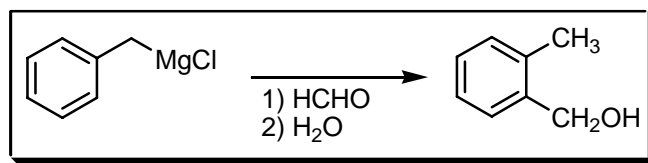
**Org. React.** : **11**, 157

- 1) N.J. Demjanov, *J. Russ. Phys. Chem. Ges.*, 1903, **35**, 375.
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- 6) D. Fattori; S. Henry; P. Vogel, *Tetrahedron*, 1993, **49**, 1649.
- 7) L. Chow; M. McClure; J. White, *Org. Biomol. Chem.*, 2004, **2**, 648.

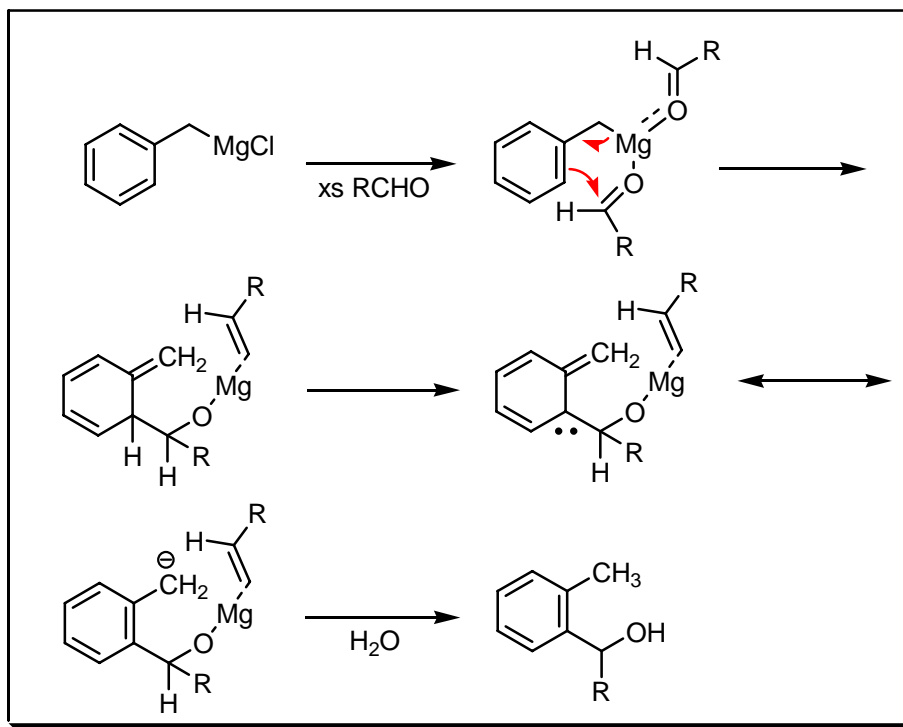
## COMMENTS :

# TIFFENEAU SYNTHESIS

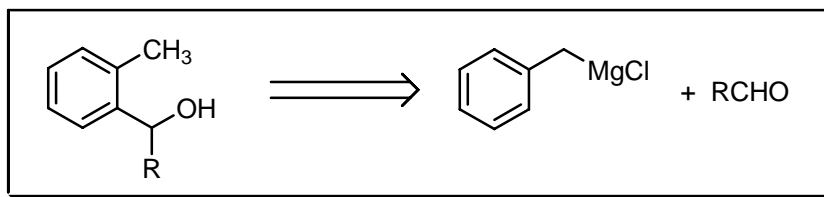
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

o-Methylbenzyl alcohols are obtained by treatment of the **Grignard** compound formed from benzyl chlorides with paraformaldehyde.

## REFERENCES :

- 1) M. Tiffeneau; Delange, *C.R. Séances Acad. Sci.*, 1903, **137**, 573.
- 2) J. Schmidlin; A. Garcia-Banús, *Ber. Dtsch. Chem. Ges.*, 1912, **45**, 3193.
- 3) H. Gilman; J.E. Kirby, *J. Am. Chem. Soc.*, 1927, **49**, 1825.

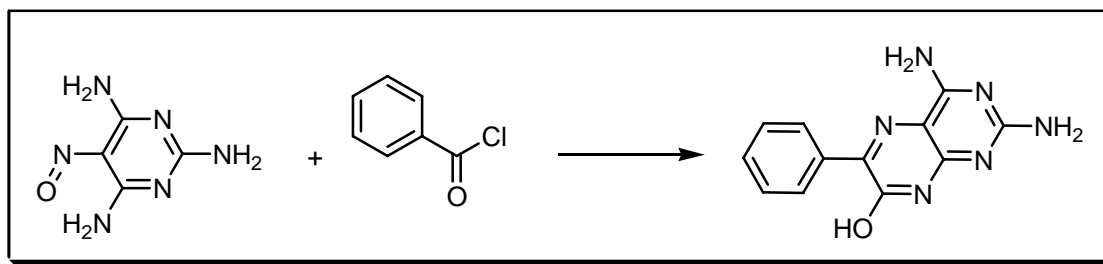
- 4) H. Gilman; J.E. Kirby, *J. Am. Chem. Soc.*, 1929, **51**, 3475.  
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8) B. van Zanten; W. Nauta, *Recl. Trav. Chim. Pays-Bas*, 1960, **79**, 1211.
- 

**COMMENTS :**

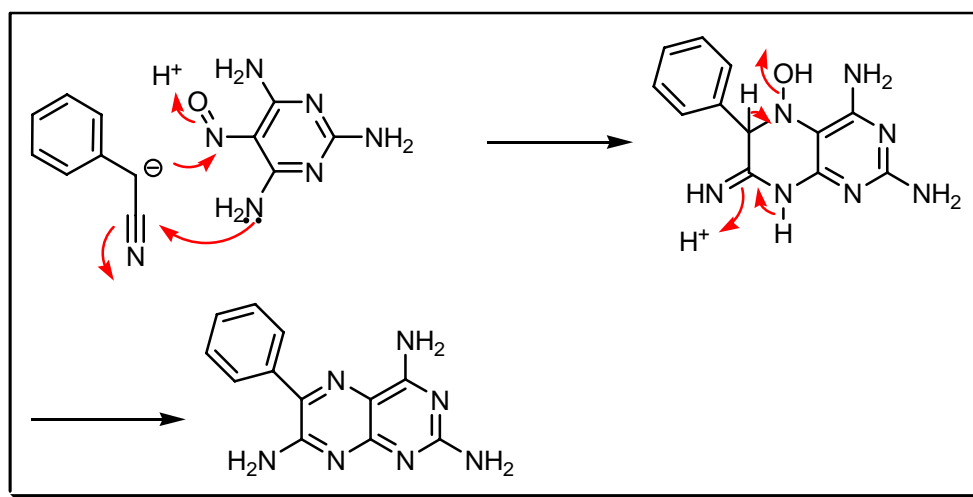
**TIMMIS PTERIDINE SYNTHESIS**

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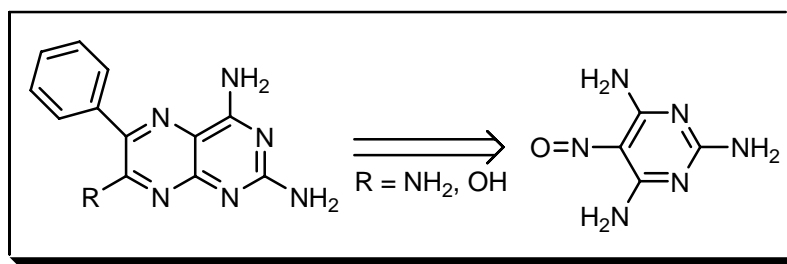
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

7-Amino and 7-hydroxy-pteridines and its derivatives are synthesised by the reaction of 4-amino-5-nitrosopyrimidines with phenylacetonitriles or phenylacetyl chlorides. In the case of the phenylacetonitriles, the use of sodium alkoxides as catalyst is necessary. See also **Blicke – Pachter**, **Boon – Polonovski**, **Isay**, and **Taylor** reactions.

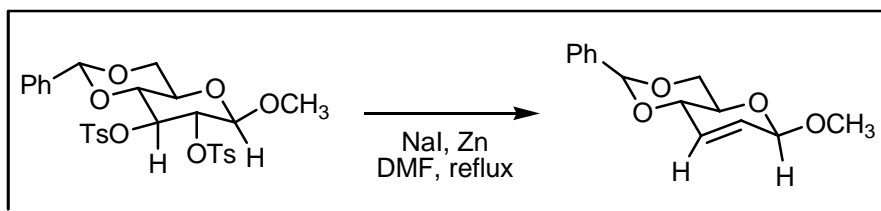
## REFERENCES :

- 1) G.M. Timmis, *Nature*, 1949, **164**, 139.
- 2) R.G.W. Spickett; G.M. Timmis, *J. Chem. Soc.*, 1954, 2887.
- 3) T.S. Osdense; G.M. Timmis, *J. Chem. Soc.*, 1955, 2032.
- 4) T.S. Osdense; G.M. Timmis, *J. Chem. Soc.*, 1955, 2036.
- 5) T.S. Osdense; G.M. Timmis, *J. Chem. Soc.*, 1955, 2038.

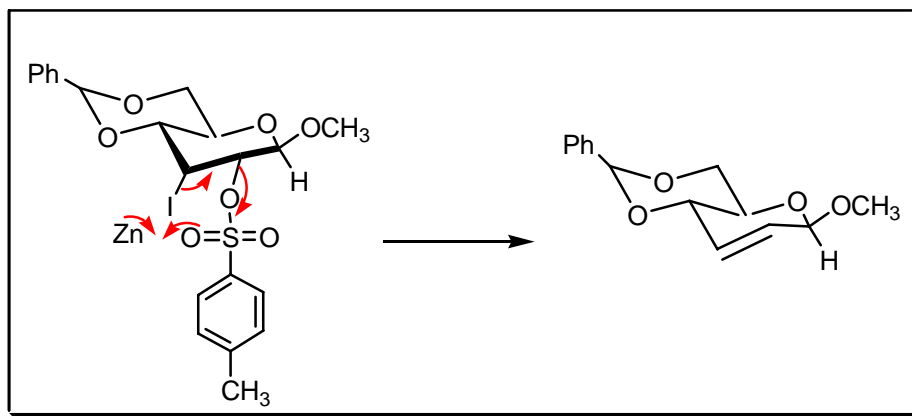
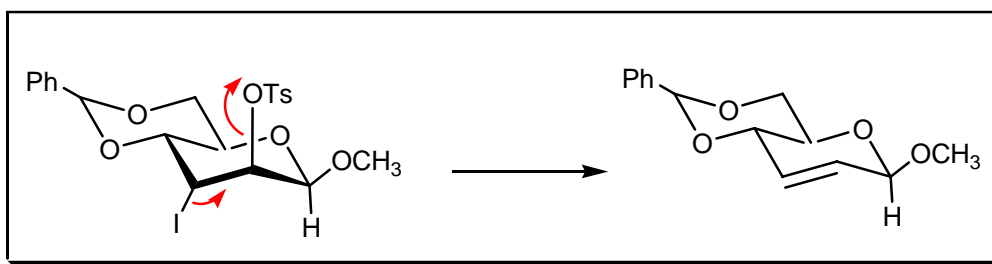
## COMMENTS :

## TIPSON – COHEN OLEFINATION

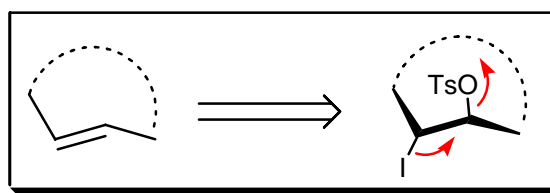
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The formation of enes from  $\alpha$ -diols, in which derived  $\alpha$ -disulfonates (two adjacent secondary tosylates) are treated with sodium iodide and zinc in refluxing DMF or butanone.

## REFERENCES :

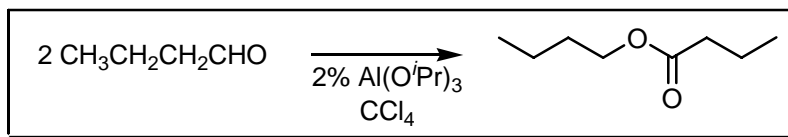
**Org. React.** : **30**, 457

- 1) R.S. Tipson; A. Cohen, *Carbohydr. Res.*, 1965, **1**, 338.
- 2) B. Fraser-Reid; B. Boctor, *Can. J. Chem.*, 1969, **47**, 393.
- 3) T. Yamazaki; K. Matsuda; H. Sugiyama; S. Seto; N. Yamaoka, *J. Chem. Soc., Perkin Trans. 1*, 1977, 1981.
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- 5) L.M. Engelhardt; M. Mocerino; R.V. Stick; A.H. White, *Aust. J. Chem.*, 1990, **43**, 1111.
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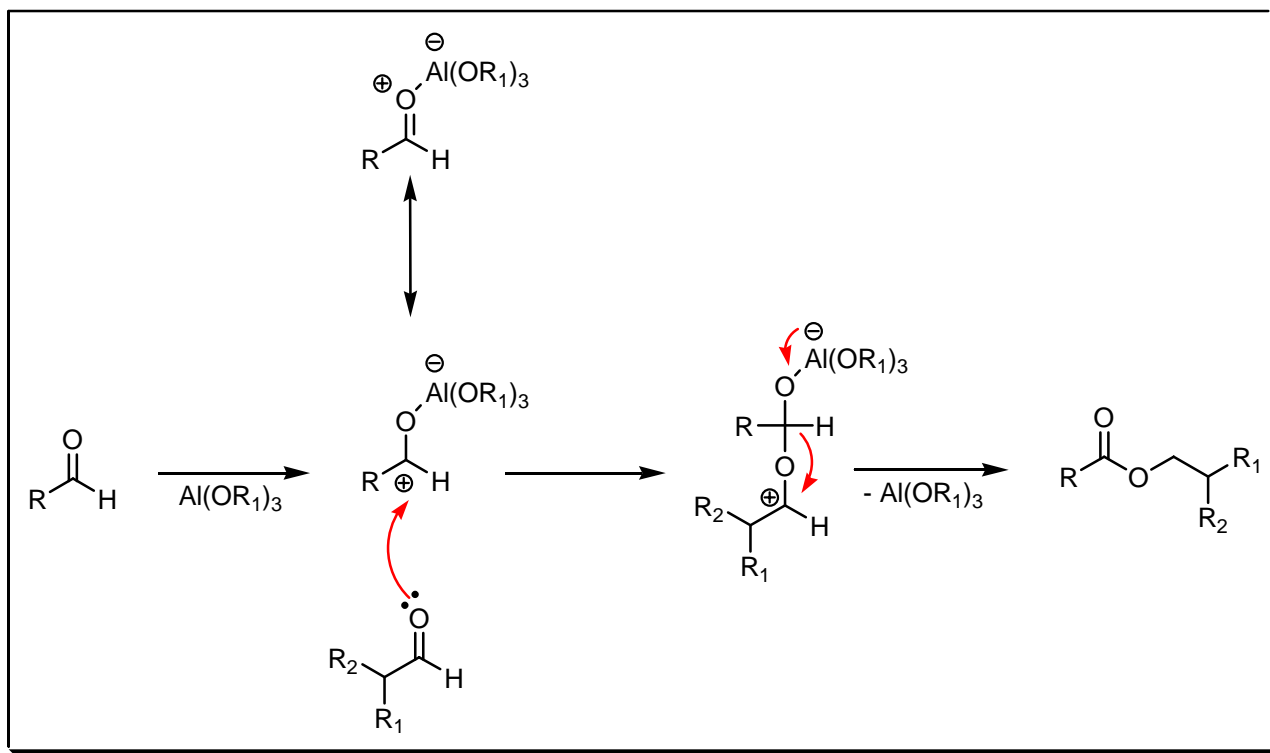
COMMENTS :

## TISHCHENKO – CLAISEN REACTION

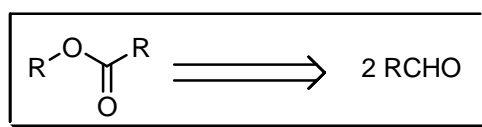
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The conversion of aldehydes to esters in the presence of metal alcoholates. One molecule of aldehyde is oxidised while the other is reduced. Crossed reactions are possible. The samarium promoted reduction is sometimes called

the **Evans – Tishchenko** reduction. Other transition metals like ruthenium and zirconocenes are also being used. See also **Cannizzaro**, **Meerwein – Ponndorf – Verley** reduction, **Nord** and **Oppenauer** oxidation reactions.

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#### REFERENCES :

**March** : 1235

**Smith – March** : 1565

**Houben – Weyl** : **E5**, 658

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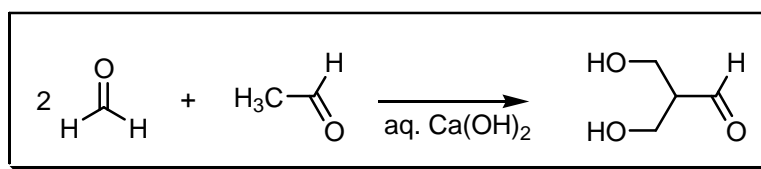
- 1) L. Claisen, *Ber. Dtsch. Chem. Ges.*, 1887, **20**, 648.
  - 2) W. Tishchenko, *J. Russ. Physik. Chem. Ges.*, 1906, **38**, 355.
  - 3) P.R. Stapp, *J. Org. Chem.*, 1973, **38**, 1433.
  - 4) D.A. Evans; A.H. Hoveyda, *J. Am. Chem. Soc.*, 1990, **112**, 6449.
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  - 6) K.M. Gillespie; I.J. Munslow; P. Scott, *Tetrahedron Lett.*, 1999, **40**, 9371.
  - 7) I. Simpura; V. Nevalainen, *Tetrahedron Lett.*, 2001, **42**, 3905.
  - 8) A.B. Smith III; D. Lee; C.M. Adams; M.C. Kozlowski, *Org. Lett.*, 2002, **4**, 4539.
  - 9) C.A. Fan; X.D. Hu; Y.Q. Tu; B.M. Wang; Z.L. Song, *Chem. Eur. J.*, 2003, **9**, 4301.
  - 10) J. Mlynarski; M. Mitura, *Tetrahedron Lett.*, 2004, **45**, 7549.
  - 11) C. Schneider; K. Klapa; M. Hansch, *Synlett*, 2005, 91.
- 

#### COMMENTS :

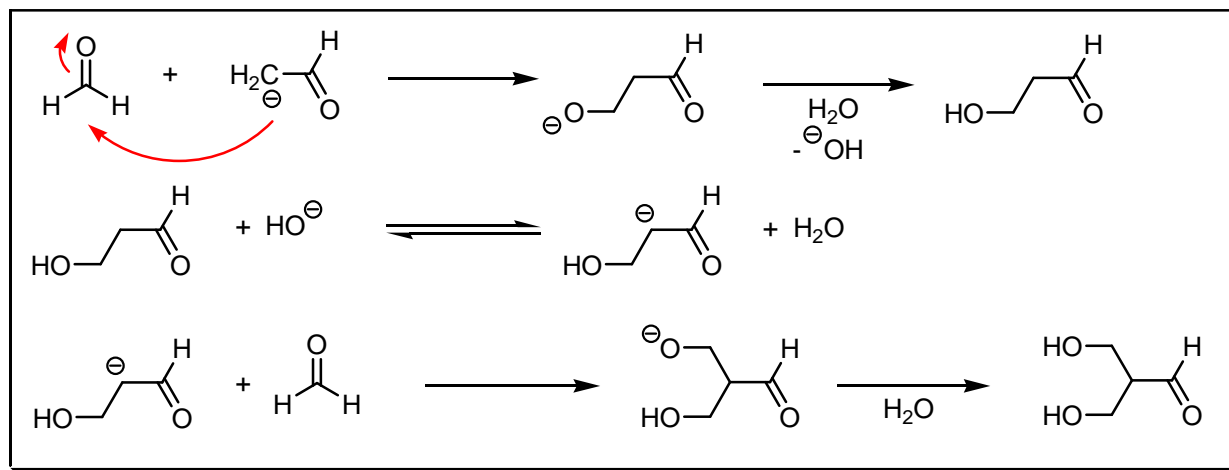
### TOLLENS ADDITION

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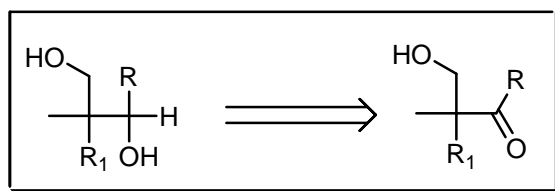
#### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The aldol addition of one, two, three or four equivalents of formaldehyde to an aldehyde or ketone in the presence of a weak base. See also **Cannizzaro** and **Mannich** reactions.

## REFERENCES :

March : 955

Smith – March : 1219, 1230

Houben – Weyl : 7/1, 89

Org. Synth. : 4, 53; 31, 101

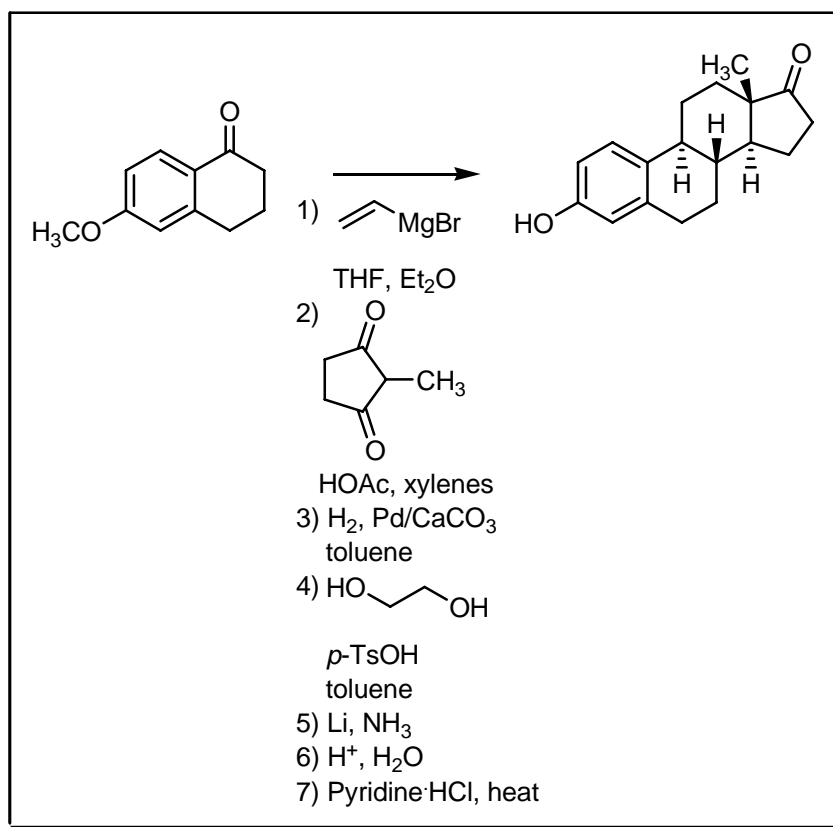
Org. Synth. Coll. Vol. : 1, 425; 4, 907

- 1) B. Tollens; P. Wigand, *Liebigs Ann. Chem.*, 1891, **265**, 316.
- 2) M. Apel; B. Tollens, *Ber. Dtsch. Chem. Ges.*, 1894, **27**, 1087.
- 3) T.J. Prosser, *J. Org. Chem.*, 1961, **26**, 242.
- 4) I.D. Jenkins, *J. Chem. Educ.*, 1987, **64**, 164.
- 5) S. Munoz; G.W. Gokel, *J. Am. Chem. Soc.*, 1993, **115**, 4899.
- 6) S. Huang; A.W.H. Mau, *J. Phys. Chem. B*, 2003, **107**, 3455.

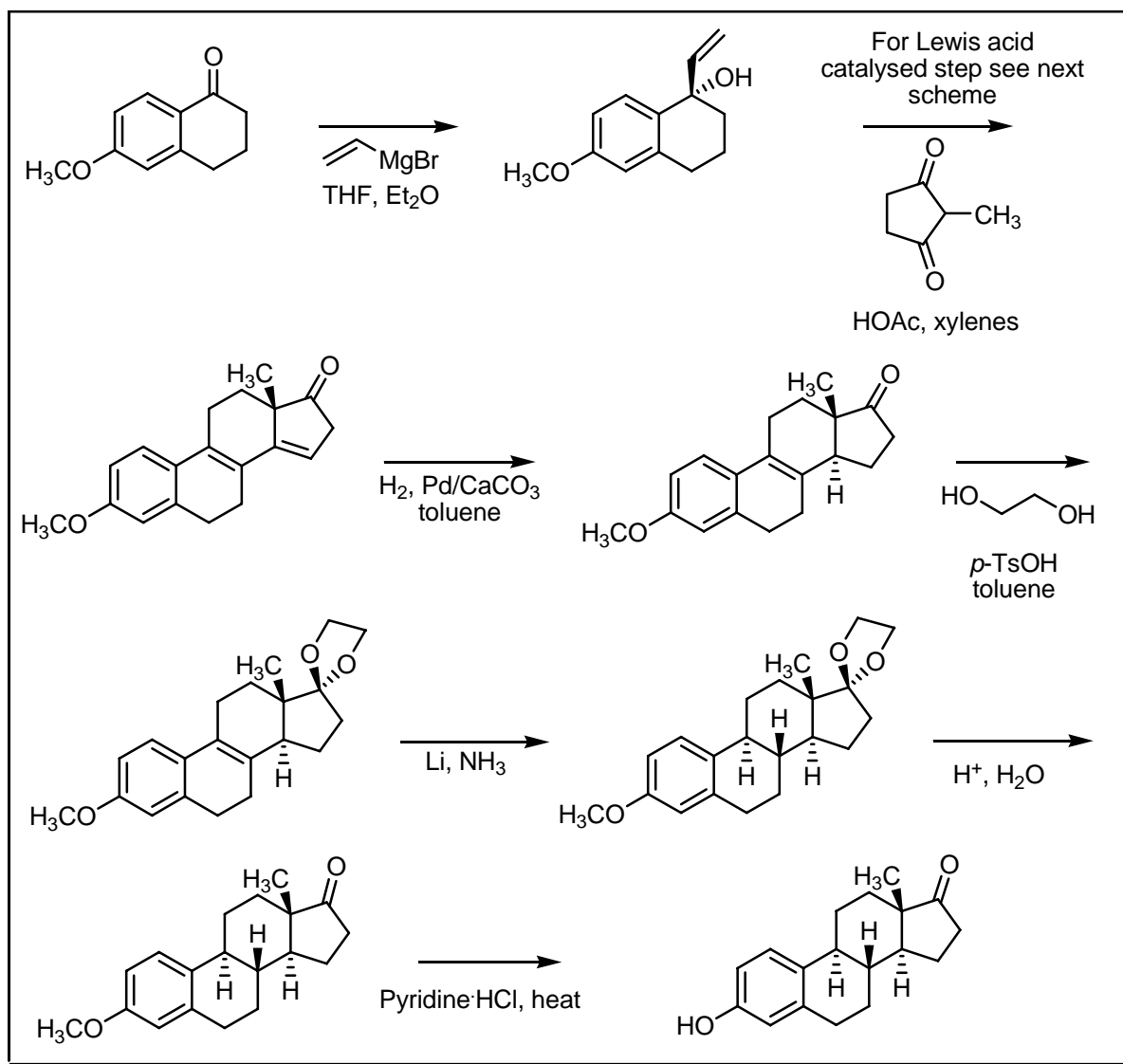
## COMMENTS :

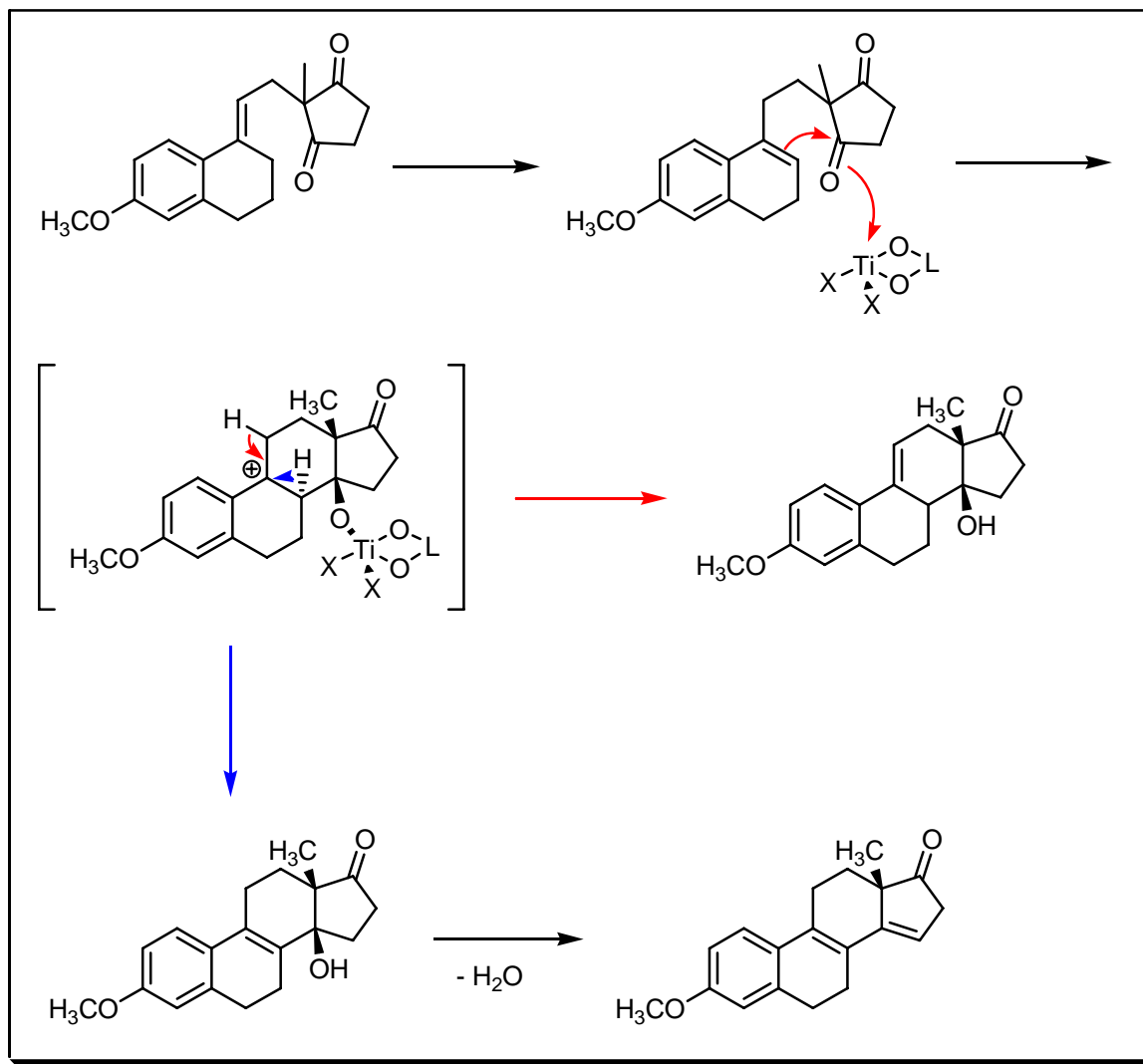


## EXAMPLE :

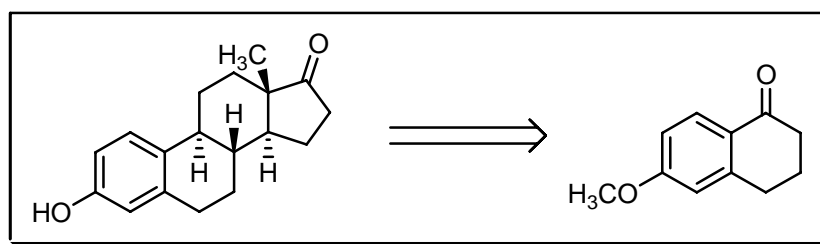


**MECHANISM :**





#### DISCONNECTION :



#### NOTES :

The main cyclisation step in the synthesis of estrone. The reaction can be Lewis acid mediated to give an asymmetric **Torgov** cyclisation in a **Prins**-type of fashion. See also **Prins** reaction.

#### REFERENCES :

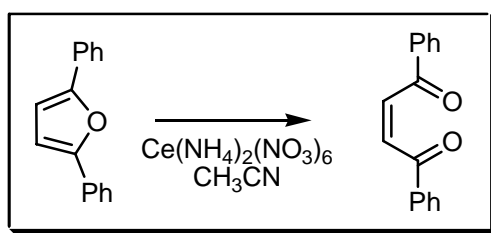
- 1) S.N. Anachenko; I.V. Torgov, *Dokl. Akad. Nauk SSSR*, 1959, **127**, 553.
- 2) C.H. Kuo; D. Taub; N.L. Wendler, *J. Org. Chem.*, 1968, **33**, 3126.
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- 4) S. Jayaraman; K. Rajagopalan, *Indian J. Chem.*, 1989, **28B**, 61.
- 5) J.-C. Blazejewski; M. Haddad; C. Wakselman, *Tetrahedron Lett.*, 1994, **35**, 2021.

**COMMENTS :**

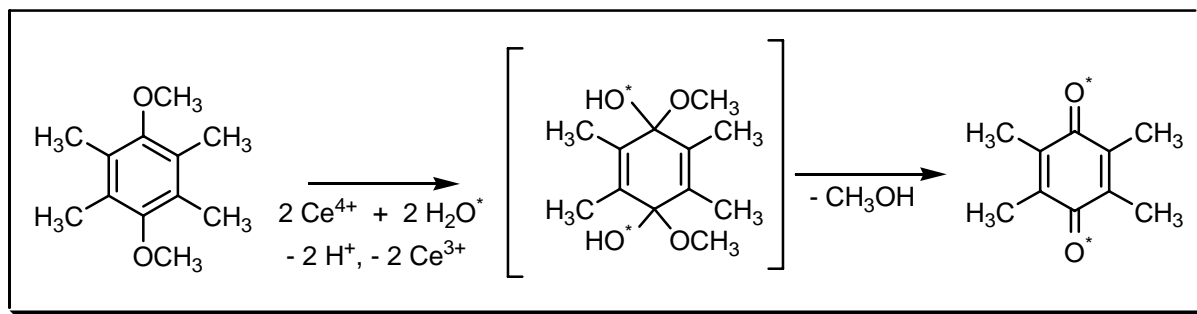
**TRAHANOVSKY ETHER OXIDATION**

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**EXAMPLE :**



**MECHANISM :**



**NOTES :**

The oxidation of aromatic ethers to carbonyl compounds with cerium ammonium nitrate.

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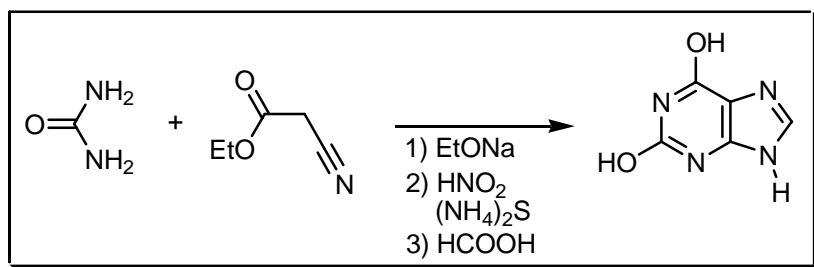
**REFERENCES :**

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  - 5) J. Laduranty; L. Lepage; Y. Lepage, *Can. J. Chem.*, 1980, **58**, 1161.
  - 6) L. Lepage; Y. Lepage, *Synthesis*, 1983, 1018.
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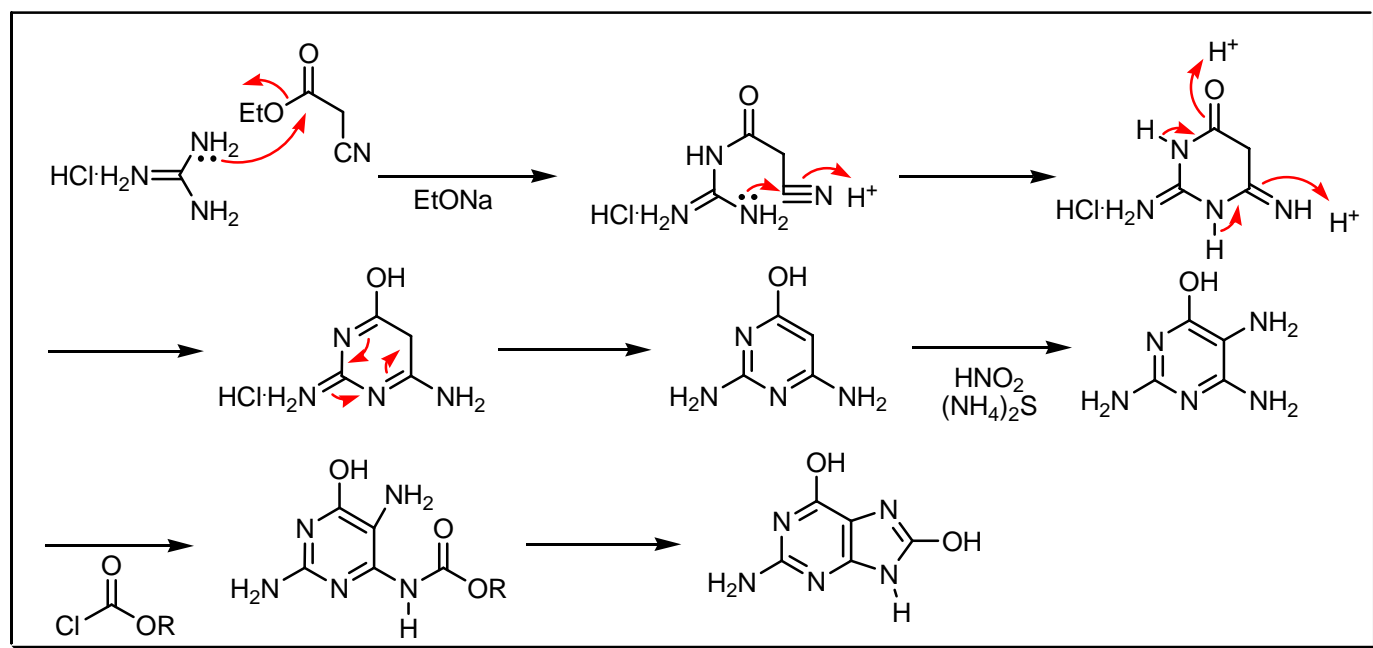
COMMENTS :

## TRAUBE PURINE SYNTHESIS

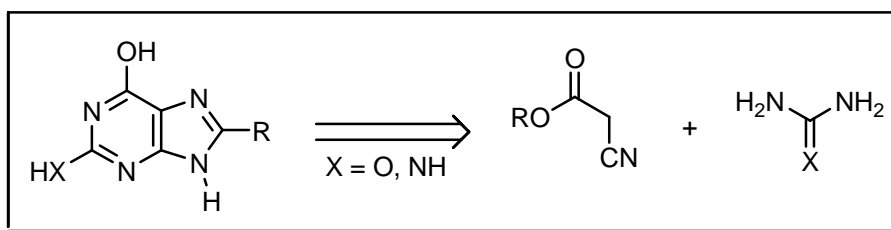
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

The pyrimidine synthesis from guanidine or urea and cyanoacetic ester, followed by reaction with nitrous acid and condensation with formic acid afford purines. See also **Behrend – Roosen**, **Fischer** and **Horbaczewski** reactions.

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## REFERENCES :

Org. Synth. : **32**, 45; **37**, 15

Org. Synth. Coll. Vol. : **4**, 245, 247

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1) W. Traube, *Ber. Dtsch. Chem. Ges.*, 1900, **33**, 1371.

2) A.R. Katritzky, *J. Chem. Soc., Quat. Rev.*, 1956, **10**, 397.

3) A.R. Katritzky, *Pure Appl. Chem.*, 1961, **11**, 178.

4) M. Melguizo; M. Nogueras; A. Sanchez, *Synthesis*, 1992, 491.

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6) K.A. Ismail; A.A. Eltombar; A. Omar; O.M. Abouwafa; N.I. Madi, *Eur. J. Med. Chem.*, 1995, **30**, 423.

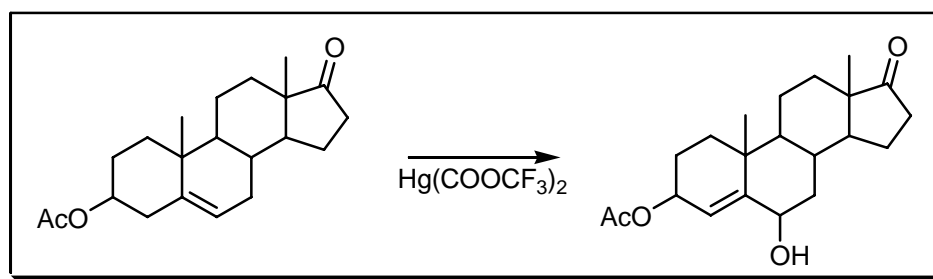
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## COMMENTS :

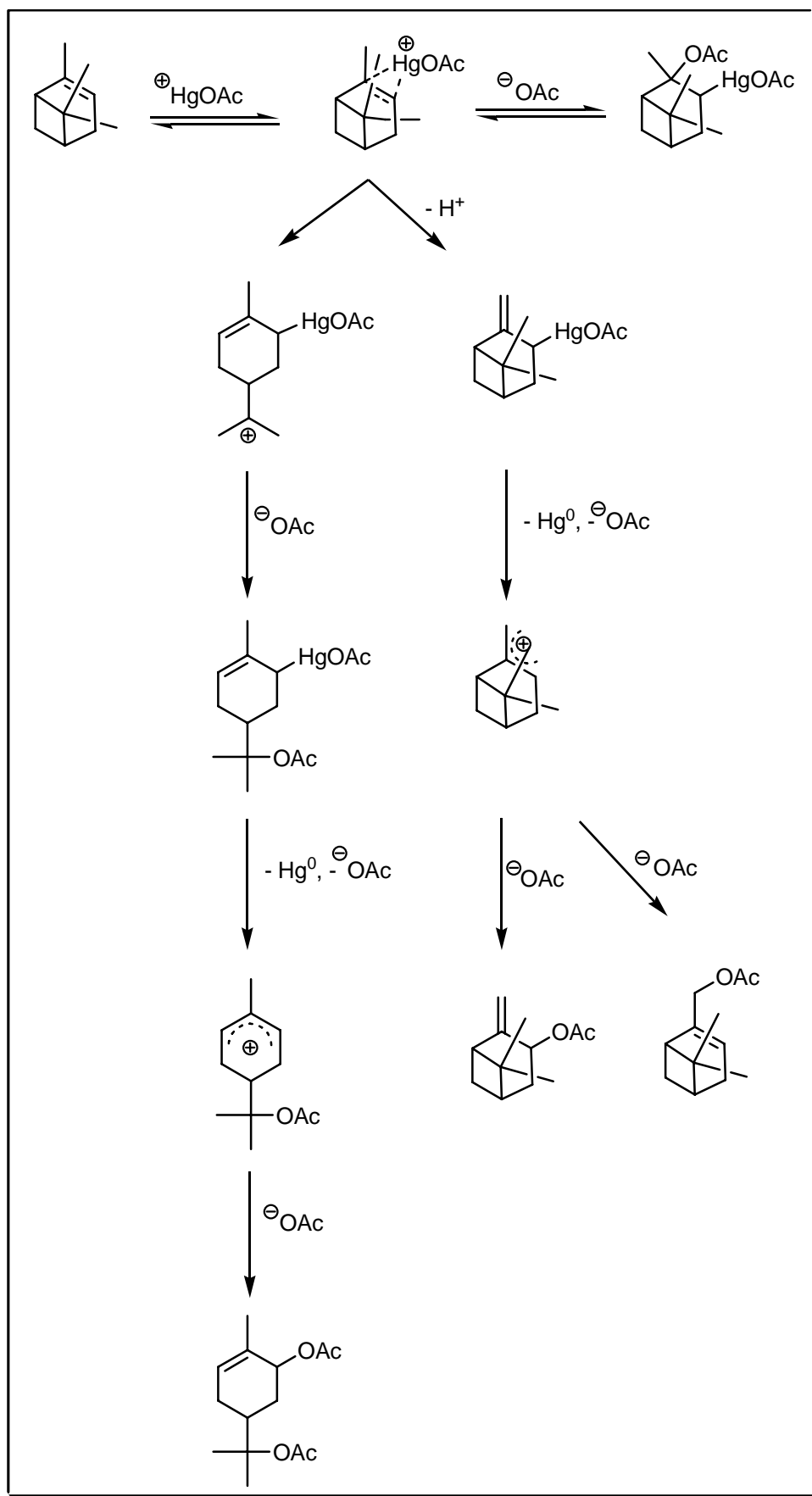
## TREIBS ALLYLIC OXIDATION

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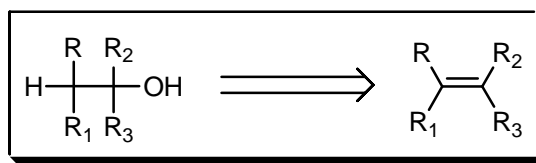
### EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The allylic oxidation of alkenes using mercuric trifluoroacetate, allylic rearrangement is possible although mercury normally stabilises the formed cation.

## REFERENCES :

March : 759

Smith – March : 993

Smith : 179

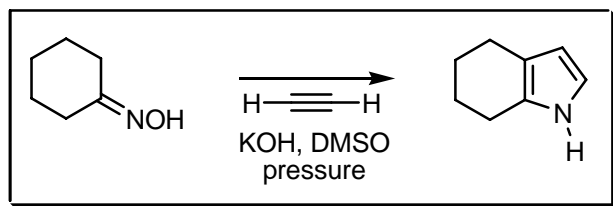
Smith 2<sup>nd</sup> : 150

- 1) W. Treibs, *Naturwissenschaften*, 1948, **35**, 125.
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- 5) R.A. Broad; J.R. Hanson; P.B. Reese, *J. Chem. Res.*, 1987, **5**, 172.

## COMMENTS :

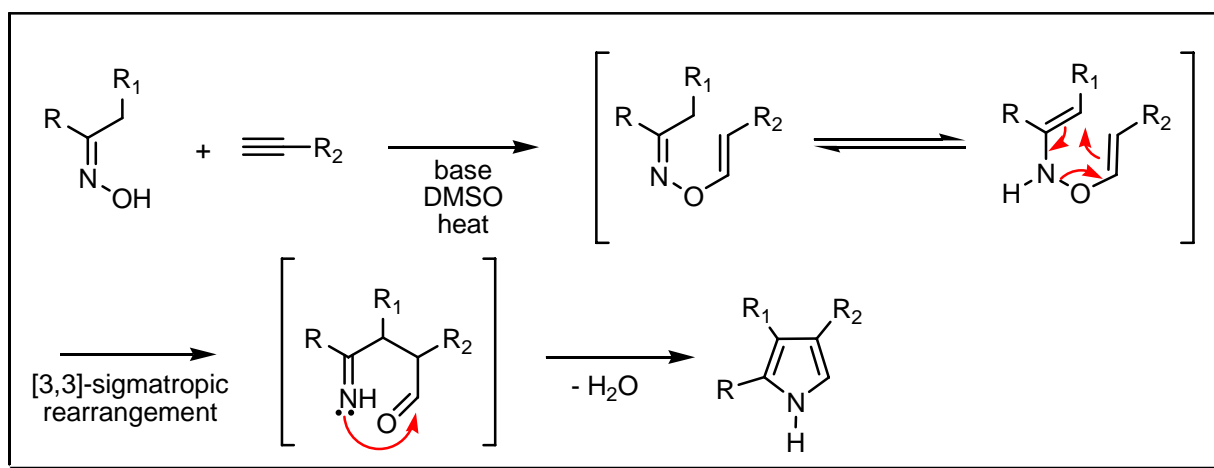
## TROFIMOV PYRROLE SYNTHESIS

### EXAMPLE :

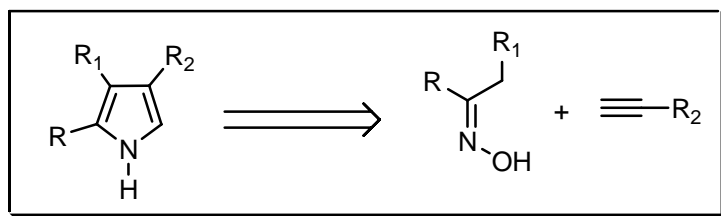




## MECHANISM :



## DISCONNECTION :



## NOTES :

Another synthesis of pyrroles derived from hetaryl alkyl ketoximes and acetylenes via a [3,3]-sigmatropic rearrangement. See also **Barton – Zard**, **Clauson–Kaas**, **Fischer – Fink**, **Grob – Camenisch**, **Hantzsch** pyrrole, **Harries** pyrrole, **Kenner**, **Knorr** pyrrole, **Miller – Plöchl**, **Paal – Knorr**, **Padwa**, **Piloty – Robinson**, **Schwanert** and **Zav'yalov** reactions.

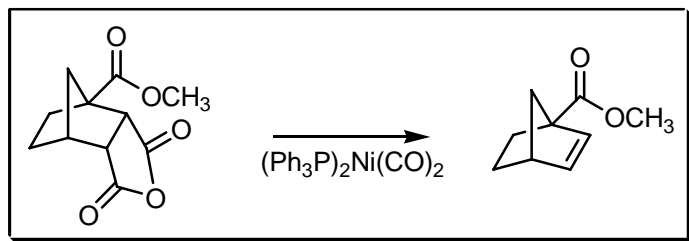
## REFERENCES :

- 1) B.A. Trofimov, *Adv. Heterocycl. Chem.*, 1990, **51**, 177.
- 2) B.A. Trofimov; A.I. Mikhaleva, *Heterocycles*, 1994, **37**, 1193.
- 3) A.M. Vasil'tsov; A.B. Zaitsev; A.I. Mikhaleva; E.Yu. Schmidt; A.V. Afo–nin, *Mendeleev Commun.*, 2001, **11**, 74.
- 4) A.M. Vasil'tsov; A.B. Zaitsev; A.I. Mikhaleva; E.Yu. Schmidt; A.V. Afo–nin, *Chem. Heterocycl. Comp.*, 2002, **415**, 66.
- 5) E.Yu. Schmidt; N.V. Zorina; A.B. Zaitsev; A.I. Mikhaleva; A.M. Vasil'tsov; P. Audebert; G. Clavier; R. Méallet–Renault; R.B. Pansu, *Tetrahedron Lett.*, 2004, **45**, 5489.
- 6) A.B. Zaitsev; R. Méallet–Renault; E.Yu. Schmidt; A.I. Mikhaleva; S. Badré; C. Dumas; A.M. Vasil'tsov; N.V. Zorina; R.B. Pansu, *Tetrahedron*, 2005, **61**, 2683.

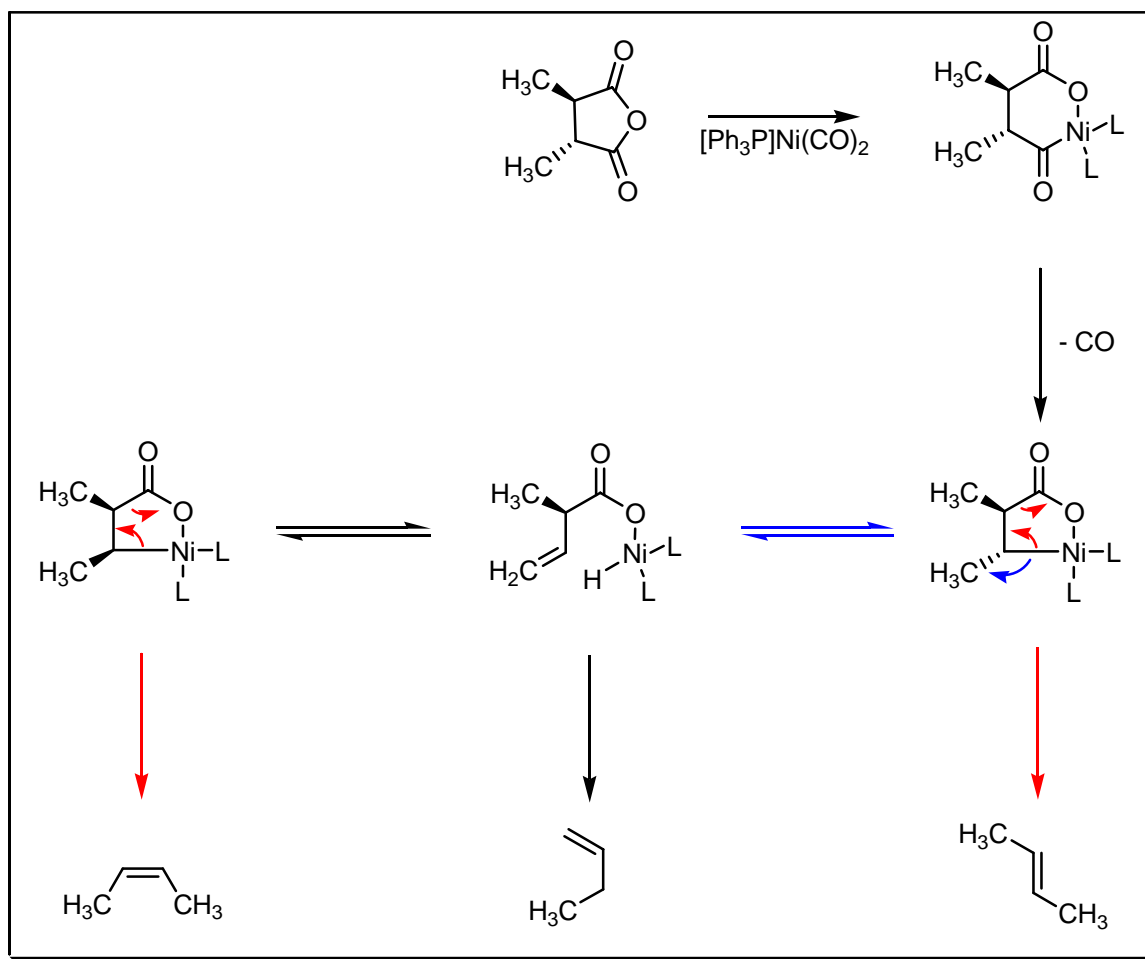
COMMENTS :

## TROST – CHEN DECARBOXYLATION

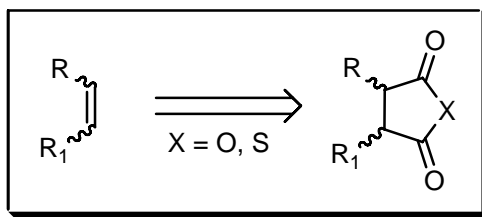
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The nickel complex catalyses the decarboxylation of dicarboxylic acid anhydrides or thioanhydrides to form alkenes.

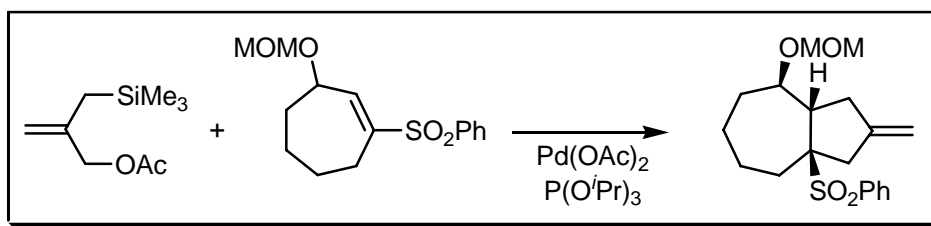
## REFERENCES :

- 1) J.D. Rose; F.S. Statham, *J. Chem. Soc.*, 1950, 69.
- 2) B.M. Trost; F. Chen, *Tetrahedron Lett.*, 1971, **12**, 2603.
- 3) T.C. Flood; A. Sharhngi, *Tetrahedron Lett.*, 1977, **18**, 3861.
- 4) G.L. Grunewald; D.P. Davis, *J. Org. Chem.*, 1978, **43**, 3074.

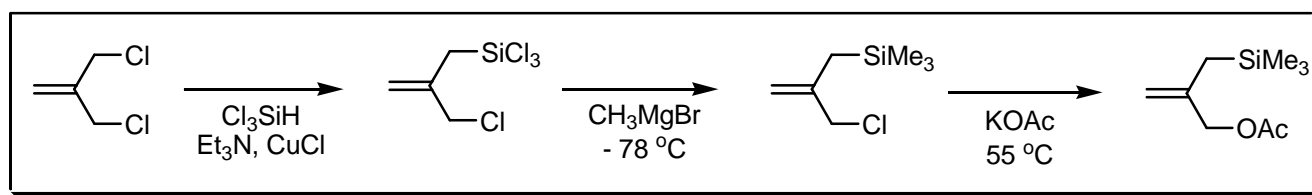
## COMMENTS :

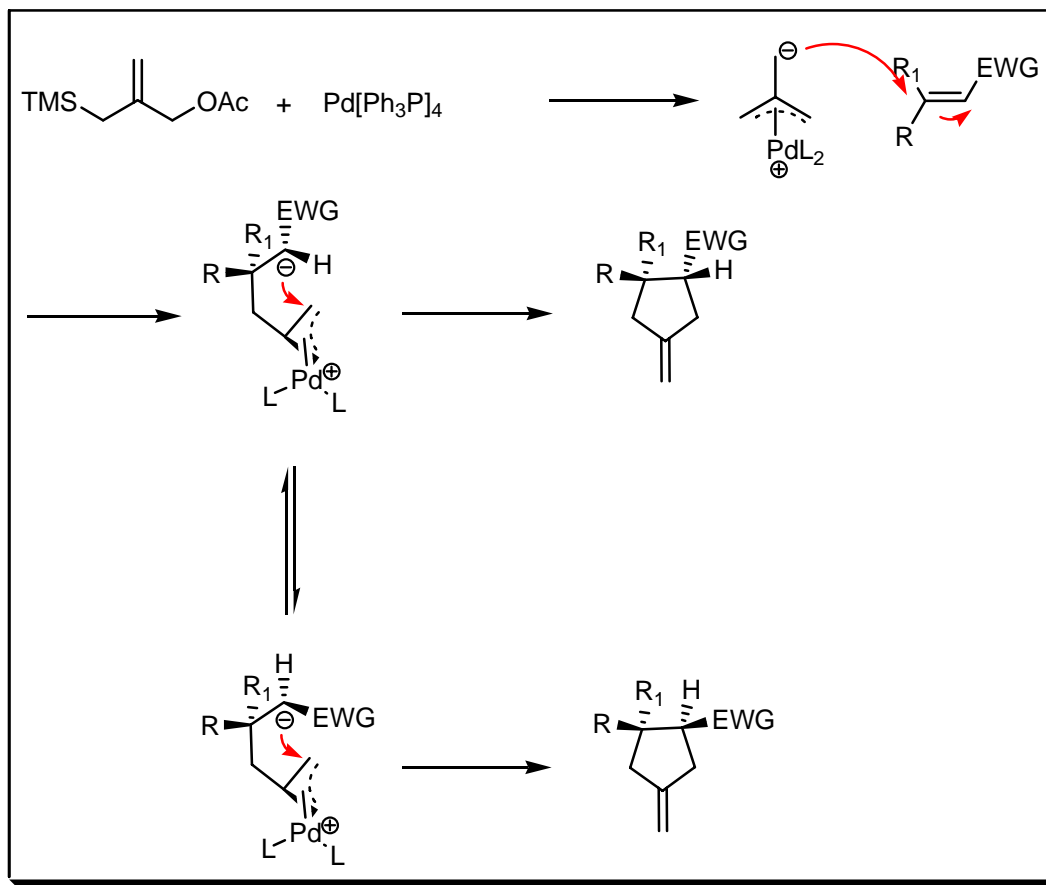
## TROST CYCLOPENTANATION

### EXAMPLE :

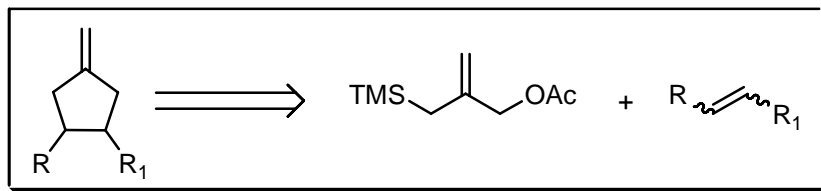


### MECHANISM :





#### DISCONNECTION :



#### NOTES :

The formation of methylenecyclopentane starting from siloxymethylallylsilane or acetoxymethylallylsilane with **Michael** acceptor olefins and palladium catalysts (*via* trimethylene methane equivalent). The geometry of (*E*)-olefins is retained in the products. The mechanism is or [3+2]-concerted or is step-wise but collapse of the intermediate enolate is faster than  $\sigma$ -bond rotation. (*Z*)-Olefins give *syn* and *anti* mixtures.

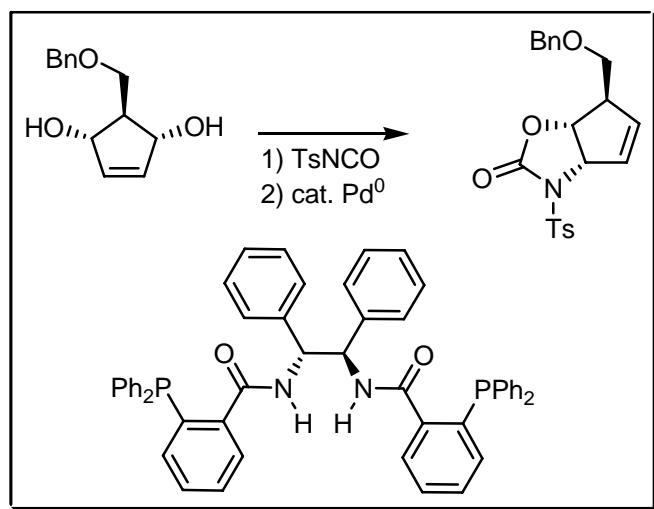
#### REFERENCES :

- 1) B.M. Trost; D.M.T. Chan, *J. Am. Chem. Soc.*, 1979, **101**, 6429.
- 2) B.M. Trost; D.M.T. Chan, *J. Am. Chem. Soc.*, 1983, **105**, 2315.
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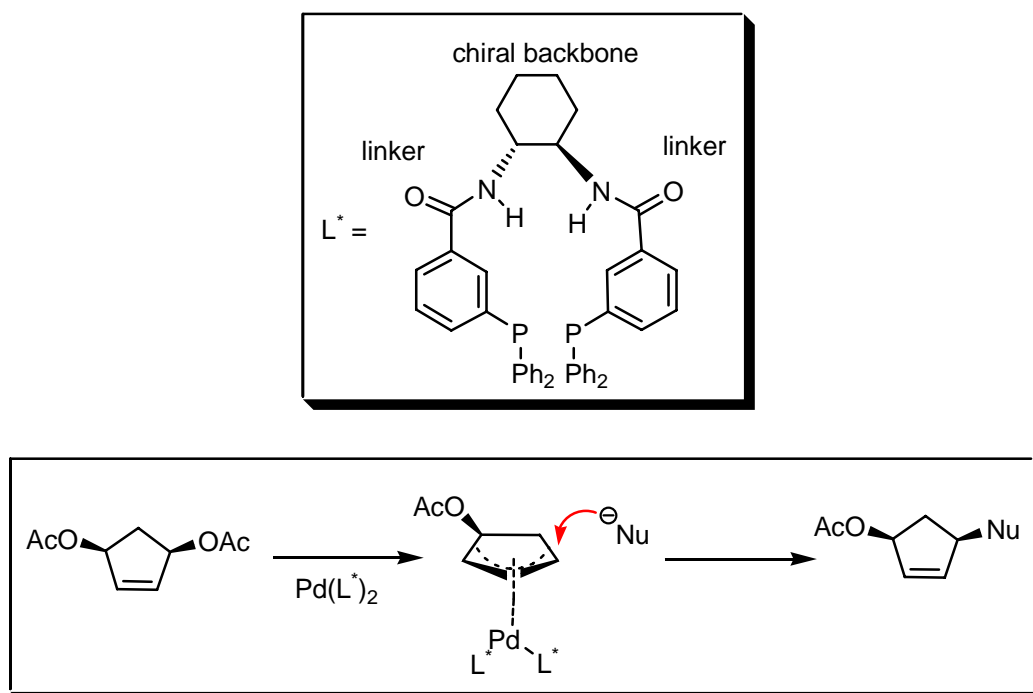
COMMENTS :

## TROST DESYMMETRISATION

EXAMPLE :



MECHANISM :



## NOTES :

A palladium-catalysed desymmetrisation using a nitrogen nucleophile (azide or amine). Where the palladium complex is derived from a chiral ligand and  $\pi$ -allylpalladium chloride. This will afford an enantiomerically pure, azide or amine containing five or six membered ring. The primary chirality of the stereogenic centres of the backbone gets translated *via* the linker units into a secondary chirality at the phosphines. See also **Bäckvall** reaction.

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## REFERENCES :

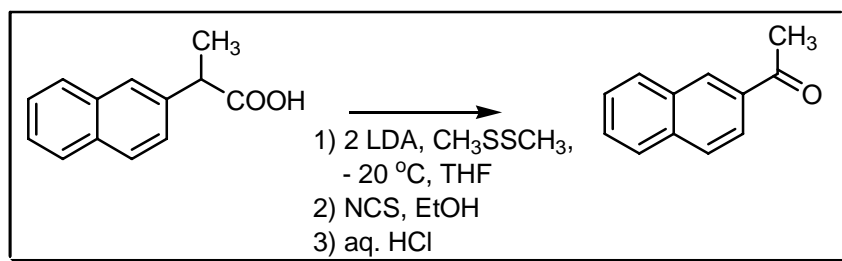
- 1) B.M. Trost; D.L. van Vranken; C. Bingel, *J. Am. Chem. Soc.*, 1992, **114**, 9327.
  - 2) B.M. Trost; R.C. Bunt, *J. Am. Chem. Soc.*, 1994, **116**, 4089.
  - 3) S.R. Pulley; B.M. Trost, *J. Am. Chem. Soc.*, 1995, **117**, 10143.
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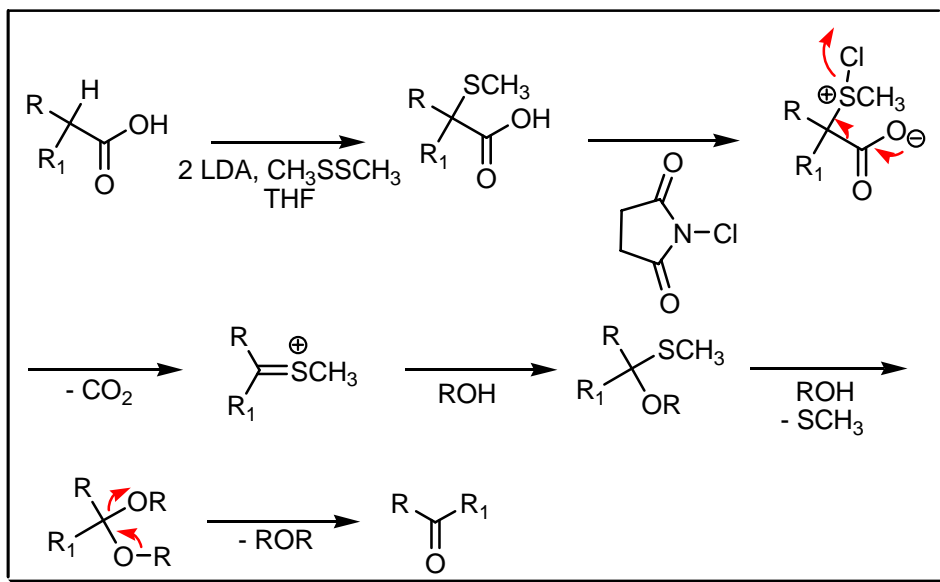
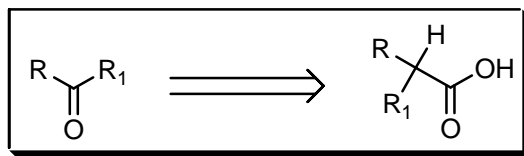
## COMMENTS :

## TROST OXIDATIVE DECARBOXYLATION

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### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

The conversion of a carboxylic acid to a ketone with the loss of one carbon atom using dimethyl disulfide as sulfenylating agent and *N*-chlorosuccinimide as oxidising reagent. See also **Barbier – Locquin – Wieland** degradation, **Gallagher – Hollander**, **Hoehn – Mason** degradation, **Krafft**, **Miescher** degradation and **Wieland – Dane** degradation reactions.

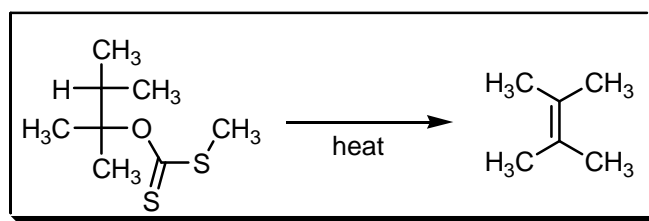
**REFERENCES :**

B.M. Trost; Y. Tamaru, *J. Am. Chem. Soc.*, 1975, **97**, 3528.

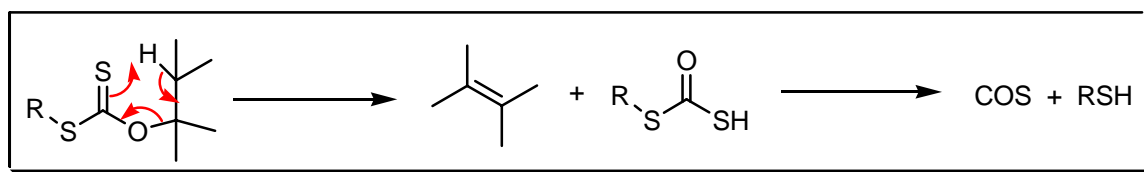
**COMMENTS :**

# TSCHUGAEFF (CHUGAEV) OLEFIN SYNTHESIS

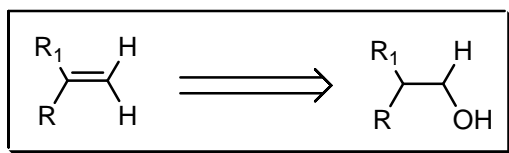
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The intramolecular *syn*-elimination of an alcohol into an olefin by the thermal decomposition of the xanthate prepared from the alcohol. It proceeds through a six-membered transition state. See also **Cope – Mamlock – Wolffenstein** reaction.

## REFERENCES :

March : 1014

Smith – March : 1330

Smith : 167

Smith 2<sup>nd</sup> : 140

Org. React. : 12, 57

Org. Synth. : 64, 57

Org. Synth. Coll. Vol. : 7, 139

- 1) L. Tschugaeff, *Ber. Dtsch. Chem. Ges.*, 1899, **32**, 3332.
- 2) G.L. O'Connor; H.R. Nace, *J. Am. Chem. Soc.*, 1952, **74**, 5454.
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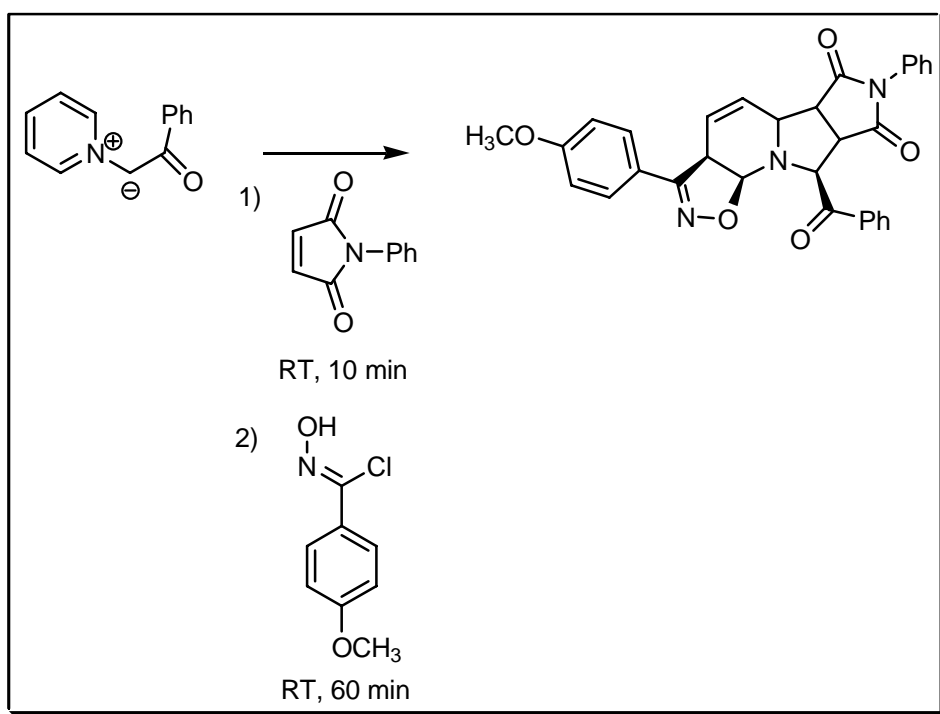
- 6) A. De Groot; B. Evenhuis; H. Wynberg, *J. Org. Chem.*, 1968, **23**, 2214.  
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8) X. Fu; J.M. Cook, *Tetrahedron Lett.*, 1990, **31**, 3409.  
9) P.S. Ray; M.J. Manning, *Heterocycles*, 1994, **33**, 1361.  
10) T. Kumamoto; N. Tabe; K. Yamaguchi; H. Yagishita; H. Iwasa; T. Ishikawa, *Tetrahedron*, 2001, **57**, 2717.
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COMMENTS :

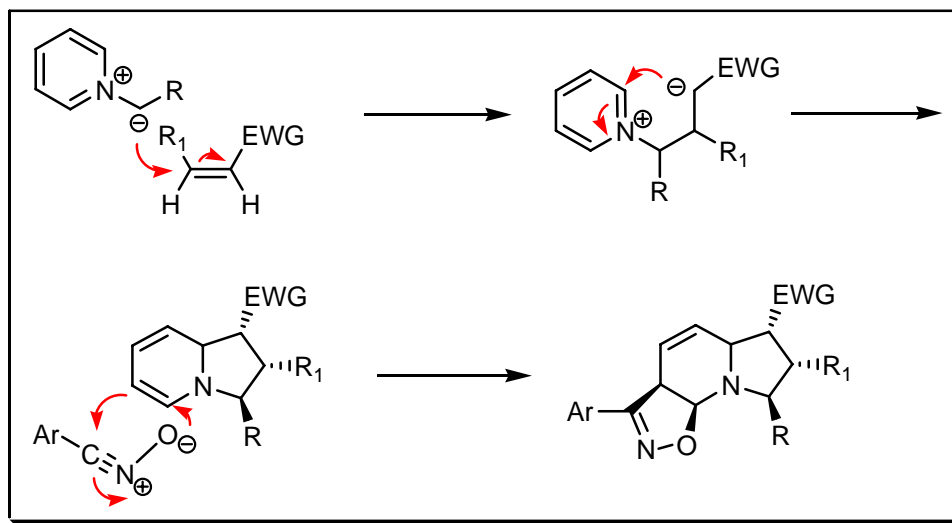
## TSUGE REACTION

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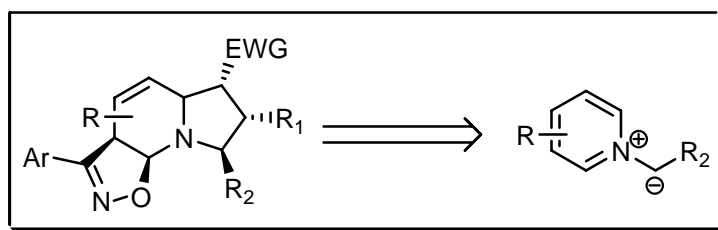
EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Pyridinium or isoquinolinium methylides undergo highly stereo- and regioselective cycloadditions with olefinic dipolarophiles to form unstable tetrahydroindolizine derivatives. One of the double bonds will react further with nitrile oxides to give isoxazole-fused tetrahydroindolizines in a good stereo- and regioselective fashion.

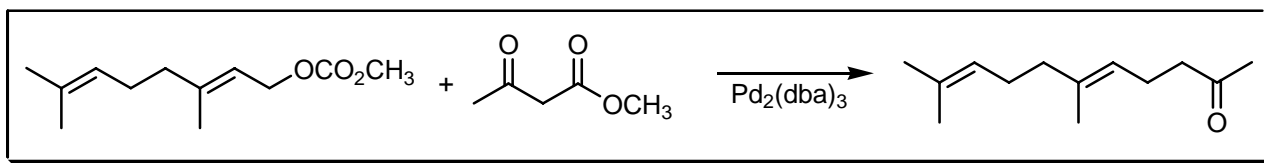
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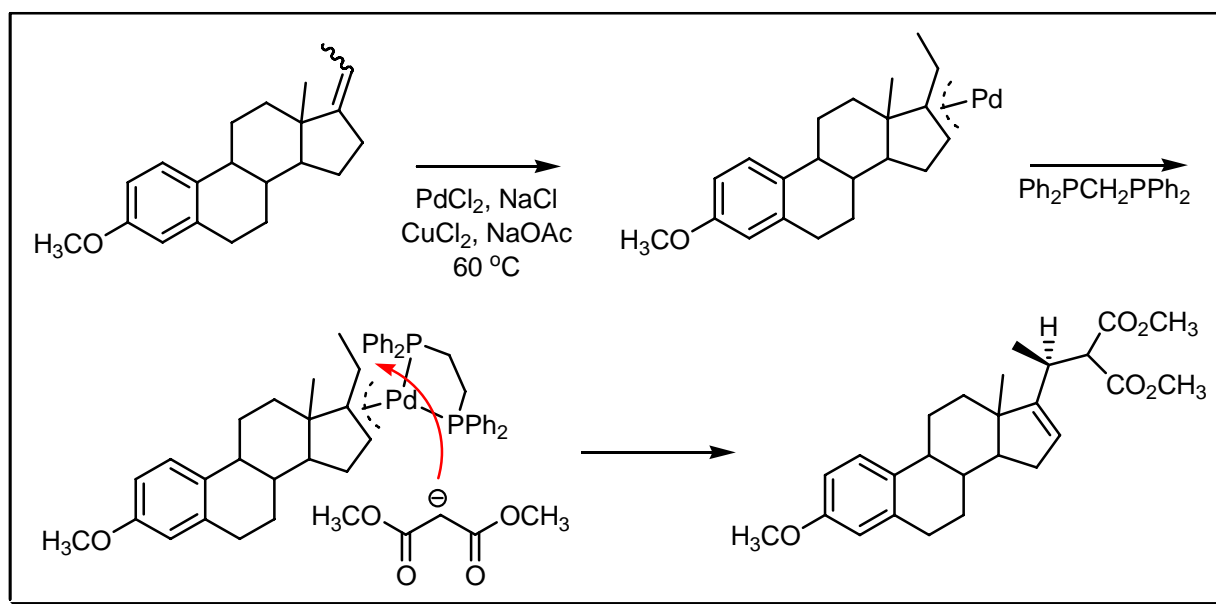
## COMMENTS :

## TSUJI – TROST ALLYLATION

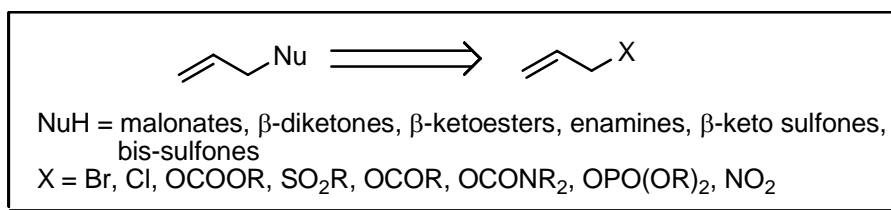
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The direct C-allylation of ketones or of tin enol ethers with Pd(0) catalysts. These transformations require rather sophisticated conditions depending mainly on the nature of the catalytic species. They allow control of regio-, diastereo-, and even enantioselectivity. Bimetallic systems containing rhodium(I) are used to activate the pronucleophiles by coordination to a cyano group. Other metals can catalyse allylic alkylations, e.g. molybdenum, tungsten, iridium and rhodium. See also **Bäckvall** reaction.

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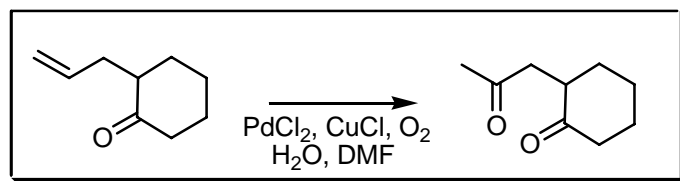
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**COMMENTS :**

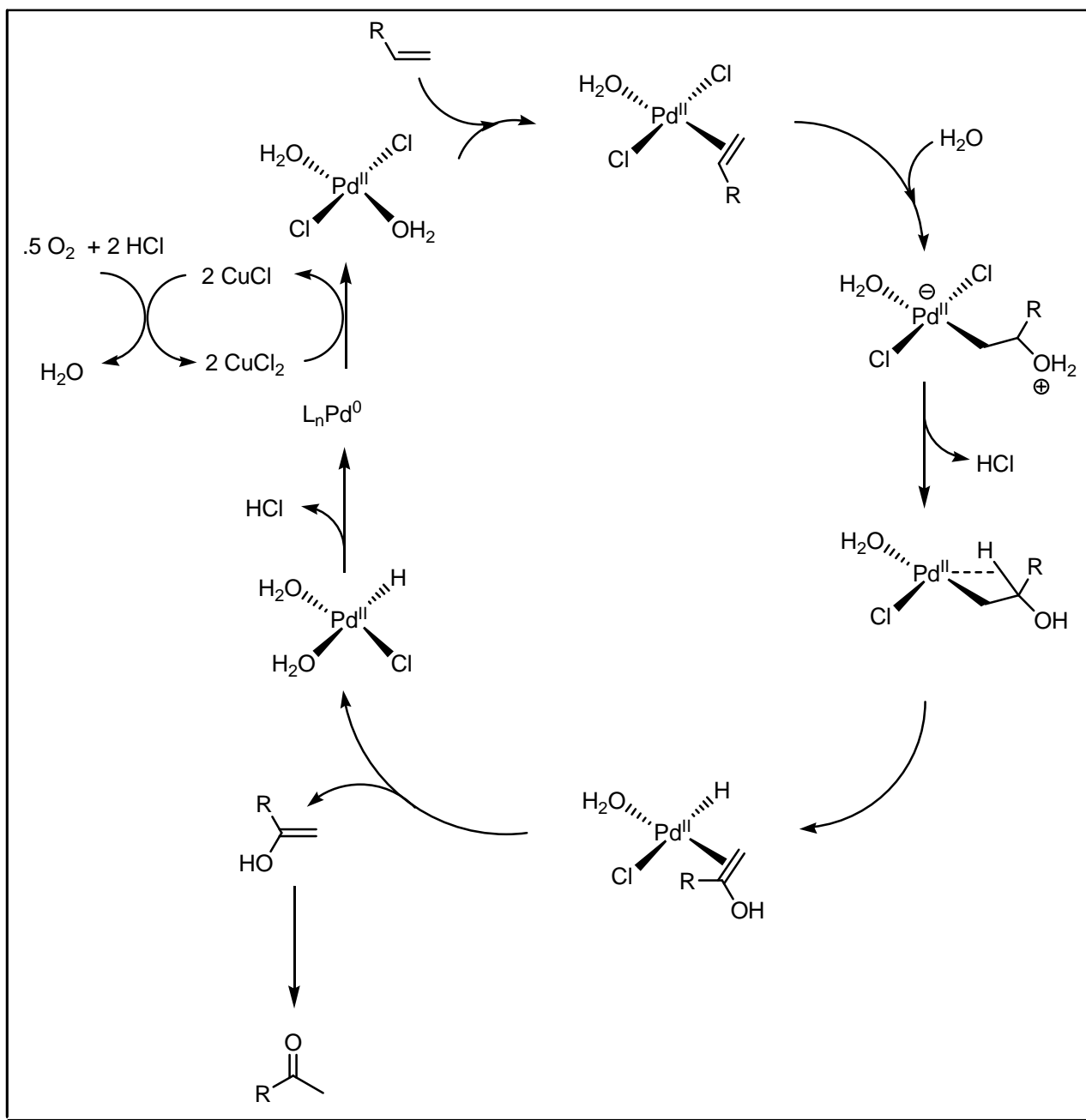
## TSUJI – WACKER OLEFIN OXIDATION

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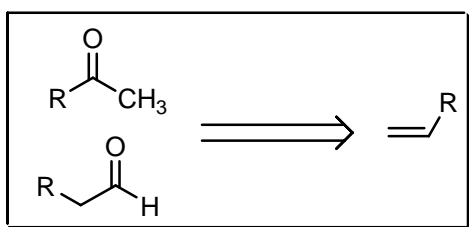
**EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

The oxidation of olefins to ketones by a palladium(II) catalyst. The unique feature is the invention of the *in situ* redox system of  $\text{PdCl}_2 - \text{CuCl}_2$ . The formation of aldehydes is also possible see **Kiers** *et al.* Water soluble palladium complexes have been reported by **Sheldon** *et al.* There are two mechanistic possibilities for the hydroxypalladation,

*syn* or *anti*, deuterium-labelling study has shown that it proceeds through a palladium-nucleophile *anti*-addition. See also **Uemura** oxidation.

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**Smith – March** : 1538

**Smith 2<sup>nd</sup>** : 278, 1110

**Houben – Weyl** : **E3**, 340; **E18**, 1088

**Science of Synthesis** : **1**, 322, 333; **10**, 417

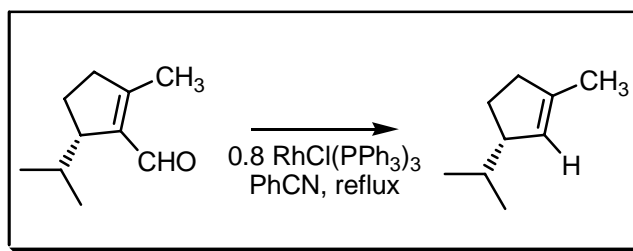
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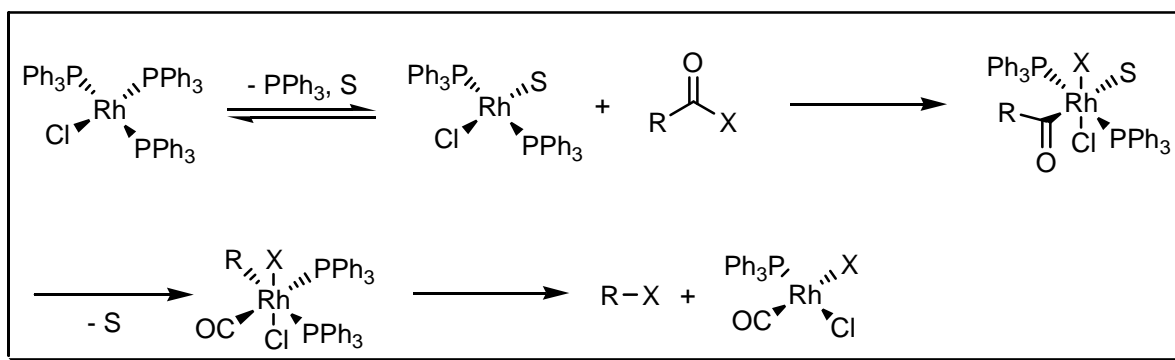
#### COMMENTS :

## TSUJI – WILKINSON REACTION

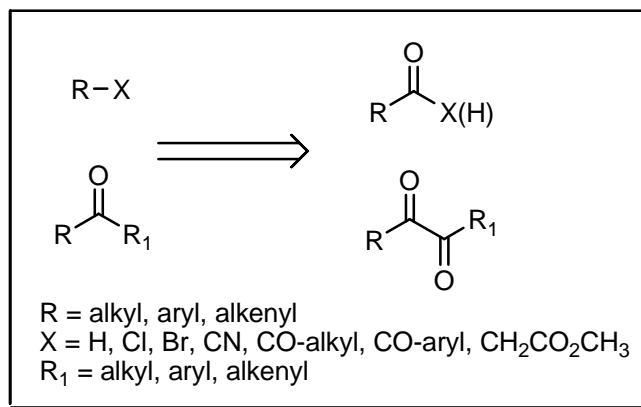
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Aldehydes, acyl halides or 1,2-diketones can be decarbonylated using Wilkinson's catalyst.

### REFERENCES :

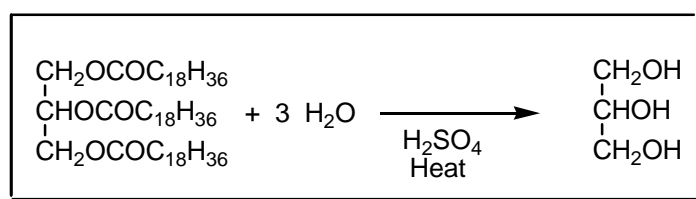
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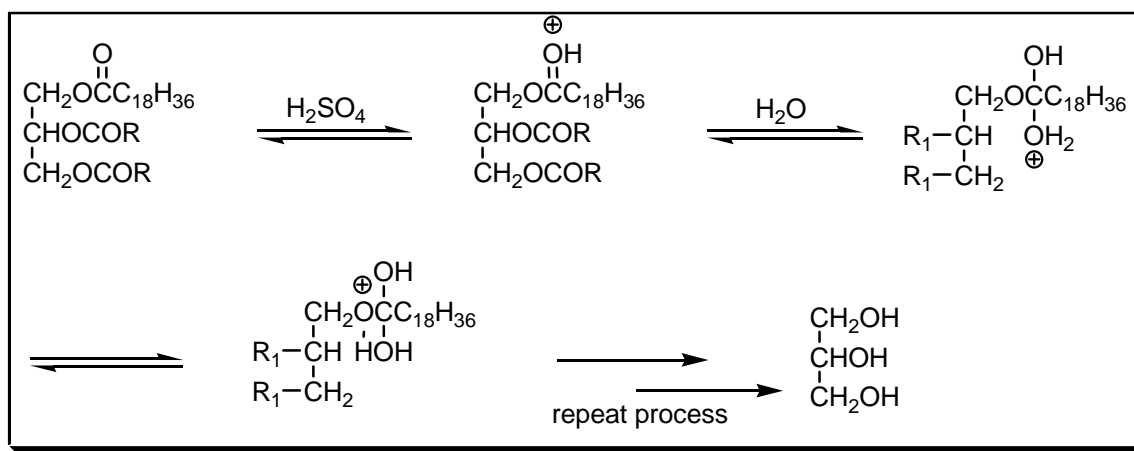
**COMMENTS :**

**TWITCHELL PROCESS**

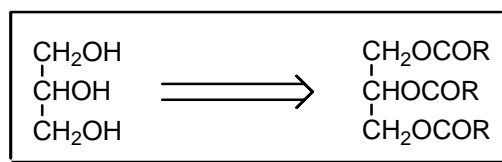
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

The hydrolysis of fatty acids with 30% sulfuric acid to afford the free fatty acid and glycerine. See also **Claisen** hydrolysis.



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March : 378

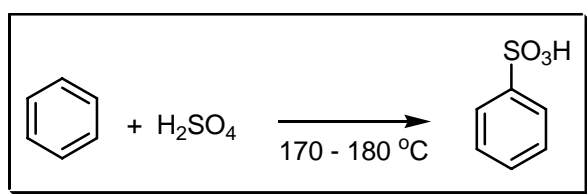
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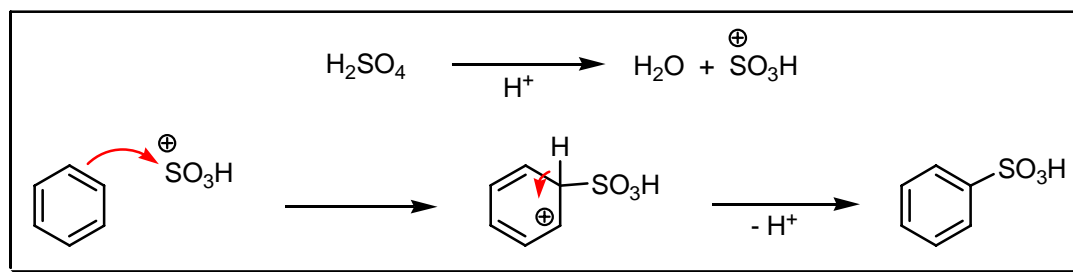
## COMMENTS :

## TYRER SULFONATION PROCESS

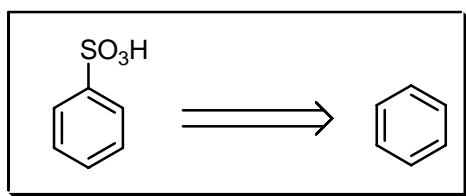
### EXAMPLE :



### MECHANISM :



**DISCONNECTION :**



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**NOTES :**

The sulfonylation of benzene with sulfuric acid.

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**REFERENCES :**

Houben – Weyl : **9**, 452

Org. React. : **3**, 141

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**COMMENTS :**

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**G**

GRAEBE – ULLMANN FLUORENE SYNTHESIS · 1768

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**U**

UEMURA OXIDATION · 1756

UGI CONDENSATION · 1757

ULLMANN – FETVADJIAN ACRIDINERING CONDENSATION ·  
1760

ULLMANN – HORNER PHENAZINE SYNTHESIS · 1761

ULLMANN – LA TORRE ACRIDINE SYNTHESIS · 1763

ULLMANN – UKITA – BUCHWALD – LI REACTION · 1765

ULLMANN DIARYL CONDENSATION · 1764

ULLMANN DIARYL ETHER SYNTHESIS · 1766

ULLMANN FLUORENONE SYNTHESIS · 1767

ULTEE CYANOHYDRIN SYNTHESIS · 1768

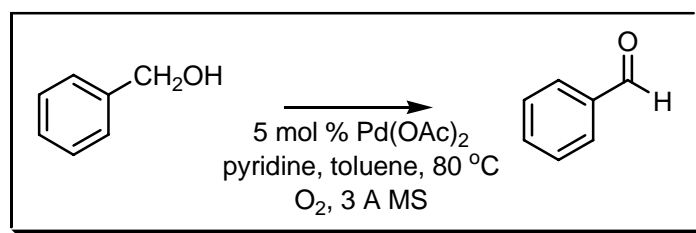
URECH CYANOHYDRIN METHOD · 1770

URECH HYDANTOIN SYNTHESIS · 1771

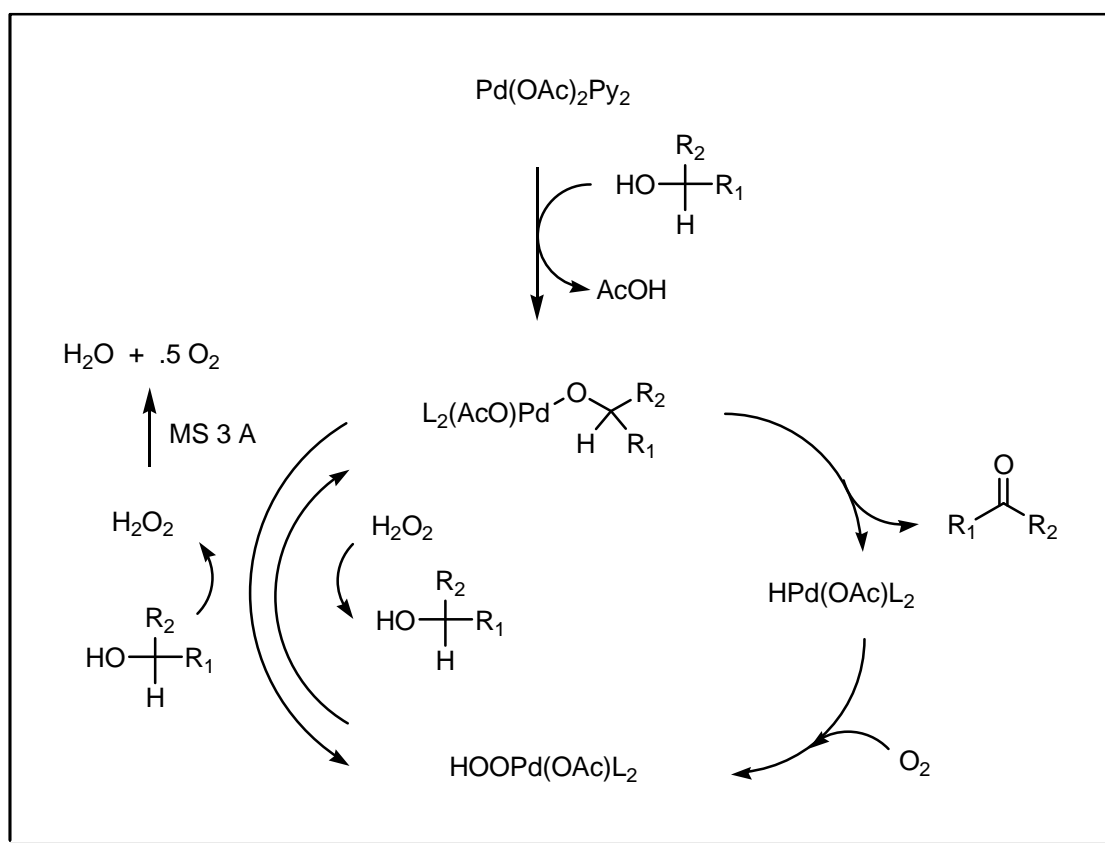
UTZINGER ALDEHYDE SYNTHESIS · 1772

## UEMURA OXIDATION

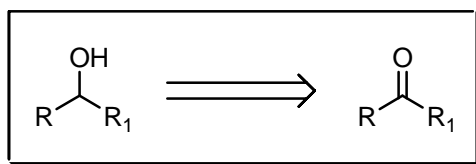
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The aerobic oxidation of primary and secondary alcohols to the corresponding carbonyl derivatives using palladium acetate and pyridine as rate accelerant. The original conditions developed for the asymmetric oxidation ( $\text{Pd}(\text{OAc})_2$ , (-)-sparteine) were rather sluggish. The **Stolz** and **Sigman** group reported that addition of *tert*-butanol and caesium carbonate increases the reaction rate. The change of solvent to chloroform allows the reaction to be preformed at

room temperature and under ambient air. Both homogeneous and heterogeneous catalysts have been reported. See also **Anelli**, **Ball – Goodwin – Morton**, **Collins**, **Corey – Kim**, **Corey – Schmidt**, **Corey – Suggs**, **David – Thieffry**, **Delépine**, **Dess – Martin**, **Einhorn** oxidation, **Fétizon**, **Jones** oxidation, **Ley**, **Maurer – Drefahl**, **Mukaiyama** oxidation, **Nicolaou**, **Oppenauer**, **Parikh – von Doering**, **Pfizzner – Moffatt**, **Pinnick**, **Sarett** and **Swern** reactions.

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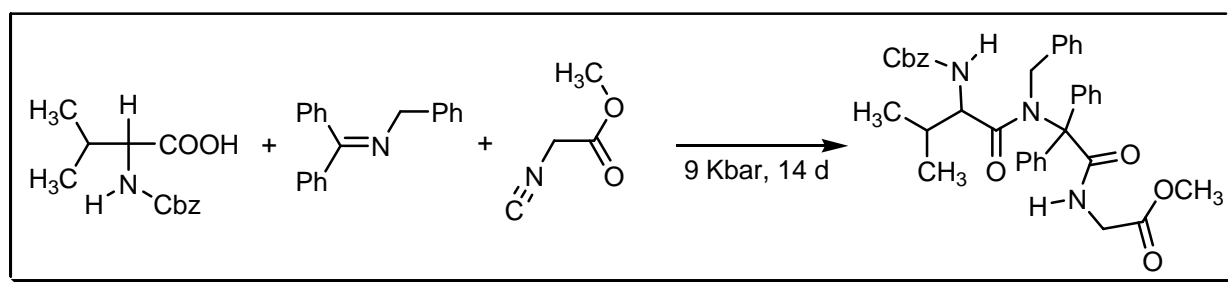
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#### COMMENTS :

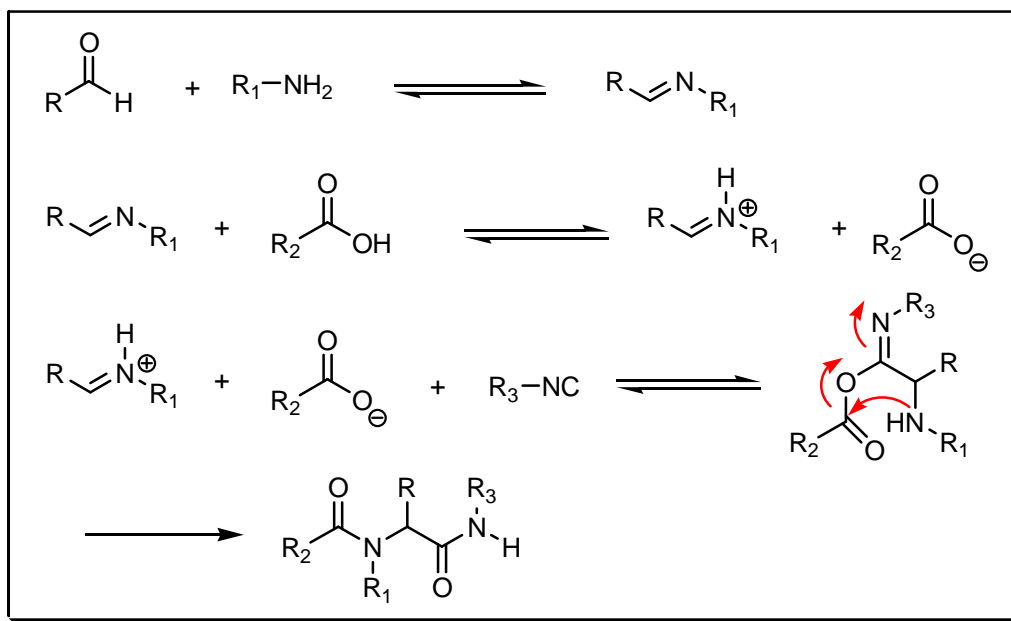
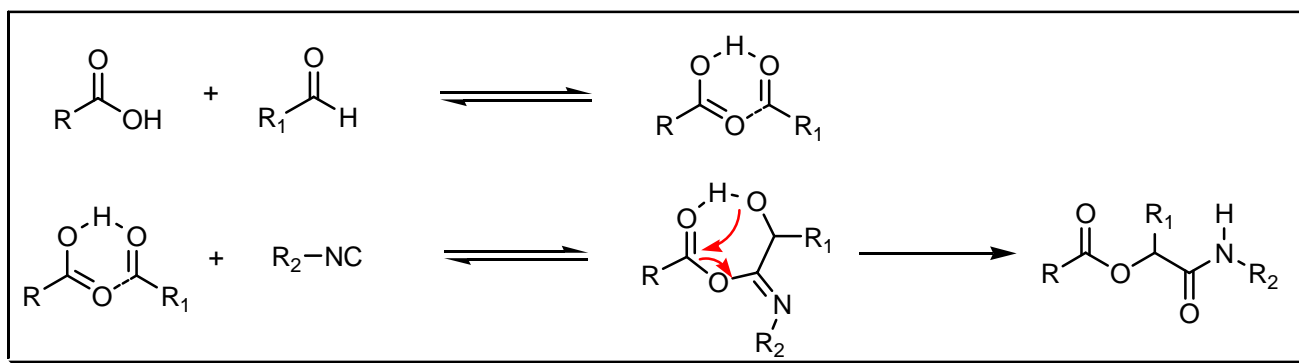
### UGI CONDENSATION

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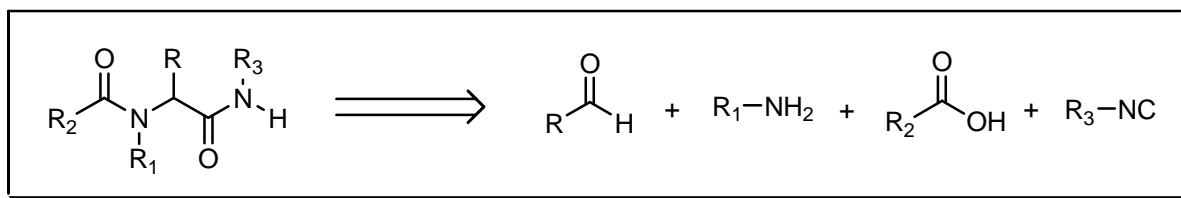
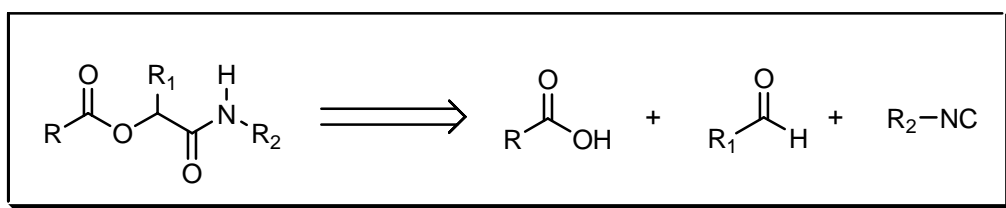
#### EXAMPLE :



# MECHANISM :



# DISCONNECTION :



## NOTES :

The peptide synthesis *via* a three, four or five component condensation (carboxylic acid, imine, isocyanide). The mechanism is still a subject of uncertainty. Simple starting reagents can give access to tetrazole derivatives, hydantoinimide derivatives, thiohydantoinimide derivatives,  $\alpha$ -acylaminocarboxamide derivatives,  $\alpha$ -amino carboxamide derivatives and  $\alpha$ -acyloxyaminocarboxamide derivatives. See also **Passerini** reaction.

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**March** : 980

**Smith – March** : 1251

**Houben – Weyl** : **E3**, 457; **E5**, 1652; **E16d**, 568, 740, 1243

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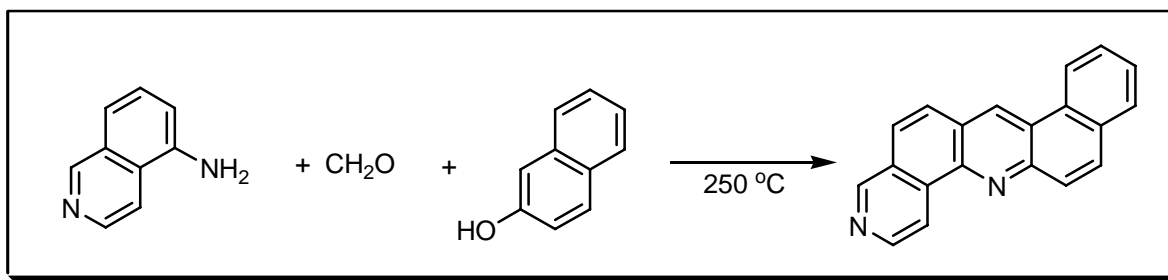
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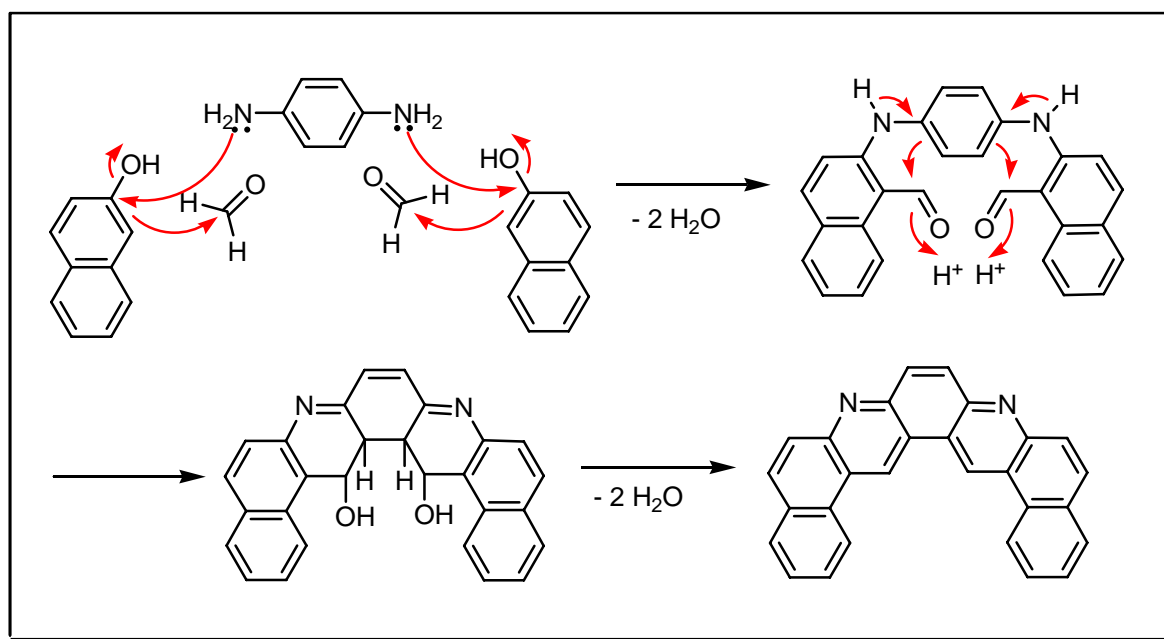


## ULLMANN – FETVADJIAN ACRIDINERING CONDENSATION

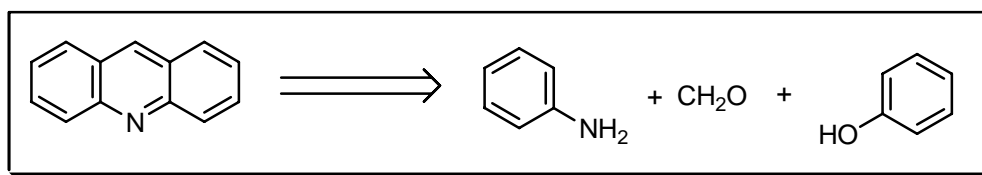
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The synthesis of polynuclear pyridines (acridines) from anilines, phenols and formaldehyde. See also **Bernthsen** acridine, **Mayer** and **Ullmann – la Torre** reactions.

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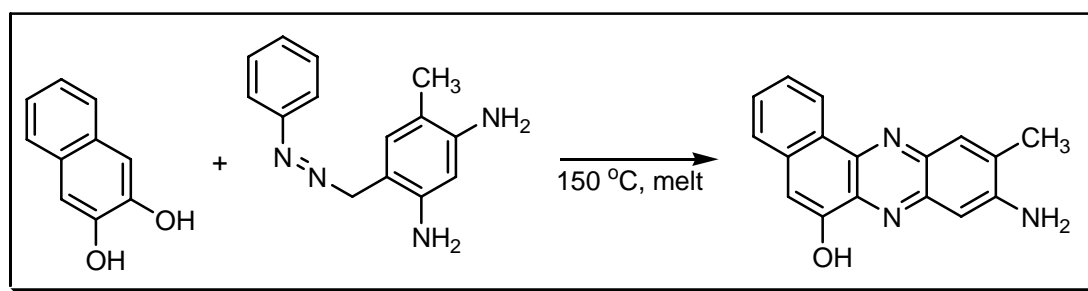
- 4) Ng.Ph. Buu-Hoï, *J. Chem. Soc.*, 1951, 2871.  
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**COMMENTS :**

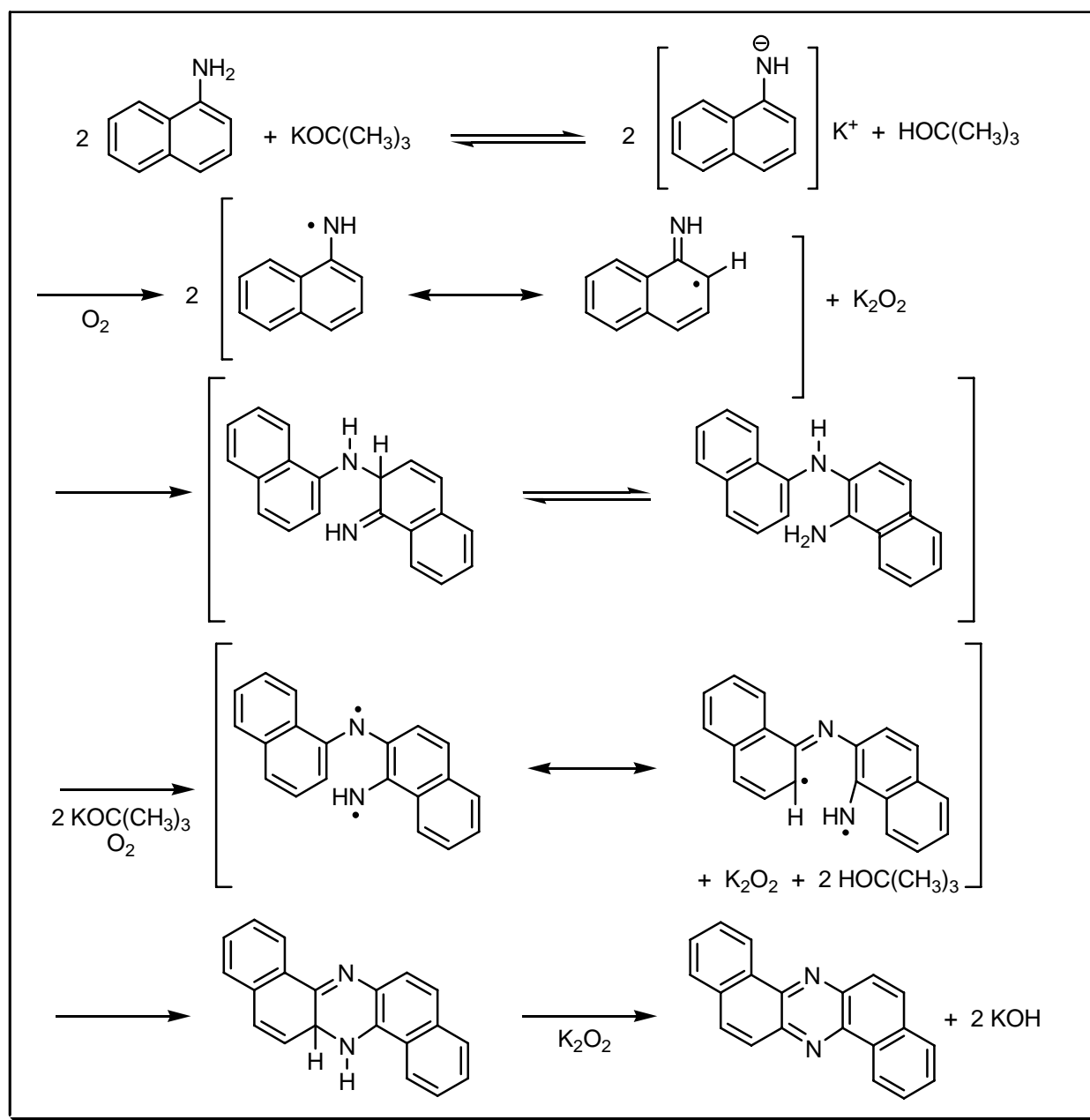
## ULLMANN – HORNER PHENAZINE SYNTHESIS

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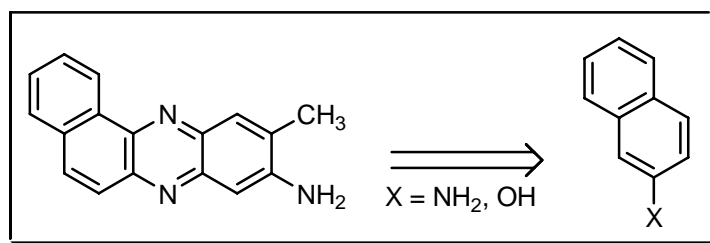
**EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of phenazine. The **Ullmann** method react 2-naphthol derivatives with 1-phenylazo-2-naphthylamine derivatives. While the **Horner** method is the autoxidation of 1-aminonaphthalene.

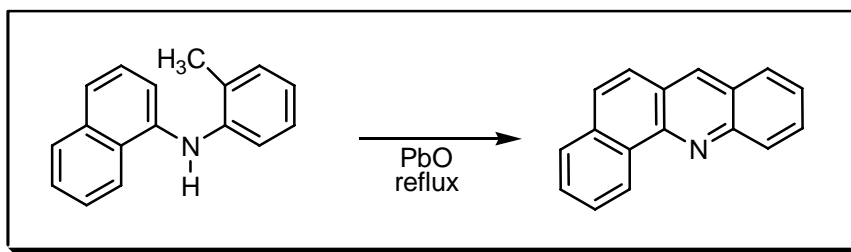
## REFERENCES :

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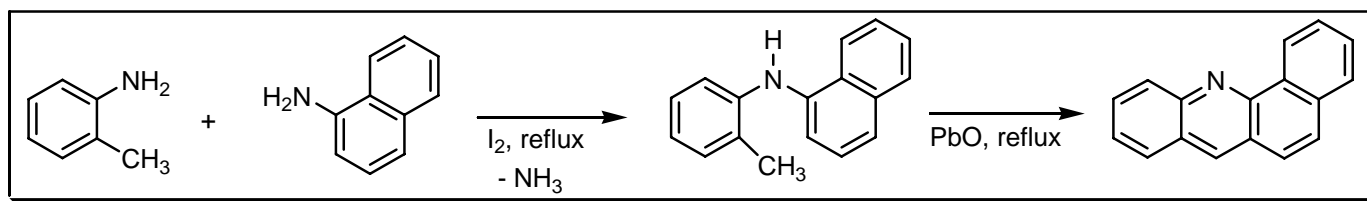
## COMMENTS :

## ULLMANN – LA TORRE ACRIDINE SYNTHESIS

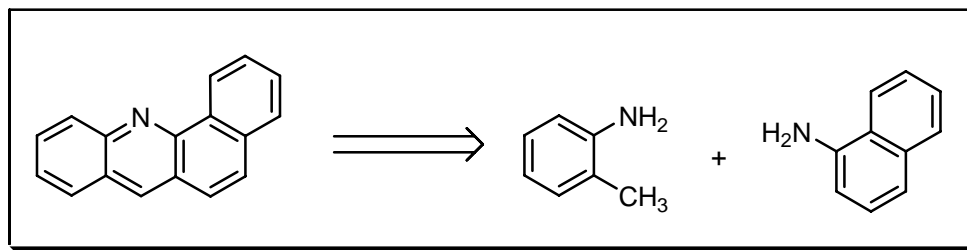
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

*o*-Methyldiarylamines cyclise with anilines in the presence of lead(II) oxide to afford acridines. See also **Bernthsen** acridine, **Mayer** and **Ullmann – Fetvadjan** reactions.

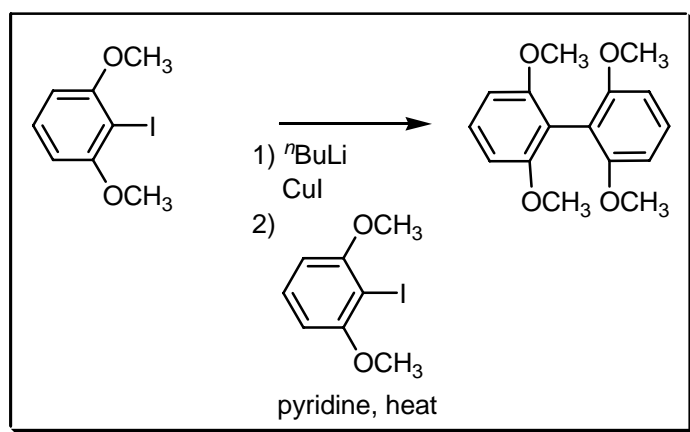
## REFERENCES :

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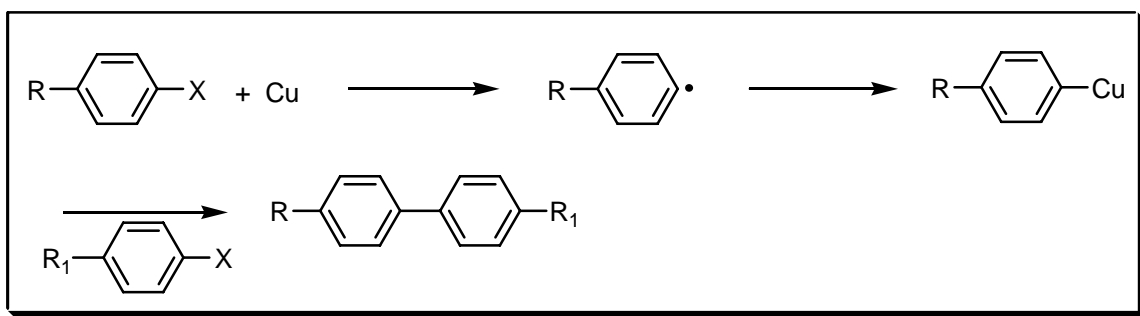
## COMMENTS :

## ULLMANN DIARYL CONDENSATION

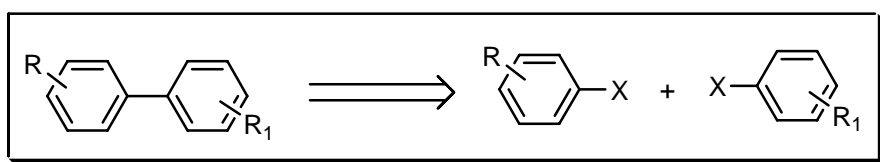
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

Diaryl derivatives are formed by the condensation of aromatic halides with itself or with other aromatic halides in the presence of metals. A large variety of conditions have been reported by several authors. There are several name reactions derived from the original **Ullmann** reaction, the most recent one **Ullmann – Ukita – Buchwald – Li** reaction. See also **Gattermann**, **Kondo – Uyeo** and **Mayer** reactions.

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**March** : 655

**Smith – March** : 871

**Smith** : 1437

**Smith 2<sup>nd</sup>** : 1185

**Houben – Weyl** : **6/3**, 86; **E8b**, 401

**Org. React.** : **2**, 224; **63**, 265

**Org. Synth.** : **20**, 45

**Org. Synth. Coll. Vol.** : **3**, 339

**Science of Synthesis** : **9**, 259, 371; **10**, 134, 140, 309, 350, 497

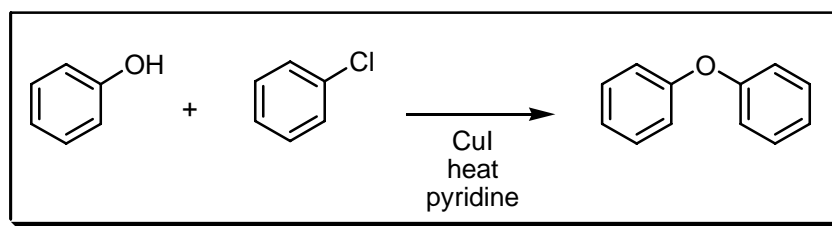
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  - 2) P.E. Fanta, *Chem. Rev.*, 1946, **38**, 139.
  - 3) H.E. Ungnade, *Chem. Rev.*, 1946, **38**, 405.
  - 4) P.E. Fanta, *Chem. Rev.*, 1964, **64**, 613.
  - 5) P.E. Fanta, *Synthesis*, 1974, 9.
  - 6) M. Tashiro, *Synthesis*, 1979, 933.
  - 7) T. Yamamoto; Y. Kurata, *Can. J. Chem.*, 1983, **61**, 86.
  - 8) A.J. Paine, *J. Am. Chem. Soc.*, 1987, **109**, 1496.
  - 9) A.I. Meyers; J.J. Willemsen, *Chem. Commun.*, 1997, 1573.
  - 10) M. Sugahara; T. Ukita, *Chem. Pharm. Bull.*, 1997, **45**, 719.
  - 11) G. Harada; M. Yoshida; M. Iyoda, *Chem. Lett.*, 2000, 160.
  - 12) G.Q. Lin; R. Hong, *J. Org. Chem.*, 2001, **66**, 2872.
  - 13) A. Hameurlaine; W. Dehaen, *Tetrahedron Lett.*, 2003, **44**, 957.
  - 14) P.-S. Wang; C.-K. Liang; M.-k. Leung, *Tetrahedron*, 2005, **61**, 2931.
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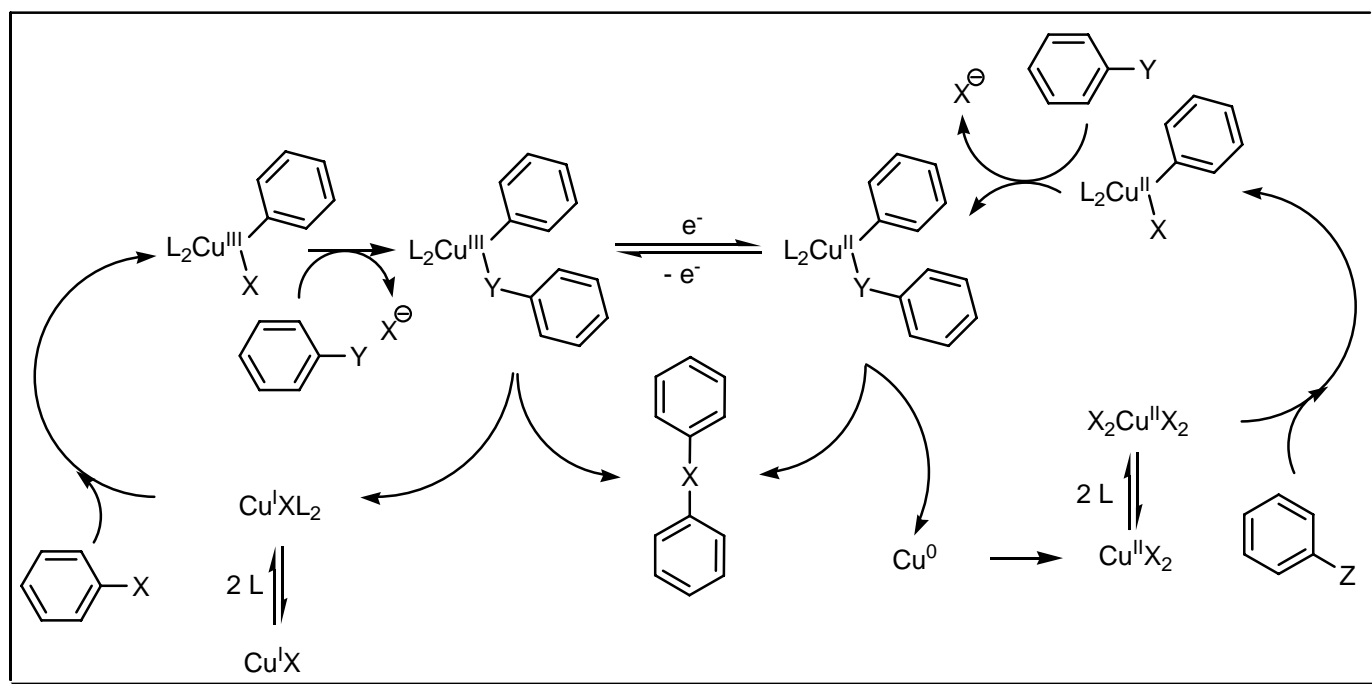
## COMMENTS :

## ULLMANN DIARYL ETHER SYNTHESIS

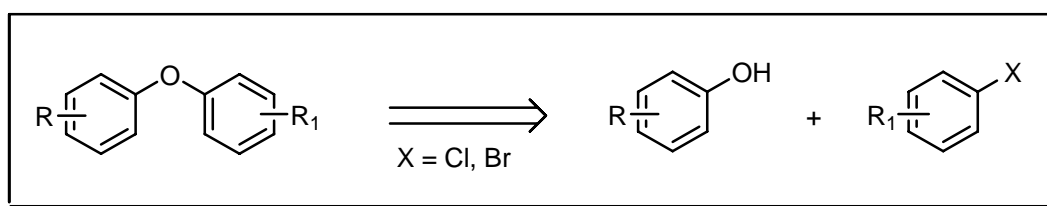
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

This reaction has traditionally been carried out under harsh conditions, usually at high temperature in pyridine as solvent. Low to moderate yields are common and the reactions between electron-rich aryl halides and electron deficient phenols typically do not work well. Milder reaction conditions have been reported by several groups.

### REFERENCES :

March : 655

Smith – March : 863

Org. Synth. : 14, 66; 26, 50

Org. Synth. Coll. Vol. : 2, 445; 3, 566

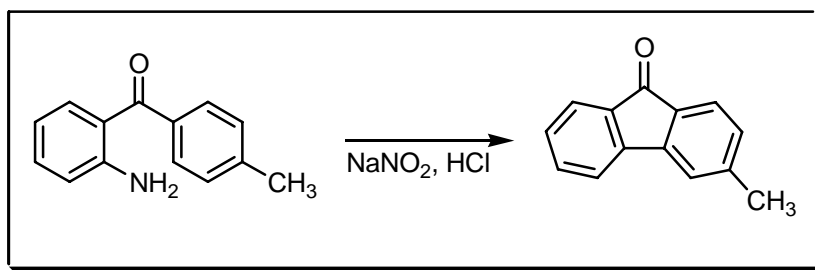
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- 1) F. Ullmann, *Ber. Dtsch. Chem. Ges.*, 1904, **37**, 853.
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  - 3) R.W. Turner; E.I. Amma, *J. Am. Chem. Soc.*, 1963, **85**, 4046.
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  - 5) J. Lindley, *Tetrahedron*, 1984, **40**, 1433.
  - 6) D.L. Boger; S.M. Sakya; D. Yohannes, *J. Org. Chem.*, 1991, **56**, 4204.
  - 7) M. Wolter; G. Nordman; G.E. Job; S.L. Buchwald, *Org. Lett.*, 2002, **4**, 973.
- 

COMMENTS :

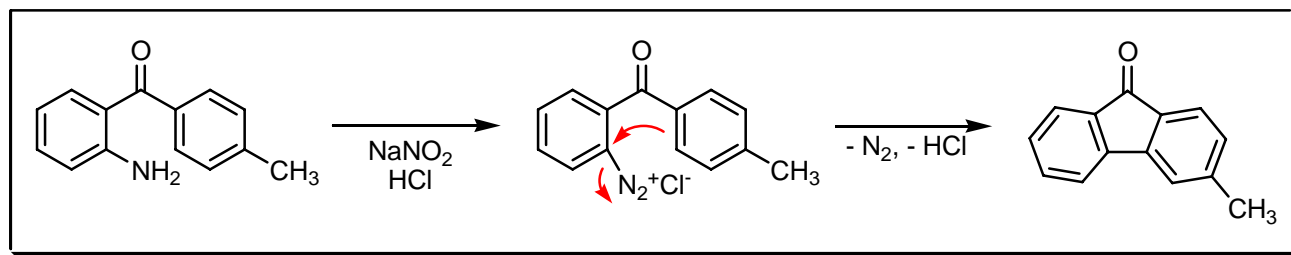
## ULLMANN FLUORENONE SYNTHESIS

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EXAMPLE :

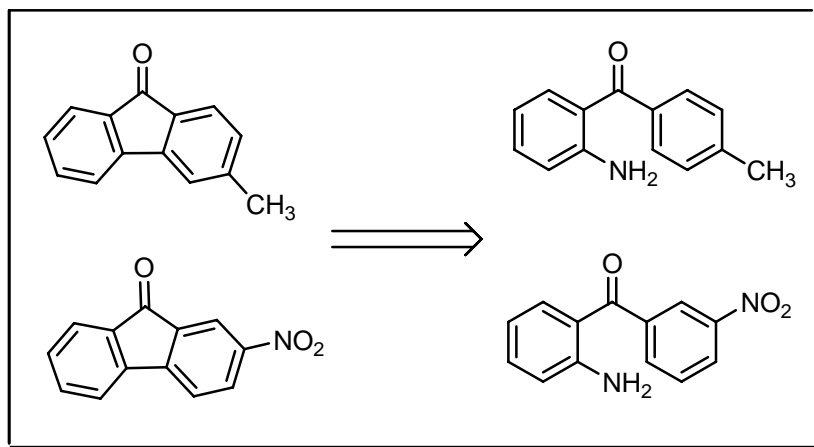


MECHANISM :





## DISCONNECTION :



## NOTES :

A 2-aminobenzophenone is diazotised to afford fluorenone. This reaction is very similar to the **Graebe – Ullmann** reaction and is sometimes called the **Graebe – Ullmann** fluorenone synthesis. See also **Gomberg – Bachmann – Hey**, **Larock** fluorene and **Pschorr** reactions.

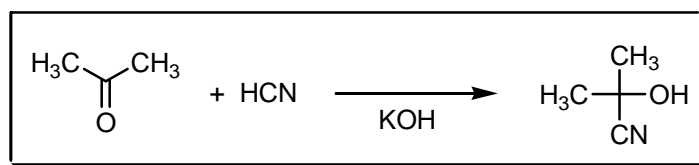
## REFERENCES :

- 1) C. Graebe; F. Ullmann, *Ber. Dtsch. Chem. Ges.*, 1894, **27**, 3484.
- 2) F. Ullmann; Ed. Mallet, *Ber. Dtsch. Chem. Ges.*, 1898, **31**, 1694.
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- 4) D.F. Detar; S.V. Sagmanli, *J. Am. Chem. Soc.*, 1950, **72**, 966.
- 5) A.J. Nunn; K. Schofield; R.S. Theobald, *J. Chem. Soc.*, 1952, 2797.
- 6) D.F. Detar; D.I. Relyea, *J. Am. Chem. Soc.*, 1954, **76**, 1680.

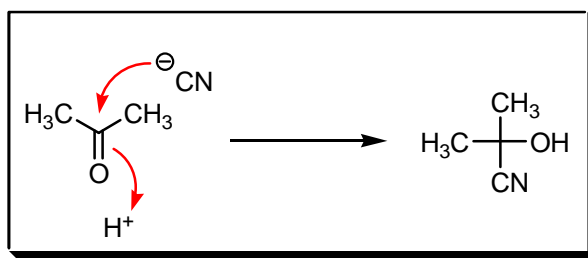
## COMMENTS :

## ULTEE CYANOHYDRIN SYNTHESIS

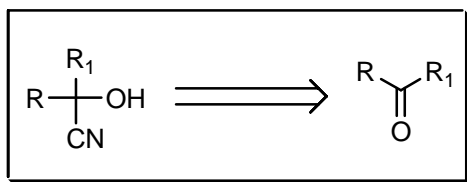
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The cyanohydrin synthesis in the presence of a base by addition of water-free hydrogen cyanide to carbonyls and ketones. See also **Bouveault – Locquin** amino acid, **von Braun** amino acid synthesis, **Bucherer – Bergs**, **Corey – Link**, **Darapsky**, **Herbst – Engel**, **Knoop – Oosterlin**, **O'Donnell**, **Schöllkopf**, **Sorensen**, **Strecker** amino acid, **Tiemann** amination, **Urech** and **Zelinsky – Stadnikoff** reactions.

## REFERENCES :

**March** : 964

**Smith – March** : 1239

**Smith** : 678

**Smith 2<sup>nd</sup>** : 575

**Houben – Weyl** : 8, 275

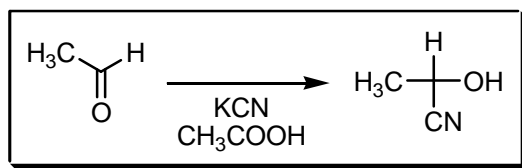
- 1) A.J. Ultee, *Ber. Dtsch. Chem. Ges.*, 1906, **39**, 1856.
- 2) A.J. Ultee, *Recl. Trav. Chim. Pays-Bas*, 1909, **28**, 1.
- 3) D.T. Mowry, *Chem. Rev.*, 1948, **42**, 189.
- 4) S.L. Shapiro; I.M. Rose; E. Roskin; L. Freedman, *J. Am. Chem. Soc.*, 1959, **81**, 386.
- 5) H. Plieniger; J. Kurze, *Liebigs Ann. Chem.*, 1964, **680**, 60.

## COMMENTS :

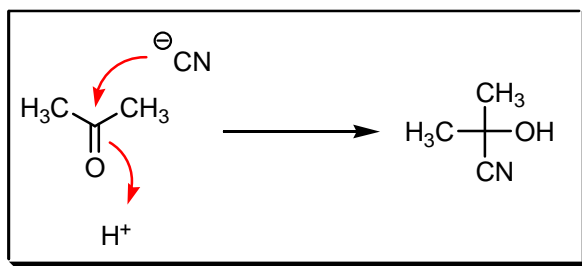
## URECH CYANOHYDRIN METHOD

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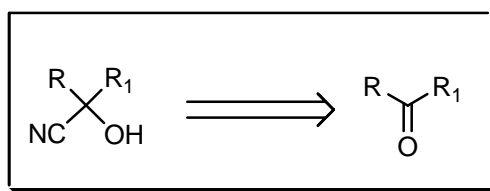
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The cyanohydrin synthesis by addition of alkali cyanide to ketones and aldehydes in the presence of acetic acid. See also **Bouveault – Locquin** amino acid, **von Braun** amino acid synthesis, **Bucherer – Bergs**, **Corey – Link**, **Darapsky**, **Herbst – Engel**, **Knoop – Oosterlin**, **O'Donnell**, **Schöllkopf**, **Sorensen**, **Strecker** amino acid, **Tiemann** amination, **Ultee** and **Zelinsky – Stadnikoff** reactions.

### REFERENCES :

**Houben – Weyl** : 8, 274

**Org. Synth.** : 13, 56; 15, 1; 27, 41; 33, 7

**Org. Synth. Coll. Vol.** : 2, 7, 387; 3, 436; 4, 58

1) F.L. Winckler, *Liebigs Ann. Chem.*, 1832, **4**, 246.

2) F. Urech, *Liebigs Ann. Chem.*, 1872, **164**, 255.

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(*Bull. Acad. Sci. USSR Div. Chem. Sci. (Engl. Transl.)*, 1981, **30**, 475.)

5) K. Mori; T. Ebata; S. Takechi, *Tetrahedron*, 1984, **40**, 1761.

6) R.S. Randad; G.H. Kulkarni, *Indian J. Chem.*, 1985, **24B**, 225.

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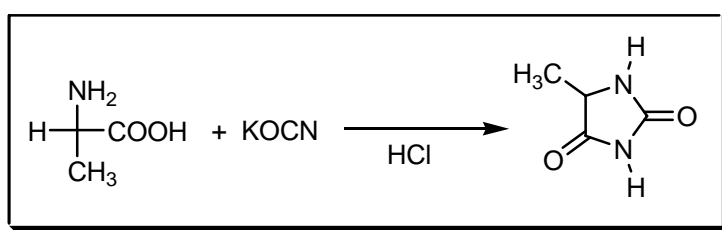
**COMMENTS :**

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**URECH HYDANTOIN SYNTHESIS**

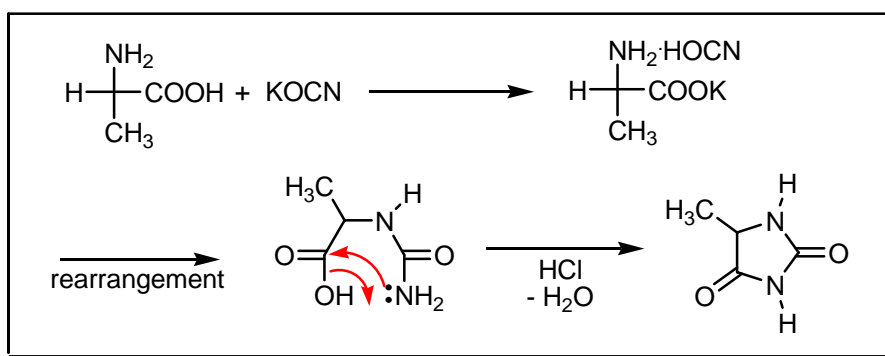
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**EXAMPLE :**



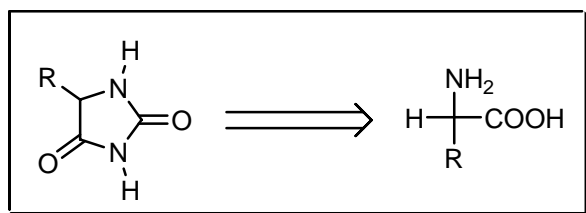
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**MECHANISM :**



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**DISCONNECTION :**



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**NOTES :**

An α-amino acid reacts with potassium cyanate to afford an hydantoin. See also **Bucherer – Bergs**, **Johnson 2-thiohydantoin** and **Schlack – Kumpf** reactions.

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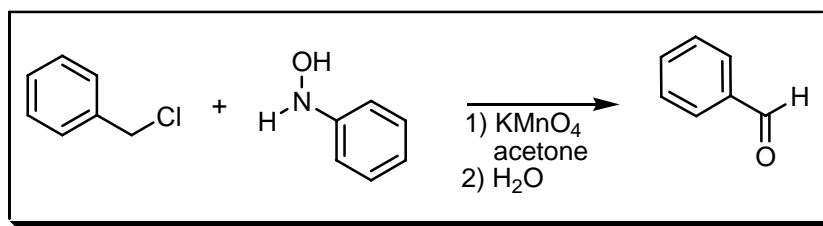
## REFERENCES :

- 1) F. Urech, *Liebigs Ann. Chem.*, 1873, **165**, 99.
- 2) W.T. Read, *J. Am. Chem. Soc.*, 1922, **44**, 1746.
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- 6) R.N. Comber; R.C. Reynolds; J.D. Friedrich; R.A. Manguikian; R.W. Buckheit; J.W. Truss; W.M. Shannon; J.A. Secrist, *J. Med. Chem.*, 1992, **35**, 3567.

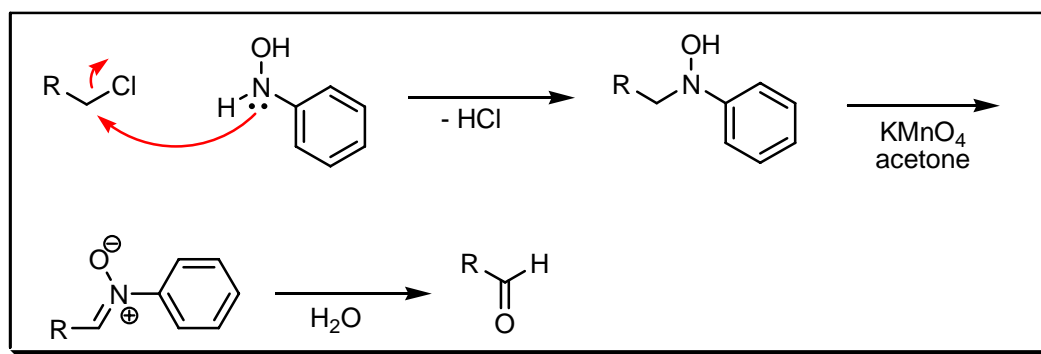
## COMMENTS :

## UTZINGER ALDEHYDE SYNTHESIS

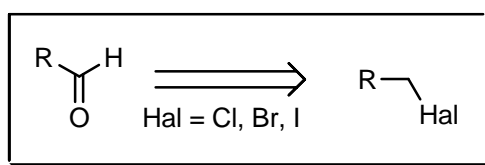
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



**NOTES :**

Alkyl and aromatic halides react in water or in ethanolic pyridine with phenylhydroxylamine to yield a substituted phenylhydroxylamine, which is oxidised by potassium permanganate in acetone, to the nitron. The latter may be quantitatively hydrolysed to the aldehyde. See also **Kröhnke – Ortoleva – King** reaction.

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**REFERENCES :**

Houben – Weyl : 7/1, 203

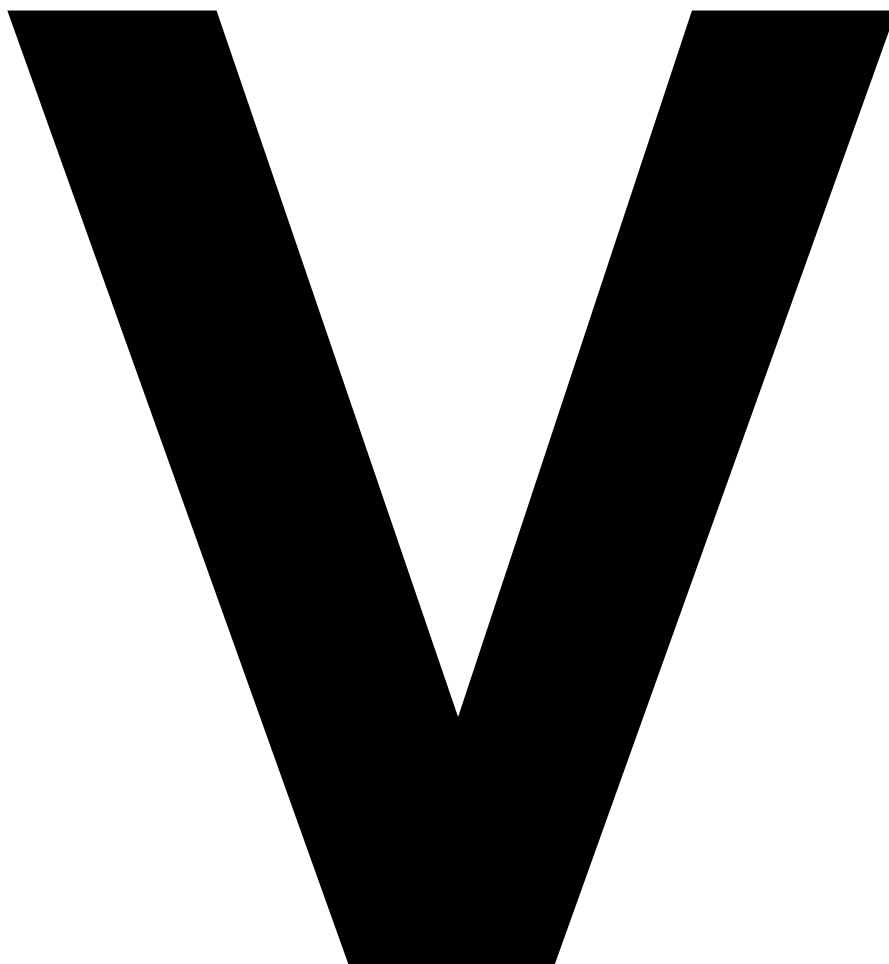
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1) G.E. Utzinger, *Liebigs Ann. Chem.*, 1944, **556**, 50.

2) H.D. Hartough, *J. Am. Chem. Soc.*, 1947, **69**, 1355.

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**COMMENTS :**



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**H**

HILBERT – JOHNSON – RIST REACTION · 1790

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**N**

NISHIMURA – CRISTESCU *N*-GLYCOSIDATION · 1790

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**V**

VARRENTRAPP OLEIC ACID REACTION · 1776

VASELLA – BERNET REACTION · 1777

VEDEJS HYDROXYLATION · 1779

VENKATARAMAN – WAGLE REACTION · 1780

VIGNEAUD du SERINE SYNTHESIS · 1782

VILSMEIER – HAACK – VIEHE REACTION · 1783

VOIGHT AMINATION · 1785

VOLHARD – ERDMANN CYCLISATION · 1786

VORBRÜGGEN – KROLIKIEWICZ REACTION · 1787

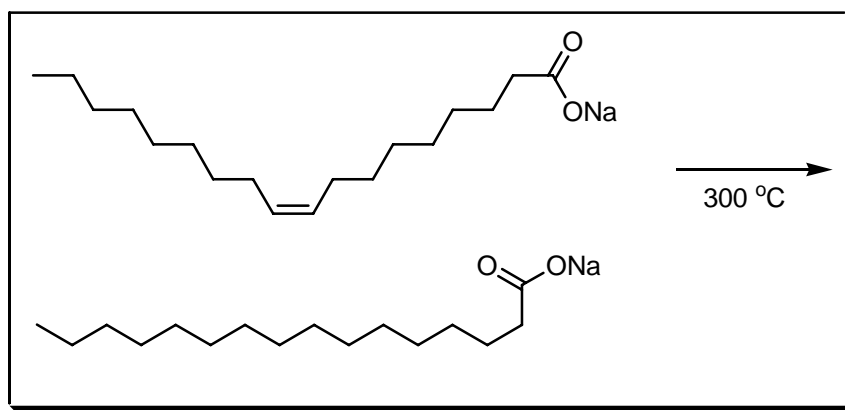
VORBRÜGGEN NUCLEOSIDE SYNTHESIS · 1789

VORLÄNDER SYNTHESIS · 1790

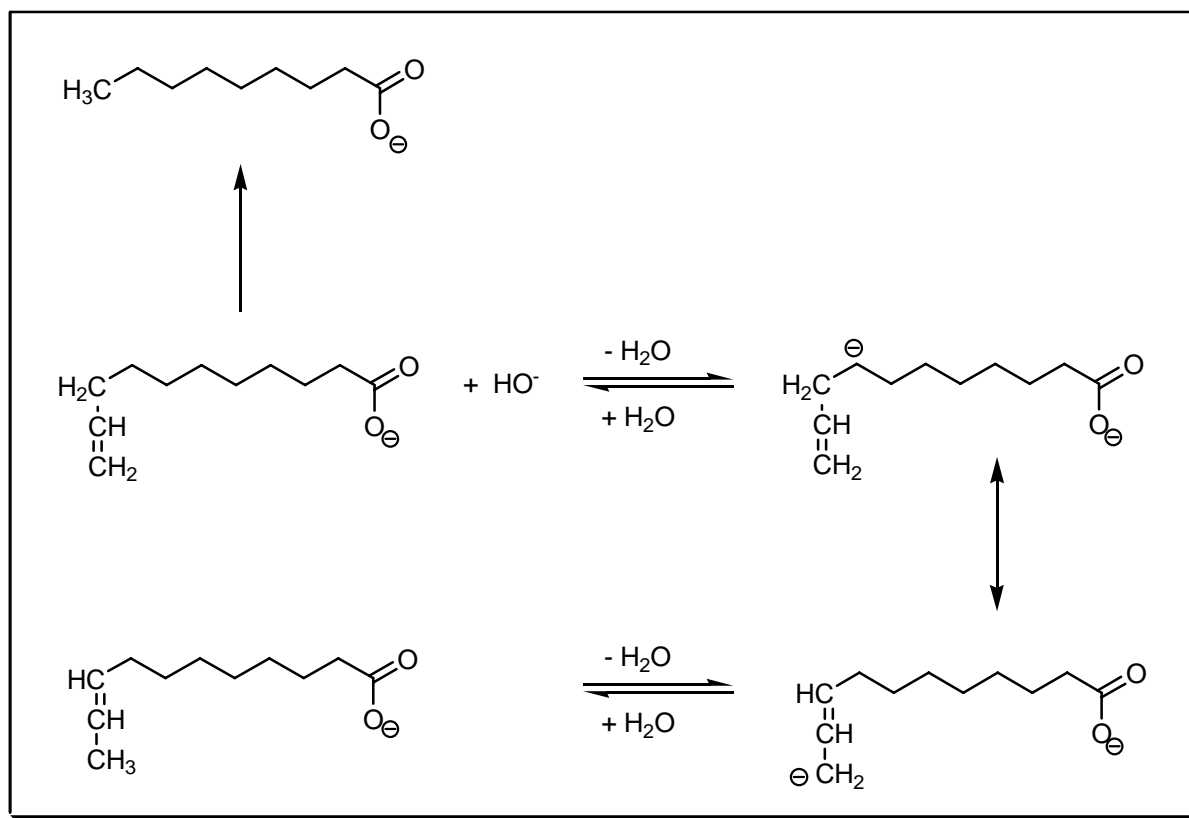


## VARRENTRAPP OLEIC ACID REACTION

### EXAMPLE :



### MECHANISM :



### NOTES :

When oleic acid is heated in an alkali melt at 300 °C a migration of the double bond to the  $\alpha,\beta$ -position occurs to afford palmitinic acid and acetic acid. Linoleic and stearolic acid give myristic acid, together with small amounts of palmitinic acid, on treatment with molten potassium hydroxide. Similar reactions occur with other olefinic acids.

## REFERENCES :

Houben – Weyl : E5, 456

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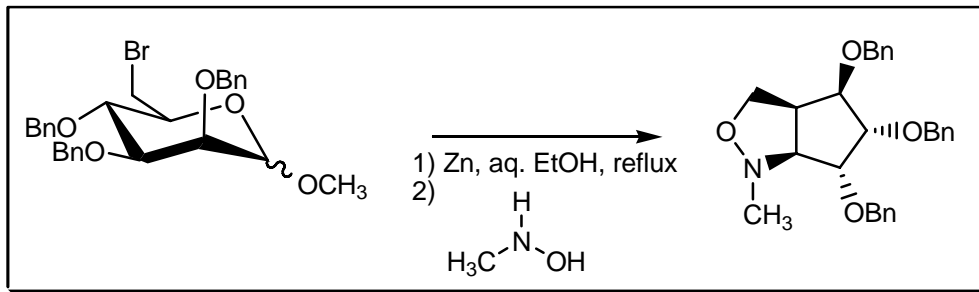
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  - 4) R.G. Ackman; R.A. Dytham; B.J. Wakefield; B.C.L. Weedon, *Tetrahedron*, 1960, **8**, 239.
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  - 6) R.G. Ackman; M.A. Bannerman; M.E. Retson; F.A. van den Heuvel, *Can. J. Chem.*, 1961, **29**, 1730.
- 

## COMMENTS :

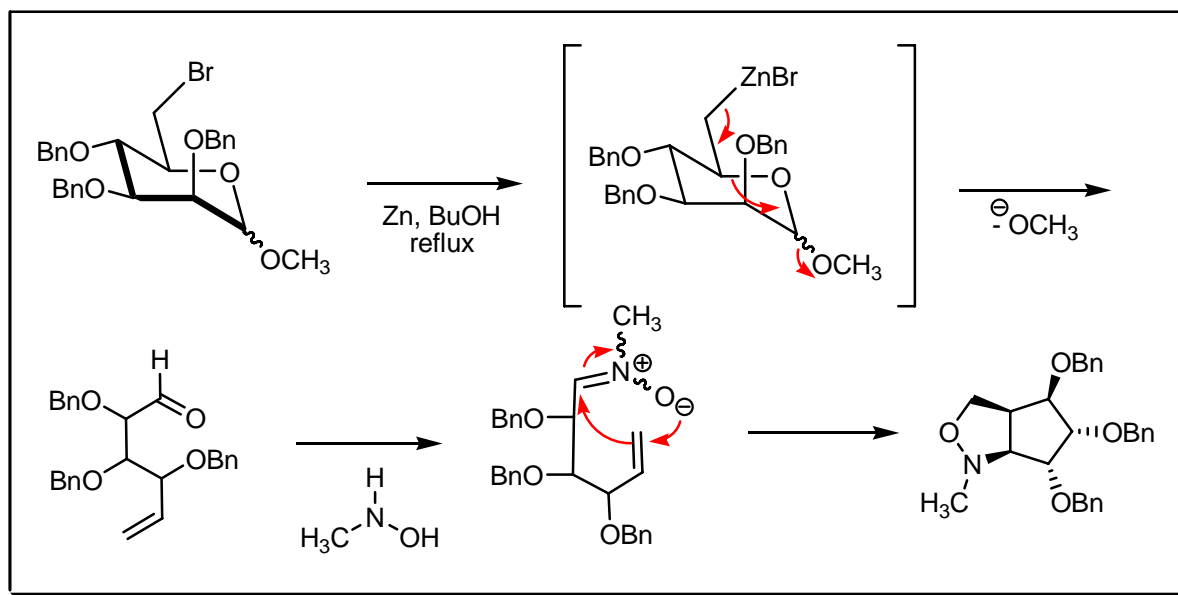
## VASELLA – BERNET REACTION

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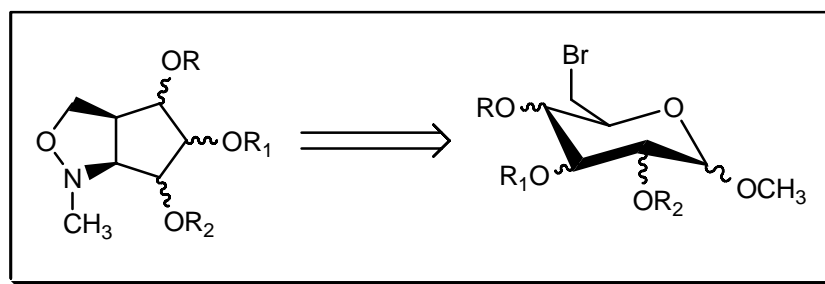
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The formation of cyclopentane derivatives derived from the monosaccharides, glucose, mannose, galactose and 6-deoxy-6-halo-hexono-1,5-*ortholactones*. The crucial steps in these syntheses are the reductive fragmentation of the 6-bromo-6-deoxy-glycosides affording the unsaturated aldehydes and the *intramolecular* cycloaddition of the corresponding nitrones.

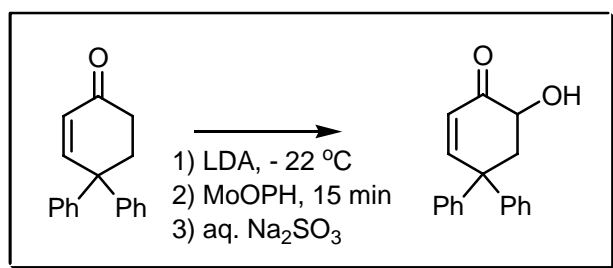
## REFERENCES :

- 1) B. Bernet; A. Vasella, *Helv. Chim. Acta*, 1979, **62**, 1990.
- 2) B. Bernet; A. Vasella, *Helv. Chim. Acta*, 1979, **62**, 2400.
- 3) B. Bernet; A. Vasella, *Helv. Chim. Acta*, 1979, **62**, 2411.
- 4) B. Bernet; A. Vasella, *Helv. Chim. Acta*, 1984, **67**, 1328.

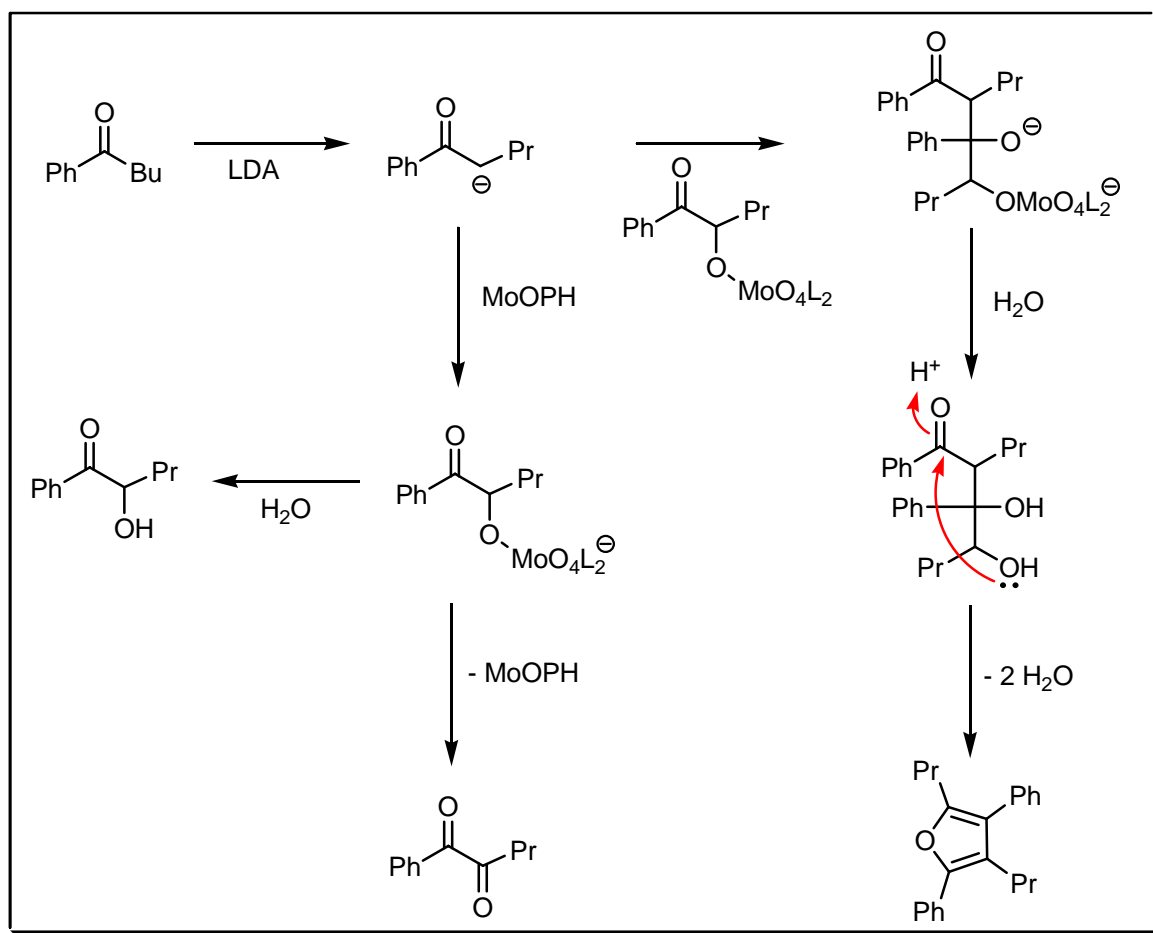
## COMMENTS :

## VEDEJS HYDROXYLATION

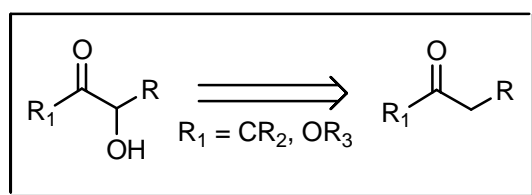
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The oxidation of enolates of ketones, esters and lactones to  $\alpha$ -hydroxy derivatives using MoOPH ( $\text{MoO}_3 \cdot \text{Py} \cdot \text{HMPA}$ ) reagent. Several side reactions under the typical conditions can take place as shown in the mechanism scheme. See also **Hassner – Rubottom**  $\alpha$ -hydroxylation reaction.

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## REFERENCES :

Smith – March : 915

Smith 2<sup>nd</sup> : 738

Org. Synth. : 64, 127

Org. Synth. Coll. Vol. : 7, 277

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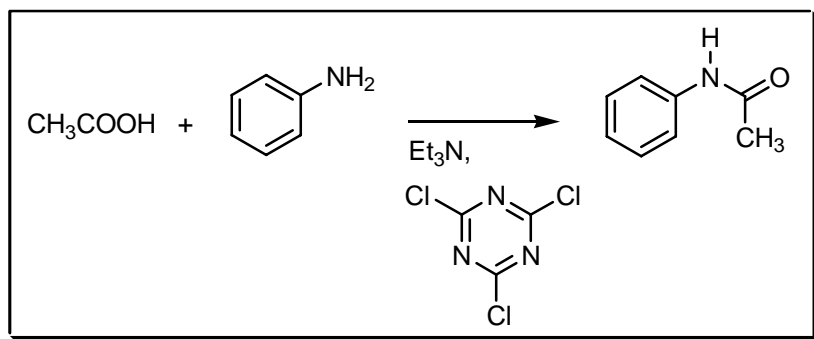
- 1) E. Vedejs; D.A. Engler; J.E. Telschow, *J. Org. Chem.*, 1978, **43**, 188.
  - 2) K. Krohn; H. Riger; K. Khanbabaei, *Chem. Ber.*, 1989, **122**, 2323.
  - 3) L.N. Mander; R.P. Robinson, *J. Org. Chem.*, 1991, **56**, 3595.
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  - 5) O. Hara; J. Takizawa; T. Yamatake; K. Makino; Y. Hamada, *Tetrahedron Lett.*, 1999, **40**, 7787.
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- 

## COMMENTS :

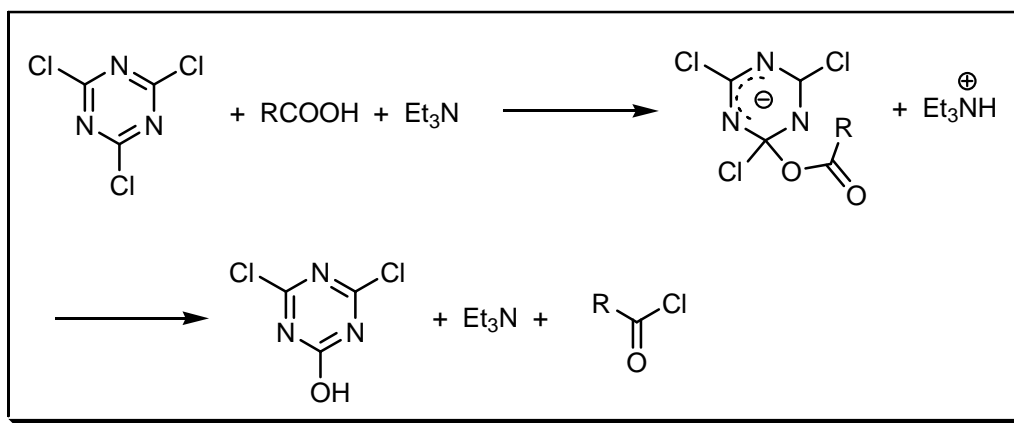
## VENKATARAMAN – WAGLE REACTION

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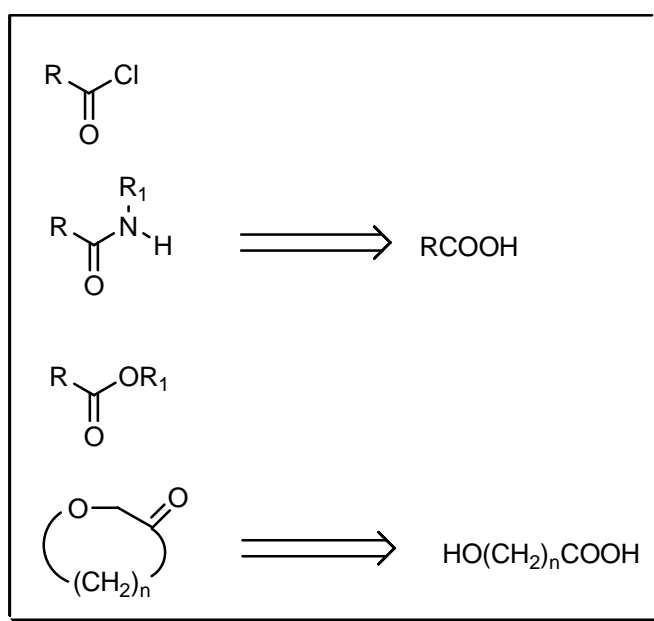
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The use of cyanuric chloride in the conversion of carboxylic acids into acid chlorides, esters, amides and peptides. The reaction is also used in the macrolactonisation of  $\omega$ -hydroxy carboxylic acids. See also **Corey – Nicolaou**, **Diels – Alder**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Kita**, **Masamune**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Vorbrüggen – Krolkiewicz**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

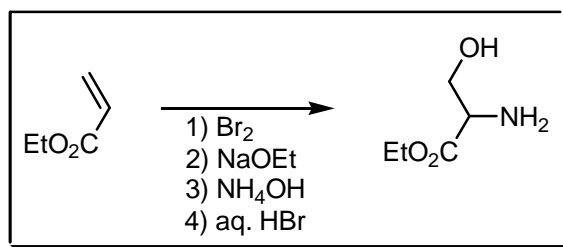
## REFERENCES :

- 1) K. Venkataraman; D.R. Wagle, *Tetrahedron Lett.*, 1979, **20**, 3037.
- 2) K. Venkataraman; D.R. Wagle, *Tetrahedron Lett.*, 1980, **21**, 1893.

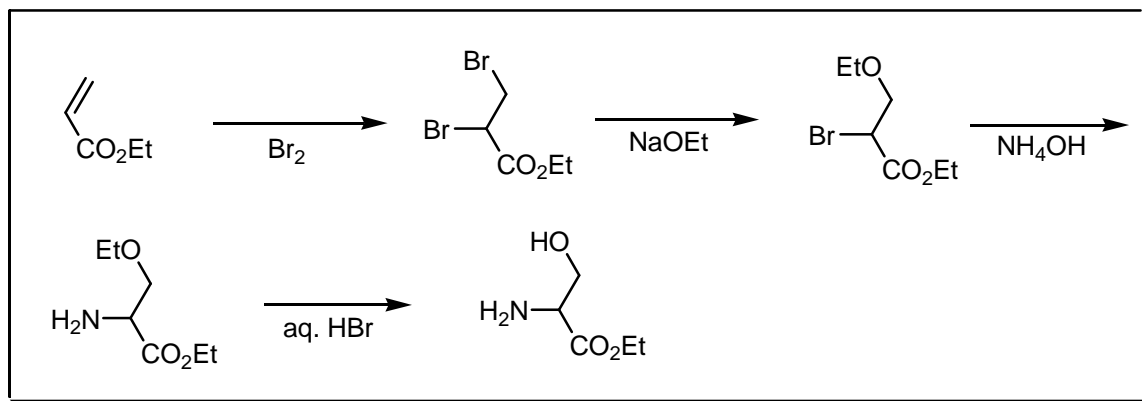
COMMENTS :

du VIGNEAUD SERINE SYNTHESIS

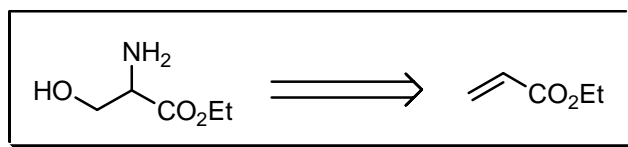
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

Ethyl acrylate is brominated to yield  $\alpha,\beta$ -dibromopropionate, which on treatment with one mole of sodium ethoxide is converted into ethyl  $\alpha$ -bromo- $\beta$ -ethoxypropionate. The latter with ammonium hydroxide gives ethyl  $\alpha$ -amino- $\beta$ -ethoxypropionate, which with aqueous hydrogen bromide yields *dl*-serine. See also **von Braun** amino acid synthesis and **Leuchs – Bergmann** reactions.

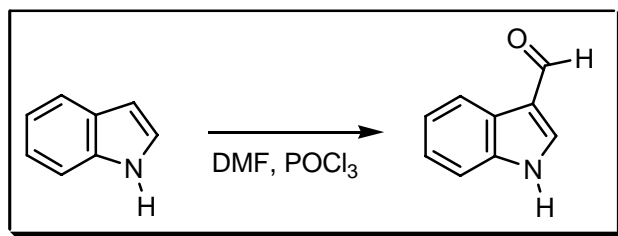
## REFERENCES :

- 1) V. du Vigneaud; J.L. Wood, *J. Biol. Chem.*, 1940, **134**, 413.
- 2) H. Bretschneider; N. Karpitschka; G. Piekarski, *Monatsh. Chem.*, 1953, **84**, 1084.

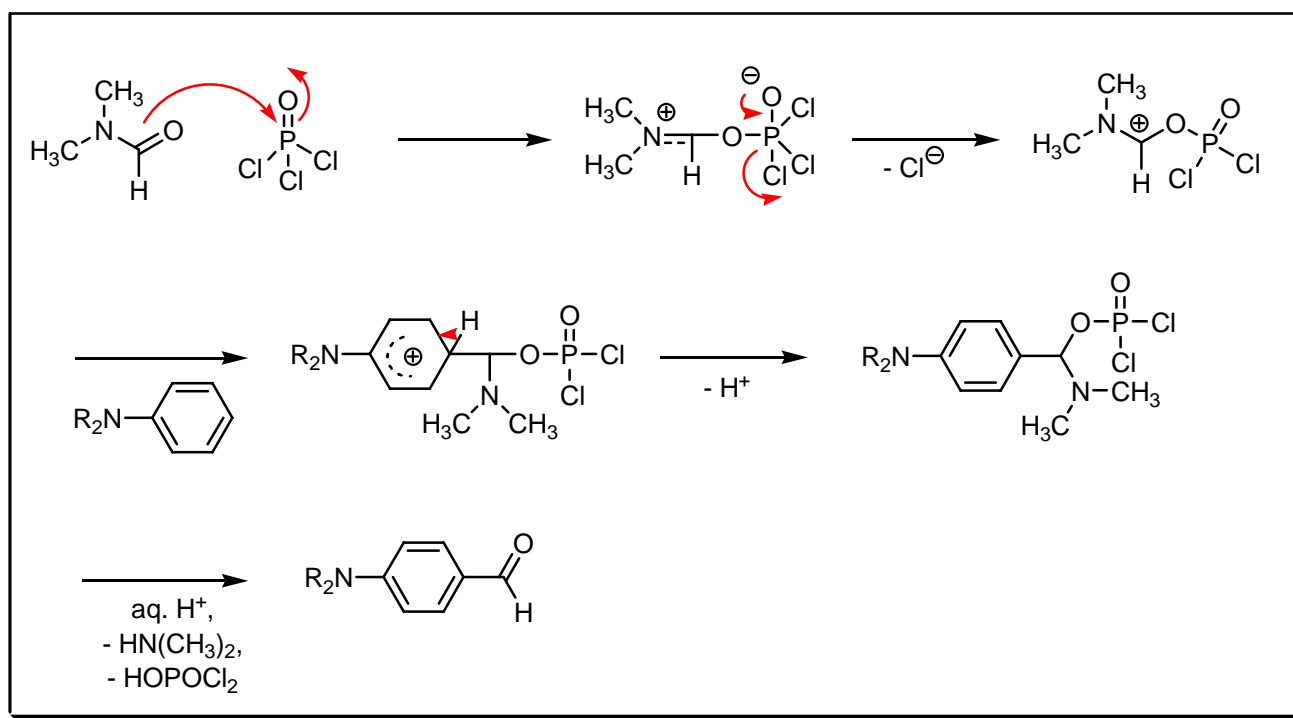
## COMMENTS :

## VILSMEIER – HAACK – VIEHE REACTION

### EXAMPLE :

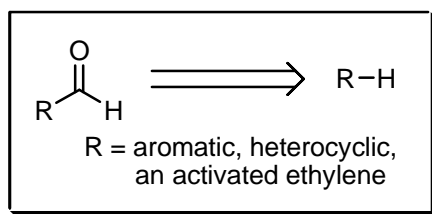


### MECHANISM :





## DISCONNECTION :



## NOTES :

Formamides react with aromatic, heterocyclic and activated ethylenic compounds in the presence of phosphorous oxychloride to produce intermediates, which on hydrolysis in acid solution yield aldehydes.  $\text{Me}_2\text{N}^+=\text{CHCl} \text{ Cl}^-$  (Vilsmeier – Haack),  $\text{Me}_2\text{N}^+=\text{CCl}_2 \text{ Cl}^-$  (Viehe). See also Friedel – Crafts, Gattermann, Gattermann – Koch and Meth–Cohn quinoline reactions.

## REFERENCES :

March : 542

Smith – March : 715, 785

Smith : 1328

Smith 2<sup>nd</sup> : 327, 1093

Houben – Weyl : **7/1**, 29; **E6a**, 95, 438; 758, 977; **E6b**, 256, 1042, 1050, 1065, 1069, 1098; **E7b**, 231; **E8a**, 608, 750, 833, 845, 987; **E8b**, 263; **E19c**, 360

Org. React. : **49**, 1; **56**, 355

Org. Synth. : **20**, 11; **33**, 27; **64**, 144

Org. Synth. Coll. Vol. : **3**, 98; **4**, 331; **7**, 323

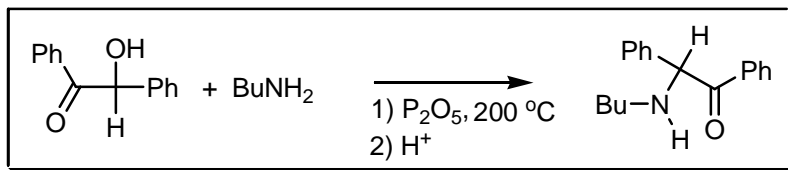
Science of Synthesis : **9**, 239, 351, 438, 509; **10**, 72, 450, 509, 511, 537, 601, 683, 717, 726

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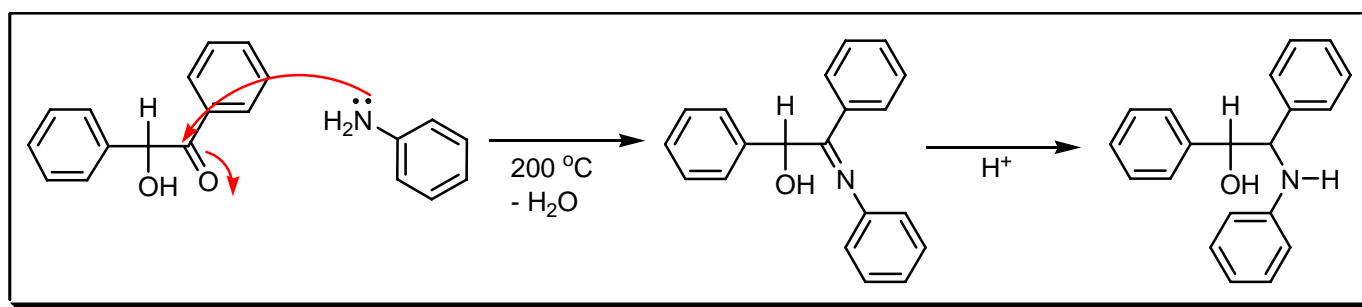
COMMENTS :

## VOIGHT AMINATION

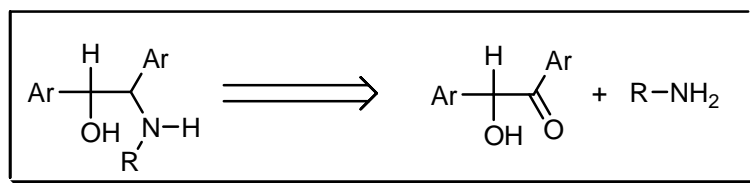
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

*N*-substituted 1,2-diaryl amino alcohols are obtained by the interaction of benzoin and primary amines. Phosphorous pentoxide or hydrochloric acid may be used as a condensing agent for aliphatic amines.

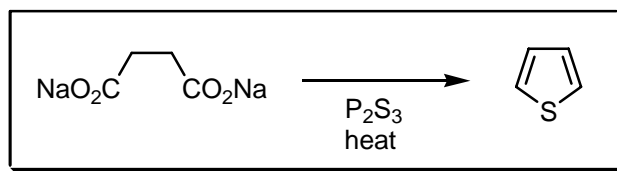
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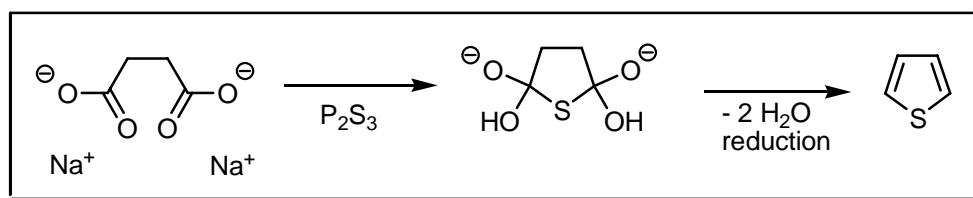
## COMMENTS :

## VOLHARD – ERDMANN CYCLISATION

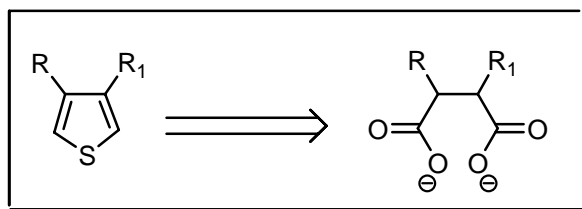
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The action of diphosphorous trisulfide on sodium succinate or a substituted sodium succinate yields a thiophene. See also **Baumann – Fromm**, **Bogert – Herrera**, **Fiesselmann**, **Hinsberg** thiophene, **Paal – Knorr** and **Willgerodt – Kindler** reactions.

## REFERENCES :

Org. React. : 6, 9

Org. Synth. : 12, 72; 34, 73

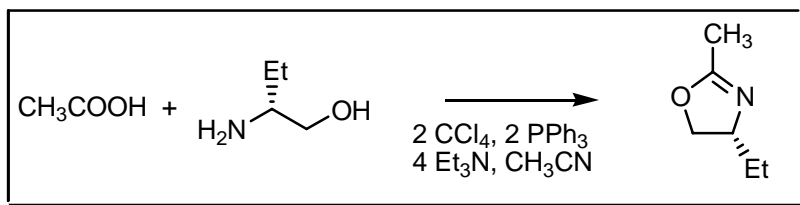
Org. Synth. Coll. Vol. : 2, 578; 4, 671

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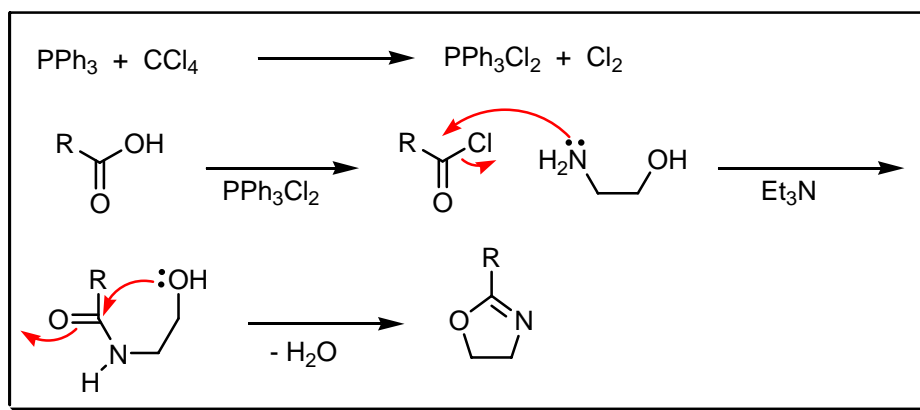
## COMMENTS :

## VORBRÜGGEN – KROLIKIEWICZ REACTION

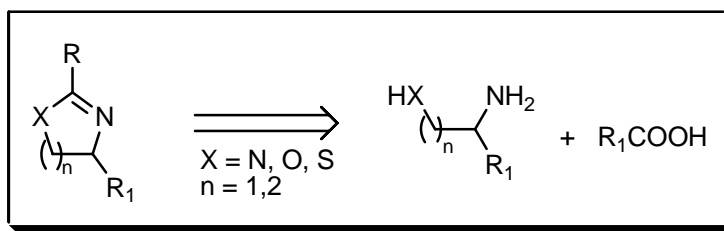
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

Carboxylic acids react readily with amino alcohols, amino mercaptans, diamines and *o*-aminophenols in the presence of triphenylphosphine- or tributylphosphine dichloride (generated *in situ* from the reaction of the phosphines with hexachloroethane or CCl<sub>4</sub>) and triethylamine in acetonitrile to form the corresponding  $\Delta^2$ -oxazolines,  $\Delta^2$ -oxazines,  $\Delta^2$ -thiazolines,  $\Delta^2$ -imidazolines, 2-substituted benzoxazoles and 2-oxazolidinones. See also **Appel**, **Corey – Nicolaou**, **Diels – Alder**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Keck** macrolactonisation, **Kita**, **Masamune**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Wittig**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

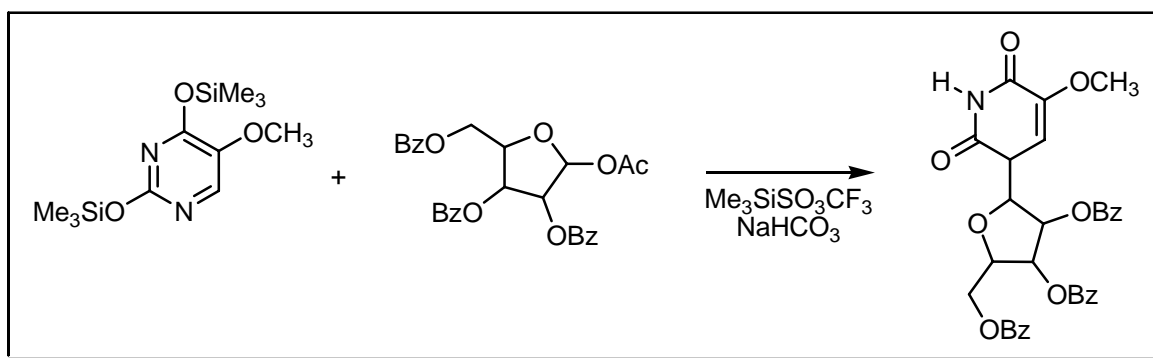
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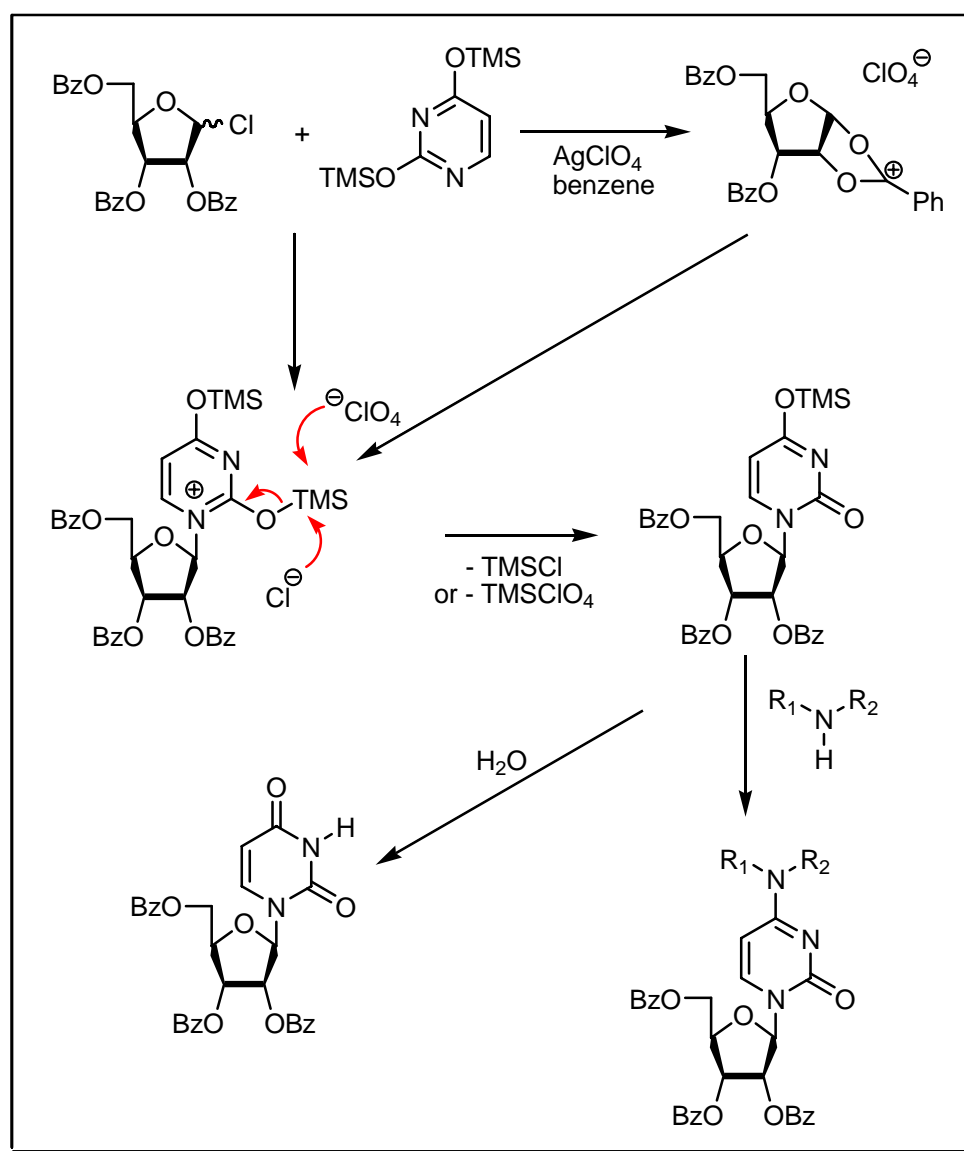
## COMMENTS :

## VORBRÜGGEN NUCLEOSIDE SYNTHESIS

### EXAMPLE :



### MECHANISM :



## NOTES :

The synthesis of nucleosides by condensation of sugars with silyl heterocycles and Lewis acids such as  $\text{SnCl}_4$ ,  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  or trimethyl triflate. In the literature also known as the **Hilbert – Johnson – Rist** reaction, although several other names show up. See also **Nishimura – Cristescu** *N*-glycosidation.

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## REFERENCES :

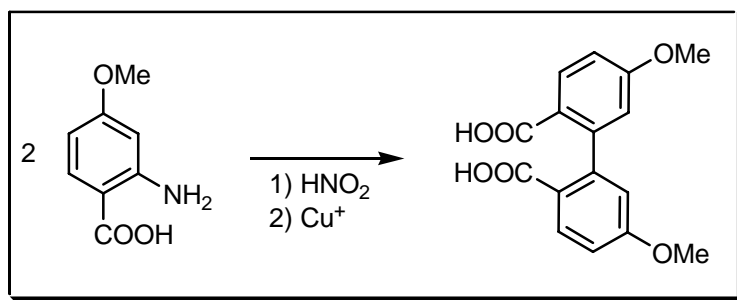
Org. React. : 55, 1

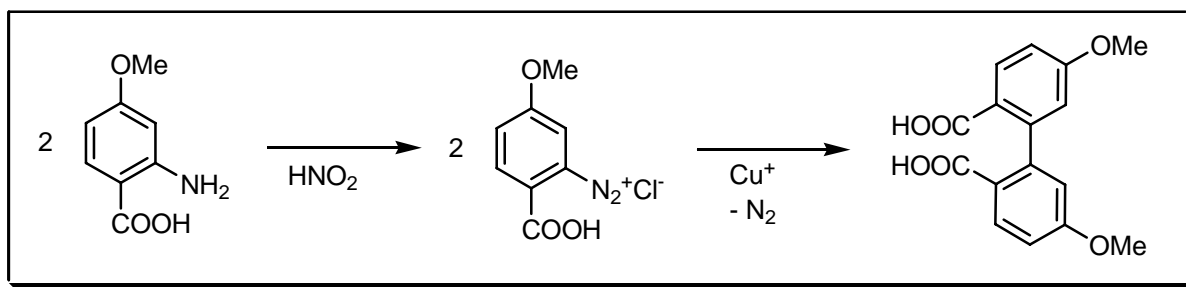
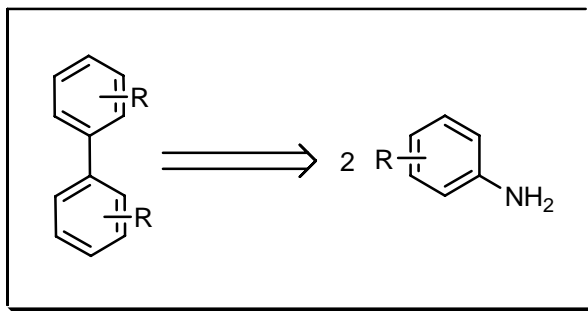
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- 

## COMMENTS :

## VORLÄNDER SYNTHESIS

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

Diphenyl dicarboxylic acids are obtained by diazotisation and subsequent reduction of a derivative of anthranilic acid by ammoniacal cuprous hydroxide. Other types of diaryl derivatives can be similarly prepared.

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Houben – Weyl : 10/3, 163; E16d, 52

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**COMMENTS :**



**W**

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**B**

BUU-HÖI MODIFICATION · 1871

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**H**

HUANG-MILON MODIFICATION · 1875

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**S**

SCHLOSSER MODIFICATION · 1865

SCHWENK MODIFICATION · 1849

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**W**

WAGNER – MEERWEIN REARRANGEMENT · 1795

WAGNER–JAUREGG ADDITION · 1794

WAKAMATSU SYNTHESIS · 1796

WAKATSUKI – YAMAZAKI – BÖNNEMANN REACTION · 1799

WALKER – HAUSER SYNTHESIS · 1801

WALLACH IMIDAZOLE SYNTHESIS · 1802

WALLACH REARRANGEMENT · 1803

WASSERMANN – BORMANN MACROCYCLIC LACTAM  
SYNTHESIS · 1805

WATANABE HETEROCYCLISATION · 1806

WATANABE INDOLE SYNTHESIS · 1808

WAWZONEK – YEAKEY REARRANGEMENT · 1809

WEERMAN DEGRADATION · 1811

WEERMAN SYNTHESIS OF INDOLE · 1812

WEIDENHAGEN IMIDAZOLE SYNTHESIS · 1813

WEIL SYNTHESIS OF ARYL ALDEHYDES · 1814

WEINREB ACYLATION · 1815

WEISS ANNULATION · 1817

WEITZ – SCHEFFER REACTION · 1818

WELDE SYNTHESIS OF DIXANTHATES · 1820

WENDER CYCLOHEPTENE SYNTHESIS · 1823

WENDER INDOLE SYNTHESIS · 1821

WENDER REACTION · 1825

WENKER RING–CLOSURE · 1826

WENZEL – IMAMOTO REDUCTION · 1827

WERNER SYNTHESIS · 1828

WESSELY – MOSER REARRANGEMENT · 1829

WESTPHAL CONDENSATION · 1830

WESTPHALEN – LETTRÉ REARRANGEMENT · 1831

WETTSTEIN OXIDATION · 1833

WEYGAND – LÖWENFELD REDUCTION · 1834

WHARTON FRAGMENTATION · 1836

WHARTON OLEFIN SYNTHESIS · 1835

WHITING – NAYLER REACTION · 1836

WIBAUT – ARENS SYNTHESIS · 1838

WICHTERLE REACTION · 1839

WIDEQVIST CYCLOPROPANE SYNTHESIS · 1841

WIDMAN – STOERMER SYNTHESIS · 1842

WIDMANN SYNTHESIS OF INDOLES · 1843

WIELAND – DANE DEGRADATION · 1844

WIELAND TRIPHENYLMETHYL RADICAL REARRANGEMENT ·  
1845

WILKE REACTION · 1847

WILLGERODT – KINDLER REDOX AMINATION · 1849

WILLIAMS – BEN-ISHAI AMINO ACID SYNTHESIS · 1851

WILLIAMSON ETHER SYNTHESIS · 1852

WINTERFELDT OXIDATION · 1854

WISLICENUS SYNTHESIS · 1855

WISSNER  $\alpha$ -FUNCTIONALISED METHYL KETONE SYNTHESIS ·  
1855

WITT DIAZOTATION · 1857

WITTE – SEELIGER REACTION · 1858

WITTIG – GILMAN REACTION · 1859

WITTIG – WITT LITHIUM EXCHANGE · 1859

WITTIG [1,2]-REARRANGEMENT · 1860

WITTIG [2,3]-REARRANGEMENT · 1861

WITTIG PHENANTHRENE SYNTHESIS · 1863

WITTIG REACTION · 1864

WOHL – AUE REACTION · 1866

WOHL – MARCKWALD SYNTHESIS · 1867

WOHL – ZIEGLER BROMINATION · 1869

WOHL DEGRADATION · 1872

WÖHLER UREA SYNTHESIS · 1873

WOLFF – KISHNER REDUCTION · 1874

WOLFF REARRANGEMENT · 1876

WOLFFENSTEIN – BÖTERS REACTION · 1878

WOLFRAM – SCHÖRNIG – HANS DORF  
CARBOXYMETHYLATION · 1880

WOLFRAM SYNTHESIS OF CYCLONITE · 1881

WOLFROM – KARABINOS REDUCTION · 1882

WOODWARD CIS-HYDROXYLATION · 1883

WOODWARD PEPTIDE SYNTHESIS · 1884

WRIGHT – WEST GERMYL MIGRATION · 1886

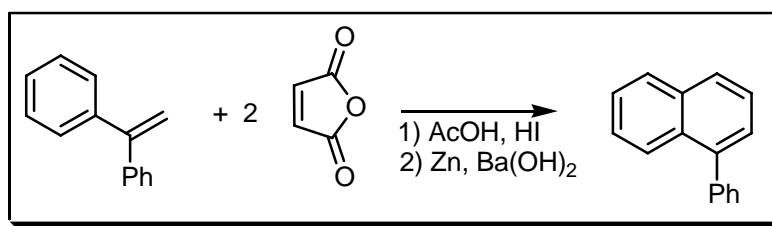
WURTZ – FITTIG REACTION · 1887

WURTZ REACTION · 1888

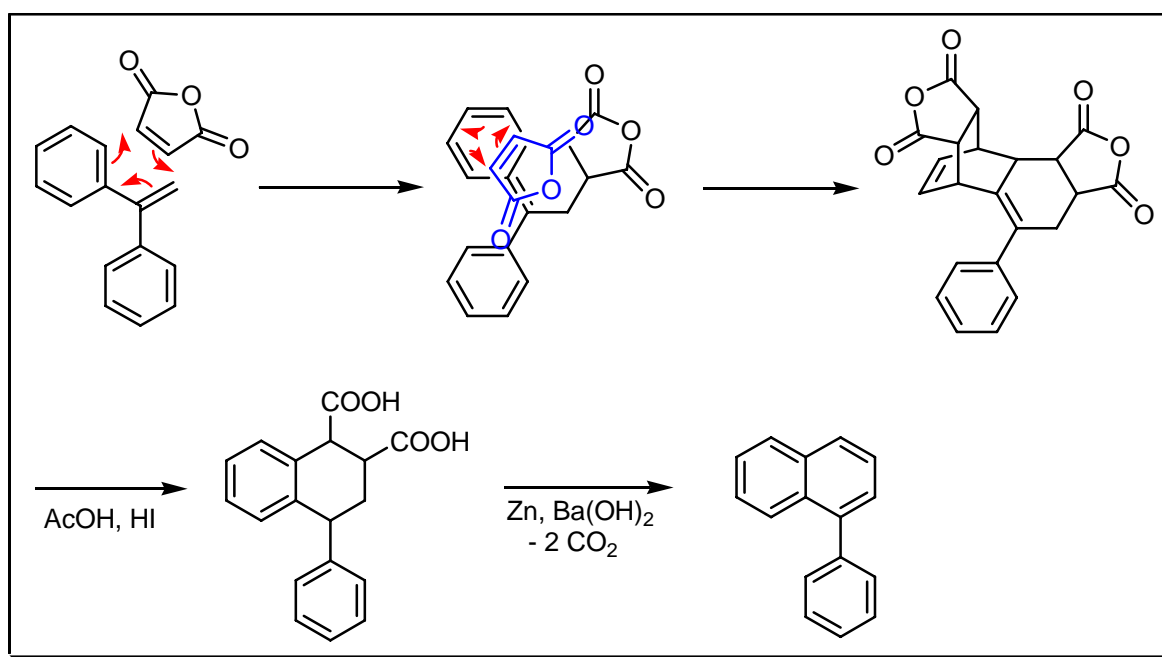
WUYTS SYNTHESIS · 1889

## WAGNER–JAUREGG ADDITION

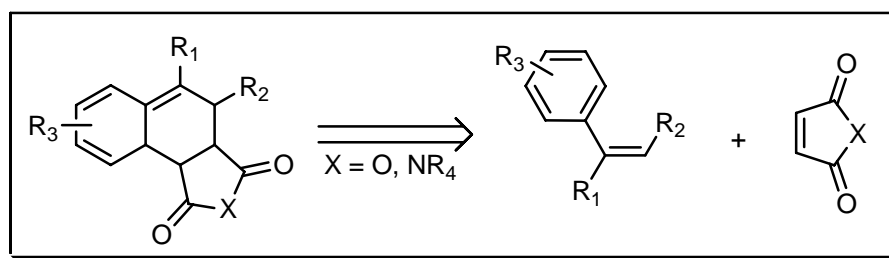
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The **Diels – Alder** reaction between an asymmetrical substituted styrene and maleic anhydride yields *bis*-adducts, which can be converted into aromatic ring systems. See also **Diels – Alder** reaction.

### REFERENCES :

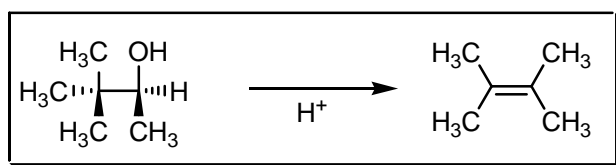
Org. React. : 4, 1

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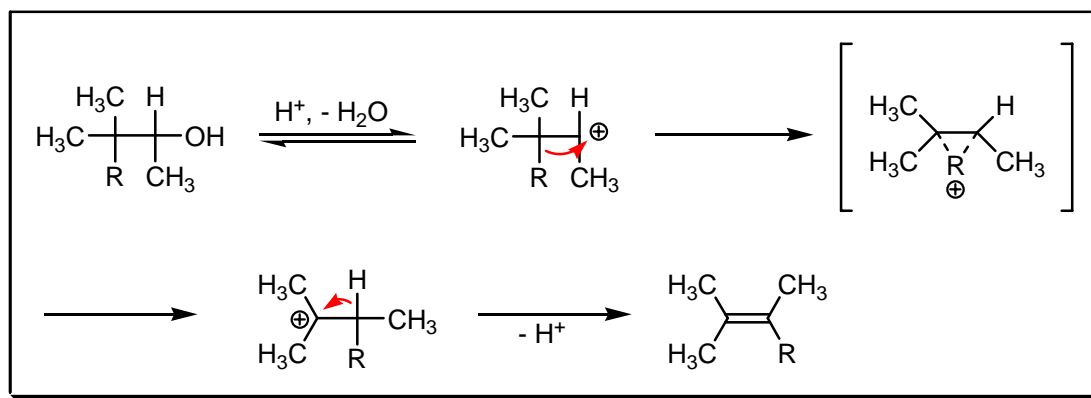
**COMMENTS :**

## WAGNER – MEERWEIN REARRANGEMENT

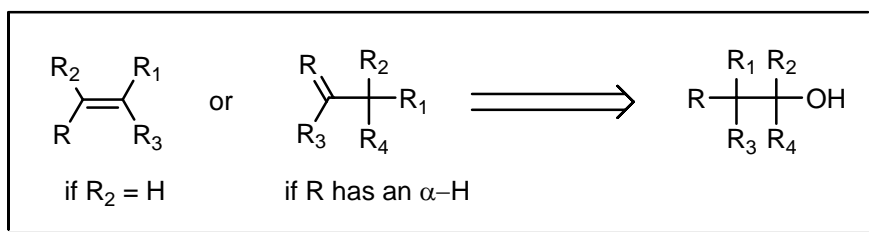
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

This is a retro-pinacolic rearrangement involving certain alkyl carbinols. These undergo heterolytic removal of an anion, or addition of a proton to form a carbonium ion, which suffers a 1,2-rearrangement to form a compound of greater stability. See also **von Baeyer – Villiger**, **Criegee**, **Demjanov** rearrangement, **Nametkin**, **von Ragué Schleyer** adamantisation and **Wallach** reactions.

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**March** : 1068

**Smith – March** : 1384, 1393

**Smith** : 1296

**Smith 2<sup>nd</sup>** : 892, 1069

**Houben – Weyl** : **E5**, 298, 316; **E19c**, 3, 72, 398; **E15**, 2524

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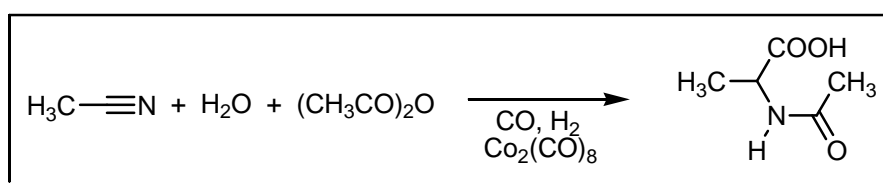
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## COMMENTS :

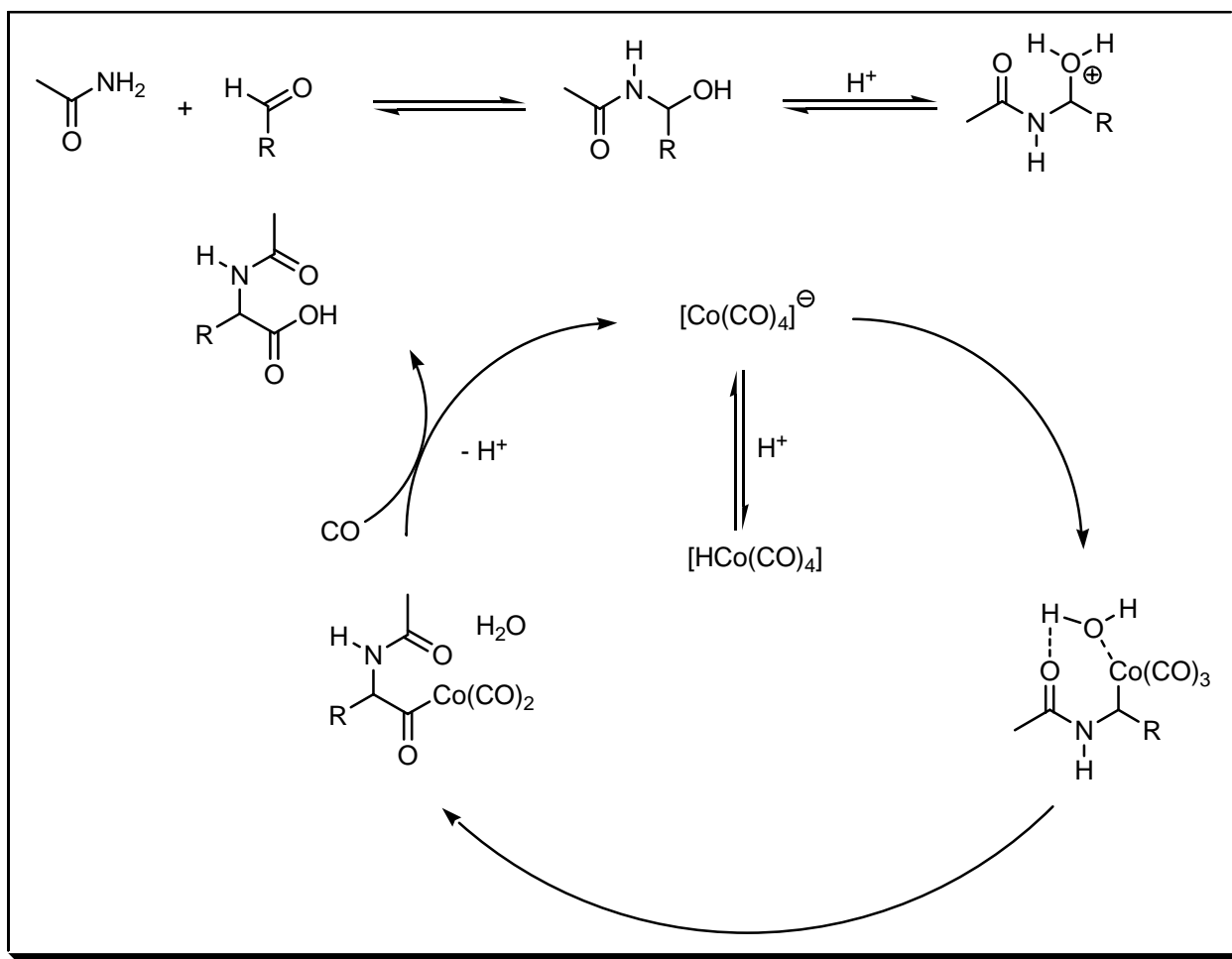
## WAKAMATSU SYNTHESIS

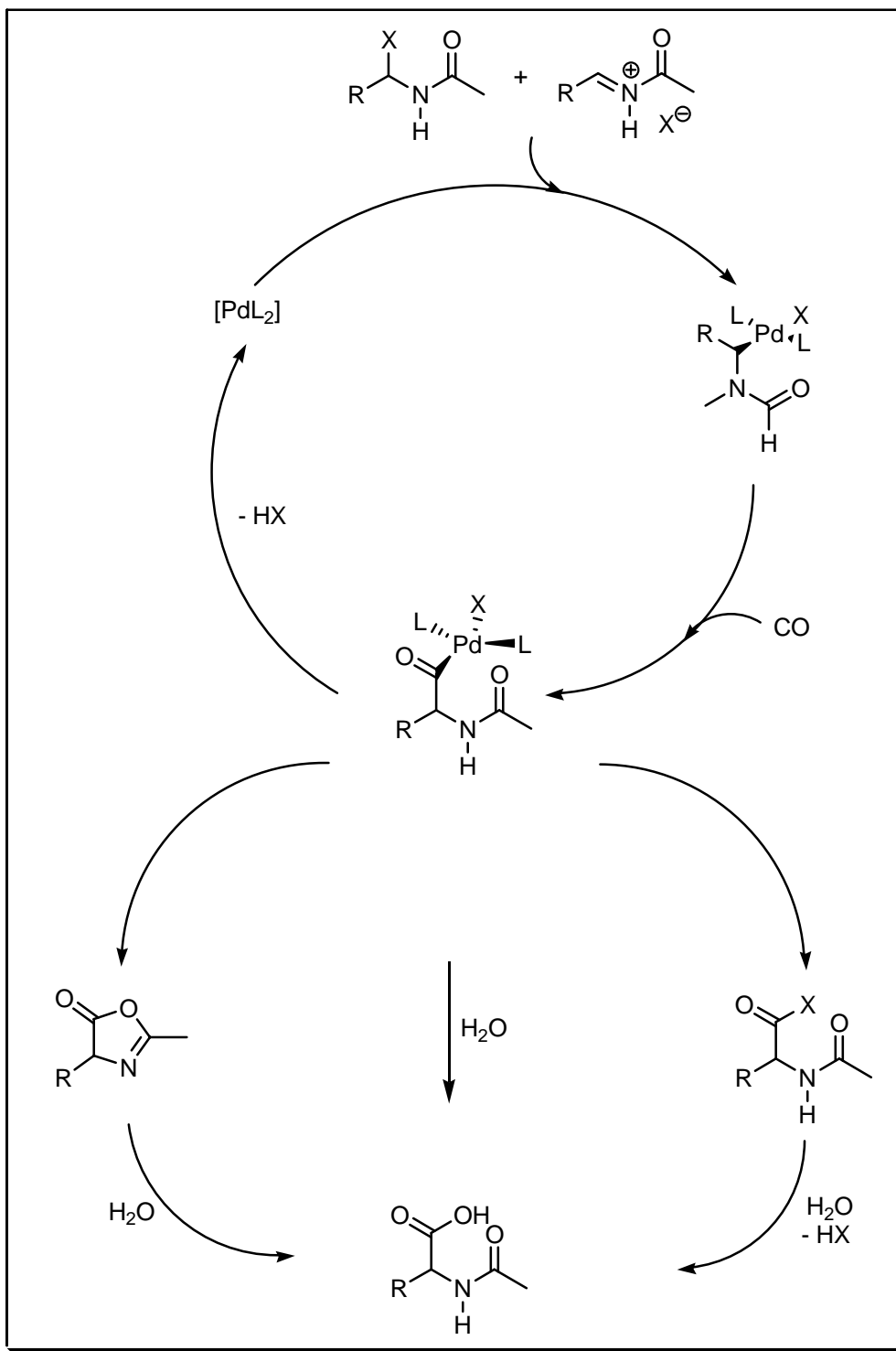
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### EXAMPLE :

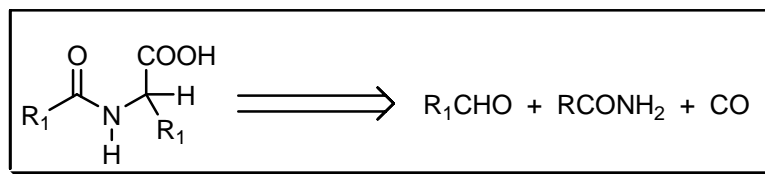


**MECHANISM :**





DISCONNECTION :



## NOTES :

Cobalt-catalysed amidocarbonylation is generally carried out at 70 – 160 °C with synthesis gas pressures of 50-200 bar in solvents such as dioxane, THF, DME, ethyl acetate, acetone or benzene.  $\text{Co}_2(\text{CO})_8$  is used in amounts of 1 – 5 mol%. Milder reactions conditions are used for the amidocarbonylation with a palladium catalyst. Temperatures of 70 – 130 °C and CO pressures of 10 – 60 bar are used. In this case the presence of halide ions are essential. For an excellent review on the subject see **Beller** and **Eckert**. See also **Arndtsen**, **Asinger**, **Biginelli**, **Mannich** and **Strecker** reactions.

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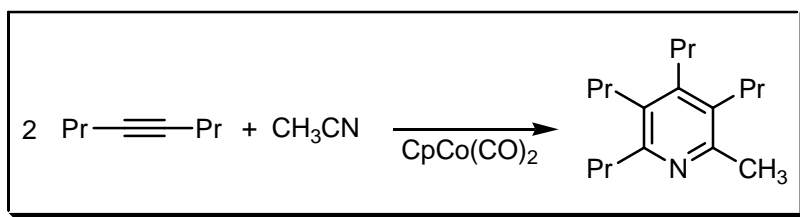
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## COMMENTS :

## WAKATSUKI – YAMAZAKI – BÖNNEMANN REACTION

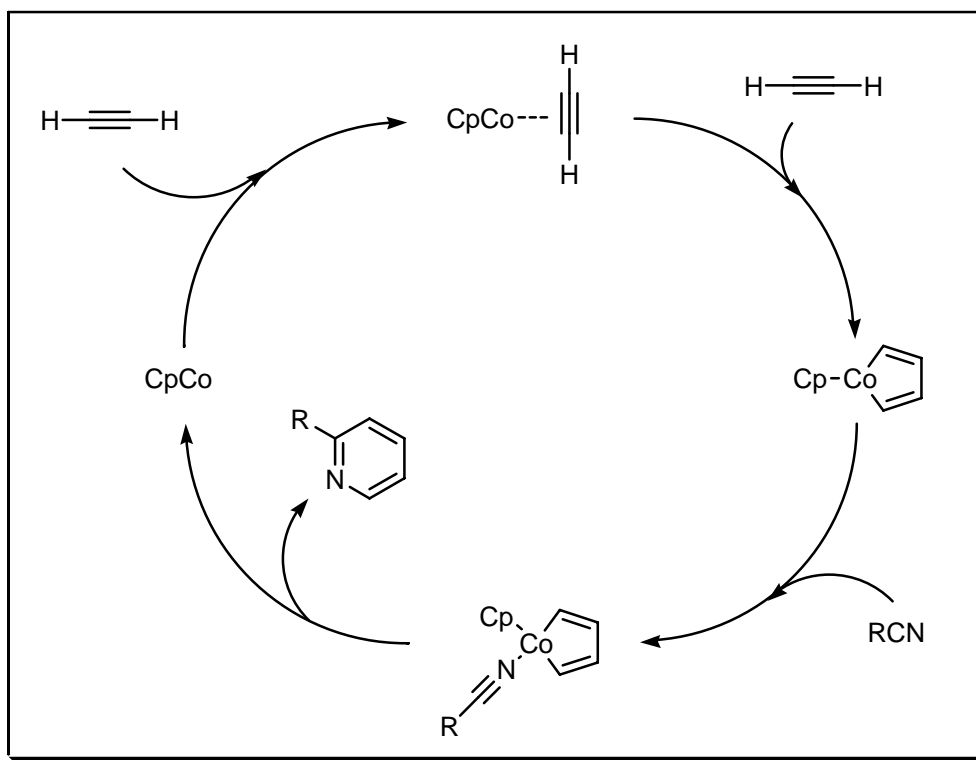
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### EXAMPLE :

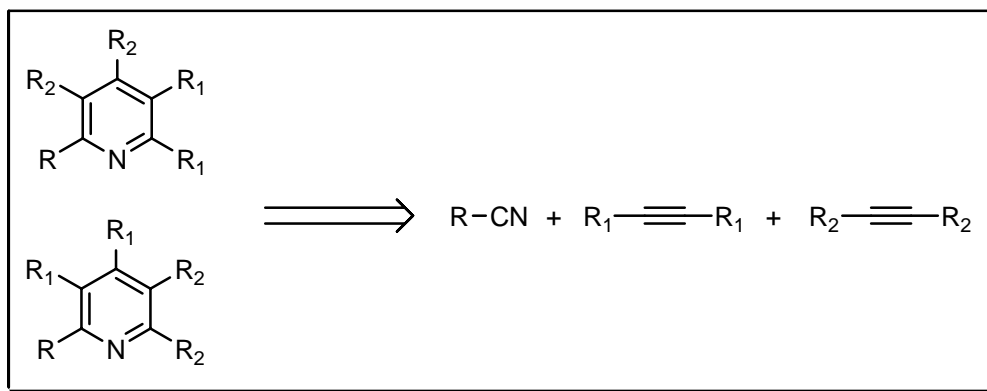




## MECHANISM :



## DISCONNECTION :



## NOTES :

Pyridine is obtained from two alkynes and a nitrile with cobalt complexes, with or without phosphane-modified cobalt-complexes. Although the method is very effective, mainly a mixture of two regio isomers will be obtained. A way around this is to react first one of the alkynes with the nitrile to give an azametallacyclopentadiene. This is reacted with the second alkyne. See also **Bohlmann – Rahtz**, **Chichibabin** pyridine, **Gattermann – Skita**, **Guareschi – Thorpe**, **Hantzsch – Beyer**, **von Meyer – Mohr**, **Petrenko – Kritschenko** and **Riehm** pyridine reactions.

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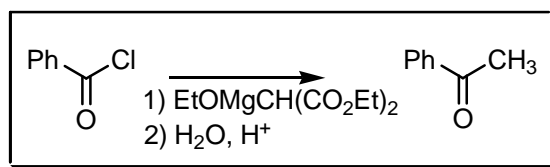
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**COMMENTS :**

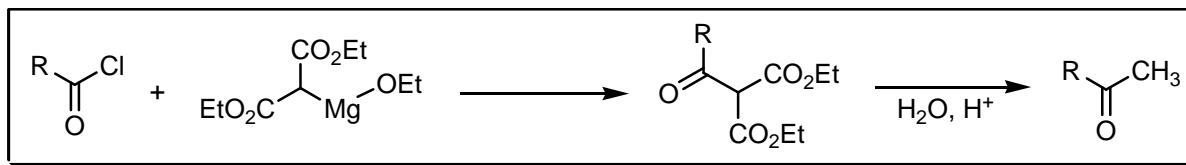
**WALKER – HAUSER SYNTHESIS**

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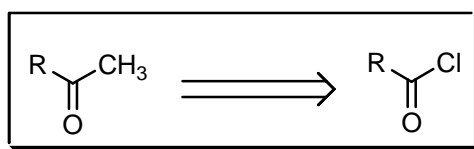
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

This synthesis involves the acylation of the sodium- or preferably the magnesium-ethoxy-derivative of diethyl malonate with the appropriate acid chloride followed by hydrolysis and decarboxylation of the two ester groups of the resulting diethyl acyl-malonate in the presence of acid.

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**REFERENCES :**

*Org. Synth.* : **30**, 70

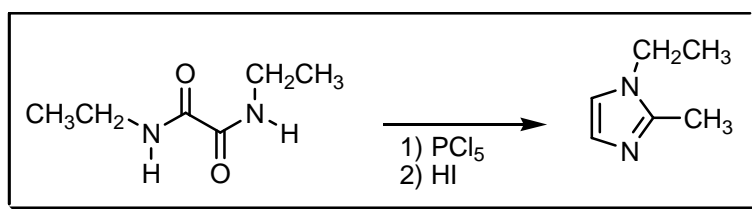
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H.G. Walker; C.R. Hauser, *J. Am. Chem. Soc.*, 1946, **68**, 1386.

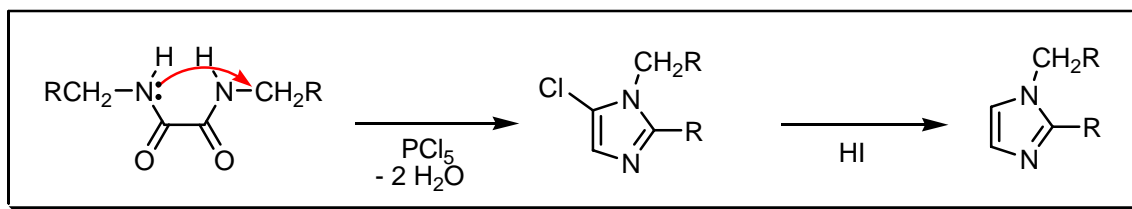
COMMENTS :

## WALLACH IMIDAZOLE SYNTHESIS

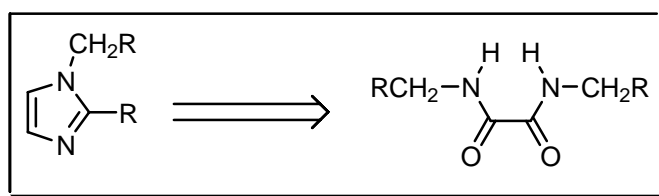
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The **Wallach** synthesis uses *N,N*-dialkyloxamides with phosphorous pentachloride to yield 5-chloro-*N,N*-alkylglyoxalines, which on treatment with hydriodic acid give the *N,N*-alkylimidazoles. See also **Akabori – Neuberg – Fischer**, **Brackeen**, **Bredereck**, **Debus – Radziszewski**, **Maquenne** and **Weidenhagen** reactions.

## REFERENCES :

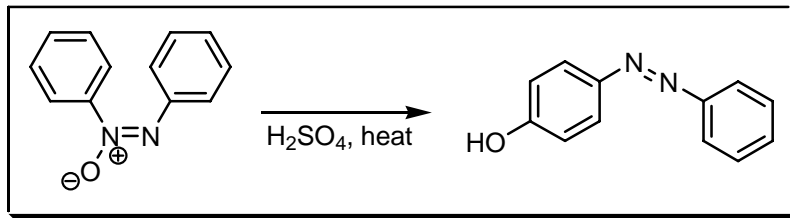
Houben – Weyl : E8c, 9, 13, 97

- 1) O. Wallach, *Liebigs Ann. Chem.*, 1877, **184**, 1.
- 2) O. Wallach; E. Schulze, *Ber. Dtsch. Chem. Ges.*, 1881, **14**, 420.
- 3) A. Mukherjee; S. Kumar; A.P. Bhaduri, *Indian J. Chem.*, 1989, **28B**, 1.
- 4) R.A. Egolf; N.D. Heindel, *J. Heterocycl. Chem.*, 1991, **28**, 577.
- 5) T. Benincori; E. Brenna; F. Sanniccolo, *J. Chem. Soc., Perkin Trans. 1*, 1993, 675.
- 6) D.J.K. Crawford; J.L. Maddocks; D.N. Jones; P. Szawlowski, *J. Med. Chem.*, 1996, **39**, 2690.

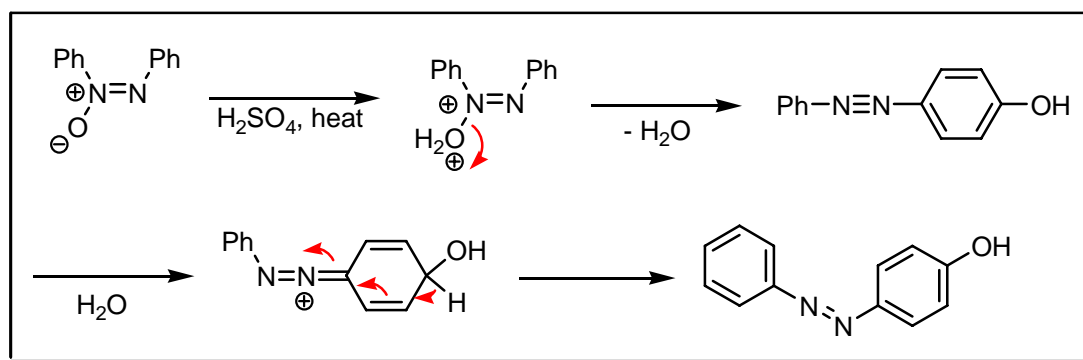
## COMMENTS :

## WALLACH REARRANGEMENT

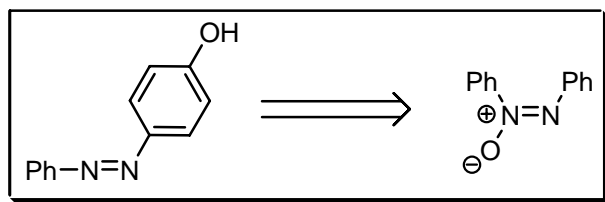
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



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## NOTES :

The acid-catalysed rearrangement of azoxybenzenes to *para*-hydroxyazobenzenes. *Ortho*-rearrangement may occur as a side reaction. The mechanism of this reaction has not been fully understood. There is also a photo-chemical **Wallach** rearrangement known affording an *ortho*-hydroxyazo compound.

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## REFERENCES :

**March** : 1155

**Smith – March** : 1464

**Houben – Weyl** : **E16d**, 121

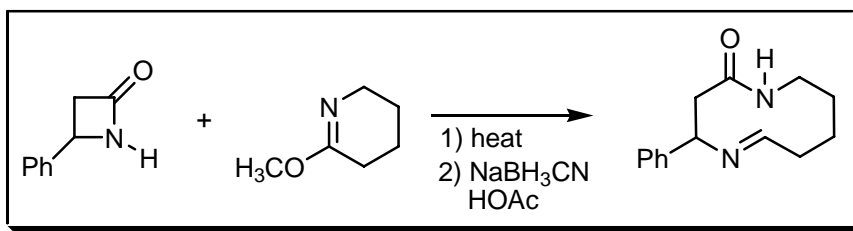
- 
- 1) O. Wallach; L. Belli, *Chem. Ber.*, 1880, **13**, 525.
  - 2) H.E. Bigelow, *Chem. Rev.*, 1931, **9**, 117.
  - 3) C.S. Hahn; H.H. Jaffé, *J. Am. Chem. Soc.*, 1962, **84**, 946.
  - 4) H. Kolck, *Z. Chem.*, 1989, **29**, 18.
  - 5) E. Buncel; K.S. Cheon, *J. Chem. Soc., Perkin Trans. 2*, 1998, 1241.
  - 6) G.R. Hodges; J.R.L. Smith; J. Oakes, *J. Chem. Soc., Perkin Trans. 2*, 1999, 1943.
  - 7) A. Lalitha; K. Pitchumani; C. Srinivasan, *J. Mol. Catal. A: Chem.*, 2000, **160**, 429.

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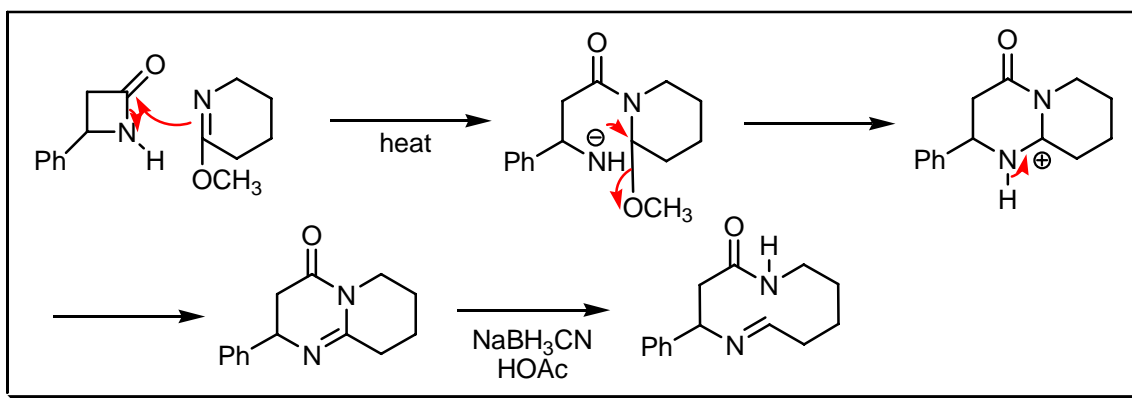
## COMMENTS :

# WASSERMANN – BORMANN MACROCYCLIC LACTAM SYNTHESIS

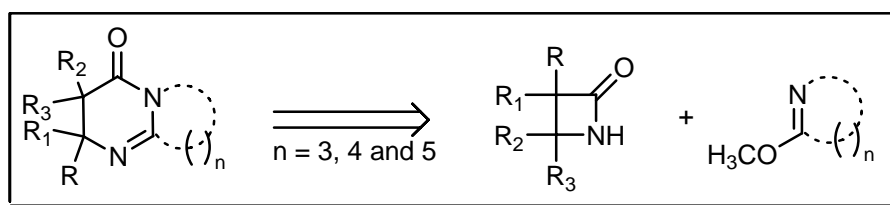
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The ring-expansion sequence of lactams by reaction with cyclic imino ethers followed by reductive ring-opening to a macrocyclic lactam.

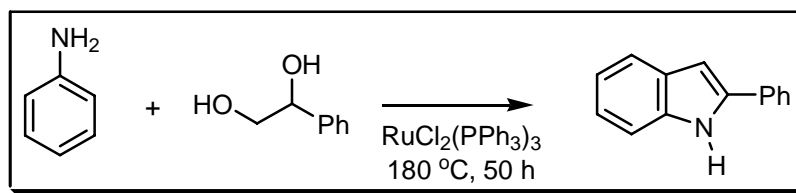
## REFERENCES :

- 1) D. Bormann, *Chem. Ber.*, 1970, **103**, 1797.
- 2) H.H. Wasserman; H. Matsuyama, *J. Am. Chem. Soc.*, 1981, **103**, 461.
- 3) H.H. Wasserman; R.P. Robinson, *Tetrahedron Lett.*, 1983, **24**, 3669.

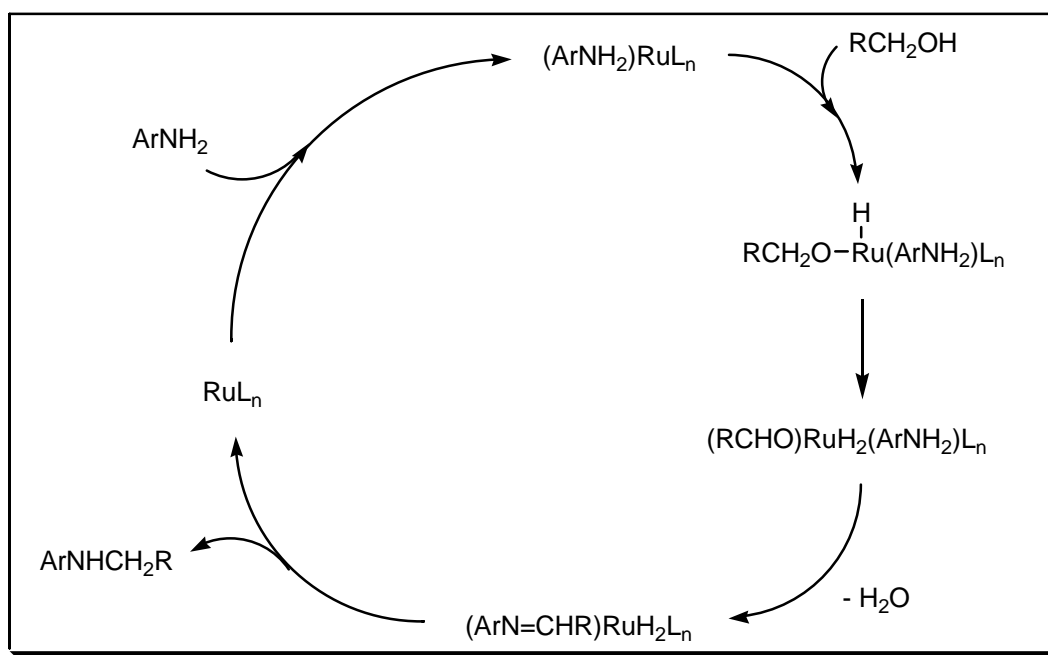
COMMENTS :

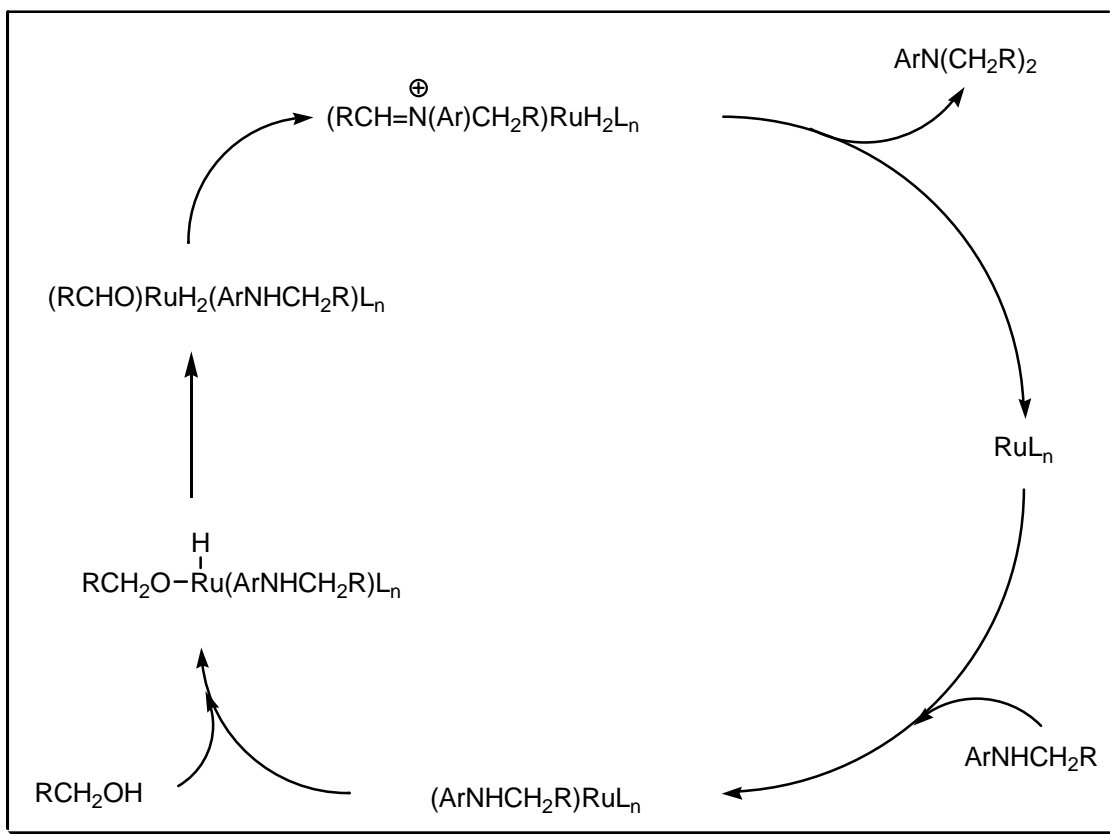
## WATANABE HETEROCYCLISATION

EXAMPLE :

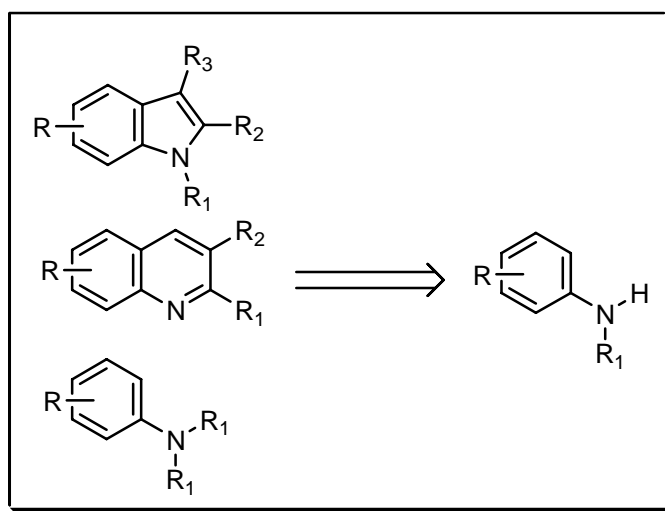


MECHANISM :





**DISCONNECTION :**



**NOTES :**

The ruthenium-catalysed *N*-alkylation or *N*-benzylation of aminoarenes with alcohols. Quinoline, indole and its derivatives can be prepared.



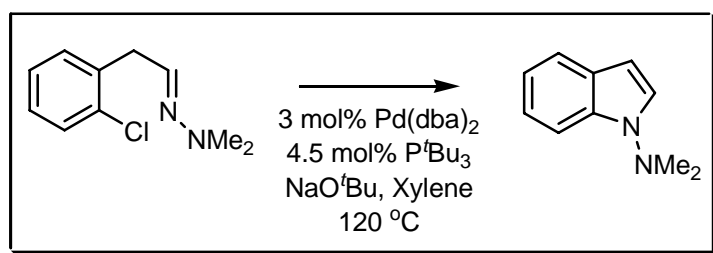
## REFERENCES :

- 1) Y. Watanabe; Y. Tsuji; Y. Ohsugi; J. Shida, *Bull. Chem. Soc. Jpn.*, 1983, **56**, 2452.
- 2) Y. Watanabe; Y. Tsuji; J. Shida, *Bull. Chem. Soc. Jpn.*, 1984, **57**, 435.
- 3) Y. Watanabe; Y. Tsuji; H. Ige; Y. Ohsugi; T. Ohta, *J. Org. Chem.*, 1984, **49**, 3359.
- 4) Y. Tsuji; K.-T. Huh; Y. Ohsugi; Y. Watanabe, *J. Org. Chem.*, 1985, **50**, 1365.
- 5) Y. Tsuji; K.-T. Huh; Y. Watanabe, *J. Org. Chem.*, 1987, **52**, 1673.

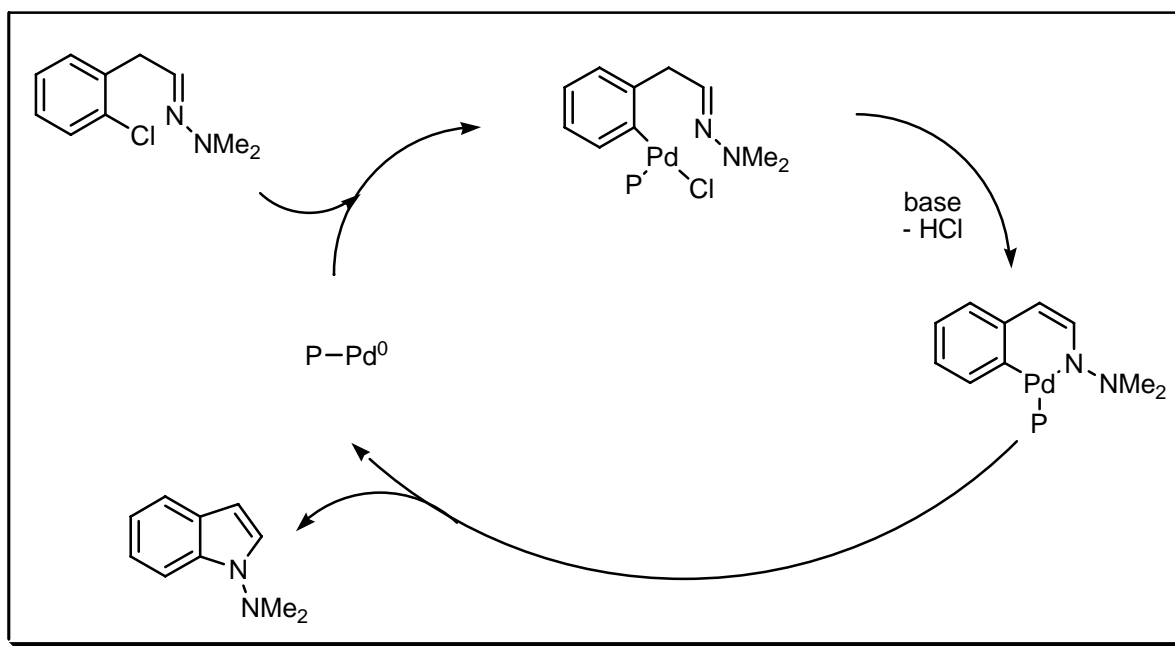
## COMMENTS :

## WATANABE INDOLE SYNTHESIS

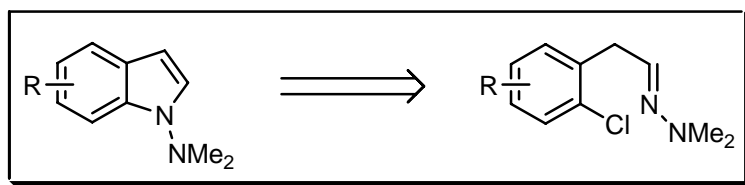
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

A palladium-catalysed synthesis of 1-amino indoles. It is assumed that the reaction proceeds *via* the mechanism shown. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

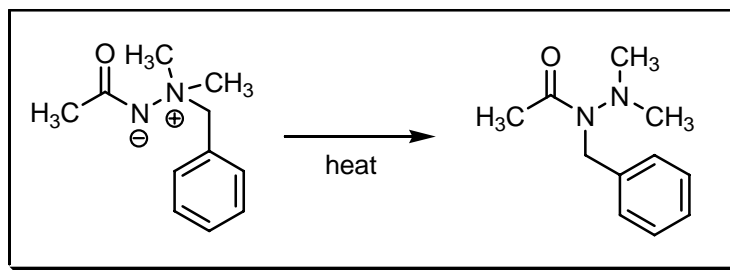
## REFERENCES :

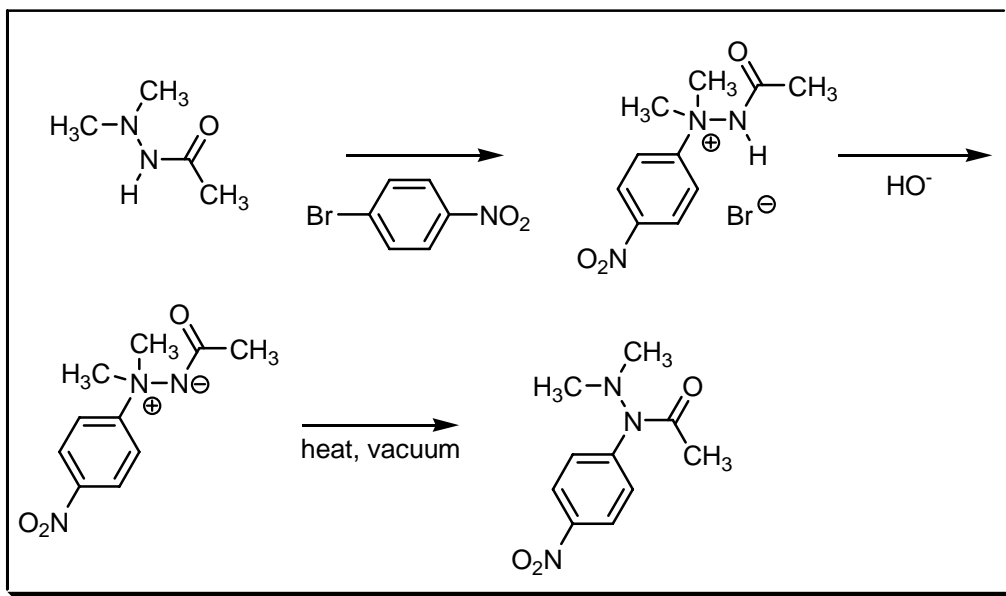
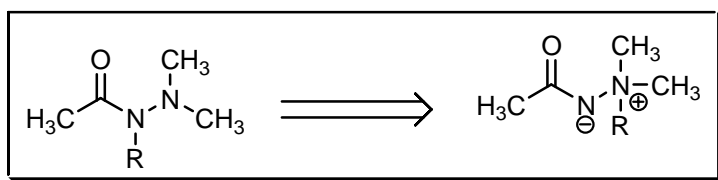
M. Watanabe; T. Yamamoto; M. Nishiyama, *Angew. Chem., Int. Ed.*, 2000, **39**, 2501.

## COMMENTS :

## WAWZONEK – YEAKEY REARRANGEMENT

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

Aminimides with benzyl groups rearrange in a similar fashion to that observed with the corresponding sulfilimines.

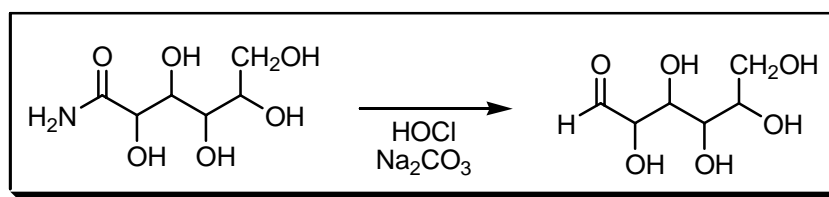
**REFERENCES :**

- 1) A.S.F. Ash; F. Challenger, *J. Chem. Soc.*, 1952, 2792.
- 2) S. Wawzonek; E. Yeakey, *J. Am. Chem. Soc.*, 1960, **82**, 5718.
- 3) S.-B. Lee; H. Jung; K.W. Lee, *Bull. Korean Chem. Soc.*, 1996, **17**, 362.

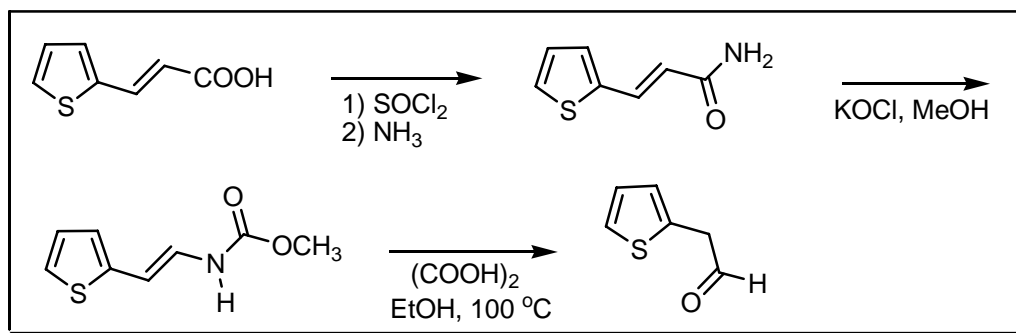
**COMMENTS :**

## WEERMAN DEGRADATION

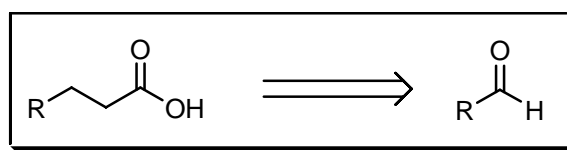
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The synthesis of lower homologue aldehydes from  $\alpha,\beta$ -unsaturated carboxamides (**Hofmann** degradation). Initially used for the degradation of aldonic acid amides. Later expanded to ethylenic amides. See also **Hofmann** degradation.

### REFERENCES :

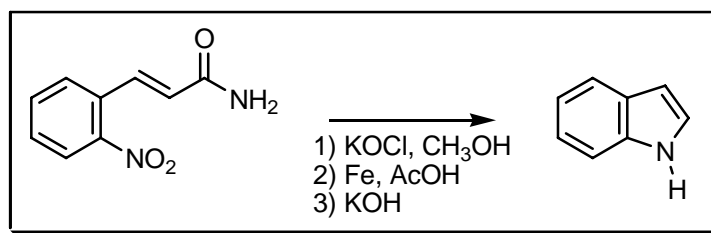
**Org. React.** : **3**, 267

- 1) R.A. Weerman, *Liebigs Ann. Chem.*, 1913, **401**, 1.
- 2) R.A. Weerman, *Recl. Trav. Chim. Pays-Bas*, 1918, **37**, 1.
- 3) C.D. Mason; F.F. Nord, *J. Org. Chem.*, 1951, **16**, 1869.
- 4) P.S. O'Colla; J.J. O'Donnell; J.A. Mulloy, *Proc. Chem. Soc.*, 1961, 300.

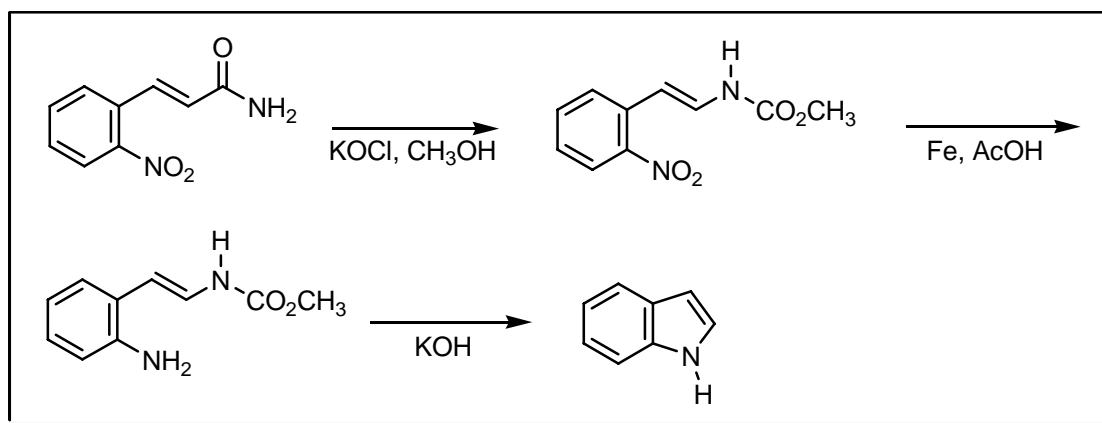
COMMENTS :

WEERMAN SYNTHESIS OF INDOLE

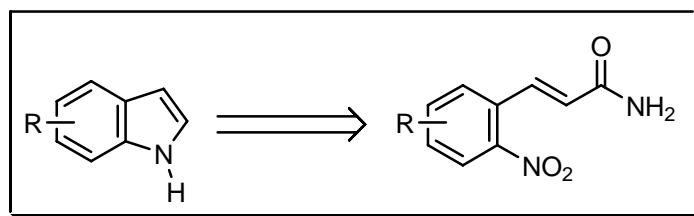
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

*o*-Nitrocinnamamide is converted by methanol and potassium hypochlorite into the methyl carbamate, which is reduced by iron in acetic acid to the corresponding *o*-amino compound. The latter is cyclised to the indole by heating with alkali. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Hofmann** degradation,

Inanaga, Iwao, Japp – Murray, Julia, Kihara, Larock indole, Leimgruber – Batcho, Lipp, Madelung indole, Magnus, Martin, Montecvecchi, Mori – Ban, Murphy, Naito, Natsume, Nenitzescu indole, Piloty – Robinson, Pschorr – Hoppe, Reissert indole, Saegusa indole, Schmid, Smith, Sugawara indole, Sundberg, Thiele – Dimroth, Thyagarajan, Watanabe heterocyclisation, Watanabe indole, Weerman, Wender, Widman, Yamamoto indole-1, Yamamoto indole-2 and Yurovskaya reactions.

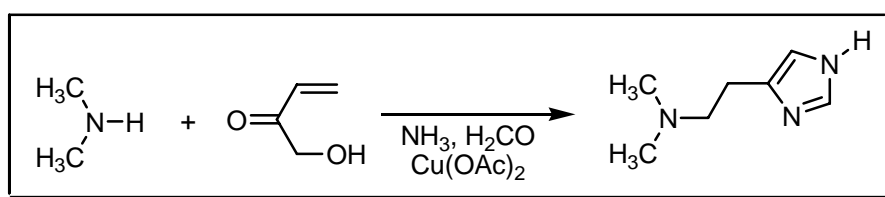
## REFERENCES :

- 1) R.A. Weerman, *Recl. Trav. Chim. Pays-Bas*, 1910, **29**, 18.
- 2) R.A. Weerman, *Liebigs Ann. Chem.*, 1913, **401**, 1.

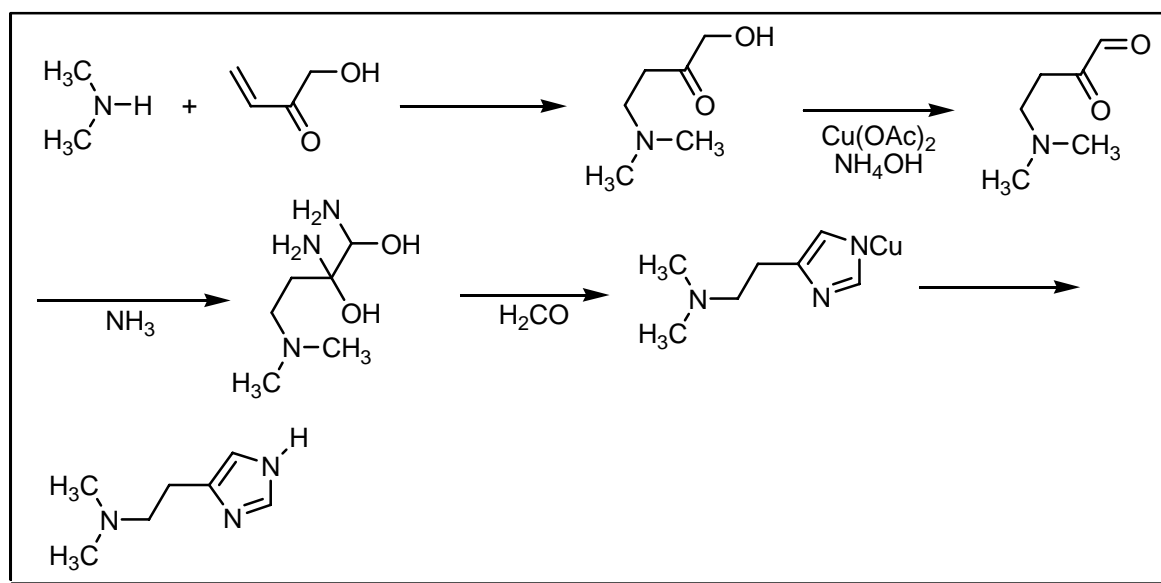
## COMMENTS :

## WEIDENHAGEN IMIDAZOLE SYNTHESIS

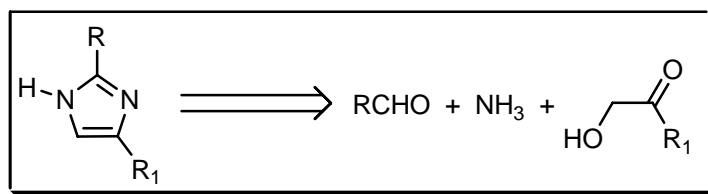
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

This is a modification of the **Debus – Radziszewski** reaction. See also **Akabori – Neuberg – Fischer**, **Brackeen**, **Bredereck**, **Debus – Radziszewski**, **Maquenne** and **Wallach** imidazole reactions.

## REFERENCES :

Houben – Weyl : **E8c**, 9, 13, 97

Org. Syn. : **24**, 64

Org. Syn. Coll. Vol. : **3**, 460

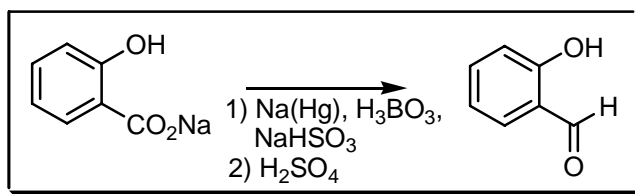
1) R. Weidenhagen, R. Herrmann, *Ber. Dtsch. Chem. Ges.*, 1935, **68**, 1953.

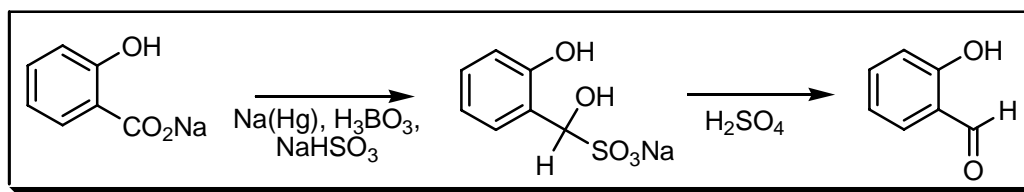
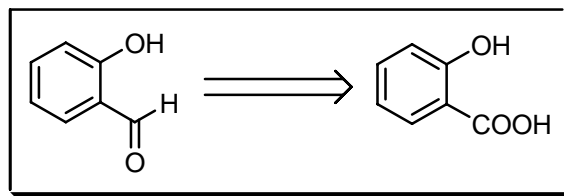
2) C.F. Huebner, *J. Am. Chem. Soc.*, 1951, **73**, 4667.

## COMMENTS :

## WEIL SYNTHESIS OF ARYL ALDEHYDES

### EXAMPLE :

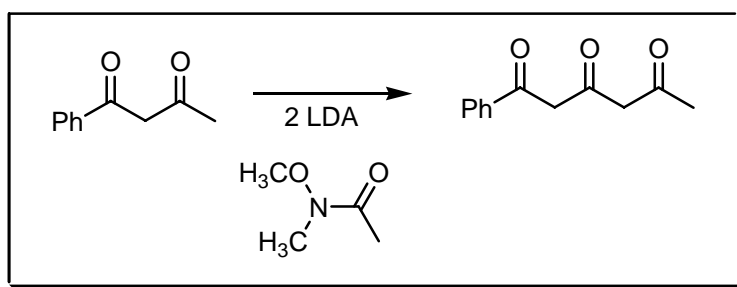


**MECHANISM :****DISCONNECTION :****NOTES :**

The sodium salt of an aromatic acid is reduced by sodium amalgam in the presence of sodium hydrogen sulfite and boric acid to yield the bisulfite addition compound, which on boiling with sulfuric acid is decomposed to araldehyde. The reaction mainly applies to *o*-hydroxyaldehydes.

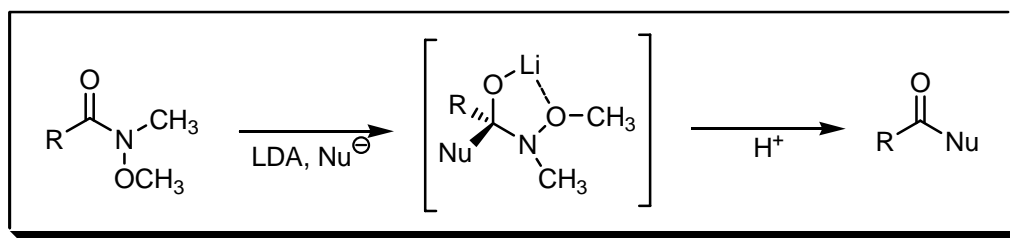
**REFERENCES :**

- 1) H. Weil, *Ber. Dtsch. Chem. Ges.*, 1908, **41**, 4147.
- 2) H. Weil; H. Ostermeier, *Ber. Dtsch. Chem. Ges.*, 1921, **54**, 3217.

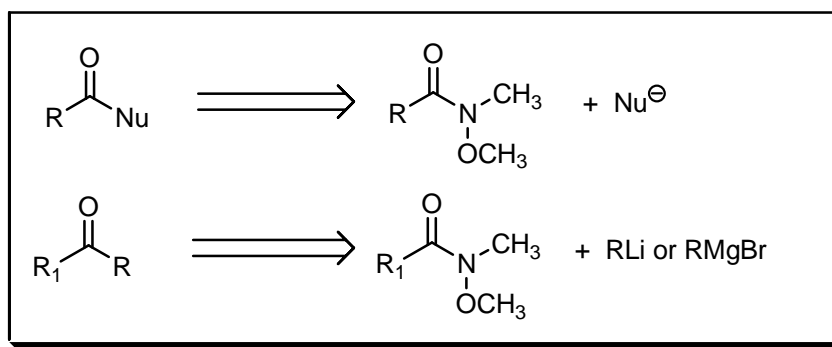
**COMMENTS :****WEINREB ACYLATION****EXAMPLE :**



### MECHANISM :



### DISCONNECTION :



### NOTES :

**Weinreb** amides are acylation reagents. The formed intermediate is stable until it is protonated upon aqueous work-up. See also **Chattaway** acylation, **Einhorn** acylation, **Galat – Elion**, **Lumière – Barbier** and **Schotten – Baumann** reactions.

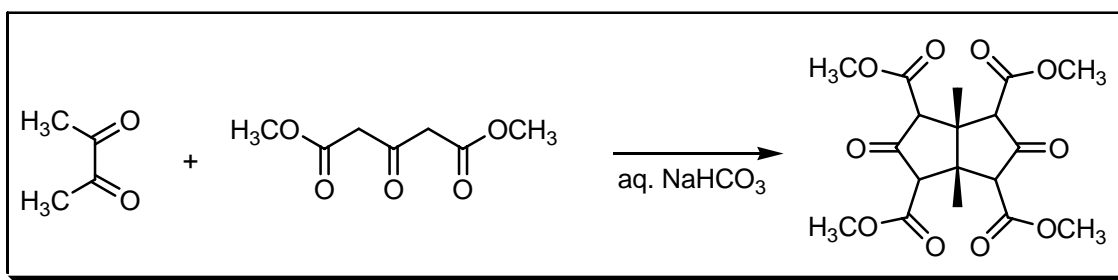
### REFERENCES :

- 1) S. Nahm; S.M. Weinreb, *Tetrahedron Lett.*, 1981, **22**, 3815.
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- 3) M. Sibi, *Org. Prep. Proced. Int.*, 1993, **25**, 15.
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- 7) J. Ruiz; N. Sotomayor; E. Lete, *Org. Lett.*, 2003, **5**, 1115.

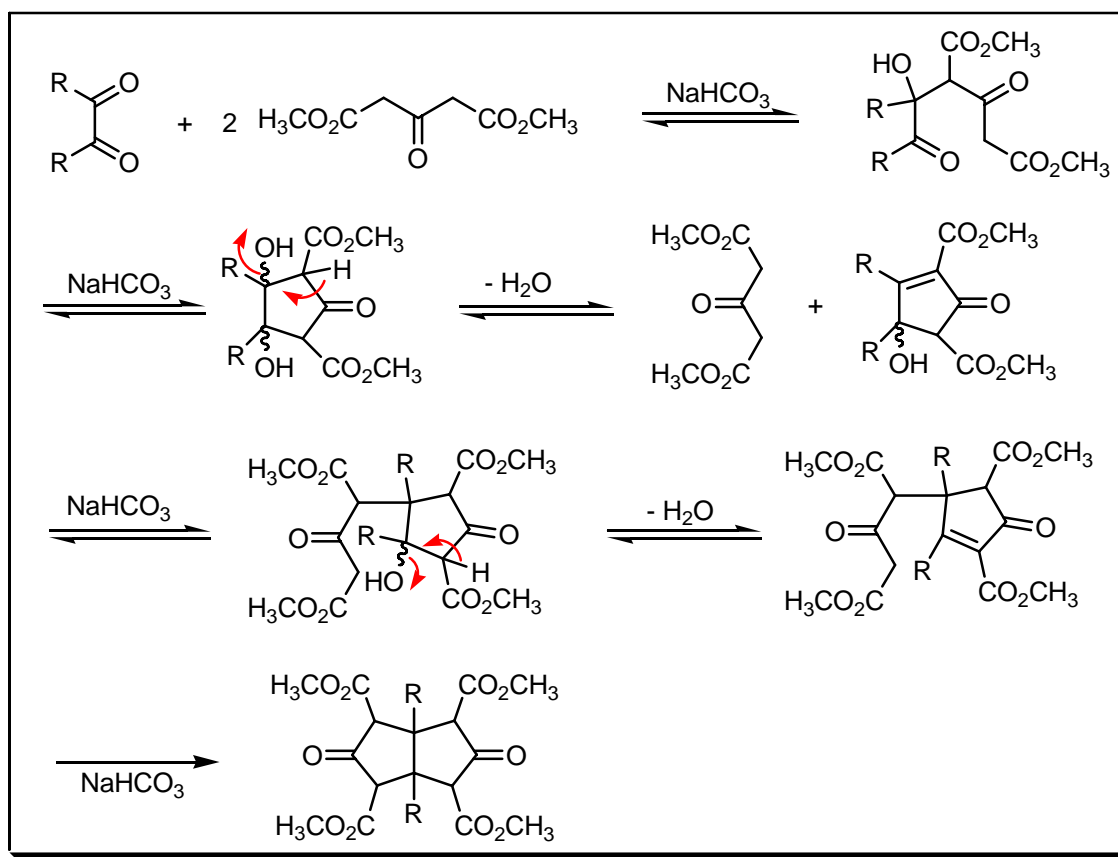
### COMMENTS :

## WEISS ANNULATION

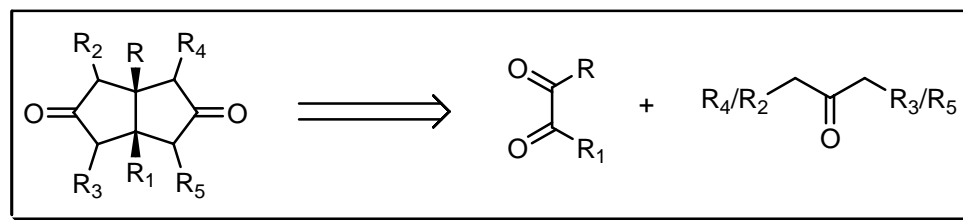
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The synthesis of fused cyclopentanones (bicyclo[3.3.0]octadiones) or of propellanes from  $\alpha$ -dicarbonyl compounds via the double aldol condensation with  $\beta$ -ketoesters.

## REFERENCES :

Org. Synth. : 64, 27

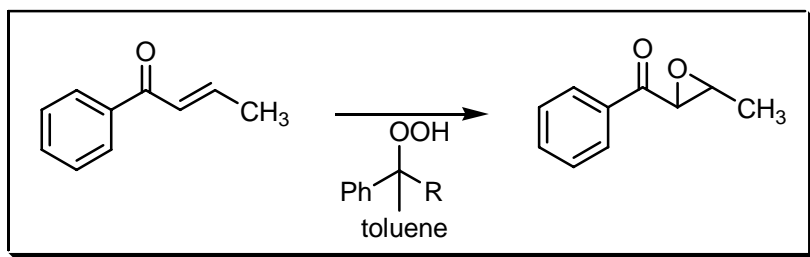
Org. Synth. Coll. Vol. : 7, 50

- 1) U. Weiss; J.M. Edwards, *Tetrahedron Lett.*, 1968, **9**, 4885.
- 2) G. Kubiak; J.M. Cook, *Tetrahedron Lett.*, 1985, **26**, 2163.
- 3) A.K. Gupta; X. Fu; J.P. Snyder; J.M. Cook, *Tetrahedron*, 1991, **47**, 3665.
- 4) X. Fu; J.M. Cook, *Aldrichimica Acta*, 1992, **25**, 43.
- 5) R.V. Williams; V.R. Gadgil; A. Vij; J.M. Cook; G. Kubiak; Q. Huang, *J. Chem. Soc., Perkin Trans. 1*, 1997, 1425.

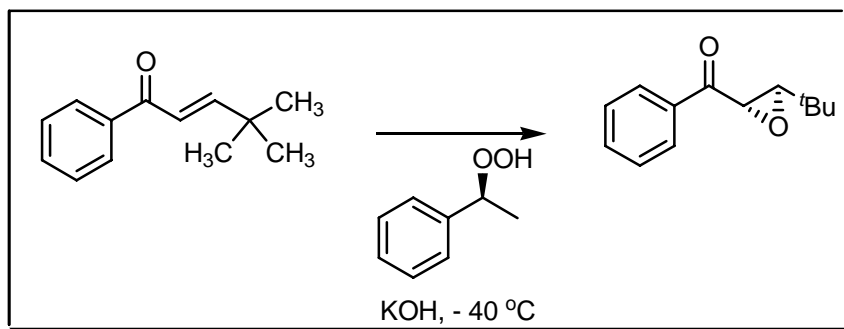
## COMMENTS :

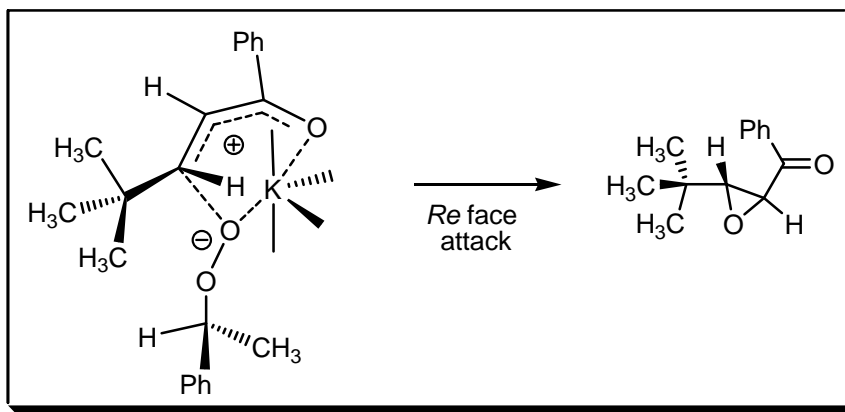
## WEITZ – SCHEFFER REACTION

### EXAMPLE :

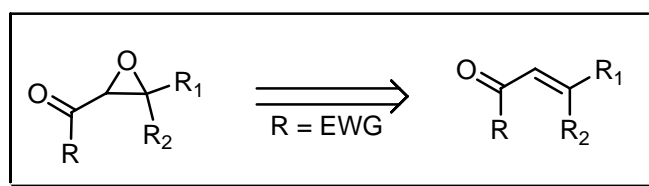


### MECHANISM :





#### DISCONNECTION :



#### NOTES :

The epoxidation of electron-deficient olefins like  $\alpha,\beta$ -enones with hydroperoxides. The asymmetric version of this reaction has gained considerable attention over the last few years using optically active hydroperoxide and metal ions. See also **Buchner – Curtius – Schlotterbeck**, **Corey – Chaykovsky**, **Jacobsen – Katsuki**, **Juliá – Colonna**, **Katsuki – Sharpless**, **Mukaiyama – Yamada**, **Prileschajew** and **Shi** reactions.

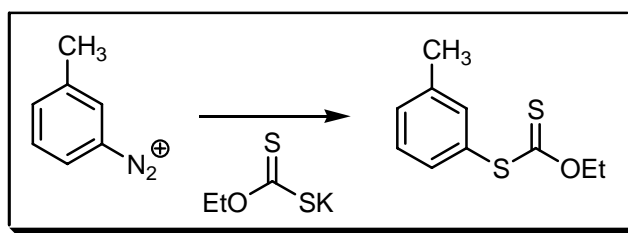
#### REFERENCES :

- 1) E. Weitz; A. Scheffer, *Ber. Dtsch. Chem. Ges.*, 1921, **54**, 2327.
- 2) H. Pluim; H. Wynberg, *J. Org. Chem.*, 1980, **45**, 2498.
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- 4) E.J. Corey; F.-Y. Zhang, *Org. Lett.*, 1999, **1**, 1287.
- 5) W. Adam; P. Bheema Rao; H.-G. Degen; C.R. Saha-Möller, *J. Am. Chem. Soc.*, 2000, **122**, 5654.
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- 7) W. Adam; P. Bheema Rao; H.-G. Degen; C.R. Saha-Möller, *Tetrahedron: Asymmetry*, 2001, **12**, 121.
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- 9) W. Adam; P. Bheema Rao; H.-G. Degen; A. Levai; T. Patonay; C.R. Saha-Möller, *J. Org. Chem.*, 2002, **67**, 259.
- 10) D.R. Kelly; E. Caroff; R.W. Flood; W. Heal; S.M. Roberts, *Chem. Commun.*, 2004, 2016.

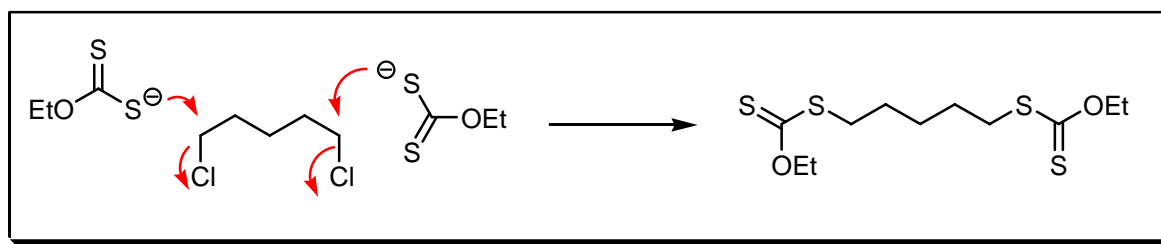
#### COMMENTS :

## WELDE SYNTHESIS OF DIXANTHATES

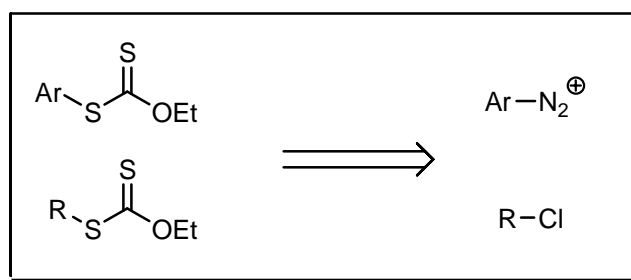
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Dixanthates are obtained by the action of alkali xanthate on alkyl dihalides in ethanol at temperatures of 20 – 50 °C. Similar reaction is possible on diazonium salts.

### REFERENCES :

Org. React. : 12, 2

Org. Synth. : 27, 81; 72, 265

Org. Synth. Coll. Vol. : 3, 809; 9, 72

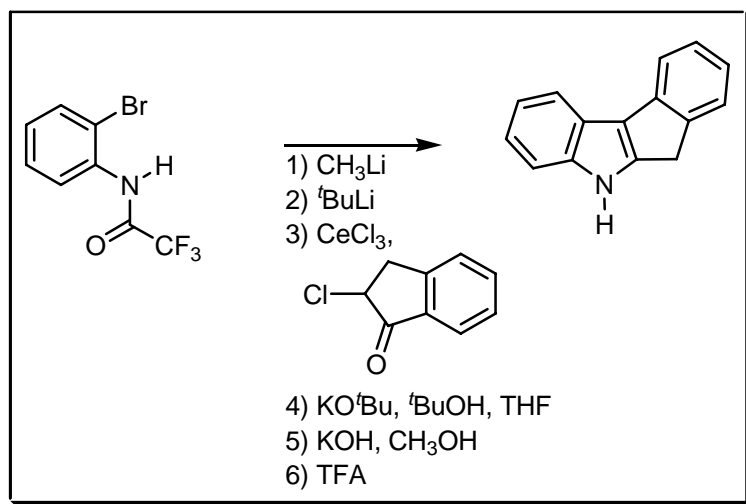
- 1) H. Welde, *J. Prakt. Chem.*, 1877, **15**, 43.
- 2) J. Leuckart, *J. Prakt. Chem.*, 1890, **41**, 179.
- 3) Ed. Bourgeois, *Recl. Trav. Chim. Pays-Bas*, 1899, **18**, 426.
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COMMENTS :

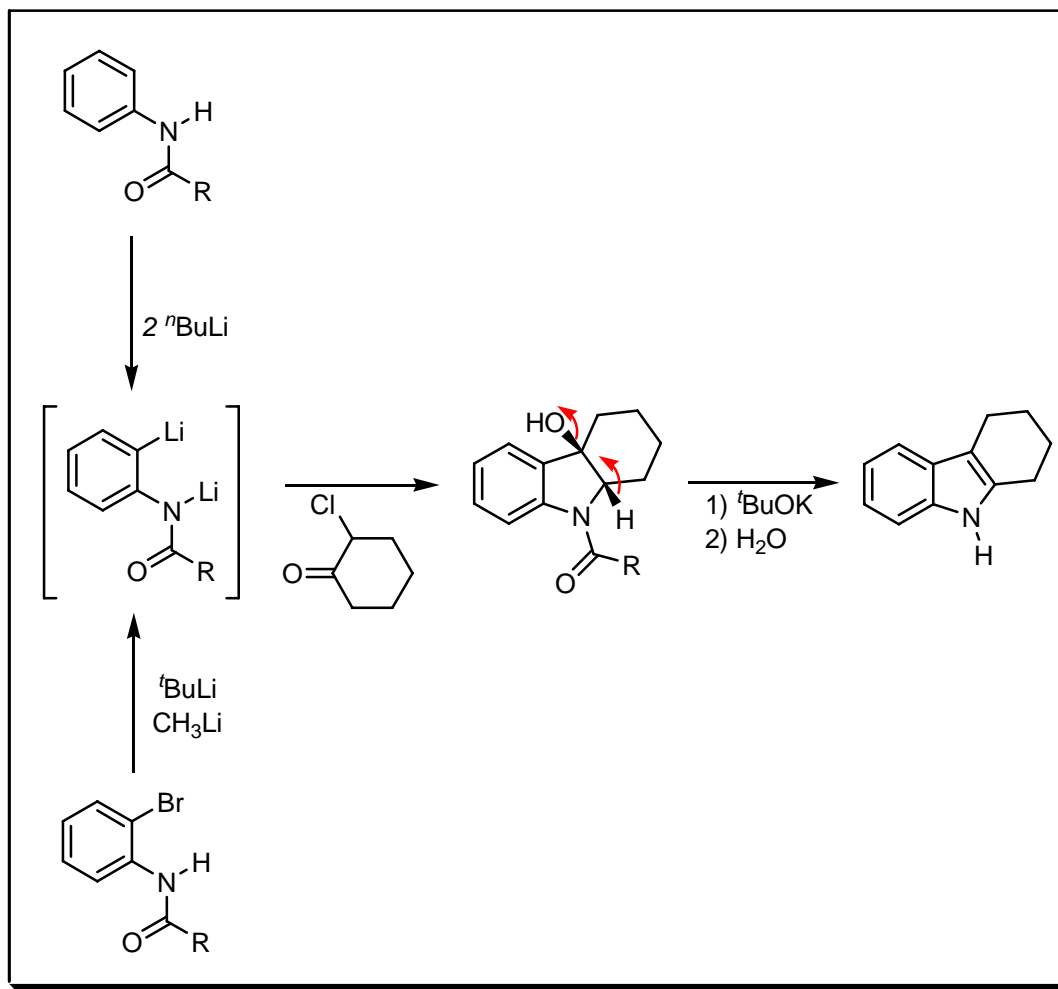
## WENDER INDOLE SYNTHESIS

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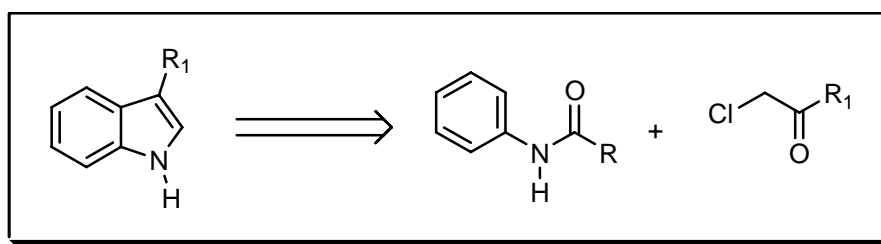
EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

This reaction starts with the *ortho*-lithiation of *N*-phenylamides. The formed dianion is reacted with  $\alpha$ -haloketones, ring-closure followed by dehydration will give the indole. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Widman**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

## REFERENCES :

- 1) P.A. Wender; A.W. White, *Tetrahedron*, 1983, **39**, 3767.
- 2) P. Hewawasam; N.A. Meanwell, *Tetrahedron Lett.*, 1994, **35**, 7303.
- 3) K. Smith; G.A. El-Hiti; G.J. Pritchard; A. Hamilton, *J. Chem. Soc., Perkin Trans. 1*, 1999, 2299.
- 4) K. Smith; G.A. El-Hiti; A.P. Shukla, *J. Chem. Soc., Perkin Trans. 1*, 1999, 2305.
- 5) K. Smith; G.A. El-Hiti; A.C. Hawes, *Synlett*, 1999, 945.

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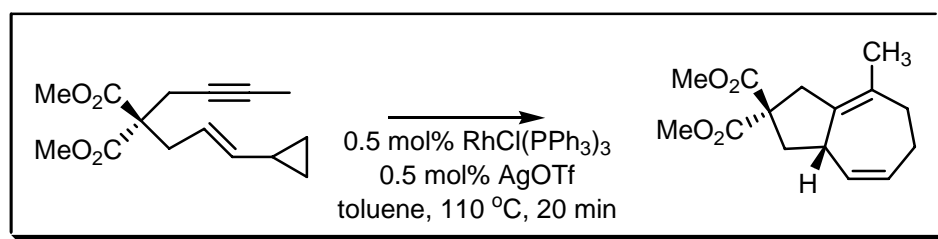
## COMMENTS :

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## WENDER CYCLOHEPTENE SYNTHESIS

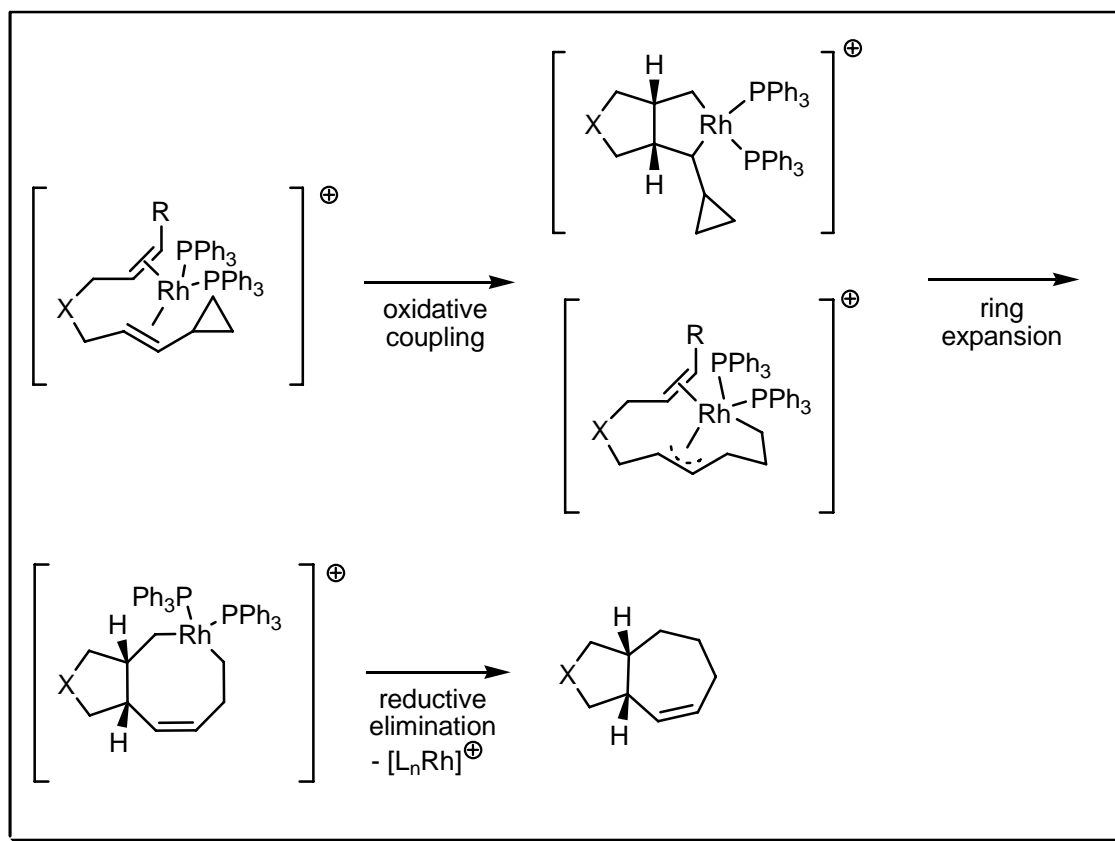
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### EXAMPLE :

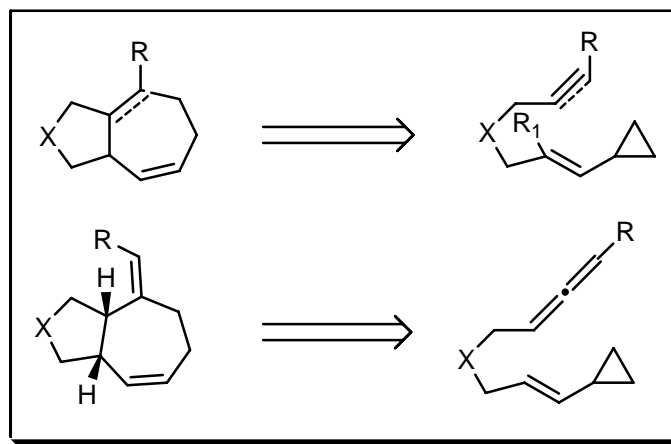




## MECHANISM :



## DISCONNECTION :



## NOTES :

The rhodium-catalysed (AgOTf, modified **Wilkinson's** catalyst or [RhCl(CO)<sub>2</sub>]<sub>2</sub>, AgOTf) *inter*- and *intramolecular* [5+2]-cycloaddition of cyclopropanes with alkynes or alkenes to afford cycloheptenes (*cis*-fused product). Vinylcyclopropanes behave like dienes because of significant p-orbital character in the strained  $\sigma$ -bond.

## REFERENCES :

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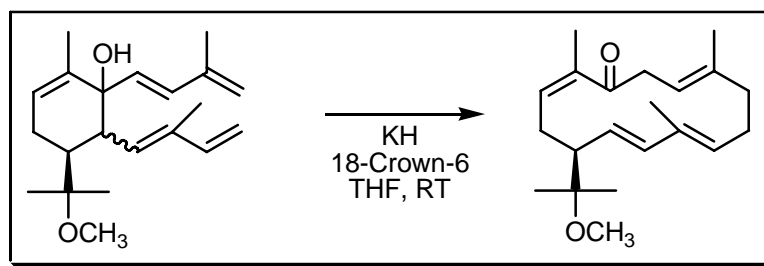
**COMMENTS :**

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**WENDER REACTION**

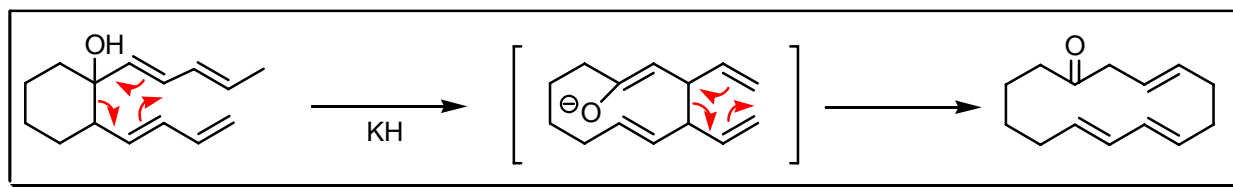
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**EXAMPLE :**



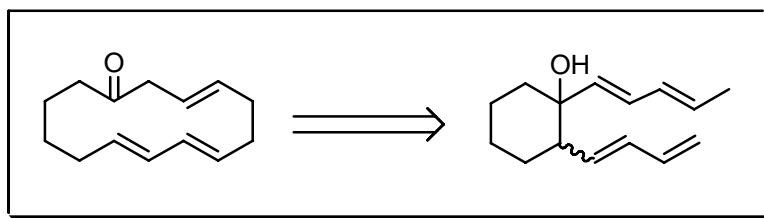
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**MECHANISM :**



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**DISCONNECTION :**



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**NOTES :**

The anionic oxy-**Cope** rearrangement is followed by a second **Cope** rearrangement. It is argued that a [5,5]-sigmatropic rearrangement directly leads to the 14-membered ring product. See also **Cope** rearrangement.

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## REFERENCES :

Smith : 1237

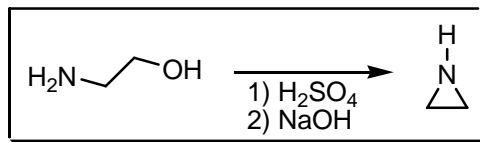
Smith 2<sup>nd</sup> : 1020

- 
- 1) P.A. Wender; S.McN. Sieburth, *Tetrahedron Lett.*, 1981, **22**, 2471.
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  - 5) P.J. Parsons; C.S. Penkett; A.J. Shell, *Chem. Rev.*, 1996, **96**, 195.
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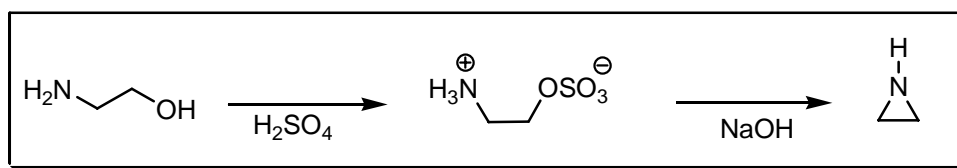
## COMMENTS :

## WENKER RING-CLOSURE

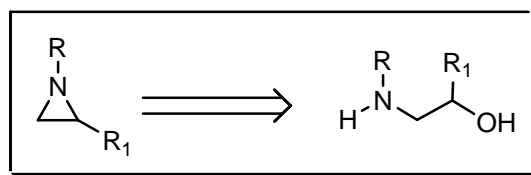
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

Ethanolamine when treated with sulfuric acid gives  $\beta$ -aminoethylsulfuric acid, which with hot alkali yields ethylenimine. See also **Blum**, **Hassner** azide aziridine, **Gabriel – Marckwald – Cromwell** ethylenimine method, **Hoch – Campbell**, **Mansuy – Evans** and **Scheiner** reactions.

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## REFERENCES :

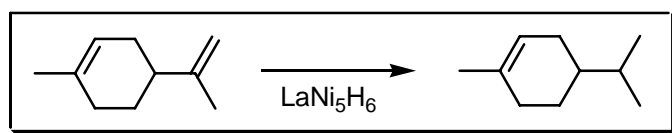
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  - 6) J-i. Park; G. Tian; D.H. Kim, *J. Org. Chem.*, 2001, **66**, 3696.
  - 7) J. Xu, *Tetrahedron: Asymmetry*, 2002, **13**, 1129.
- 

## COMMENTS :

## WENZEL – IMAMOTO REDUCTION

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### EXAMPLE :



## NOTES :

The selective reductions of  $\text{C}=\text{C}$ , aldehydes and ketones with LaNi alloy. After the hydrometallation a reductive elimination takes place.

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## REFERENCES :

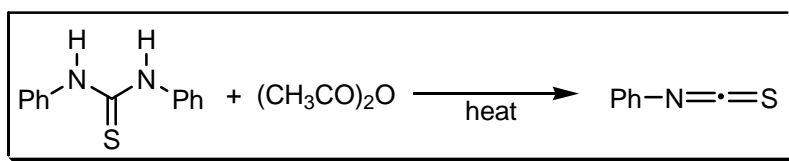
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  - 2) T. Imamoto; T. Mita; M. Yokoyama, *J. Chem. Soc., Chem. Commun.*, 1984, 163.
  - 3) T. Imamoto; T. Mita; M. Yokoyama, *J. Org. Chem.*, 1987, **52**, 5695.
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## COMMENTS :

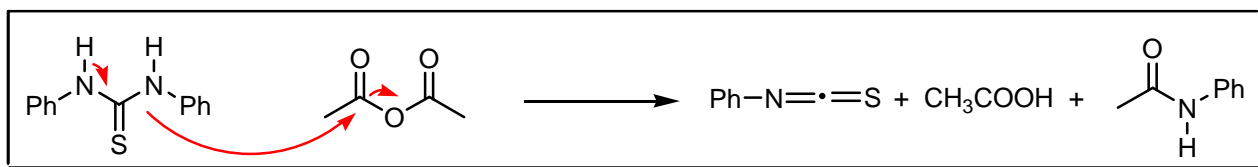
## WERNER SYNTHESIS

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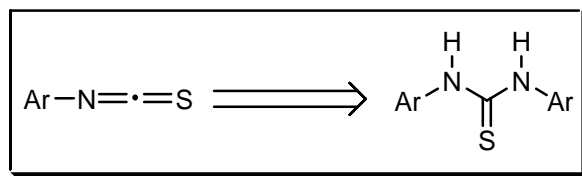
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Aryl isothiocyanates are obtained by heating *N,N'*-diarylthioureas with acetic anhydride followed by fractional distillation of the resulting mixture. See also **Hugershoff** reaction.

### REFERENCES :

Org. Synth. : 36, 56

Org. Synth. Coll. Vol. : 4, 700

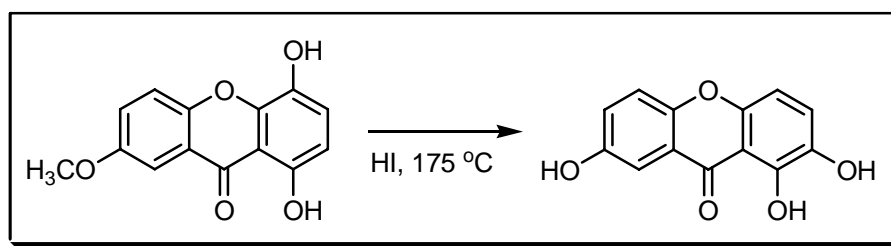
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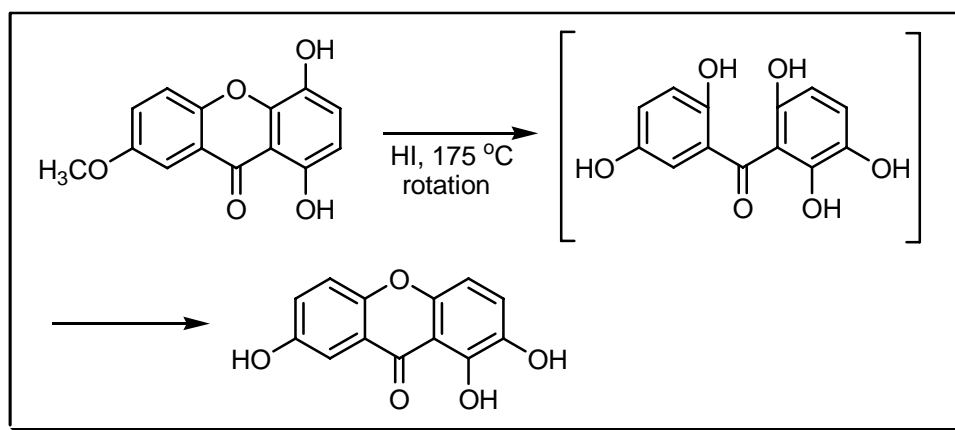
### COMMENTS :

## WESSELY – MOSER REARRANGEMENT

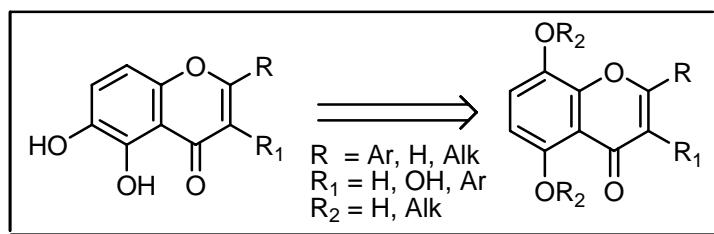
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

5,8-Dialkoxy- or dihydroxy-flavones rearrange on treatment with hydriodic (or sulfuric) acid, through the intermediate diaroylmethanes, to yield the corresponding 5,6-dihydroxyflavones. The rearrangement has been found to occur with other pyrone derivatives, e.g. isoflavones, flavonols, chromones, chromonols and xanthenes.

### REFERENCES :

Houben – Weyl : E7b, 55

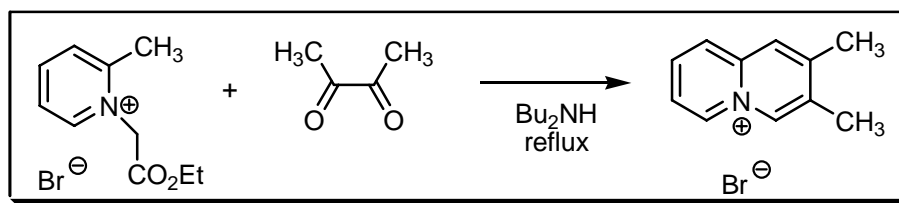
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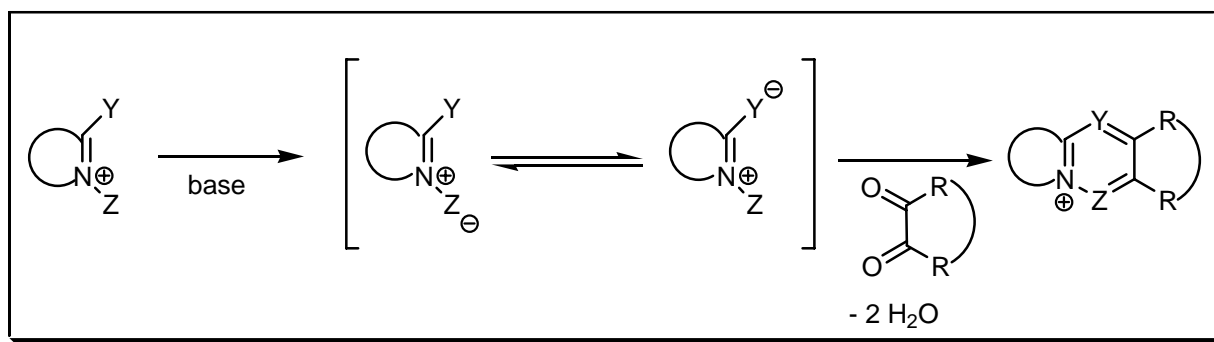
COMMENTS :

## WESTPHAL CONDENSATION

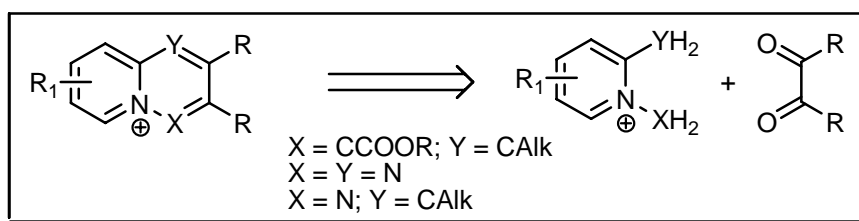
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

This is one of the easiest methods for preparing bicyclic systems with a bridgehead quaternary nitrogen atom. The reaction can be done on solid-phase support.

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## REFERENCES :

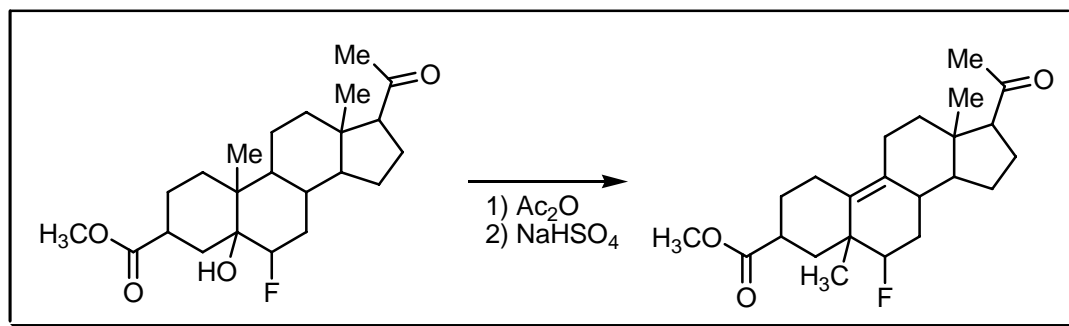
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## COMMENTS :

## WESTPHALEN – LETTRÉ REARRANGEMENT

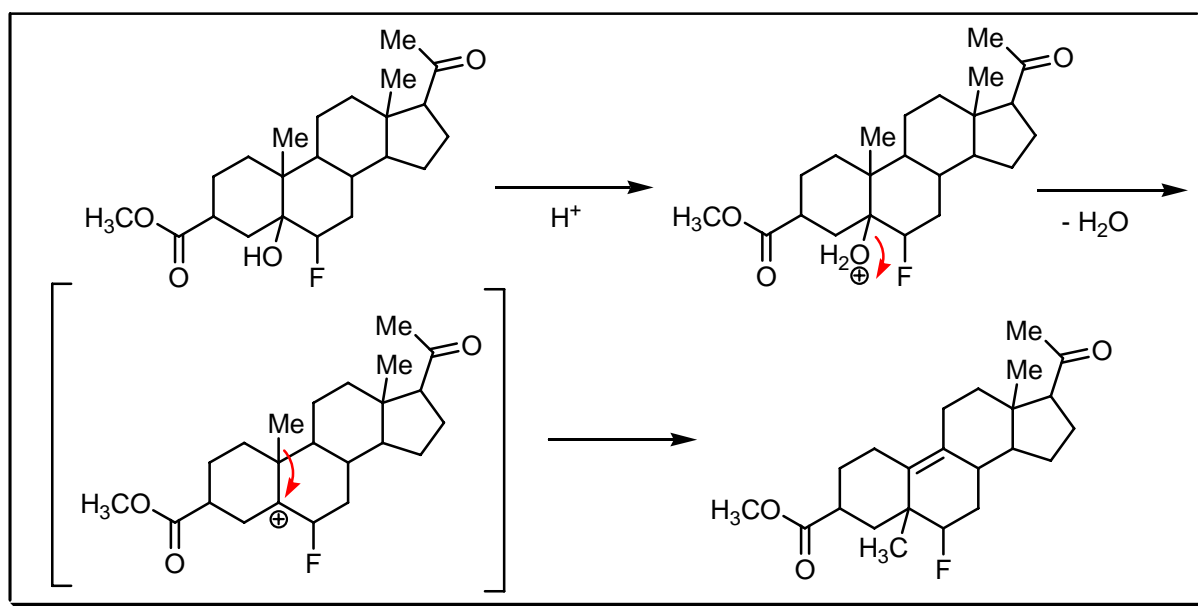
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### EXAMPLE :

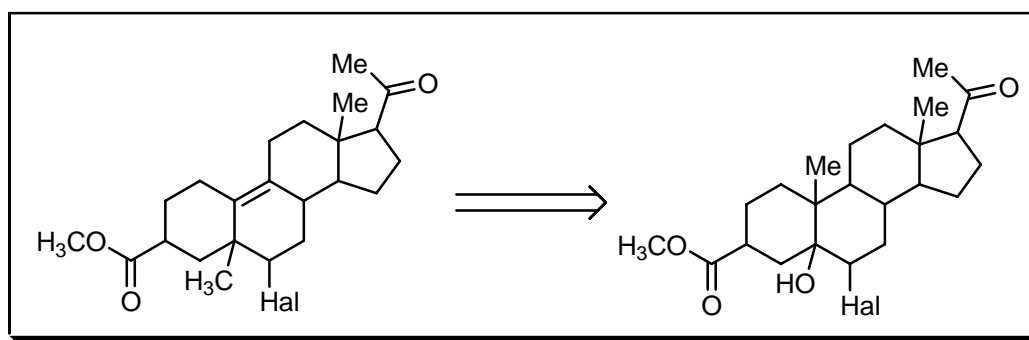




### MECHANISM :



### DISCONNECTION :



### NOTES :

This is the carbocation rearrangement of steroidal *tert*-alcohols. The position next to the formed carbocation ion has to be a halogen atom. See also **Wagner – Meerwein** rearrangement.

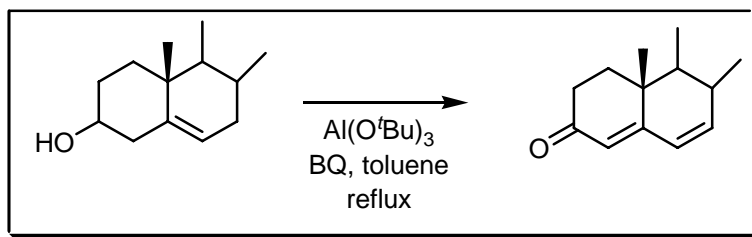
### REFERENCES :

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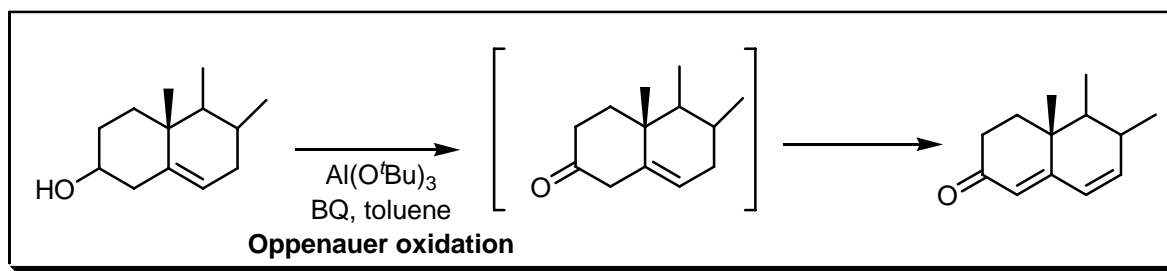
COMMENTS :

## WETTSTEIN OXIDATION

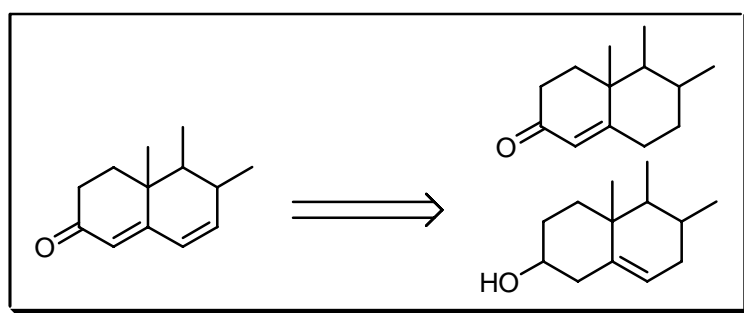
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

3 $\beta$ -Hydroxy-5-enic steroids (steroidal allylic alcohols), e.g., preg-5-en-3 $\beta$ -ol-20-one are oxidised by the **Oppenauer** method with aluminium *tert*-butoxide, using benzoquinone in boiling toluene as a hydrogen acceptor, to yield a 4,6-dien-3-one, e.g., 6-dehydroprogesterone. The reaction can give low yields. **Sondheimer** *et al.* published a similar route using manganese dioxide. See also **Oppenauer** reaction.

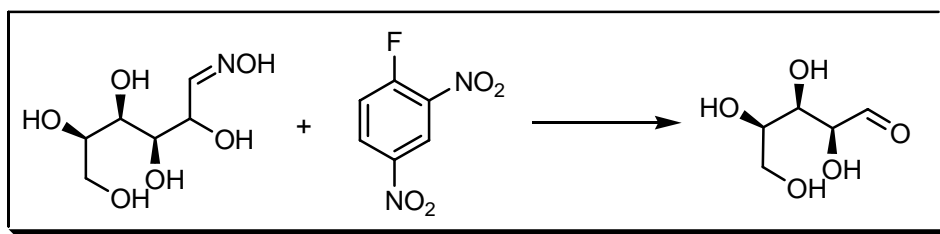
## REFERENCES :

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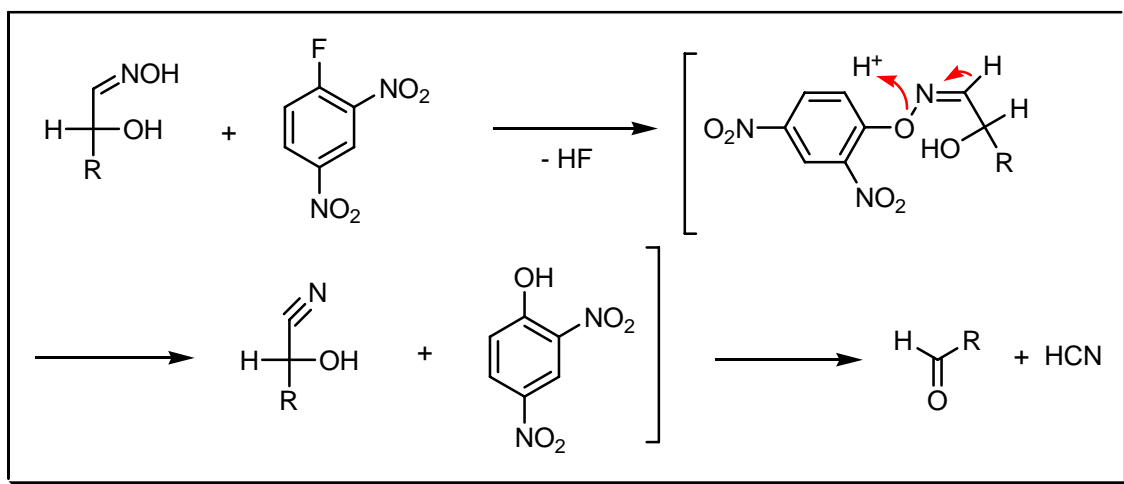
## COMMENTS :

## WEYGAND – LÖWENFELD REDUCTION

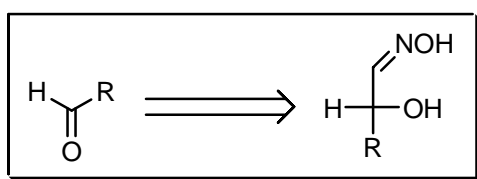
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



## NOTES :

The sugar oxime degradation with 2,4-dinitrofluorophenol (**Sanger reagent**) in bicarbonate solution. See also **Wohl** reaction.

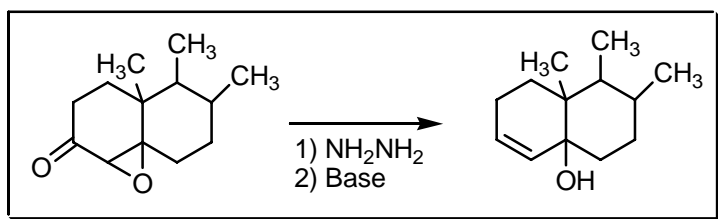
## REFERENCES :

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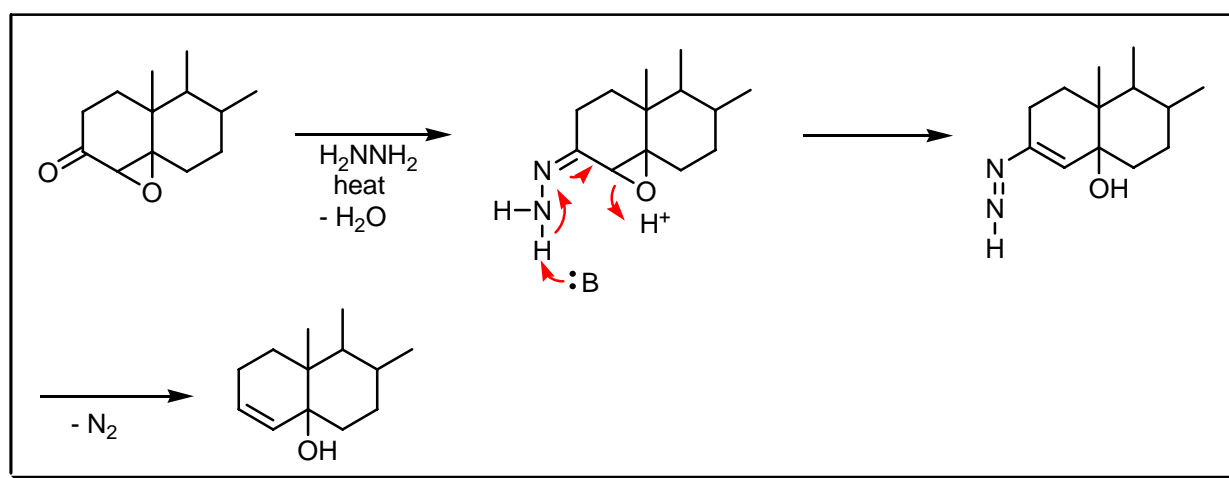
## COMMENTS :

## WHARTON OLEFIN SYNTHESIS

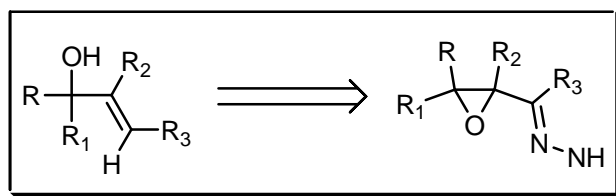
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The conversion of  $\alpha$ -haloketones to olefins using hydrazine. Also the reduction  $\alpha,\beta$ -epoxy ketones to allyl alcohols. This reaction can be considered an eliminative **Wolff – Kishner** reduction. Some authors call this reaction the **Wharton** fragmentation reaction, this fragmentation is the base-induced fragmentation of cyclic 1,3-diol monosulphate esters to give medium-sized cyclic alkenes. See also **Eschenmoser – Tanabe**, **Grob**, **Marshall – Minnaard** fragmentation and **Wolff – Kishner** reactions.

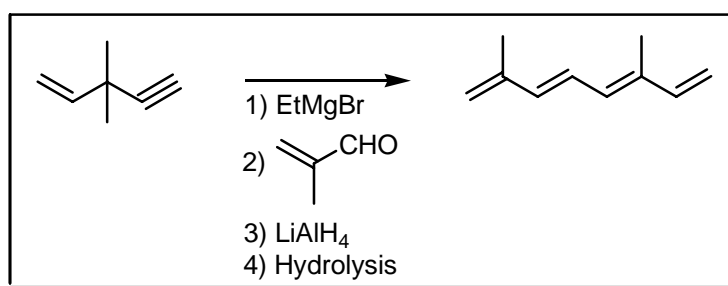
## REFERENCES :

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- 7) M. DiFilippo; F. Fezza; I. Izzo; F. De Riccardis; G. Sodano, *Eur. J. Org. Chem.*, 2000, 3247.
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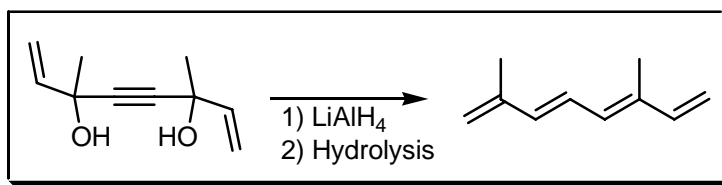
## COMMENTS :

## WHITING – NAYLER REACTION

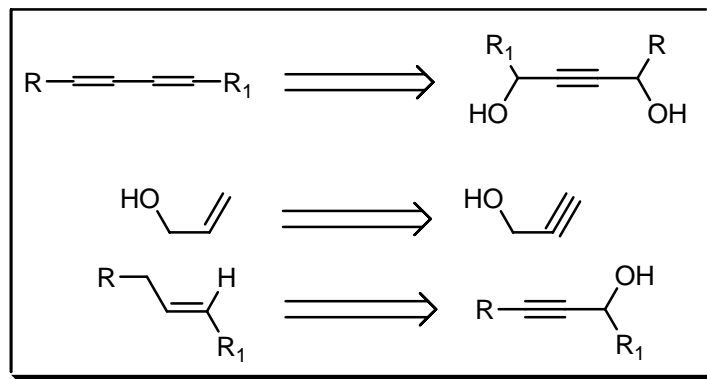
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Alkenes and alkynyls are normally not reduced by lithium aluminium hydride however propargylic alcohol derivatives are an exception. See also **Favorskii – Babayan** and **Isler** reaction.

### REFERENCES :

Smith : 358

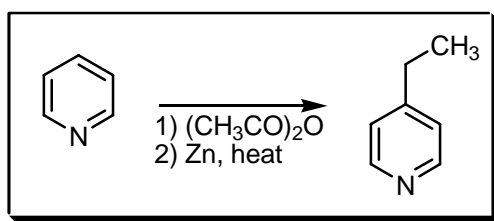
Smith 2<sup>nd</sup> : 319

- 1) P. Naylor; M.C. Whiting, *J. Chem. Soc.*, 1954, 4006.
- 2) O. Isler; M. Montavon; R. Rüegg; P. Zeller, *Helv. Chim. Acta*, 1956, **39**, 454.
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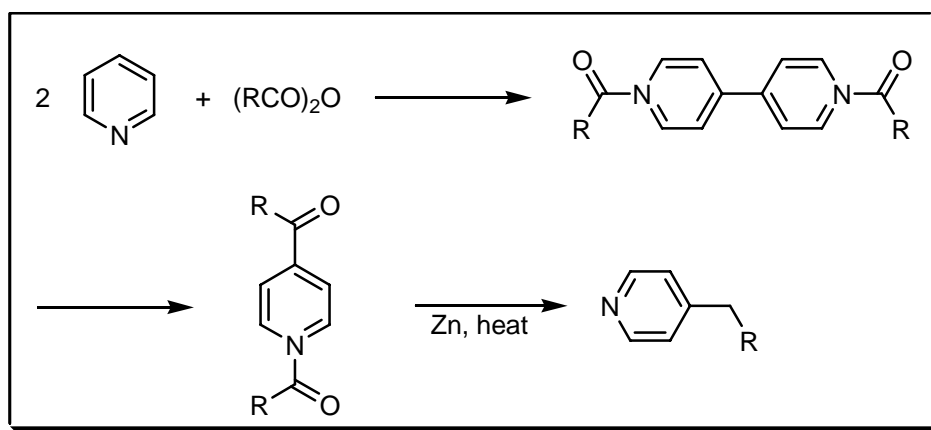
### COMMENTS :

## WIBAUT – ARENS SYNTHESIS

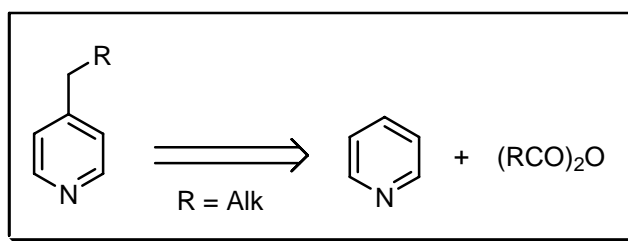
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Certain 4-alkylpyridine derivatives are formed by the treatment of dry pyridine with an acid anhydride and zinc dust. See also **Comins** and **Friedel – Crafts** reactions.

### REFERENCES :

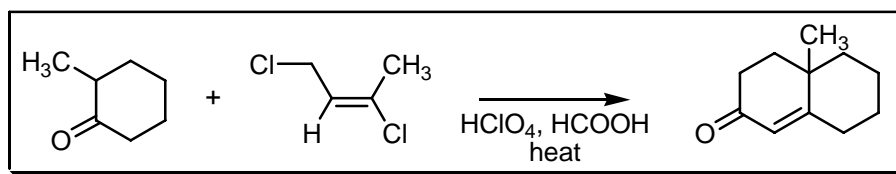
Houben – Weyl : E7b, 674

- 1) J.P. Wibaut; J.F. Arens, *Recl. Trav. Chim. Pays-Bas*, 1941, **60**, 119.
- 2) W. Solomon, *J. Chem. Soc.*, 1946, 934.
- 3) J.P. Wibaut; D. van der Vennen, *Recl. Trav. Chim. Pays-Bas*, 1947, **66**, 236.
- 4) I.P. Kutney; T. Tabata, *Can. J. Chem.*, 1963, **41**, 695.

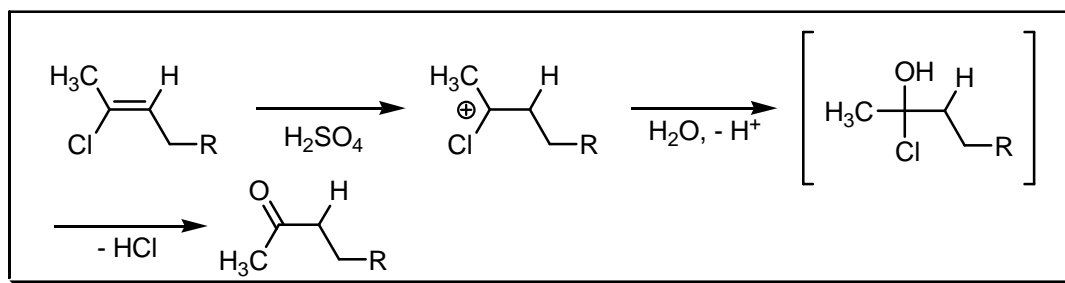
**COMMENTS :**

## WICHTERLE REACTION

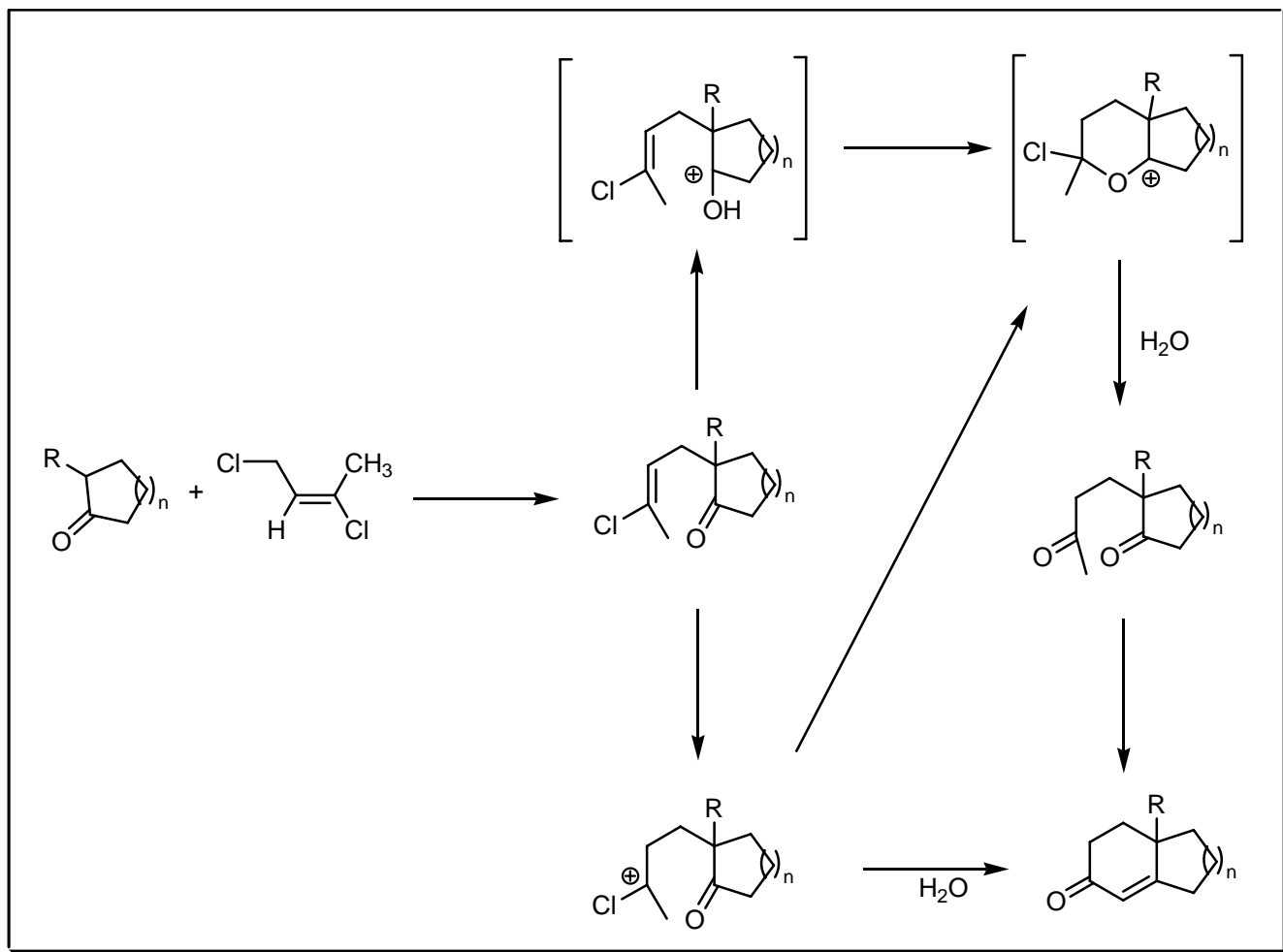
**EXAMPLE :**



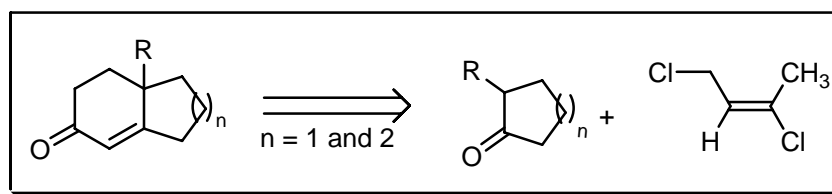
**MECHANISM :**







#### DISCONNECTION :



#### NOTES :

The modification of the **Robinson** annulation in which 1,3-dichloro-*cis*-2-butene is used instead of methyl vinyl ketone. In general the **Wichterle** reaction is the conversion of vinylic halides to ketones with the possibility of additional cyclocondensation. The mechanism is still a matter of speculation. See also **Robinson – Mannich** annulation.

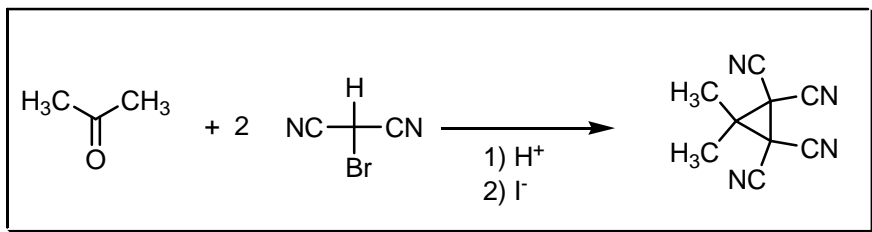
#### REFERENCES :

- 1) O. Wichterle; J. Procházka; J. Hofmann, *Coll. Czech. Chem. Commun.*, 1948, **13**, 300.
- 2) M. Kobayashi; T. Matsumoto, *Chem. Lett.*, 1973, 957.
- 3) H. Yoshioka; K. Takasaki; M. Kobayashi; T. Matsumoto, *Tetrahedron Lett.*, 1979, **20**, 3489.
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- 5) M. Hudlický, *Coll. Czech. Chem. Commun.*, 1993, **58**, 2229.

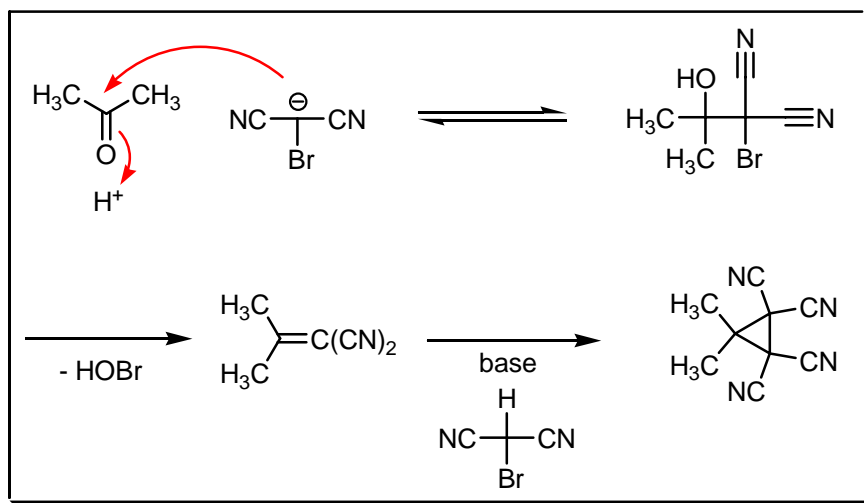
COMMENTS :

## WIDEQVIST CYCLOPROPANE SYNTHESIS

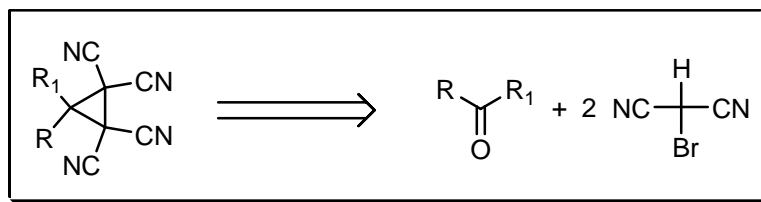
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

Tetracyanocyclopropane is prepared from bromomalonitrile and ketones. The name is sometimes also spelled as **Widequist**.

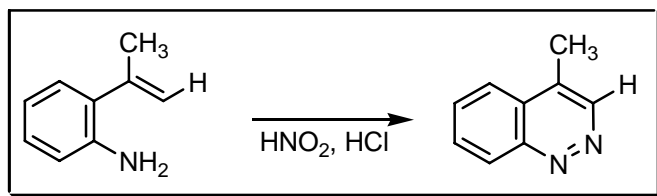
## REFERENCES :

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- 3) R.M. Scibner; G.N. Sausen; W.W. Pritchard, *J. Org. Chem.*, 1960, **25**, 1440.
- 4) H. Hart; Y.C. Kim, *J. Org. Chem.*, 1966, **31**, 2784.

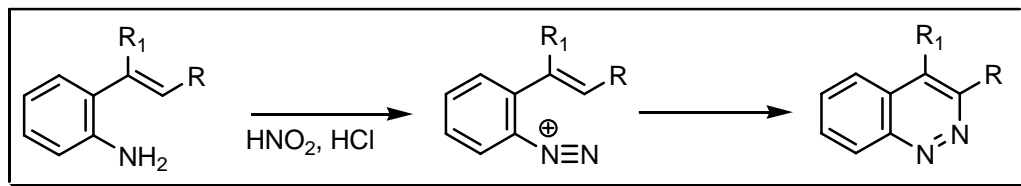
## COMMENTS :

## WIDMAN – STOERMER SYNTHESIS

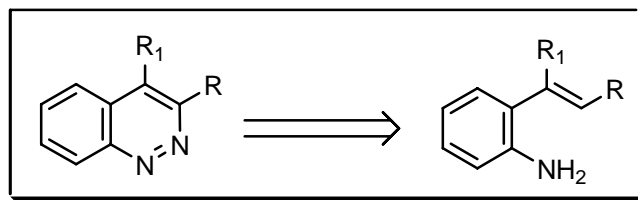
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Cinnolines are obtained by the diazotisation and cyclisation of  $\alpha$ -amino-arylethylenes. See also **Borsche – Koelsch**, **Neber – Bossel**, **Pschorr** and **von Richter** cinnoline reactions.

## REFERENCES :

- 1) O. Widman, *Ber. Dtsch. Chem. Ges.*, 1884, **17**, 722.
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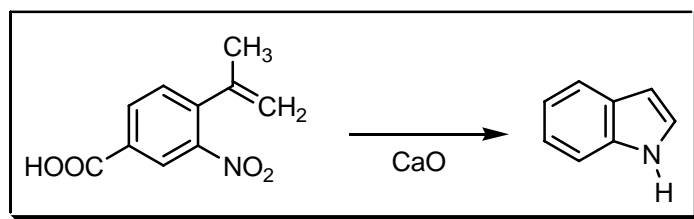
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## COMMENTS :

## WIDMAN SYNTHESIS OF INDOLES

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### EXAMPLE :



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### NOTES :

Indoles are obtained in low yield by dry distillation of o-nitrophenylalkenes with calcium oxide. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Yamamoto** indole-1, **Yamamoto** indole-2 and **Yurovskaya** reactions.

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## REFERENCES :

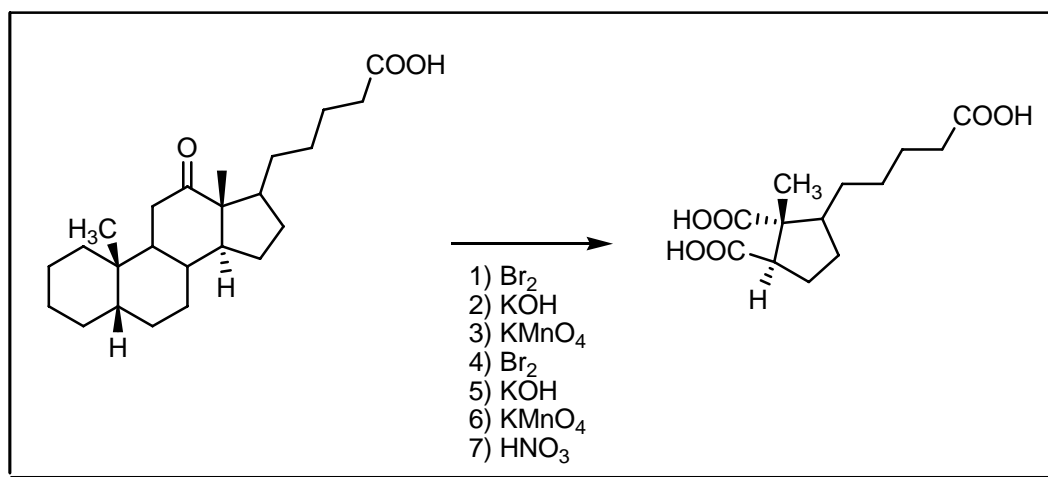
- O. Widman, *Ber. Dtsch. Chem. Ges.*, 1882, **15**, 2547.

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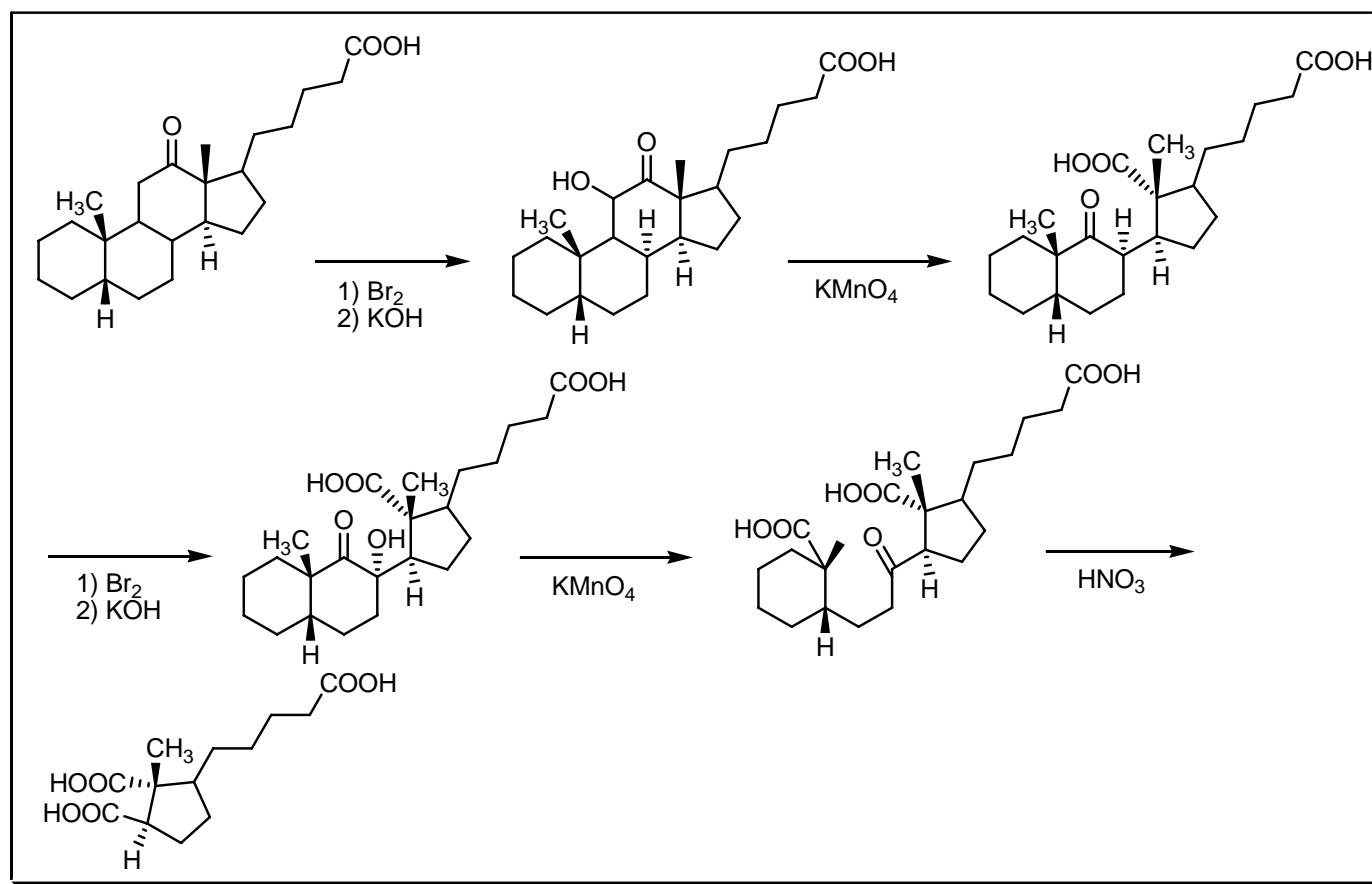
## COMMENTS :

## WIELAND – DANE DEGRADATION

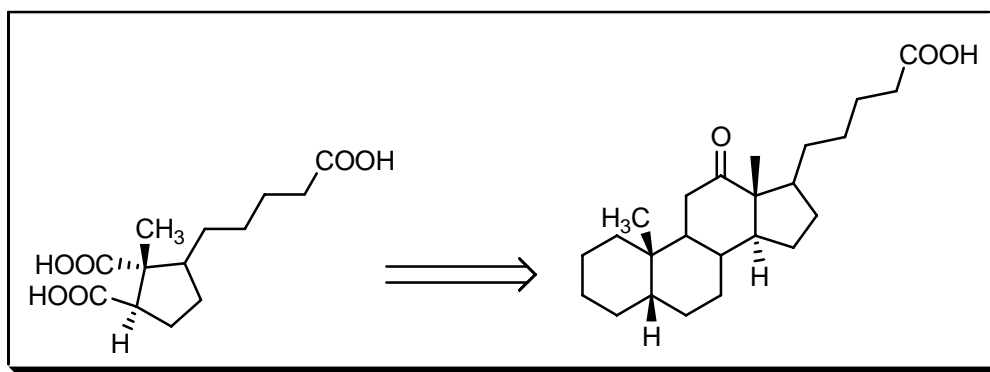
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

A complex series of reactions by which, e.g. 12-ketocholanic acid is converted into a *trans*-tricarboxylic acid. The result of this degradation enables a *trans* configuration to be assigned to the CD rings of the bile-acid and determines the position of the angular methyl group at C(13). See also **Barbier – Locquin – Wieland** degradation, **Miescher** degradation, **Hoehn – Mason** degradation and **Trost** oxidative decarboxylation reactions.

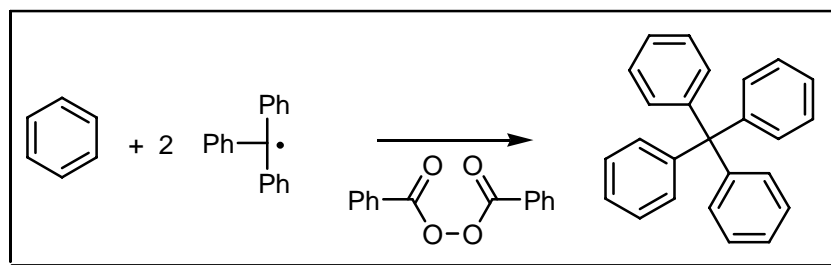
## REFERENCES :

H. Wieland; E. Dane, *Hoppe Seylers Z. Physiol. Chem.*, 1933, **216**, 91.

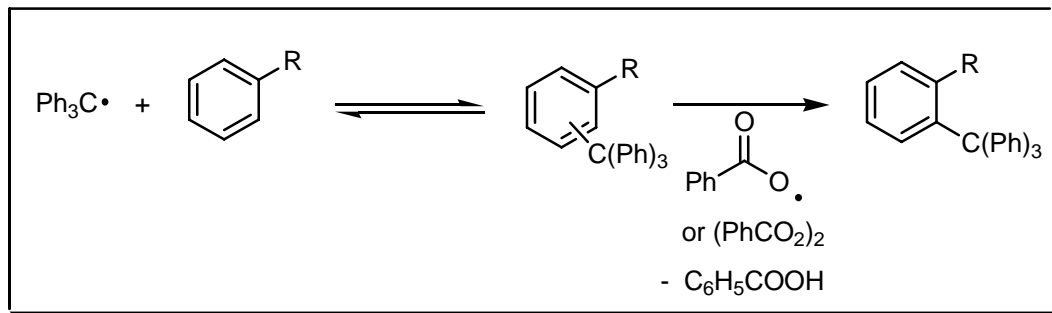
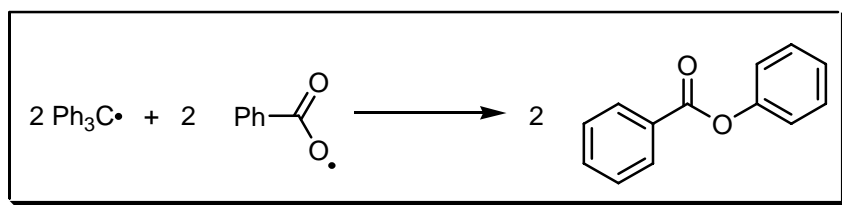
## COMMENTS :

## WIELAND TRIPHENYLMETHYL RADICAL REARRANGEMENT

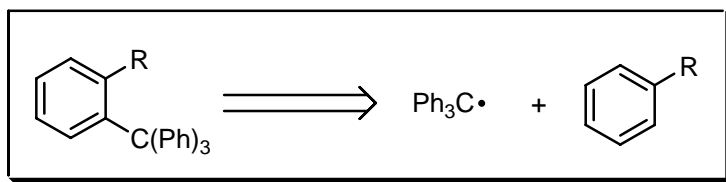
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

A triphenylmethyl radical attacks aromatic substrates in the presence of benzoylperoxide.

## REFERENCES :

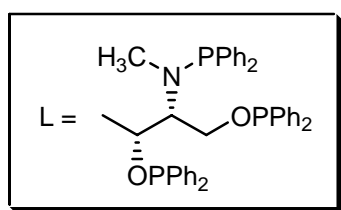
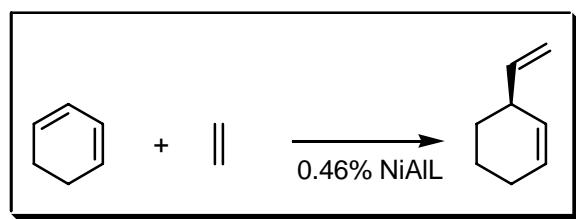
Smith – March : 241

- 1) H. Wieland, *Ber. Dtsch. Chem. Ges.*, 1911, **44**, 2550.
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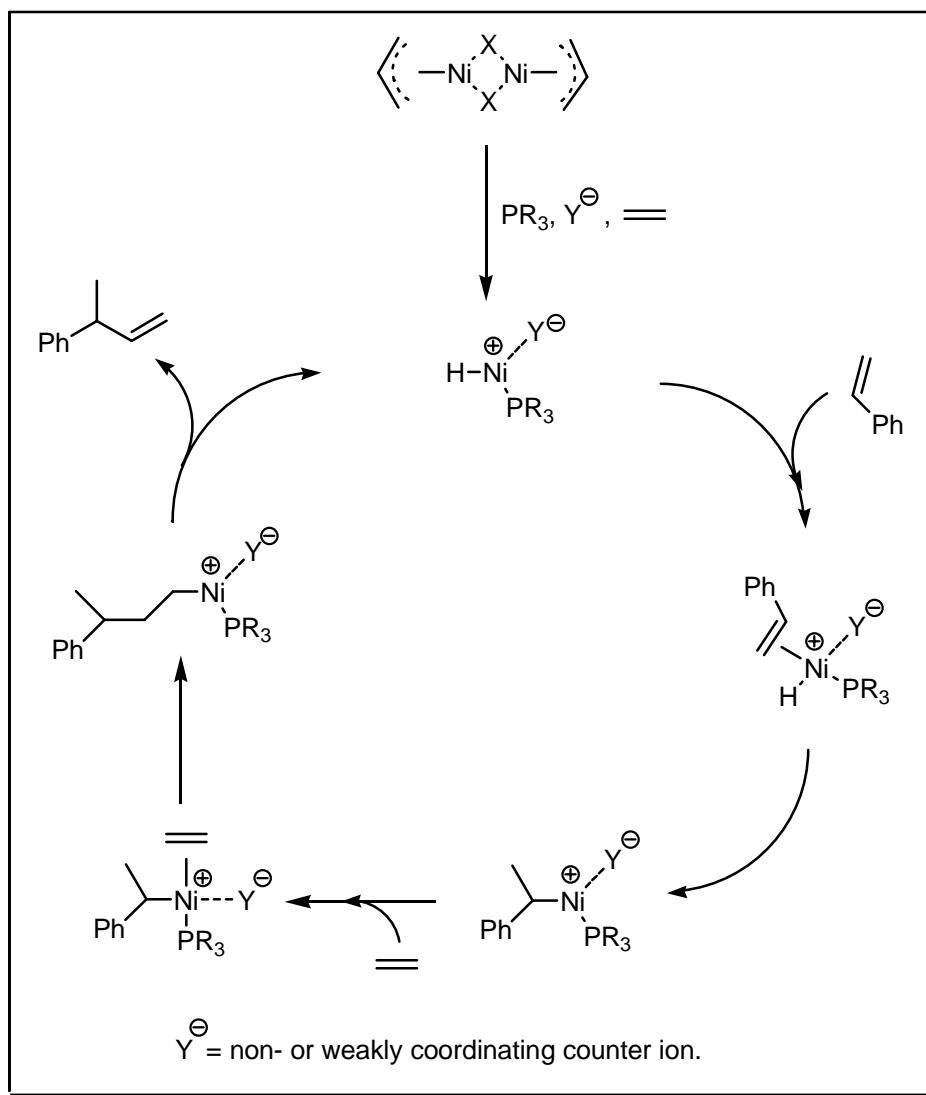
## COMMENTS :

## WILKE REACTION

### EXAMPLE :

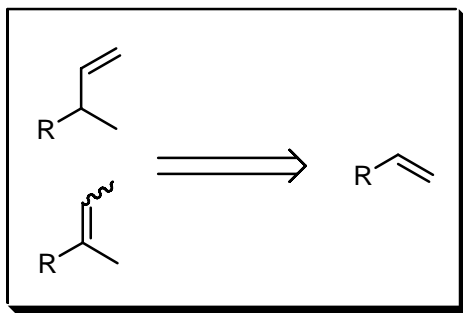


### MECHANISM :





## DISCONNECTION :



## NOTES :

The enantioselective hydrovinylation of olefins is highly atom economic, requires low catalyst loading and low pressure. The classical **Wilke** reaction uses **Ziegler**-type catalysts made from tetrabutyltitanate and triethylaluminium. In later versions nickel and palladium are used as metals.

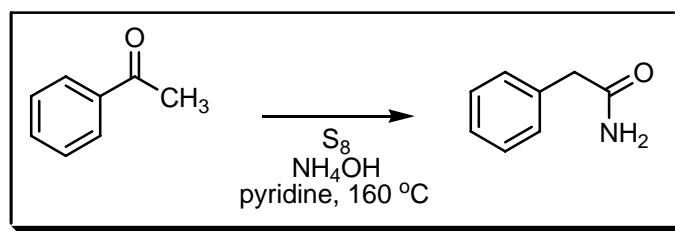
## REFERENCES :

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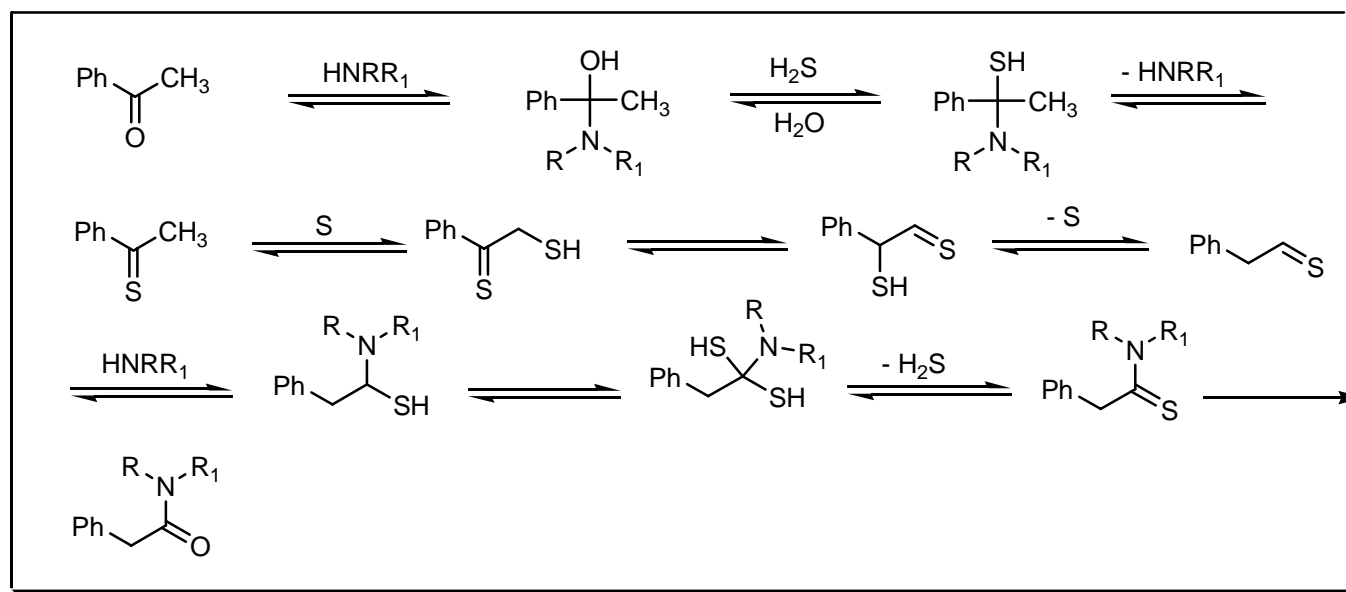
## COMMENTS :

## WILLGERODT – KINDLER REDOX AMINATION

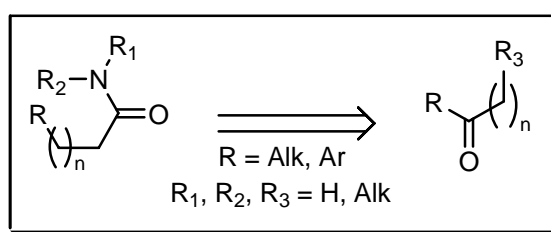
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The rearrangement of aromatic and aliphatic ketones to amides by heating with sulfur (**Kindler** modification, **Willgerodt** used  $(NH_4)_2S_x$ ) and ammonia or amines. For volatile amines the corresponding hydrogen chloride salts can be used. The **Schwenk** modification is based on the **Kindler** variation of the **Willgerodt** reaction, the carbonyl compound is treated with morpholine and sulfur to yield the morpholide of the corresponding thio-acetic acid. This may be hydrolysed with alkali to yield an arylacetic acid. There are several mechanisms proposed in the literature, the most interesting one is the mechanism by **Carmack**. See also **Asinger**, and **Pummerer** reactions.

## REFERENCES :

March : 1236

Smith – March : 1567

Houben – Weyl : **E3**, 635; **E5**, 1232; **E8a**, 18, 1084; **E15**, 2029; **E6a**, 208; **E8b**, 988

Org. React. : **3**, 83; **6**, 439

Org. Synth. : **74**, 257

Org. Synth. Coll. Vol. : **9**, 99

Science of Synthesis : **9**, 539

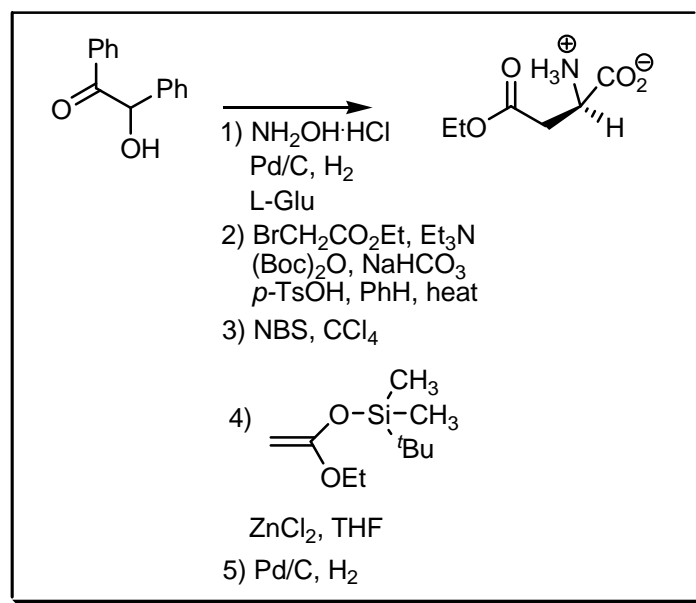
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  - 2) K. Kindler, *Liebigs Ann. Chem.*, 1923, **431**, 193.
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  - 13) M.M. Alam; S.R. Adapa, *Synth. Commun.*, 2003, **33**, 59.
  - 14) H.R. Darabi; K. Aghapoor; M. Tajbaksh, *Tetrahedron Lett.*, 2004, **45**, 3981.
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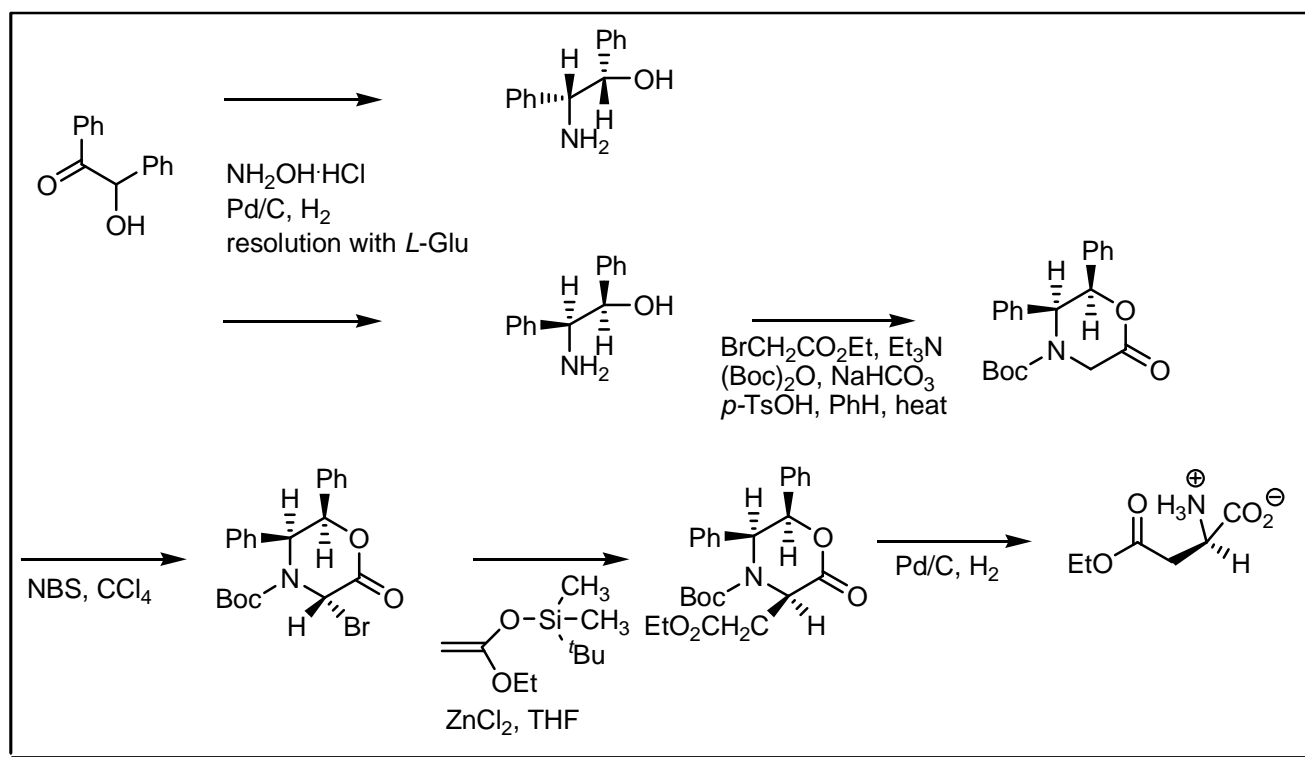
## COMMENTS :

# WILLIAMS – BEN-ISHAI AMINO ACID SYNTHESIS

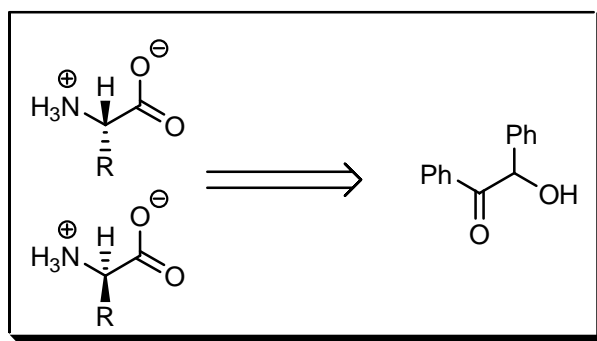
## EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Optically active oxazin-2-ones serve as an electrophilic glycine template for the asymmetric synthesis of amino acids.

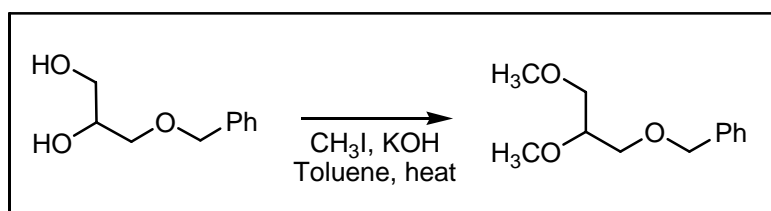
## REFERENCES :

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- 3) P.J. Sinclair; D. Zhai; J. Reibenspeis; R.M. Williams, *J. Am. Chem. Soc.*, 1986, **108**, 1103.
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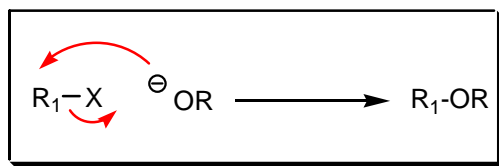
## COMMENTS :

## WILLIAMSON ETHER SYNTHESIS

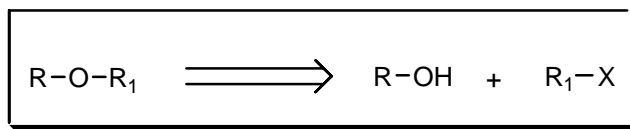
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Ethers are synthesised by the interaction of an alkyl halide and an alkali alkoxide. See also **Robertson – Robinson** and **Ullmann** diaryl reactions.

## REFERENCES :

**March** : 386

**Smith – March** : 477

**Smith** : 132

**Smith 2<sup>nd</sup>** : 106, 227, 543

**Houben – Weyl** : 6/3, 24; **E6b**, 62

**Org. Synth.** : 25, 9

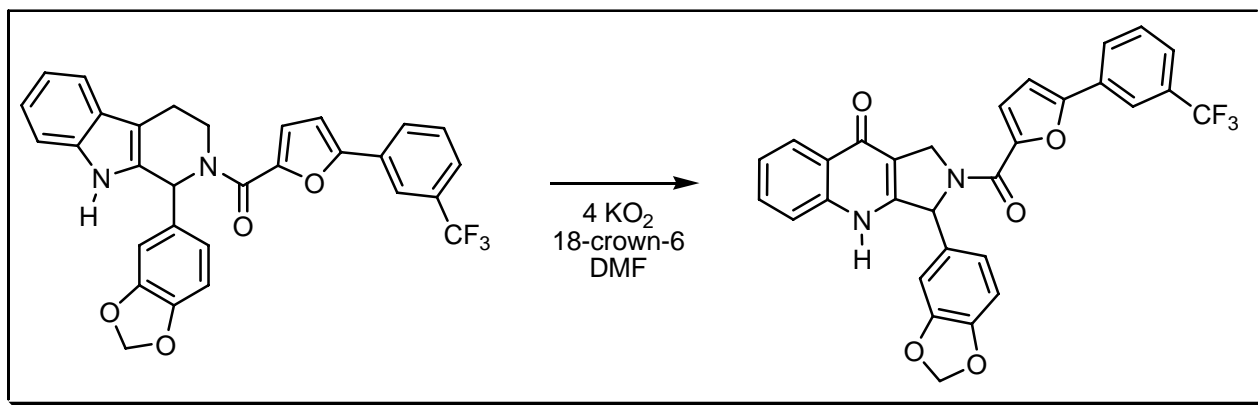
**Org. Synth. Coll. Vol.** : 3, 140

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- 2) O.C. Dermer, *Chem. Rev.*, 1934, **14**, 385.
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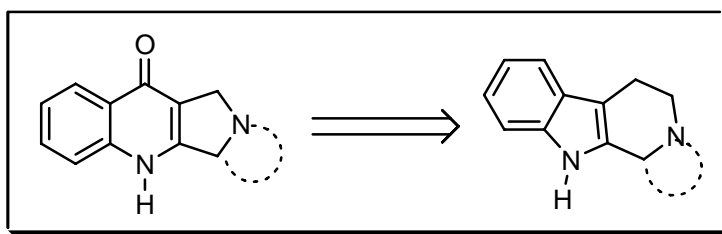
## COMMENTS :

## WINTERFELDT OXIDATION

### EXAMPLE :



### DISCONNECTION :



### NOTES :

In the classic example substituted indole derivatives are oxidised on treatment with potassium *tert*-butylate followed by oxygen. Nowadays potassium superoxide is used and is more superior.

### REFERENCES :

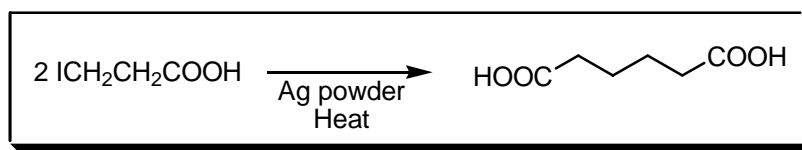
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### COMMENTS :

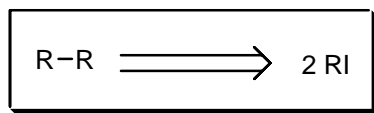
## WISLICENUS SYNTHESIS

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### EXAMPLE :



### DISCONNECTION :



### NOTES :

In the classic example aliphatic dibasic acids are obtained by action of metals (Ag, Ce, Al, U) on halogeno mono basic acids. See also **Fittig** and **Wurtz** reactions.

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### REFERENCES :

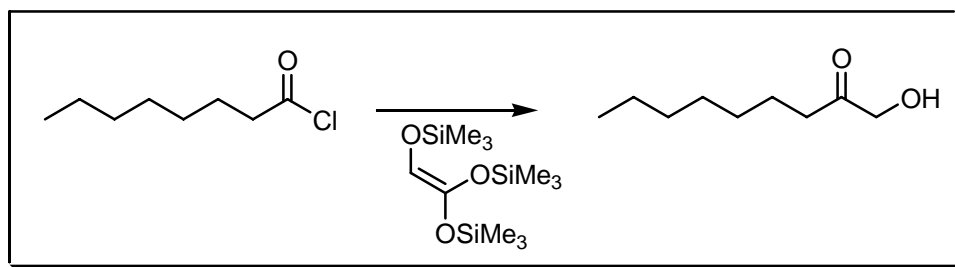
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### COMMENTS :

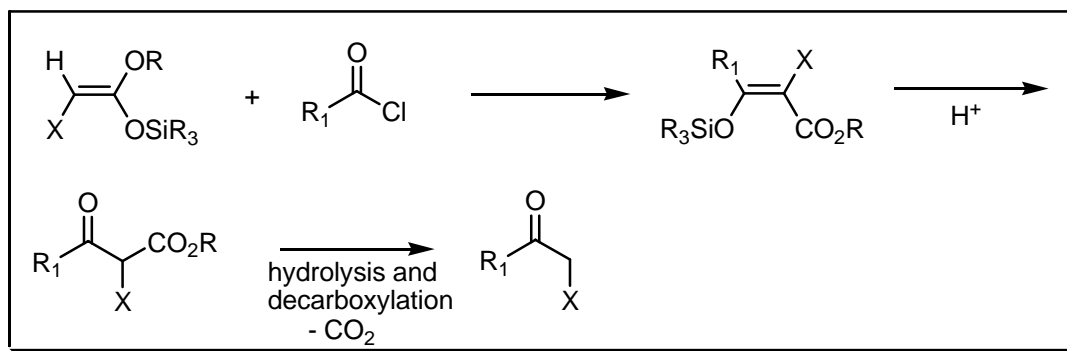
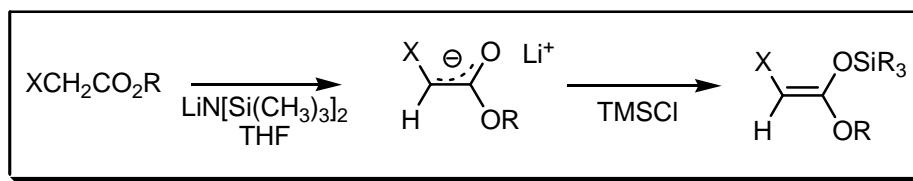
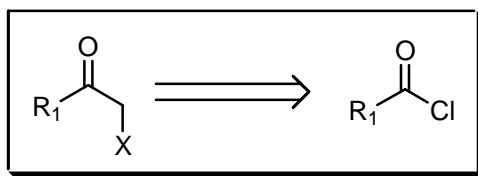
## WISSNER $\alpha$ -FUNCTIONALISED METHYL KETONE SYNTHESIS

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### EXAMPLE :





**MECHANISM :****DISCONNECTION :****NOTES :**

The conversion of acyl chlorides to functionalised ( $\text{OH}$ ,  $\text{OCH}_3$ ,  $\text{OPh}$ ,  $\text{SCH}_3$ ) ketones using silylated ketene acetals.

**REFERENCES :**

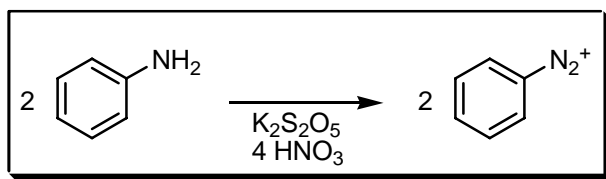
- 1) A. Wissner, *Tetrahedron Lett.*, 1978, **19**, 2749.
- 2) A. Wissner, *J. Org. Chem.*, 1979, **44**, 4617.
- 3) A. Wissner; J.E. Birnbaum; D.E. Wilson, *J. Med. Chem.*, 1980, **23**, 715.

**COMMENTS :**

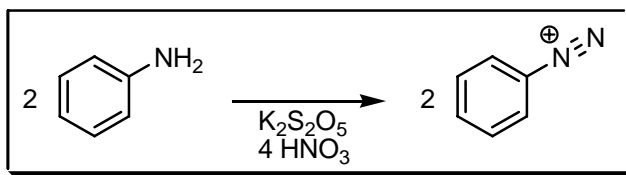
## WITT DIAZOTATION

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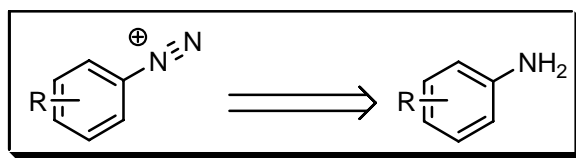
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The diazotation of aromatic amines in concentrated nitric acid with a reducing agent. See also **Balz – Schiemann**, **Cadogan** arylation, **Craig** exchange, **Demjanov** rearrangement, **Gattermann** diazo, **Gattermann** sulfinic acid, **Griess** deamination, **Knoevenagel** diazotation, **Körner – Contardi**, **Meerwein** arylation, **Sandmeyer** diazonium and **Schwechten** reactions.

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### REFERENCES :

**March** : 635

**Smith – March** : 816

**Smith 2<sup>nd</sup>** : 167, 1057

**Org. React.** : 2, 262

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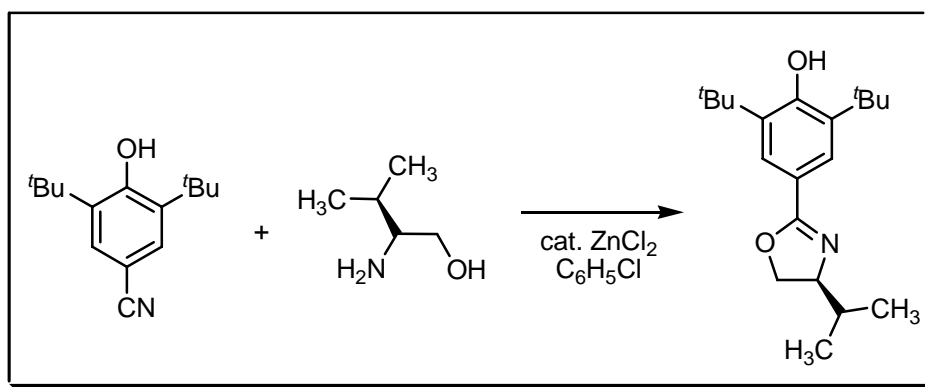
O.N. Witt, *Ber. Dtsch. Chem. Ges.*, 1909, **42**, 2953.

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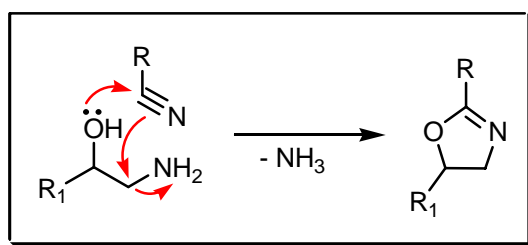
### COMMENTS :

## WITTE – SEELIGER REACTION

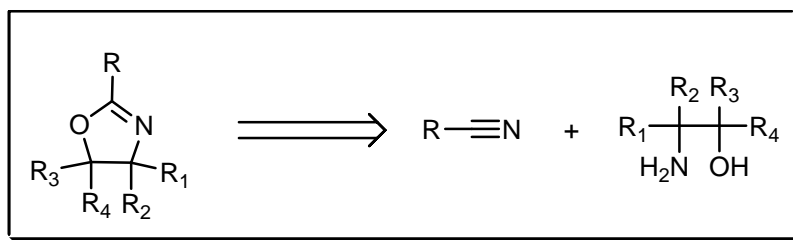
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The formation of 2-oxazolines from nitriles and amino alcohols using zinc chloride as catalyst. In addition, oxazines can be prepared this way. See also **Vorbrüggen – Krolkiewicz** reaction.

### REFERENCES :

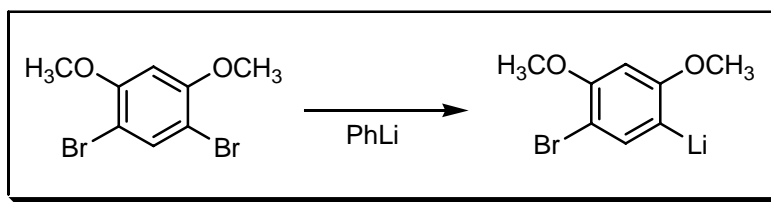
- 1) H. Witte; W. Seeliger, *Liebigs Ann. Chem.*, 1974, 996.
- 2) C. Bolm; K. Weickhardt; M. Zehnder; T. Ranff, *Chem. Ber.*, 1991, **124**, 1173.
- 3) A. Scheurer; P. Mosset; W. Bauer; R.W. Saalfrank, *Eur. J. Org. Chem.*, 2001, 3067.

COMMENTS :

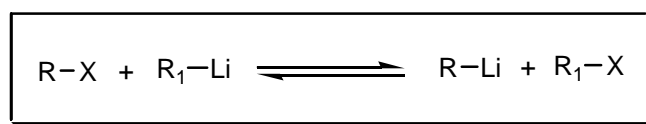
## WITTIG – GILMAN REACTION

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EXAMPLE :



MECHANISM :



NOTES :

An organo lithium species ( $R_1-Li$ ) reacts reversibly with an alkyl halide (mostly Br, I) to produce a new organo lithium species ( $R-Li$ ) *via* a metal-halogen exchange. There are several mechanisms proposed, but the equilibrium favours the organo lithium species possessing the best group to stabilise the carbanionic center. This reaction is also known as **Wittig – Witt** lithium exchange. See also **Wurtz** coupling.

REFERENCES :

Smith : 724

Smith 2<sup>nd</sup> : 611

Houben – Weyl : 4/2, 783; E7b, 622

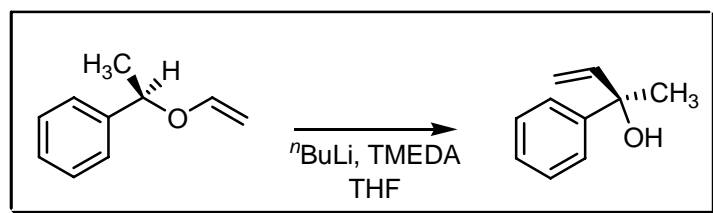
Org. React. : 6, 339

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  - 2) H. Gilman; W. Langham; A.L. Jacoby, *J. Am. Chem. Soc.*, 1939, **61**, 106.
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  - 6) L. Green; B. Chauder; V. Snieckus, *J. Heterocycl. Chem.*, 1999, **36**, 1453.
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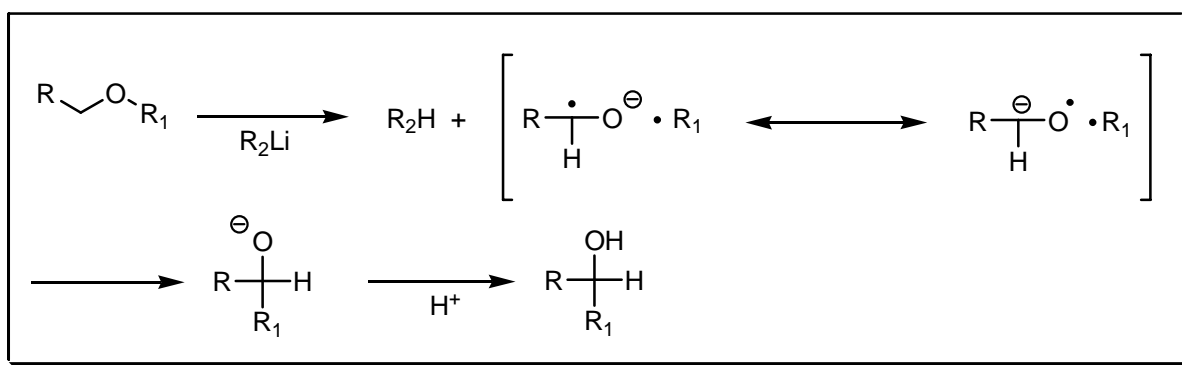
COMMENTS :

## [1,2]-WITTIG REARRANGEMENT

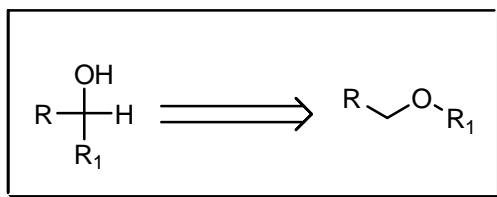
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The non-concerted rearrangement of ethers with alkyl lithium to an atom with a lone pair of electrons to yield alcohols via a [1,2]-shift. The reaction can also be samarium diiodide induced. See also **Meisenheimer** and **Stevens** rearrangement reactions.

## REFERENCES :

March : 1102

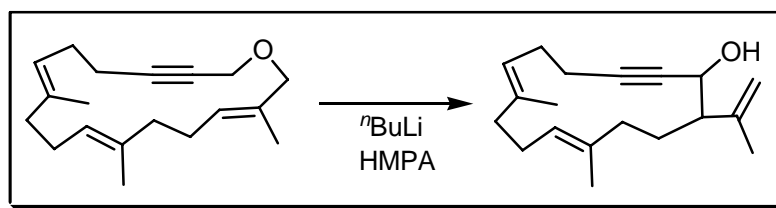
Smith – March : 1421

- 1) G. Wittig; L. Löhmann, *Liebigs Ann. Chem.*, 1942, **550**, 260.
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- 5) R.W. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, 1979, **18**, 563.
- 6) T. Nakai; K. Mikami, *Chem. Rev.*, 1986, **86**, 885.
- 7) K. Tomooka; H. Yamamoto; T. Nakai, *Liebigs Ann. Chem.*, 1997, 1275.
- 8) K. Tomooka; T. Inoue; T. Nakai, *Chem. Lett.*, 2000, 418.
- 9) L. Lemiègre; T. Regnier; J.-C. Combret; J. Maddaluno, *Tetrahedron Lett.*, 2003, **44**, 373.
- 10) O. Miyata; T. Koizumi; H. Asai; R. Iba; T. Naito, *Tetrahedron Lett.*, 2004, **45**, 3893.

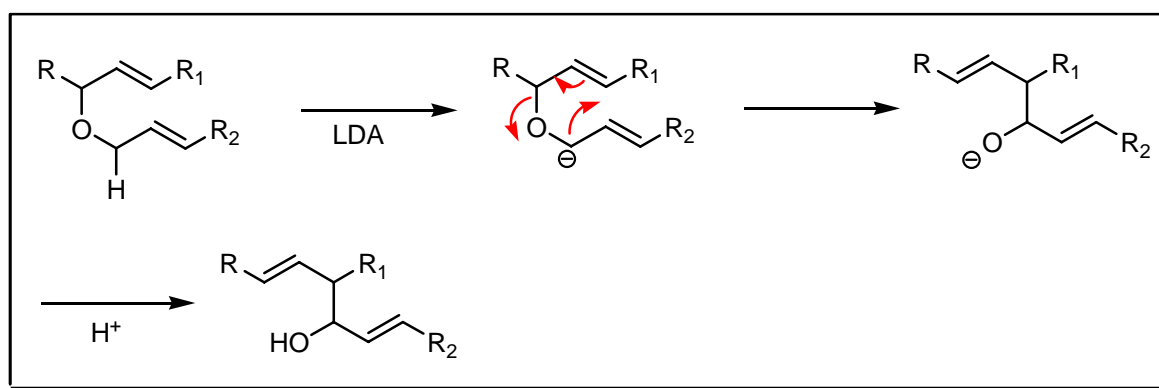
## COMMENTS :

## [2,3]-WITTIG REARRANGEMENT

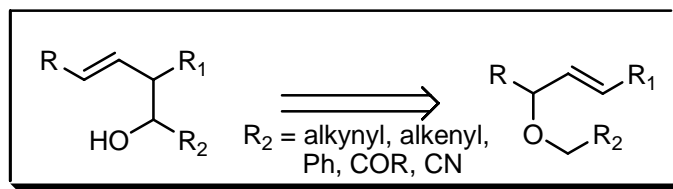
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

Certain benzyl and allyl ethers rearrange ([2,3]-sigmatropic rearrangement) on treatment with a base (LDA, <sup>t</sup>BuLi, NaNH<sub>2</sub>) to yield secondary and tertiary alcohols. Aza-[2,3] rearrangements have also been published. See also **Meisenheimer**, **Mislow – Evans** and **Sommelet – Hauser** reactions.

## REFERENCES :

**Smith – March** : 558, 1453

**Houben – Weyl** : 12/1, 120

**Org. React.** : 46, 105

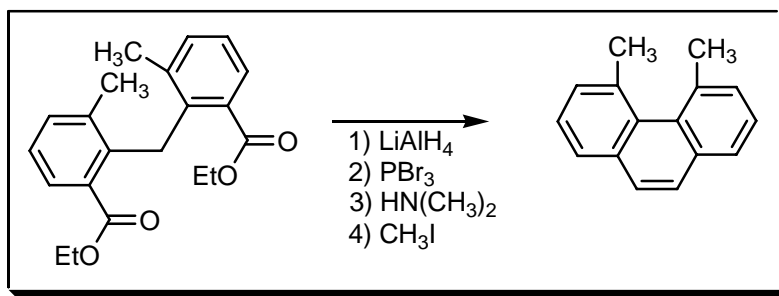
**Science of Synthesis** : 9, 270

- 1) G. Wittig; L. Löhmann, *Liebigs Ann. Chem.*, 1942, **550**, 260.
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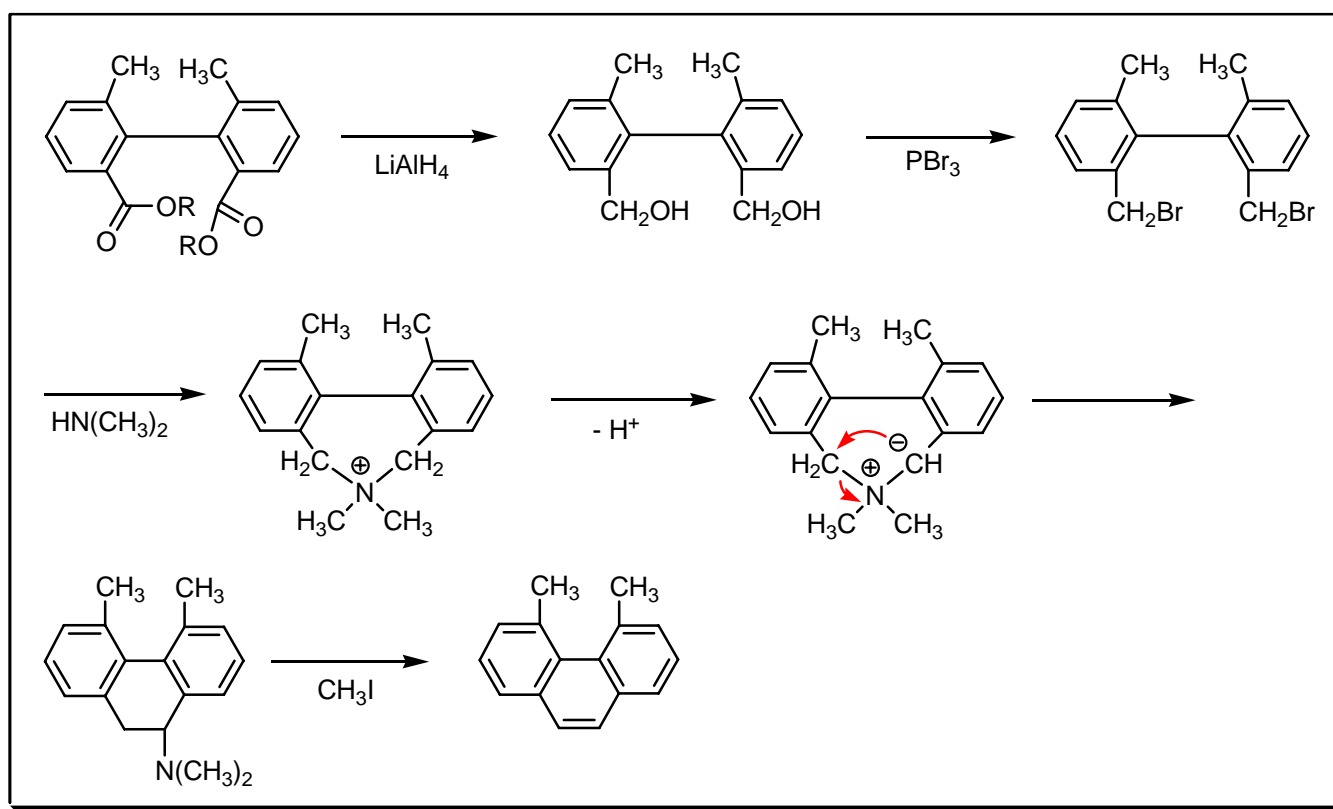
## COMMENTS :

## WITTIG PHENANTHRENE SYNTHESIS

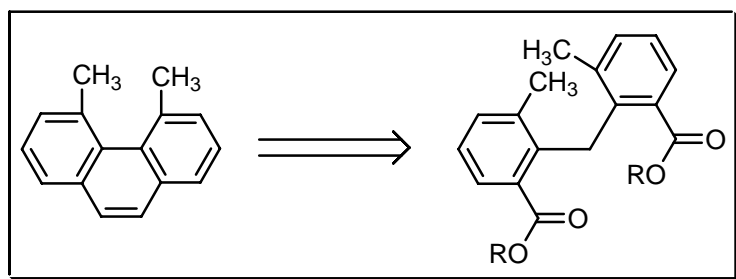
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :





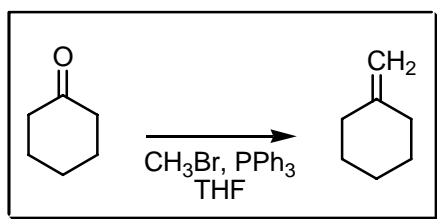
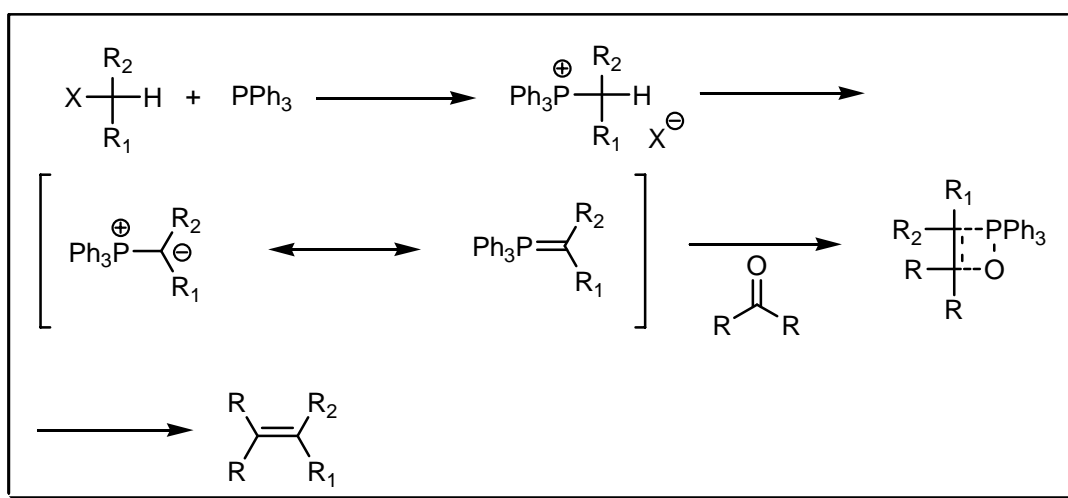
**NOTES :**

The synthesis of phenanthrene *via* ylide-isomerisation of a quaternary cyclic ammonium salt. See also **Haworth** polynuclear aromatics reaction.

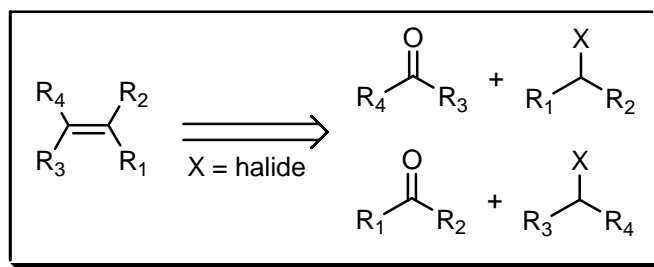
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  - 3) A.J. Floyd; S.F. Dyke; S.E. Ward, *Chem. Rev.*, 1976, **76**, 509.
- 

**COMMENTS :****WITTIG REACTION****EXAMPLE :****MECHANISM :**

## DISCONNECTION :



## NOTES :

Triphenylphosphine methylene and derivatives substituted in the methylene group react with aldehydes and ketones, whereby the carbonyl oxygen is exchanged for the methylene group to yield triphenylphosphine oxide and the corresponding unsaturated compound. In the **Schlosser** variant a salt is used as base in which the cation can block the oxygen atom. Then *tert*-butyl alcohol is added, this protonates the oxygen atom and ring-closure cannot take place and the more favourable conformation is formed (*trans*). In the **aza-Wittig** reaction an iminophosphorane formed in a **Staudinger** reaction is reacted with the ketones. Solvent-free **Wittig** reactions have also been reported. See also **Corey – Kwiatkowski**, **Corey – Nicolaou**, **Diels – Alder**, **Eastwood**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Horner – Wadsworth – Emmons**, **Hunsdiecker** ring-closure, **Julia – Paris – Kocienski – Lythgoe**, **Keck** macrolactonisation, **Kita**, **Krief – Reich – Chow**, **Masamune**, **McMurry**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Nysted**, **Petasis** reaction, **Peterson**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Staudinger**, **Steglich – Hassner**, **Still – Gennari**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Takeda**, **Tebbe**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Kroliekiewicz**, **Yamaguchi** and **Yamamoto** macrolactonisation reactions.

## REFERENCES :

**March** : 956

**Smith – March** : 1231

**Smith** : 782

**Smith 2<sup>nd</sup>** : 656

**Houben – Weyl** : **12/1**, 120; **E15**, 2523

**Org. React.** : **14**, 270

**Org. Synth.** : **40**, 66; **75**, 153

**Org. Synth. Coll. Vol.** : **5**, 751

**Science of Synthesis** : **9**, 146, 479, 488, 537

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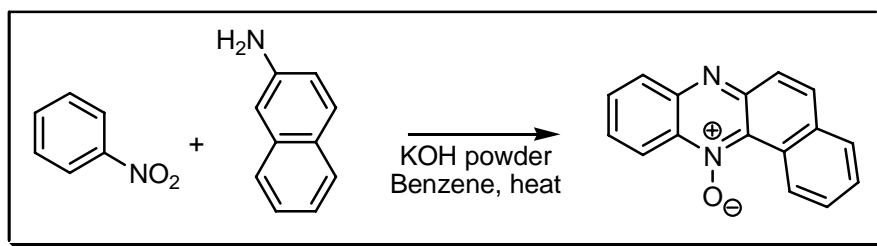
**COMMENTS :**

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**WOHL – AUE REACTION**

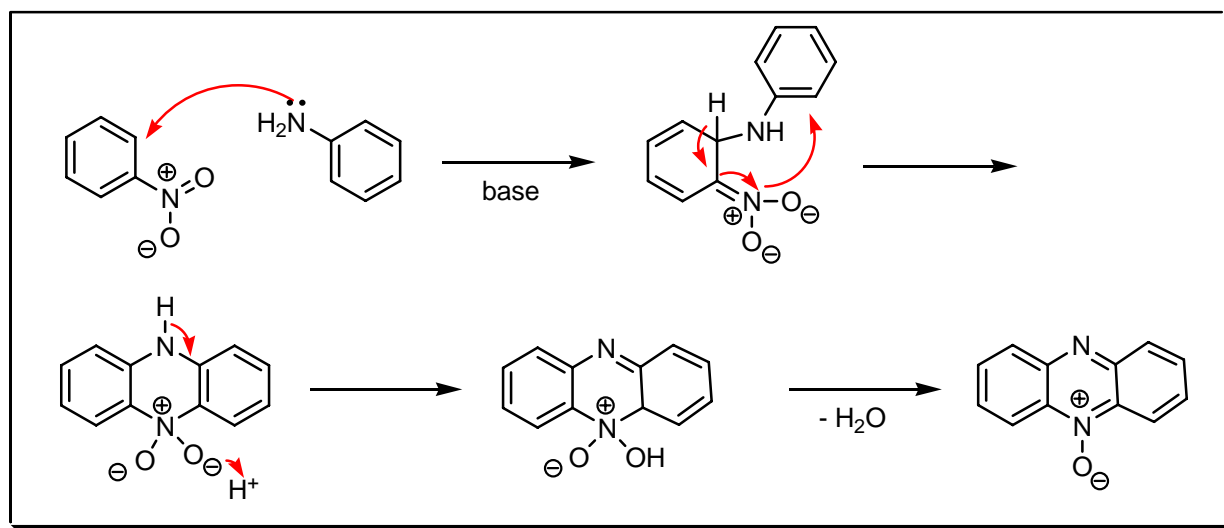
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**EXAMPLE :**

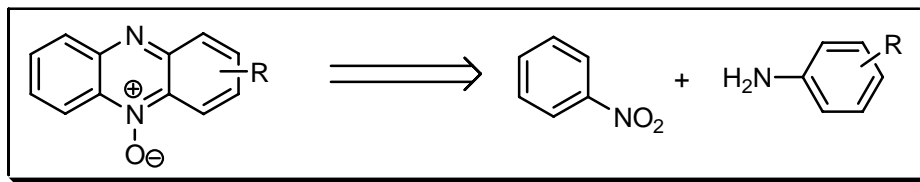


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**MECHANISM :**



## DISCONNECTION :



## NOTES :

Phenazine-*N*-oxide is synthesised from anilines and nitrobenzene. For a more exact and detailed reaction mechanism see **Yoshioka** *et al.*

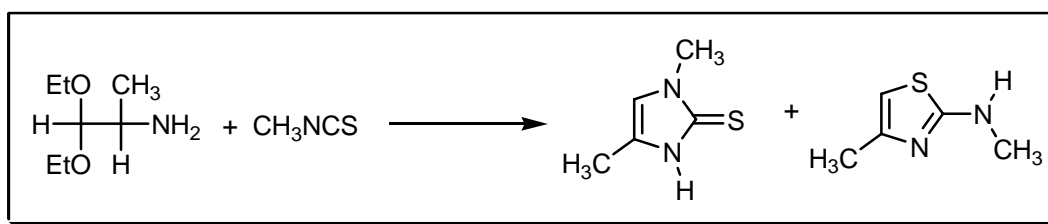
## REFERENCES :

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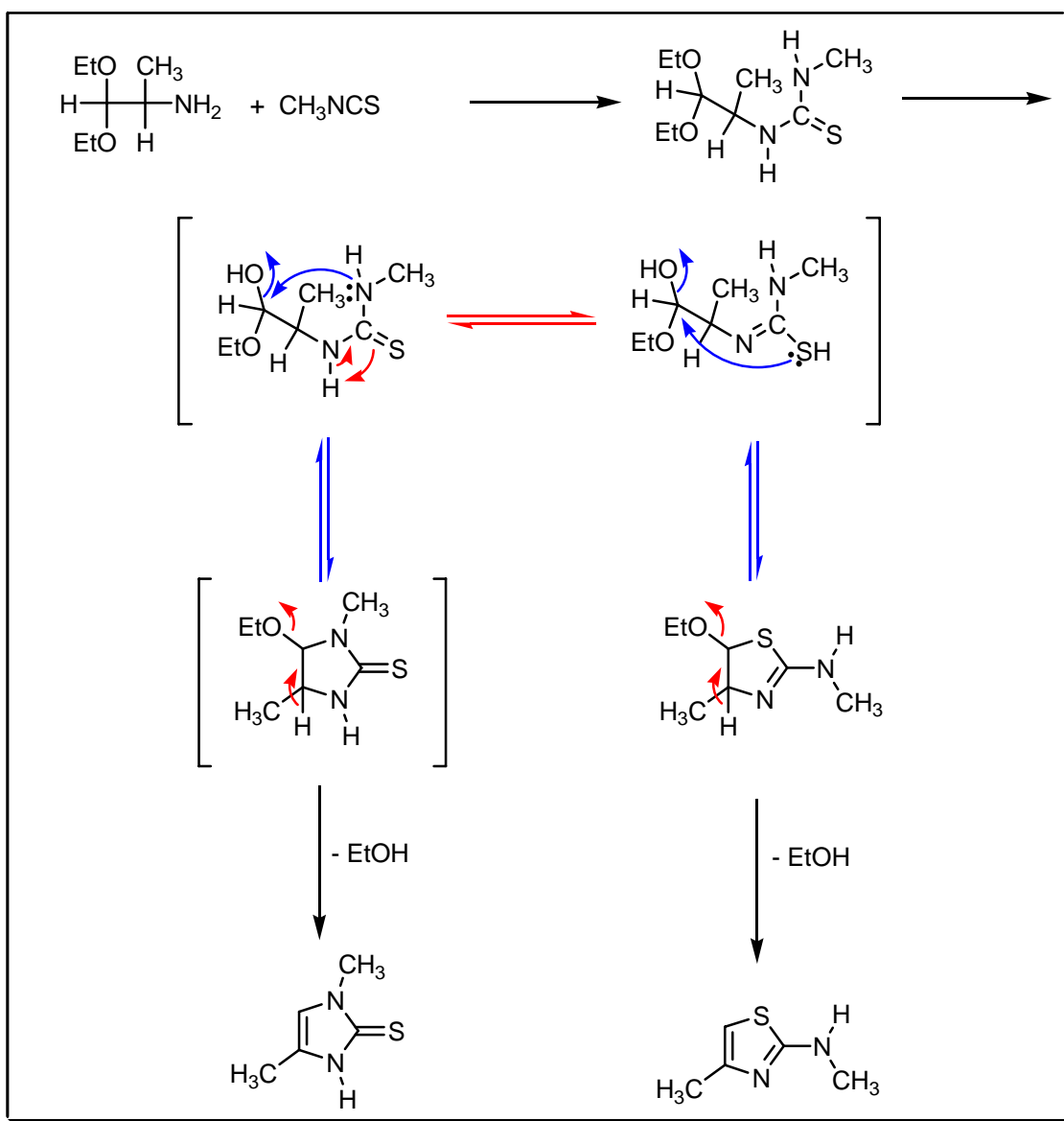
## COMMENTS :

## WOHL – MARCKWALD SYNTHESIS

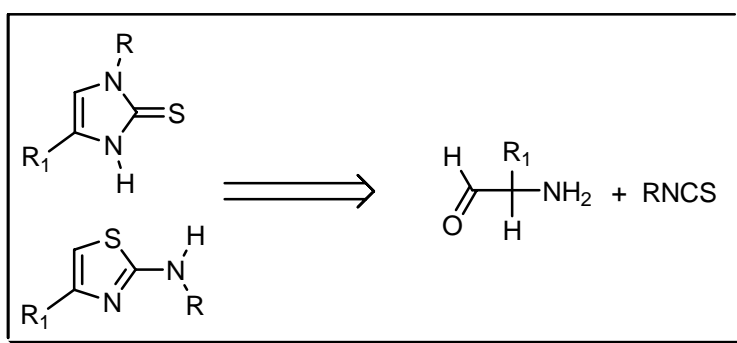
### EXAMPLE :



# MECHANISM :



# DISCONNECTION :



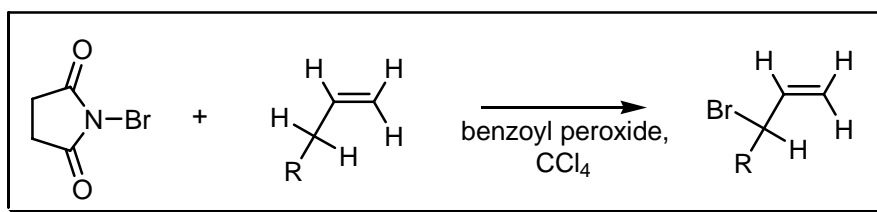
**NOTES :**

An  $\alpha$ -amino aldehyde (an acetal can also be used) or ketone reacts with potassium thiocyanate or alkyl- or aryl-isothiocyanate to give a substituted thiourea which with acid yields a glyoxazoline-2-thiol. The 2-thiol group can be removed by oxidation. In certain instances substituted  $\alpha$ -amino-acetals yield thiazolines or mixtures of glyoxalines, thiazolines and thiazoles. See also **Debus**, **Maquenne**, **Radziszewski**, **Wallach** and **Weidenhagen** reactions.

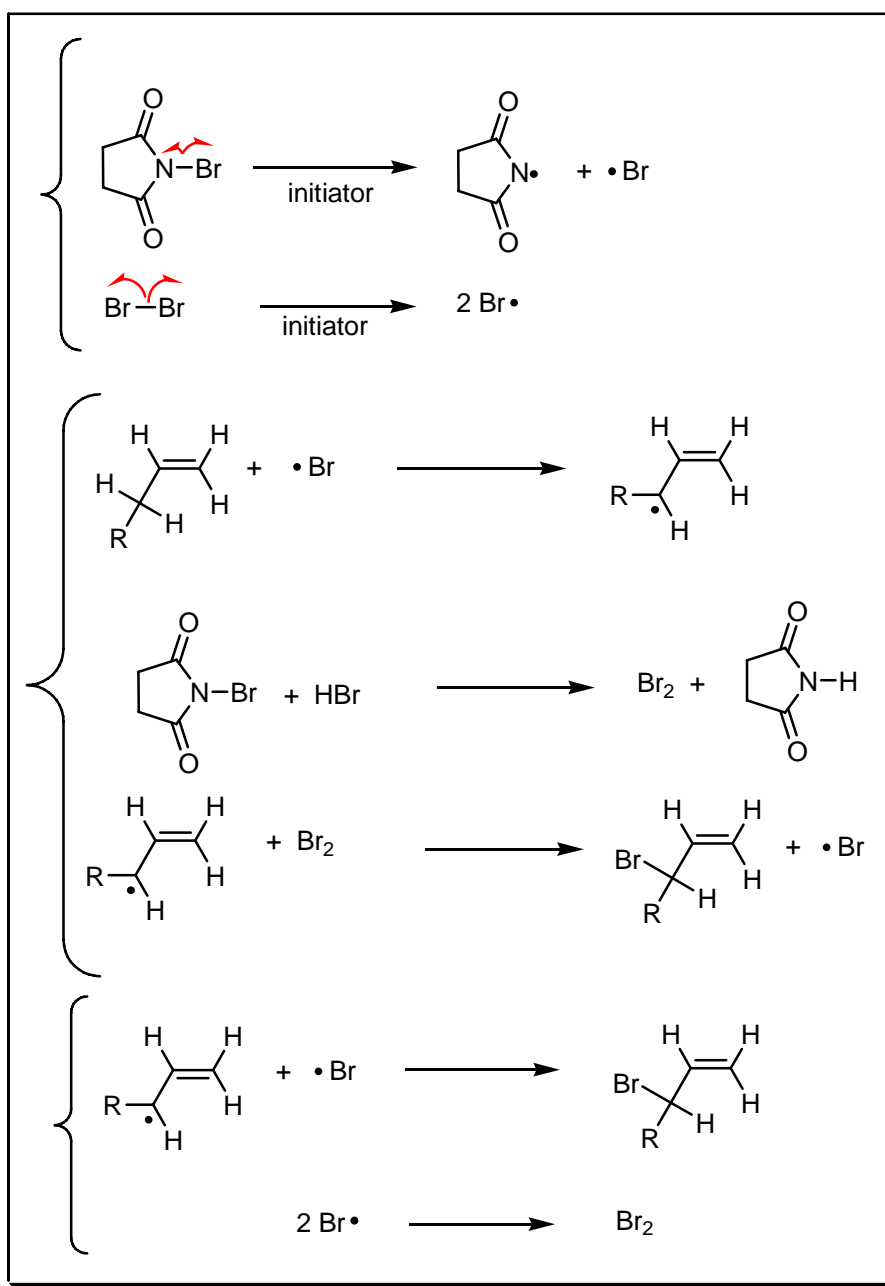
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**REFERENCES :**

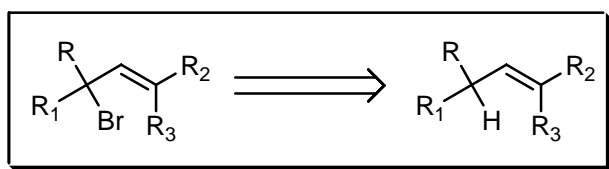
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- 

**COMMENTS :****WOHL – ZIEGLER BROMINATION****EXAMPLE :**

# MECHANISM :



# DISCONNECTION :



## NOTES :

The use of *N*-haloamides, especially *N*-bromosuccinimide (NBS) as brominating agents, *e.g.*, for the bromination of olefins. The method is of value in the production of  $\alpha$ -bromoketones. In some cases dehydrobromination occurs to introduce a new double bond. Certain applications of the reaction require the use of catalysts, *e.g.* light, benzoyl peroxide, metal chlorides. The **Buu-Hoï** modification uses *N*-chlorosuccinamide to chlorinate aliphatic compounds in the presence of peroxybenzoyl. NBS can also be used to brominate non-olefinic substrates.

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## REFERENCES :

**March** : 694

**Smith – March** : 911

**Smith** : 156

**Smith 2<sup>nd</sup>** : 126

**Houben – Weyl** : **5/4**, 221; **8**, 657; **E8d**, 80

**Org. Synth.** : **38**, 8; **42**, 26; **46**, 81; **56**, 49

**Org. Synth. Coll. Vol.** : **4**, 108; **5**, 145; **6**, 462

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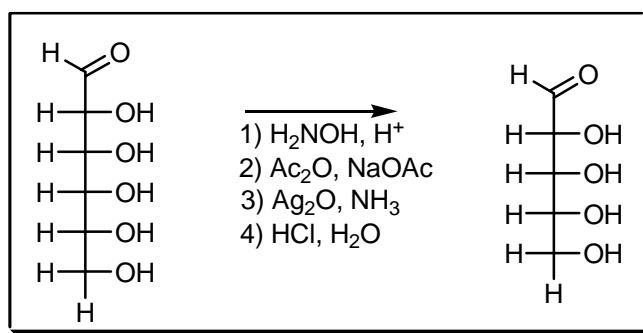
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## COMMENTS :

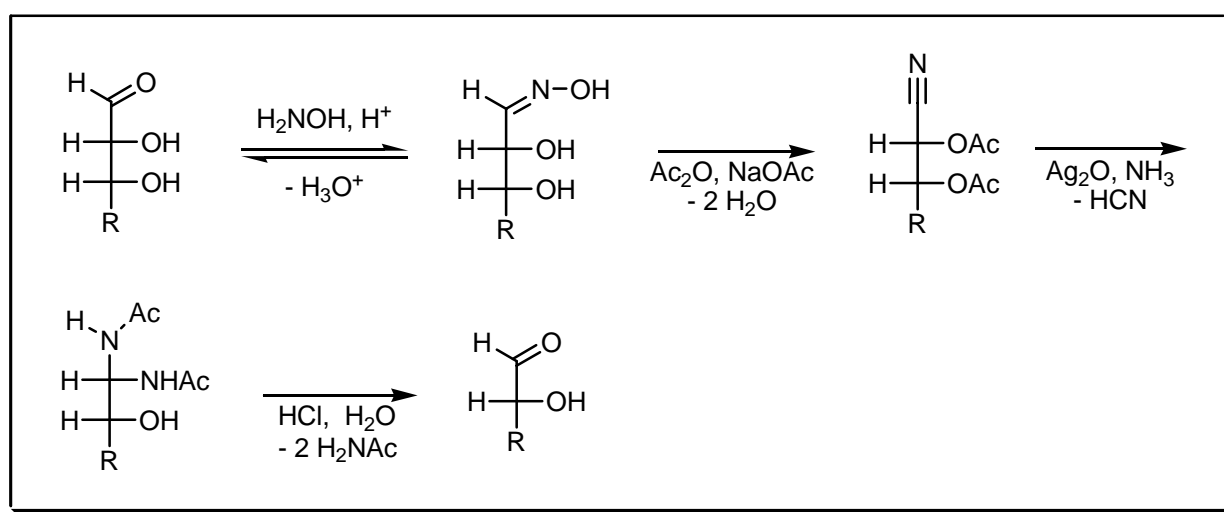


## WOHL DEGRADATION

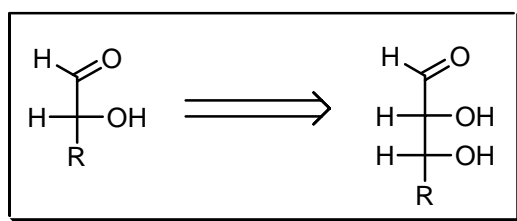
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

An aldose oxime is acetylated to yield the nitrile of the corresponding acetylated aldonic acid, which with ammoniacal silver oxide or ammonia yields the diacetimido compound of the aldose containing one carbon less than the original aldose. The diacetimido compound is then hydrolysed to the lower aldose. The method is nowadays of limited value. See also **Kiliani – Fischer**, **Ruff – Fenton**, **Weerman** degradation and **Zemplén** reactions.

## REFERENCES :

Org. Synth. : 20, 74

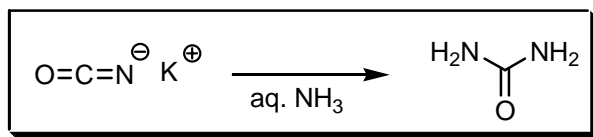
Org. Synth. Coll. Vol. : 3, 690

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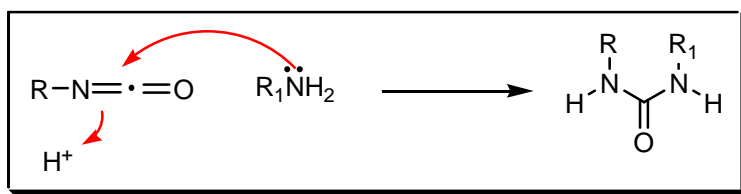
## COMMENTS :

## WÖHLER UREA SYNTHESIS

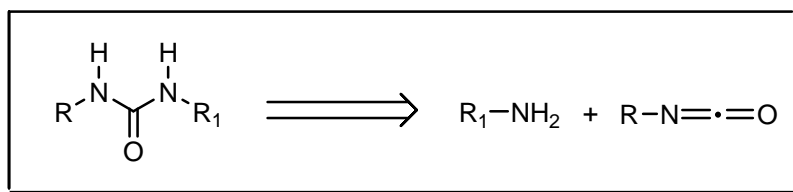
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



**NOTES :**

The classical formation of urea from an aqueous solution of ammonia to a salt of isocyanate. See also **Bosch – Meiser** reaction.

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**REFERENCES :**

**Smith – March** : 1191

**Org. Synth.** : **17**, 16; **21**, 83; **28**, 89; **31**, 8; **36**, 8; **37**, 52; **45**, 89; **56**, 95

**Org. Synth. Coll. Vol.** : **2**, 79; **3**, 617, 735; **4**, 49; 180; 213; 515; 700; **5**, 801; **6**, 951

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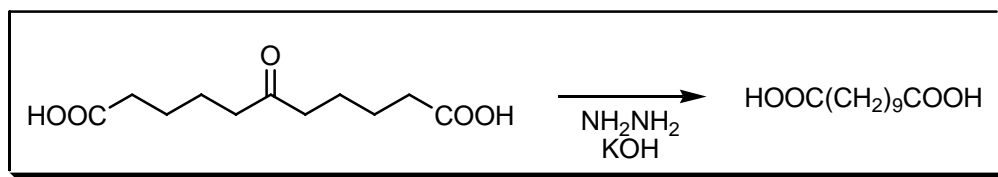
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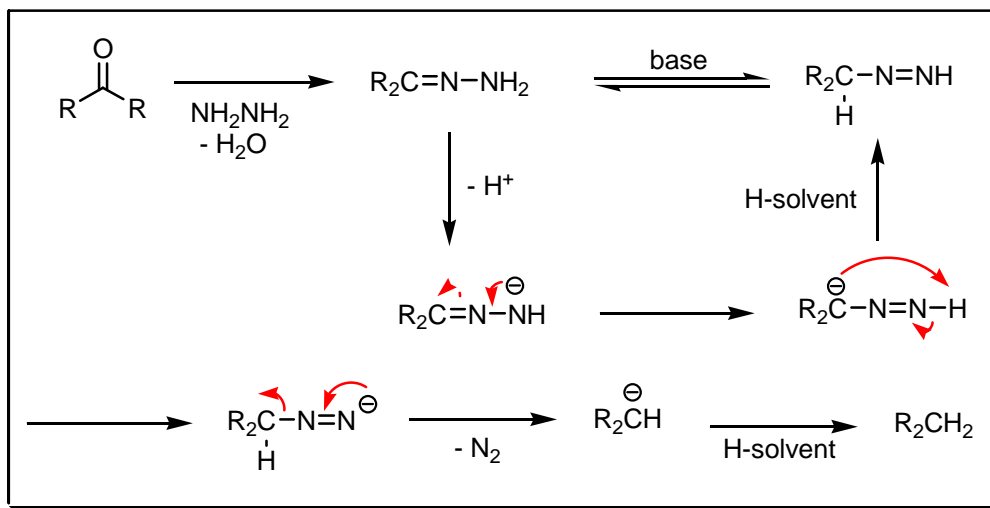
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4) G. Kauffman; S. Chooljian, *Chem. Ind. (London)*, 2000, **23**, 774.

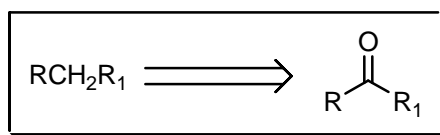
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**COMMENTS :****WOLFF – KISHNER REDUCTION****EXAMPLE :**

## MECHANISM :



## DISCONNECTION :



## NOTES :

The carbonyl group in aldehydes and ketones can be reduced to a methylene group by heating the azine, hydrazone or semicarbazone with an alkaline catalyst, e.g. potassium hydroxide or sodium ethoxide.  $\alpha,\beta$ -Unsaturated carbonyl compounds react abnormally. Certain hydroxy and amino-ketones may undergo elimination to yield an olefin (**Kishner** reduction elimination). In the original procedure, the carbonyl was heated with hydrazine hydrate and a base. This method has been almost completely replaced by the **Huang-Milon** modification, where the reaction is carried out in refluxing diethylene glycol. See also **Clemmensen**, **Schwenk**, and **Wolfrom – Karabinos** reactions.

## REFERENCES :

March : 1209

Smith – March : 1547

Smith : 473

Smith 2<sup>nd</sup> : 411, 1094, 1136

Houben – Weyl : 5/1a, 251; E6a, 407, 719; E8a, 904; E8b, 525; E14b, 596

Org. React. : 4, 378

Org. Synth. : 43, 34

Org. Synth. Coll. Vol. : 5, 533

Science of Synthesis : 10, 322, 340, 619, 737, 783

1) N. Kishner, *J. Russ. Phys. Chem. Ges.*, 1911, **43**, 582.

2) L. Wolff, *Liebigs Ann. Chem.*, 1912, **394**, 1912.

3) Huang-Milon, *J. Am. Chem. Soc.*, 1946, **68**, 2487.

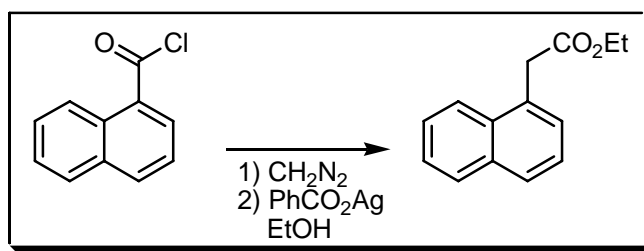
- 4) H.H. Szmant; C.M. Harmuth, *J. Am. Chem. Soc.*, 1964, **86**, 2909.  
5) T. Momose; O. Muraoka, *Tetrahedron Lett.*, 1978, **19**, 1125.  
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9) C.G. Bashore; I.J. Samardjiev; J. Bordner; J.W. Coe, *J. Am. Chem. Soc.*, 2003, **125**, 3268.  
10) M.E. Furrow; A.G. Myers, *J. Am. Chem. Soc.*, 2004, **126**, 5436.
- 

**COMMENTS :**

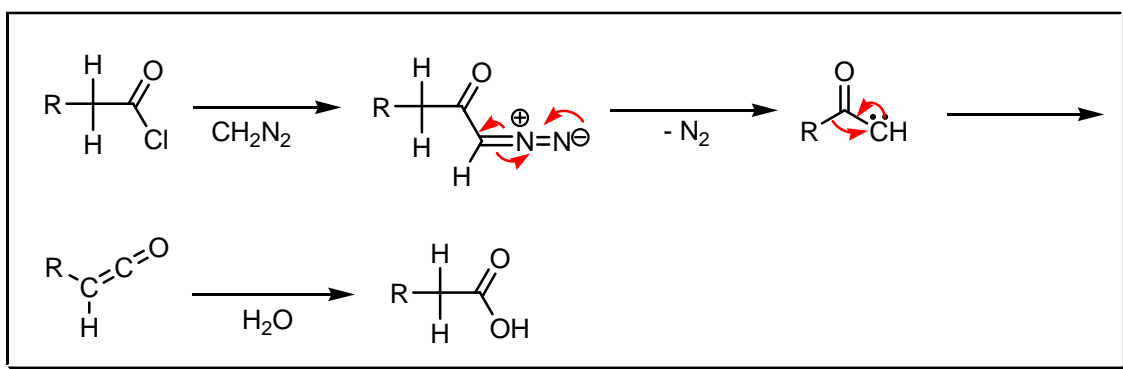
## WOLFF REARRANGEMENT

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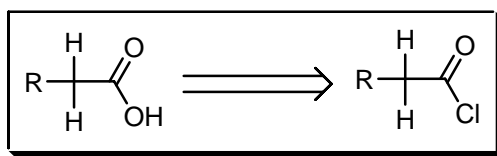
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

$\alpha$ -Diazoketenes can be converted by heating in solvents with or without heterogeneous or homogeneous catalysts, into nitrogen and a ketene, or into products that would be formed from the ketene by reaction with such hydroxy- and amino-compounds as are present in solution. Amines and silver oxide, Raney nickel, silver benzoate dissolved in triethylamine, and ultra-violet light are among the catalysts employed. See also **Arndt – Eistert**, **Clibbens – Nierenstein**, **Curtius**, **Lossen**, **Schmidlin** and **Süs** reactions.

## REFERENCES :

**March** : 201, 1083

**Smith – March** : 1250, 1405

**Smith** : 1453

**Smith 2<sup>nd</sup>** : 1199

**Houben – Weyl** : **E6a**, 702; **E11**, 241, 1334, 1415; **E14b**, 1371; **E15**, 2393, 2578; **E16b**, 463, 538, 597, 934; **E19b**, 1055, 1232, 1431, 1679

**Org. React.** : **1**, 39

**Org. Synth.** : **52**, 53

**Org. Synth. Coll. Vol.** : **6**, 840

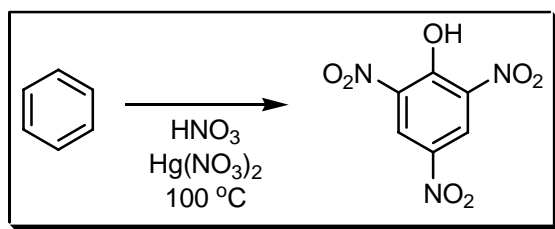
**Science of Synthesis** : **9**, 27, 71, 505

- 1) L. Wolff, *Liebigs Ann. Chem.*, 1912, **394**, 25.
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- 3) J. Meinwald; P.G. Gassman, *J. Am. Chem. Soc.*, 1960, **82**, 2857.
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- 9) W. Kirmse, *Eur. J. Org. Chem.*, 2002, 2193.
- 10) P.H. Dussault; C. Xu, *Tetrahedron Lett.*, 2004, **45**, 7455.
- 11) J.R. Davies; P.D. Kane; C.J. Moody; A.M.Z. Slawin, *J. Org. Chem.*, 2005, **70**, 5840.

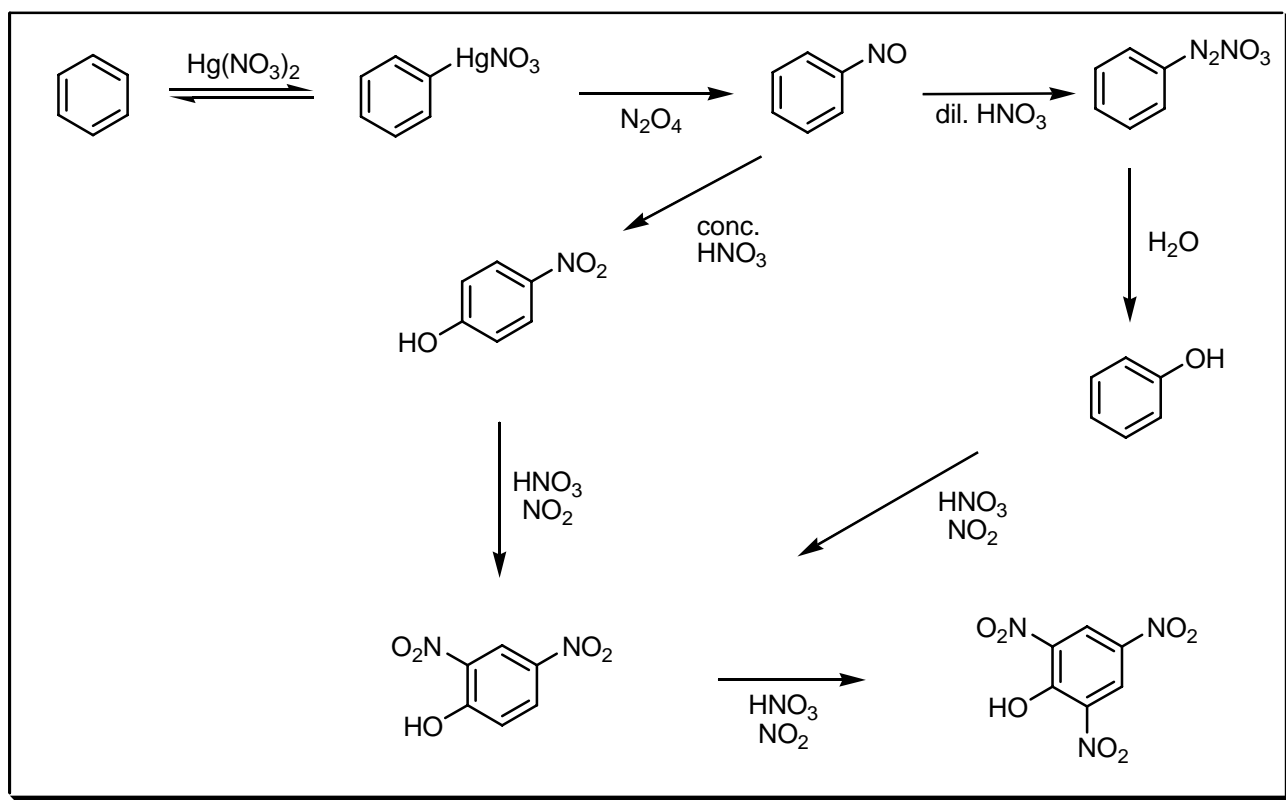
COMMENTS :

## WOLFFENSTEIN – BÖTERS REACTION

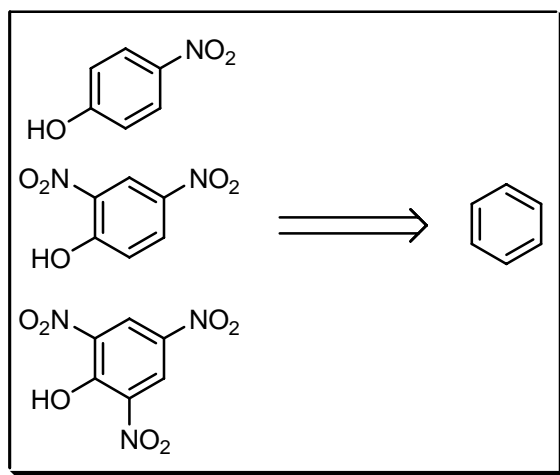
EXAMPLE :



MECHANISM :



## DISCONNECTION :



## NOTES :

The hydroxynitration of aromatic compounds to nitrophenols with nitric acid or higher oxides of nitrogen in the presence of a mercury salt as catalyst. See also **Zincke** halogenphenol nitration.

## REFERENCES :

Houben – Weyl : 10/1, 815

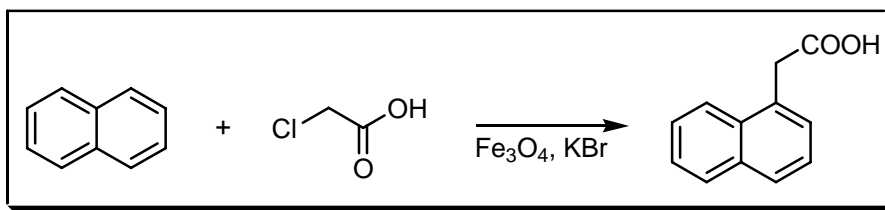
- 1) O. Böters; R. Wolffenstein, *U.S. Patent*, 1909, 923761.
- 2) O. Böters; R. Wolffenstein, *Ber. Dtsch. Chem. Ges.*, 1913, **46**, 586.
- 3) T.L. Davies, *J. Am. Chem. Soc.*, 1922, **44**, 1588.
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## COMMENTS :

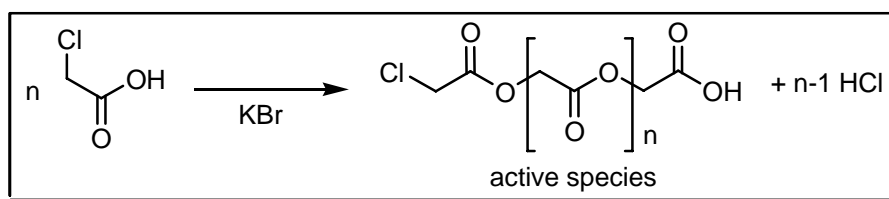


## WOLFRAM – SCHÖRNIG – HANSDORF CARBOXYMETHYLATION

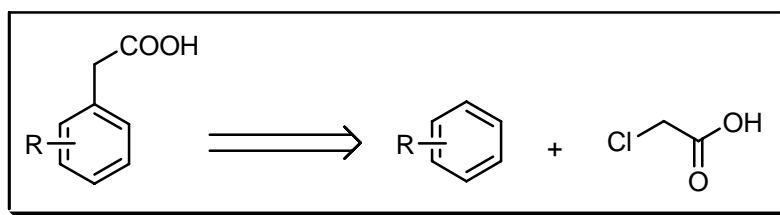
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The carboxymethylation of aromatics in the presence of oxidants or thermally or by photochemical means to afford aromatic acetic acids. See also **Kolbe – Schmitt** and **Reimer – Tiemann** reactions.

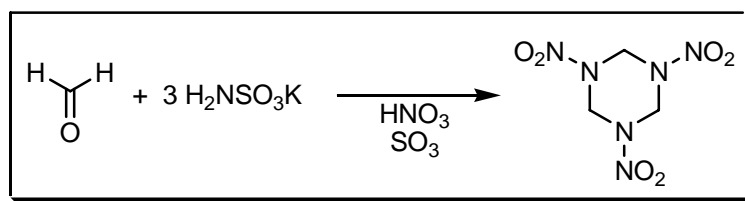
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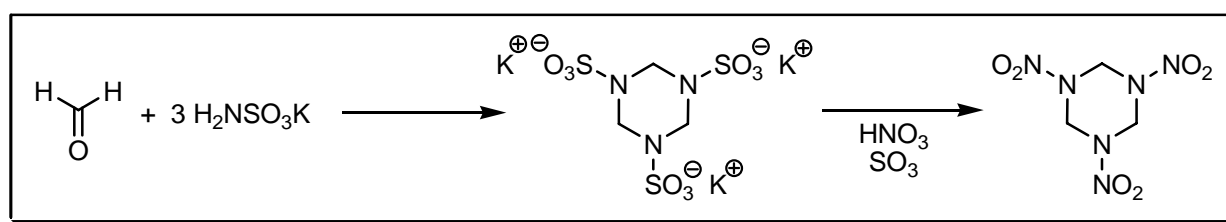
### COMMENTS :

## WOLFRAM SYNTHESIS OF CYCLONITE

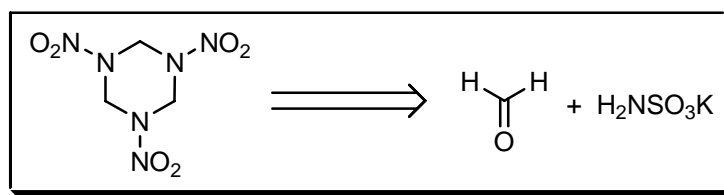
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

Formaldehyde reacts with potassium sulfamate to yield tripotassium 1,3,5-triazocyclohexane-1,3,5-trisulfonate that is nitrated to cyclonite using absolute nitric acid and sulfur dioxide. See also **Ebele – Schiessler – Ross, Hale** and **Knoffler – Bachmann** reactions.

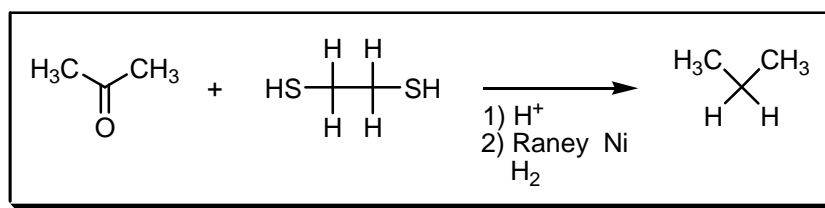
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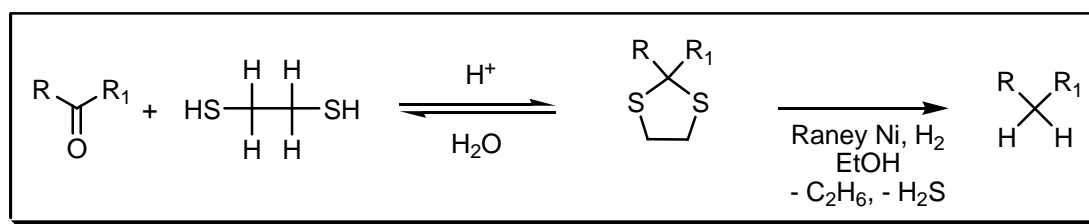
### COMMENTS :

## WOLFROM – KARABINOS REDUCTION

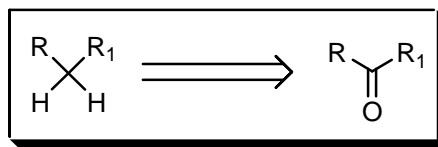
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The carbonyl groups of aldehydes and ketones can be reduced to the hydrocarbon stage by the hydrogenolysis of their thioacetals with Raney nickel in dilute ethanolic solution. See also **Clemmensen**, **Corey – Seebach** and **Wolff – Kishner** reactions.

### REFERENCES :

Houben – Weyl : 5/1a, 327

Org. React. : 8, 229

1) M.L. Wolfrom; J.V. Karabinos, *J. Am. Chem. Soc.*, 1944, **66**, 909.

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3) H. Hauptmann, *J. Am. Chem. Soc.*, 1947, **69**, 562.

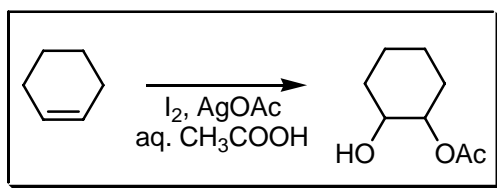
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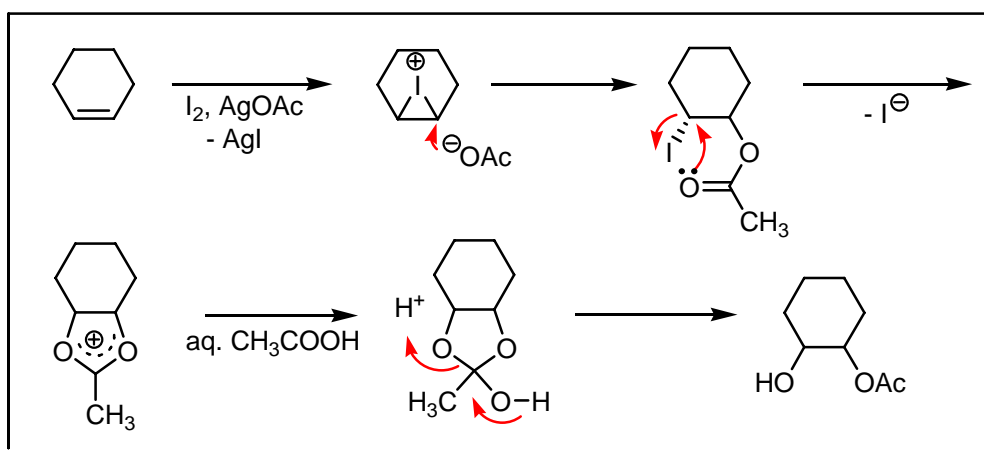
COMMENTS :

## WOODWARD C/S-HYDROXYLATION

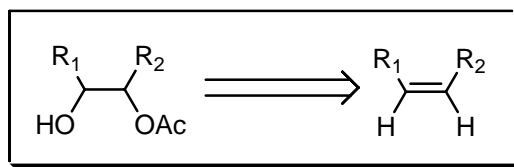
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

An olefinic compound is *cis*-hydroxylated by treatment with iodine and silver acetate in wet acetic acid followed by alkaline hydrolysis of the mixed mono- and di-acetates first formed. See also **Bäckvall**, **Birnbaum** – **Simonini**, **Brown**, **Milas**, **Prévost** and **Sharpless** dihydroxylation reactions.

REFERENCES :

Smith – March : 1050

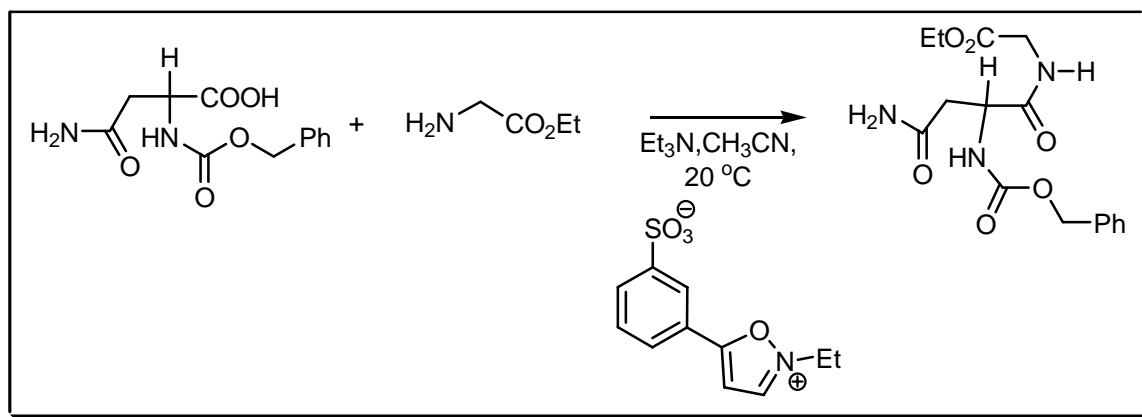
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COMMENTS :

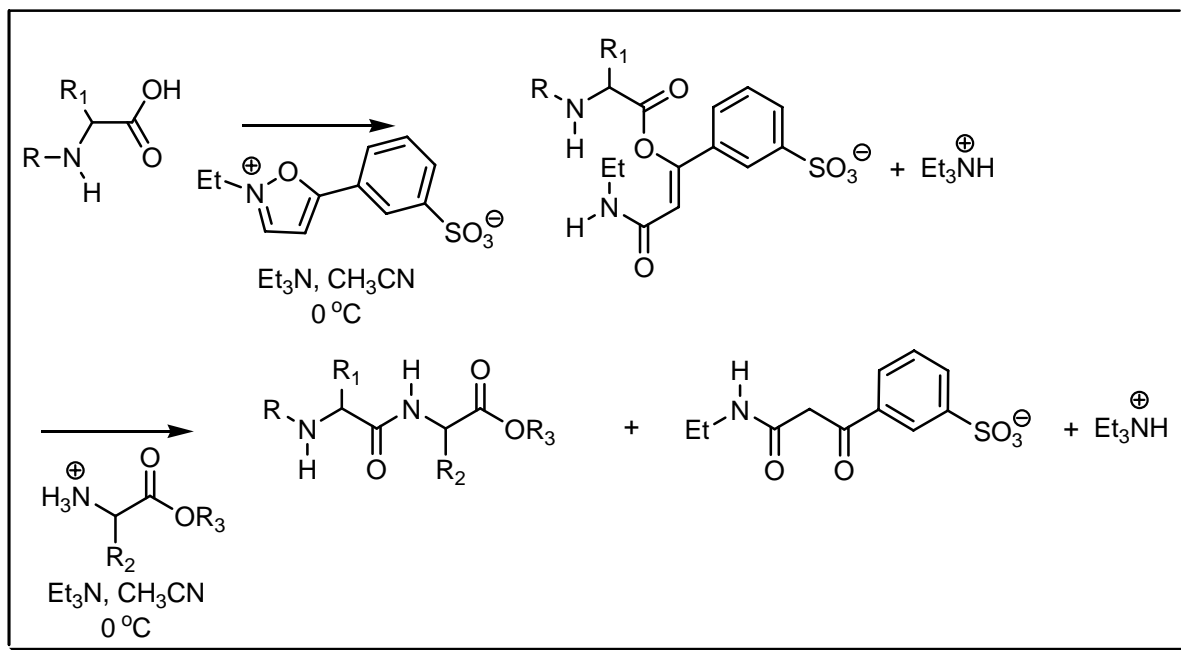
## WOODWARD PEPTIDE SYNTHESIS

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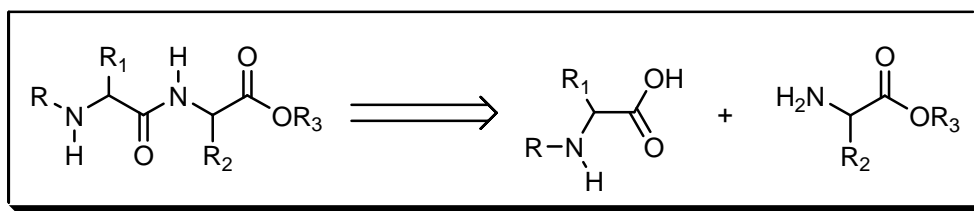
EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The peptide synthesis mediated by *N*-ethyl-5-phenylisoxazolium-3'-sulphonate (**Woodward reagent K**).

## REFERENCES :

**Org. Synth.** : **56**, 88

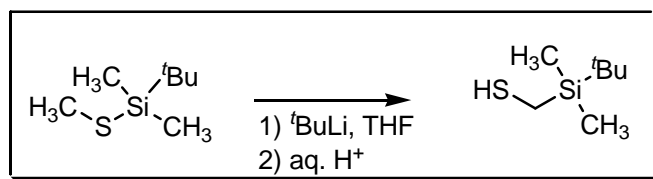
**Org. Synth. Coll. Vol.** : **6**, 263

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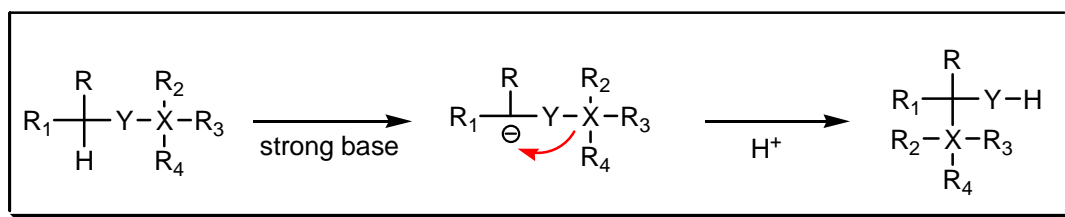
COMMENTS :

## WRIGHT – WEST GERMYL MIGRATION

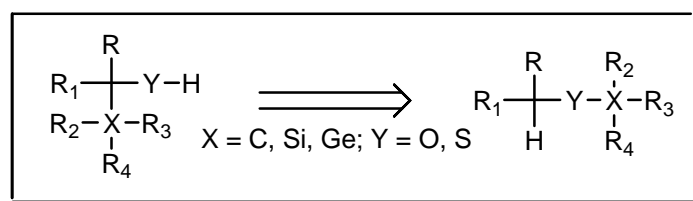
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The transformation of silyl and germynyl ethers or sulfides into their isomeric alcohols or thiols. These reactions, similar to the **Wittig** rearrangement, take place through electrophilic rearrangements in the presence of excess strong base. See also **Brook** rearrangement and **[1,2]-Wittig** rearrangement.

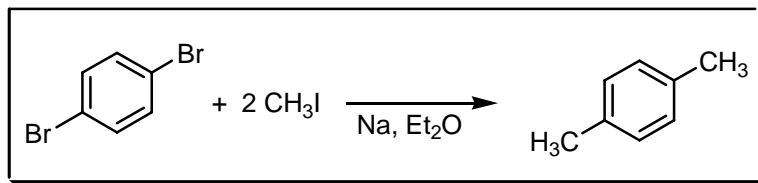
REFERENCES :

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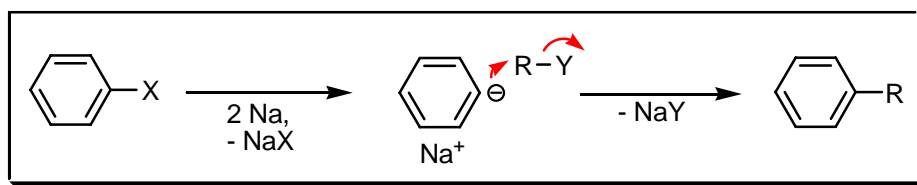
COMMENTS :

## WURTZ – FITTIG REACTION

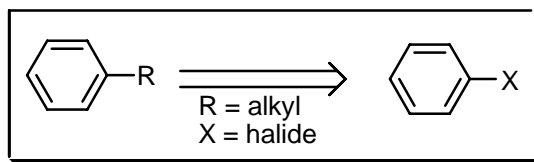
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

This is the **Wurtz** reaction carried out on a mixture of alkyl and aryl halides.

REFERENCES :

March : 449

Smith – March : 535

Houben – Weyl : 5/1a, 480; E19a, 876

Org. Synth. : 25, 11; 51, 55

Org. Synth. Coll. Vol. : 3, 157; 6, 133

1) A. Wurtz, *Ann. Chim. (Paris)*, 1855, **44**, 275.

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**COMMENTS :**

## WURTZ REACTION

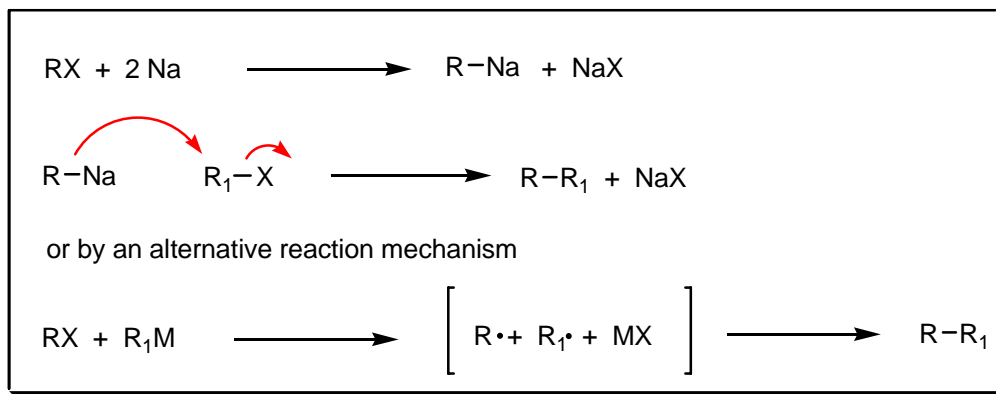
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**EXAMPLE :**



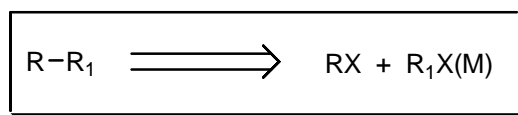
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**MECHANISM :**



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**DISCONNECTION :**



## NOTES :

The synthesis of alkyl hydrocarbons by the interaction of alkyl halides with sodium or finely divided silver or copper. Tetraphenylethylene has been used as catalyst. The reaction has been extended to silicon and tin compounds. The reaction has had limited utility due to many side reactions. See also **Wislicenus**, **Wurtz – Grignard** and **Wurtz – Fittig** reactions.

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## REFERENCES :

**March** : 449

**Smith – March** : 535

**Smith** : 726

**Smith 2<sup>nd</sup>** : 613

**Houben – Weyl** : **5/1b**, 451; **E19a**, 101, 876

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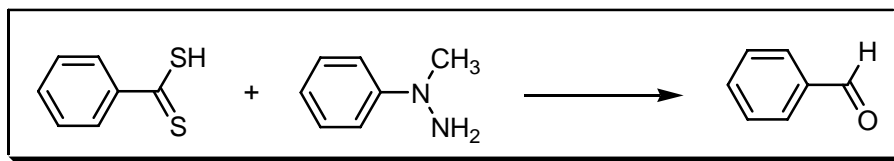
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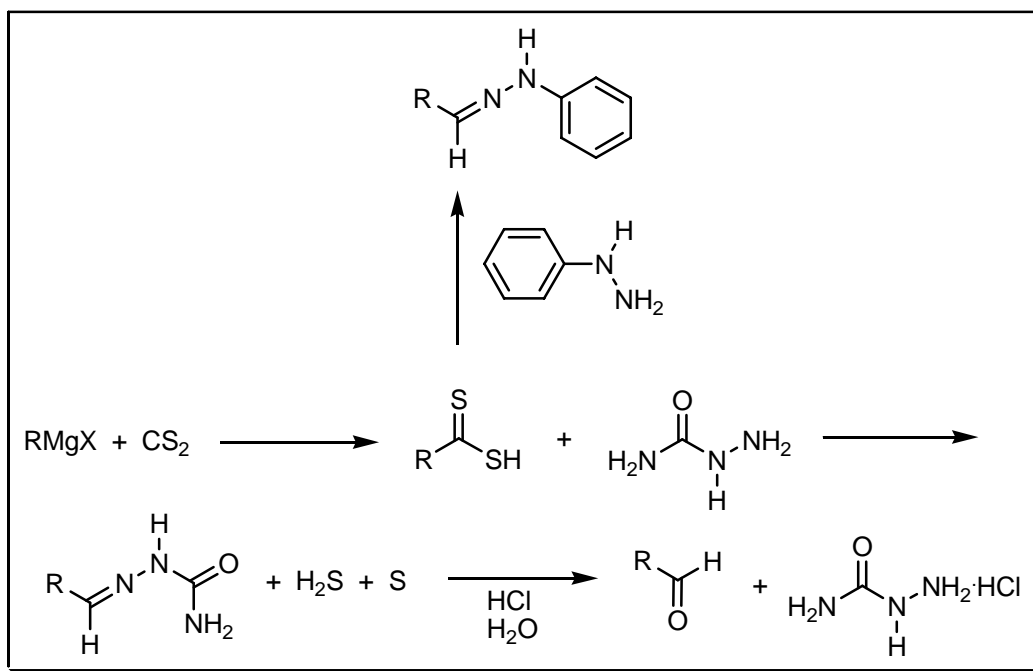
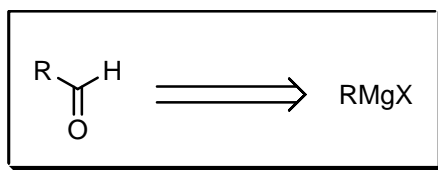
## COMMENTS :

## WUYTS SYNTHESIS

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### EXAMPLE :



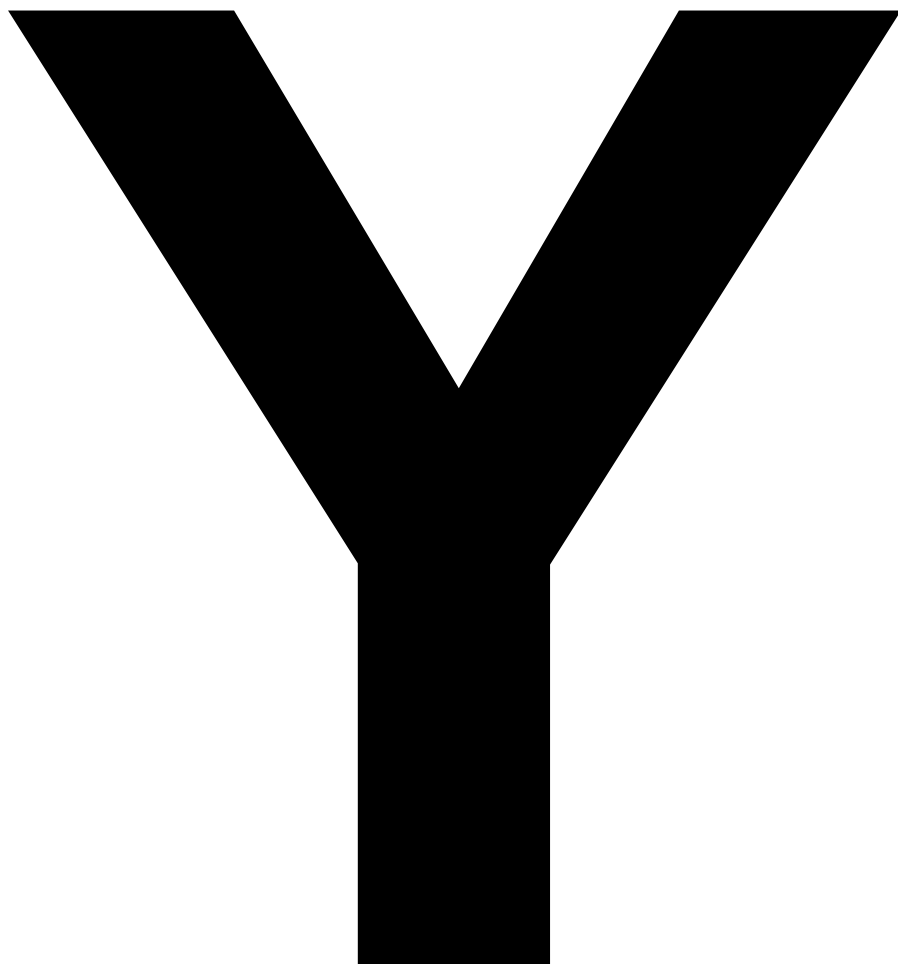
**MECHANISM :****DISCONNECTION :****NOTES :**

Aromatic aldehydes are obtained from the corresponding dithio-acids and *N,N*-methylphenylhydrazine, semicarbazide, or hydroxylamine followed by hydrolysis. The dithio-acid is prepared by the action of carbon disulfide on a **Grignard** reagent. See **McFadyen – Stevens** reaction.

**REFERENCES :**

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**COMMENTS :**



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## Y

YAMADA PEPTIDE COUPLING · 1893

YAMAGUCHI – HIRAO REACTION · 1894

YAMAGUCHI REACTION · 1895

YAMAMOTO ALLYLATION · 1897

YAMAMOTO INDOLE-1 SYNTHESIS · 1899

YAMAMOTO INDOLE-2 SYNTHESIS · 1901

YAMAMOTO KETONE SYNTHESIS · 1903

YAMAMOTO MACROLACTONISATION · 1905

YAMAZAKI – CLAUSEN GUANINE SYNTHESIS · 1906

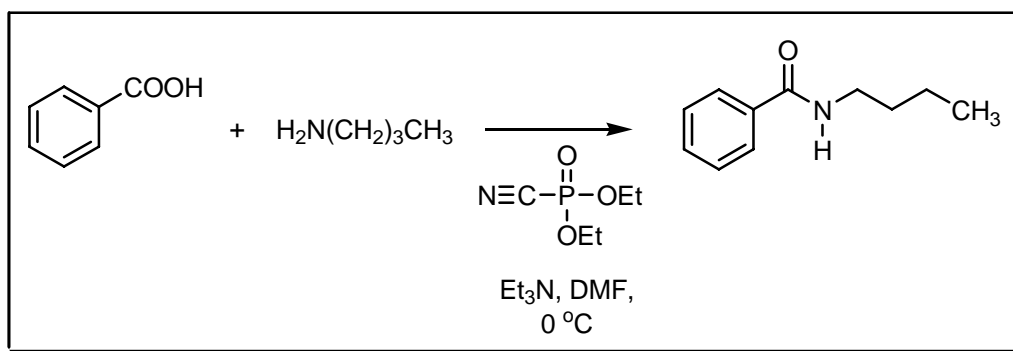
YAMAZAKI CYANOANILINE SYNTHESIS · 1908

YANG CYCLISATION · 1909

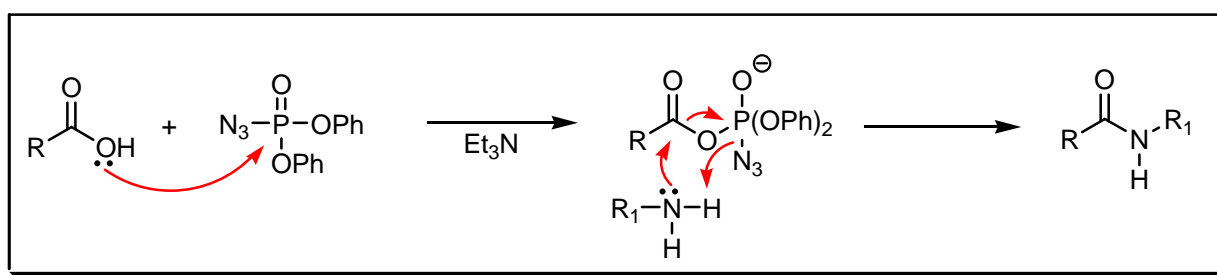
YUROVSKAYA INDOLE SYNTHESIS · 1911

## YAMADA PEPTIDE COUPLING

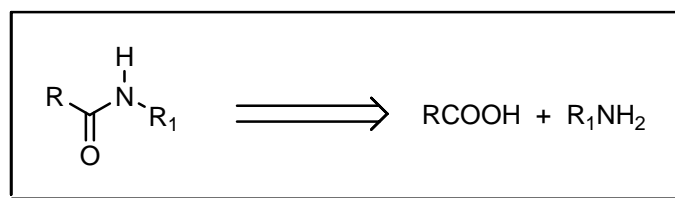
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The use of diphenylphosphoryl azide (DPPA) or diethylphosphoryl cyanide (DEPC) as an efficient coupling reagent for the amide bond formation of peptides from carboxyl and amino components. See also **Kita** reaction.

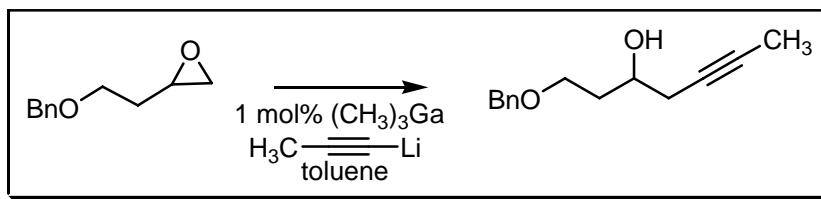
### REFERENCES :

- 1) T. Shioiri; K. Ninomiya; S-i. Yamada, *J. Am. Chem. Soc.*, 1972, **94**, 6203.
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- 4) A. Guzman; E. Diaz, *Synth. Commun.*, 1997, **27**, 3035.
- 5) M. Mizuno; T. Shioiri, *Tetrahedron Lett.*, 1998, **39**, 9209.
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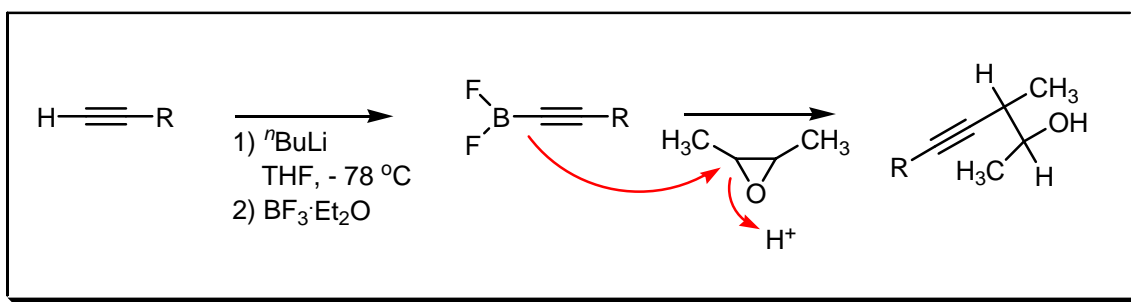
COMMENTS :

## YAMAGUCHI – HIRAO REACTION

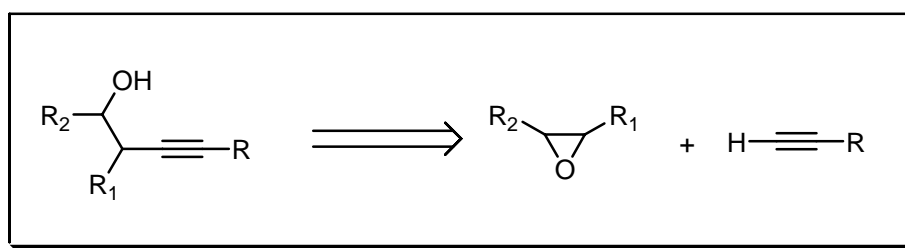
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The alkylation of lithioacetylides by substituted epoxides using  $\text{BF}_3\cdot\text{Et}_2\text{O}$ . The use of  $\text{BF}_3\cdot\text{THF}$  affords higher yields. Trimethylgallium has also been used to catalyse this reaction.

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- 2) K. Utimoto; C. Lambert; Y. Fukuda; H. Shiragami; H. Nozaki, *Tetrahedron Lett.*, 1984, **25**, 5423.
- 3) A.B. Evans; D.W. Knight, *Tetrahedron Lett.*, 2001, **42**, 6947.

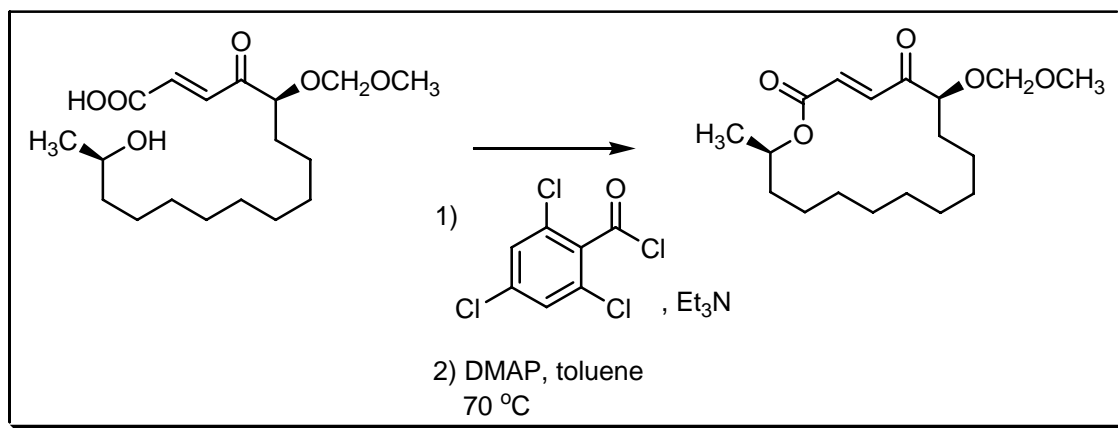
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## COMMENTS :

## YAMAGUCHI REACTION

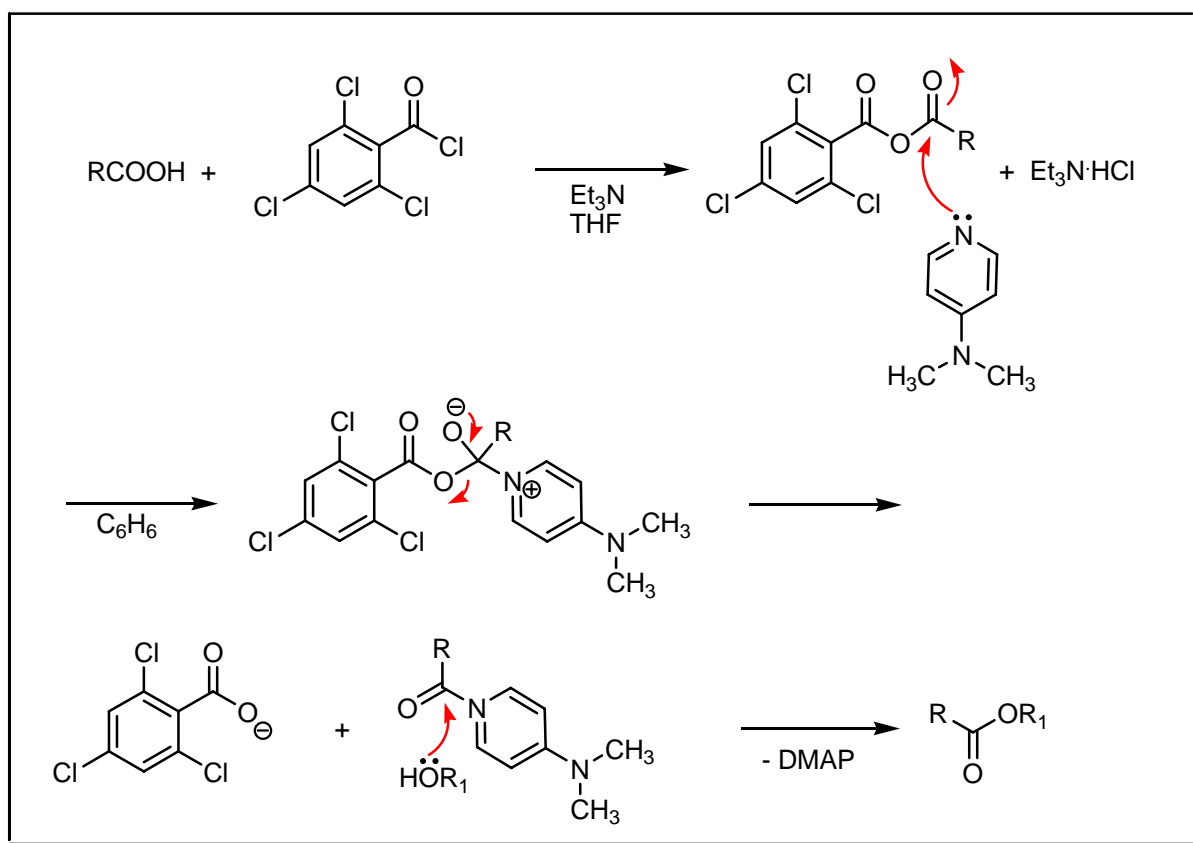
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### EXAMPLE :

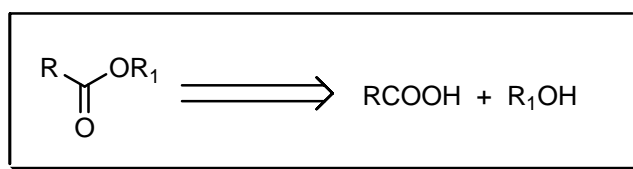




## MECHANISM :



## DISCONNECTION :



## NOTES :

The rapid and mild esterification or macrolactonisation method using 2,4,6-trichlorobenzoyl chloride as coupling reagent. The reaction has a high reaction rate and lacks any by-products. See also **Corey – Kwiatkowski**, **Corey – Nicolaou**, **Diels – Alder**, **Eastwood**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Hunsdiecker** ring-closure, **Julia – Paris – Kocienski – Lythgoe**, **Keck** macrolactonisation, **Kita**, **Krief – Reich – Chow**, **Masamune**, **McMurry**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Petasis** reaction, **Peterson**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Still – Gennari**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Takeda**, **Tebbe**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolakiewicz**, **Wittig** and **Yamamoto** macrolactonisation reactions.

## REFERENCES :

Smith 2<sup>nd</sup> : 527, 540

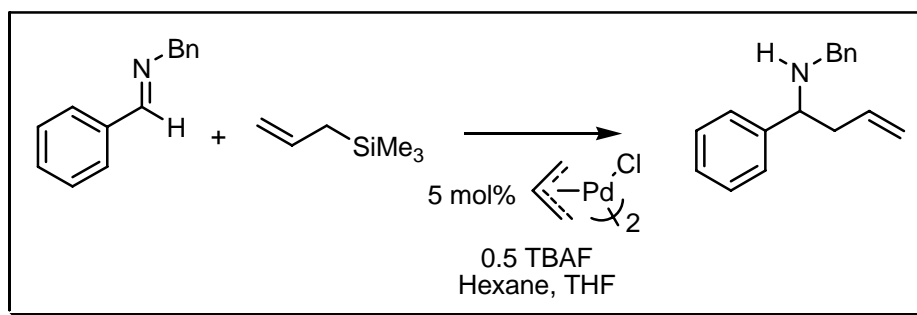
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  - 6) M. Berger; J. Mulzer, *J. Am. Chem. Soc.*, 1999, **121**, 8393.
  - 7) Y. Kobayashi; H. Okui, *J. Org. Chem.*, 2000, **65**, 612.
  - 8) A.K. Ghosh; Y. Wang; J.T. Kim, *J. Org. Chem.*, 2001, **66**, 8973.
  - 9) P.R. Blakemore; C.C. Browder; J. Hong; C.M. Lincoln; P.A. Nagorny; L.A. Robarge; D.J. Wardrop; J.D. White, *J. Org. Chem.*, 2005, **70**, 5449.
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**COMMENTS :**

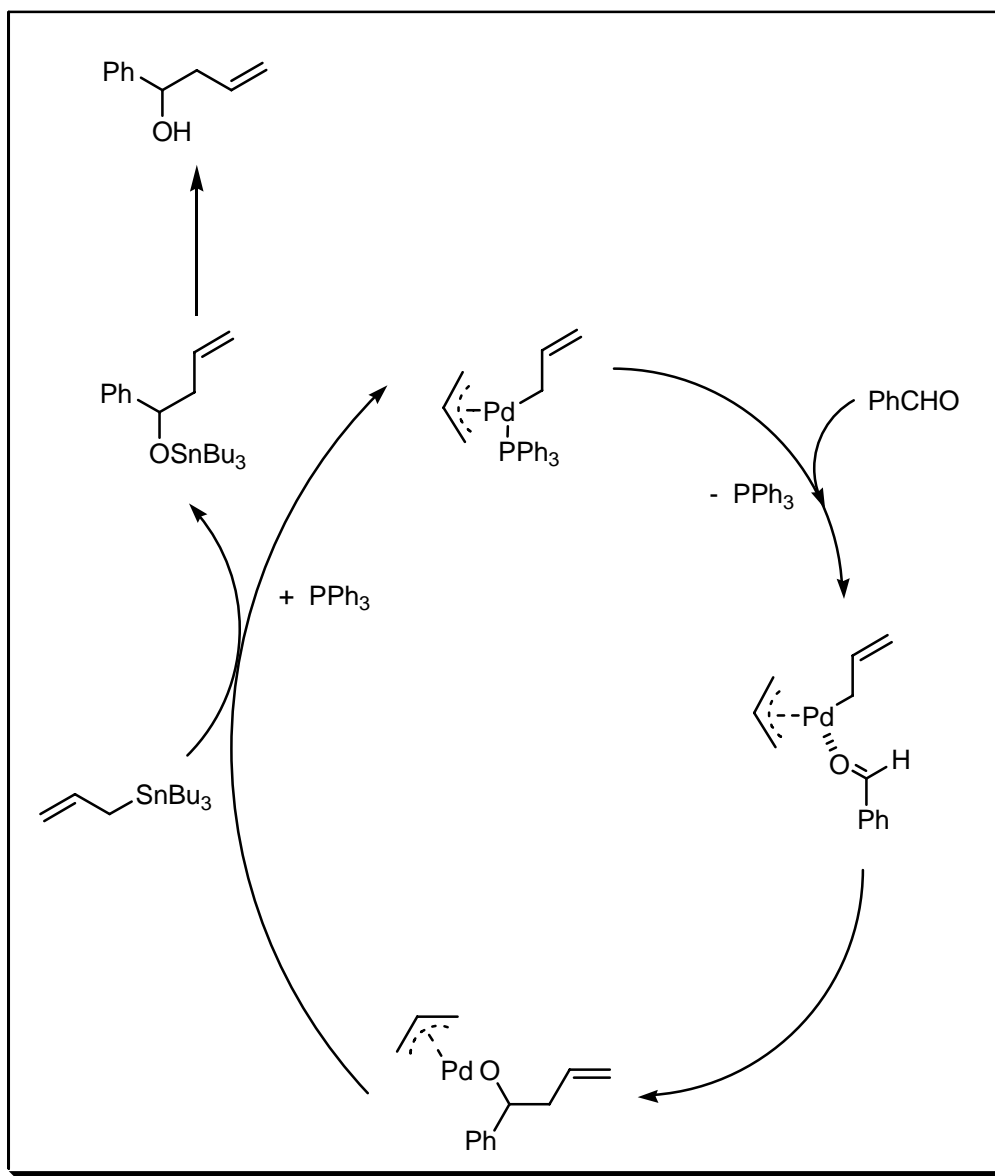
## YAMAMOTO ALLYLATION

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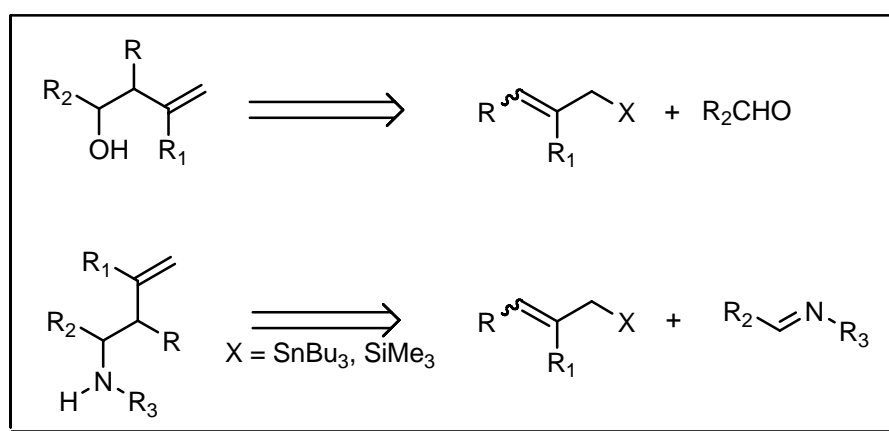
**EXAMPLE :**



## MECHANISM :



## DISCONNECTION :



## NOTES :

The asymmetric allylation of imines and aldehydes catalysed by chiral  $\pi$ -allylpalladium. See also **Hiyama** coupling.

## REFERENCES :

- 1) H. Nakamura; H. Iwama; Y. Yamamoto, *J. Am. Chem. Soc.*, 1996, **118**, 6641.
- 2) H. Nakamura; K. Nakamura; Y. Yamamoto, *J. Am. Chem. Soc.*, 1998, **120**, 4242.
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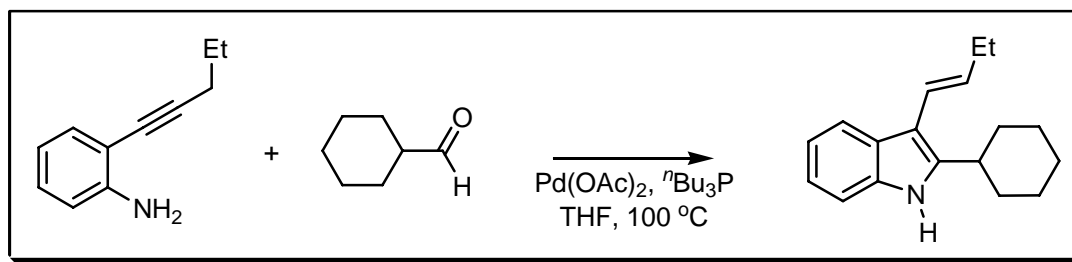
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## COMMENTS :

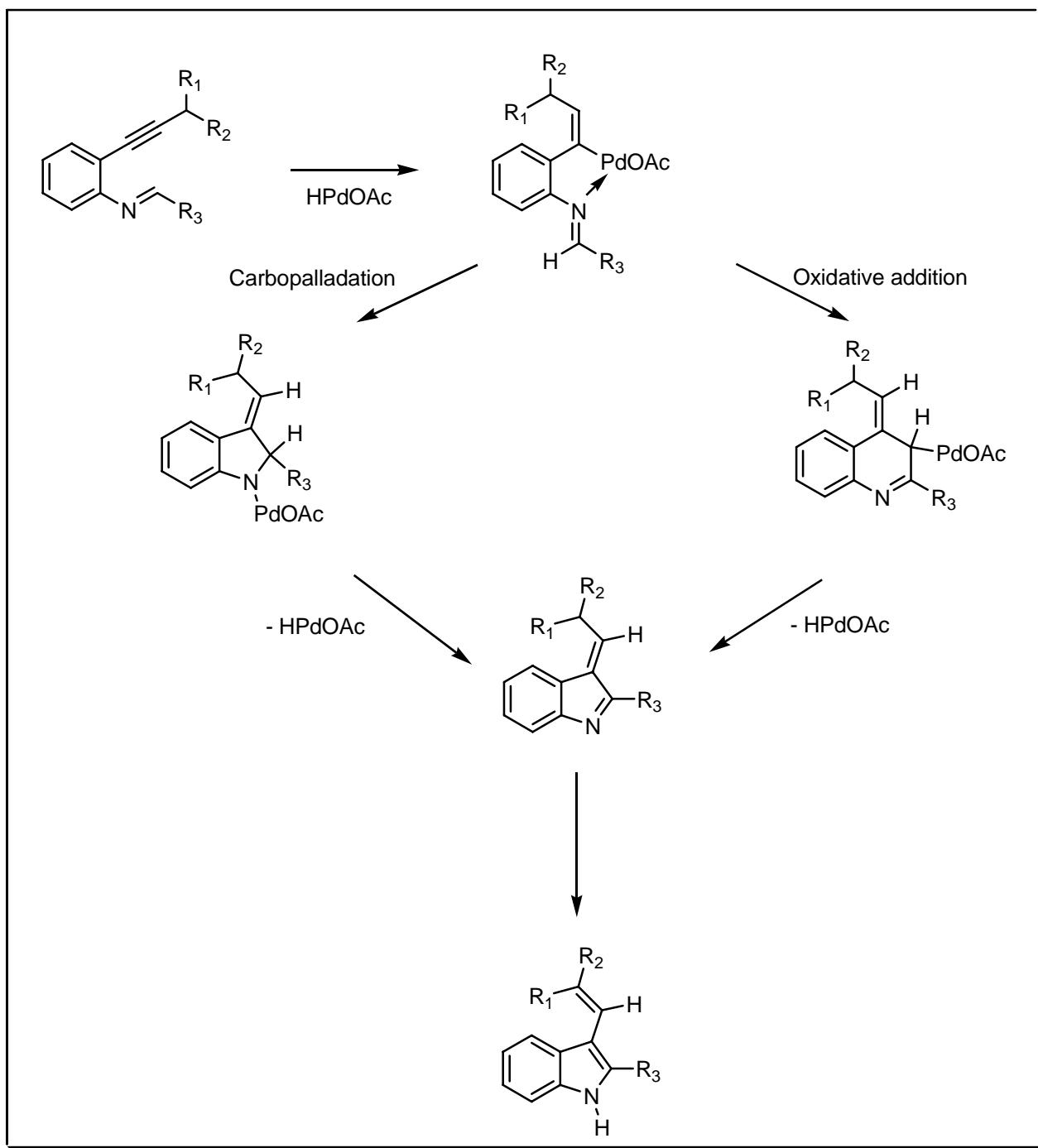
## YAMAMOTO INDOLE-1 SYNTHESIS

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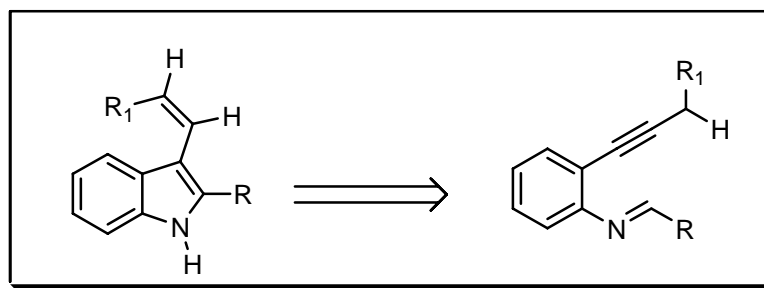
### EXAMPLE :



# MECHANISM :



# DISCONNECTION :



## NOTES :

The three component coupling for the synthesis of indole. The palladium-catalysed *intramolecular* cyclisation of an alkyne and imine on an aromatic ring will afford 3-alkenylindoles. Also tandem copper-catalysed tandem reaction between imines and alcohols to afford indoles. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu** indole, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert** indole, **Saegusa** indole, **Schmid**, **Smith**, **Sugasawa** indole, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender**, **Widman**, **Yamamoto** indole-2 and **Yurovskaya** reactions.

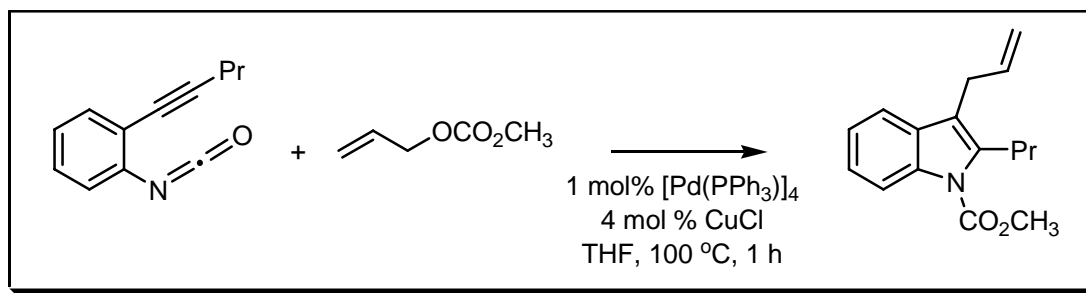
## REFERENCES :

- 1) A. Takeda; S. Kamijo; Y. Yamamoto, *J. Am. Chem. Soc.*, 2000, **122**, 5662.
- 2) S. Kamijo; Y. Sasaki; Y. Yamamoto, *Tetrahedron Lett.*, 2004, **45**, 35.

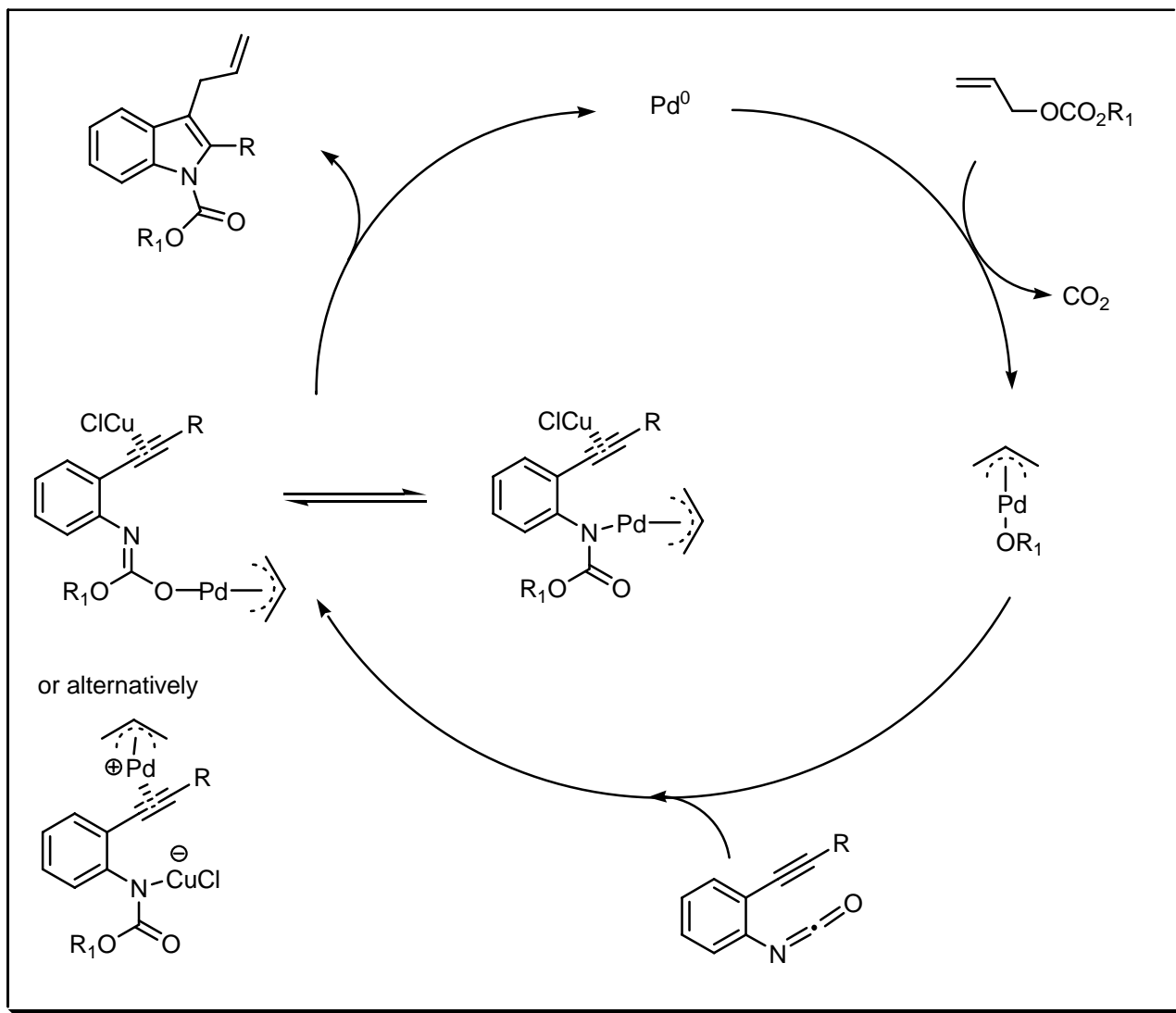
## COMMENTS :

## YAMAMOTO INDOLE-2 SYNTHESIS

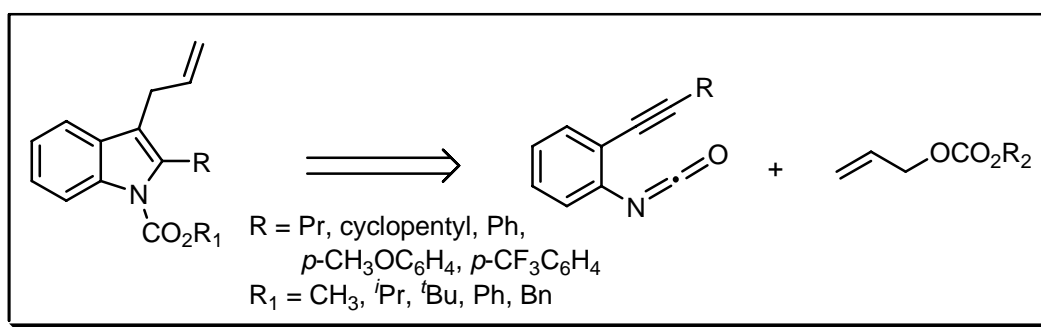
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The coupling of 2-alkynylphenylisocyanates and allylic carbonates using a palladium-copper(I) bimetallic catalyst to afford indoles. The role of  $\text{CuCl}$  is not fully understood but it is believed that it behaves as a Lewis acid to activate the alkynyl function. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman** indole, **Fischer** indole, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman** indole, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock** indole, **Leimgruber – Batcho**, **Lipp**, **Madelung** indole, **Magnus**, **Martin**,

**Montevecchi, Mori – Ban, Murphy, Naito, Natsume, Nenitzescu** indole, **Piloty – Robinson, Pschorr – Hoppe, Reissert** indole, **Saegusa** indole, **Schmid, Smith, Sugasawa** indole, **Sundberg, Thiele – Dimroth, Thyagarajan, Watanabe** heterocyclisation, **Watanabe** indole, **Weerman** indole, **Wender, Widman, Yamamoto** indole-1 and **Yurovskaya** reactions.

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#### REFERENCES :

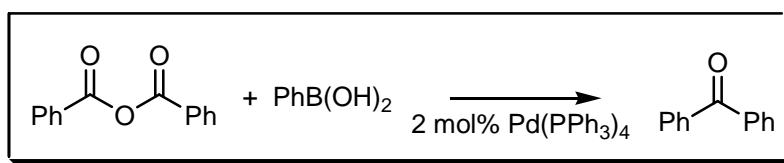
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  - 2) S. Kamijo; Y. Yamamoto, *J. Org. Chem.*, 2003, **68**, 4764.
- 

#### COMMENTS :

### YAMAMOTO KETONE SYNTHESIS

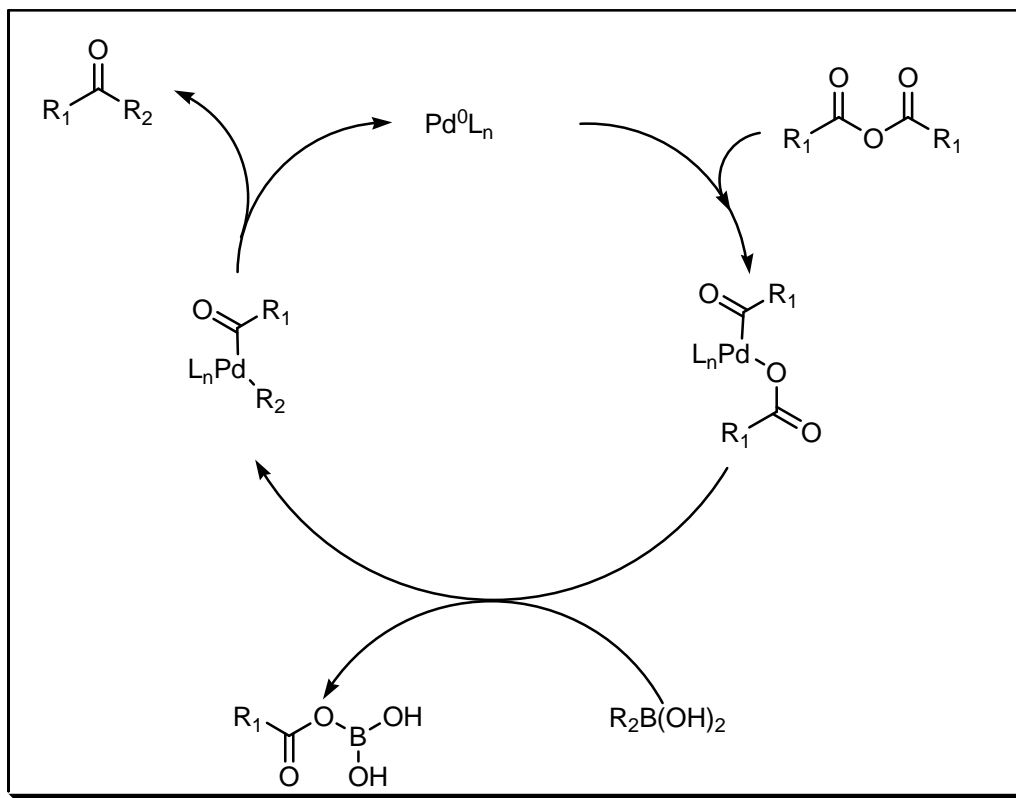
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#### EXAMPLE :

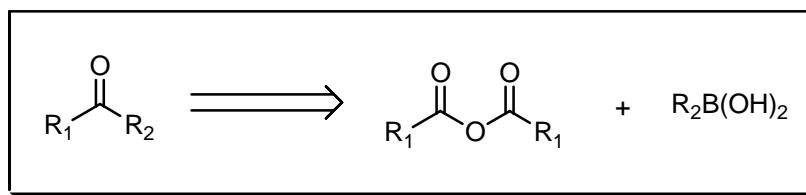




## MECHANISM :



## DISCONNECTION :



## NOTES :

The treatment of a carboxylic anhydride or ester with organoboron compounds in the presence of a palladium catalyst affords ketones. See also **Suzuki – Miyaura** reaction.

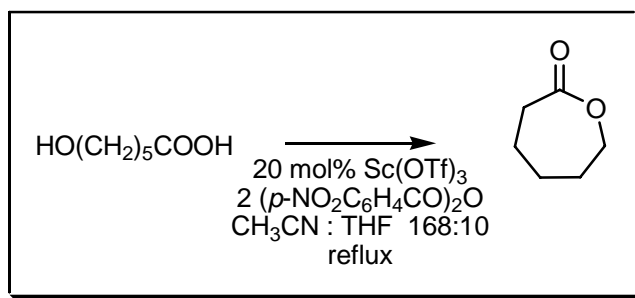
## REFERENCES :

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- 2) K. Nagayama; F. Kawataka; M. Sakamoto; I. Shimizu; A. Yamamoto, *Chem. Lett.*, 1995, 367.
- 3) K. Nagayama; I. Shimizu; A. Yamamoto, *Chem. Lett.*, 1998, 1143.
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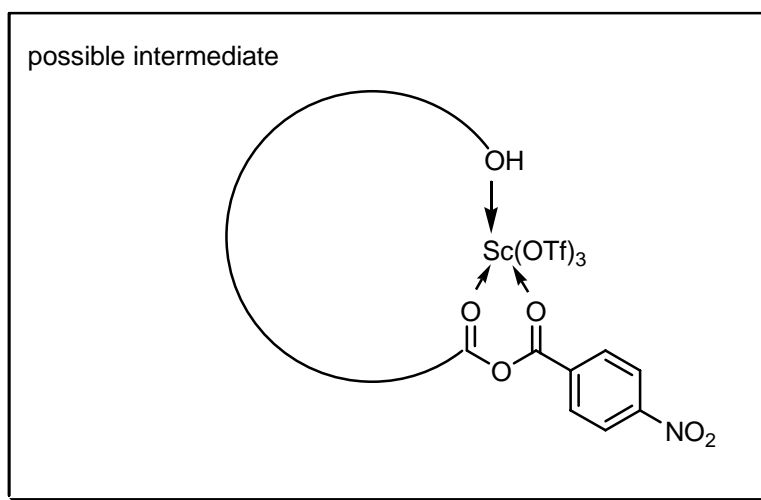
COMMENTS :

## YAMAMOTO MACROLACTONISATION

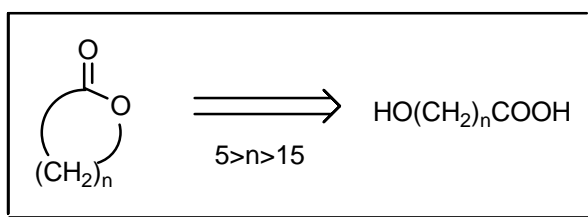
EXAMPLE :



MECHANISM :



DISCONNECTION :



## NOTES :

Scandium trifluoromethanesulfonate is a practical and useful Lewis acid for the selective macrolactonisation of  $\omega$ -hydroxy carboxylic acids. The exact mechanism is not fully understood. See also **Corey – Kwiatkowski**, **Corey – Nicolaou**, **Diels – Alder**, **Eastwood**, **Hanessian** macrolactonisation, **Hansley – Prelog – Stoll**, **Hunsdiecker** ring-closure, **Julia – Paris – Kocienski – Lythgoe**, **Keck** macrolactonisation, **Kita**, **Krief – Reich – Chow**, **Masamune**, **McMurry**, **Michael** condensation, **Mitsunobu**, **Mukaiyama** macrolactonisation-1, **Mukaiyama** macrolactonisation-2, **Murai** rearrangement, **Nagarajan – Kumar – Rao**, **Nozaki – Hiyama – Kishi (Takai – Utimoto)**, **Petasis reaction**, **Peterson**, **Raphael**, **Roush**, **Ružička** large ring synthesis, **Schmidt** macrolactonisation, **Spassow**, **Staab**, **Stacey**, **Steglich – Hassner**, **Still – Gennari**, **Stille – Migita – Kosugi**, **Story**, **Suzuki – Miyaura**, **Takeda**, **Tebbe**, **Thorpe – Ziegler**, **Venkataraman – Wagle**, **Vorbrüggen – Krolakiewicz**, **Wittig** and **Yamaguchi** reactions.

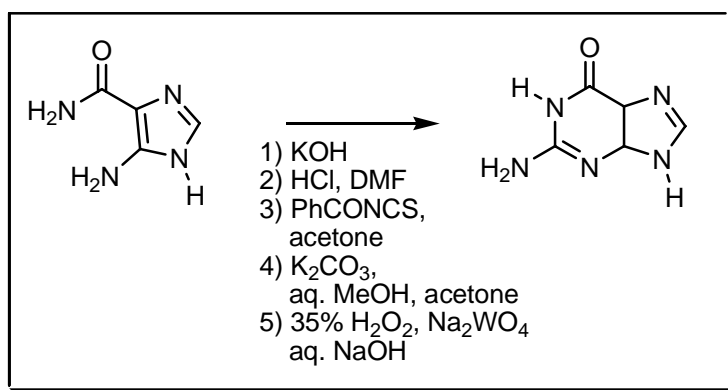
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- 2) K. Ishihara; M. Rubota; H. Kurihara; H. Yamamoto, *J. Org. Chem.*, 1996, **61**, 4560.
- 3) K.C. Nicolaou; A. Ritzén; K. Namoto; R.M. Buey; J.F. Díaz; J.M. Andreu; M. Wartmann; K.-H. Altmann; A. O'Brate; P. Giannakakou, *Tetrahedron*, 2002, **58**, 6413.

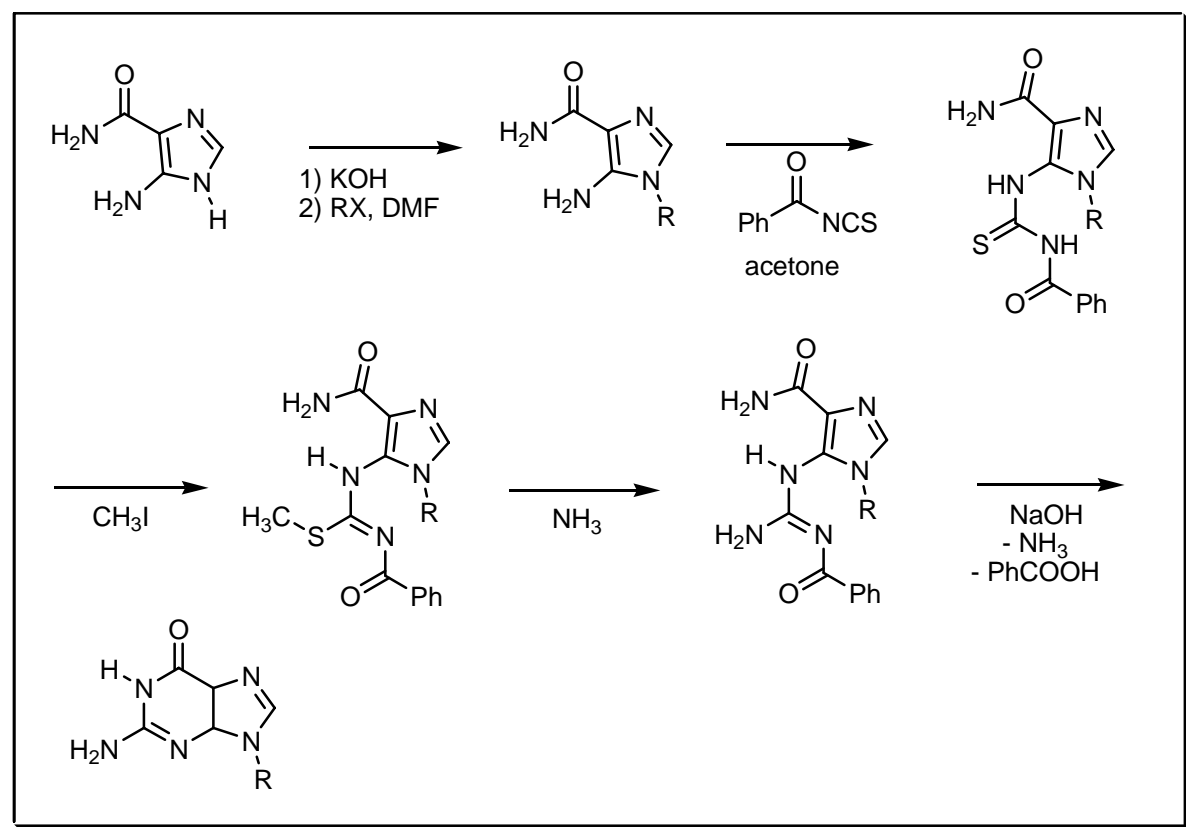
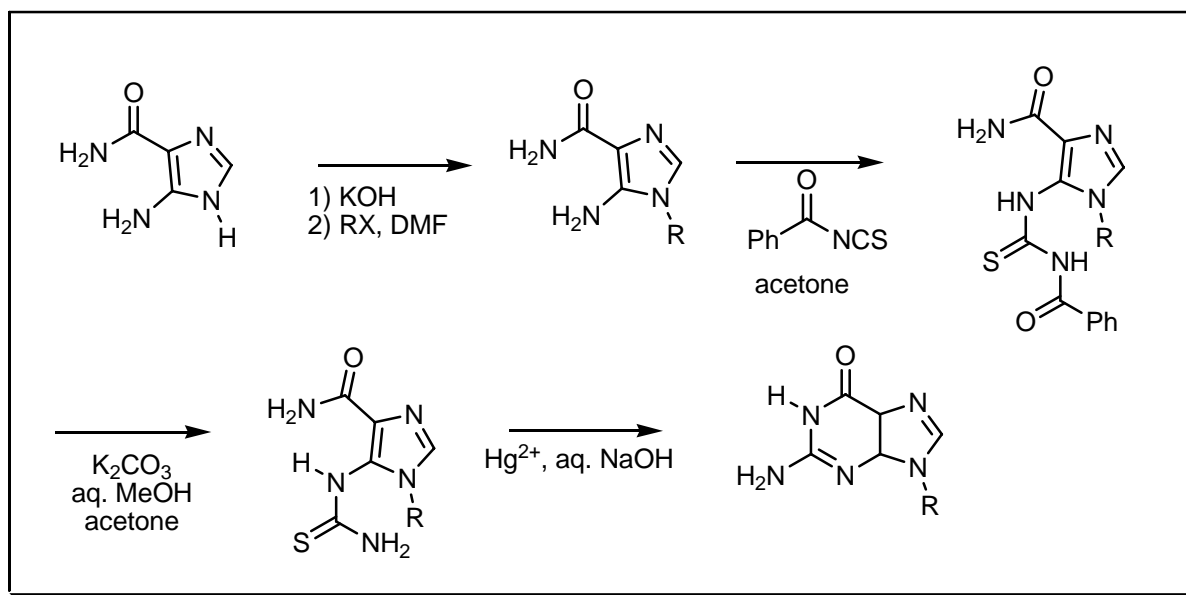
## COMMENTS :

## YAMAZAKI – CLAUSEN GUANINE SYNTHESIS

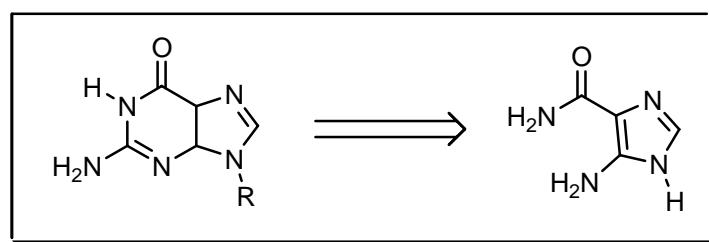
### EXAMPLE :



# MECHANISM :



# DISCONNECTION :

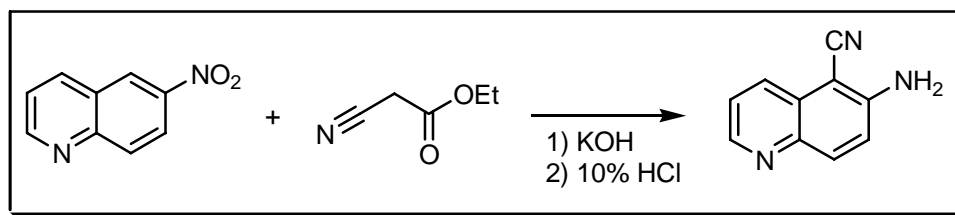
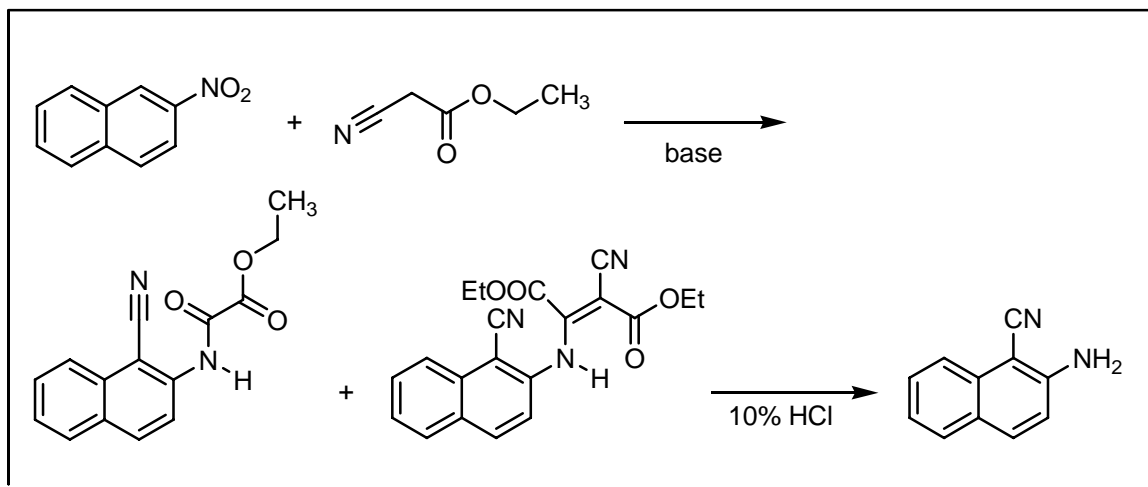


**NOTES :**

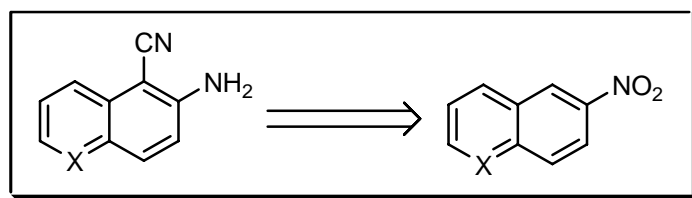
The simple and efficient synthesis of 9-substituted guanines starting from 5-aminoimidazole-4-carboxamide.

**REFERENCES :**

- 1) A. Yamazaki; I. Kumashiro; T. Takenishi, *J. Org. Chem.*, 1967, **32**, 1825.
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- 3) M.P. Groziak; J.W. Chern; L.B. Townsend, *J. Org. Chem.*, 1986, **51**, 1065.
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**COMMENTS :****YAMAZAKI CYANOANILINE SYNTHESIS****EXAMPLE :****MECHANISM :**

## DISCONNECTION :



## NOTES :

The synthesis of *o*-aminoarylnitriles from nitroquinolines, nitronaphthalenes, and *m*-substituted (CF<sub>3</sub>, COCH<sub>3</sub>, and COPh) nitrobenzenes. The exact mechanism has not yet been established.

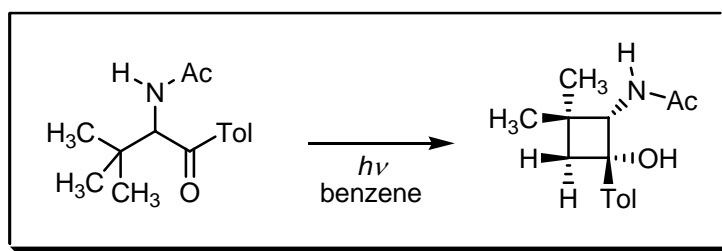
## REFERENCES :

- 1) Y. Tomioka; A. Mochiike; J. Himeno; M. Yamazaki, *Chem. Pharm. Bull.*, 1981, **29**, 1286.
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- 3) Y. Tomioka; K. Ohkubo; M. Yamazaki, *Chem. Pharm. Bull.*, 1985, **33**, 1360.
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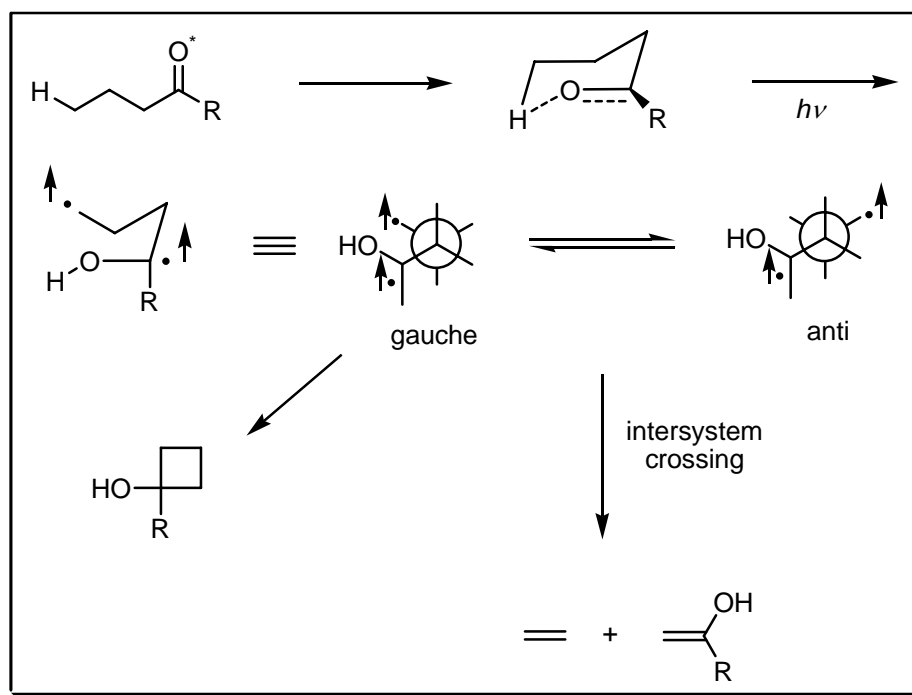
## COMMENTS :

## YANG CYCLISATION

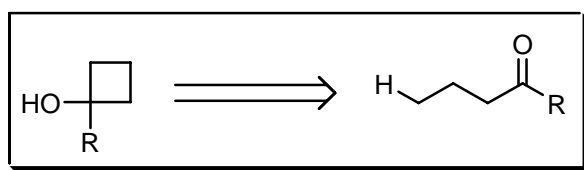
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The **Yang** cyclisation is the formation of cyclobutanols from 1-hydroxytetramethylene biradicals, which are produced via photochemical  $\gamma$ -hydrogen abstraction. From one chiral molecule up to 8 diastereoisomers can be formed. **Norrish** type I and type II fragmentation products are observed. See also **Norrish** type 1 and type 2 reactions.

## REFERENCES :

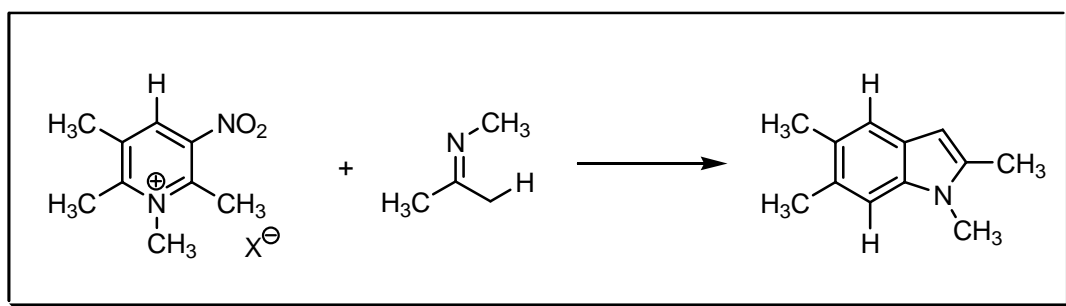
- 1) N.C. Yang; D.-D. H. Yang, *J. Am. Chem. Soc.*, 1958, **80**, 2913.
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- 6) R.R. Sauers; L.A. Edberg, *J. Org. Chem.*, 1994, **59**, 7061.
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- 11) S. Saphier; Y. Hu; S.C. Sinha; K.N. Houk; E. Keinan, *J. Am. Chem. Soc.*, 2005, **127**, 132.

COMMENTS :

## YUROVSKAYA INDOLE SYNTHESIS

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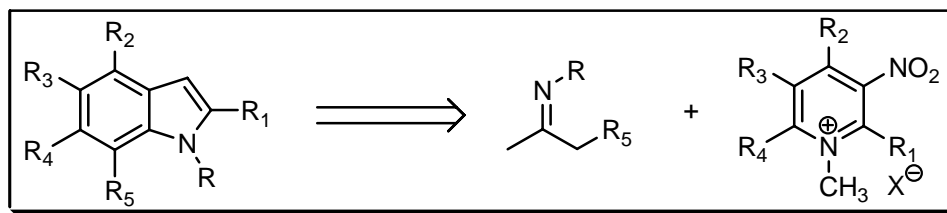
EXAMPLE :





The reaction scheme illustrates the synthesis of a substituted indole derivative through a series of 11 intermediates and transition states. The starting material is a substituted pyridine with a methyl group at the nitrogen and a substituent  $X^-$  at the 4-position. The reaction proceeds via a series of intermediates, including a 1,2-dihydropyridine, a 1,2-dihydropyridine with a methyl group at the nitrogen, a 1,2-dihydropyridine with a methyl group at the nitrogen, a 1,2-dihydropyridine with a methyl group at the nitrogen, a 1,2-dihydropyridine with a methyl group at the nitrogen, a 1,2-dihydropyridine with a methyl group at the nitrogen, a 1,2-dihydropyridine with a methyl group at the nitrogen, a 1,2-dihydropyridine with a methyl group at the nitrogen, a 1,2-dihydropyridine with a methyl group at the nitrogen, a 1,2-dihydropyridine with a methyl group at the nitrogen, and a 1,2-dihydropyridine with a methyl group at the nitrogen. The final product is a substituted indole derivative.

## DISCONNECTION :



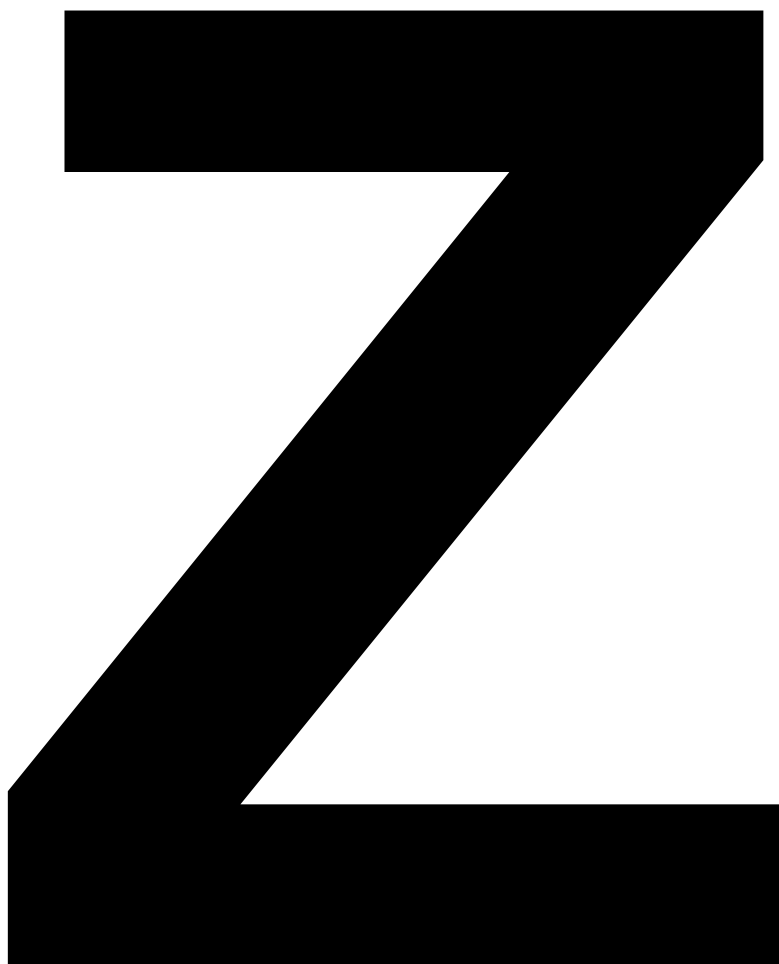
## NOTES :

The formation of indoles by the reaction of 3-nitropyridinium salts with *N*-alkyl-2-ketimines. The more alkyl substituents on the pyridinium the better the yield of the indole. See also **von Baeyer – Emmerling**, **von Baeyer – Jackson**, **Bailey – Liebeskind**, **Bartoli**, **Bischler – Möhlau**, **Cadogan – Sundberg**, **Couture**, **Engler**, **Feldman indole**, **Fischer indole**, **Foulds – Robinson**, **Fukuyama**, **Fürstner**, **Gassman indole**, **Grandberg**, **Hegedus**, **Hemetsberger – Knittel**, **Inanaga**, **Iwao**, **Japp – Murray**, **Julia**, **Kihara**, **Larock indole**, **Leimgruber – Batcho**, **Lipp**, **Madelung indole**, **Magnus**, **Martin**, **Montevecchi**, **Mori – Ban**, **Murphy**, **Naito**, **Natsume**, **Nenitzescu indole**, **Piloty – Robinson**, **Pschorr – Hoppe**, **Reissert indole**, **Saegusa indole**, **Schmid**, **Smith**, **Sugasawa indole**, **Sundberg**, **Thiele – Dimroth**, **Thyagarajan**, **Watanabe heterocyclisation**, **Watanabe indole**, **Weerman indole**, **Wender**, **Widman**, **Yamamoto indole-1** and **Yamamoto indole-2** reactions.

## REFERENCES :

M.A. Yurovskaya; A.Z. Afanasyev; F.V. Maximova; Y.G. Bundel, *Tetrahedron*, 1993, **49**, 4945.

## COMMENTS :



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**C**

CLAYTON – JENSEN REACTION · 1947

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**Z**

ZAGOUMENNY DIPHENYL CARBINOL SYNTHESIS · 1916

ZAV'YALOV PYRROLE SYNTHESIS · 1916

ZEISEL SYNTHESIS · 1918

ZEISS KETONE TRANSFER · 1919

ZELINSKY – STADNIKOFF AMINONITRILE SYNTHESIS · 1922

ZELINSKY ALDEHYDE SYNTHESIS · 1921

ZEMPLÉN SUGAR DEGRADATION · 1923

ZIEGLER – HAFNER AZULENE SYNTHESIS · 1925

ZIEGLER – NATTA POLYMERISATION · 1926

ZIEGLER ALKYLATION · 1928

ZIEGLER ALUMINIUMALKYL OXIDATION · 1929

ZIEGLER TERTIARY HIGHER FATTY ACIDS SYNTHESIS · 1930

ZIMMER REARRANGEMENT · 1931

ZIMMERMAN REACTION · 1933

ZINCKE – KÖNIG PYRIDINIUM SALTS · 1934

ZINCKE – SUHL CYCLOHEXADIENONE SYNTHESIS · 1936

ZINCKE DIARYLMETHANE SYNTHESIS · 1937

ZINCKE DISULFIDE CLEAVAGE · 1938

ZINCKE HALOGENPHENOL NITRATION · 1940

ZININ REACTION · 1941

ZININ REARRANGEMENT · 1942

ZINKE – CORNFORTH MODIFICATION · 1945

ZINKE – ZIEGLER SYNTHESIS · 1944

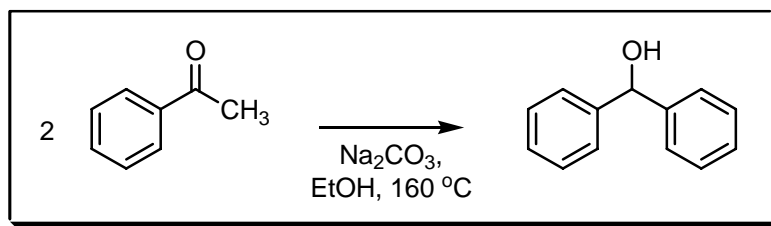
ZINNER SYNTHESIS · 1946

ZINOVEV – SOBOROVSKI REACTION · 1947

## ZAGOUMENNY DIPHENYL CARBINOL SYNTHESIS

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### EXAMPLE :



### NOTES :

Diphenyl carbinol is obtained by heating benzophenone, ethanol and alkali in a sealed tube at 160 °C for five hours. In addition, zinc can be used. See also **Hammick** picolinic acid decarboxylation.

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### REFERENCES

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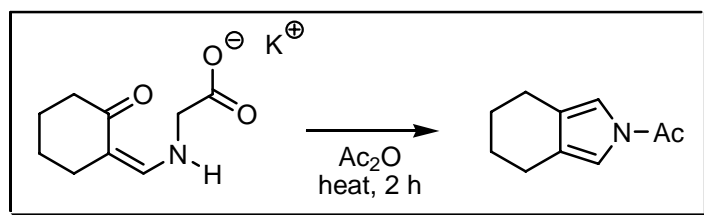
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### COMMENTS :

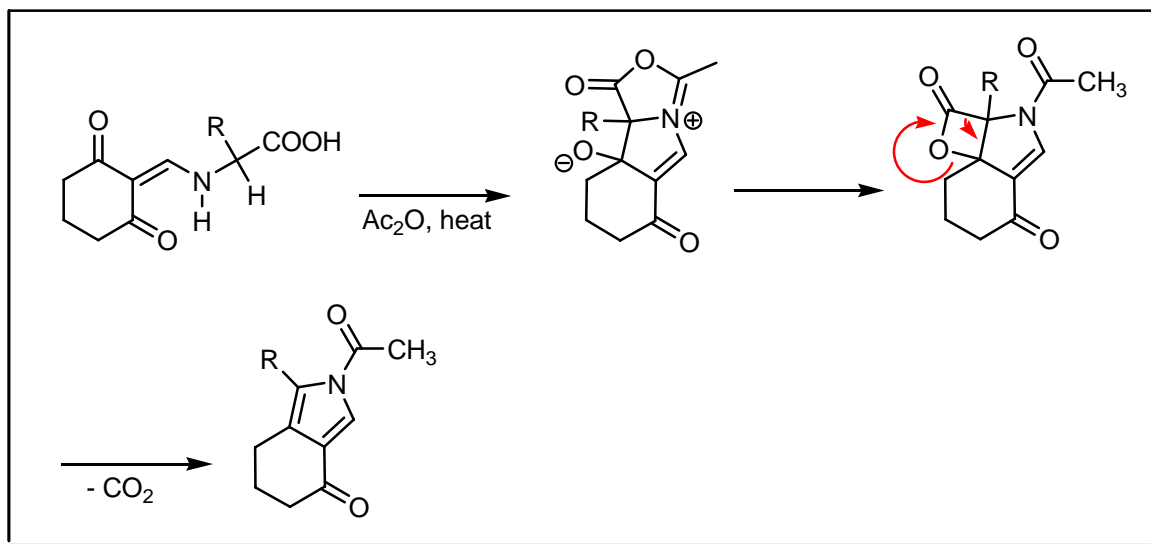
## ZAV'YALOV PYRROLE SYNTHESIS

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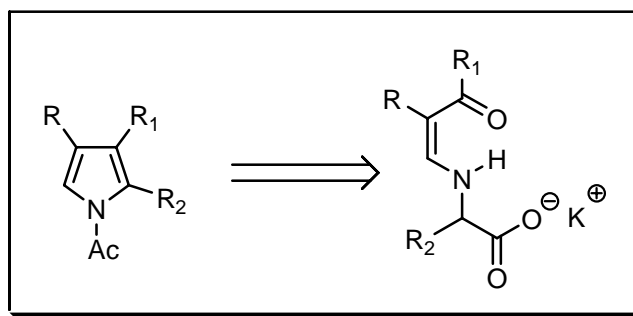
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

The potassium salts of amino acid derived alkenones are heated in acetic anhydride. The pyrrole ring is formed after decarboxylation and dehydration. See also **Barton – Zard**, **Clauson-Kaas**, **Fischer – Fink**, **Grob – Camenisch**, **Hantzsch** pyrrole, **Harries** pyrrole, **Kenner**, **Knorr** pyrrole, **Miller – Plöchl**, **Paal – Knorr**, **Padwa**, **Piloty – Robinson**, **Schwanert** and **Trofimov** reactions.

## REFERENCES :

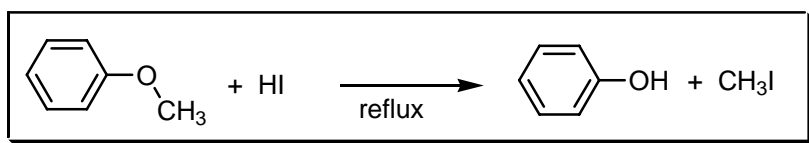
- 1) S.I. Zav'yalov; I.F. Mustafaeva; N.I. Aronova; N.N. Makhova, *Izv. Akad. Nauk. SSSR, Ser Khim.*, 1973, 2572. (*Proc. Acad. Sci. USSR (Eng.*, 1973, 2505.)
- 2) N.J. Bach; E.C. Kornfeld; N.D. Jones; M.O. Chaney; D.E. Dorman; J.W. Paschal; J.A. Clemens; E.B. Smalstig, *J. Med. Chem.*, 1980, **23**, 481.
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- 6) C.D. Gabutt; J.D. Hepworth; B.M. Heron; M.R.J. Elsegood; W. Clegg, *Chem. Commun.*, 1999, 289.
- 7) K.-M. Cheung; P.M. Shoolingin-Jordan, *Synthesis*, 2001, 1627.

## COMMENTS :

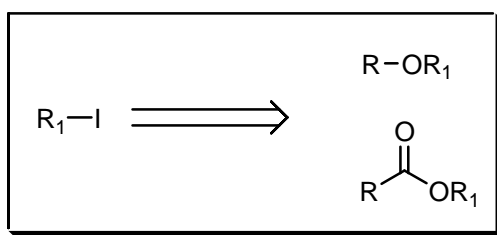
## ZEISEL SYNTHESIS

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### EXAMPLE :



### DISCONNECTION :



### NOTES :

The removal of alkyl groups from methoxy and ethoxy compounds with boiling hydrogen iodide or TMS-iodide. See also **Appel – Robinson**, **Gustus** cleavage, **Herzig – Meyer**, **Jung – Olah – Voronkov**, **Mann** dealkylation, **Prey**, and **Stoermer** dealkylation reactions.

### REFERENCES :

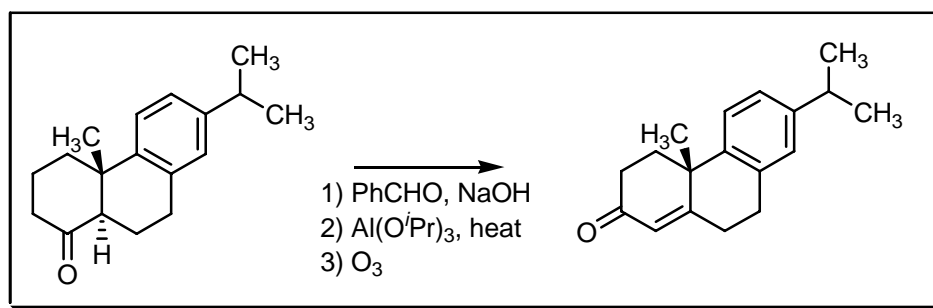
**Houben – Weyl** : **2**, 404

- 1) S. Zeisel, *Monatsh. Chem.*, 1885, **6**, 989.
- 2) S. Zeisel, *Monatsh. Chem.*, 1886, **7**, 406.
- 3) S. Zeisel; R. Fanto, *Z. Anal. Chem.*, 1903, **42**, 549.
- 4) H.J. Backer, *Recl. Trav. Chim. Pays-Bas*, 1952, **71**, 740.
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- 6) T.G. Miller; R.J. Hronek, *Anal. Chem.*, 1985, **57**, 2091.
- 7) A.M.T. Magalhaes; P.M. Chalk, *Analyst*, 1986, **111**, 77.

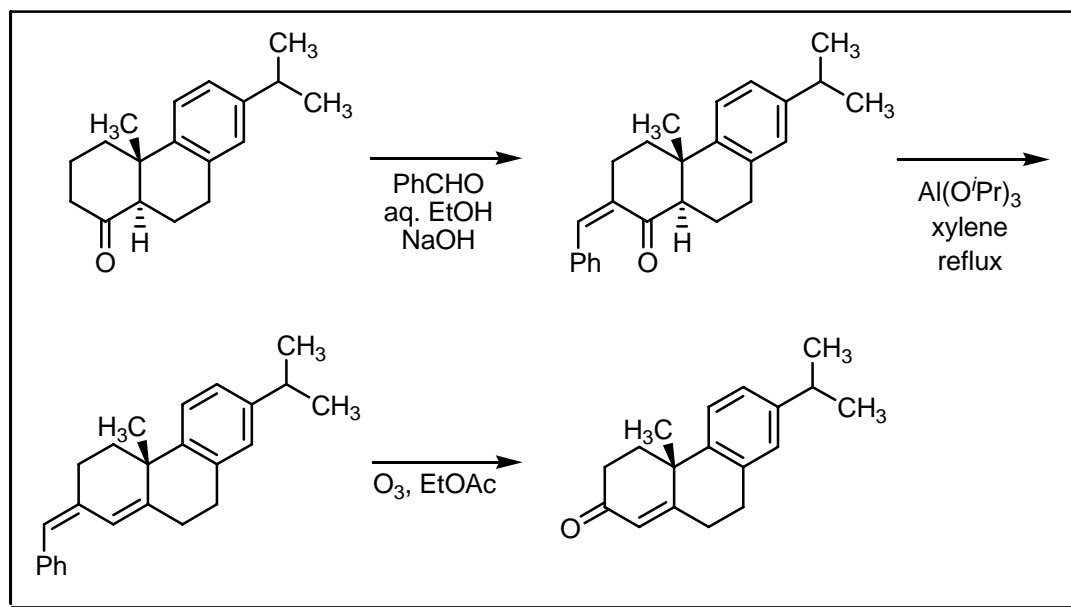
COMMENTS :

## ZEISS KETONE TRANSFER

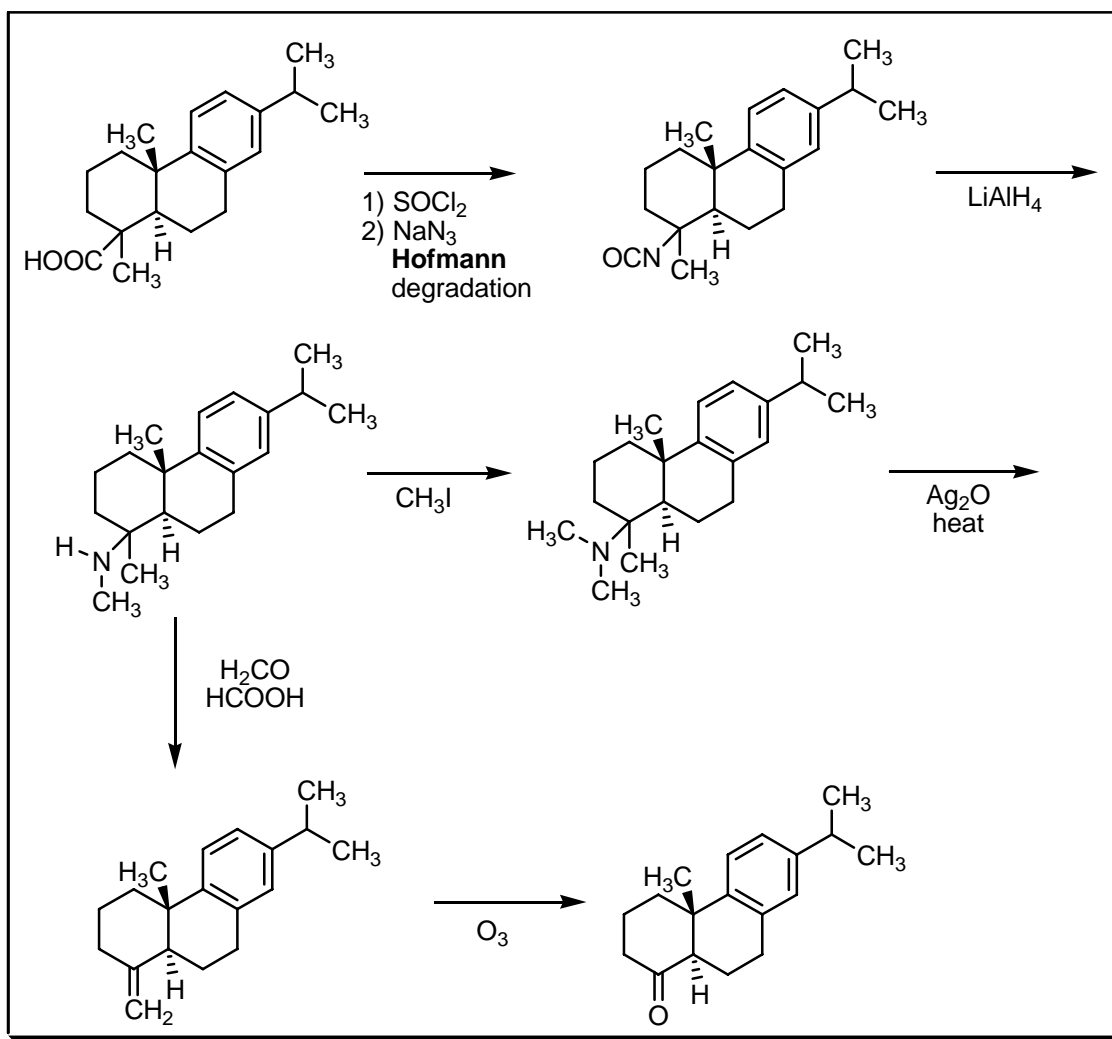
EXAMPLE :



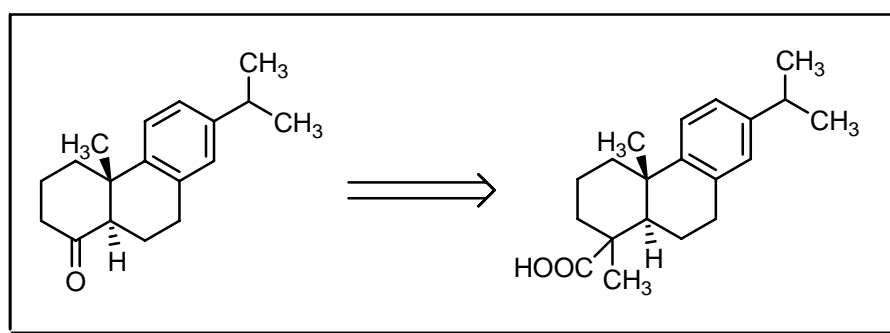
MECHANISM :







#### DISCONNECTION :



#### NOTES :

The basic transformation is the movement of the A-ring carbonyl function to an adjacent ring carbon atom in steroidal systems.

#### REFERENCES :

- 1) H.H. Zeiss; W.B. Martin, jr., *J. Am. Chem. Soc.*, 1953, **75**, 5935.
- 2) J.W. Huffman; R.F. Stockel, *J. Org. Chem.*, 1963, **28**, 506.
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- 5) E.E. van Tamelen; J.P. Demers; E.G. Taylor; K. Koller, *J. Am. Chem. Soc.*, 1980, **102**, 5424.  
6) A. Abad; C. Agulló; M. Arnó; L.R. Domingo; R.J. Zaragoza, *Org. Prep. Proced. Int.*, 1991, **23**, 323.

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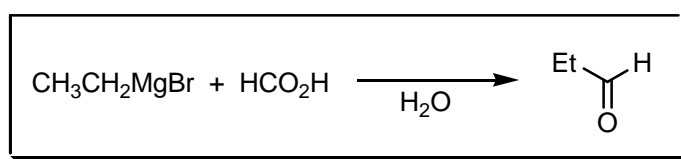
COMMENTS :

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## ZELINSKY ALDEHYDE SYNTHESIS

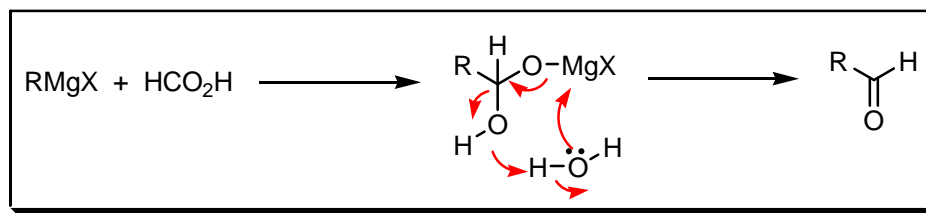
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EXAMPLE :



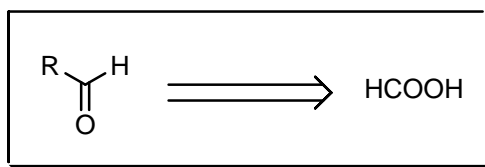
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MECHANISM :



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DISCONNECTION :



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NOTES :

Aldehydes are obtained by the hydrolysis of the complex formed by the interaction of a **Grignard** reagent and formic acid. See also **Bodroux – Chichibabin** reaction.

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REFERENCES :

*Org. Synth.* : 6, 22

*Org. Synth. Coll. Vol.* : 1, 188

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2) L.I. Smith; J. Nichols, *J. Org. Chem.*, 1941, **6**, 489.  
3) F. Sato; K. Oguro; H. Watanabe; M. Sato, *Tetrahedron Lett.*, 1980, **21**, 2869.  
4) M. Bogavac; L. Arsenijevic; S. Pavlov; V. Arsenijevic, *Tetrahedron Lett.*, 1984, **25**, 1843.

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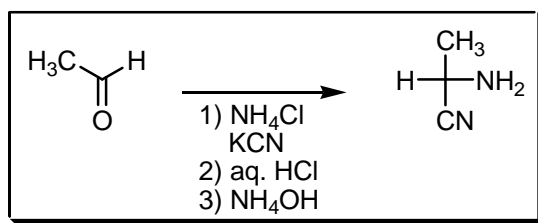
**COMMENTS :**

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**ZELINSKY – STADNIKOFF AMINONITRILE SYNTHESIS**

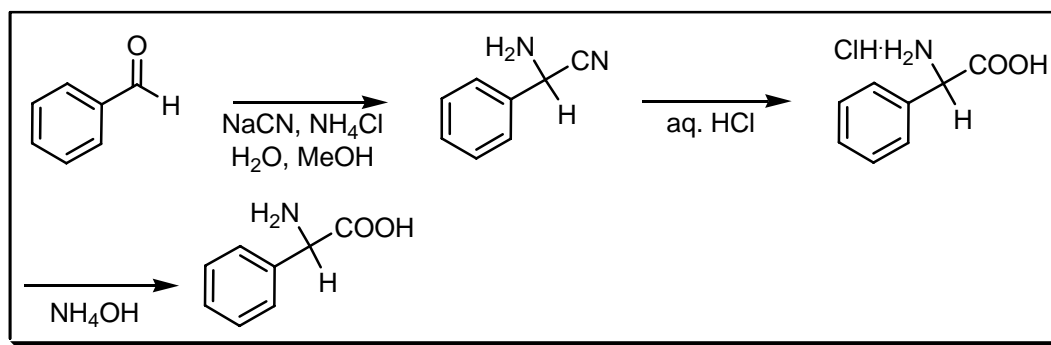
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**EXAMPLE :**



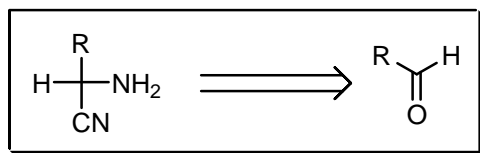
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**MECHANISM :**



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**DISCONNECTION :**



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**NOTES :**

This reaction forms *in situ*  $\text{NH}_3$  and  $\text{HCN}$ . These reactants react with the carbonyl group and afford  $\alpha$ -amino acids after hydrolysis. See also **Bouveault – Locquin** amino acid, **von Braun** amino acid synthesis, **Bucherer – Bergs**,

Darapsky, Herbst – Engel, Knoop – Oosterlin, O'Donnell, Schöllkopf, Sorensen, Strecker amino acid, Tiemann amination, Ultee and Urech reactions.

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#### REFERENCES :

Houben – Weyl : 8, 280

Org. Synth. : 9, 4; 11, 4; 22, 13, 23; 24, 9

Org. Synth. Coll. Vol. : 1, 21; 2, 29; 3, 66, 84, 88

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1) N. Zelinsky; G. Stadnikoff, *Ber. Dtsch. Chem. Ges.*, 1906, **39**, 1722.

2) D.T. Mowry, *Chem. Rev.*, 1948, **42**, 189.

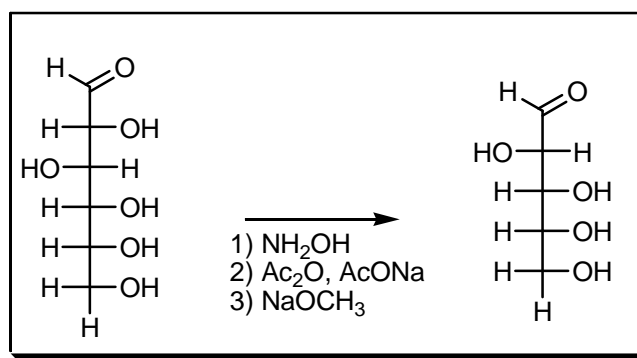
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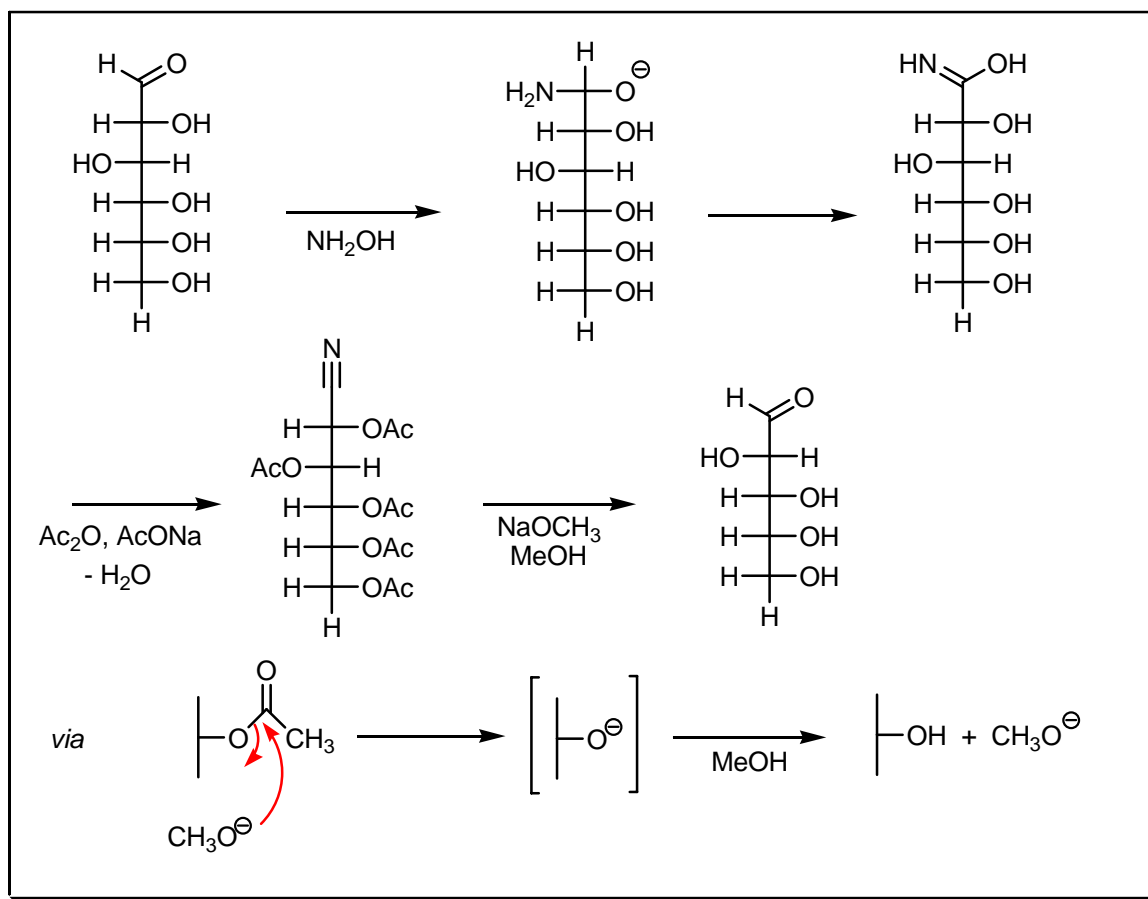
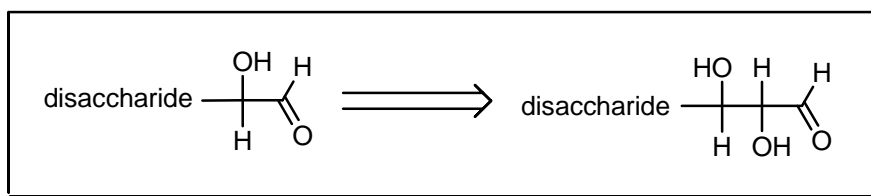
#### COMMENTS :

### ZEMPLÉN SUGAR DEGRADATION

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#### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

This method is developed for the degradation of disaccharides. Hydrolysis with  $\text{NH}_3$  and  $\text{Ag}_2\text{O}$  (**Wohl** degradation) to form diacetamide compounds is not possible due to hydrolysis of the disaccharides at the same time. The acetylated nitrile is converted directly to the aldose by the alkoxide. See also **Wohl** reaction.

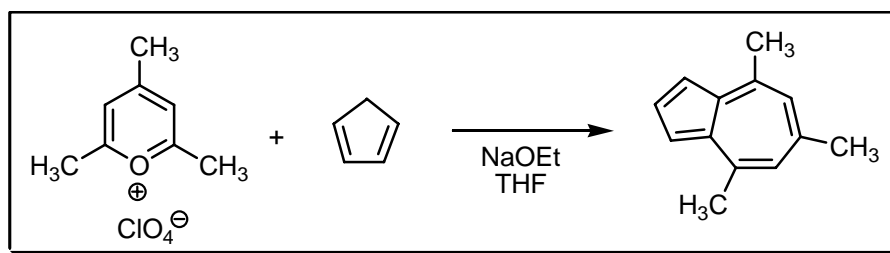
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- 7) E. Osz; K. Czifrak; T. Deim; L. Szilagyi; A. Benyei; L. Somsak, *Tetrahedron*, 2001, **57**, 5429.

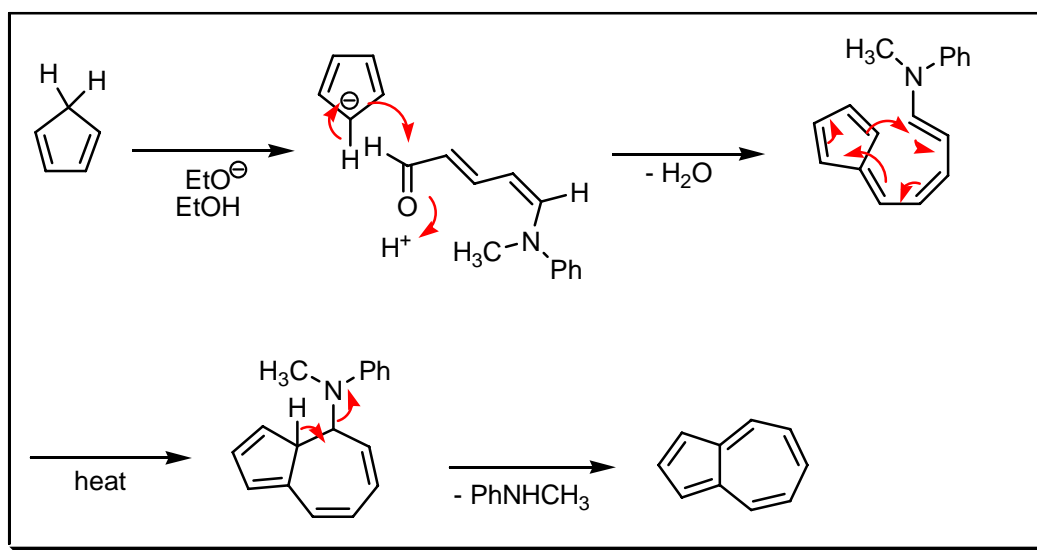
## COMMENTS :

## ZIEGLER – HAFNER AZULENE SYNTHESIS

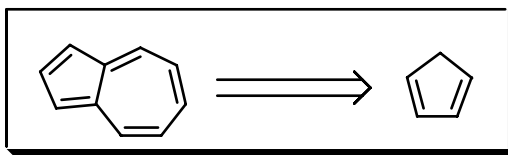
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The first step is the deprotonation to form the cyclopentadienyl anion, followed by condensation with the carbonyl of the **Zincke** aldehyde. The thermal cyclisation is followed by elimination of the secondary amine.

## REFERENCES :

**Org. Synth.** : **44**, 94; **62**, 134

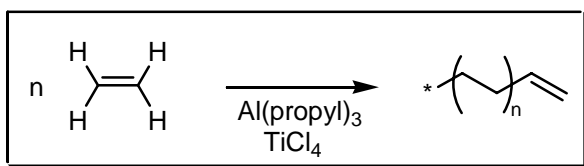
**Org. Synth. Coll. Vol.** : **5**, 1088; **7**, 15

- 1) K. Ziegler; K. Hafner, *Angew. Chem.*, 1955, **67**, 301.
- 2) K. Hafner, *Angew. Chem.*, 1958, **70**, 419.
- 3) R.W. Alder; G. Whittaker, *J. Chem. Soc., Perkin Trans. 2*, 1975, 714.
- 4) L.T. Scott; M.A. Kirms, *J. Am. Chem. Soc.*, 1981, **103**, 5875.

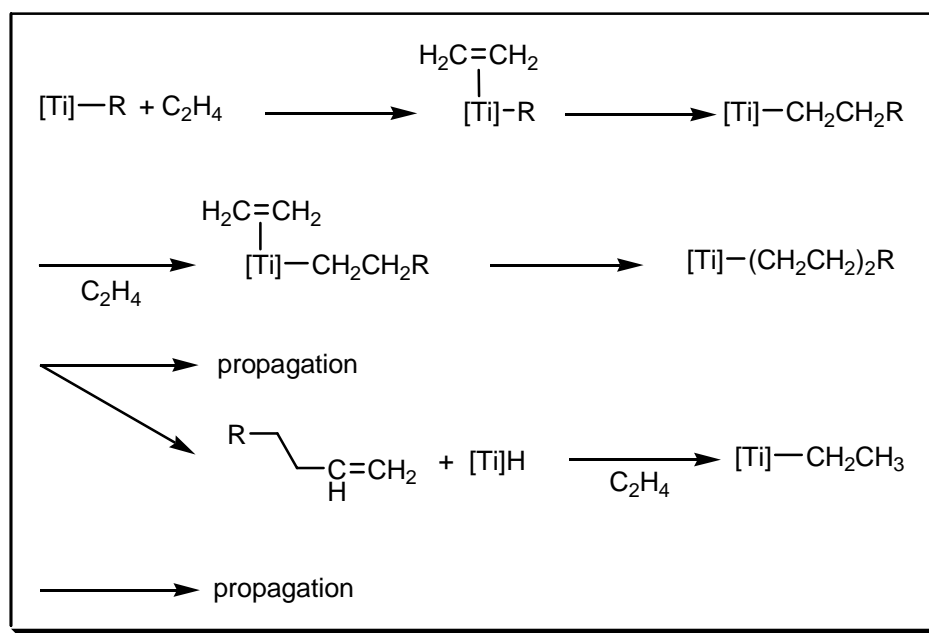
## COMMENTS :

## ZIEGLER – NATTA POLYMERISATION

### EXAMPLE :



## MECHANISM :



## NOTES :

Ethene is polymerised by trialkylaluminium compounds and traces of a transition metal belonging to group 4, 5, or 6. The polymerisation takes place at room temperature and at normal pressure. According to the **Cossee – Arlman** mechanism, propagation of the polymer occurs exclusively at the titanium centre. The exact nature of the propagation step was controversial for some time. Recent studies show that  $\alpha$ -agostic species are important. The use of vanadium-based catalysts allows for the preparation of high-molecular-weight polymers with narrow molecular-weight distributions, although the activity of these catalysts is inferior to other known systems.

## REFERENCES :

Houben – Weyl : 14/1, 578

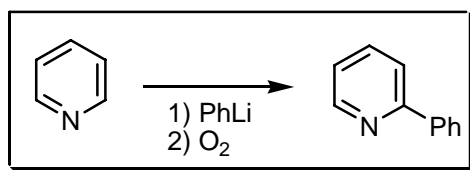
- 1) K. Ziegler; E. Holzkamp; H. Breil; H. Martin, *Angew. Chem.*, 1955, **67**, 426.
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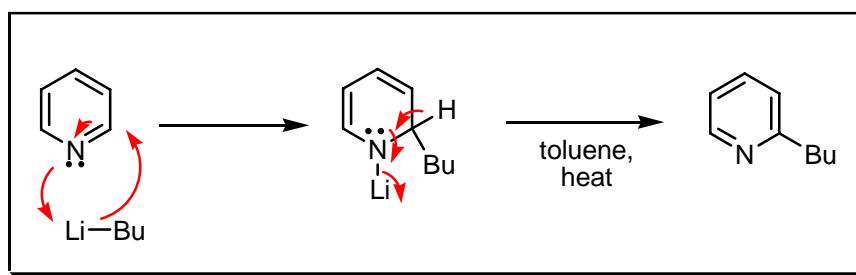
COMMENTS :

## ZIEGLER ALKYLATION

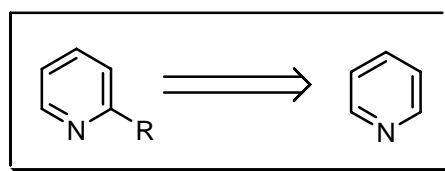
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The alkylation of heterocyclic nitrogen compounds. The unshared pair of electrons on the nitrogen combines with the lithium, so the extra pair of ring electrons has a place to go; it becomes the new unshared pair on the nitrogen.

REFERENCES :

March : 666

Smith – March : 871

Org. Synth. : 18, 70

Org. Synth. Coll. Vol. : 2, 517

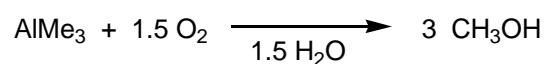
- 1) K. Ziegler; H. Zeiser, *Ber. Dtsch. Chem. Ges.*, 1930, **63**, 1847.
  - 2) R.A. Abramovitch; G.A. Poulton, *J. Chem. Soc., Chem. Commun.*, 1967, 274.
  - 3) C.S. Giam; J.L. Stout, *J. Chem. Soc., Chem. Commun.*, 1969, 142.
  - 4) H. Vorbrüggen; M. Maas, *Heterocycles*, 1988, **27**, 2659.
  - 5) D.R. Armstrong; R.E. Mulvey; D. Barr; R. Snaith; D. Reed, *J. Organomet. Chem.*, 1988, **350**, 191.
- 

**COMMENTS :**

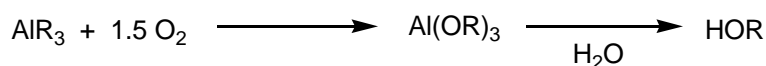
## ZIEGLER ALUMINIUMALKYL OXIDATION

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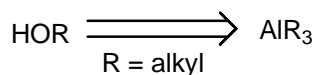
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

The oxidation of trialkylaluminium compounds with air followed by hydrolysis to afford primary alcohols. This is due to the fact that only terminal double bonds react.

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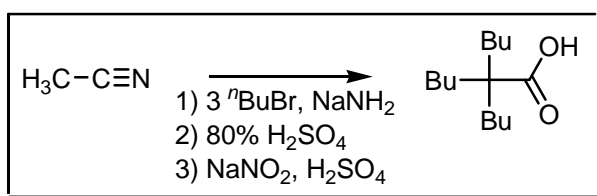
**REFERENCES :**

- 1) K. Ziegler, *Angew. Chem.*, 1952, **64**, 323.
  - 2) K. Ziegler; H.-G. Gellert; H. Martin; K. Nagel; J. Schneider, *Liebigs Ann. Chem.*, 1954, **589**, 91.
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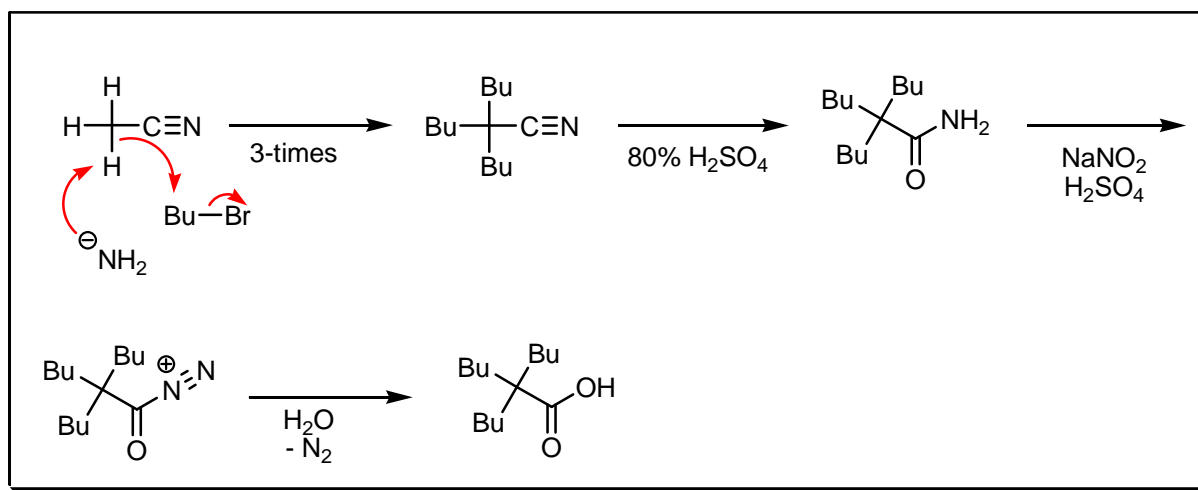
COMMENTS :

## ZIEGLER TERTIARY HIGHER FATTY ACIDS SYNTHESIS

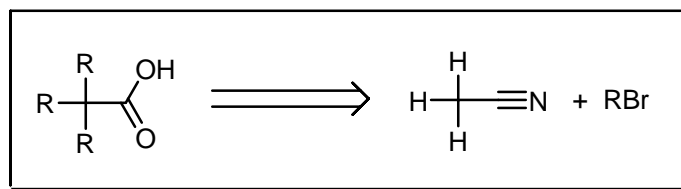
EXAMPLE :



MECHANISM :



DISCONNECTION :

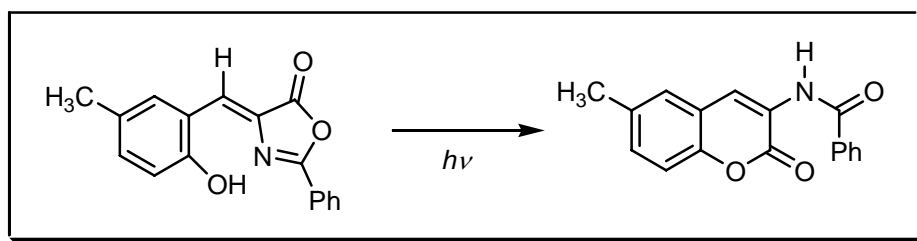


NOTES :

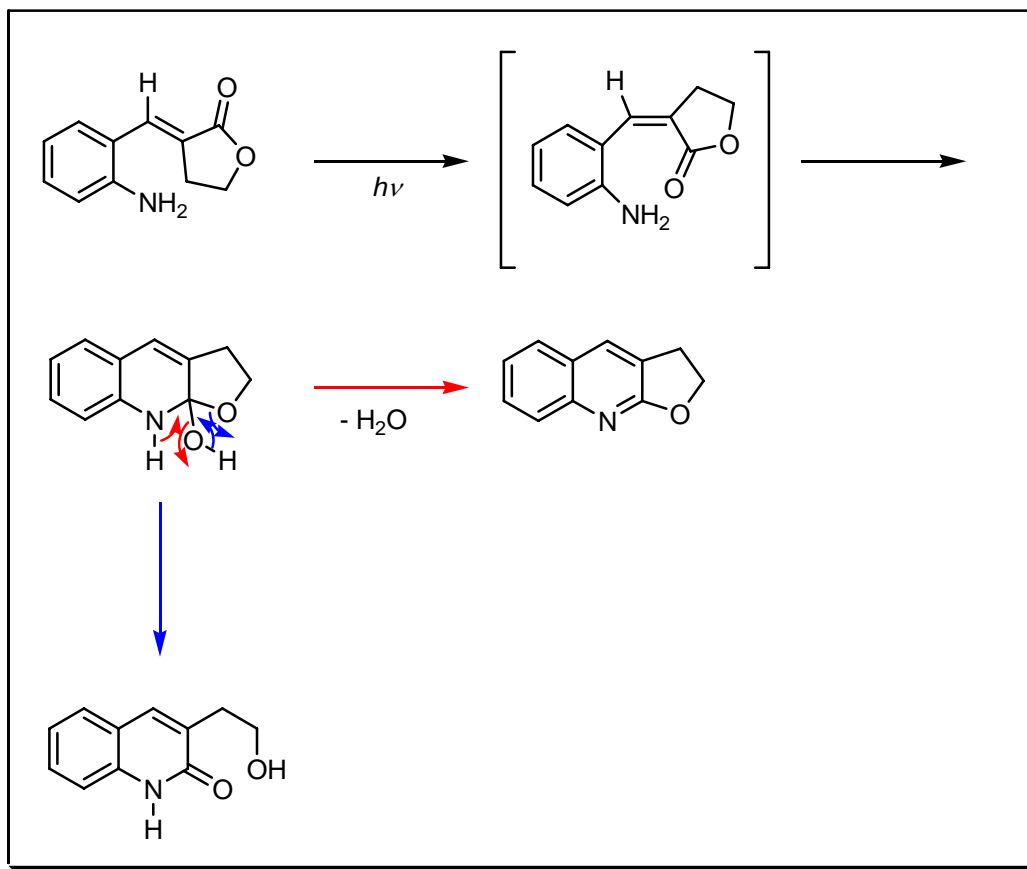
An alkyl nitrile is alkylated with an alkyl halide in the presence of sodamide. The resulting tertiary nitrile is hydrolysed with 80% sulfuric acid to give the amide, which yields the tertiary fatty acid on treatment with sodium nitrite in sulfuric acid. Compare with the **Haller – Bauer** reaction. See also **Haller – Bauer** reaction.

**REFERENCES :**

- 1) K. Ziegler; H. Ohlinger, *Liebigs Ann. Chem.*, 1932, **495**, 84.  
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- 

**COMMENTS :****ZIMMER REARRANGEMENT****EXAMPLE :**

## MECHANISM :



## NOTES :

This is the (photolytic) rearrangement from  $\alpha$ -methylenelactones, -lactams and thiolactones. A wide variety of compounds can be obtained including carbostyryl, dihydrocoumarin and quinolines.

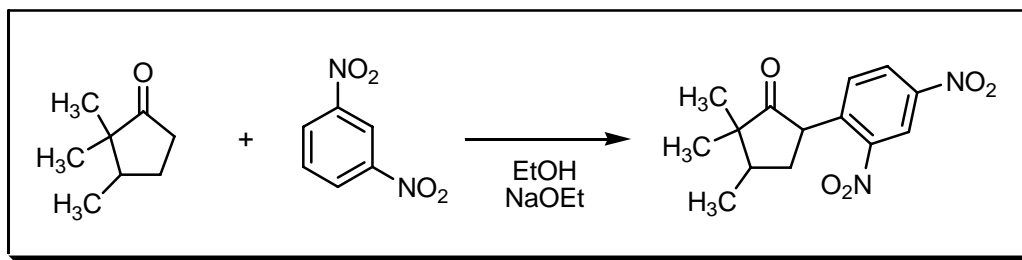
## REFERENCES :

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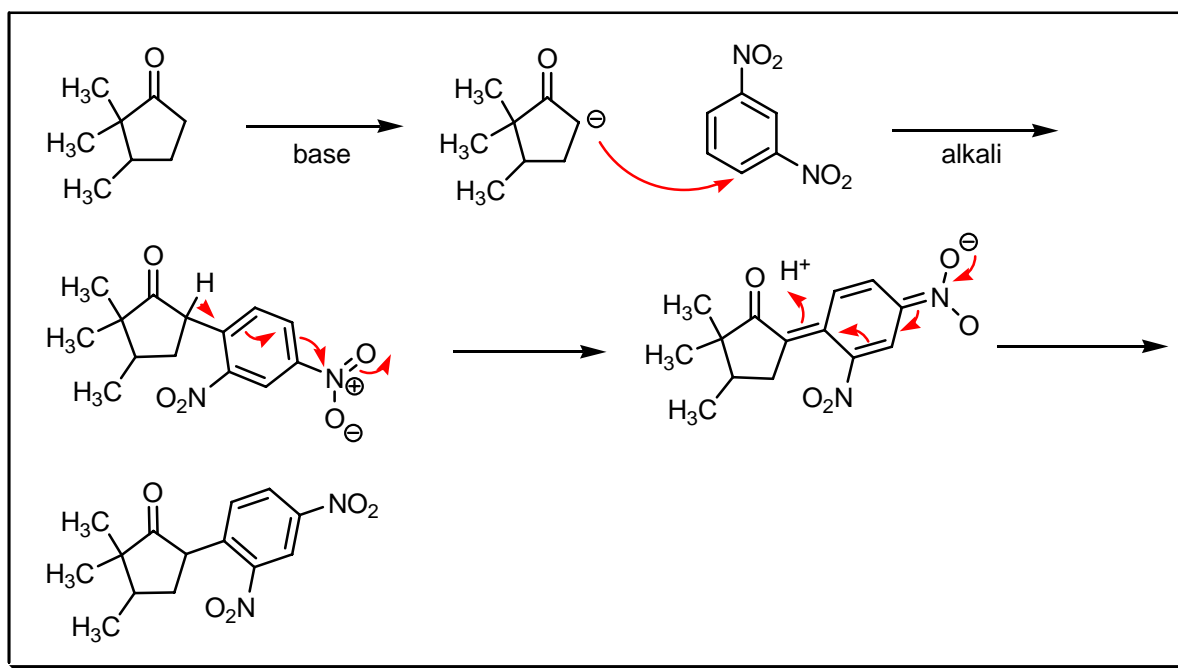
## COMMENTS :

## ZIMMERMAN REACTION

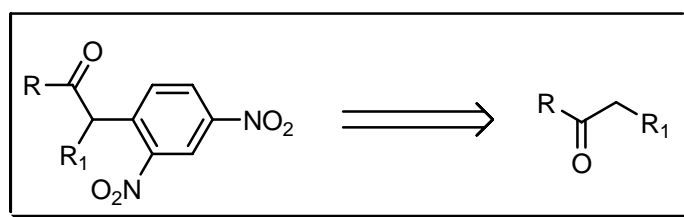
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The reaction that occurs between methylene ketones and aromatic polynitro compounds in the presence of an ethanolic solution of sodium ethoxide (**Janovsky** used aqueous sodium hydroxide). When applied to 17-oxosteroids, the coloured compounds formed can be used for the quantitative determination of 17-oxosteroids. See also **Meisenheimer – Janovsky** reaction.

## REFERENCES :

- 1) W. Zimmermann, *Z. Physiol. Chem.*, 1935, **233**, 257.
- 2) M. Ishidate; T. Sakaguchi, *J. Pharm. Soc. Japan*, 1950, **70**, 444.
- 3) O. Neunhoeffer; K. Thewalt; W. Zimmermann, *Z. Physiol. Chem.*, 1961, **323**, 116.
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- 5) H. Hoffmeister; C. Rufer, *Chem. Ber.*, 1965, **98**, 2376.
- 6) C.S. Feldkamp; R. Watkins; R.J. Thibert; E. Epstein; B. Zak, *Microchem. J.*, 1977, **22**, 201.

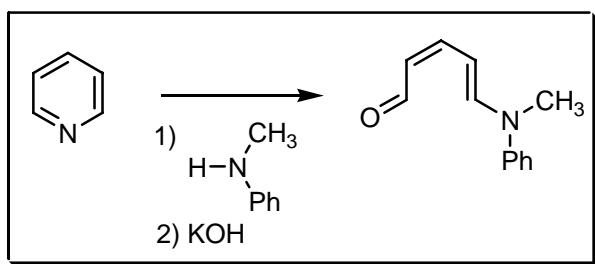
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## COMMENTS :

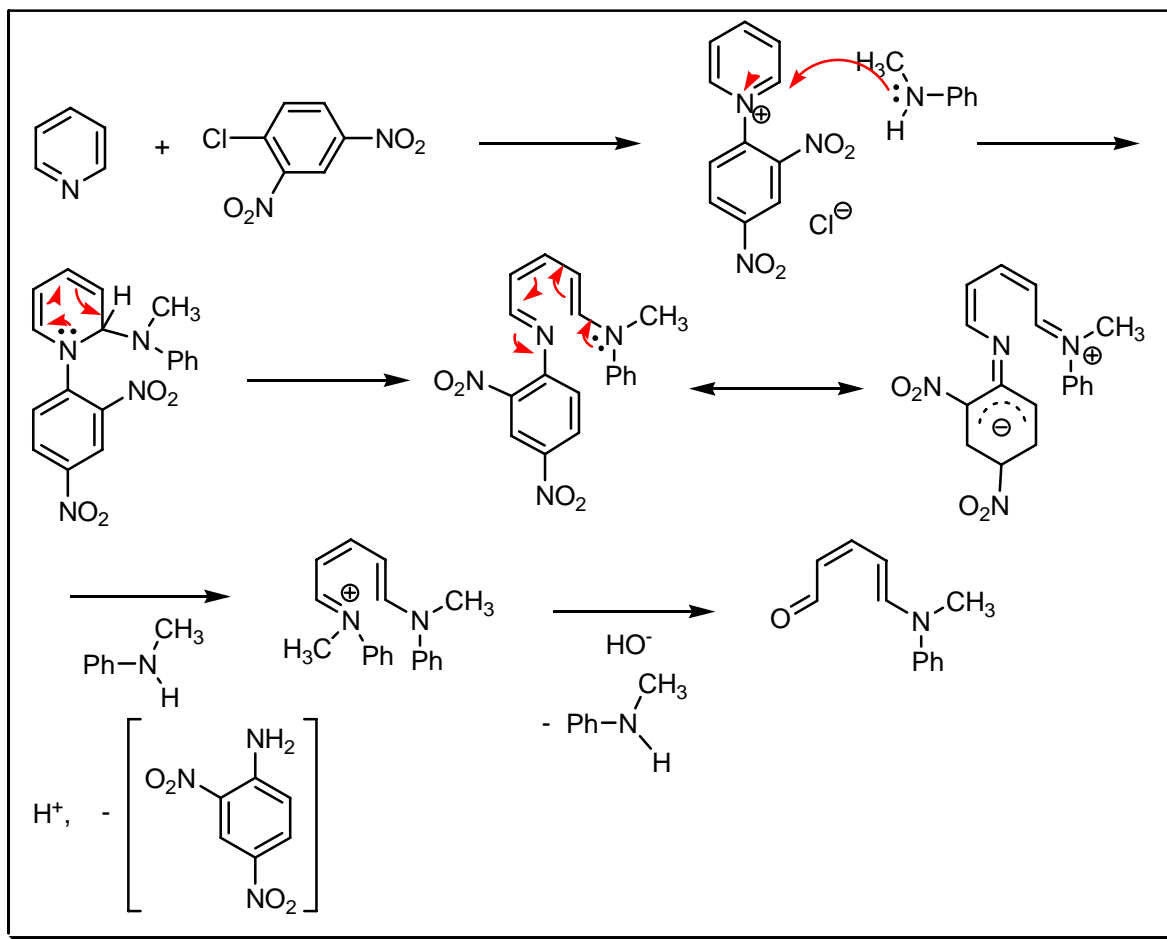
## ZINCKE – KÖNIG PYRIDINIUM SALTS

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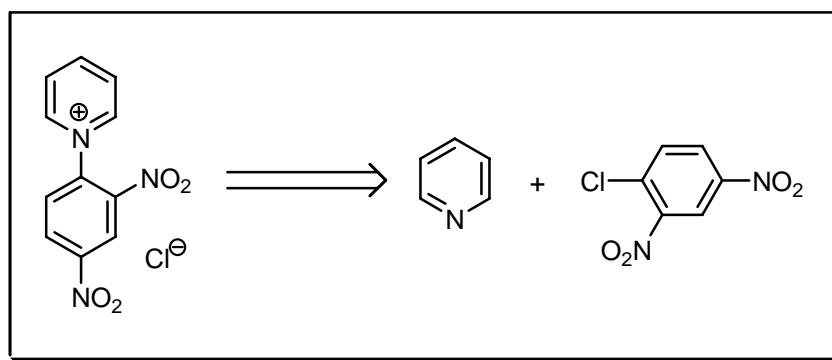
### EXAMPLE :



## MECHANISM :



## DISCONNECTION :



## NOTES :

Instead of 1-bromo-2,4-dinitrobenzene (used by **Zincke**), methyl aniline or bromocyanide (used by **König**) can be used. The initial formed salts are called the **Zincke** salts. See also **Allan – Loudon** reaction.

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Houben – Weyl : E3, 86

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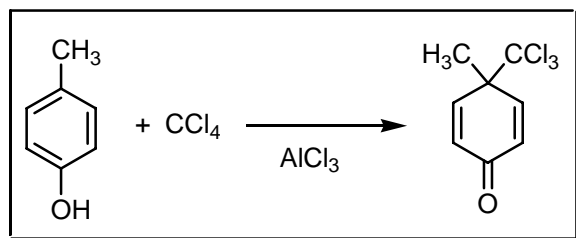


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- 5) A. Diez; L. Vilaseca; I. Lopez; M. Rubiralta; C. Marazano; D.S. Grierson; H.P. Husson, *Heterocycles*, 1991, **32**, 2139.
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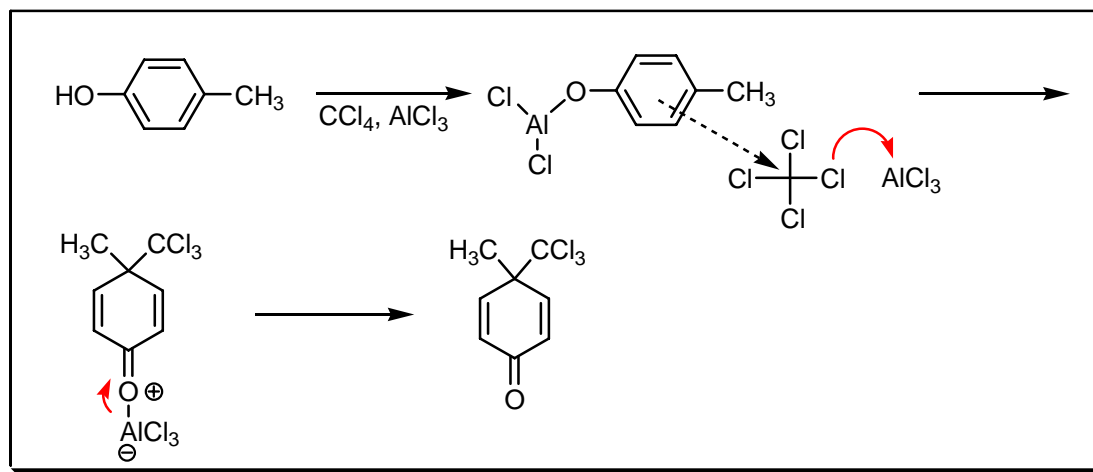
**COMMENTS :**

## ZINCKE – SUHL CYCLOHEXADIENONE SYNTHESIS

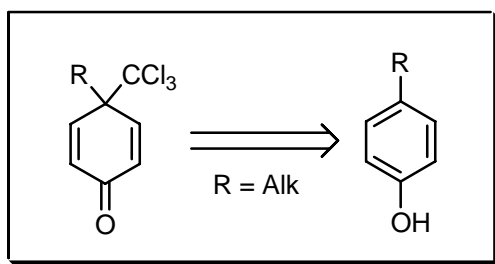
**EXAMPLE :**



**MECHANISM :**



## DISCONNECTION :



## NOTES :

$p$ -Alkylated phenols react with carbon tetrachloride in the presence of aluminium chloride to yield 4,4-disubstituted cyclohexadienones. See also **Friedel – Crafts** reaction.

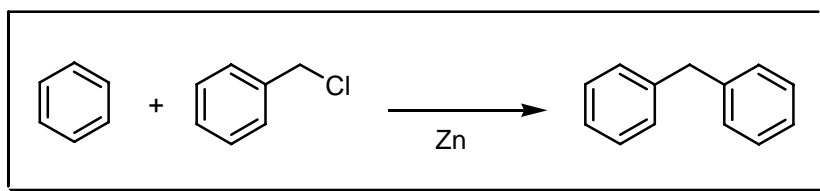
## REFERENCES :

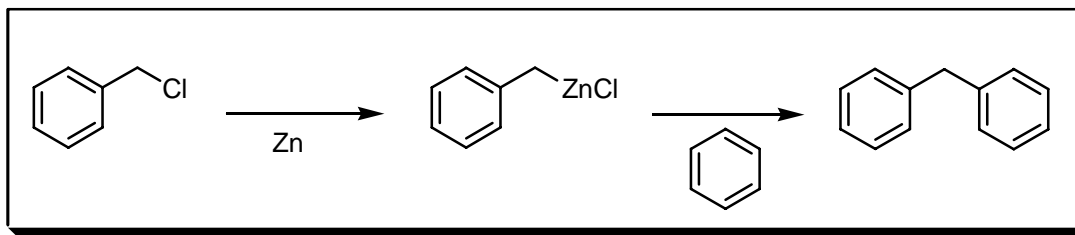
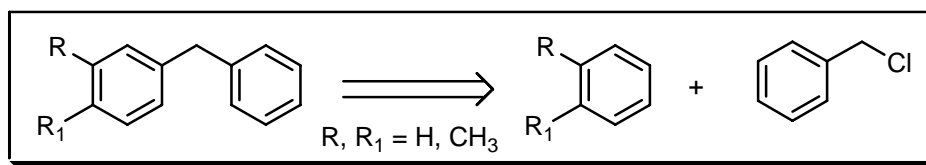
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- 4) S.V. Sergeev; V.A. Nikanorov; V.I. Rozeberg; O.A. Reutov, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1988, **37**, 790.

## COMMENTS :

## ZINCKE DIARYLMETHANE SYNTHESIS

### EXAMPLE :



**MECHANISM :****DISCONNECTION :****NOTES :**

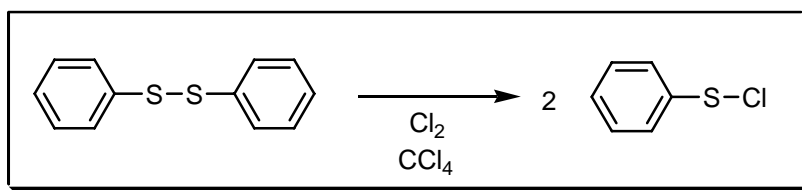
This method is exemplified by the reaction of benzene and benzyl chloride, when heated in the presence of zinc dust or other metallic catalyst, gives diphenylmethane.

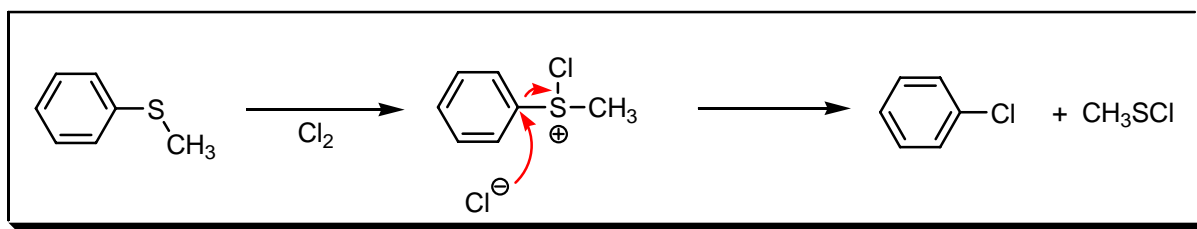
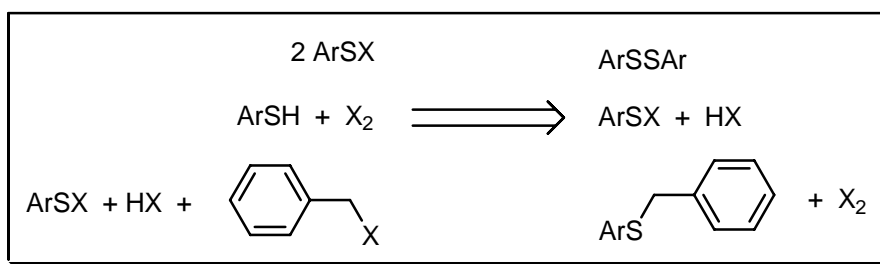
**REFERENCES :**

Org. Synth. : 14, 34

Org. Synth. Coll. Vol. : 2, 232

Th. Zincke, *Liebigs Ann. Chem.*, 1871, **159**, 367.

**COMMENTS :****ZINCKE DISULFIDE CLEAVAGE****EXAMPLE :**

**MECHANISM :****DISCONNECTION :****NOTES :**

The reaction of chlorine or bromine on aryldisulfides, thiophenols or arylbenzylsulfides to afford aromatic and aliphatic sulfenylhalogenides. *Ortho* or *para* nitro groups suppress halogenation of the phenyl ring.

**REFERENCES :**

Houben – Weyl : **9**, 268

Org. Synth. : **11**, 455; **15**, 55

Org. Synth. Coll. Vol. : **2**, 455, 471

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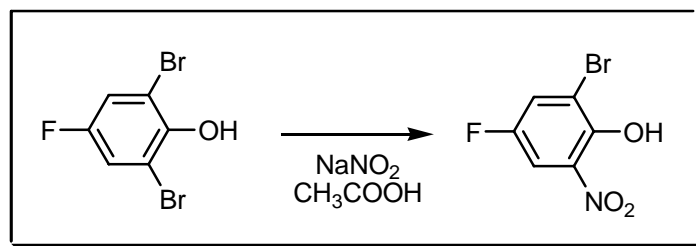
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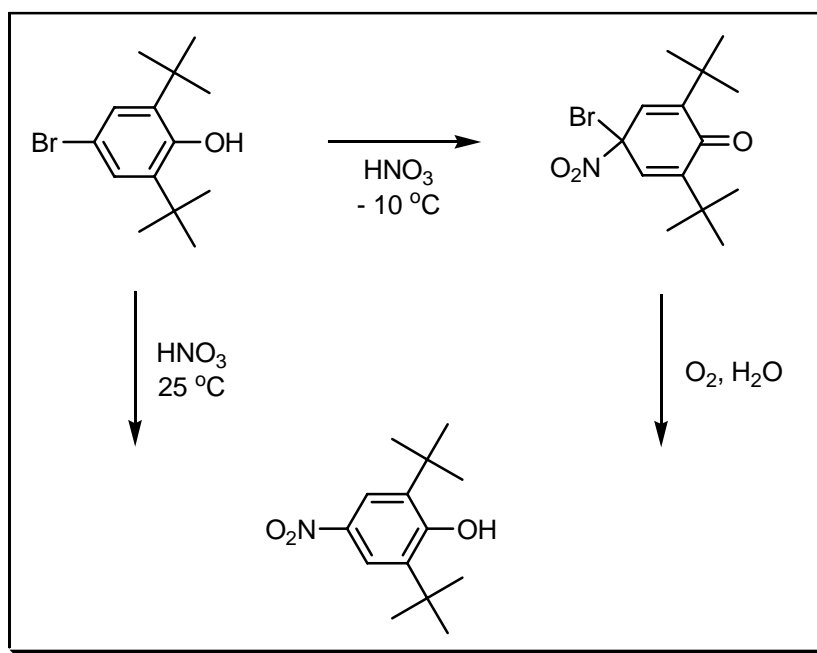
**COMMENTS :**

## ZINCKE HALOGENPHENOL NITRATION

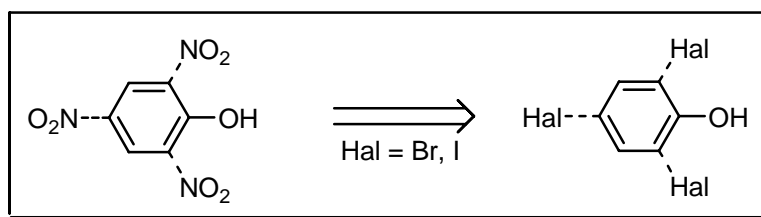
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

The replacement of *o*- and *p*-bromine or iodine atoms (not fluorine or chlorine) in phenols by nitro groups using nitrous acid or a nitrite in acidic acid. See also **Wolffenstein – Bötters** reaction.

### REFERENCES :

Houben – Weyl : 10/1, 821

- 1) Th. Zincke, *J. Prakt. Chem.*, 1900, **61**, 561.
- 2) L.C. Raiford, *Am. Chem. J.*, 1910, **43**, 393.
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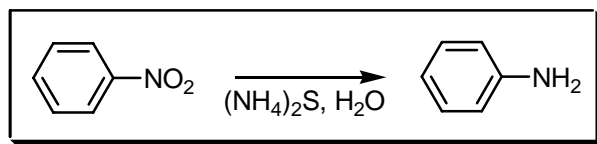
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**COMMENTS :**

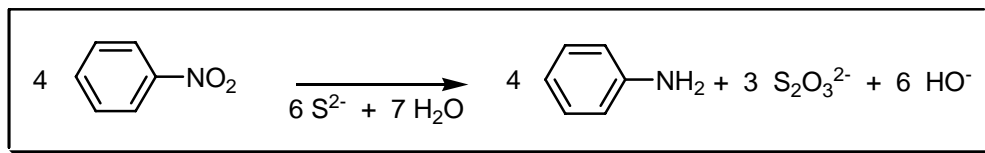
## ZININ REACTION

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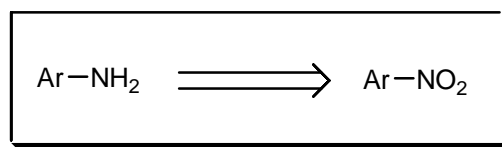
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



**NOTES :**

This is the reduction of nitro compounds to amines using sulfides or polysulfides. See also **Béchamp** reduction.

**REFERENCES :**

**March :** 1216

**Smith – March :** 1553

**Org. React. :** 20, 455

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- 1) N. Zinin, *J. Prakt. Chem.*, 1842, **27**, 140.
- 2) K. Brand, *J. Prakt. Chem.*, 1906, **74**, 449.
- 3) M. Hojo; Y. Takagi; Y. Ogata, *J. Am. Chem. Soc.*, 1960, **82**, 2459.

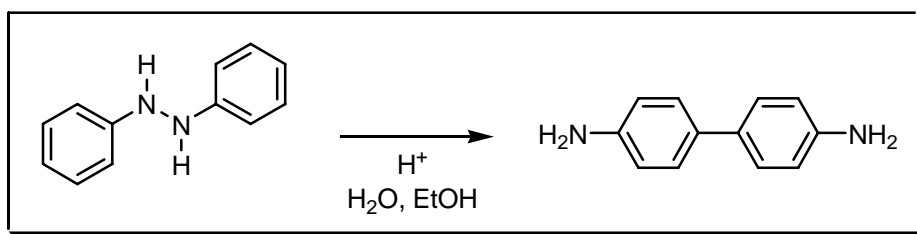
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**COMMENTS :**

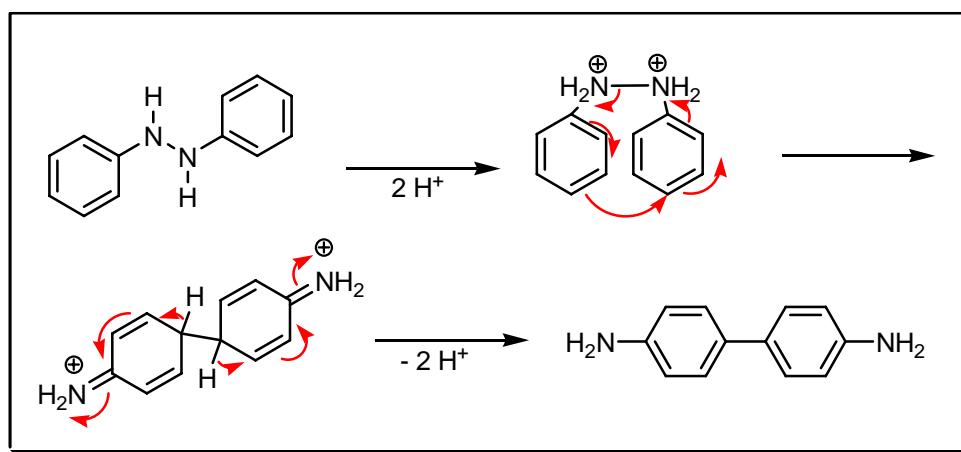
**ZININ REARRANGEMENT**

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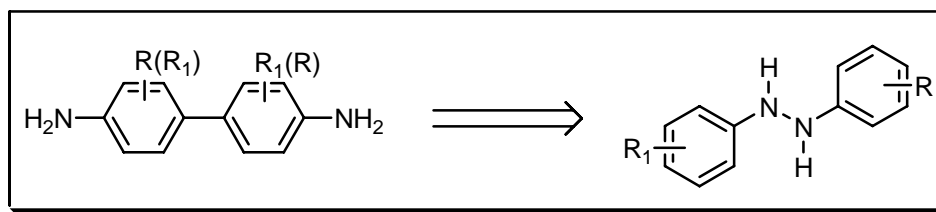
**EXAMPLE :**



**MECHANISM :**



**DISCONNECTION :**



## NOTES :

1,2-Diphenyl hydrazine is converted to 4,4'-diaminobiphenyl under acidic conditions. The mechanism involves a [5,5]-sigmatropic rearrangement. Even with the *para* position occupied the rearrangement can still take place. This reaction is maybe better known as the benzidine rearrangement.

---

## REFERENCES :

**March** : 1144

**Smith – March** : 1455

**Houben – Weyl** : 4/2, 58; 11/1, 839

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1) N. Zinin, *J. Prakt. Chem.*, 1845, **36**, 93.

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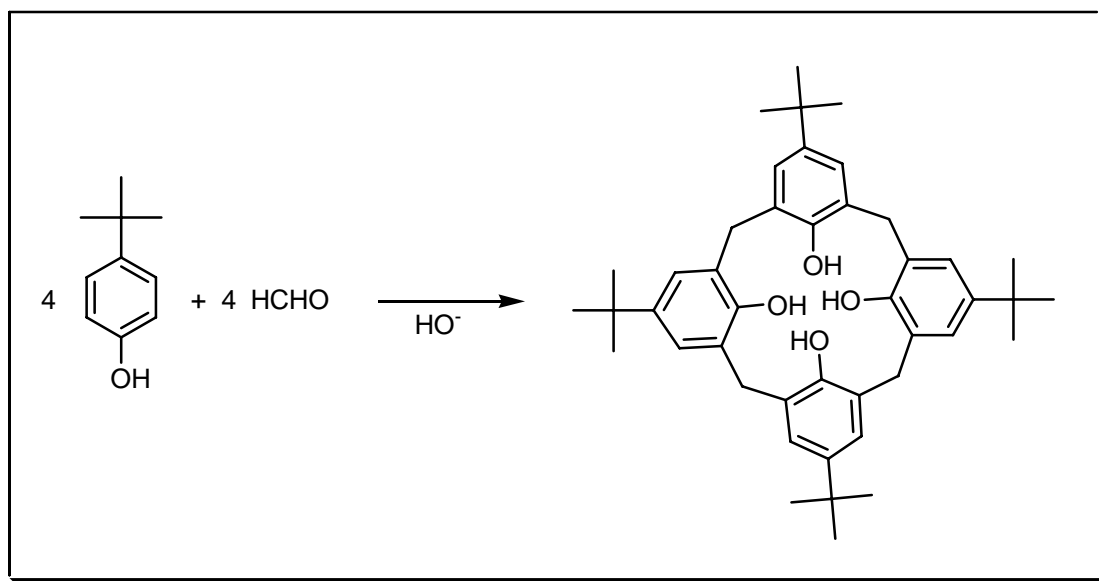
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## COMMENTS :

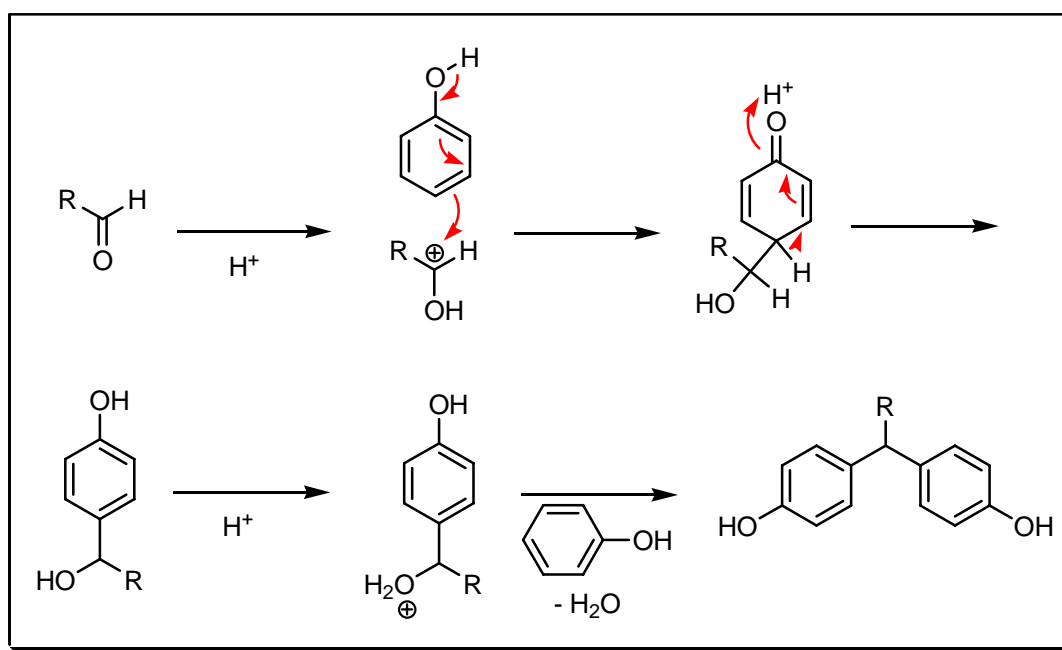


## ZINKE – ZIEGLER SYNTHESIS

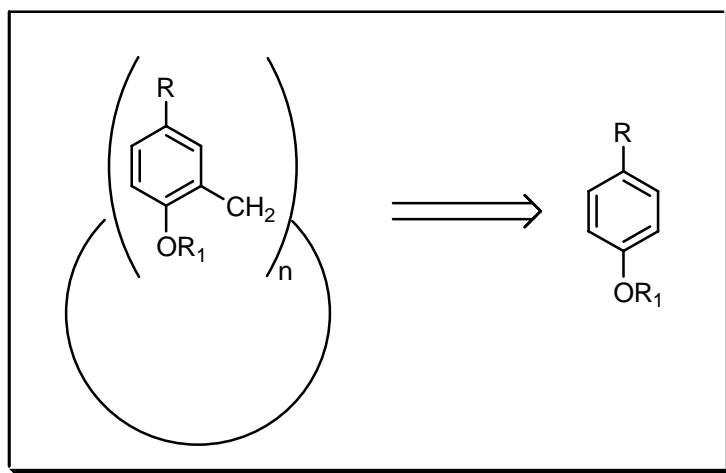
### EXAMPLE :



### MECHANISM :



## DISCONNECTION :



## NOTES :

The synthesis of calixarenes from formaldehyde and phenols or resorcinols under basic conditions. The shapes range from baskets to wheels. There is a synthetic modification better known as the **Zinke – Cornforth** modification. See also **Baekeland**, **von Baeyer** aldehyde and **Lederer – Manasse** reactions.

## REFERENCES :

**March** : 84

**Smith – March** : 106

**Org. Synth.** : 68, 234

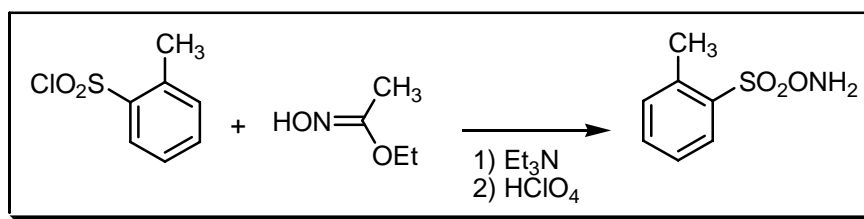
**Org. Synth. Coll. Vol.** : 8, 75, 77

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- 5) C.D. Gutsche, *Acc. Chem. Res.*, 1983, **16**, 161.
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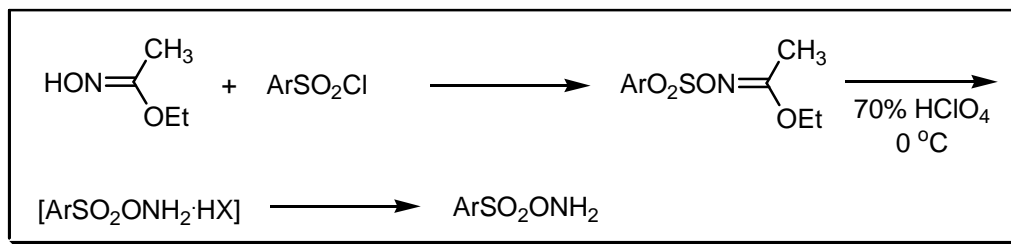
COMMENTS :

## ZINNER SYNTHESIS

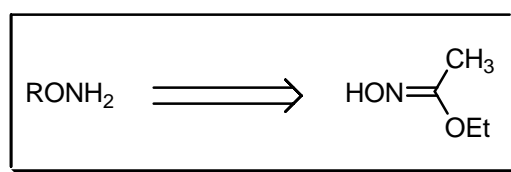
EXAMPLE :



MECHANISM :



DISCONNECTION :



NOTES :

The preparation of O-aryloyl-, O-carbalkoxy-, O-arylsulfonyl-, and O-nitrophenyl hydroxylamines starting with ethylhydroxamate. **Zinner's** method has been improved by **Tamura et al.**

## REFERENCES :

- 1) G. Zinner, *Angew. Chem.*, 1957, **69**, 204.
- 2) G. Zinner, *Angew. Chem.*, 1957, **69**, 480.
- 3) G. Zinner, *Chem. Ber.*, 1958, **91**, 302.
- 4) Y. Tamura; J. Minamikawa; K. Sumoto; S. Fujii; M. Ikeda, *J. Org. Chem.*, 1973, **38**, 1239.
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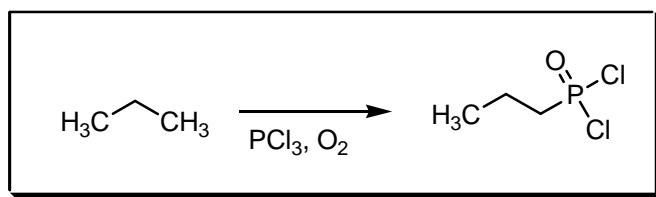
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## COMMENTS :

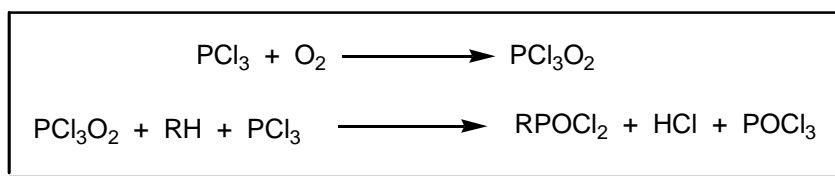
## ZINOVEV – SOBOROVSKI REACTION

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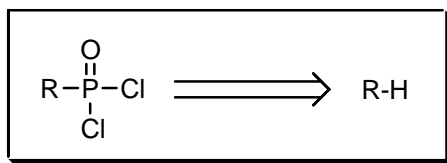
### EXAMPLE :



### MECHANISM :



### DISCONNECTION :



### NOTES :

It involves the synthesis of dichloroanhydrides or of alkylphosphonic acids by oxidative phosphorylation of hydrocarbons. With long chain hydrocarbons, branching takes place. This reaction is also known under the name of **Clayton – Jensen** reaction. See also **McBride** reaction.

## REFERENCES :

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  - 2) W.L. Jensen; R.C. Noller, *J. Am. Chem. Soc.*, 1949, **71**, 2384.
  - 3) L.S. Soborovski; Yu.M. Sinovev; M.A. Englin, *Ber. Akad. Wiss. USSR*, 1950, **73**, 333.
  - 4) R. Graf, *Chem. Ber.*, 1952, **85**, 9.
  - 5) G. Geiseler; F. Asinger; M. Fedtke, *Chem. Ber.*, 1960, **93**, 765.
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### Other books:

Thin Layer Chromatography Visualisation Reagents, 1<sup>st</sup> Edition. Available as E-book or ring bound. Prices £15.00 and £20 +P&P.

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