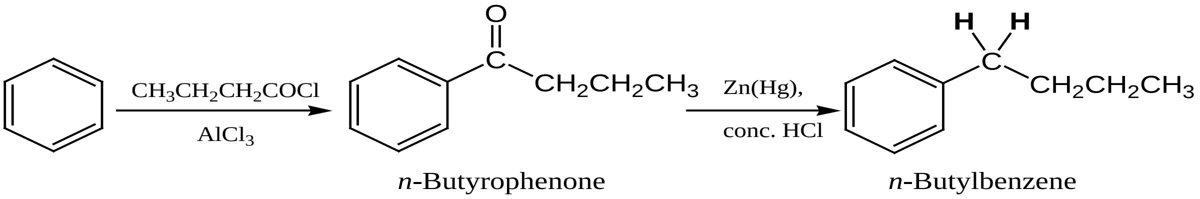
CLEMMENSEN REDUCTION

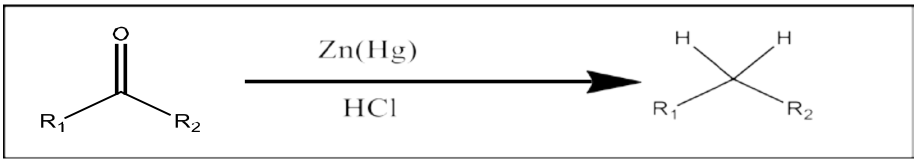
1. This reaction was first reported by Clemmensen of Park Davis in 1913.
2. It is the reduction of carbonyl groups (in aldehyde and ketone) to
3. methylene group.
4. This reaction done with zinc amalgam and hydrochloric acid and it is generally known as Clemmensen reduction.
5. The Clemmensen reduction is particularly effective at reducing aryl- alkyl ketones, such as those formed in a Friedel-Crafts acylation.

The **Clemmensen reduction** is most commonly used to convert acylbenzenes (from Friedel-Crafts acylation) to alkylbenzenes, but it also works with other ketones or aldehydes that are **not sensitive to acid**. The carbonyl compound is **heated** with an excess of amalgamated zinc (zinc treated with mercury; **Zn (Hg),** and concentrated hydrochloric acid **(HCl)**. The actual reduction occurs by a complex mechanism on the surface of the zinc.



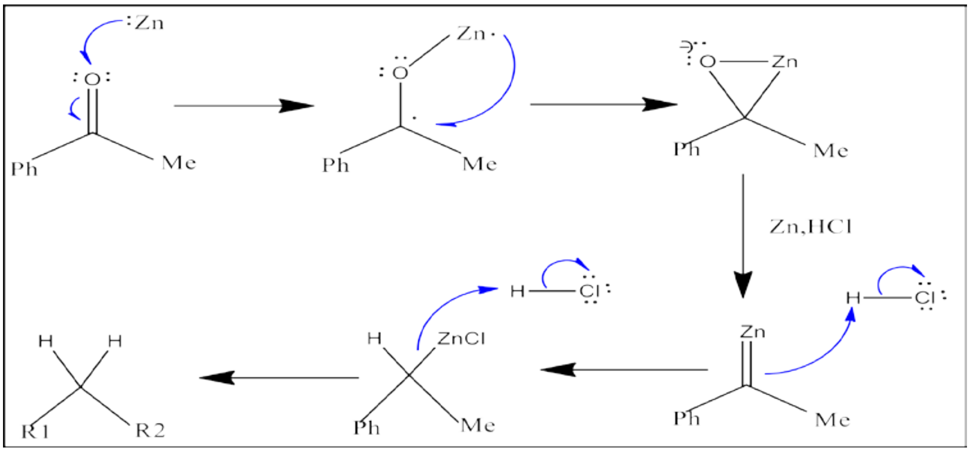
The **Clemmensen reduction** uses zinc and mercury in the presence of strong acid.

The general reaction is



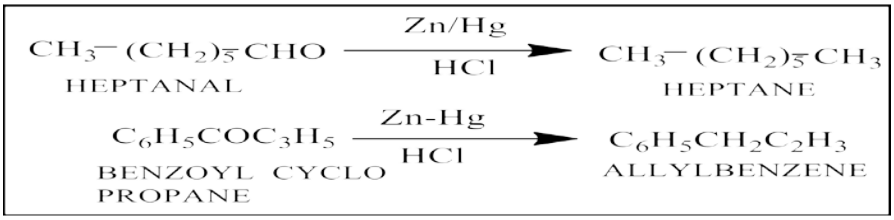
R1=Alkyl, Aryl R2= H, Alkyl, Aryl

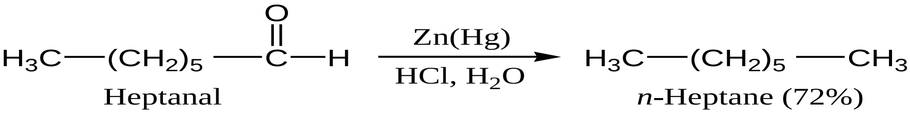
Mechanism:

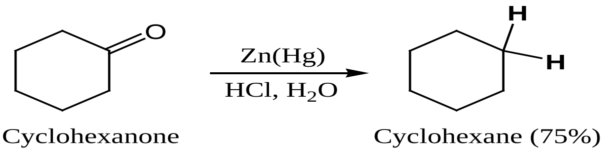


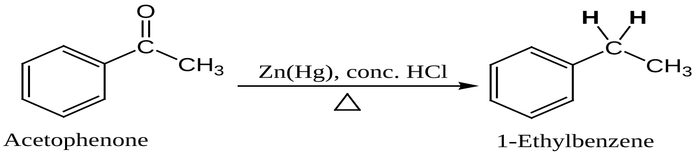
Applications:

1. This reaction has widely used to convert a carbonyl group into a methylene group.
2. It’s important application in the preparation of polycyclic aromatics and aromatics containing unbranched side hydrocarbon chains.
3. This reaction helps to reduce the aliphatic and mixed aliphatic-aromatic carbonyl compounds.







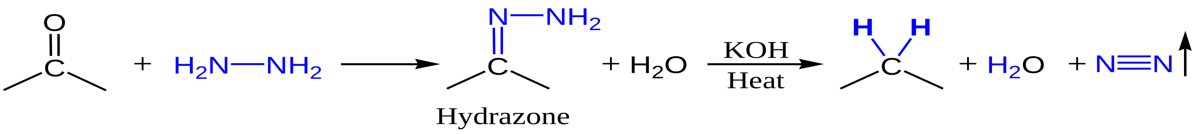


WOLFF–KISHNER REACTION

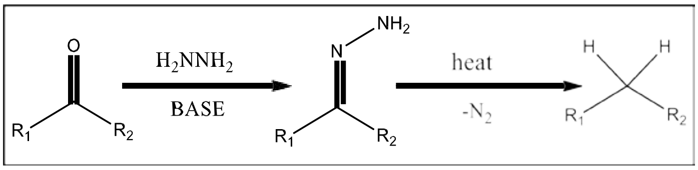
1. The Wolff– Kishner reduction was discovered independently by N. Kishner in 1911 and L. Wolff in 1912.
2. The Wolff– Kishner reduction is a reaction used in organic chemistry to convert carbonyl functionalities into methylene groups.
3. The Wolff-Kishner reduction is an organic reaction used to convert an aldehyde or ketone to an alkane using hydrazine, base, and thermal conditions.

4. Because of the Wolff–Kishner reduction requires highly basic conditions, it is unsuitable for base-sensitive substrates.

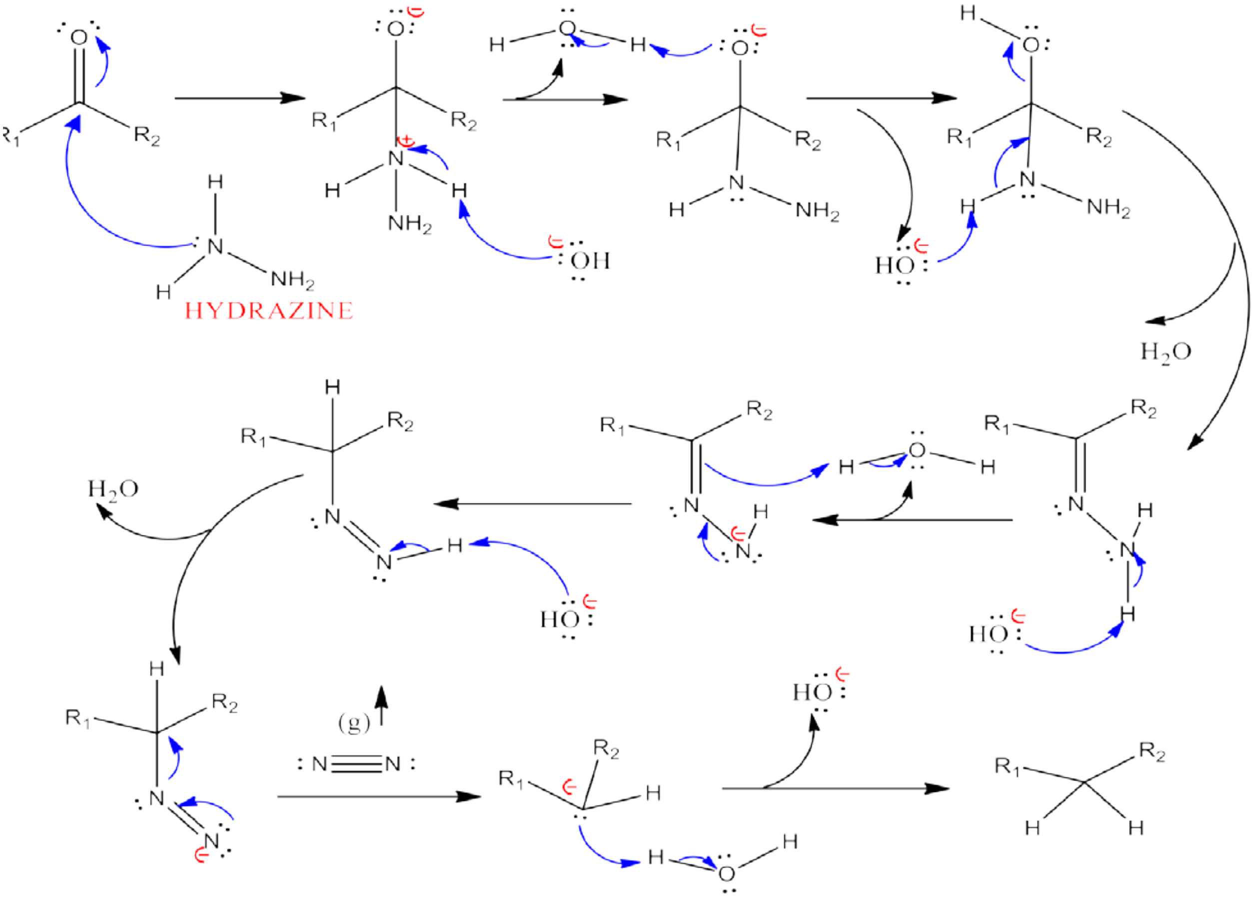
Compounds that cannot survive treatment with hot acid can be deoxygenated using the **Wolff–Kishner reduction.** The ketone or aldehyde is converted to its **hydrazone**, which is **heated** with Hydrazine **(NH_2NH_2)**, and **strong base** such as **KOH**. Ethylene glycol, diethylene glycol, or another high-boiling solvent is used to facilitate the high temperature (140-200°C) needed in the second step.



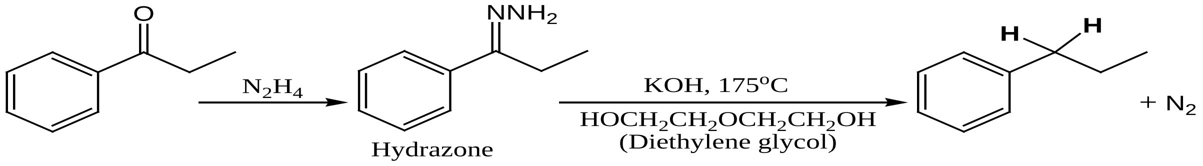
The general reaction is

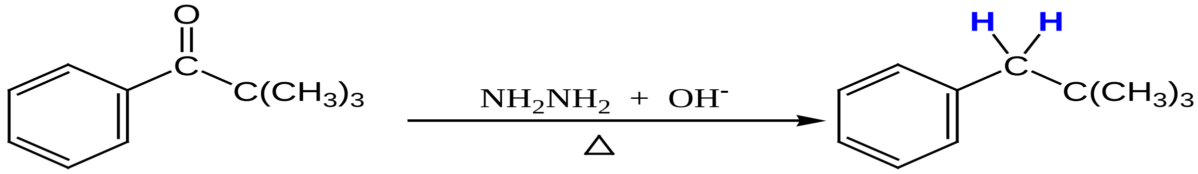


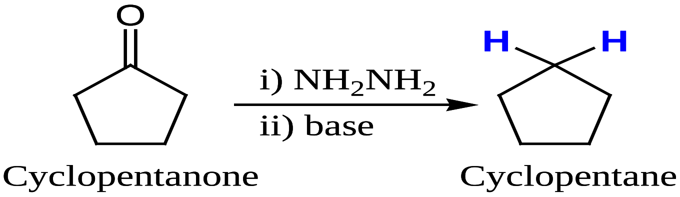
Mechanism:



Examples:







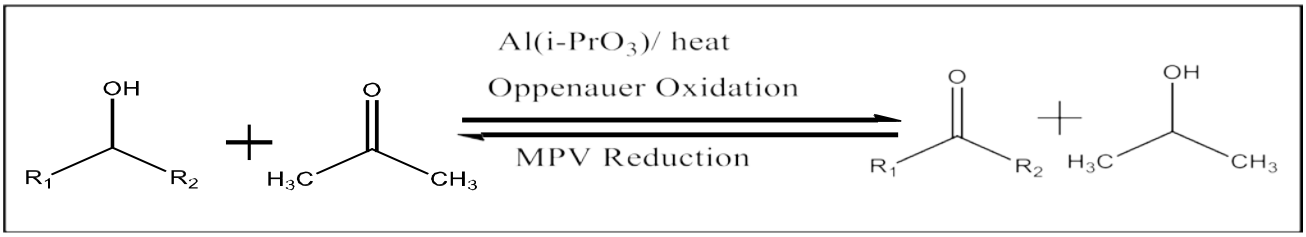
Applications:

1. This reaction has very broad application in organic synthesis, especially for the multiwalled carbon nanotubes.
2. In 2011, Pettus and Green reduced a tricyclic carbonyl compound using the Huang Minlon modification of the Wolff–Kishner reduction. Several attempts towards decarbonylation of tricyclic allylic acetate containing ketone failed and the acetate functionality had to be removed to allow successful Wolff–Kishner reduction. Finally, the allylic alcohol was prepared via oxyplumbation.
3. The Wolff–Kishner reduction has also been used on kilogram scale for the synthesis of a functionalized imidazole substrate.

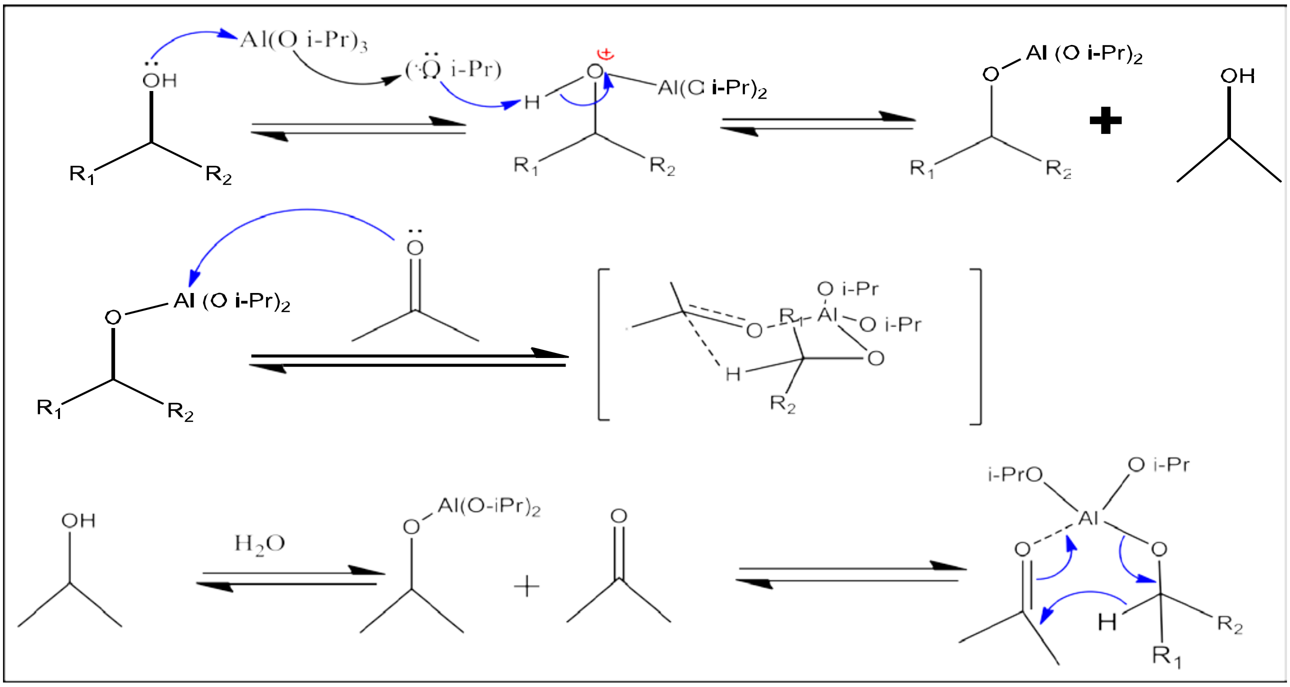
OPPENAUER OXIDATION

1. Named after Rupert Viktor Oppenauer.
2. It is a gentle method for selectively oxidizing secondary alcohols to ketones.
3. The reaction is the opposite of Meerwein– Ponndorf –Verley reduction.
4. The alcohol is oxidized with aluminium isopropoxide in excess acetone.
5. This shifts the equilibrium toward the product side.
6. The oxidation is highly selective for secondary alcohols and does not oxidize other sensitive functional groups such as amines and sulfides,
7. Though primary alcohols can be oxidized under Oppenauer conditions, primary alcohols are seldom oxidized by this method due to the competing aldol condensation of aldehyde products.
8. The Oppenauer oxidation is still used for the oxidation of acid labile substrates.

The general reaction is

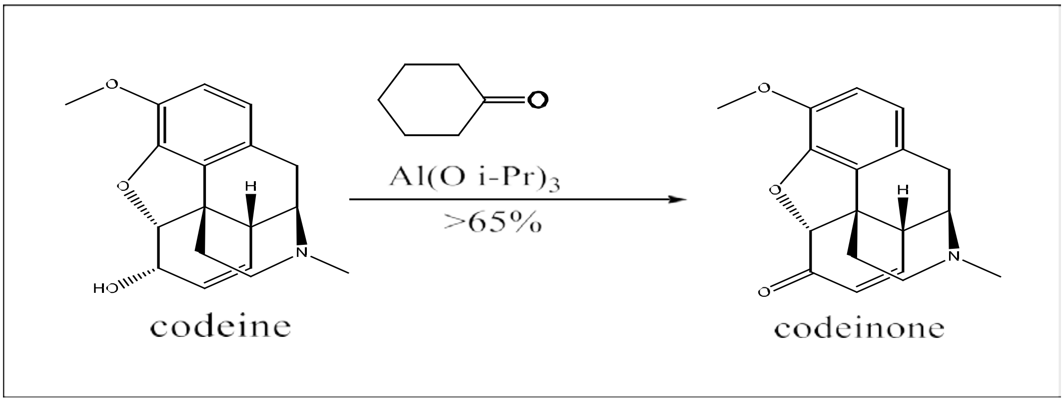


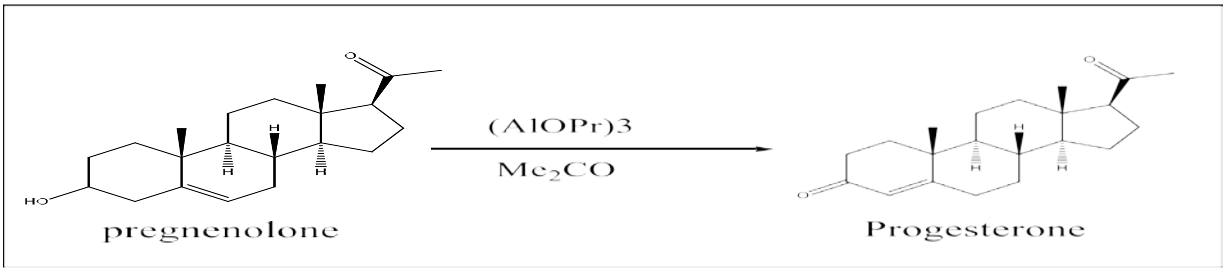
Mechanism:

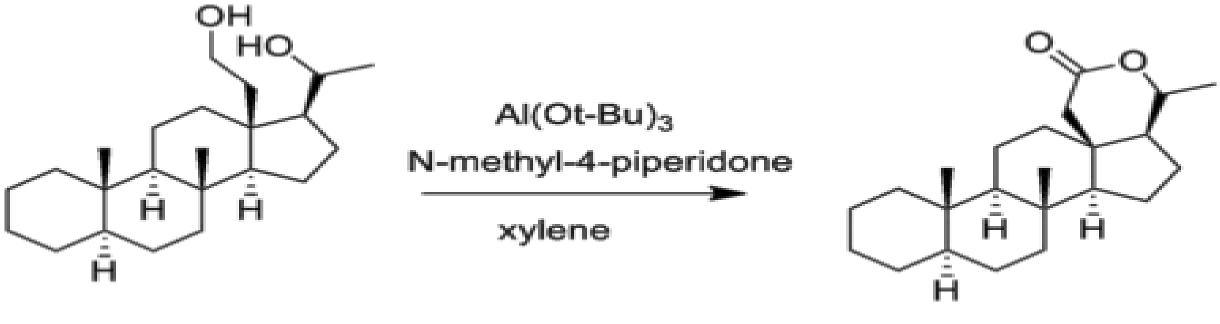


Applications:

1. The Oppenauer oxidation is used to prepare analgesics in the pharmaceutical industry such as morphine and codeine. For instance, codeinone is prepared by the Oppenauer oxidation of codeine.
2. The Oppenauer oxidation is also used to synthesize hormones.
3. Progesterone is prepared by the Oppenauer oxidation of pregnenolone.
4. The Oppenauer oxidation is also used in the synthesis of lactones from 1,4 and 1,5 diols.





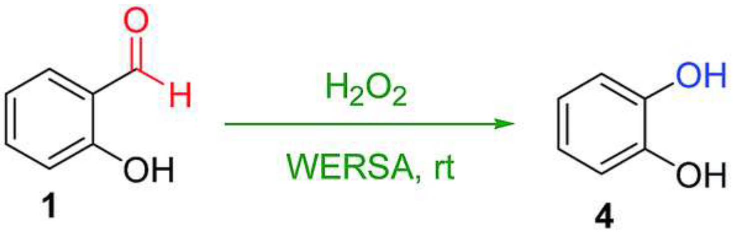


DAKIN REACTION

1. The oxidation of aldehydes and ketones to the corresponding phenols is known as **Dakin reaction**.
2. The reaction works best if the aromatic aldehyde or ketone is electron rich.

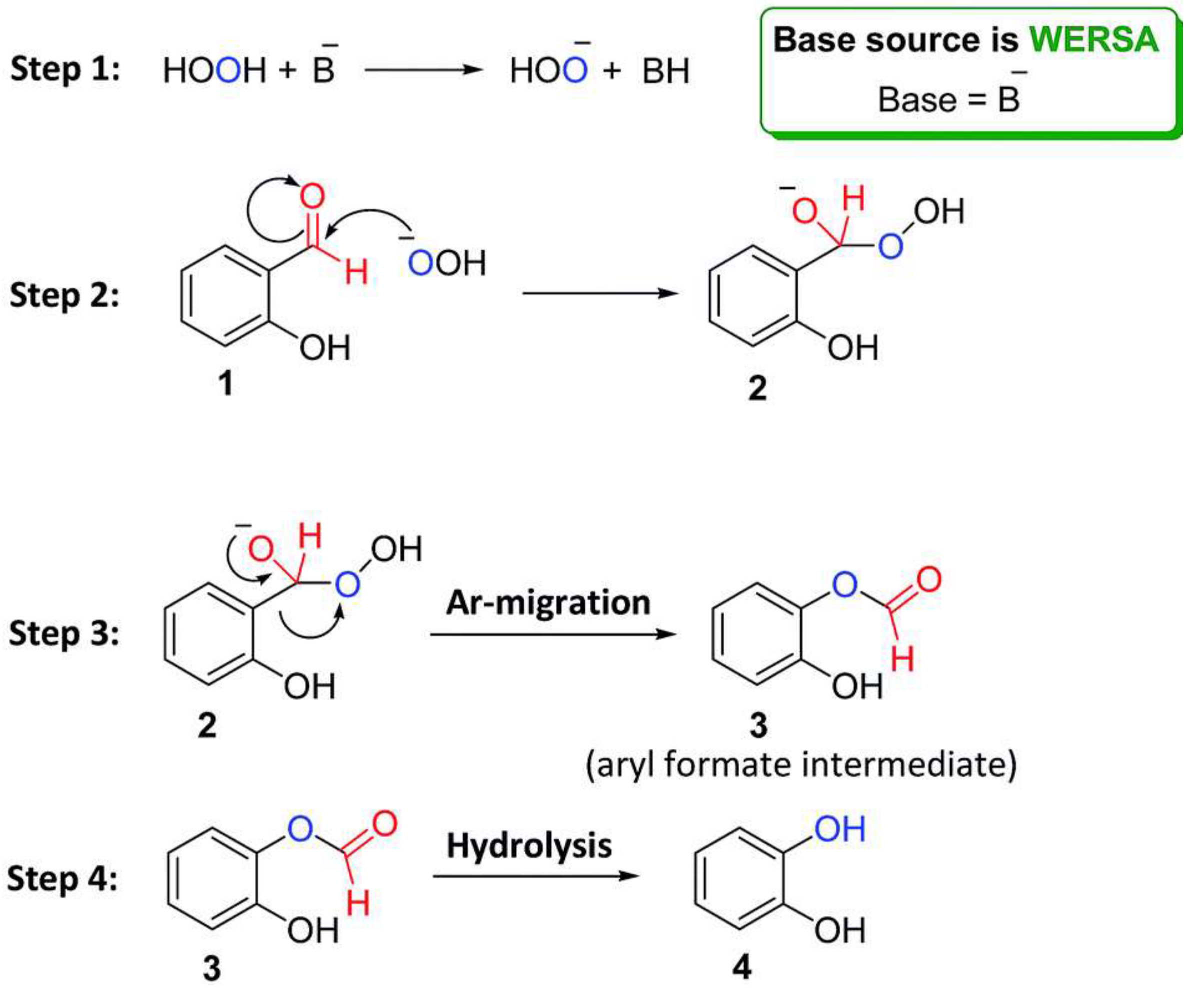
3. The reagents used in Dakin Reaction are; Alkaline H_2O_2, acidic H_2O_2, Peroxybenzoic acid($C_2H_4O_3$), 30% H_2O_2 with aryl selenium compounds as activators and Urea-H_2O_2 adduct.

The general reaction is



[WERSA (water extract of rice straw ashes) as a neat reaction medium]

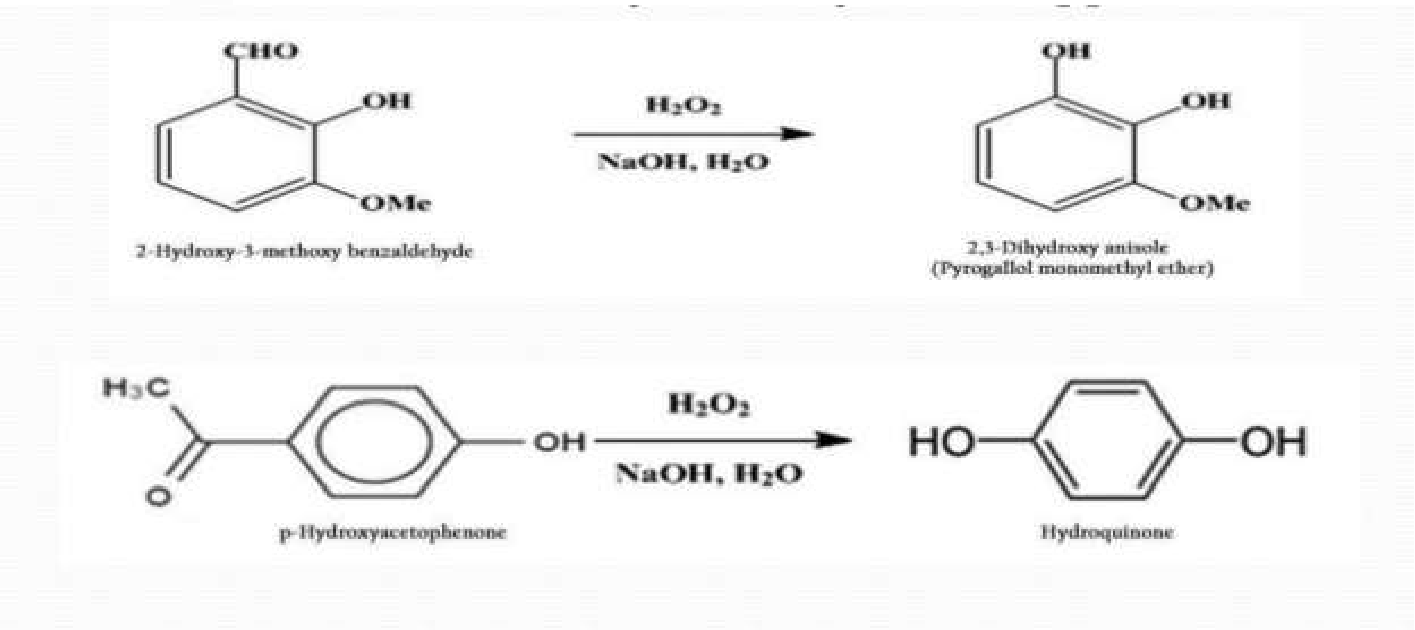
Mechanism:



Application:

It is used in the preparation of synthetic compounds

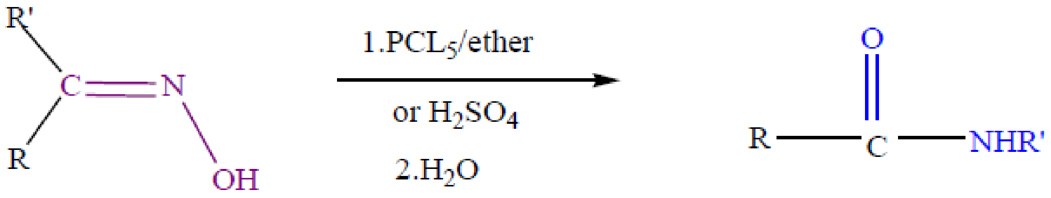
1. The Dakin oxidation is most commonly used to synthesize benzenediols and alkoxyphenols.
2. Catechol, for example, is synthesized from a-hydroxy and O-alkoxy phenyl aldehydes and ketones and is used as the starting material for synthesis of several compounds, including the catecholamines, catecholamine derivatives and 1,4-tertbutlycatechol a common antioxidant and polymerization inhibitor.
3. Other synthetically useful products of the Dakin reaction include guaiacol, a precursor of several flavorants.
4. Hydroquinone, a common photograph developing agent; and 2-tertbutyl-4-hydrooxyanisole and 3-tertbutyl-4- hydrooxyanisole, two antioxidants commonly used to preserve packaged food.
5. Dakin's solution is used to prevent and treat skin and tissue infections that could result from cuts, scrapes and pressure sores.
6. It is also used before and after surgery to prevent surgical wound infections.
7. Dakin's solution is a type of hypochlorite solution. It is made from bleach that has been diluted and treated to decrease irritation.
8. Chlorine, the active ingredient in Dakin's solution, is a strong antiseptic that kills most forms of bacteria and viruses.
9. Protect the surrounding healthy skin with a moisture barrier ointment (e.g., petroleum jelly) or skin sealant as needed to prevent irritation.



BECHMANN REARRANGEMENT

1. The Beckmann rearrangement, named after the German chemist Ernst Otto Beckman (1853–1923).
2. It is an acid catalyzed conversion of keto **oximes** to **N substituted amides** usually called the Bechmann rearrangement.

Reaction:

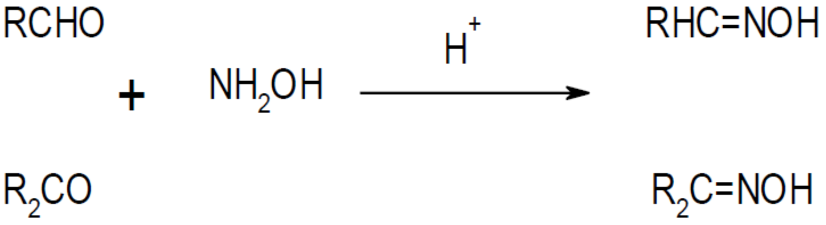


OXIMES

- In organic chemistry, compounds containing the grouping ***C = N-OH***, derived from **aldehyde** and **Ketones** by condensing them with **hydroxylamine**.
- Two types of oximes are known:

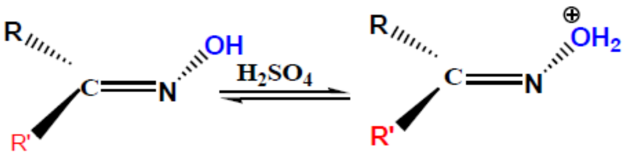
Aldoxime: combination of aldehyde with hydroxylamine.
Ketoxime: Combination of Ketones with hydroxylamine.

The general reaction is

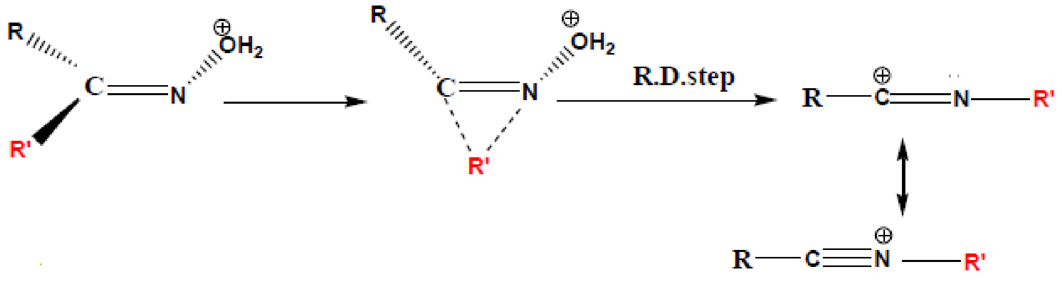


Mechanism:

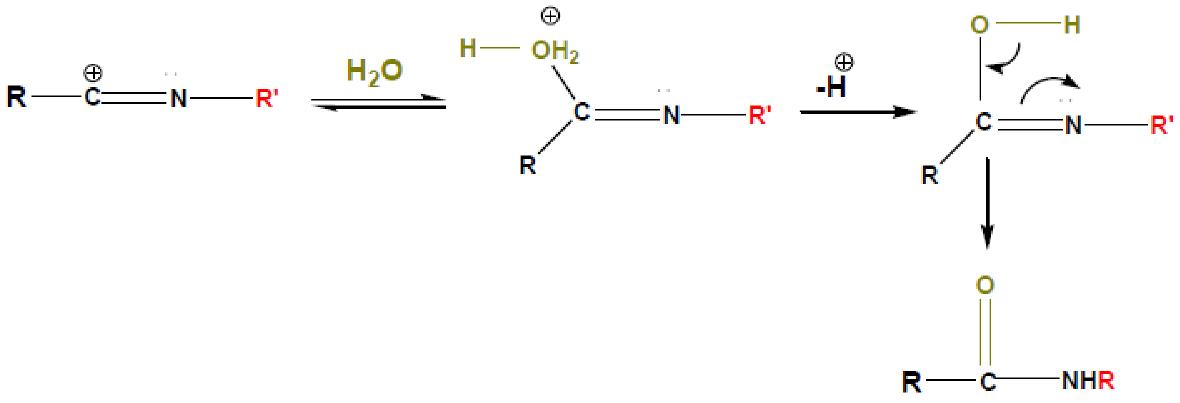
Step 1: Formation of a better leaving group



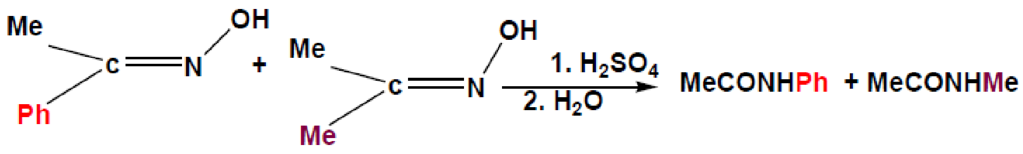
Step 2: Ionization step (migration of anti group (leaving group) loss of leaving group)



Step 3: Nucleophilic attach by water molecule to carbenium ion



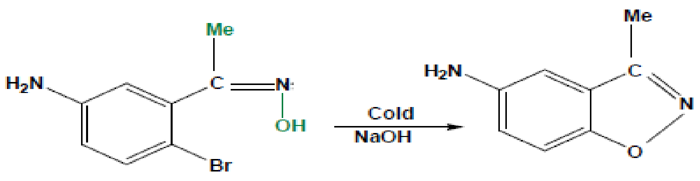
In stereo chemistry Reaction is **intramolecular.**



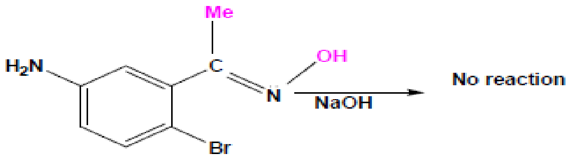
In **high polarity solvent rate of reaction is fast**. Rate of reaction also increase as **stability of leaving group** (anion)increase.

$CH_3COO^{-} < ClCH_2COO < PhSO3^{-}$

It is found that the **migrating group** is always **anti (i.e. tras)** to the hydroxy group, thus the reaction is steriospecific



(1) (3)



(2)

E.g.the rearrangement of the two isomeric **oximes of 2-bromo-5-nitrophenyl isooxamines**.
OH and Me gr.in isomer (1) are **close** enough for reaction ,and **anti(trans)** to each other.

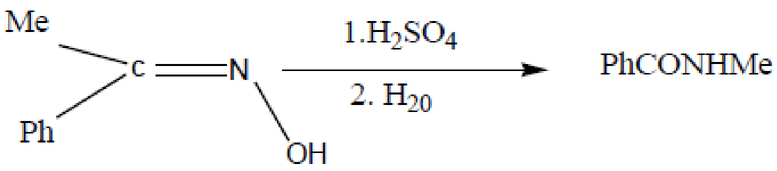
Direct exchange of the leaving group and the migrating group do not occure between N and C atom.

$$Ph_2CNOH \xrightarrow[\text{Bechmann rearrangemen}]{H_2{}^{18}O} PhCONHP \quad + PhC\,{}^{18}ONHPh$$

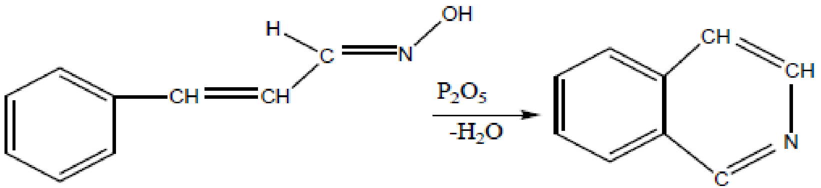
Oxygen atom come from medium

Application:

This reaction offers good method of preparing anilides



Synthesis of **isoquinoline**



cinnamaldehyde oxime Isoquinoline

SCHMIDT REACTION

1. It is a type of Named Rearrangement reaction.
2. Rearrangement reaction is also called Molecular Rearrangement.
3. This rearrangement involves migration of an alkyl or aryl group with its bonding electrons from carbon to the adjacent nitrogen atom.

Carboxylic acids and hydrazoic acids react in presence of concentrated sulphuric acids to give amines.

$$RCOOH + N_3H \xrightarrow{H_2SO_4} R-NH_2 + CO_2\uparrow + N_2\uparrow$$

Schmidt reaction also occur in ketones

$$R_2CO + N_3H \xrightarrow{H_2SO_4} RCONHR + N_2\uparrow$$

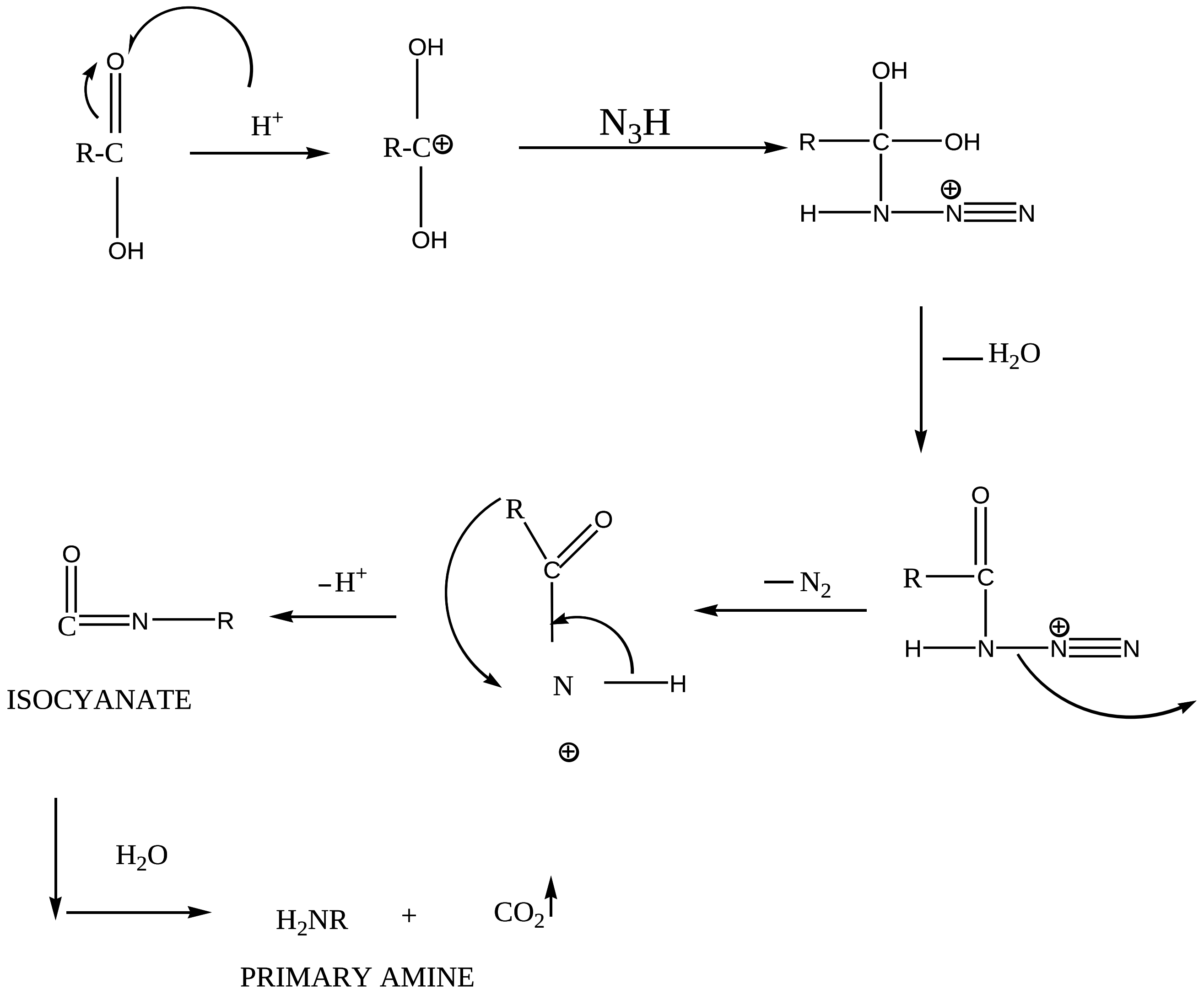
Aldehydes: This reaction closely releated to Hofmann and Curtius reaction, of all which involves formation of isocyanate intermediate through the migration of group from carbon to nitrogen.

This rearrangement closely resemble the Beckmann rearrangement.

The general reaction is

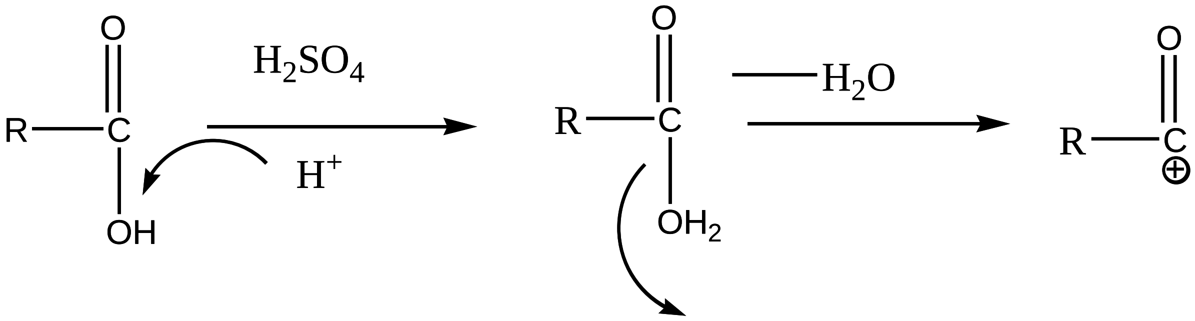
$$\underset{\text{ALDEHYDE}}{RCHO} + \underset{\text{HYDRAZOIC ACID}}{N_3H} \xrightarrow{H_2SO_4} \underset{\text{NITRILE}}{RC\equiv N} + \underset{\text{N-FORMYL DERIVATIVES}}{RNHCHO}$$

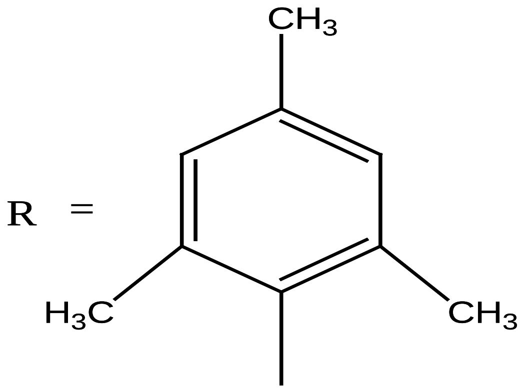
Mechanism:



O
R-C
OH
H+
OH
R-C⊕
OH
N3H
OH
R
C
OH
H
N
⊕
N
N
— H2O
O
R
C
H
N
⊕
N
N
— N2
R
O
C
N
H
⊕
–H+
O
C
N
R
ISOCYANATE
H2O
H2NR
+
CO2
PRIMARY AMINE

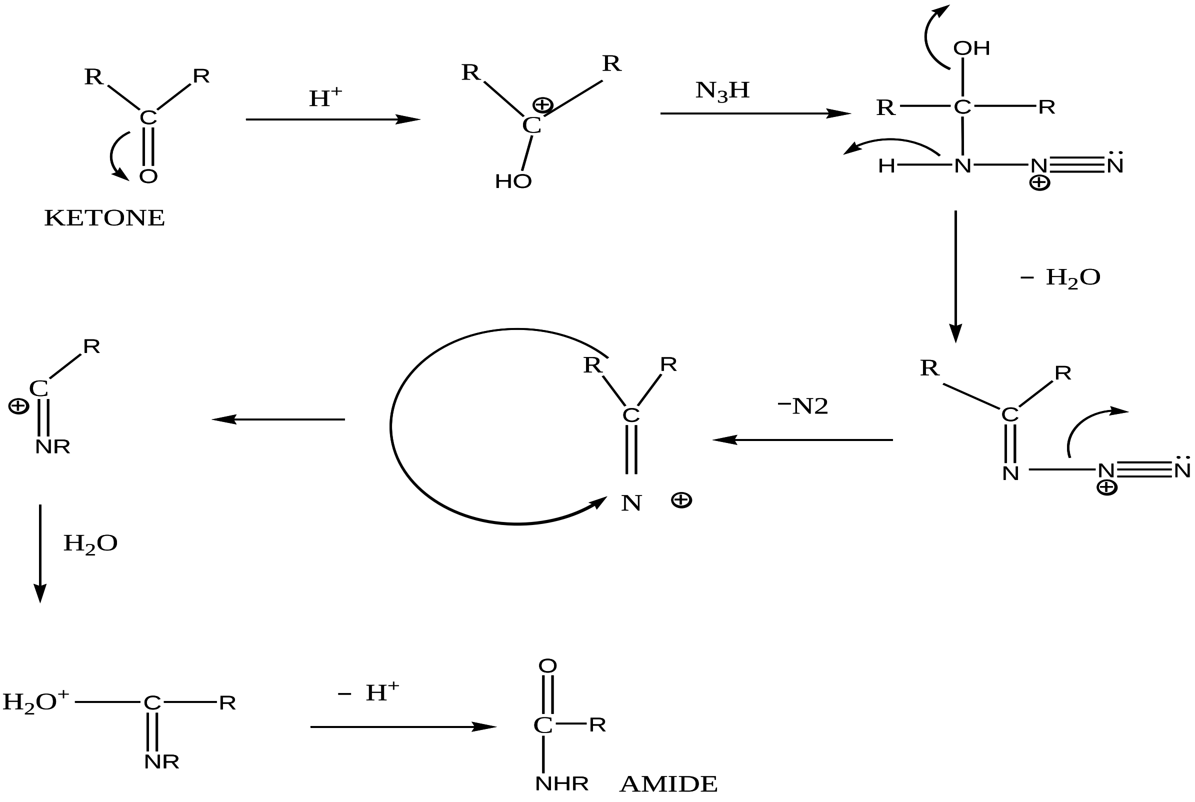
Sterically **hindered acids**:



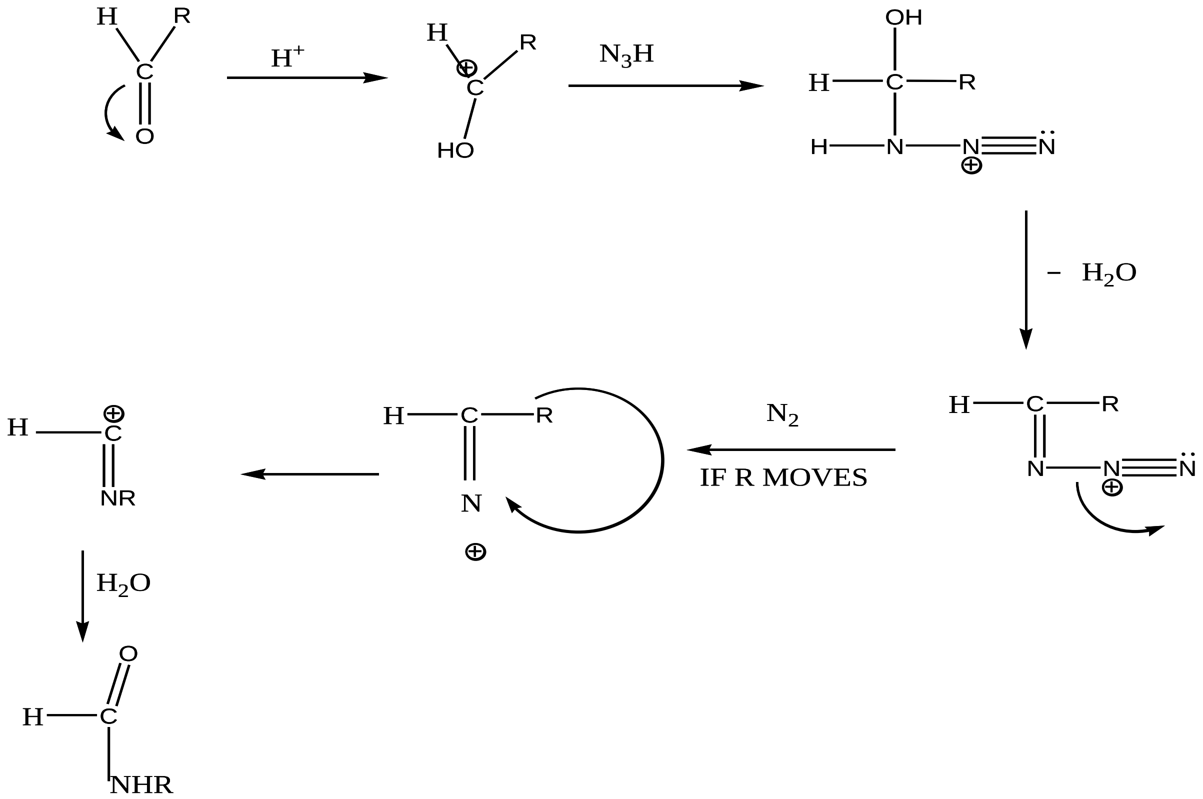


2,4,6 Trimethyl benzoic acid

Reaction with **Ketone**:



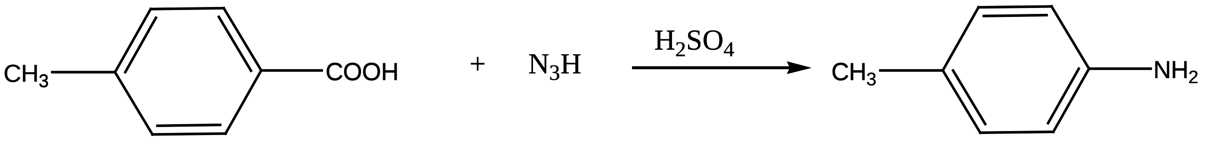
Mechanism:



FORMYL DERIVATIVE OF PRIMARY AMINE

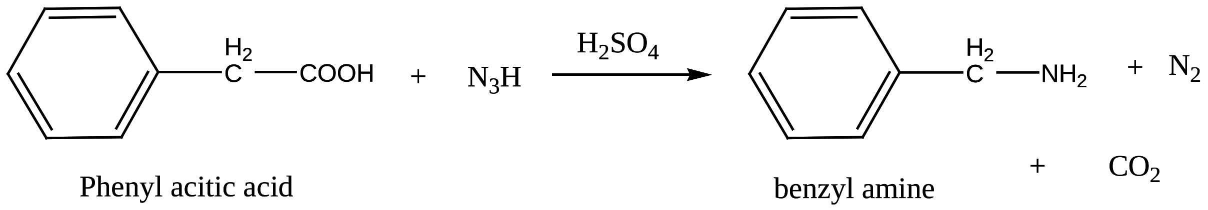
Application:

Preparation of **Primary Amines**- (It is a direct method for the preparation of primary amines from carboxylic acid and give usually better yield than the hofmann or curtius reaction)

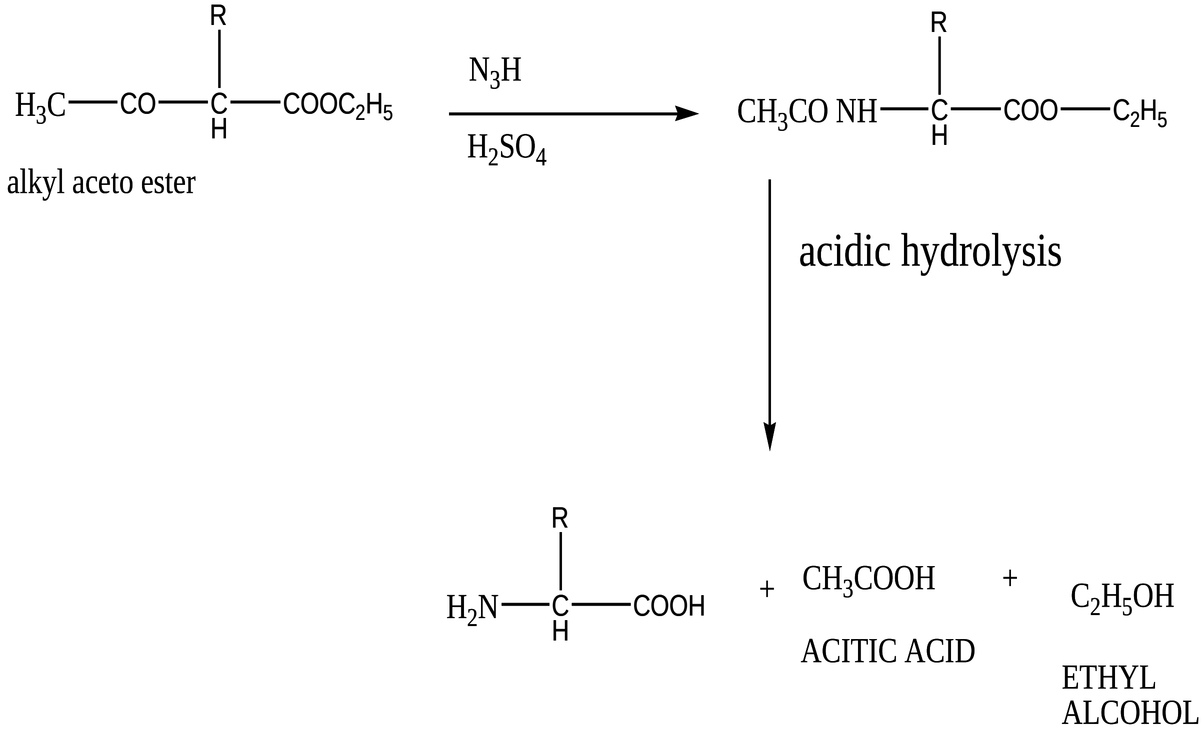


para toluic acid

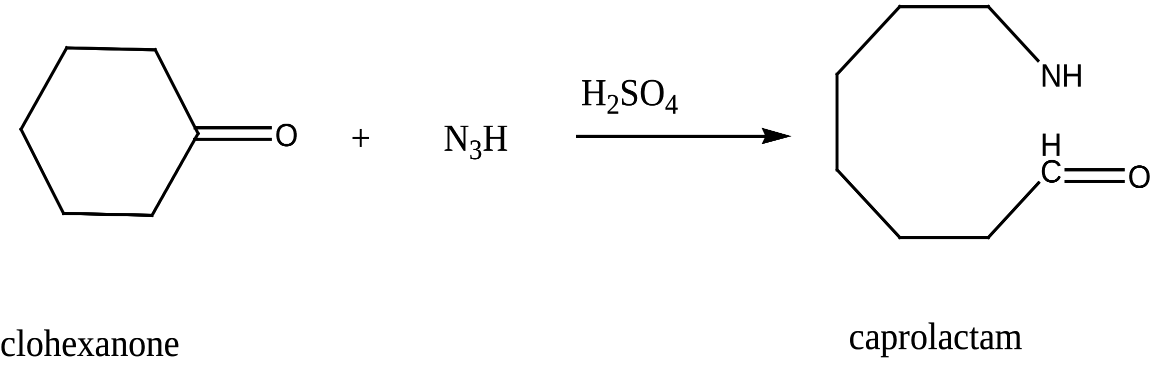
para toluidine



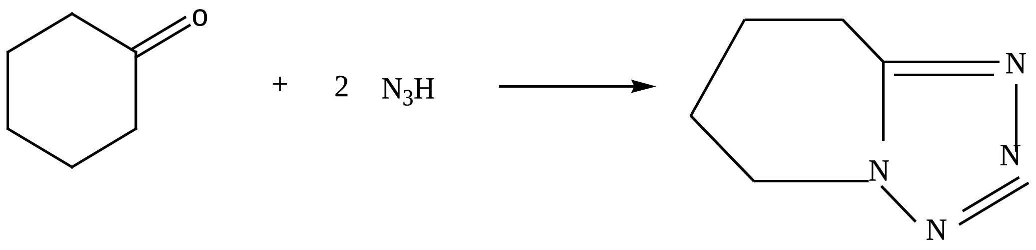
Preparation of **aminoacids**



Preparation of **lactones**



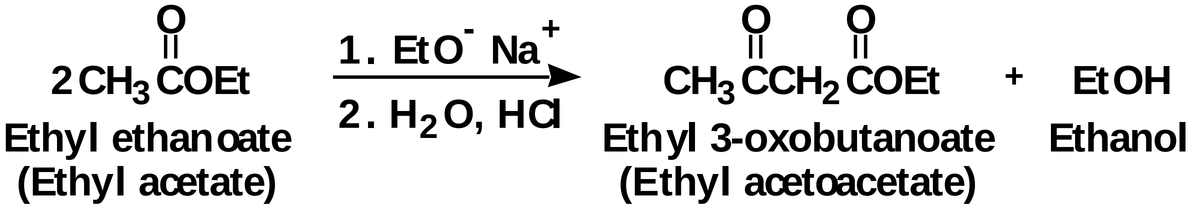
If excess of hydrazoic acid used: cyclic ketones gives tetrazoles



CLAISEN-SCHMIDT CONDENSATION

1. Condensation of an aromatic aldehyde with an aliphatic aldehyde or ketones in the presence of a base or an acid to form an alpha-beta-unsaturated aldehyde or ketone with high chemoselectivity.
2. This is also known as an acetoacetic ester condensation or cross aldol condensation.
3. This reaction aids in effecting carbon – carbon bond formation in organic synthesis.
4. When we have two carbonyl groups adjacent to a methylene group, the acidity of the a) H is greatly increased. Because of the acidity of their methylene hydrogens, malonic esters, ethylacetoacetate and b)dicarbonyl compounds and others are often called active hydrogen compounds.

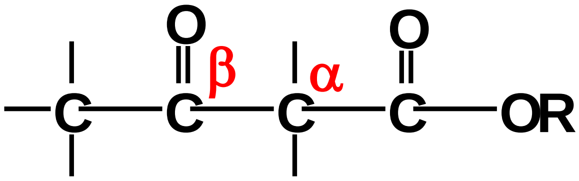
Esters also form enolate anions which participate in nucleophilic acyl substitution.



$$2\,CH_3\overset{O}{\overset{\|}{C}}OEt \xrightarrow[2.\ H_2O,\ HCl]{1.\ EtO^-\ Na^+} CH_3\overset{O}{\overset{\|}{C}}CH_2\overset{O}{\overset{\|}{C}}OEt + EtOH$$

Ethyl ethanoate (Ethyl acetate)
Ethyl 3-oxobutanoate (Ethyl acetoacetate)
Ethanol

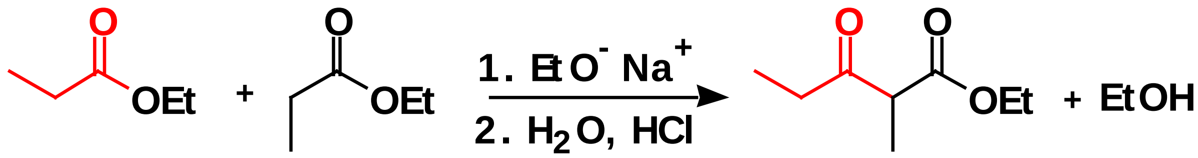
The product of a Claisen condensation is a b-ketoester



A β-ketoester

Recognition Element

Claisen condensation of **ethyl propanoate**

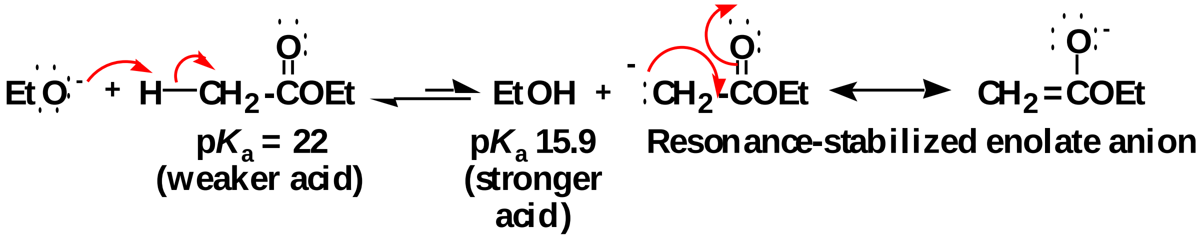


Ethyl propanoate **Ethyl propanoate** **Ethyl 2-methyl-3-oxopentanoate (racemic)**

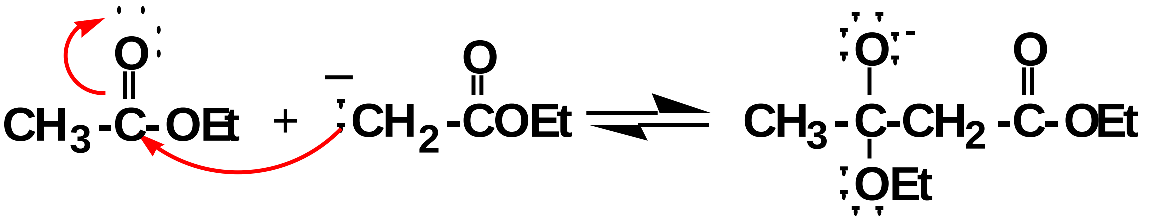
Here the enolate part of one ester molecule has replaced the alkoxy group of the other ester molecule.

Mechanism:

Step 1: Formation of an enolate anion.

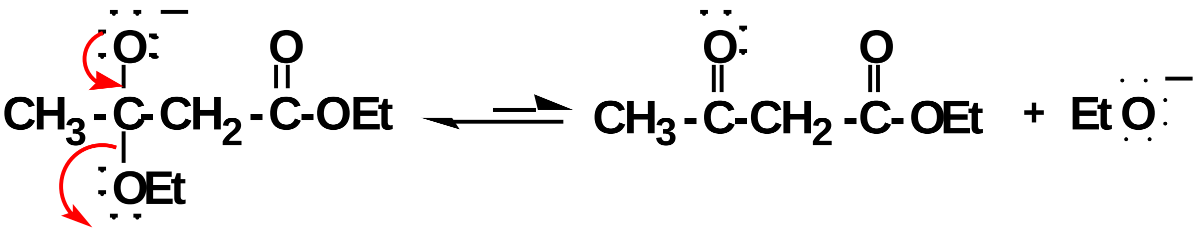


Step 2: Attack of the enolate anion on a carbonyl carbon gives a TCAI.

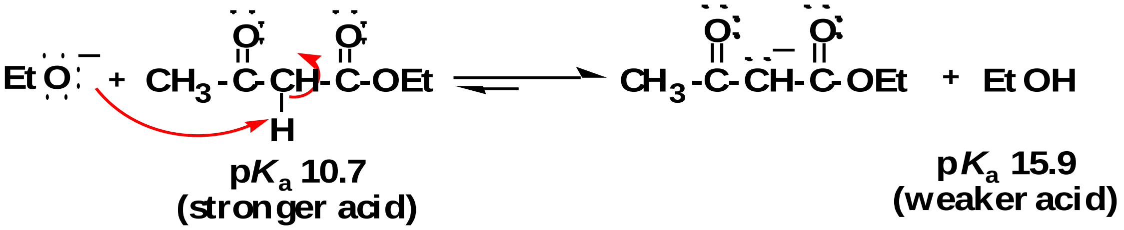


A tetrahedral carbonyl addition intermediate

Step 3: Collapse of the TCAI gives a b-ketoester and an alkoxide ion.



Step 4: An acid-base reaction drives the reaction to completion. This consumption of base must be anticipated.



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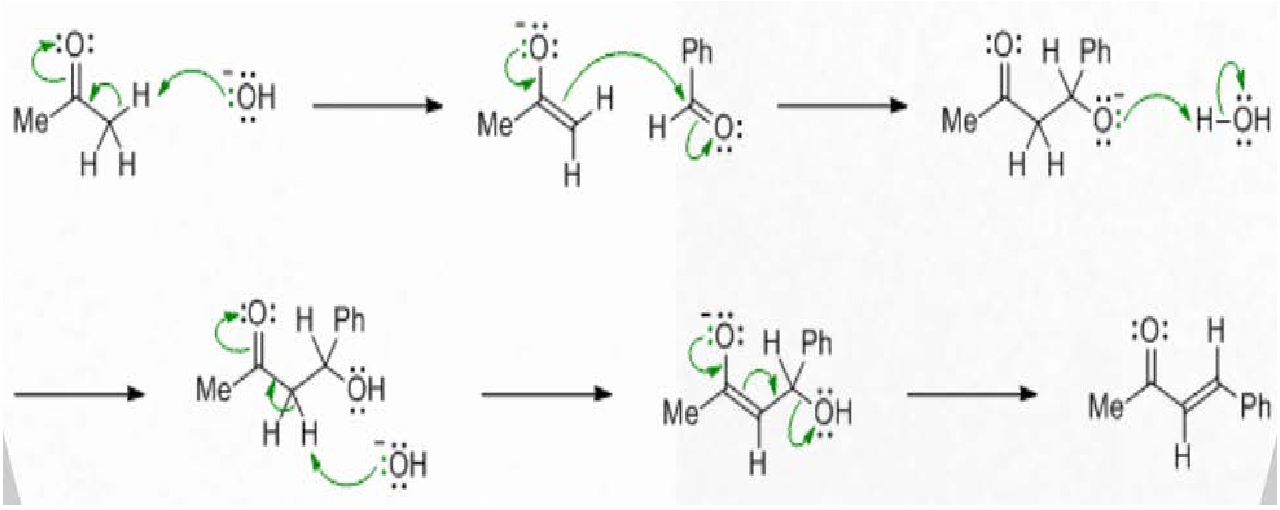

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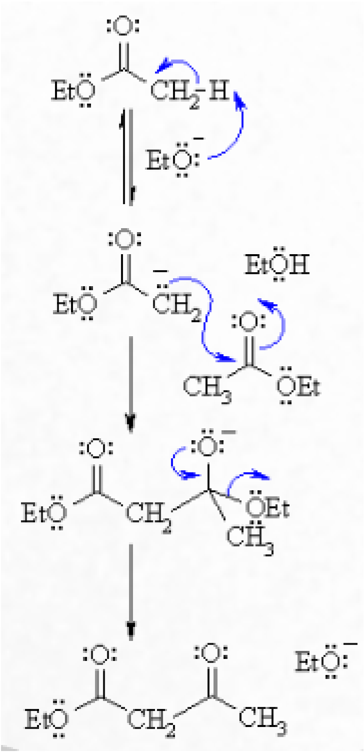
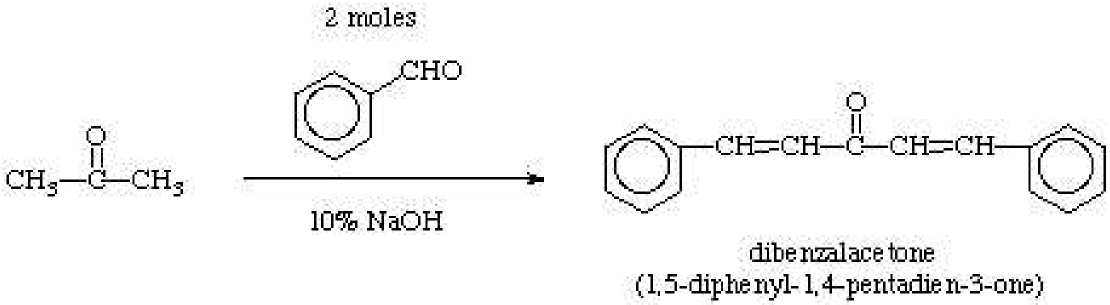
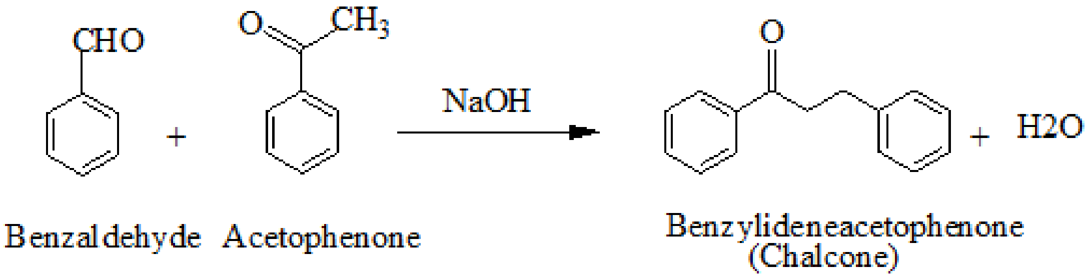


Application:

Preparation of **dibenzalacetone** and **cinnamaldehyde**

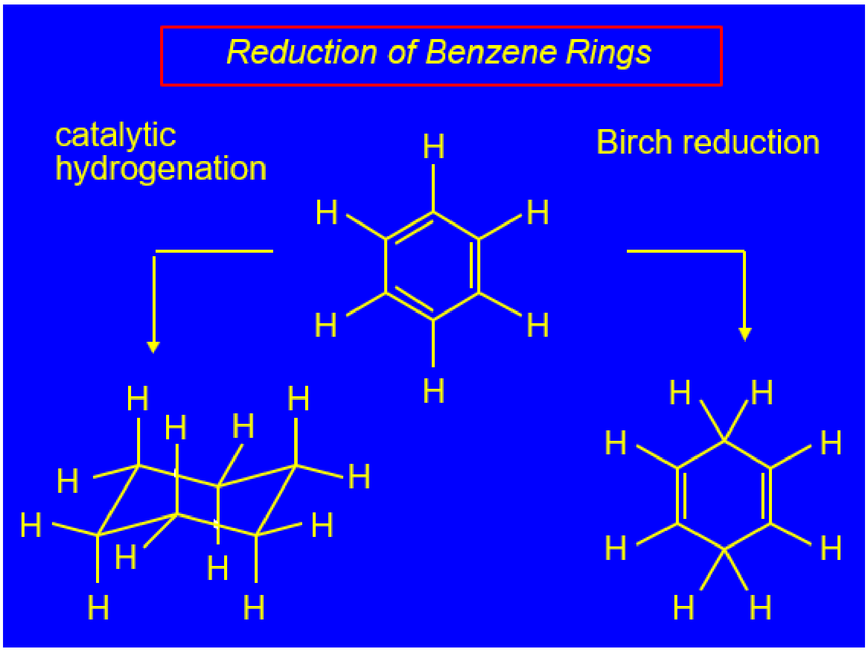


Preparation of **Bezylidenacetophenone**



BRICH REDUCTION

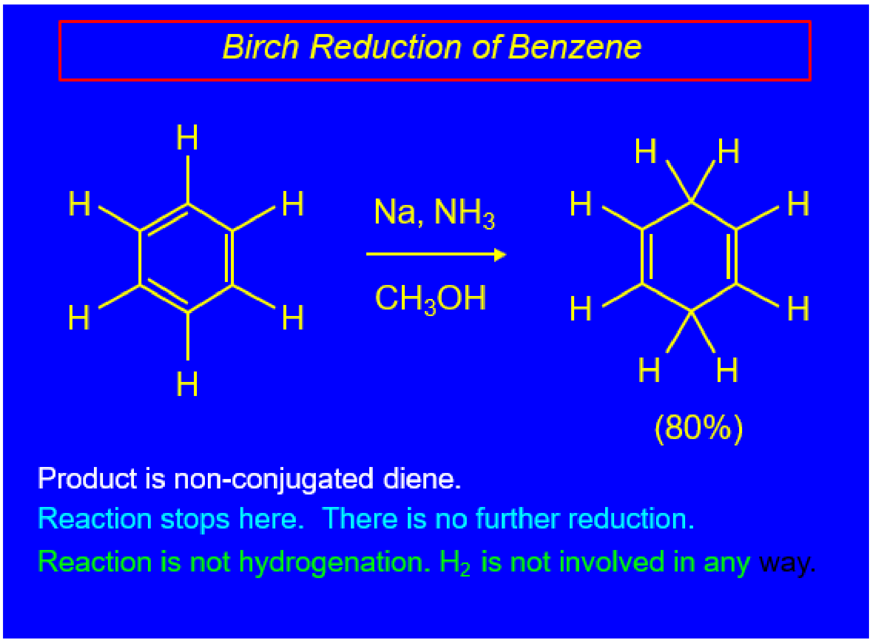
Reduction of benzene ring may take place by two methods. 1. Catalytic dehydrogenation, 2. Brich reduction.



Reduction of Benzene Rings

catalytic hydrogenation

Birch reduction



Birch Reduction of Benzene

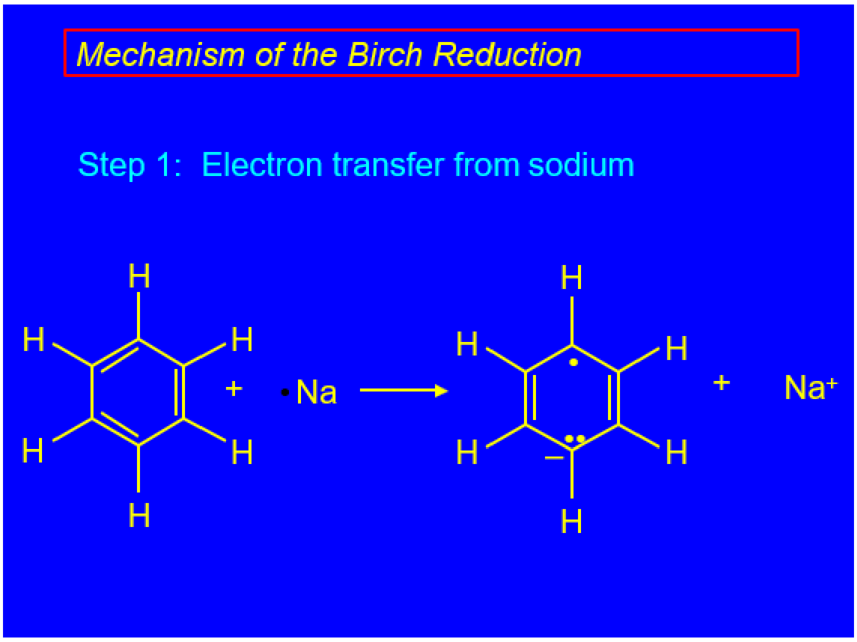
$\xrightarrow[CH_3OH]{Na,\ NH_3}$

(80%)

Product is non-conjugated diene.

Reaction stops here. There is no further reduction.

Reaction is not hydrogenation. H_2 is not involved in any way.

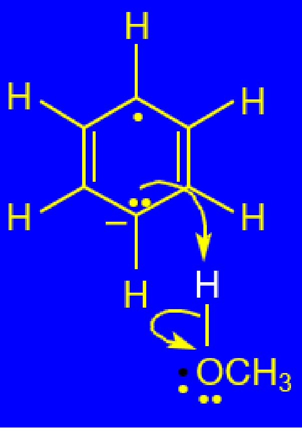


Mechanism of the Birch Reduction

Step 1: Electron transfer from sodium

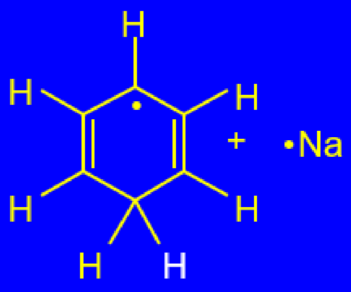
Mechanism of the Birch Reduction

Step 2: Proton transfer from methanol



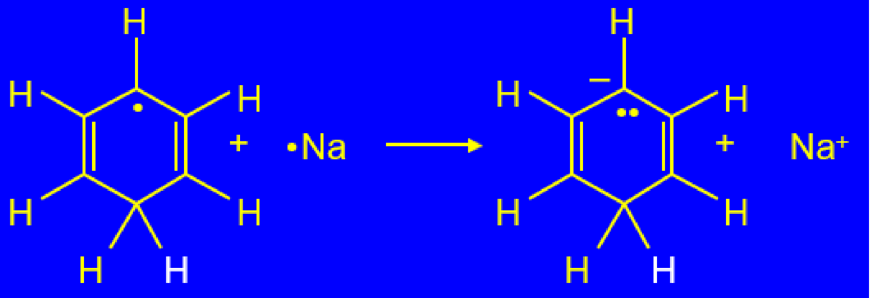
Mechanism of the Birch Reduction

Step 3: Electron transfer from sodium



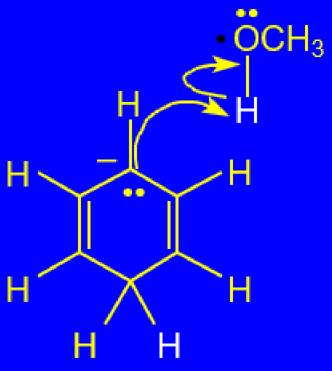
Mechanism of the Birch Reduction

Step 3: Electron transfer from sodium



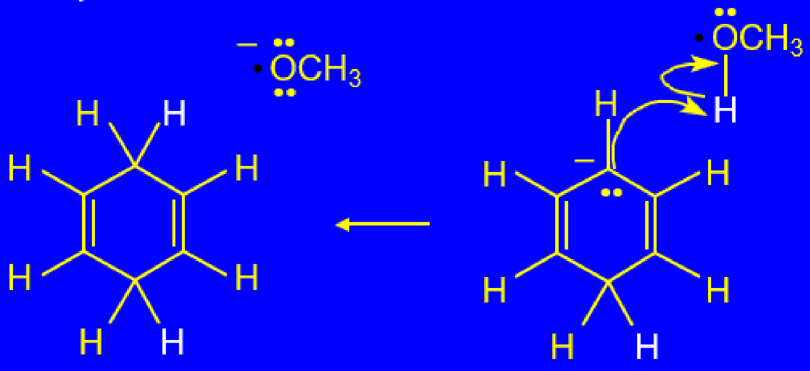
Mechanism of the Birch Reduction

Step 4: Proton transfer from methanol

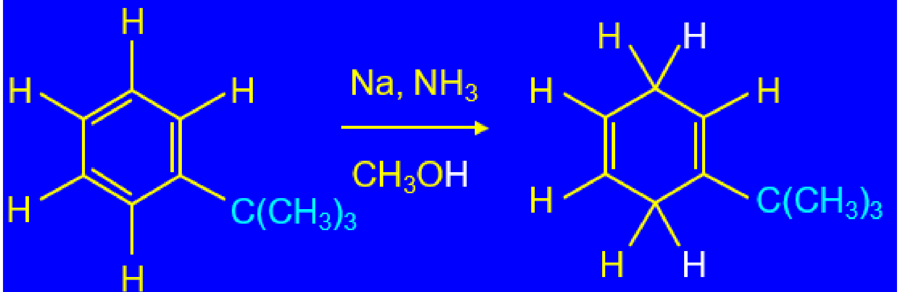


Mechanism of the Birch Reduction

Step 4: Proton transfer from methanol



Birch Reduction of an Alkylbenzene



(86%)

If an alkyl group is present on the ring, it ends up as a substituent on the double bond.