Loknete Dr. Balasaheb Vikhe Patil (Padma Bhushan Awardee)
Pravara Rural Education Society
Arts, Science & Commerce College Kolhar

# Oxidation and Reduction Reactions

**Class- M.Sc.-I**

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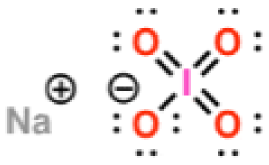
# Oxidation and Reduction Reactions

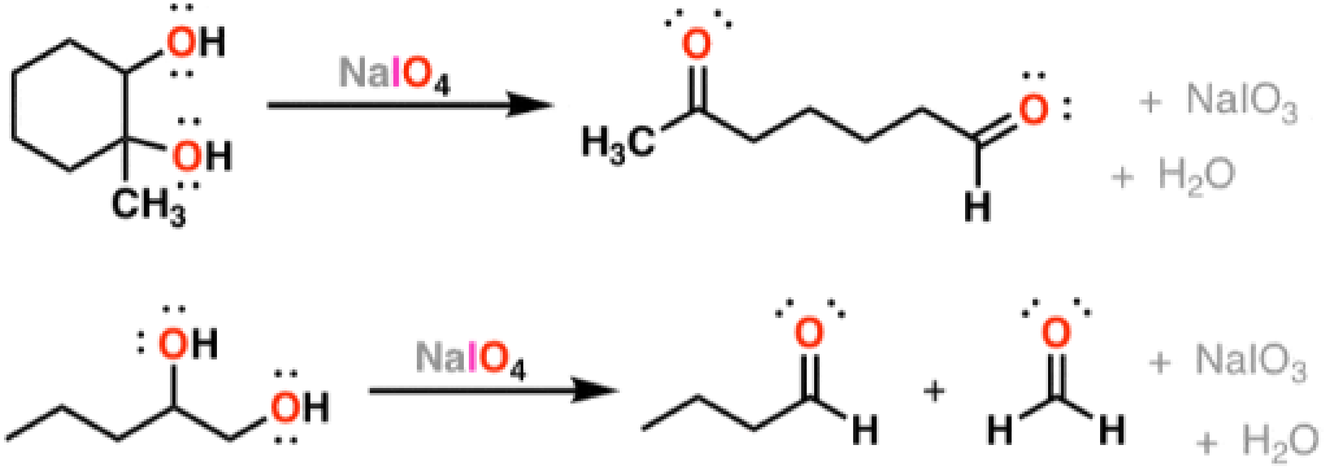
**Oxidizing Agent:-** In chemistry an oxidizing agent is a substance that has ability to oxidize other substance. In other words to accept their electrons.

**1. $NaIO_4$:-** Sodium periodate is oxidizing agent used to open saccharide rings between vicinal diols leaving two aldehyde groups.

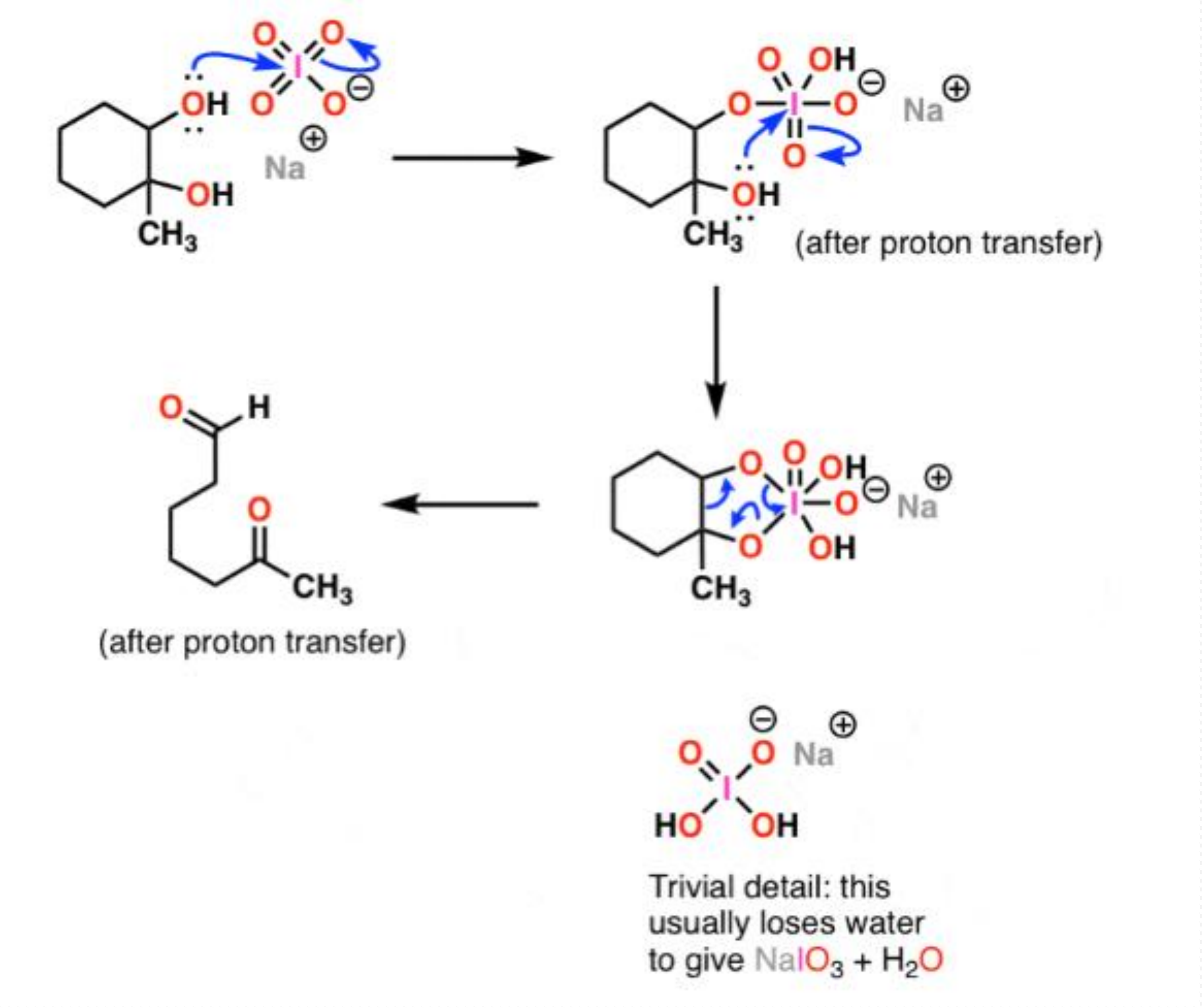


Sodium periodate ($NaIO_4$)

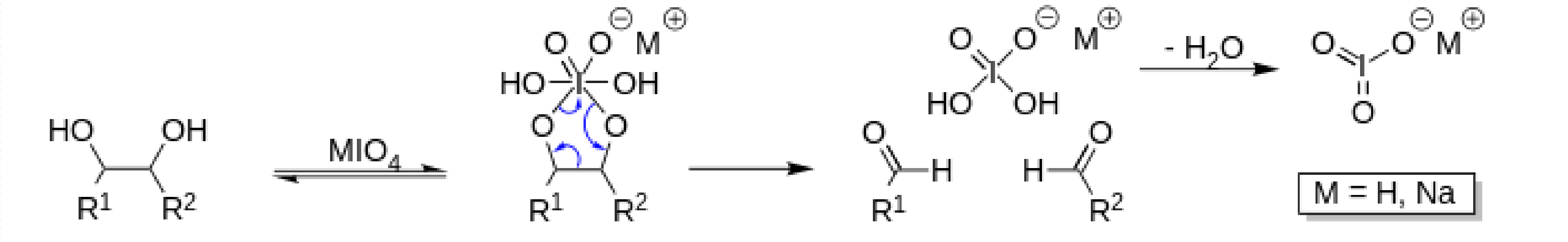
Cleavage of diols to give aldehyde/ketones.

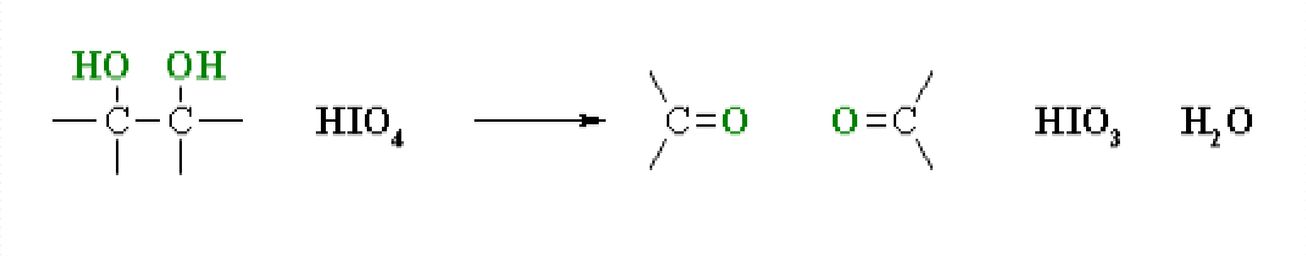


# Mechanism:-


(after proton transfer)
(after proton transfer)
Na
Trivial detail: this usually loses water to give $NaIO_3 + H_2O$

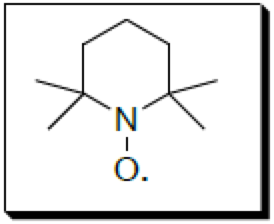
**2. $HIO_4$:-** $HIO_4$ is oxidizing agent similar to $NaIO_4$. Periodic acid is the highest oxoacid of iodine in which iodine exist in oxidation state +7. Periodic acid will cleave vicinal diols into two aldehyde or ketone. Periodic acid can be used to open saccharide rings.





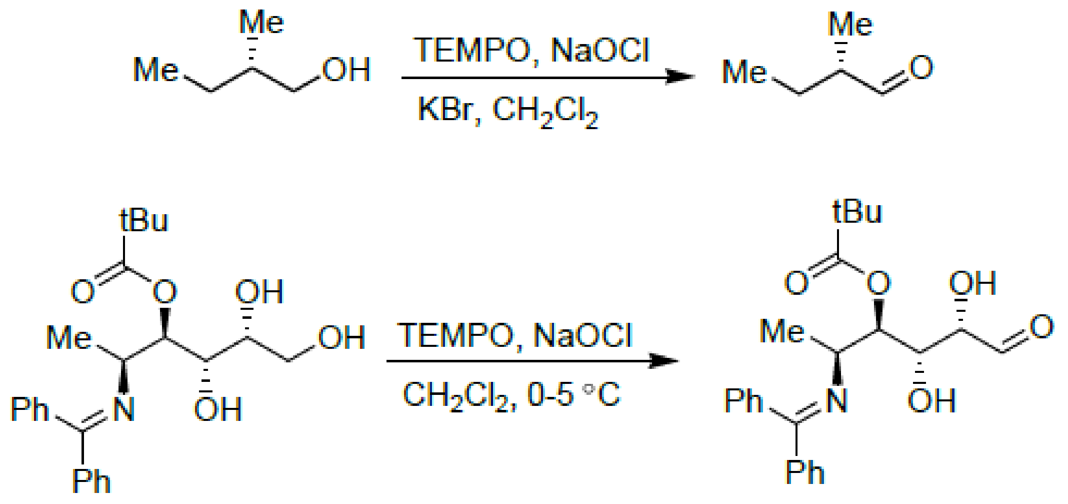
## 3. TEMPO- (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl:-

TEMPO is organic heterocyclic compound bearing a radical oxygen atom. This compound was prepared by Lebedev and Kazarnowskii in 1960 from the oxidation of 2,2,6,6-tetramethylpiperidine. In conjugation with other oxidizing agents, this reagent provides mild conditions for oxidations.

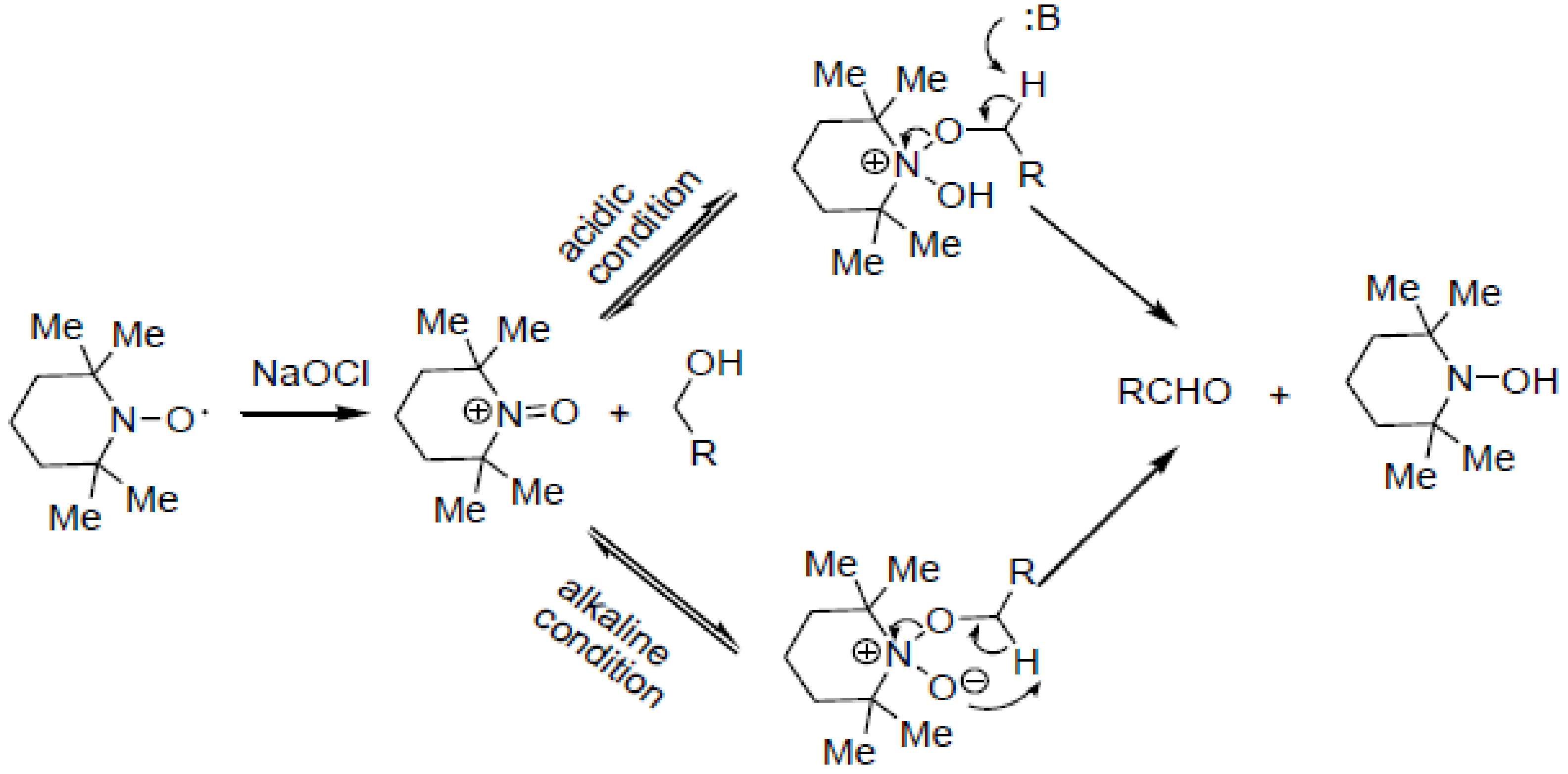


TEMPO

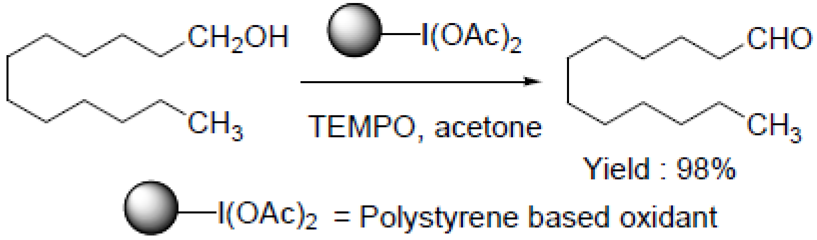
TEMPO is a mild catalyst for the oxidation of alcohols to give carbonyl compounds. NaOCl is usually used as a co-oxidant for the regeneration of the catalyst. The reactions with primary alcohols exhibit greater reactivity compared to secondary alcohols. Thus, primary alcohols could be chemoselectively oxidized in the presence of secondary alcohols.



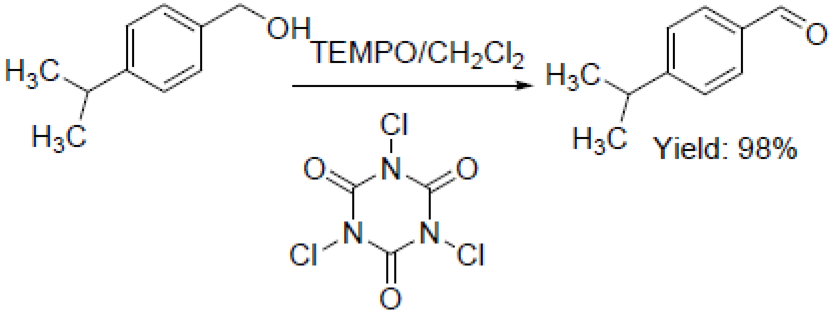
# Mechanism:-


NaOCl
acidic condition
alkaline condition
:B
Me
N–O·
⊕N=O
OH
R
⊕N
O
H
OH
O⊖
RCHO
+
N–OH

1.

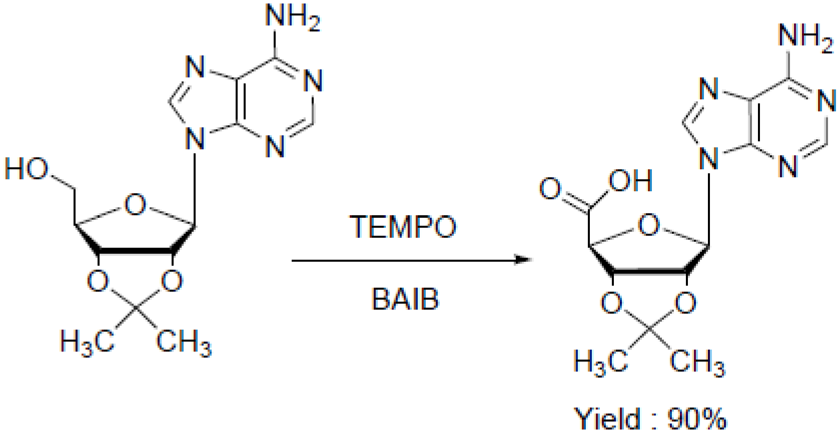


2.



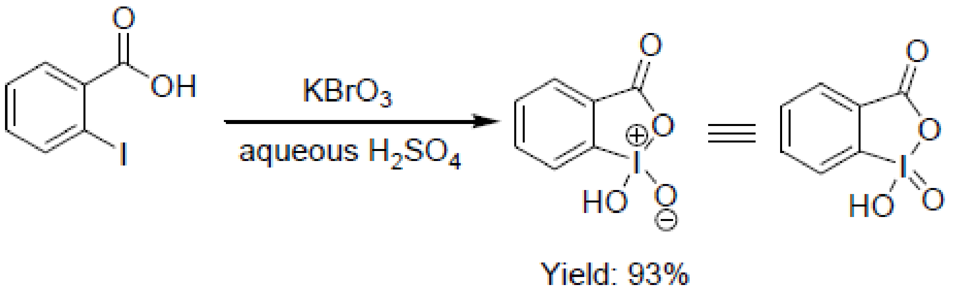
Trichloroisocyanuric acid

3.

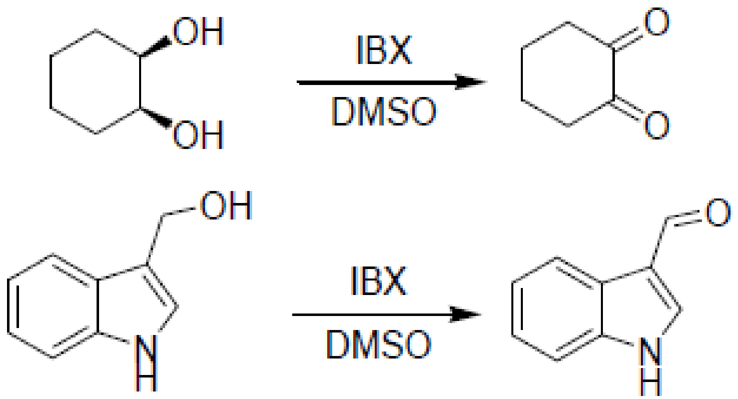


**4. IBX- (2-Iodoxybenzoic acid):-** 2-Iodoxybenzoic acid (IBX) is an organic compound prepared by oxidation of 2-iodobenzoic acid with potassium bromate in aqueous sulfuric acid. This is used for the oxidation of alcohols to give carbonyl compounds. The only drawback is that it is insoluble in common organic solvents but soluble in highly polar solvent such as DMSO.

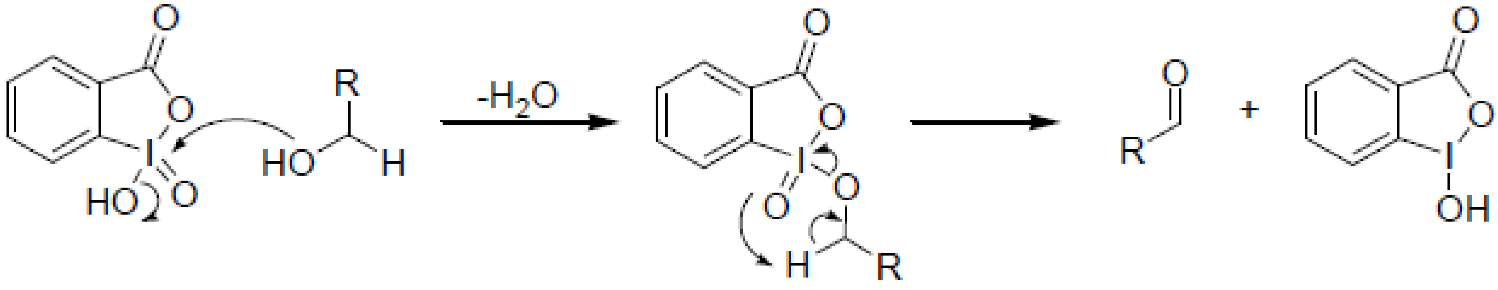
Preparation:- The oxidation of 2-iodobenzoic acid in aqueous sulfuric acid with potassium bromate gives IBX.



The alcohols are oxidized to aldehydes and ketones when treated with IBX. The reaction occurs smoothly without affecting other functional groups.



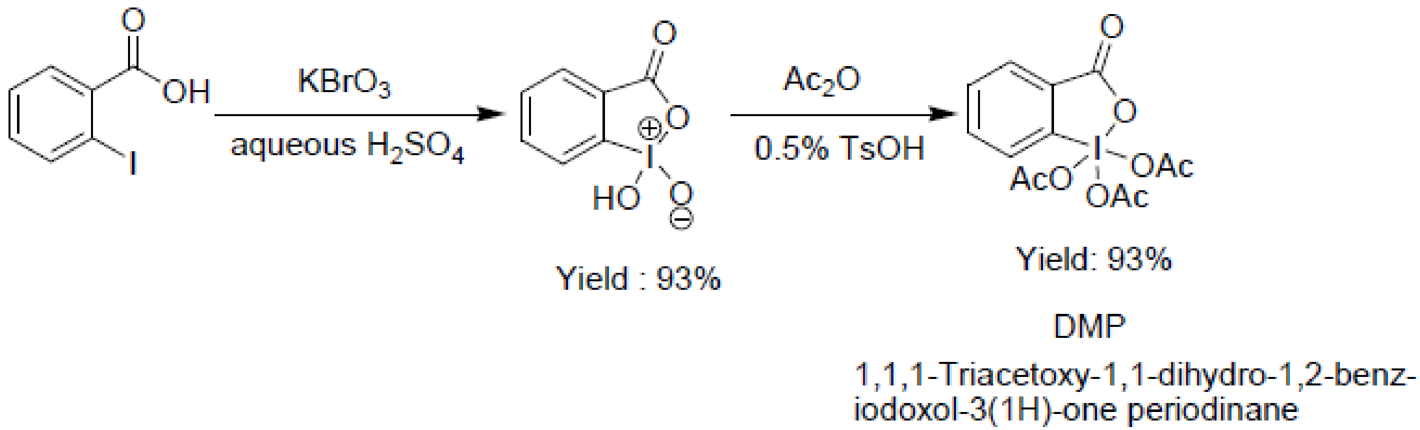
## Mechanism:-



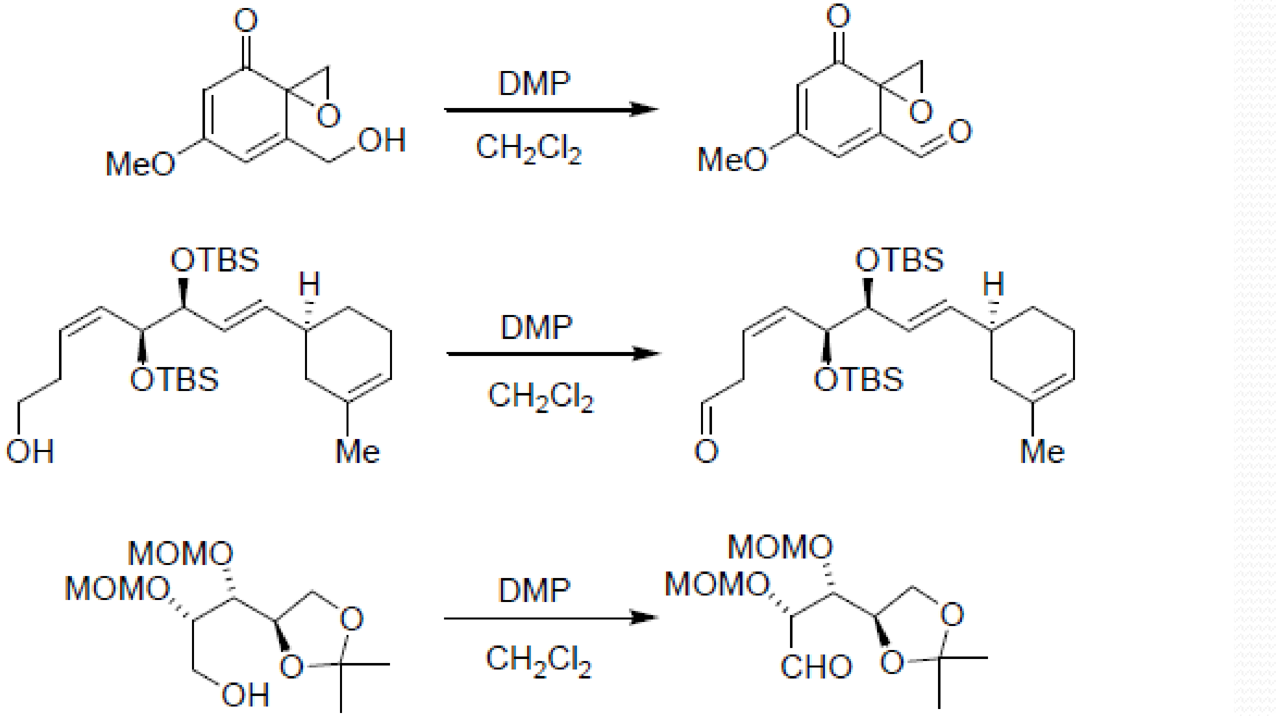
**5. Dess-Martin Periodinane (DMP):-** The Dess-Martin periodinane is a hypervalent iodine compound developed by Daniel Benjamin Dess and James Cullen Martin. It is a selective oxidizing agent and works under essentially neutral conditions.

Preparation:-

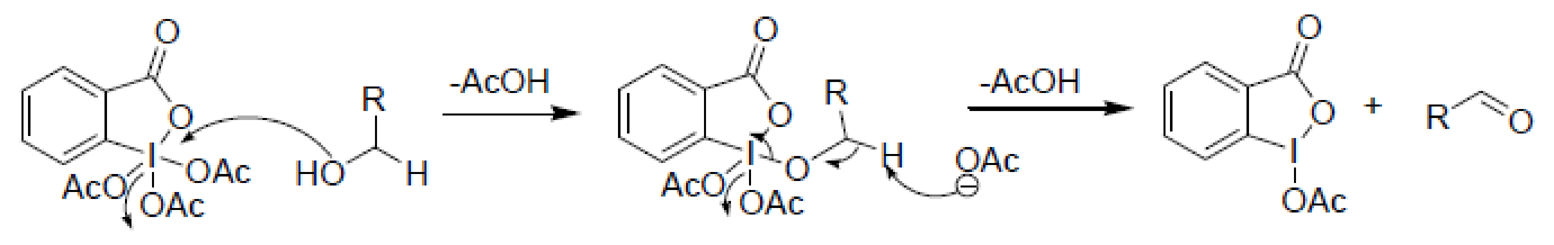
The DMP is prepared by treating 2-iodobenzoic acid with potassium bromate and then acetylated with acetic anhydride in presence of catalytic amount of toluenesulphonic acid. This reagent has indefinite shelf-life in a sealed container, however, hydrolysis occurs exposure to moisture.

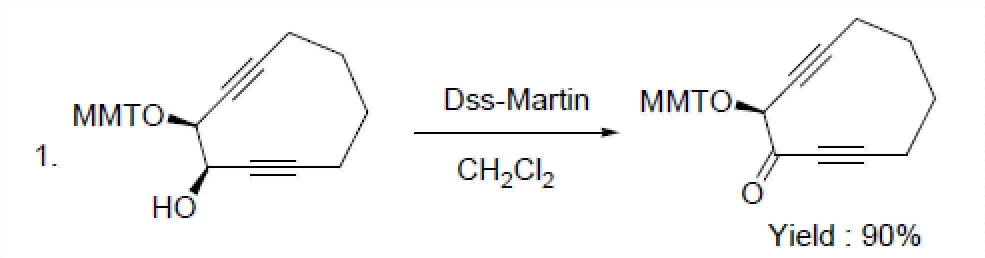


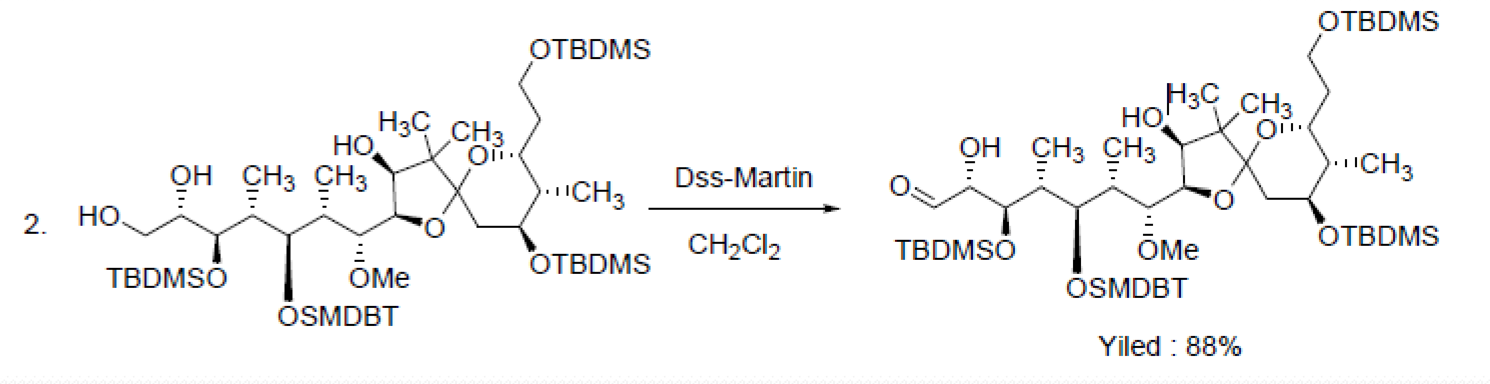
DMP oxidizes alcohols to give aldehydes and ketones under neutral or near neutral conditions. The reaction is mild and the alcohols can be selectively oxidized in presence of other selective functional groups at room temperature. There is no over oxidation of the carbonyl compounds to carboxylic acids. Furthermore, simple product isolation makes this protocol much useful.


O
O
MeO
OH
DMP
CH2Cl2
O
O
MeO
O
OTBS
H
OTBS
OH
Me
DMP
CH2Cl2
OTBS
H
OTBS
O
Me
MOMO
MOMO
O
O
OH
DMP
CH2Cl2
MOMO
MOMO
O
CHO
O

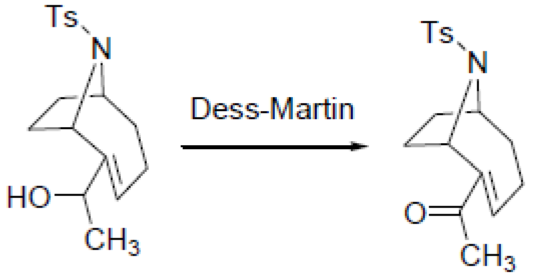
**Mechanism:-** The alcohol replaces labile acetate group from the iodine to give the intermediate that can undergo reductive elimination by oxidizing alcohol to give the carbonyl compound.





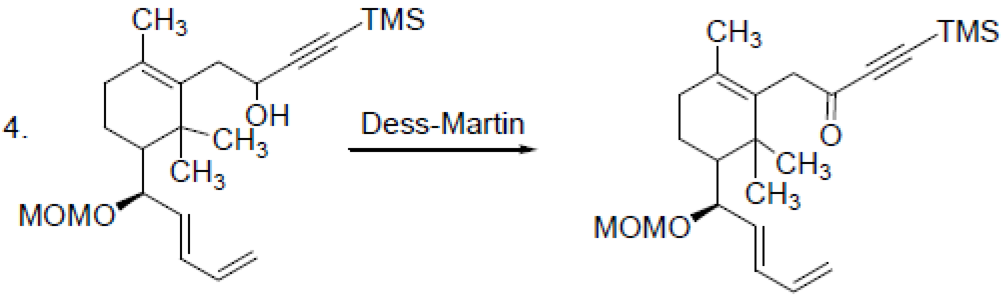


3.



Yield: 86%

4.



Yield : 55%

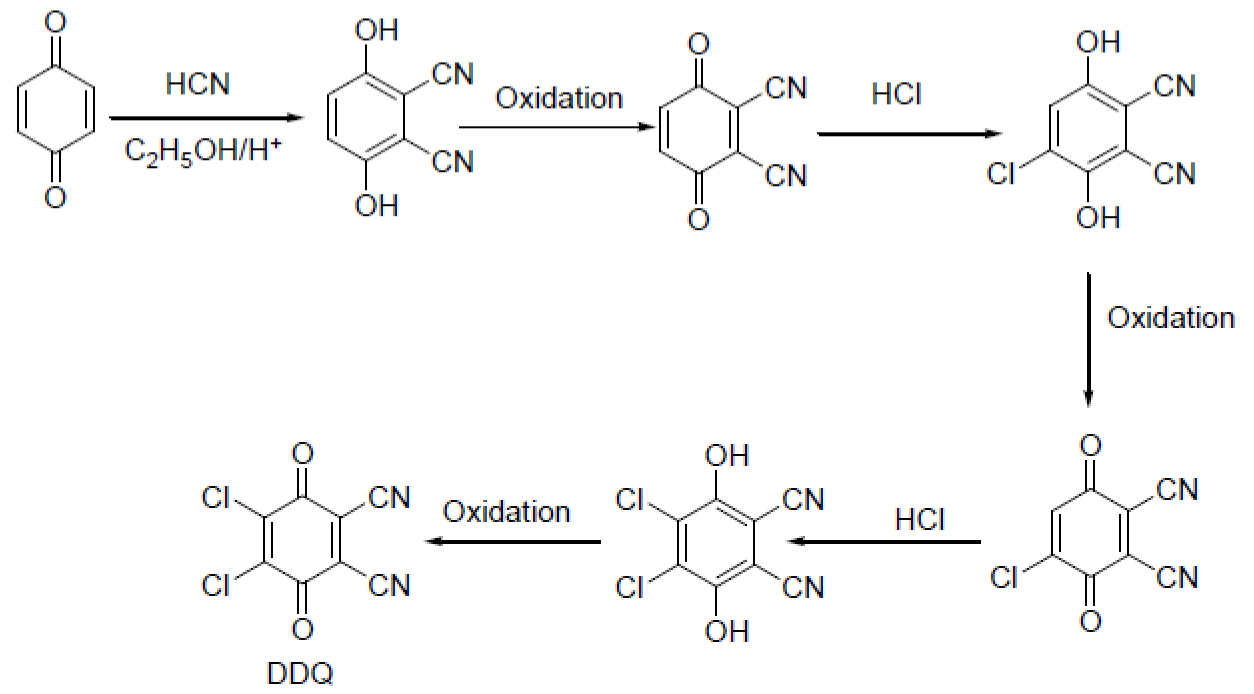
5.

Yield : 92%

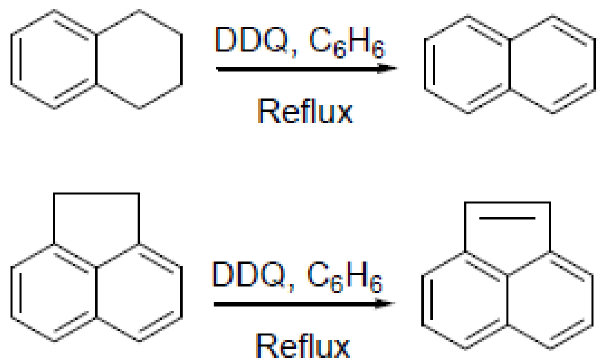
## 6. DDQ (2,3-Dichloro-5,6-dicyano-1,4-benzoquinone):-

Quinones are used for dehydrogenation reactions. Among them, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) is an important reagent. DDQ is very reactive and used under anhydrous conditions because it decomposes in the presence of water. The reaction is carried out in inert solvents such as benzene, THF and dioxane. Solution of DDQ in benzene is red in colour because of the formation of charge transfer complex. After dehydrogenation, DDQ is reduced to hydroquinone that is a yellow solid and insoluble in benzene. Hence, the progress of the dehydrogenation can be monitored.

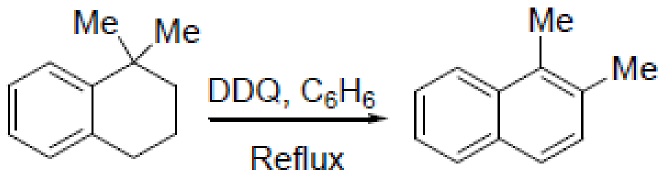
Preparation:- DDQ is very convenient to handle and is commercially available. It can be synthesized as described by Thiele and Genther procedure from the reactions of benzoquinone with HCN/HCl followed by oxidation.



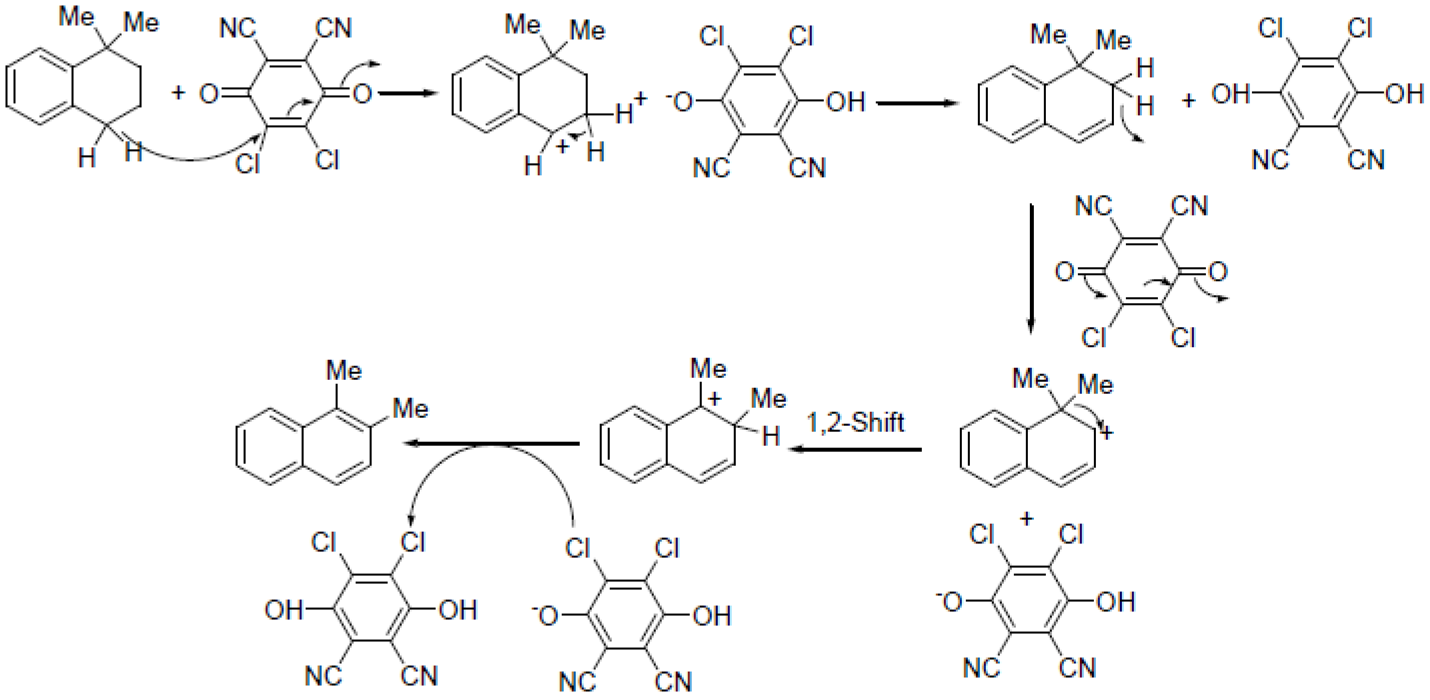
**Aromatization:-** DDQ is an effective reagent for the dehydrogenation of hydroaromatic compounds to give aromatic compounds. The procedure can be applied for the synthesis of heterocyclic compounds such as pyrroles, pyrazoles, indoles, furans and thiophenes. Many substituents do not interfere in the reaction. For example, using DDQ in boiling benzene tetralin and acenaphthene can be converted into naphthalene and acenaphthylene, respectively.



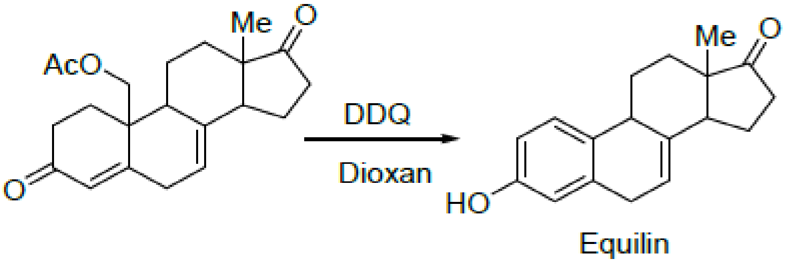
In the case of hydroaromatic compound with blocking group rearrangement has been observed. For example, in 1,1-dimethyl-1,2,3,4-tetrahydronaphthalene, the aromatization takes place with 1,2-rearrangement of the methyl group.



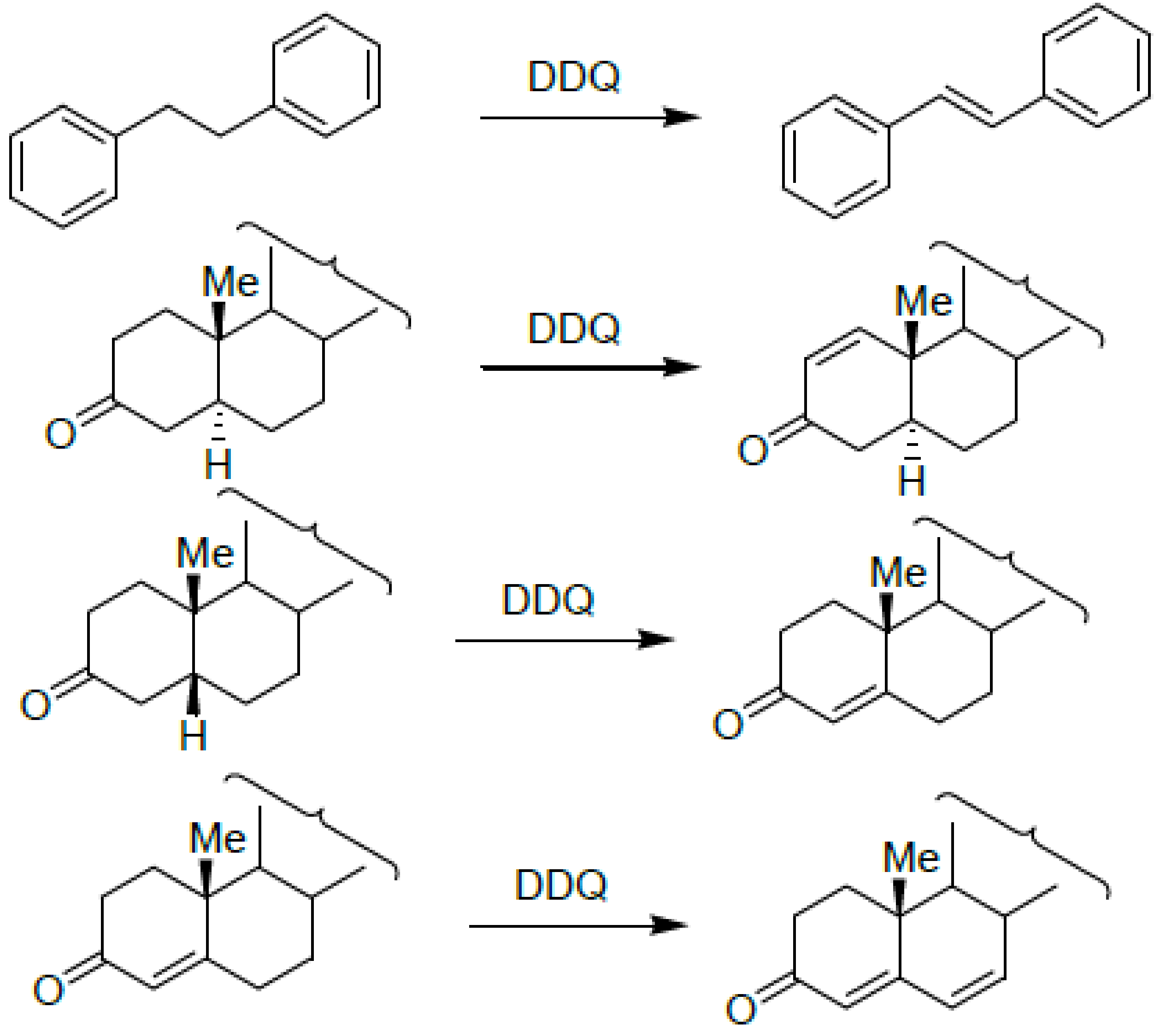
**Mechanism:-**



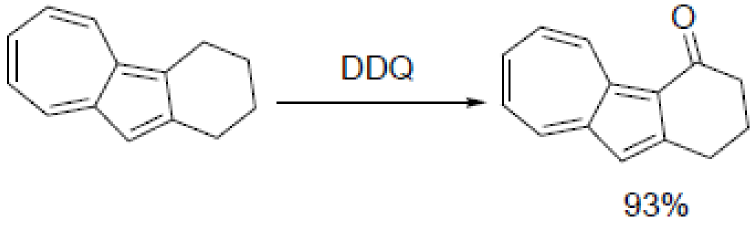
This process has been extensively used in steroid chemistry for aromatization. For example, DDQ has been used for aromatization in the synthesis of equilin.



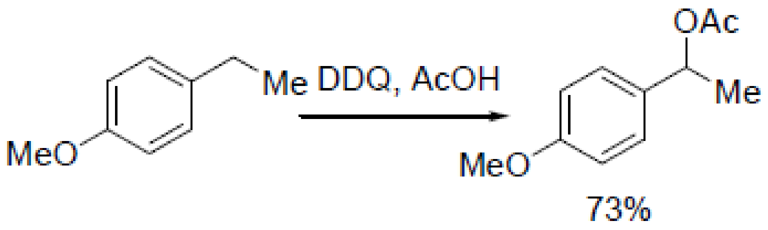
**Formation of conjugated double bonds:-** DDQ is used for dehydrogenation of organic compound for extending conjugation. For example, 1,2-diphenylethane can be converted in to trans-stilbene in high yield. In similar way, ketones can be transformed into-unsaturated carbonyl compounds, which have been considerably employed in steroid chemistry. The products are generally obtained in high yield and the substituents commonly encountered are not affected.


DDQ
DDQ
Me
H
O
Me
H
O
DDQ
Me
H
O
Me
O
DDQ
Me
O
Me
O

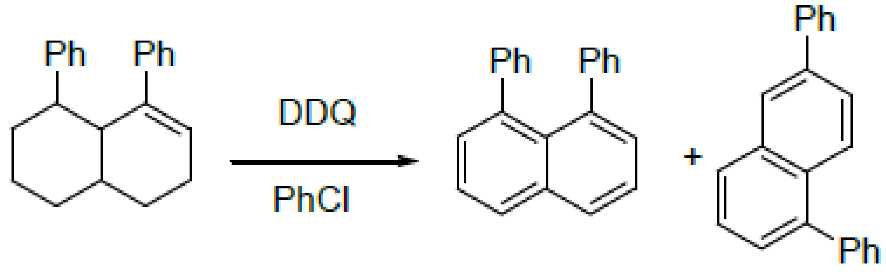
**Allylic Oxidation:-** The oxidation of benzylic C-H bonds can be carried with DDQ to afford carbonyl compounds. The reactions in aqueous acetic acid proceeds via an intermediate benzylic acetate, which is hydrolyzed under the reaction conditions. In some cases, the benzylic acetate can be isolated.



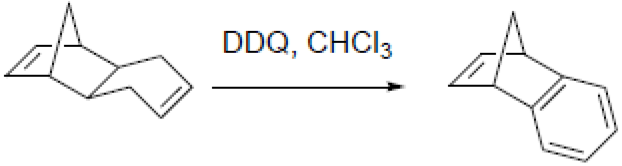
Scheme 9



**Isomerization:-** The compounds that are difficult to dehydrogenate give a mixture of isomeric products. The isomeric products could be formed due to fragmentation of intermediate carbonium ion followed by ring closure and dehydrogenation.

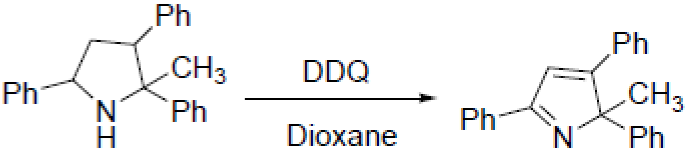


1.



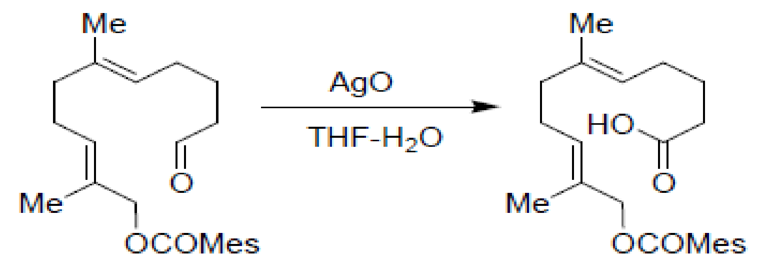
Yield : 100%

2.



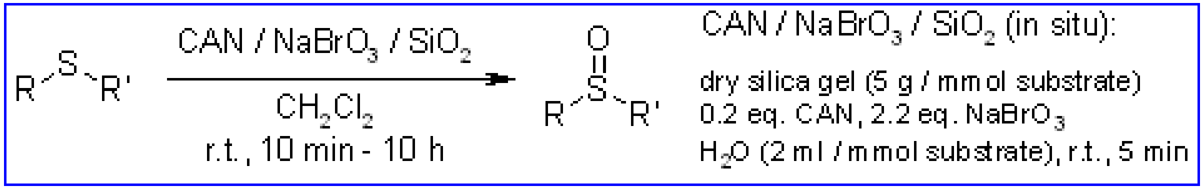
Yield : 81%

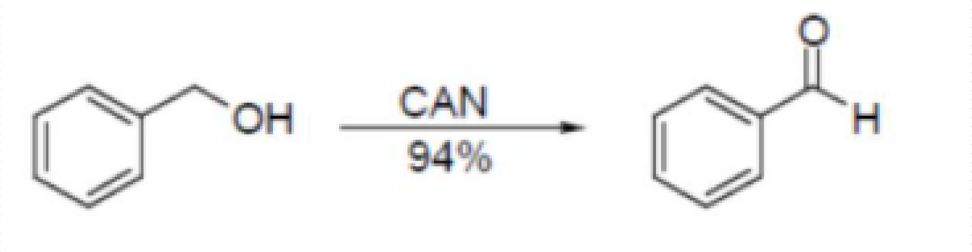
**7. $Ag_2O$:-** Silver oxide has been found to catalyze the oxidation of aldehydes to give carboxylic acids in good yield.

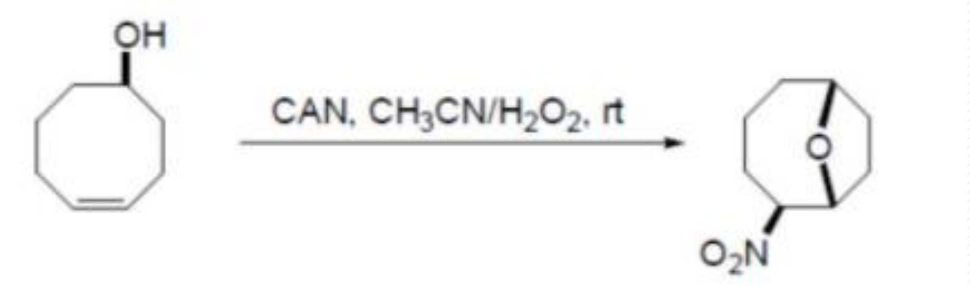


**8. CAN (Cerium Ammonium Nitrate):-** Cerium (IV) ammonium nitrate ($(NH_4)_2Ce(NO_3)_6$) is a one-electron oxidizing agent that is used for oxidative addition reactions of electrophilic radicals to alkenes, enabling intermolecular and intramolecular carbon-carbon and carbon-heteroatom bond formation. CAN also oxidizes secondary alcohols into ketones and benzylic alcohols into aldehydes.

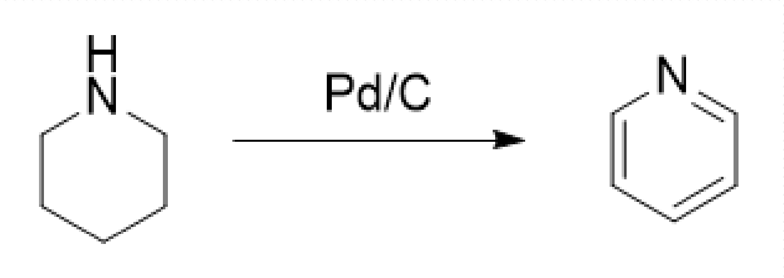

OH
R
R'
0.1 - 0.2 eq. CAN
0.1 eq. TEMPO
$O_2$ (stream)
$CH_3CN$, reflux, 15 - 210 min
O
R
R'
R: Ar, vinyl
R': alkyl, H

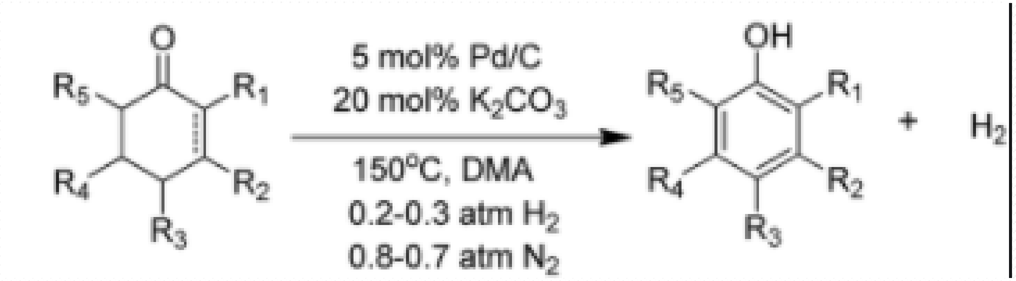

R
S
R'
CAN / $NaBrO_3$ / $SiO_2$
$CH_2Cl_2$
r.t., 10 min - 10 h
O
S
R
R'
CAN / $NaBrO_3$ / $SiO_2$ (in situ):
dry silica gel (5 g / mmol substrate)
0.2 eq. CAN, 2.2 eq. $NaBrO_3$
$H_2O$ (2 ml / mmol substrate), r.t., 5 min


OH
CAN
94%
O
H


OH
CAN, $CH_3CN/H_2O_2$, rt
O
$O_2N$

**9. Pd-C:-** In the conversion of piperidine to pyridine, palladium on carbon (Pd/C) is used.





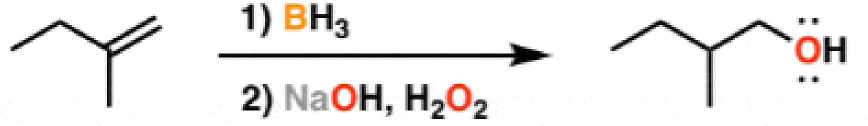
**Reducing Agent:-** In chemistry an reducing agent is a substance that has ability to reduce other substance. In other words to loose their electrons.

A reducing agent is an element or compound that loses or donates an electron to an electron recipient in redox chemical reaction.

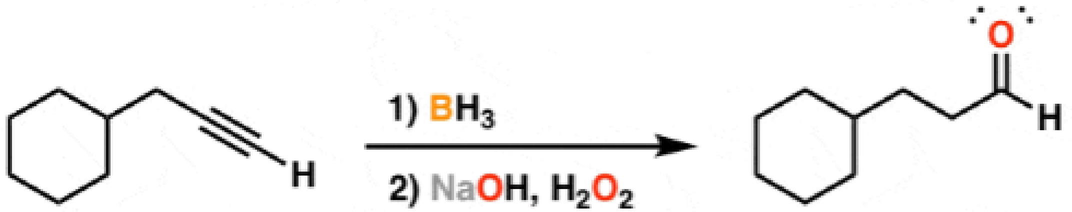
**1. Boranes and Hydroboration Reactions:-** Borane doesn’t exist as $BH_3$. Two molecules of $BH_3$ tend to associate with themselves to give $B_2H_6$. Alternatively $BH_3$ readily forms stable compounds with Lewis bases such as tetrahydrofuran (THF) and dimethyl sulfide. These can also perform the hydroboration of alkenes and alkynes.

**Hydroboration of Alkenes and Alkynes:-** The most important use of $BH_3$ is for the hydroboration of alkenes and alkynes.

Hydroboration reaction of Alkenes.



Hydroboration reaction of Alkynes.

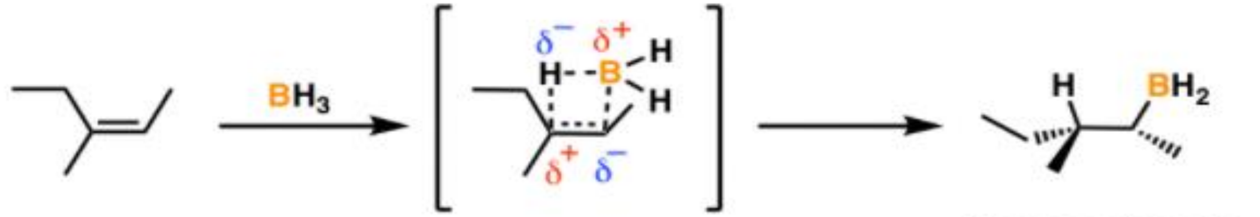


The reaction is selective to form the less substituted alcohol (Regioselective). The reaction is proceed through anti-Markovnikoff rule. The reaction always produces the product where the new H and OH are syn to each other (Stereospecific).

$BH_3$ react with alkynes gives less substituted alcohols.

Mechanism:- It proceeds through two steps.

**Step-I- Hydroboration.**

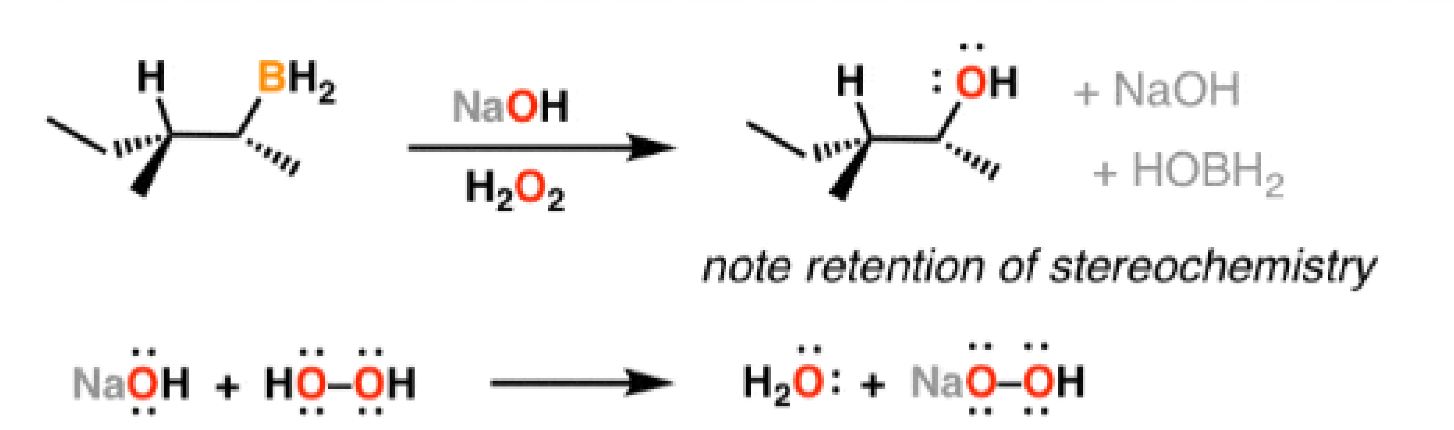


**syn addition**
*the transition state is concerted*

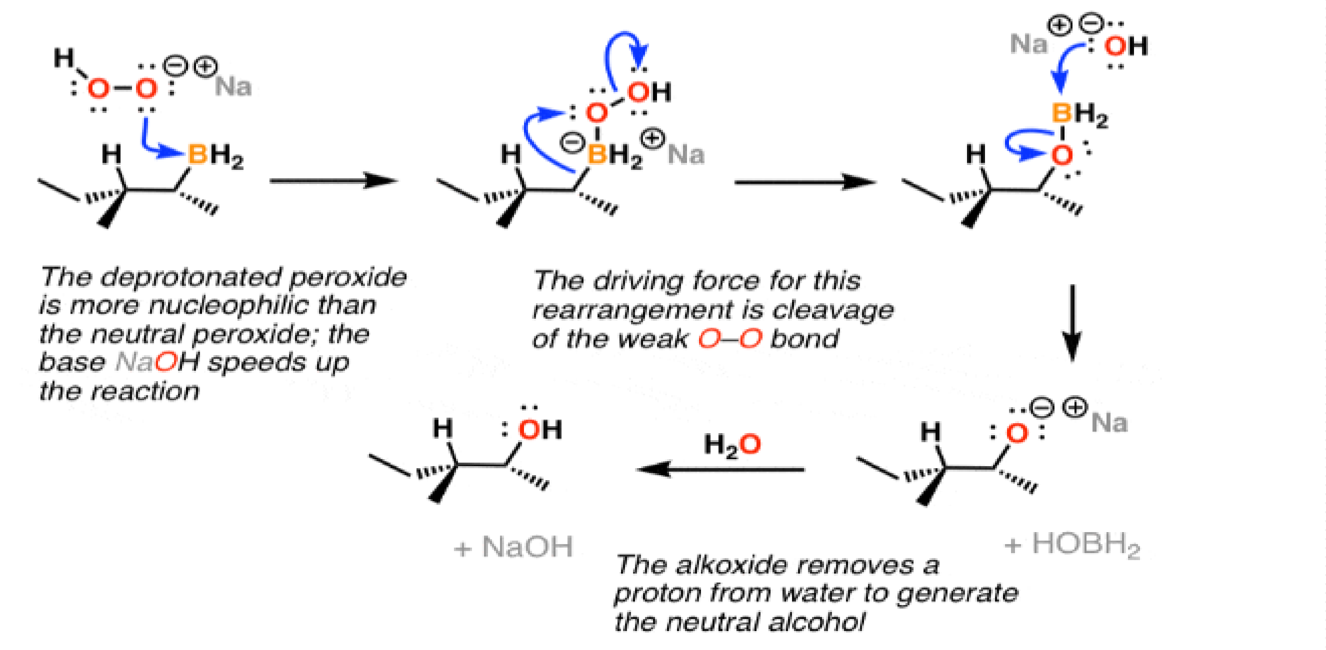
*If excess alkene is present, the two remaining B-H bonds can do subsequent hydroborations*

Hydroboration can happen up to 3 times with $BH_3$, since there are 3 B-H bonds. The OH goes exactly where the boron was, without changing the stereochemistry.

**Step-II- Oxidation Step.** The second step of the hydroboration reaction is an oxidation that replaces the C-B bond with a C-O bond.



*note retention of stereochemistry*



The deprotonated peroxide is more nucleophilic than the neutral peroxide; the base NaOH speeds up the reaction

The driving force for this rearrangement is cleavage of the weak O–O bond

The alkoxide removes a proton from water to generate the neutral alcohol

The two reagents added (NaOH and $H_2O_2$) each play a vital role.

There are 4 steps.

1. In the first step, NaOH removes a proton from $H_2O_2$, which makes it a better nucleophile.

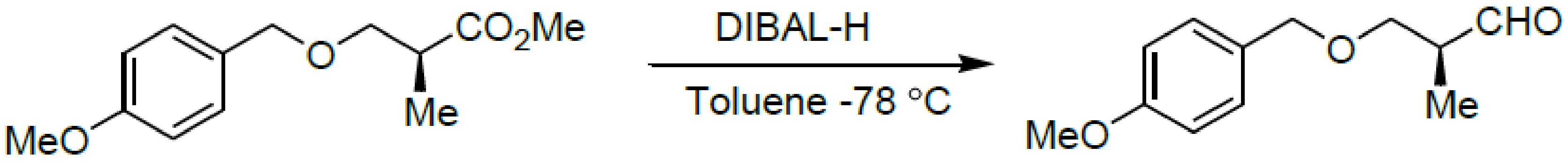
2. The resulting conjugate base of $H_2O_2$ then attacks boron.

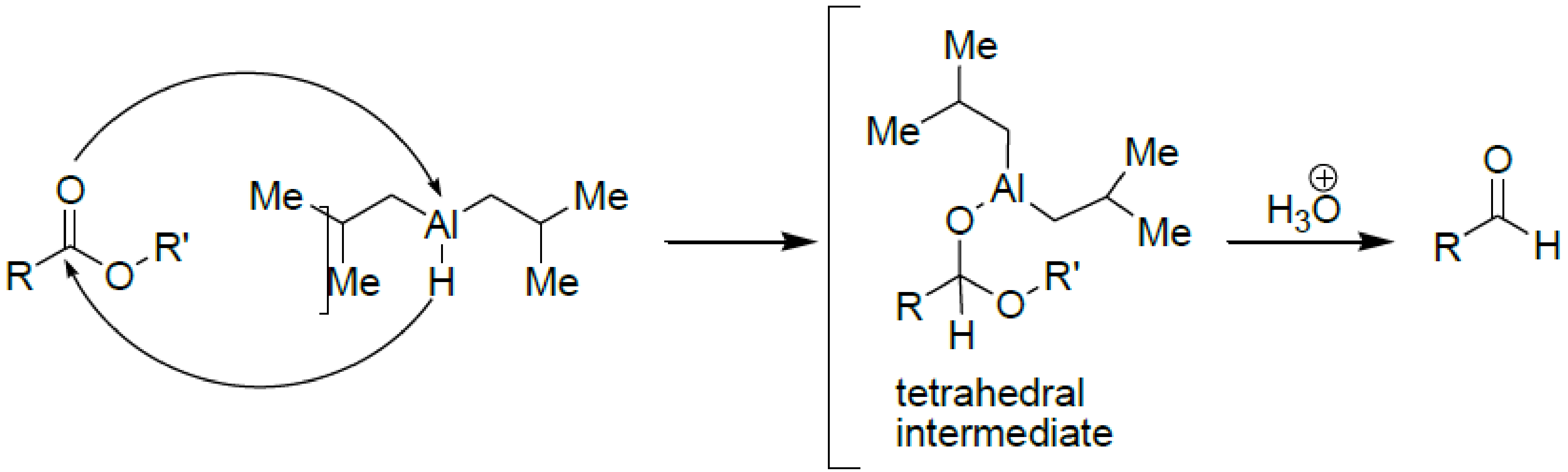
3. This sets up the third – key – step, which is rearrangement – shifting of the C-B bond to form a C-O bond, breaking the weak O-O bond in the process. In the third step, -OH attacks the boron, which releases the negatively charged alcohol (called an alkoxide).

4. Finally, protonation of this with water leads to formation of the neutral alcohol.

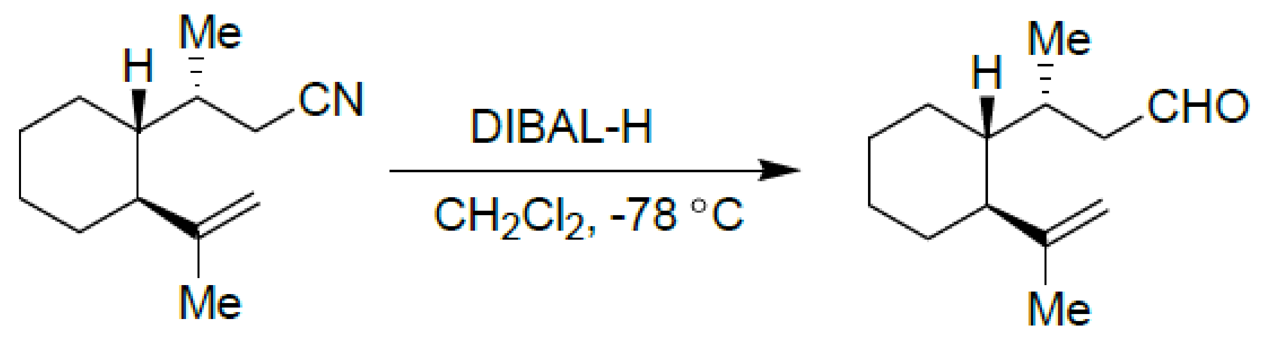
**2. Diisobutylaluminium hydride (DIBAL):-** Diisobutylaluminium hydride is a commercially available selective reducing agent. It can selectively reduce esters and nitriles to the corresponding aldehydes. The reaction is carried out in inert and moisture free atmosphere.

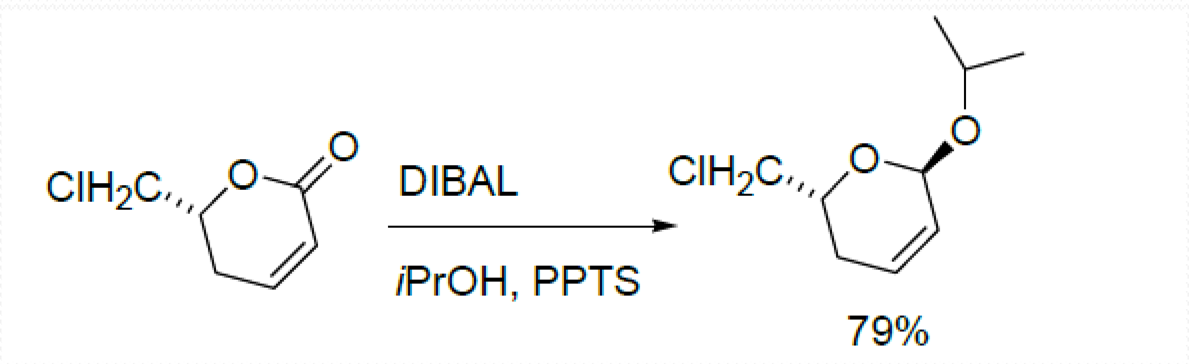
**Reduction of Esters to aldehydes:-** The esters are selectively reduced to the corresponding aldehydes at low temperature. The DIBAL-H transfer one hydride to the ester group and forms a tetrahedral intermediate which is stable at low temperature. The hydrolytic work up of the intermediate gives the desired aldehyde. The presence of alkoxy or amino group to the close proximity can stabilize the tetrahedral intermediate and hence give better result.

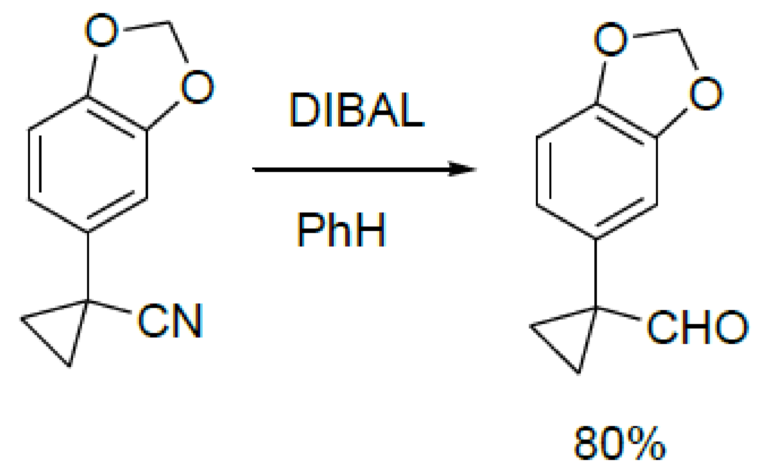

DIBAL-H
Toluene -78 °C
MeO
CO2Me
Me
CHO


R
O
R'
Me
Al
H
H3O+
tetrahedral intermediate

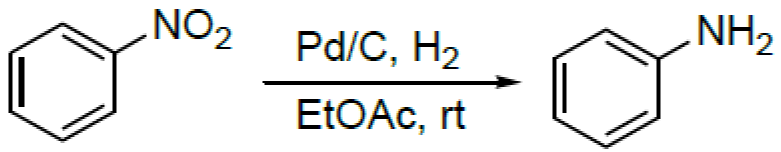
**Reduction of Nitriles:-** The nitriles are selectively reduced to the corresponding aldehydes with one equivalent of DIBAL-H at low temperature. The use of two equivalent of DIBAL-H gives the corresponding primary amine.



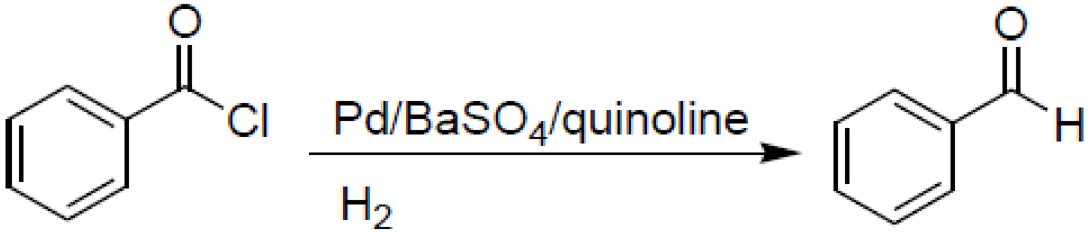




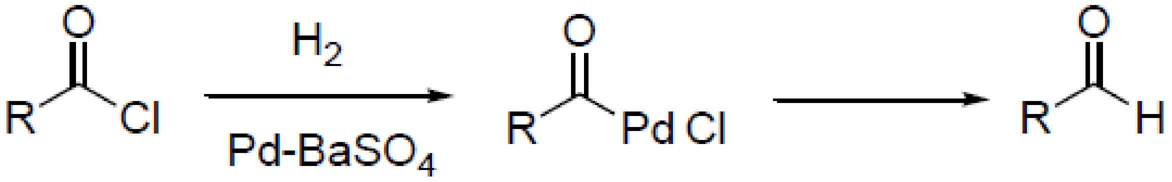
**3. $H_2$/Pd-C:-** Reduction of Aromatic Nitro compounds- The aromatic nitro compounds can be reduced to give the corresponding amines when treated with molecular hydrogen in the presence of Pt, Pd or Ni catalyst. The reaction is generally performed in methanol, ethanol or ethyl acetate at ambient temperature.

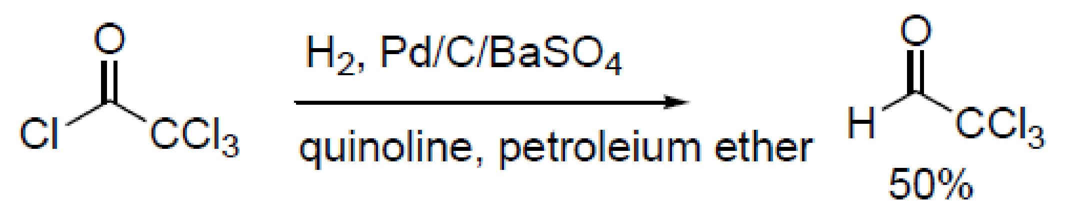


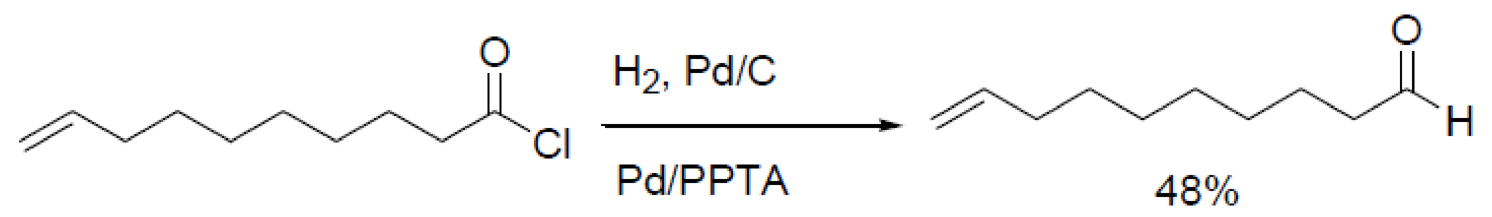
**Reduction of Acid Chlorides-** Acid chlorides undergo reduction to give the corresponding aldehydes in the presence of molecular hydrogen and palladium catalyst. When Pd/$BaSO_4$/quinoline is used as a catalyst along with molecular hydrogen the reaction is called Rosenmund reaction.

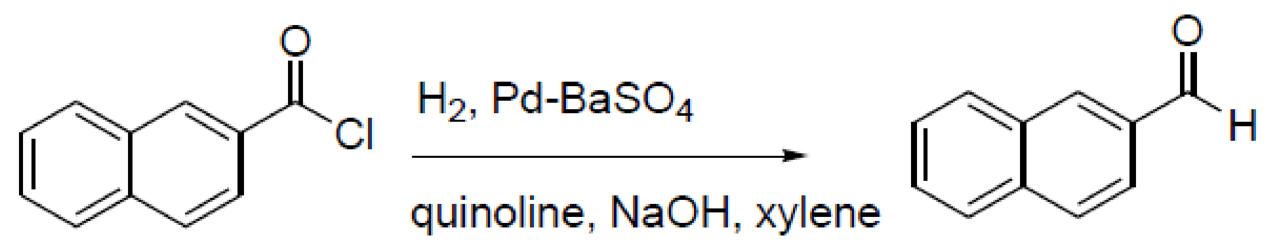


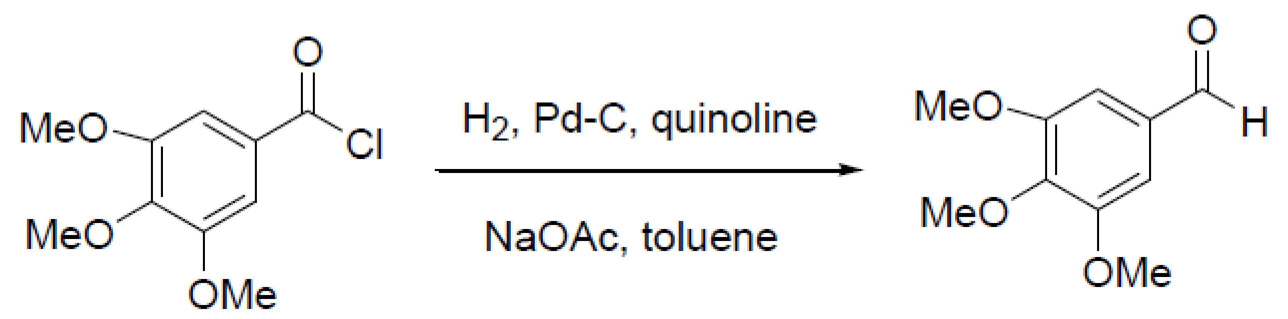
## Proposed Mechanism:-



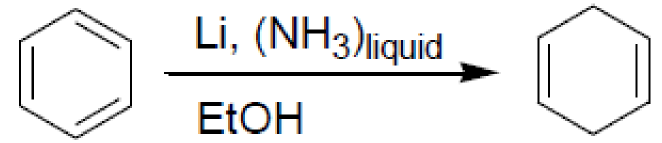

O
Cl
CCl3
H2, Pd/C/BaSO4
quinoline, petroleium ether
O
H
CCl3
50%


O
Cl
H2, Pd/C
Pd/PPTA
O
H
48%


O
Cl
H2, Pd-BaSO4
quinoline, NaOH, xylene
O
H

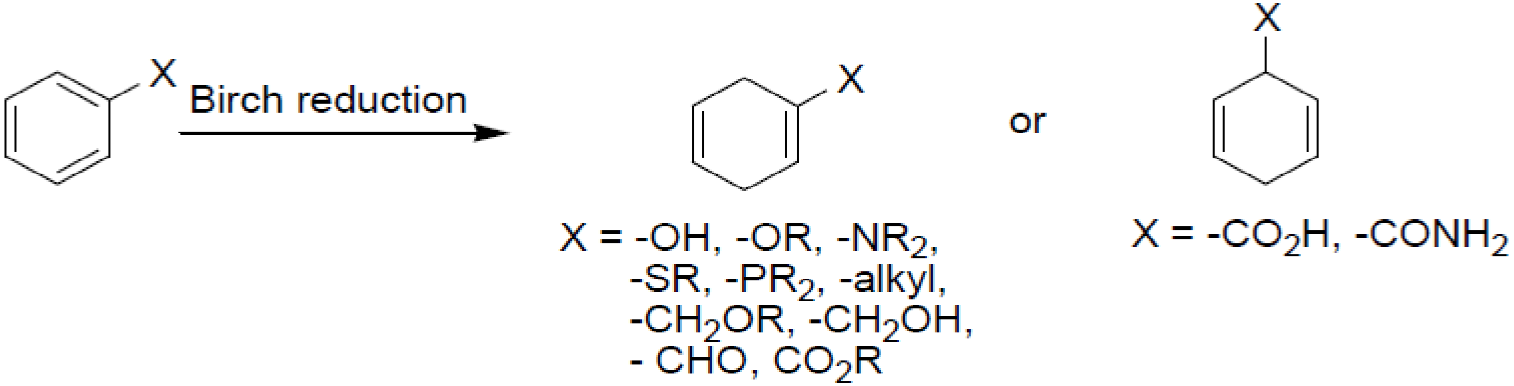

O
Cl
MeO
MeO
OMe
H2, Pd-C, quinoline
NaOAc, toluene
O
H
MeO
MeO
OMe

**4. Birch Reduction:-** The reduction of aromatic compounds to 1,4-cyclohexadiene compounds in presence of alkali metal, liquid ammonia and an alcohol is called Birch reduction. A variety of aromatic compounds containing electron donating or electron withdrawing groups could be readily converted to the corresponding 1,4-cyclohexadiene derivatives.



The regioselectivity towards the products in Birch reduction of substituted aromatic compound depends on the nature of the substituents.

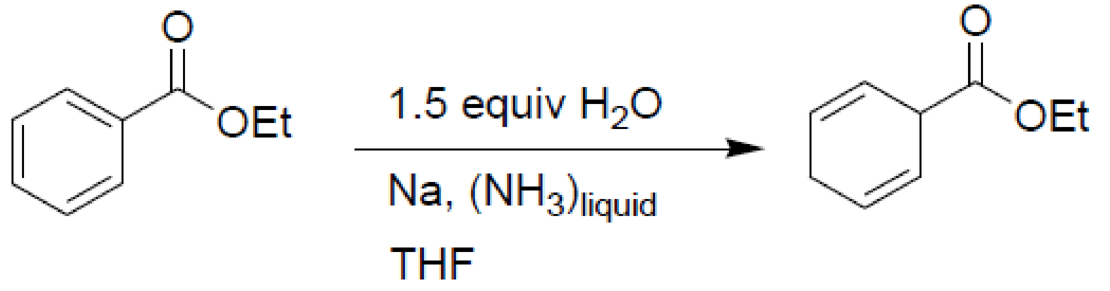
For example, the electron donating substituent such as alkyl or alkoxy group remains on the unreduced carbon where as electron withdrawing groups such as carboxylic acid or primary amide on reduced carbon almost exclusively.



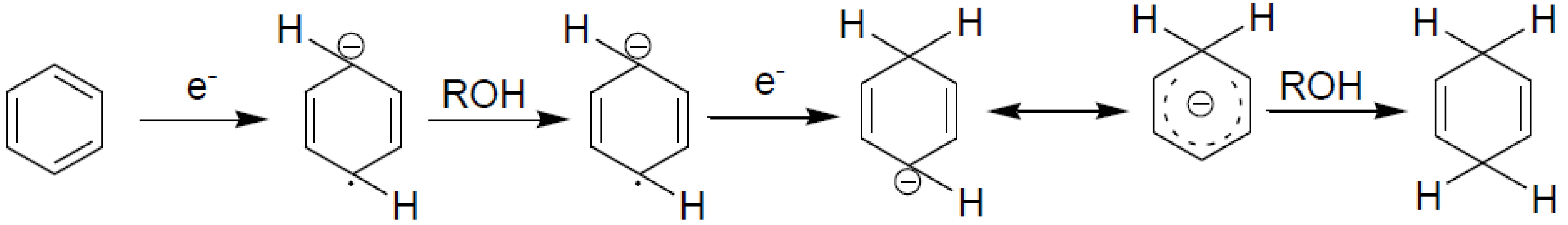
X = -OH, -OR, $-NR_2$, -SR, $-PR_2$, -alkyl, $-CH_2OR$, $-CH_2OH$, - CHO, $CO_2R$

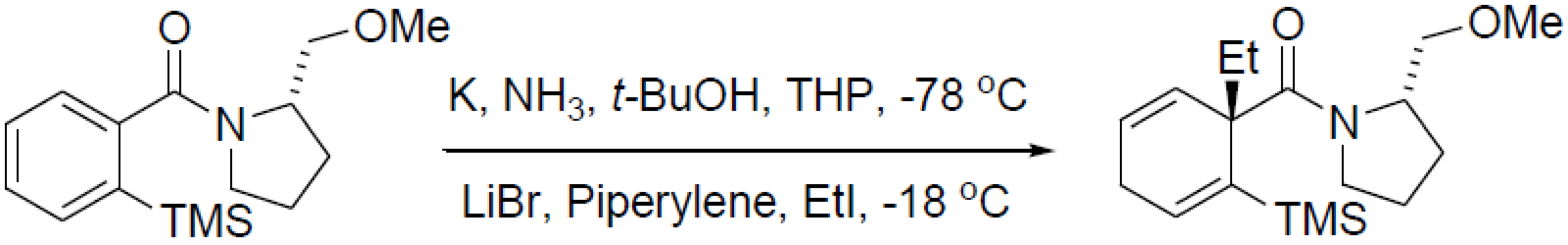
X = $-CO_2H$, $-CONH_2$

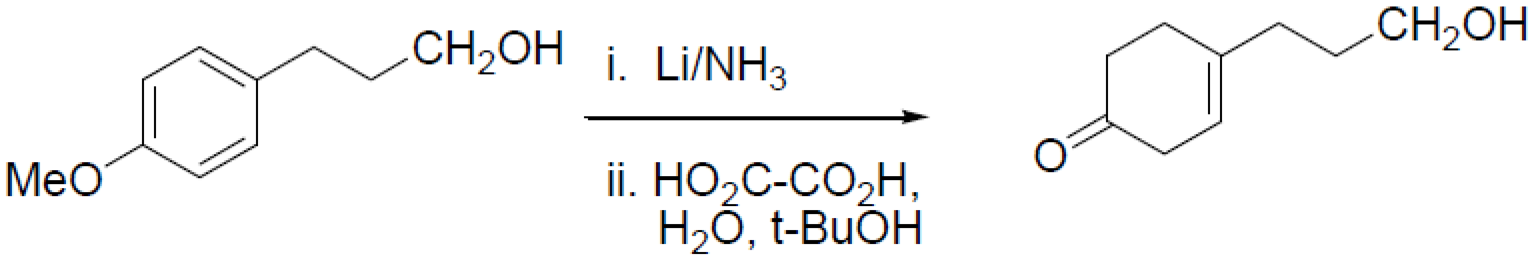
The aldehydes and esters groups are in electron donation side because these are reduced to the corresponding alcohols in Birch condition before the reduction of aromatic ring. The addition of one or two equivalent of water or t-BuOH to the $NH_3$ before the addition of metal can preserve the ester group in Birch reduction.

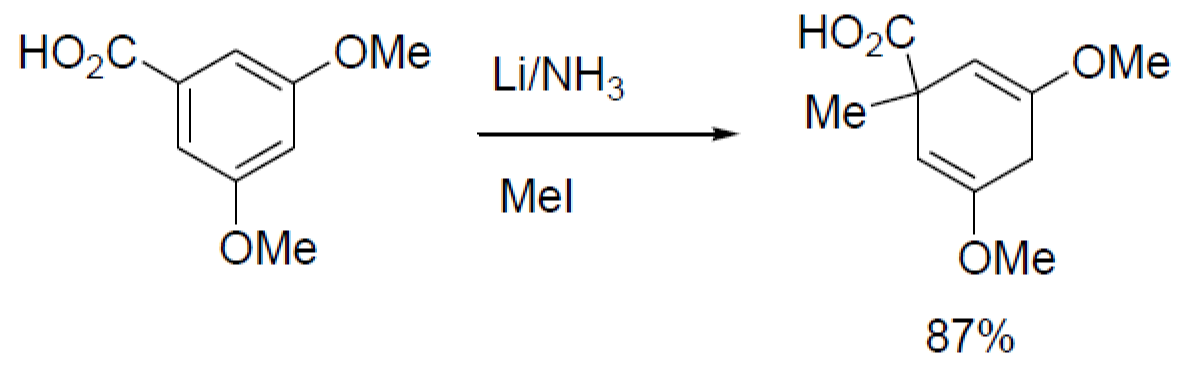


**Mechanism:-** The solvated electron accepts an electron and generates the radical anion which then takes a proton from the alcohol and forms a radical intermediate. The radical intermediate then takes another electron and converts to the carbanion which on protonation gives the desired 1,4-cyclohexadiene derivatives. The role of alcohol is to supply the proton because the $NH_3$ is not sufficient acidic to supply the proton to all the intermediate anion.

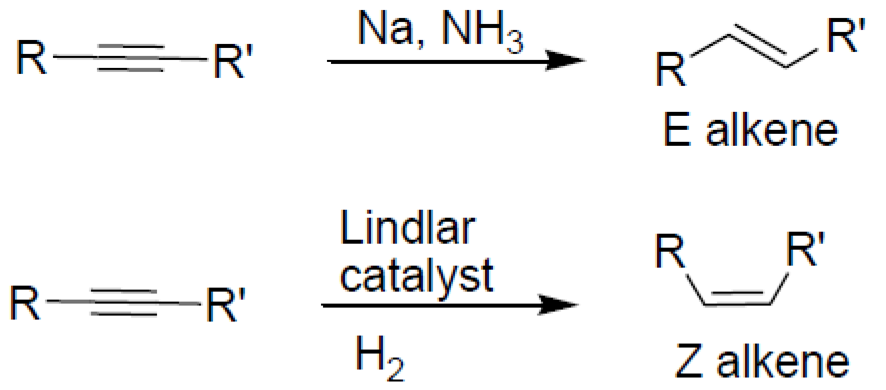

e-
H
H
ROH
H
H
e-
H
H
H
H
ROH
H
H
H
H


O
OMe
N
TMS
K, NH3, t-BuOH, THP, -78 °C
LiBr, Piperylene, EtI, -18 °C
Et
O
OMe
N
TMS

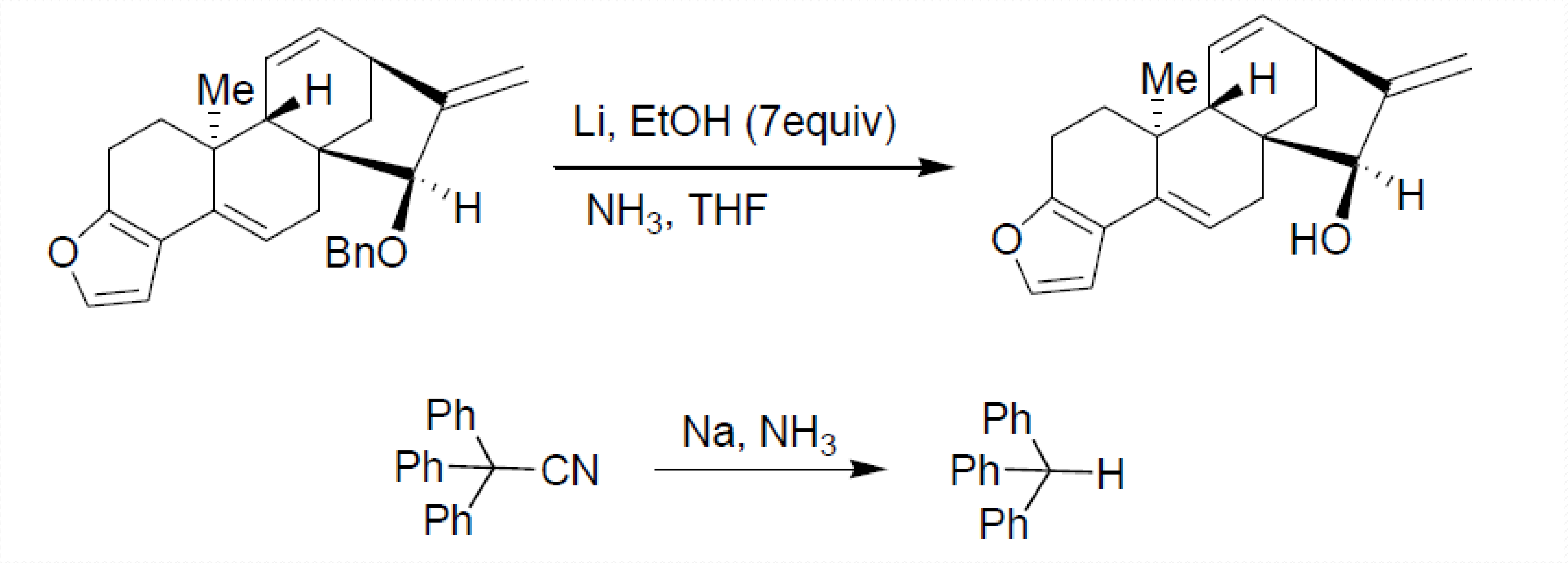

CH2OH
MeO
i. Li/NH3
ii. HO2C-CO2H, H2O, t-BuOH
CH2OH
O



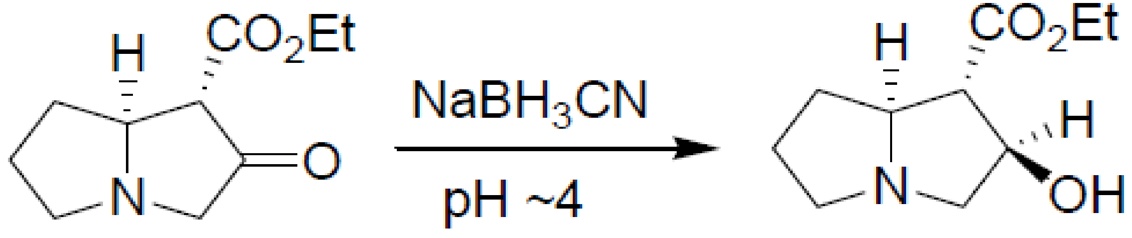
**Reduction of Alkynes:-** The reduction of alkynes to trans alkenes selectively is carried out by the dissolved metal in ammonia. This reaction specifically gives the trans alkenes ( E-alkenes) where as the reduction with Lindlar catalyst gives the cis alkenes ( Z alkenes).

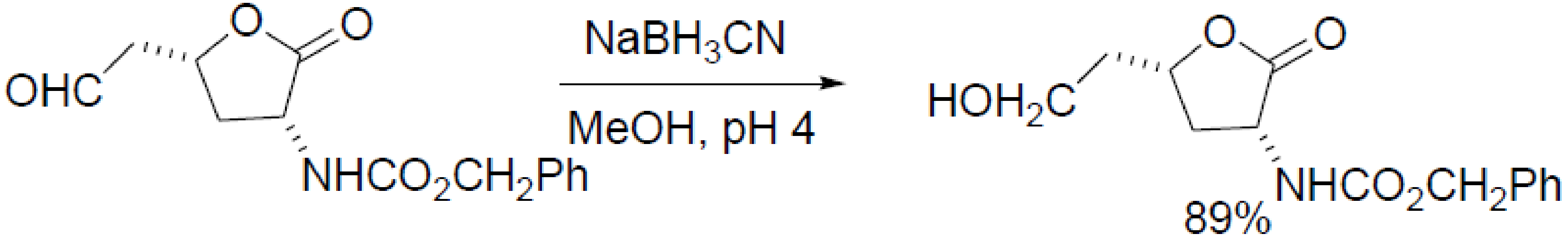


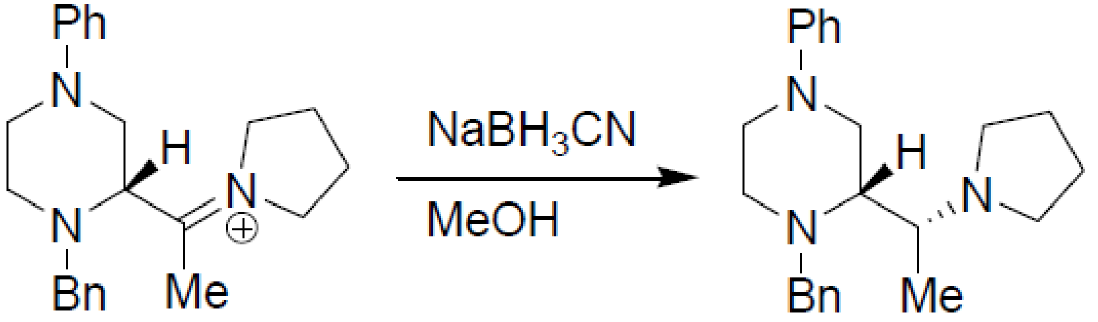
**Reductive Deprotection of Benzyl group:-** The benzyl group and cyano group (alkyl nitrile) could be deprotected by dissolved metal in ammonia.



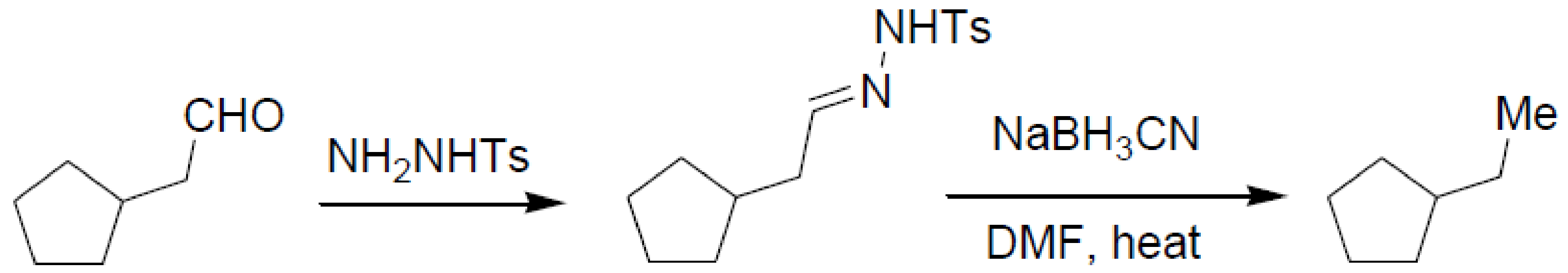
**5. Sodium Cyanoborohydride ($NaBH_3CN$):-** $NaBH_3CN$ is less reactive reducing agent than sodium borohydride due to the presence of electron withdrawing cyano group. Reaction of $NaBH_4$ with HCN gives $NaBH_3CN$, which is soluble in THF, MeOH, $H_2O$, HMPA and DMF. $NaBH_3CN$ cannot reduce the aldehyde or ketones in neutral condition but it reduces the protonated aldehydes and ketones at around pH 3. The iminium ion could be reduced to the corresponding amine with almost quantitative yield.



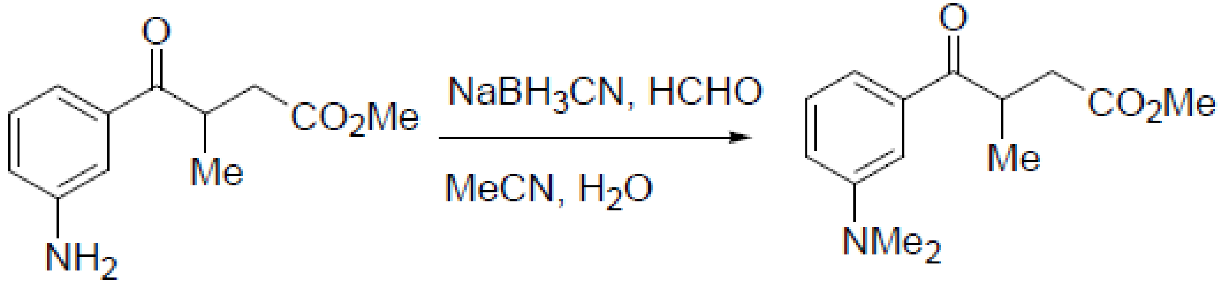




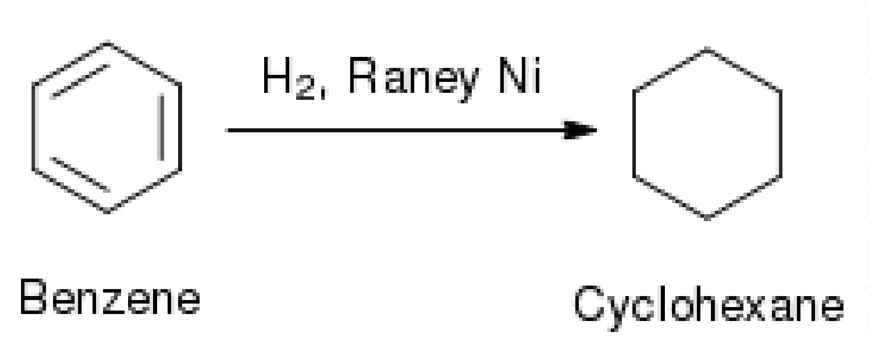
The other important reaction is the deoxygenation of carbonyl compound via tosyl hydrazone formation. It can reduce tosyl hydrazone to the corresponding hydrocarbon.



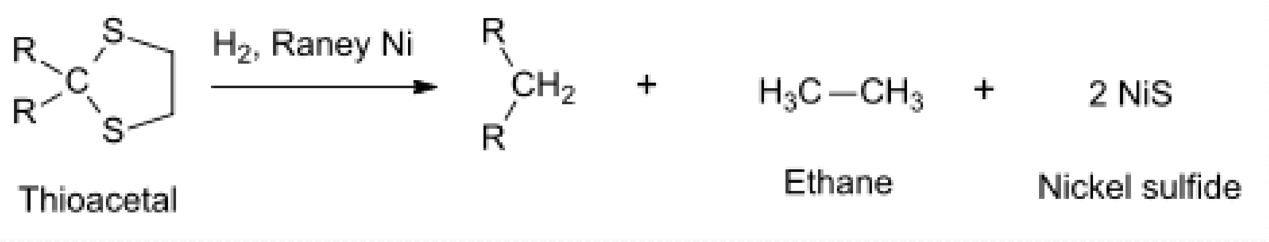
It is also useful for the reductive alkylation of amines. For example, dimethylamino derivative can be prepared from the amine by treatment with HCHO and $NaBH_3CN$, even in the presence of functional groups such as conjugated ketones and ester.

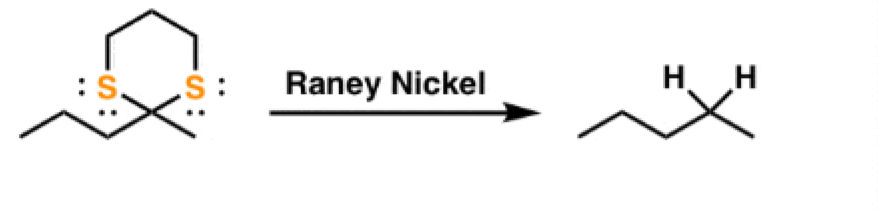


**6. Raney Ni:-** Raney Nickel also called spongy nickel is a fine grained solid composed mostly of nickel derived from a nickel aluminium alloy. Raney nickel is used as a reagent and as a catalyst in organic chemistry. It was developed in 1926 by American engineer Murray Raney for the hydrogenation of vegetable oils. Reduction of benzene ring is very hard to achieve through other chemical means, but can be effected by using Raney nickel. Other heterogeneous catalysts, such as those using platinum group elements, may be used to similar effect, but these tends to be more expensive to produce than Raney nickel.

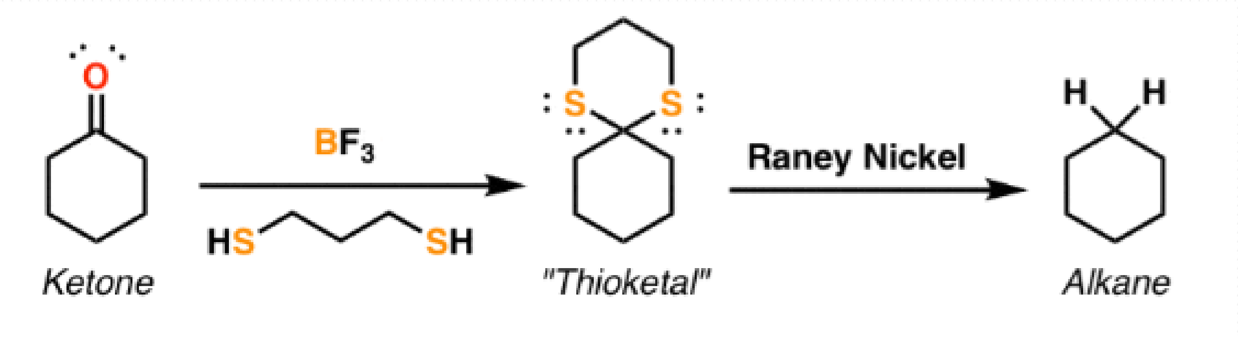


**Desulfurization:-** Raney nickel is used in organic synthesis for desulfurization. For example thioacetals will be reduced to hydrocarbons in the last step of the Mozingo reduction.

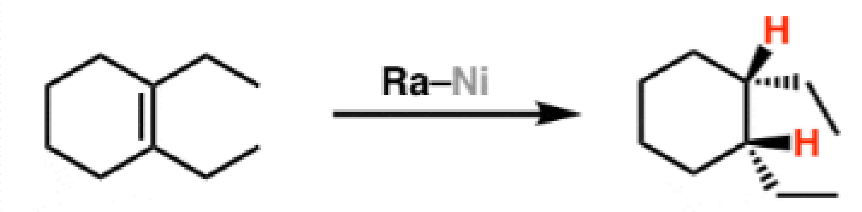




## Conversion of ketones to alkanes:-



## Hydrogenation catalyst:-

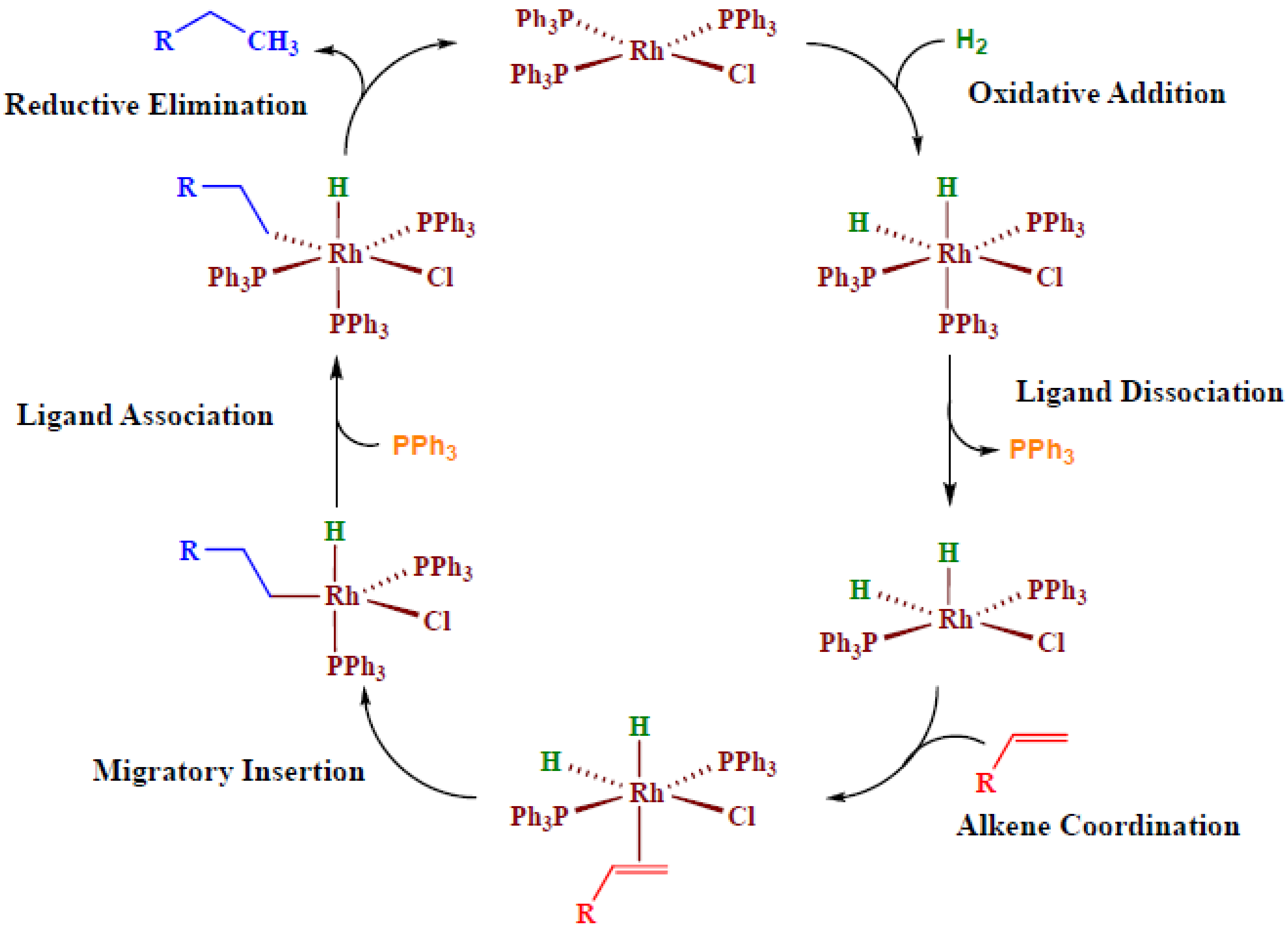


**7. Wilkinson’s Catalyst:-** Wilkinson’s catalyst is the common name for chloridotris(triphenylphosphine)rhodium(I), a coordination complex of rhodium with formula $[RhCl(PPh_3)_3]$. It is a red-brown colored solid that is soluble in hydrocarbon solvents such as benzene, and more so in tetrahydrofuran or chlorinated solvents such as dichloromethane. The compound is widely used as a catalyst for hydrogenation of alkenes.

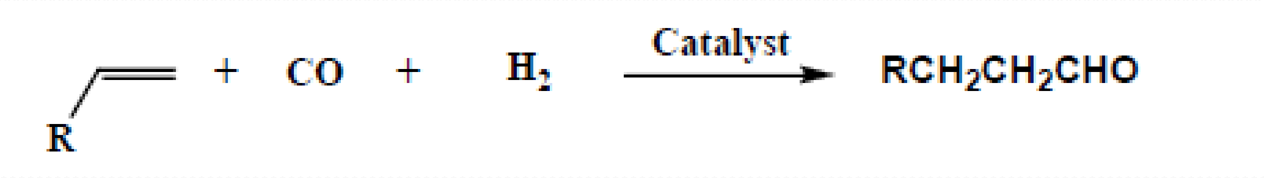
Wilkinson’s Catalyst

# Hydrogenation of Alkenes:-

## Wilkinson's Catalyst

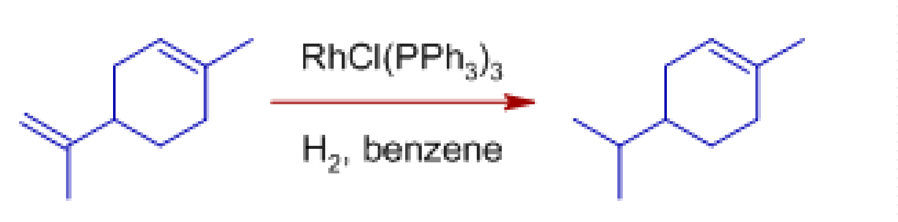


# Hydroformylation:-

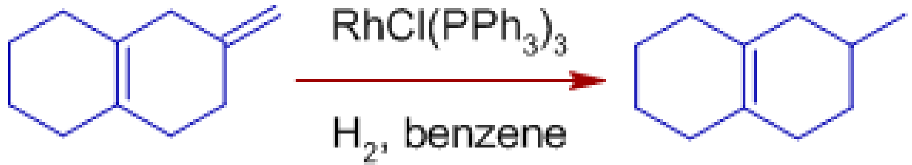


A less common but more appropriate name is hydrocarbonylation.

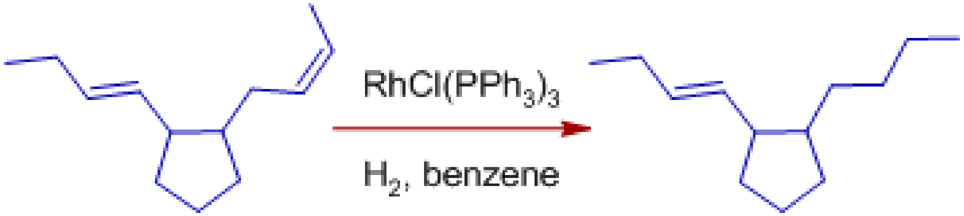
Wilkinson’s catalyst can be used to achieve selective hydrogenations. Less substituted and sterically less hindered double bonds are selectively hydrogenated.



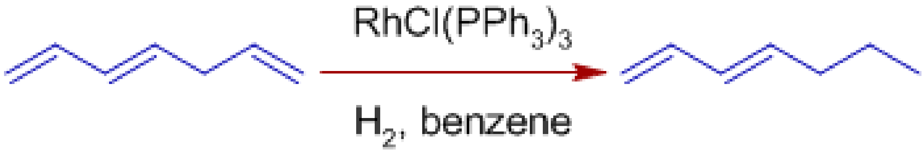
Exocyclic double bonds are selectively hydrogenated over endocyclic double bonds.



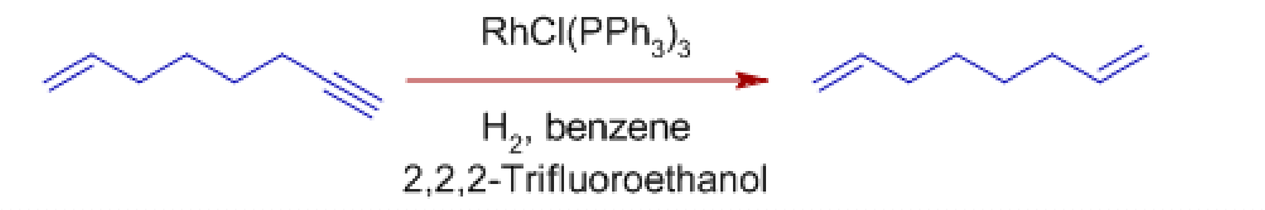
Cis alkenes are reduced rapidly than trans alkenes.



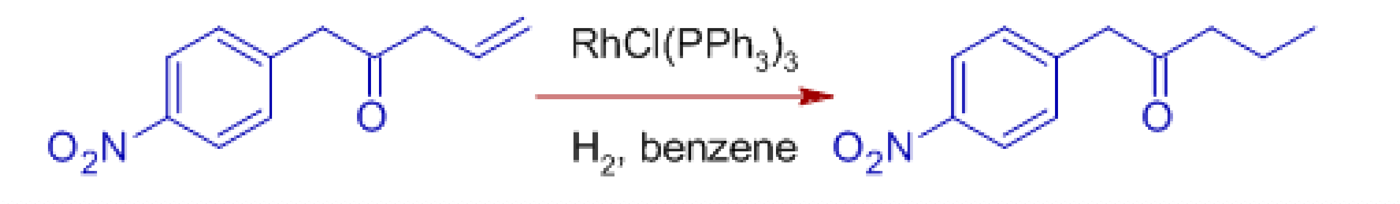
Isolated double bonds are rapidly hydrogenated over conjugated dienes.



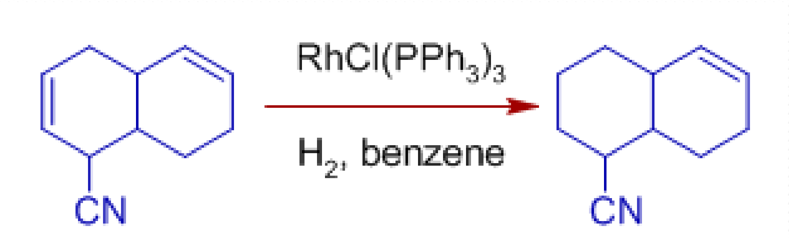
Terminal alkynes are hydrogenated more rapidly than terminal alkenes. The selectivity can be enhanced by using acidic alcoholic co-solvents.



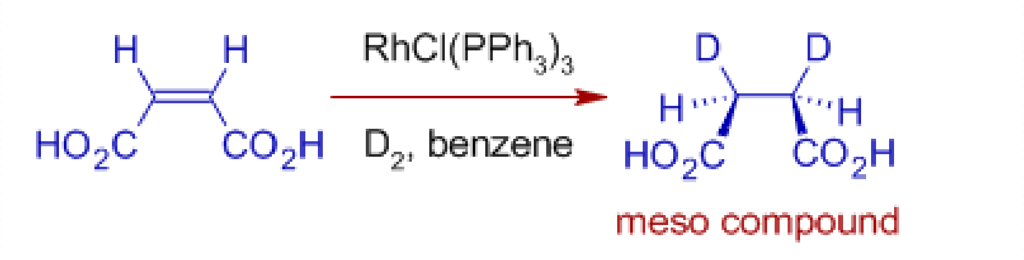
Functional groups like C=O, C=N, $NO_2$, Aryl, $CO_2R$ etc., are unaffected. The compatibility of Wilkinson’s catalyst with polar multiple bonds indicates the metal hydride bond is primarily covalent in character.



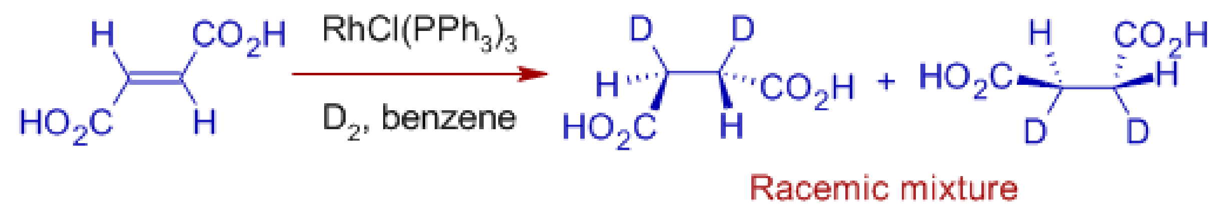
Unsaturated substrates containing polar functionality are hydrogenated more rapidly. It may be due to easy coordination of olefin to the catalyst that is assisted by polar functional group.



Hydrogenations catalyzed by Wilkinson’s catalyst involve stereospecific syn hydrometallation of the multiple bond followed by stereospecific reductive elimination. Hence the hydrogenation of olefins or alkynes result in syn addition products. E.g. Hydrogenation of Maleic acid or Fumaric acid with $D_2$ in presence of Wilkinson’s catalyst is diastereoselective. Hydrogenation of Maleic acid with $D_2$ give meso compound exclusively.



Whereas, with fumaric acid, a racemic mixture is formed.




Thank you!