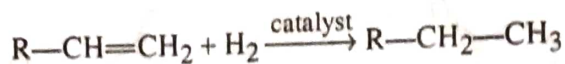


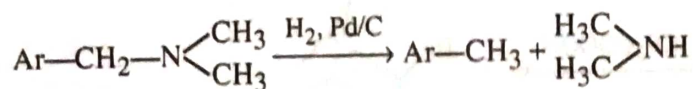
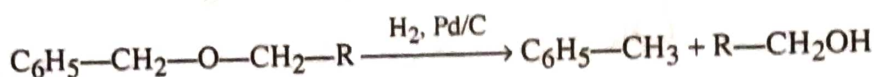
Reduction

3.0 INTRODUCTION

The reduction can be defined as: The removal of oxygen or the addition of hydrogen or the addition of electrons to an organic substrate. Thus the reductive processes fall into three categories: the removal of oxygen, the addition of hydrogen, and the gain of electrons. The addition of hydrogen may be subdivided into hydrogenation, the addition of hydrogen to an unsaturated system, e.g.

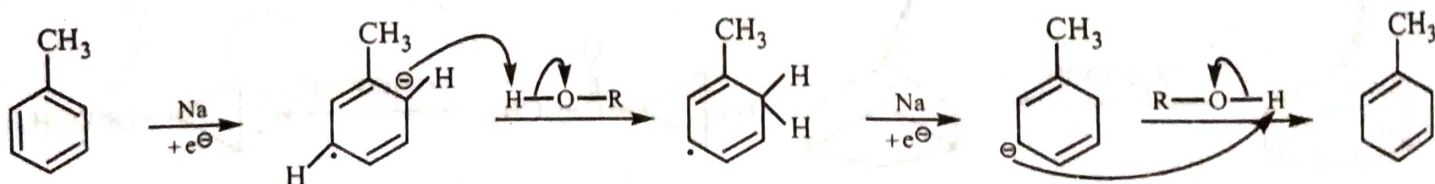


and hydrogenolysis, the addition of hydrogen with concomitant bond-rupture, e.g.

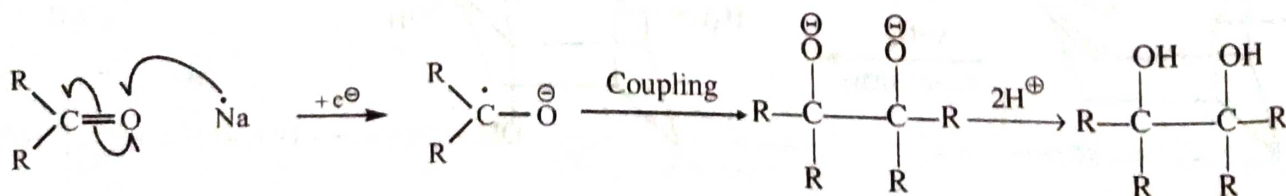


Mechanistically, there are three pathways for reduction:

(i) By the addition of electrons, followed either by the uptake of protons (Scheme-1) or by coupling (Scheme-2).

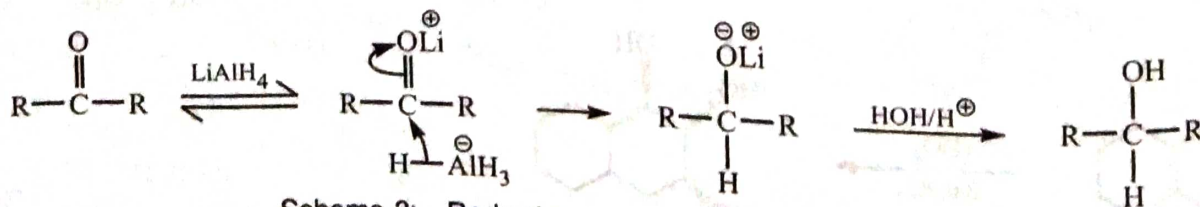


Scheme-1: Addition of electron followed by uptake of proton



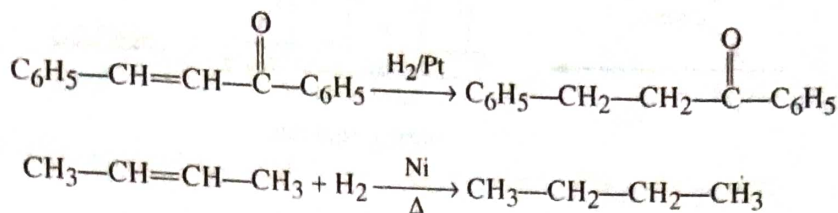
Scheme-2: Addition of electron followed by coupling

(2) By the transfer of hydride ion: hydride ion is involved in reduction by complex metal hydrides of boron and aluminium and alkoxides of aluminium (Scheme-3).

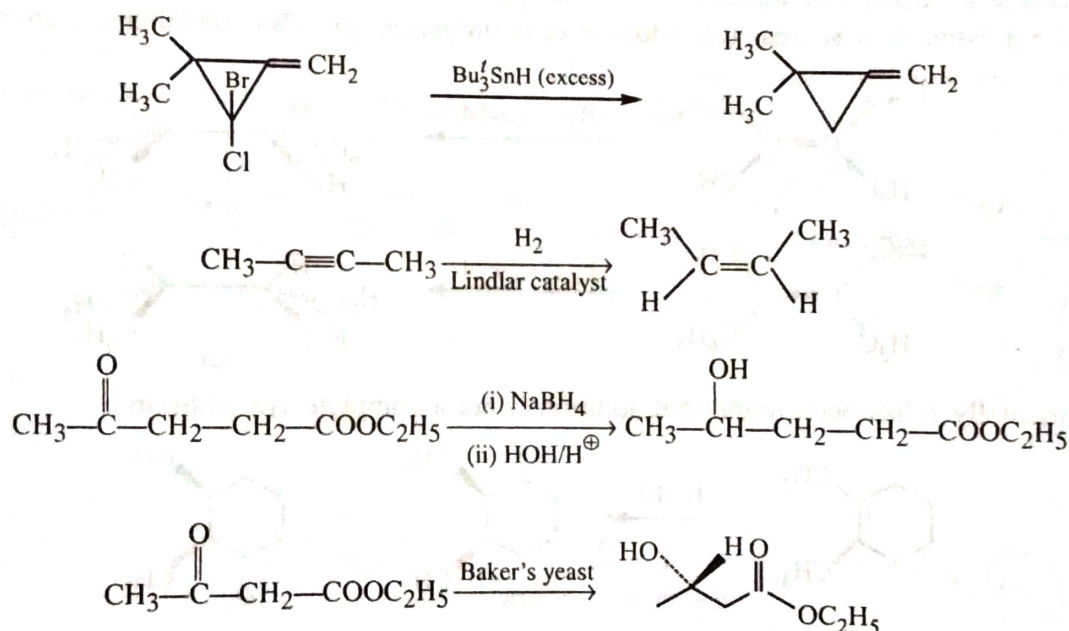


Scheme-3: Reduction by the transfer of hydride ion

(3) By the addition of molecular hydrogen in the presence of catalyst: catalytic reduction is carried out in the presence of molecular hydrogen and catalyst such as palladium, Adam's catalyst, Raney nickel, etc.



Each method has its advantages. In many reductions either methods may be used equally well. Complete reduction of an unsaturated compound can generally be achieved without any difficulty. The aim is often selective reduction of one group in a molecule in the presence of other unsaturated groups. Both catalytic and chemical methods of reduction offer considerable scope in this direction, and the method of choice in a particular case will often depend on the selectivity required and on the stereochemistry of the desired product (Scheme 4).



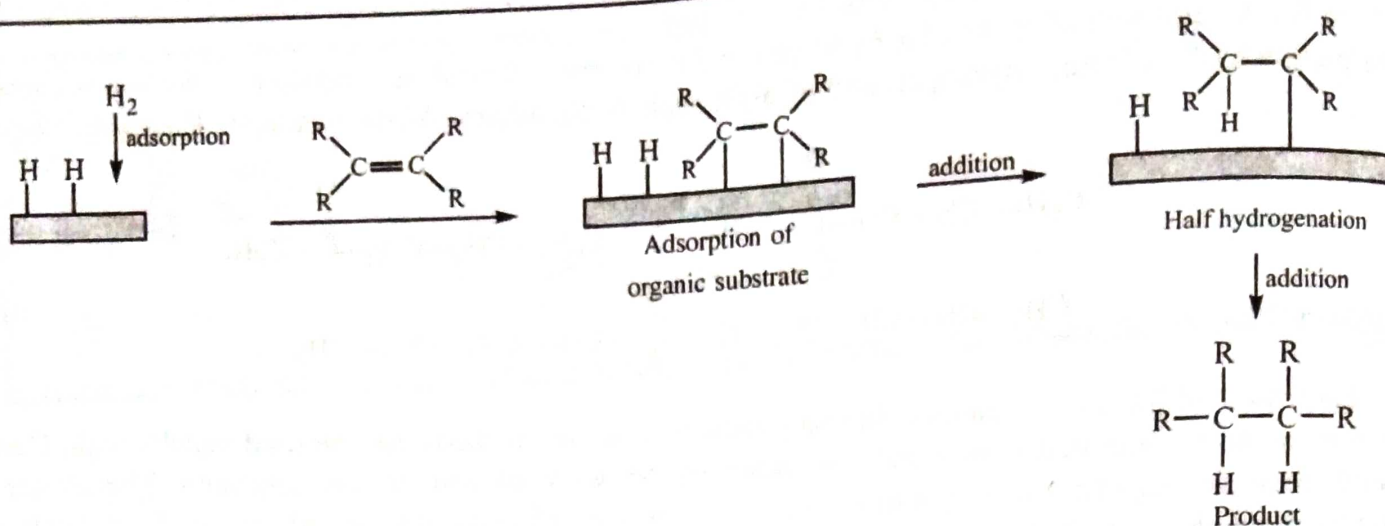
3.1 REDUCTION OF HYDROCARBONS

3.1.1 Reduction of Alkenes

(1) Catalytic hydrogenation

Catalytic hydrogenation is one of the most convenient methods for the reduction of alkenes. The method consists in string the substrate with a catalyst in a suitable solvent in an atmosphere of hydrogen. Catalytic hydrogenation can be classified into two categories. This classification is based on the homogeneity of the reaction.

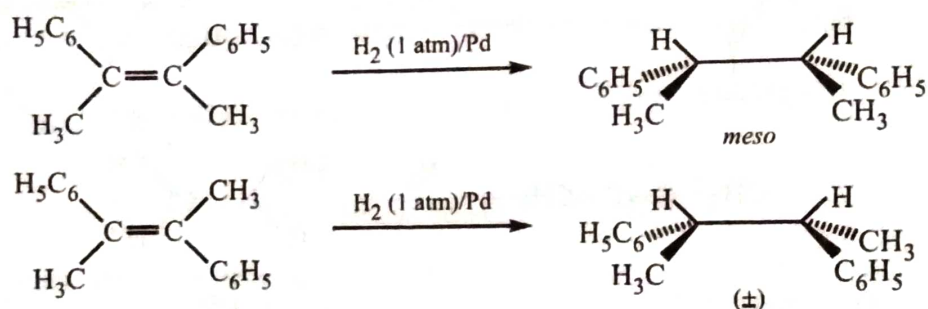
(A) Heterogeneous Hydrogenation: A number of heterogeneous catalysts have been used for catalytic hydrogenation. Modern procedures involve a transition metal catalysts (Rh, Pt, Pd are the most common) adsorbed on to a solid support (such as carbon or alumina). The catalytic reduction takes place between gaseous hydrogen and an organic compound. The reduction takes place at the surface of the catalyst which adsorbs both hydrogen and the organic compound and facilitates their contact. Transfer of hydrogen takes place from the catalyst to the molecule, resulting in reduction (Scheme-5).



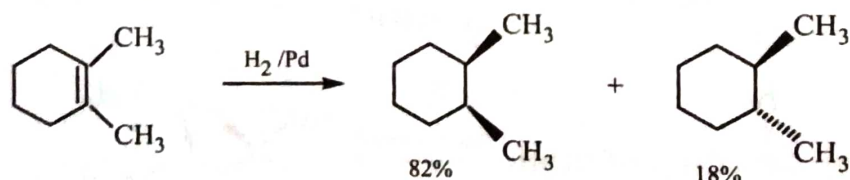
Scheme 5: Catalytic hydrogenation of alkenes

Although elevated temperature and pressure invariably increase the rate of hydrogenation, the reaction usually proceed in a satisfactory manner at room temperature under the one atmosphere of hydrogen gas.

From the Scheme-5, it is clear that addition of hydrogen is *syn*. Thus reaction is stereospecific reaction.

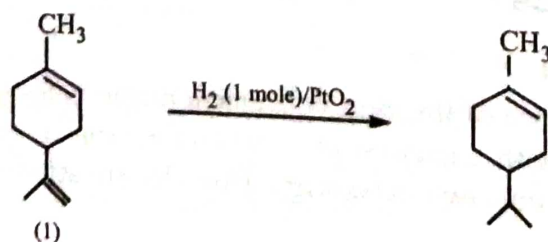


Experimentally it has been found that addition is not a complete *syn* addition.

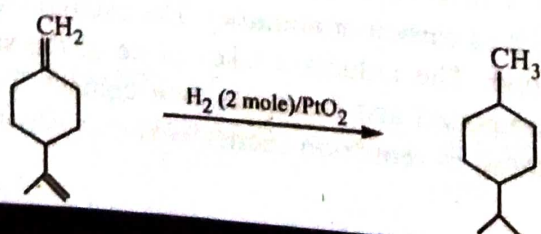


Lack of complete *syn* addition may be explained if we suppose that all steps except for the last step of the Scheme-5 are reversible.

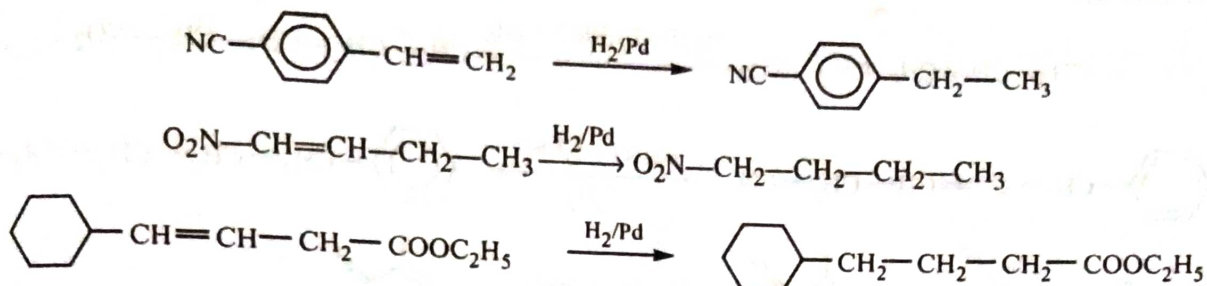
The ease of reduction of an alkene decreases with the degree of substitution of the double bond, and this sometimes allows selective reduction of one double bond in a molecule which contains more than one double bond, e.g.



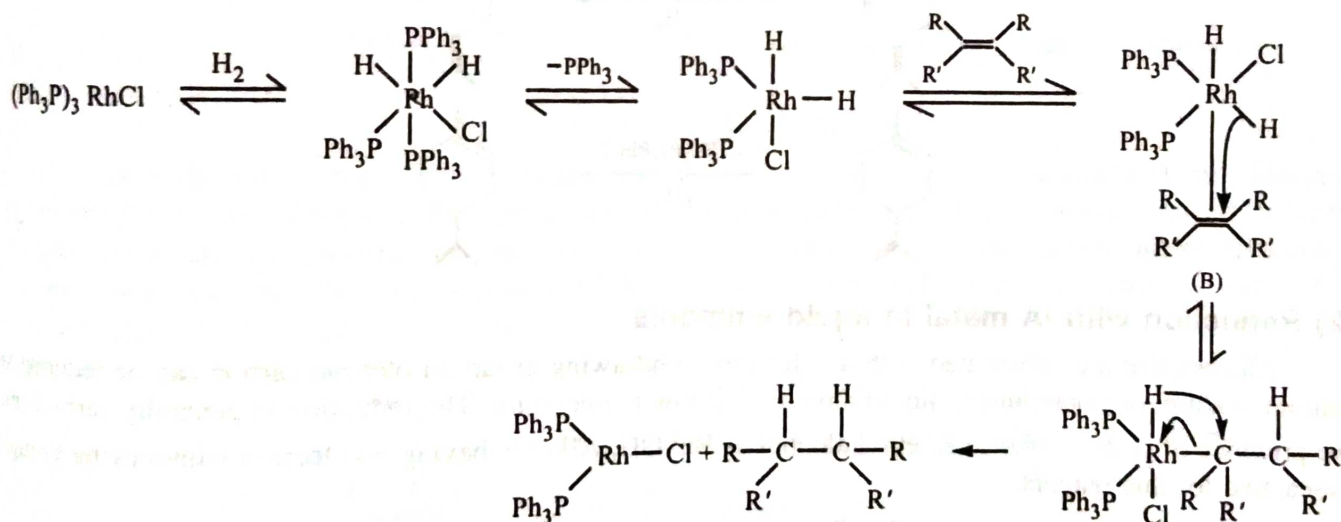
In contrast, the isomeric compound of (1), in which both double bonds are disubstituted, gives only the completely reduced product.



Selective reduction of carbon-carbon double bonds in compounds containing other unsaturated groups can usually be accomplished, except in the presence of $-\text{C}\equiv\text{C}-$, aromatic $-\text{NO}_2$ and $-\text{COX}$. The best catalyst for selective reduction is palladium, e.g.

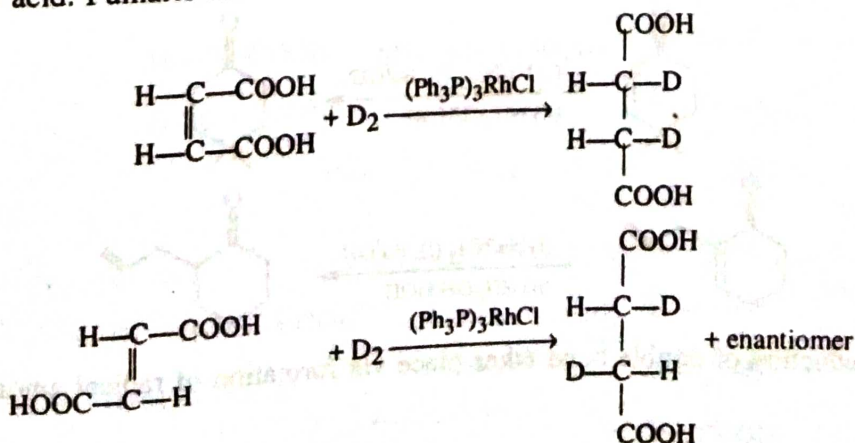


(B) Homogeneous Hydrogenation: Wilkinson's catalyst ($(\text{Ph}_3\text{P})_3\text{RhCl}$) is a most useful homogeneous catalyst of alkenes. This catalyst is soluble in solvents such as methyl alcohol or ethyl alcohol. Addition of hydrogen to a red solution of the catalyst promotes the formation of yellow complex (A). Formation of (A) takes place by oxidative addition of hydrogen and dissociation of a bulky phosphine ligand from the metal. In fact, dissociation of a phosphine ligand opens up a coordination site for the alkene to attach itself to the metal. The next step in the mechanism involves the concerted addition of a metal hydrogen bond across the coordinated alkene to form complex (B). Both atoms (H and Rh) are added *syn* fashion to the alkene. Finally, reductive elimination leads the formation of the product (Scheme-6).

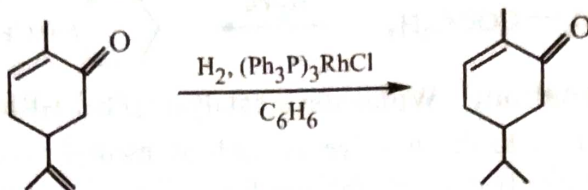
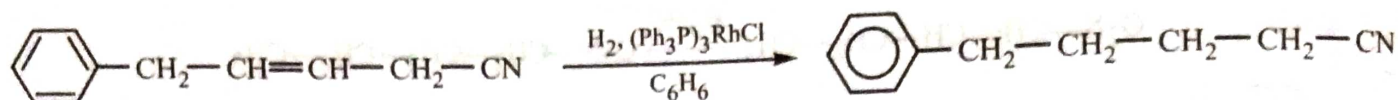
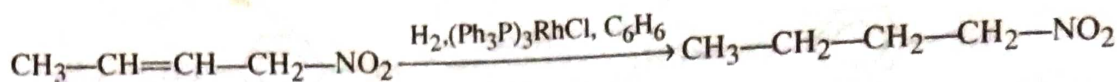


Scheme-6

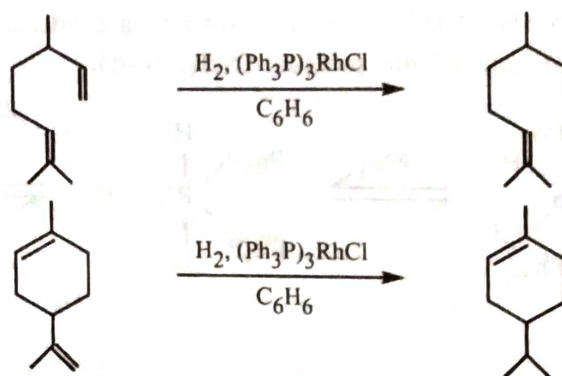
Syn addition is shown by catalysed reduction of maleic acid with deuterium which gives *meso* dideuterated succinic acid. Fumaric acid on the other hand gives (*dl*) mixture.



This catalyst is used for the hydrogenation of non-conjugated alkenes. Functional groups such as oxo, nitro, cyano, halo and azo are not reduced under the reaction conditions in the presence of triphenylphosphine rhodium chloride.

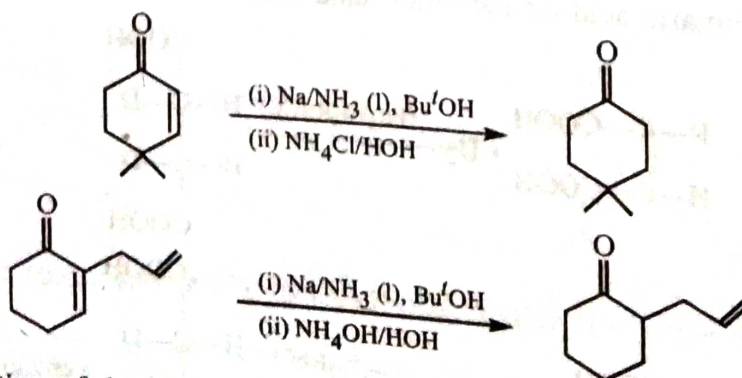
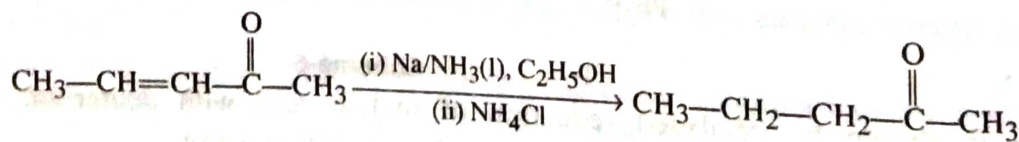


Mono- and disubstituted double bonds are reduced much more rapidly than tri and tetrasubstituted ones, permitting the partial hydrogenation of compounds containing different types of double bonds.

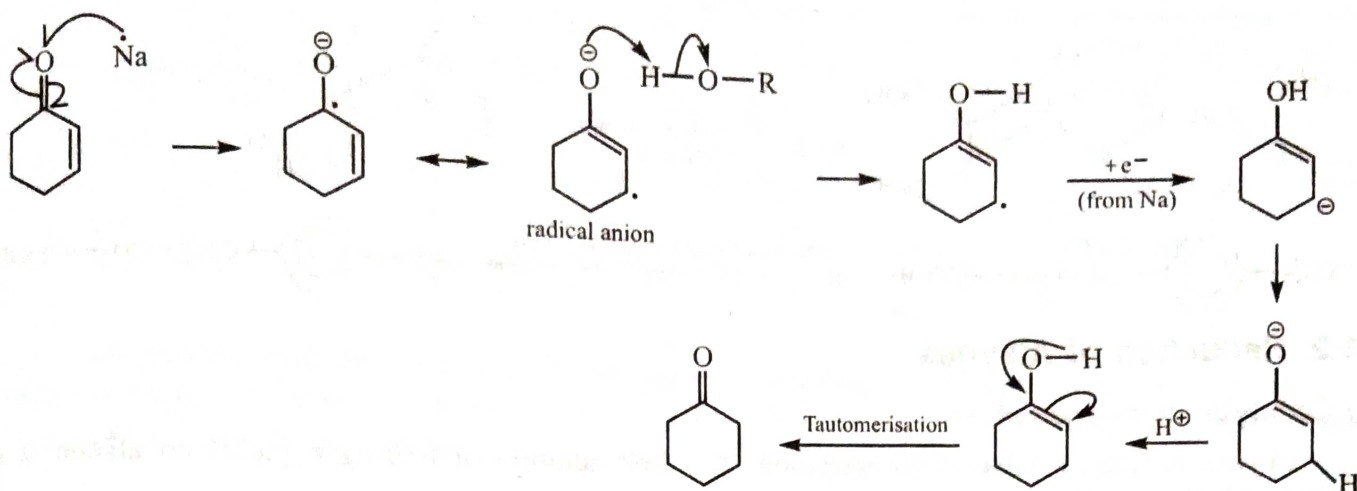


(2) Reduction with IA metal in liquid ammonia

Alkenes that are substituted with an electron-withdrawing group on olefinic carbon can be reduced with lithium, sodium or potassium in liquid ammonia at low temperature. The reduction is generally carried out in the presence of proton donor, *i.e.*, ethyl alcohol or Bu^tOH . Alkenes having no electron withdrawing group are unreactive for this reagent.

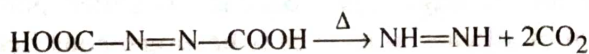
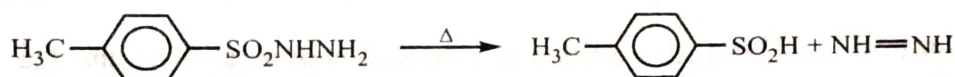
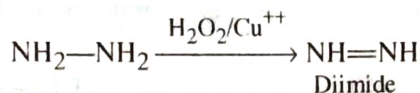


In such cases reduction of double bond takes place via formation of radical anion as follows:

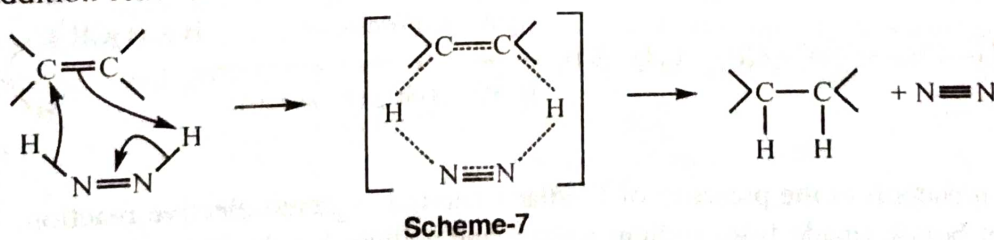


(3) Reduction with diimide

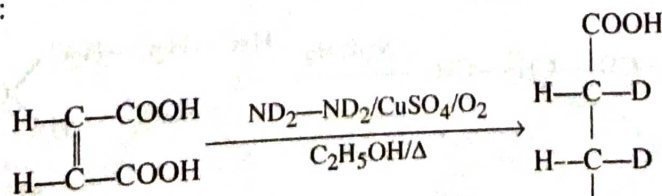
Diimide is unstable compound and is prepared *in situ* usually by the oxidation of hydrazine or by thermal decomposition of *p*-toluenesulphonylhydrazine or azo dicarboxylic acid.



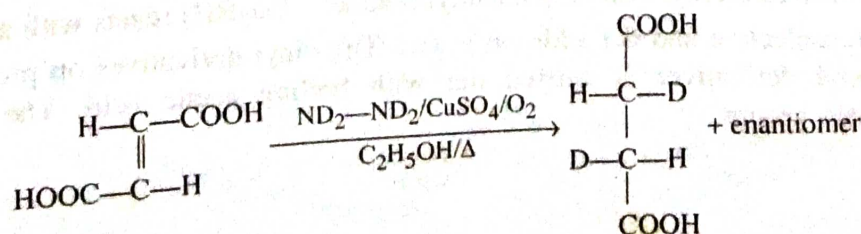
Diimide is a highly selective reagent for the reduction of carbon-carbon double bond. The reaction of diimide with alkenes is a concerted group transfer reaction proceeding through a six-membered cyclic transition state. It results in predominant *syn* (*cis*) addition of hydrogen on to the double bonds (Scheme-7). The mechanism explains the high stereospecificity of the reaction, and couples the driving force of nitrogen formation with the addition reaction.

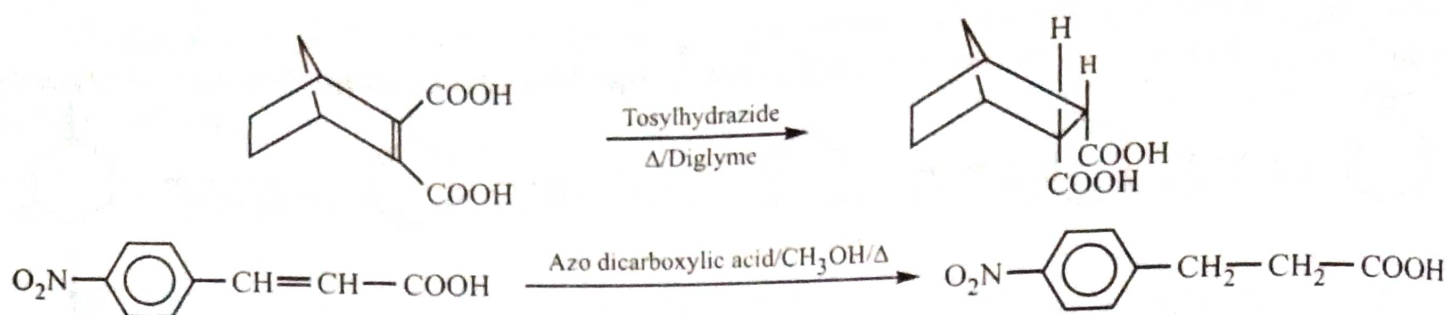


Some examples are:



meso form

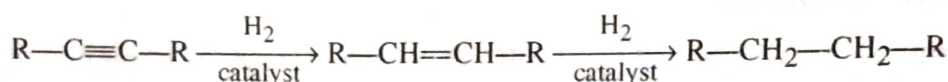




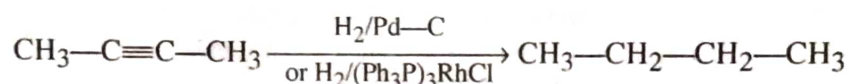
3.1.2 Reduction of Alkynes

(1) Catalytic hydrogenation

Alkynes undergo catalytic hydrogenation. The first addition of hydrogen yields an alkene: a second addition of hydrogen gives an alkane.

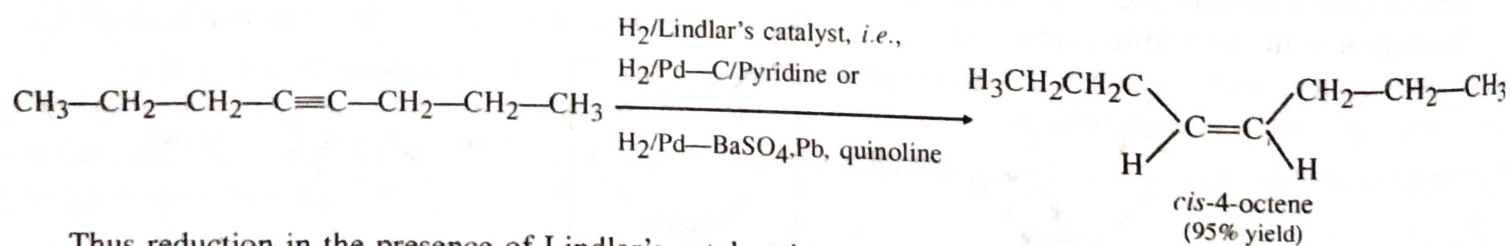


The catalyst in the above reaction may be heterogeneous or homogeneous.



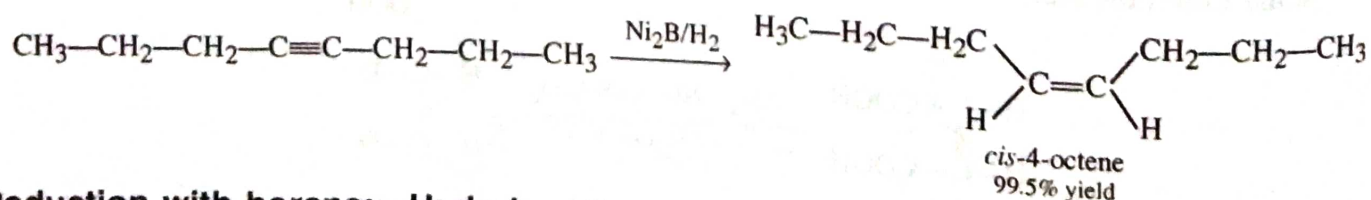
The utility of catalytic hydrogenation is enhanced considerably by the fact that hydrogenation of an alkyne may be stopped at the alkene stage. This reduction is called partial reduction of alkynes. The best method for the partial reduction of alkynes to alkenes is heterogeneous hydrogenation with Lindlar's catalyst. Lindlar's catalyst is essentially Pd that had been poisoned with Pb^{++} and an amine (quinoline or pyridine).

This catalyst is ineffective for alkenes. In the presence of Lindlar's catalyst non-terminal alkynes convert into *cis* alkenes. In fact, catalytic hydrogenation of alkynes is one of the best ways to prepare *cis*-alkenes



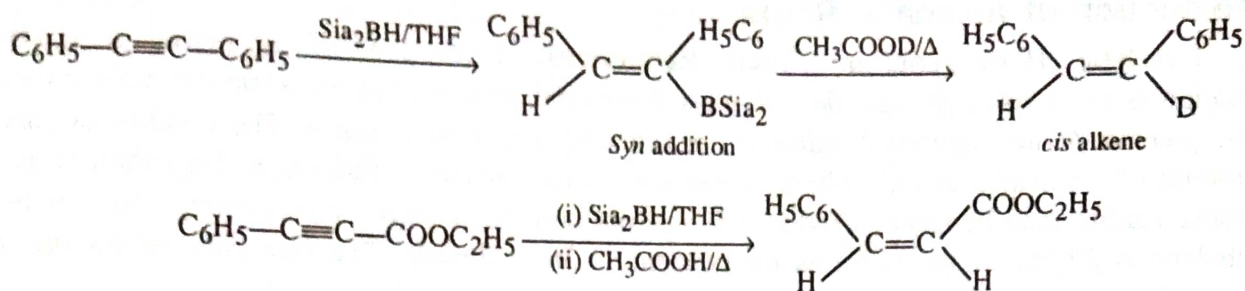
Thus reduction in the presence of Lindlar's catalyst is stereoselective reaction.

Nickel boride (made from sodium acetate and sodium borohydride) is an excellent alternative catalyst for the conversion of alkynes into *cis* alkenes.

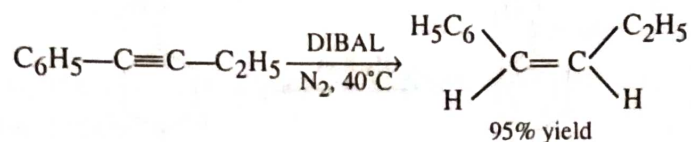


(2) Reduction with borane: Hydroboration of alkynes

A sterically hindered dialkyl borane (Disiamyl borane: Si_2BH) reacts with alkyne to give vinyl borane. The reaction is stereoselective and the addition is *syn*. The vinyl derivatives on protonolysis give *cis* alkenes. Protonolysis of vinyl derivatives is carried out with boiling acetic acid. The reagent is inert towards NO_2 , COOR and halo groups.

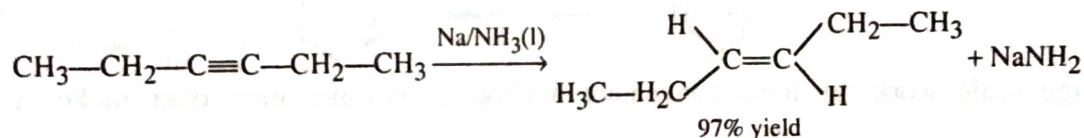


Alkynes can also be reduced to *cis* alkenes with diisobutyl aluminium hydride (DIBAL). The reduction with this reagent is carried out in the presence of inert atmosphere at 40°C. This reagent is selective one because it is inert for most of the functional groups except $-\text{C}\equiv\text{C}$, $-\text{COOR}$ and $-\text{CN}$.



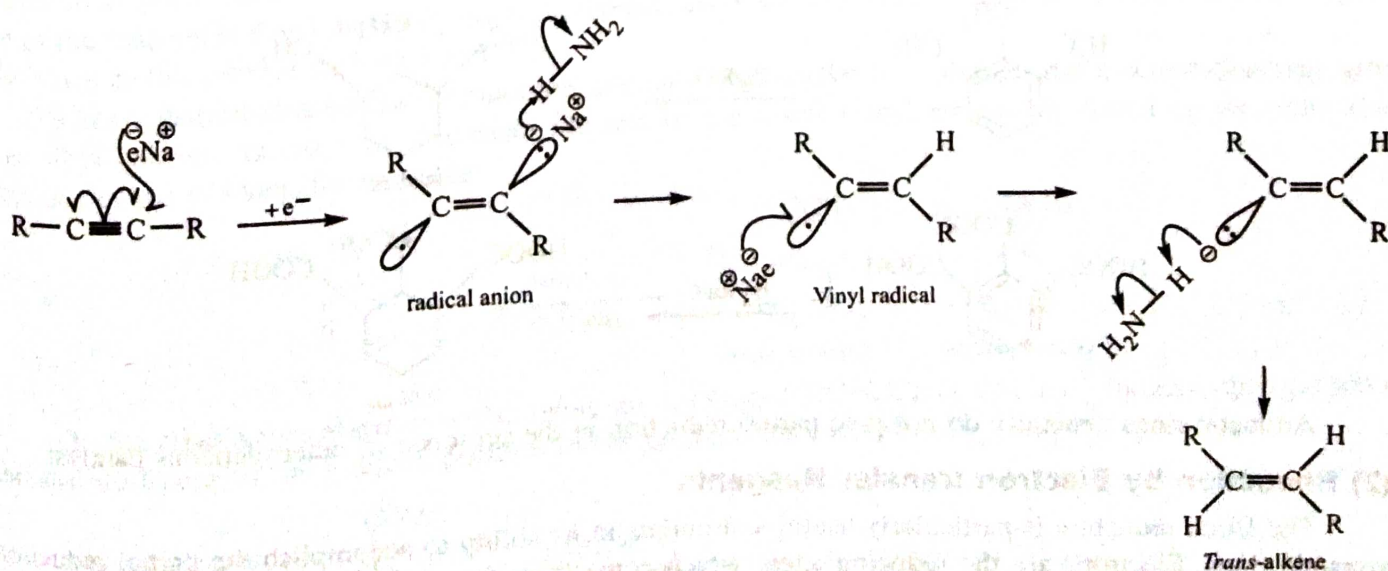
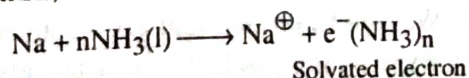
(3) Reduction with IA metals in liquid ammonia

Reaction of a non-terminal alkyne with a solution of an alkali metal (usually Na or Li or K) in liquid ammonia gives a *trans*-alkene.



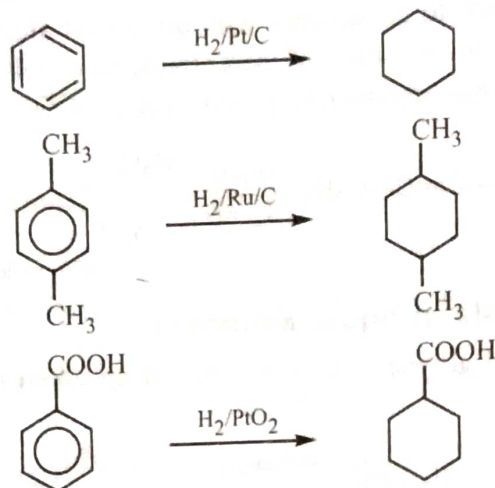
The reduction of alkynes with sodium in liquid ammonia is complementary to catalytic hydrogenation of alkynes.

The mechanism of the reduction proceeds via addition of an electron to the alkyne to form a radical anion which adopts *trans* geometry. The radical anion is such a strong base that it readily removes a proton from ammonia to give vinylic radical. The vinylic radical picks up another electron to give the vinyl anion. Finally, protonation of this anion leads to the observed *trans*-alkene (Scheme-8). Fortunately ordinary alkenes do not react with the solvated electron, the reaction stops at the *trans*-alkene stage.

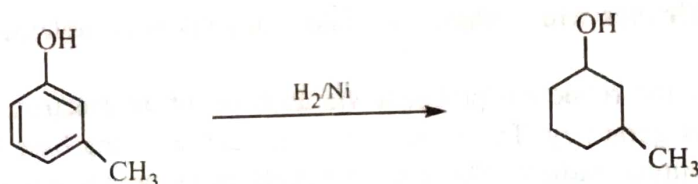


3.1.3 Reduction of Aromatic Rings

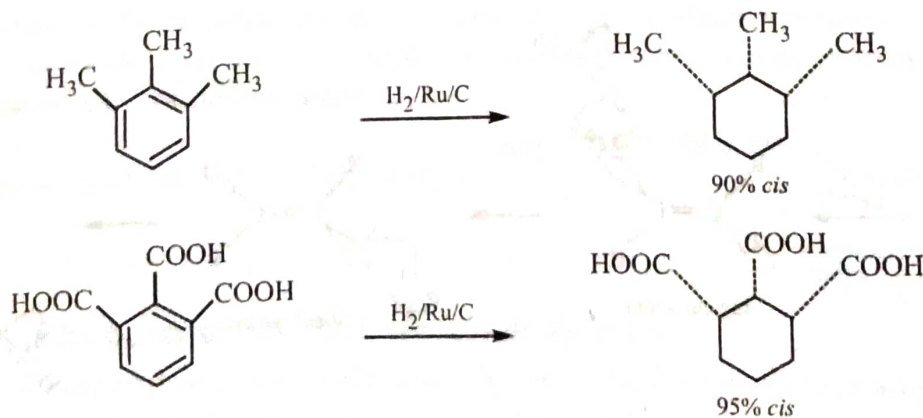
(1) **Catalytic Hydrogenation (Total Reduction):** Reduction of aromatic rings by catalytic hydrogenation is more difficult than that of most functional groups because aromatic stabilisation energy is lost in the process. More vigorous conditions are required due to this reason. The conditions vary according to the amount of resonance energy which is lost during the course of reduction. Naphthalene is reduced to tetralin more readily than benzene is reduced to cyclohexane because resonance energy for per benzene ring of naphthalene is 29 kcal/mole whereas for benzene is 36 kcal/mole. The best catalysts for the purpose are platinum rhodium and ruthenium.



For large scale work the most convenient method is hydrogenation over nickel at 150-200°C and 90-200 atm.



Stereogenic centres are formed when substituted aromatic compounds are reduced by hydrogenation. As we would expect one face of an aromatic ring to be adsorbed onto the metal surface, the subsequent addition of hydrogen to come from the metal. We would predict that *cis* diastereomers would be formed preferentially. This is indeed the case, although the level of stereoselectivity is not always high.

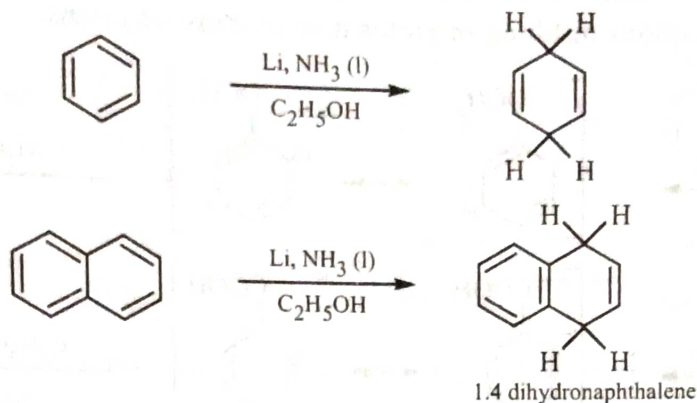


Aromatic rings generally do not give partial reduction in the presence of heterogeneous catalyst.

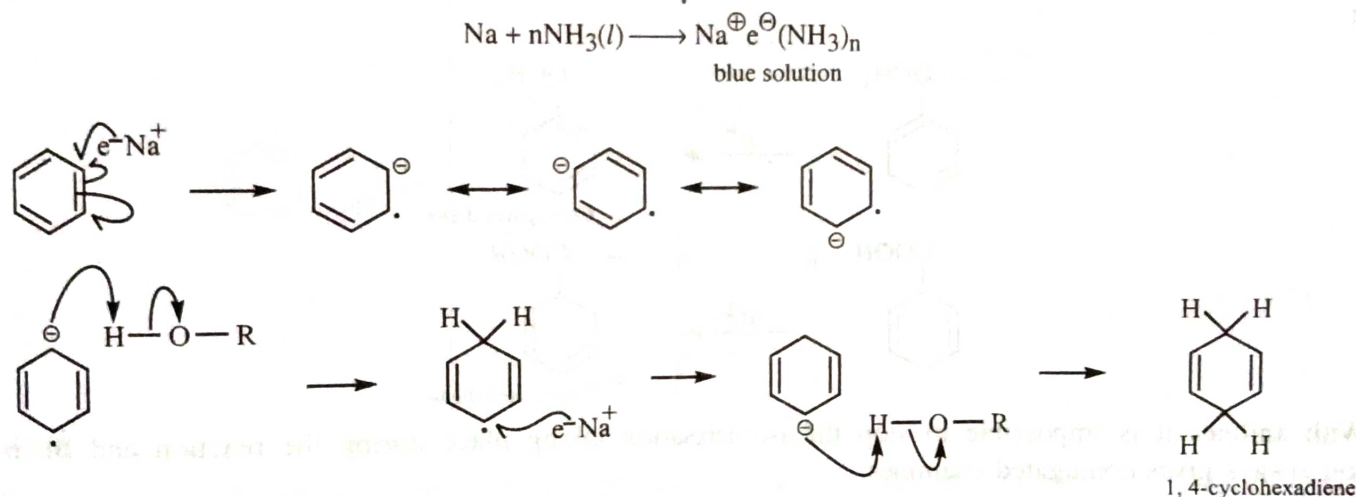
(2) Reduction by Electron transfer Reagents

The Birch reduction is particularly useful and unique in its ability to accomplish the partial reduction of aromatic rings. Electrons are the reducing agent which come from the group IA metals like Na, Li or K in

liquid ammonia. When aromatic rings are reduced by Li in liquid ammonia, usually in the presence of an alcohol (e.g. ethanol, 2-propanol or *t*-butyl alcohol), 1,4-addition of hydrogen takes place and non-conjugated cyclohexadienes are produced.



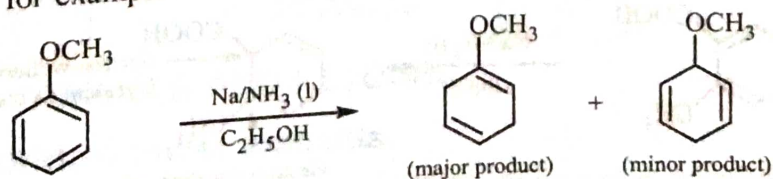
The mechanism of reduction involves sequential addition of an electron, followed by protonation of the radical anion species so formed (Scheme-9).



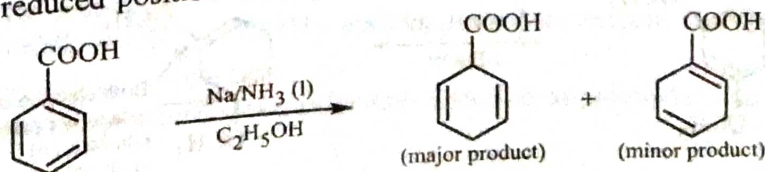
Scheme-8

Formation of a 1,4-cyclohexadiene is quite general in this type of reduction, but the reason for its formation in preference to the more stable conjugated 1,3-cyclohexadiene is not clearly understood. However, one of the reasons is that kinetically controlled reactions of cyclohexadienyl anions with electrophiles typically take place at this central carbon, *i.e.*, C-4.

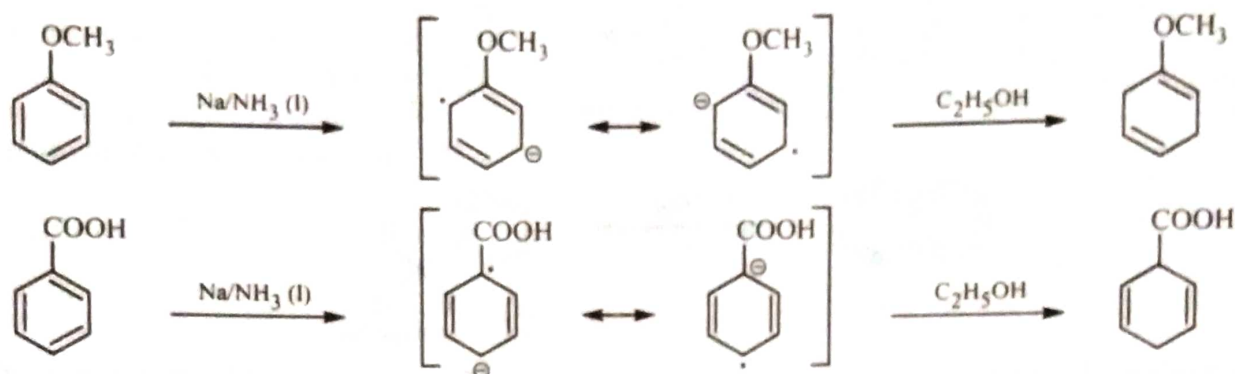
When substituted aromatic compounds are subjected to Birch reduction, the electron-donating groups (e.g. alkyl, alkoxy, amino, etc.) decreases the rate of the reaction and are mainly found on the non-reduced positions of the product, for example:



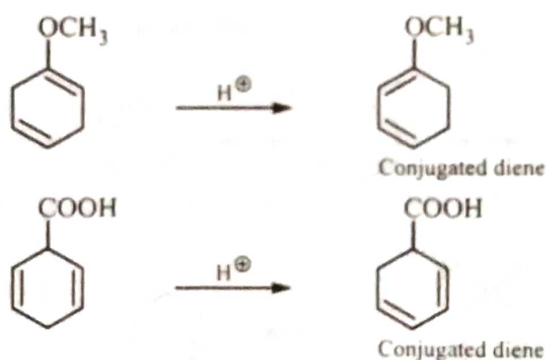
On the other hand, electron-withdrawing groups (e.g., COOH, CHO, CH, etc.) increase the reaction rate and are mainly found on the reduced position of the product, for example:



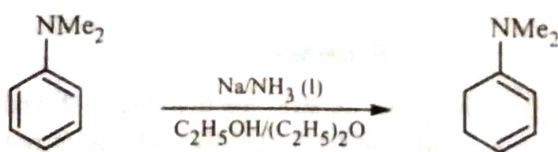
It is general principle that electron donating groups promote *ortho*, *meta* reduction while electron-withdrawing groups promote *ipso*, *para* reduction. The explanation for this is based on the distribution of electron density in the intermediate radical anions. Electron-donating groups stabilise electron density at *ortho* and *meta* positions, and protonation occurs at these positions, while electron-withdrawing groups stabilise electron density at the *ipso* positions resulting in protonation at these positions.



If one wants the conjugated dienes as product, it is quite a simple matter to isomerise them using an acid catalyst.

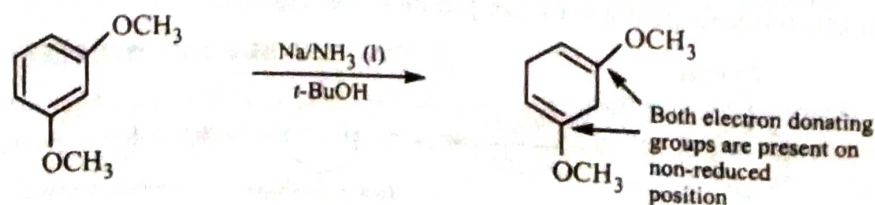
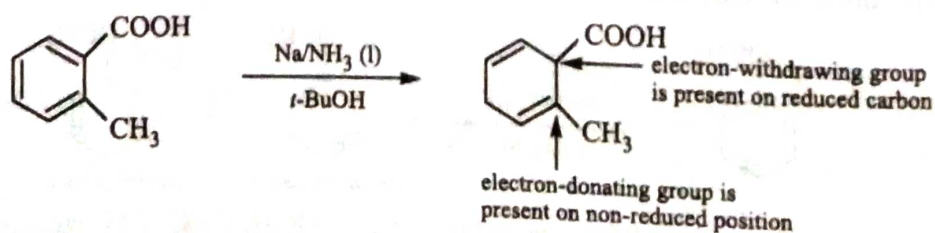


With anilines it is impossible to stop the isomerisation taking place during the reaction and Birch reduction always gives conjugated enamines.

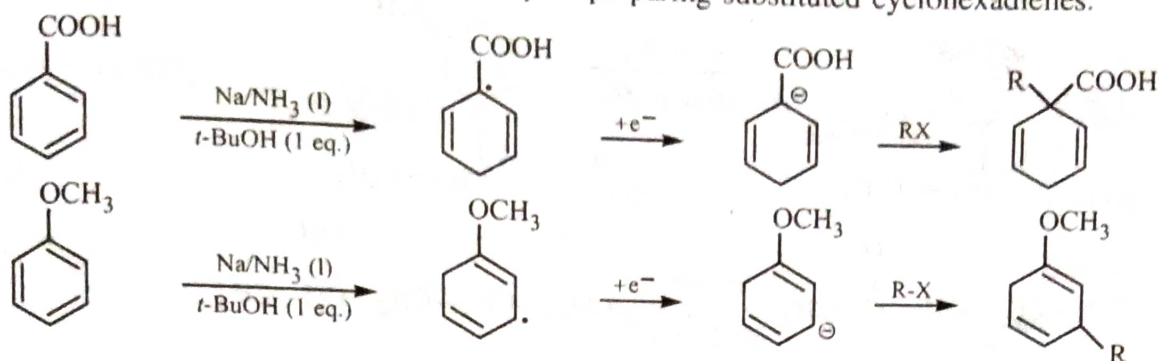


Reduction of aromatic rings with lithium or calcium in amines (not ammonia) proceeds further and cyclohexenes are obtained instead of 1,4-cyclohexadienes.

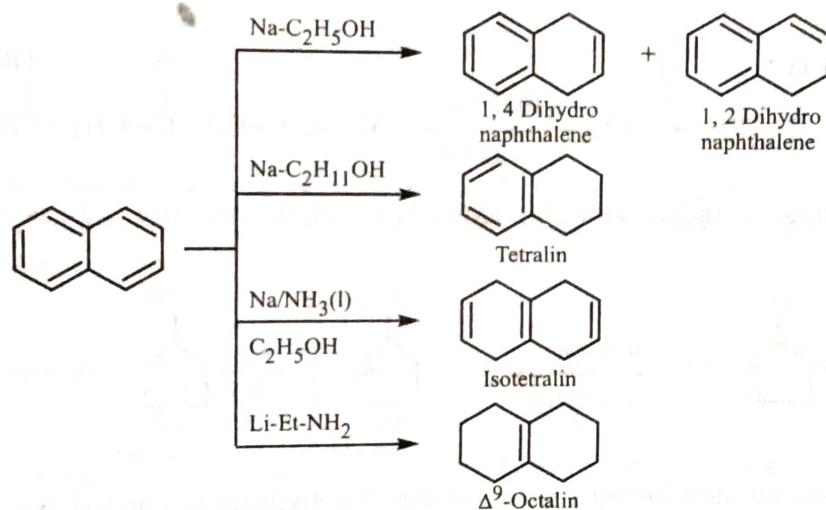
The rules described above regarding orientation can be readily applied to the reduction of more complex polysubstituted benzenes.



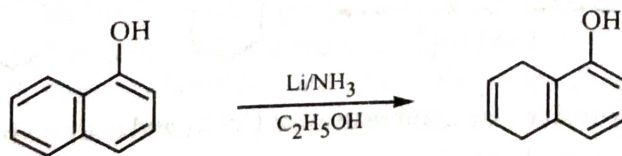
If Birch reduction is carried out in the presence of one equivalent of proton donor, then the enolate formed has no proton source to quench it. Under these conditions the enolate can be alkylated by the use of alkyl halides. This procedure is an effective way of preparing substituted cyclohexadienes.



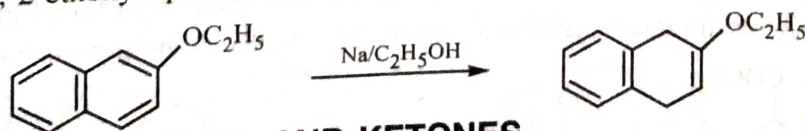
A variety of products can be obtained with naphthalene. Nature of products depend on the nature of proton donor and reaction conditions.



The reduction of 1-naphthol and 2-ethoxynaphthol provides an interesting contrast. 1-Naphthol is reduced by lithium in ammonia containing ethanol in the unsubstituted ring. This is because electron-donating groups decrease the reactivity of the ring.



On the other hand, 2-ethoxynaphthalene is reduced in the substituted ring.



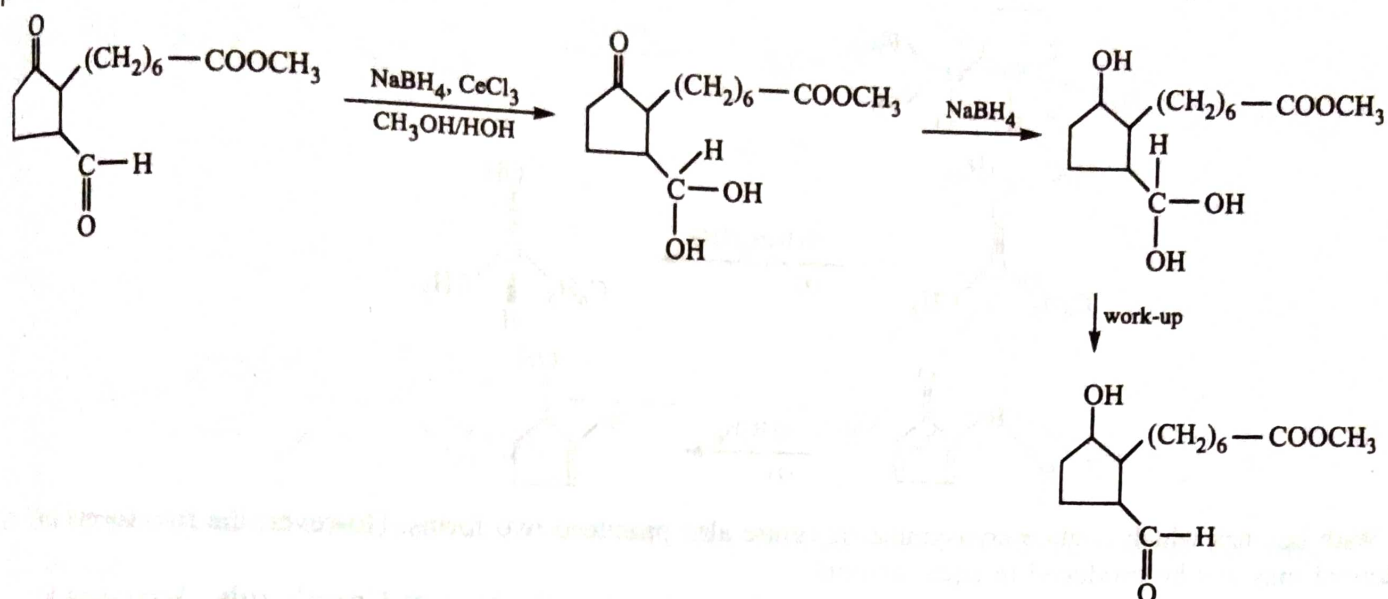
3.2 REDUCTION OF ALDEHYDES AND KETONES

3.2.1 Reduction by hydride-transfer reagents

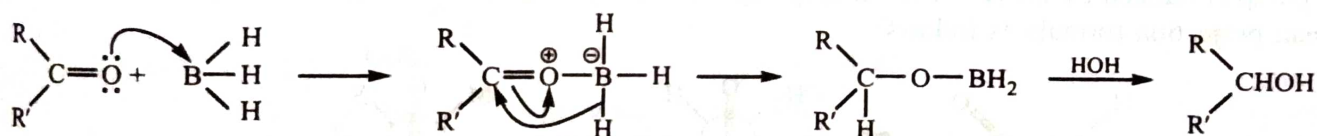
The reduction of aldehydes to primary alcohols and ketones to secondary alcohols is normally easy to accomplish using sodium borohydride or lithium aluminium hydride. Lithium aluminium hydride is a powerful reagent commonly used in ether solutions. Lithium aluminium hydride reduces a wide range of functional groups, including —COOH , COOR , —CN , —CONH_2 , epoxide, etc. This reagent can be inconvenient to use since contact with water or alcohol may cause fire.

In contrast, sodium borohydride is more specific for the reduction of aldehydes and ketones. It is milder

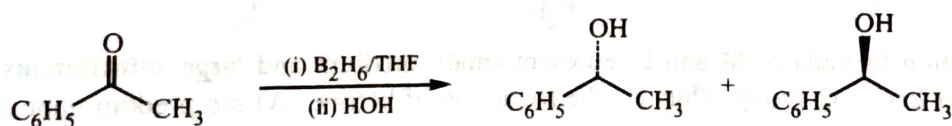
It is believed that, under the reaction conditions the more reactive aldehyde group is protected as the hydrate which is stabilised by complexation with the cerium ion and is regenerated during isolation of the product.



Aldehydes and ketones can also be reduced with borane. Reduction of carbonyl groups by borane takes place by addition of the electron deficient borane to the oxygen atom, followed by the irreversible transfer of hydride ion from boron to the carbon.



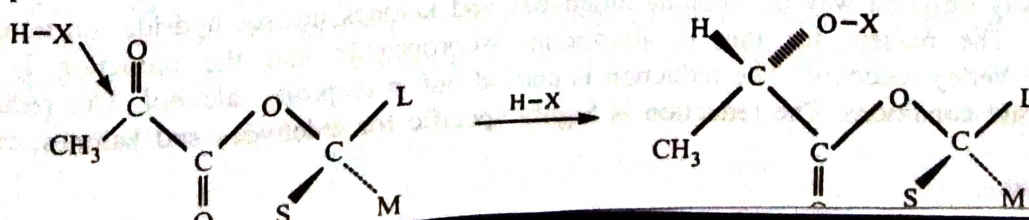
Under normal conditions, reduction of a prochiral ketone leads to racemic mixture of secondary alcohols.



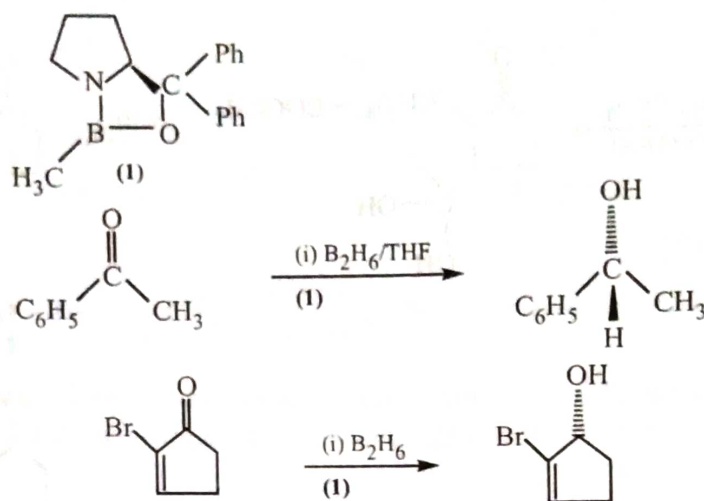
In case of prochiral ketones, the major enantiomeric form can be predicted by **Prelog's rule**. This rule relates to the course of asymmetric synthesis when a reducing agent is added to a ketonic group. According to this rule if the steric difference between large (L) and small (S) groups attached to the carbonyl group is large enough the reducing agent attacks from the less hindered face (over S) to give the corresponding alcohol as shown below:



This rule is mainly used in the case of α -ketoesters of a chiral alcohol. If the relative configuration of the ketoester is (I), the reducing agent will attack the ketonic carbon from the less hindered side, *i.e.*, from the side of the group S as shown below:

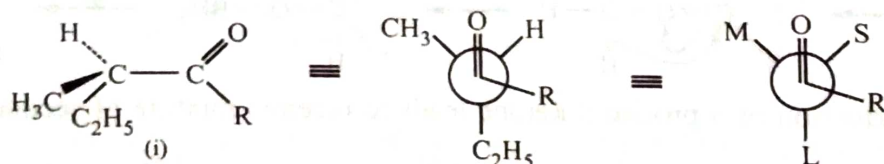


However, prochiral ketone produces only single enantiomers when reduction is carried out with B_2H_6 in the presence of chiral nonracemic ligand. The best ligand is oxazaborolidine complex (1). For example:

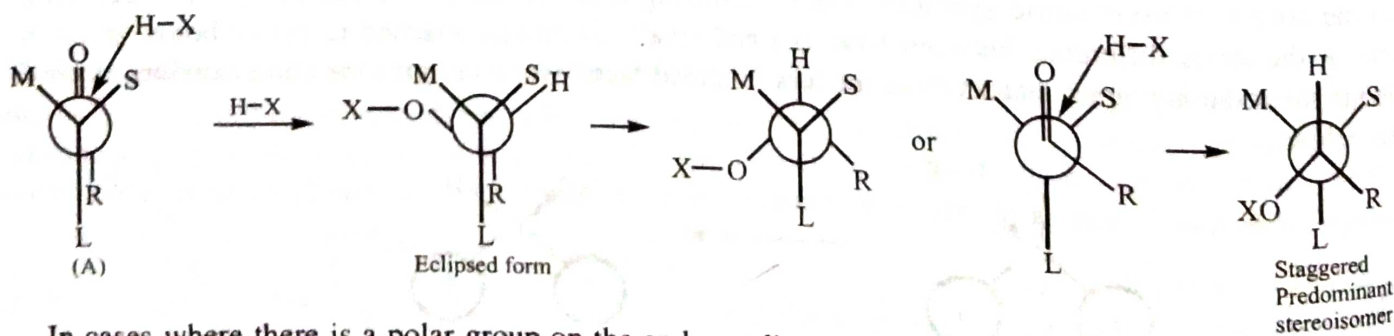


With ketones which contain an asymmetric centre also produced two forms. However, the two forms of the alcohol may not be produced in equal amount.

The main product formed in these reactions can be predicted on the basis of **Cram's rule**. According to Cram's rule that diastereomer predominates in the product which is formed by approach of the reagent to the less hindered side of the carbonyl group when the rotational conformation of the molecule is such that the carbonyl group is flanked by the two least bulky groups on the adjacent chiral centre. This may be represented by Newman projection formula as follows:

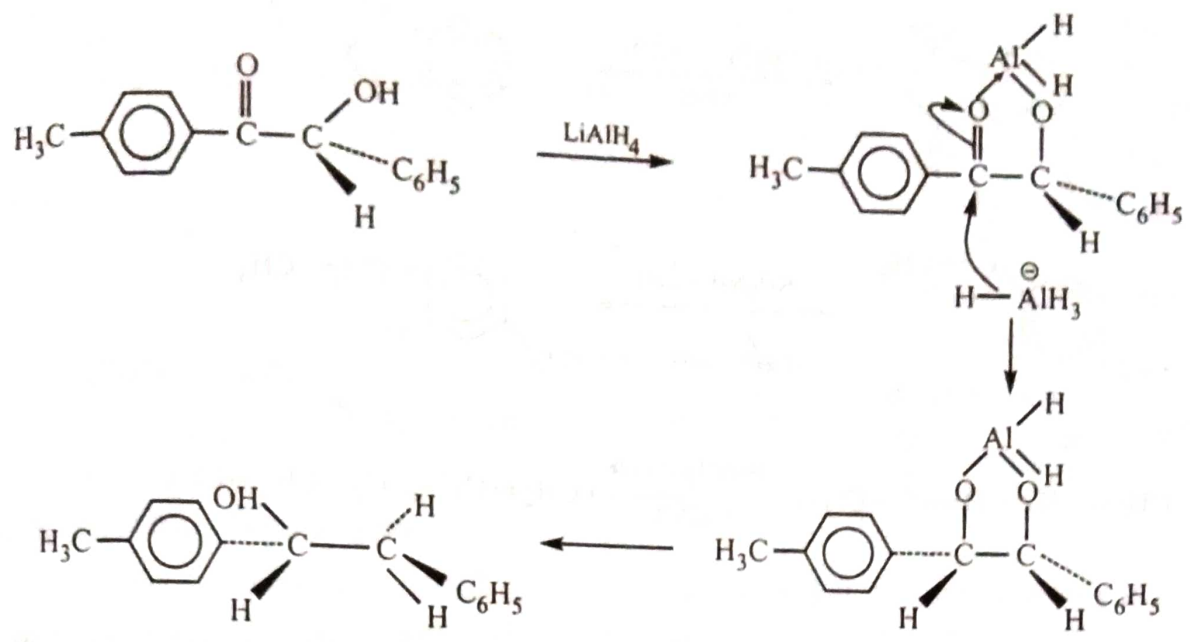


In Newman projection formula S , M and L represent small, medium and large substituents on adjacent chiral carbon with respect to $C=O$ group. Thus for the reduction of ketone (A) the predominant alcohol arises by the attack of the reducing agent (say metal hydride) on the less hindered side of the carbonyl group in the conformation shown below:

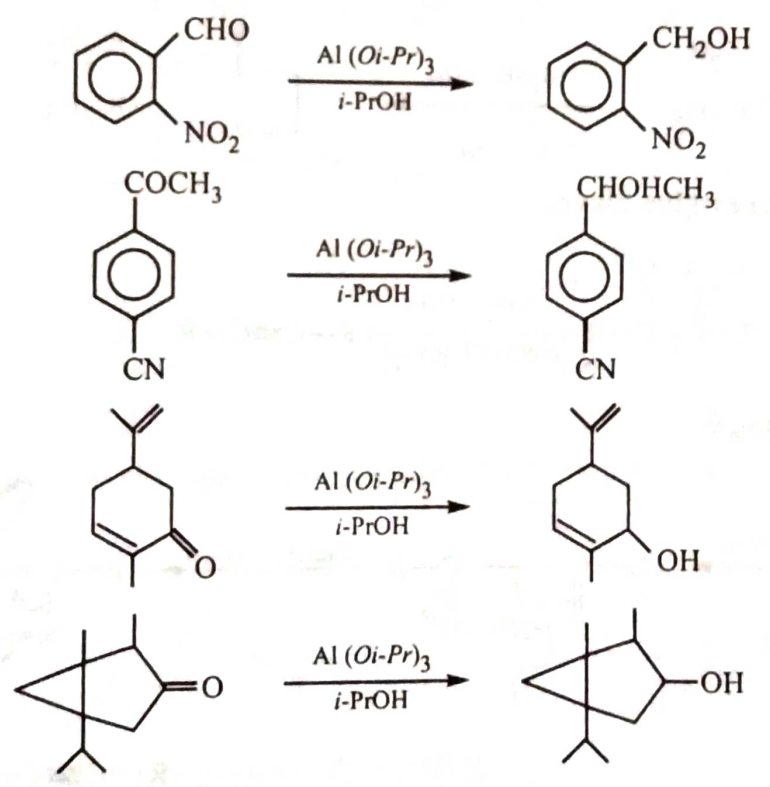


In cases where there is a polar group on the carbon adjacent to the carbonyl group Cram's rule may not be followed, because the conformation of the carbonyl compound in the transition state is no longer determined solely by steric factor. In α -hydroxy and α -amino ketones, reaction is thought to proceed through a relatively rigid chelate compound as shown on the next page.

A fundamentally different way of reducing aldehydes and ketones utilises hydride ion transfer from a secondary alcohol. The reagent for this is aluminium isopropoxide and the reduction is known as Meerwein-Ponndorf-Verley reduction. The reduction is carried out in isopropyl alcohol. This reduction takes place under very mild conditions. The reduction is highly specific for aldehydes and ketones; other groups



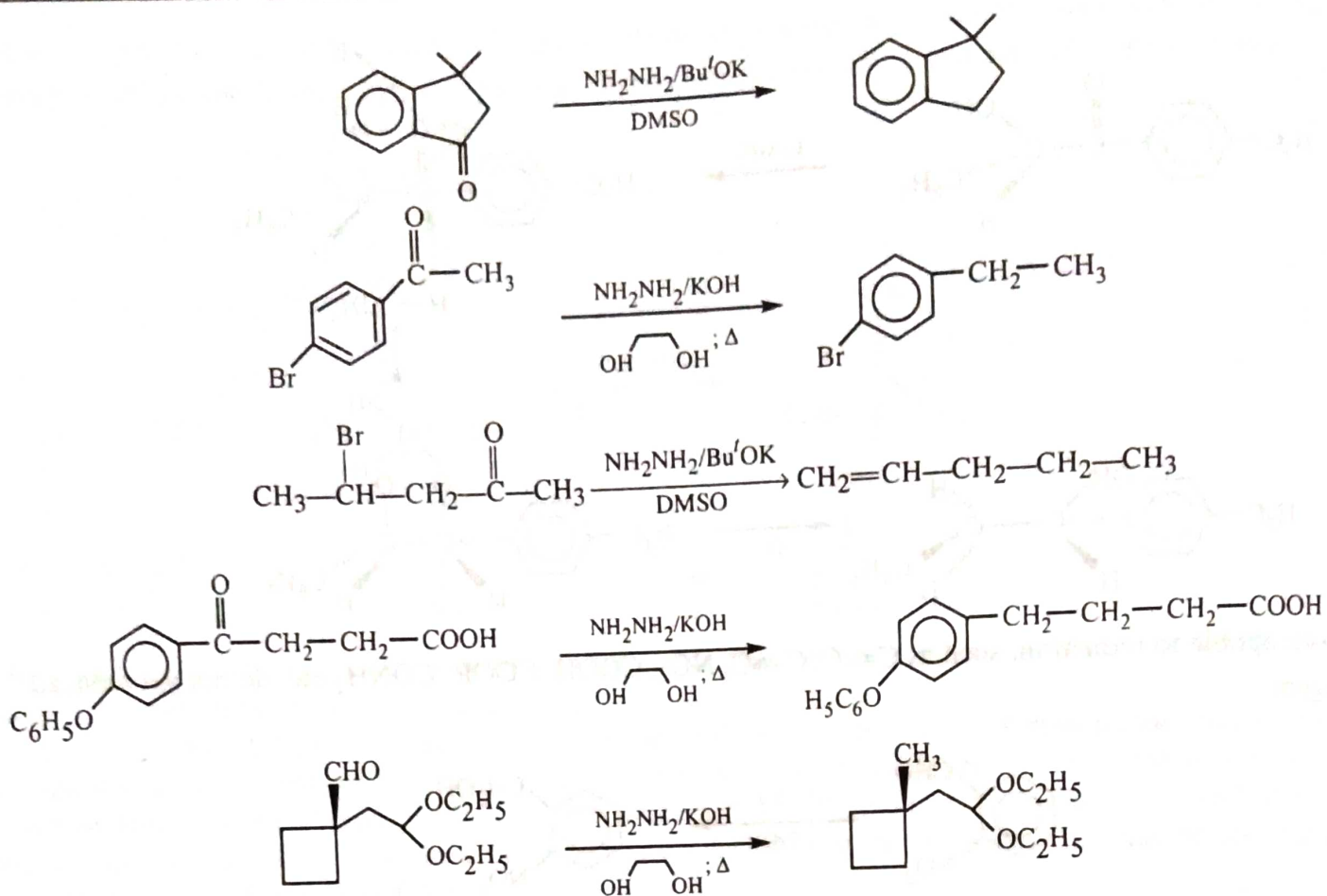
which are susceptible to reduction, such as C=C, C≡C, NO₂, COOH, COOR, CONH₂ etc. do not get reduced by this reagent.



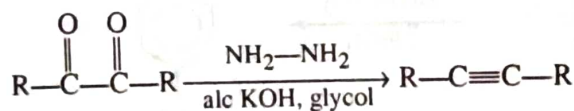
2.2 Reductive Cleavage of a carbon-oxygen double bond

CO group of aldehydes and ketones can be reduced to CH₂ group by Wolff-Kishner reduction, Clemmensen reduction or Mozingo reaction.

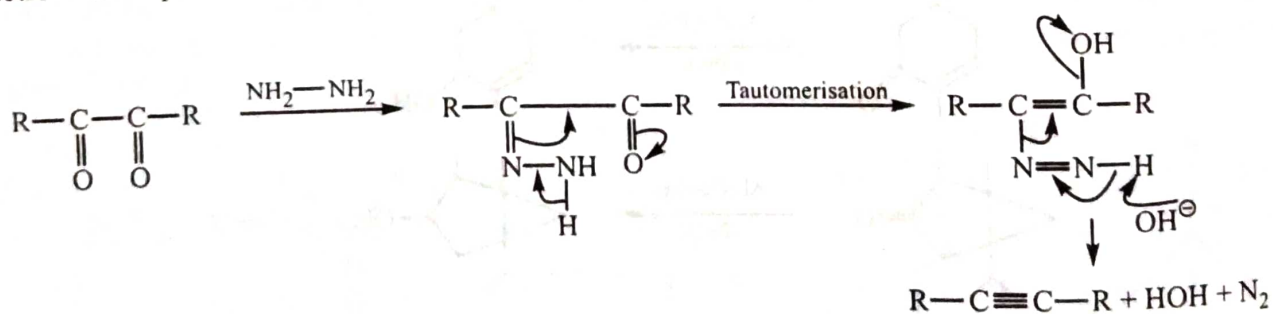
Wolff-Kishner reduction is effected by heating a mixture of the carbonyl compound, hydrazine hydrate and sodium or potassium hydroxide in a high boiling solvent (diethylene glycol) at 180-200°C for several hours. Excellent yields of the reduced product are obtained with potassium *t*-butoxide in DMSO, reduction can often be carried out at room temperature. This reduction cannot be used for those carbonyl compounds which have acid sensitive groups (such as halo group and tosyl group present in aliphatic systems).



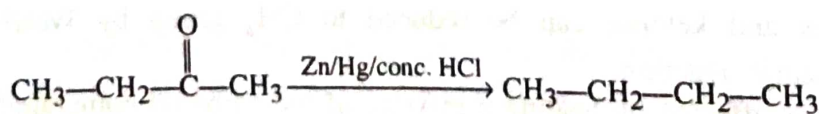
On the other hand, α -diketones give alkyenes.



Reaction takes place as follows:

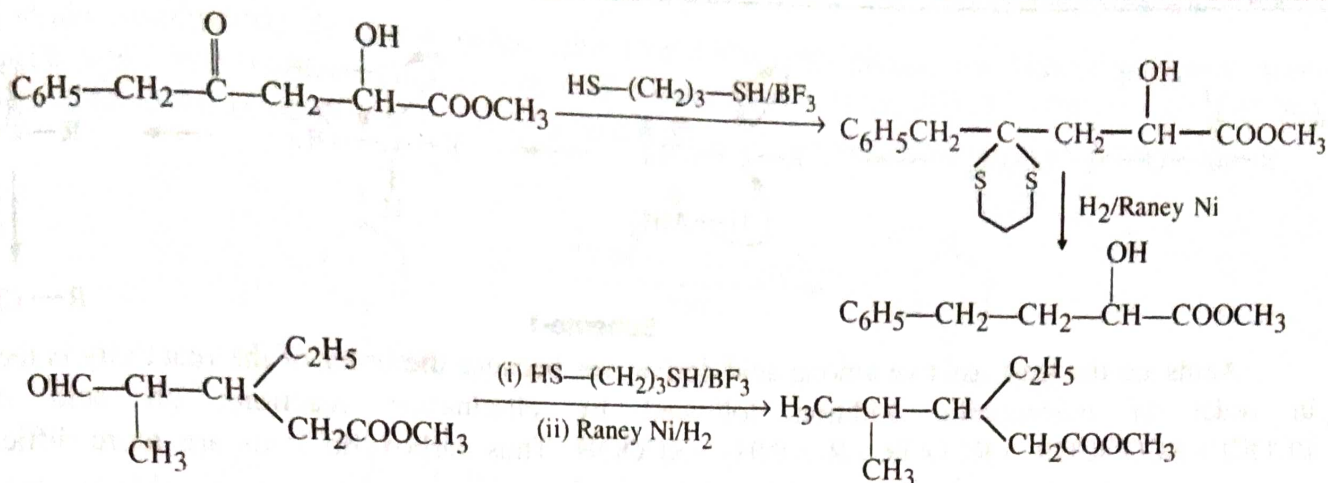


In Clemmensen reduction carbonyl compound is refluxed with Zn/Hg in the presence of conc. HCl.



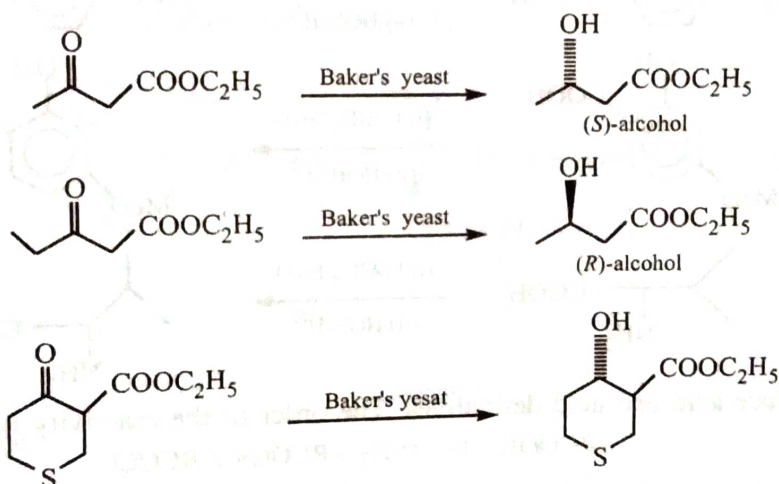
The conditions employed in this method are strongly acidic and may give rise to side reactions. This reduction is not applicable for acid sensitive compounds.

Conversion of a carbonyl group to a thioacetal, followed by hydrogenolysis is another way to convert CO into CH_2 group. This reduction takes place under neutral conditions. Hence CO group can be reduced to $-\text{CH}_2-$ by this method in all types of compounds (*i.e.*, acid sensitive as well as base sensitive).

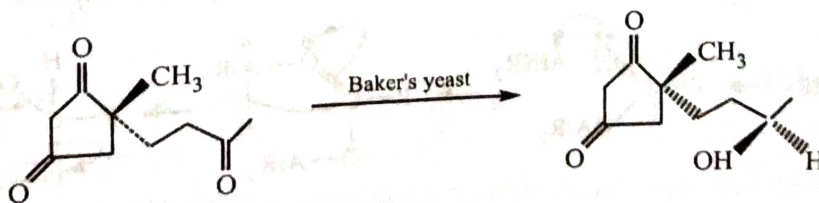


3.2.3 Enzymatic Reduction

The ketonic carbonyl group of β -keto esters and cyclic ketones are also very conveniently reduced with high stereoselectivity by fermenting Baker's yeast. Thus, reduction of ethyl acetoacetate with Baker's yeast gives the (*S*)-alcohol. On the other hand reduction of ethyl β -ketovalerate gives the (*R*)-alcohol.

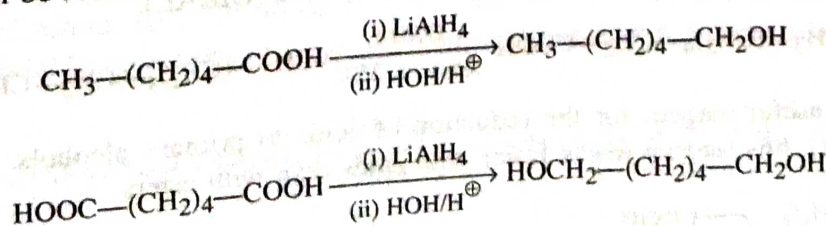


The ketonic moiety in the side chain of cyclopentanone could be selectively reduced to the (*R*) alcohol with Baker's yeast.

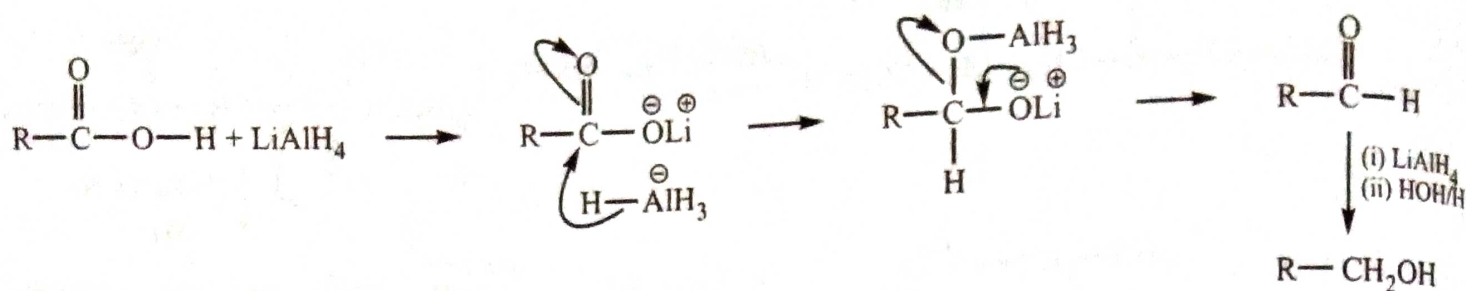


3.3 REDUCTION OF CARBOXYLIC ACIDS

Carboxylic acids can be reduced to primary alcohols with lithium aluminium hydride, alanes and boranes.

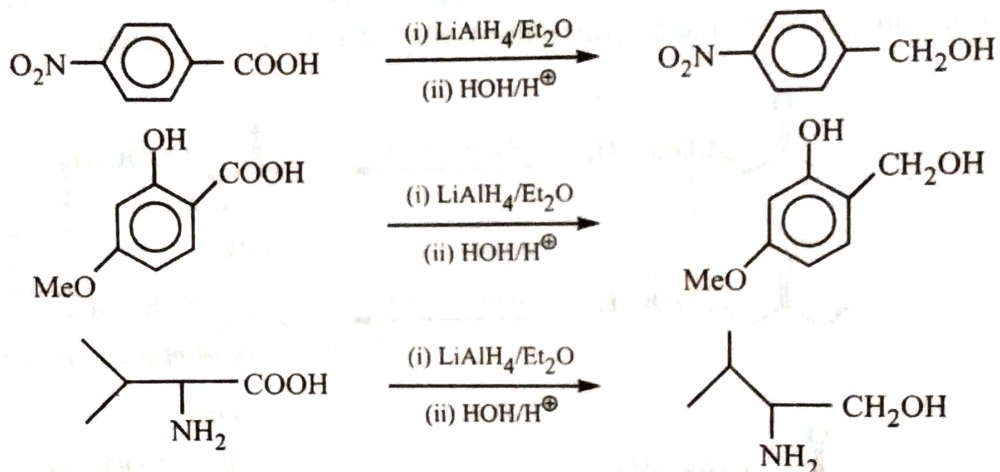


In this reduction acid first converts into aldehydes and then finally into primary alcohols (Scheme-1).



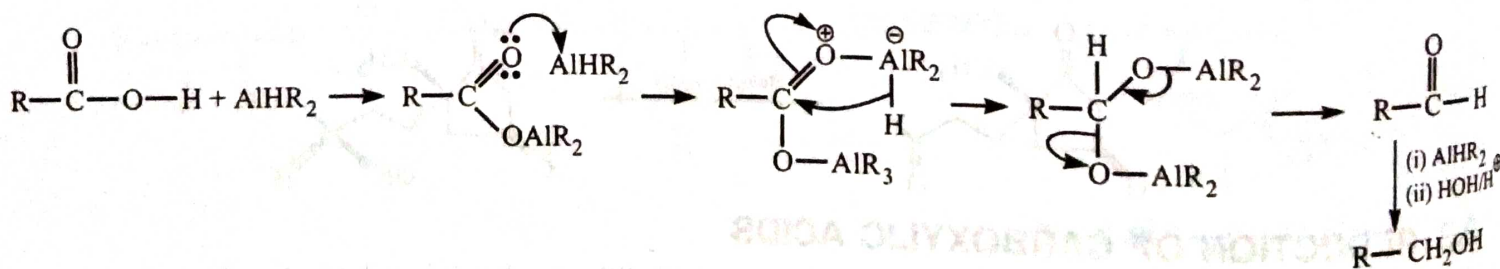
Scheme-1

Acids are the least reactive among acid derivatives because the order of the reactivity is the same as that in order of nucleophilic addition followed by elimination reactions on acid derivatives: $\text{RCOCl} > \text{RCOOCOR} > \text{RCOOR} > \text{RCONH}_2 > \text{RCOOH}$. Thus carboxylic acids are more difficult to reduce among acid derivatives. Thus lithium aluminium hydride can be used to reduce acids but this can require vigorous conditions and is also not selective because lithium aluminium hydride is very powerful reducing agent and reduce most of the commonly encountered organic functional groups such as carbonyl, ester, amide, acid chloride aliphatic nitro, cyanide and epoxide, etc.

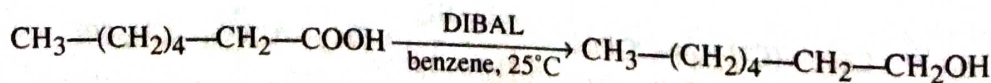


Alanes also reduce acid and acid derivatives. The order of the reactivity is almost the exact opposite: $\text{RCOOH} > \text{RCONH}_2 > \text{RCOOR} > \text{RCOCl}$

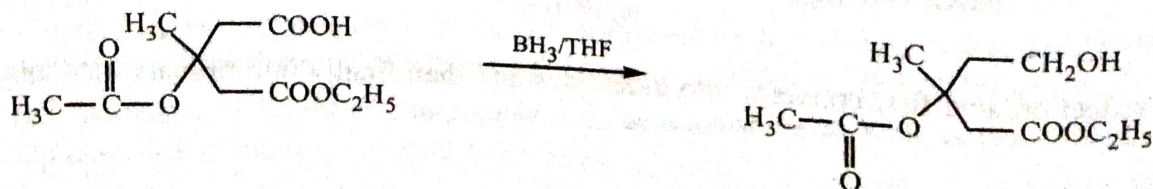
This is because the crucial step is the formation of a complex in which the alane acts as an electrophile so that it is the capacity for donation of an electron-pair by an organic compound that is important:



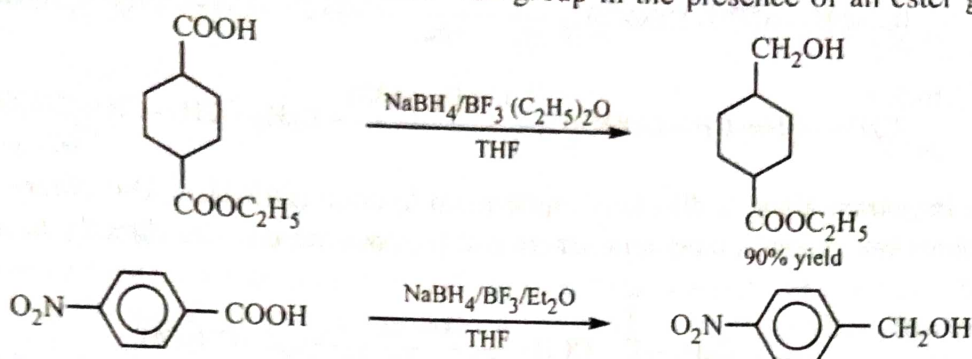
The most important alane is disobutyl aluminium hydride (DIBAL).



Diborane is a useful reagent for the reduction of acids to primary alcohols. However, unlike hydride donor such as LiAlH_4 , this reagent reacts faster with acids than with esters.



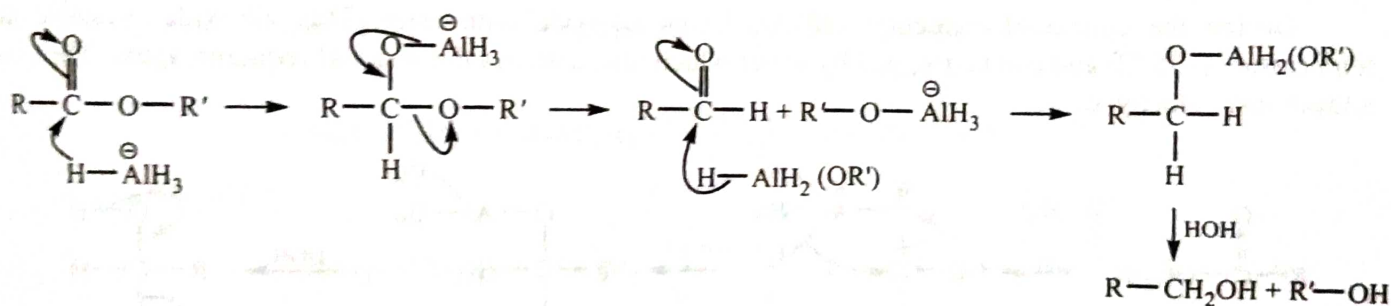
Sodium borohydride does not reduce the free carboxylic group, but borane prepared from sodium borohydride and boron trifluoride etherate in THF converts acids to alcohols at 0-25°C in 89-90% yields. This reagent is suitable for selective reduction of a free acid group in the presence of an ester group.



3.4 REDUCTION OF ESTERS

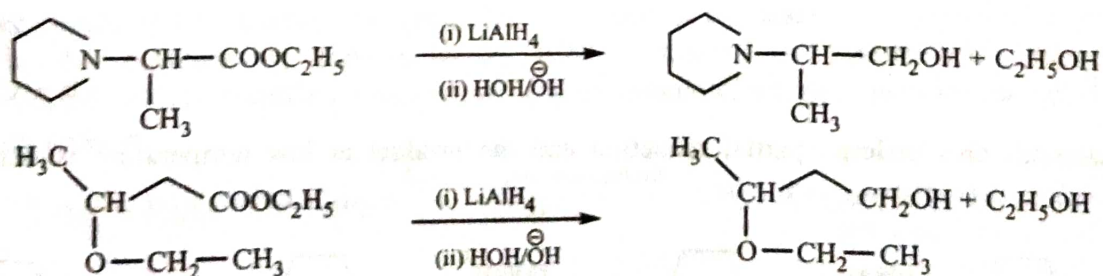
The reduction of esters to primary alcohols is best accomplished by powerful reducing agents such as LiAlH_4 , diisobutyl aluminium hydride and LiBH_4 .

The reduction of ester requires 0.5 mole of lithium aluminium hydride and probably involves formation and reduction of the corresponding aldehyde (Scheme-1).



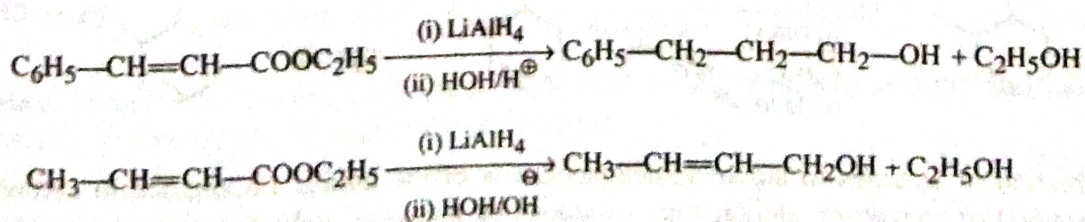
Scheme-1

Some examples are:



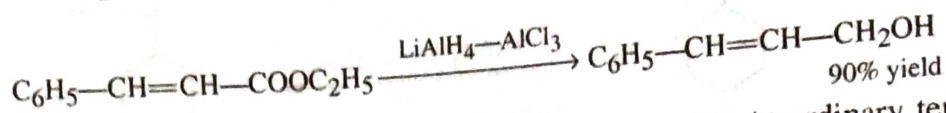
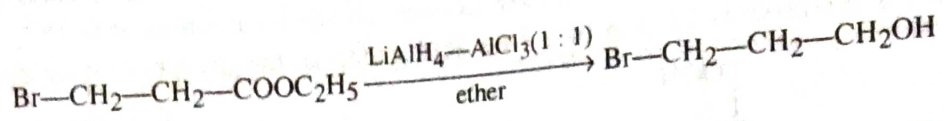
The reduction of ester with lithium aluminium hydride is not selective because it is very powerful reducing agent and reduces most of the commonly encountered organic functional groups such as carbonyl, cyano aliphatic nitro, epoxide and halide, etc.

α , β -unsaturated esters, specially those in which the double bond is also conjugated with an aromatic ring, are more comfortably converted to saturated alcohol on treatment with an excess of lithium aluminium hydride.

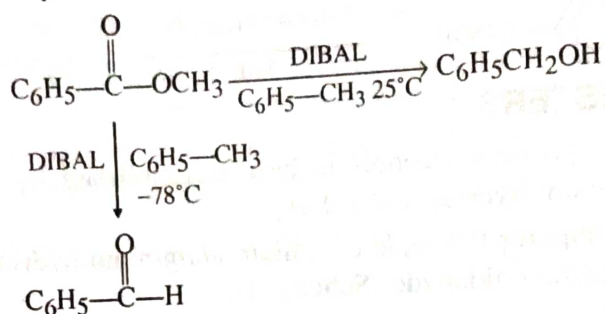


Alanes also reduce esters. Alane, formed *in situ* from lithium aluminium hydride and aluminium chloride,

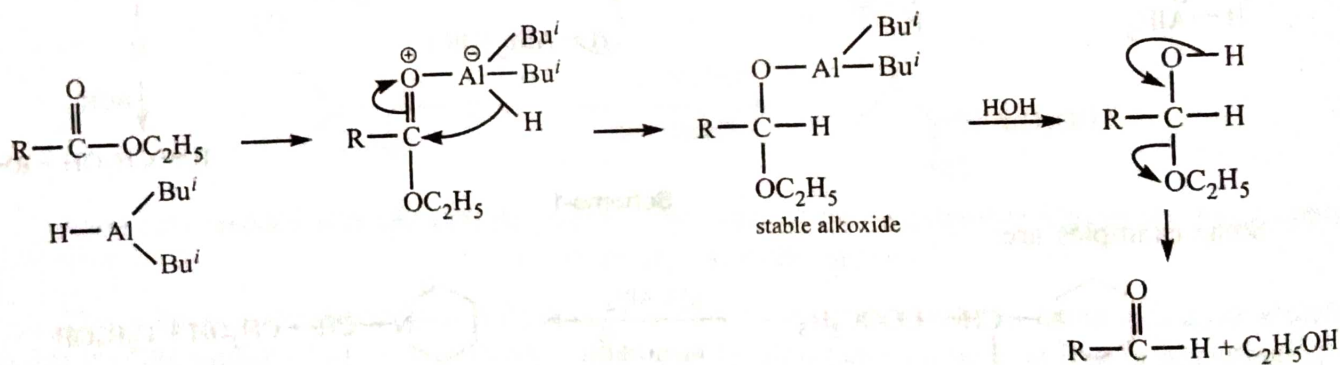
reduces esters in THF. Because it does not reduce some other functional groups it is well suited for selective reduction.



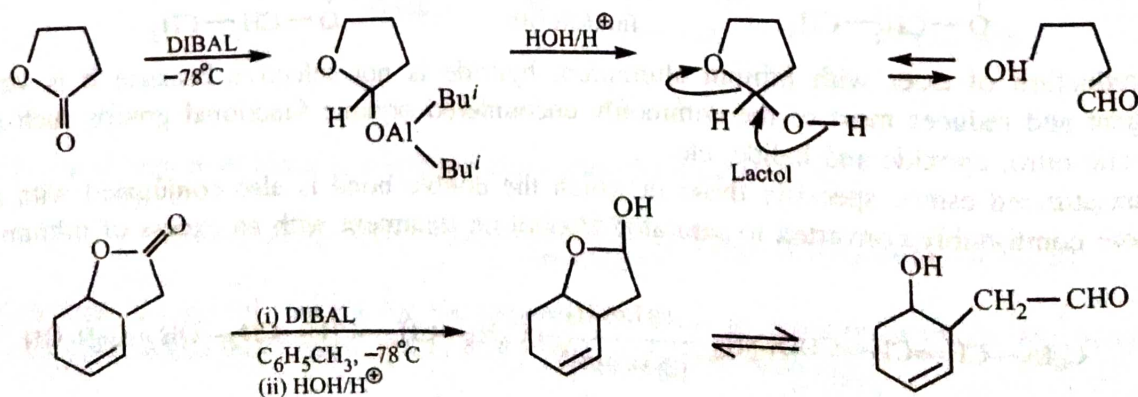
The most important alane is diisobutyl aluminium hydride (DIBAL). At ordinary temperature esters are reduced to alcohols but at low temperature esters and lactones are reduced directly to aldehydes.



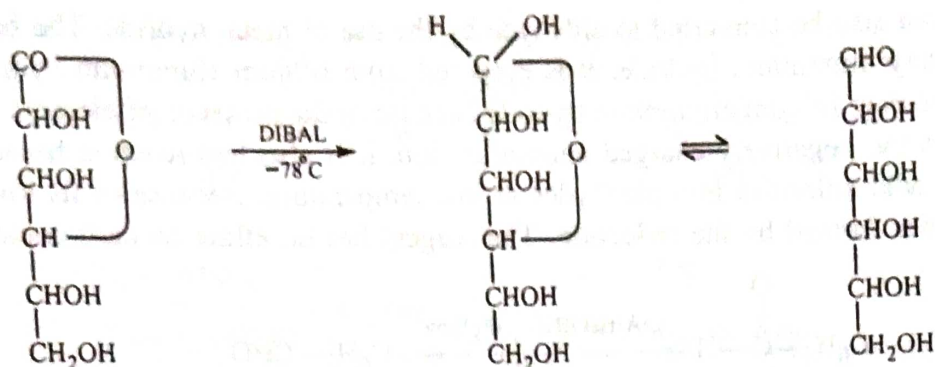
During the course of reduction DIBAL forms alkoxide with ester. This alkoxide is stable at low temperature (-78°C) and can be trapped by water which also destroys the residual reducing agent. The resulting adduct form aldehyde.



Lactones also undergo partial reduction and the product at low temperature is hemiacetal known as lactols.

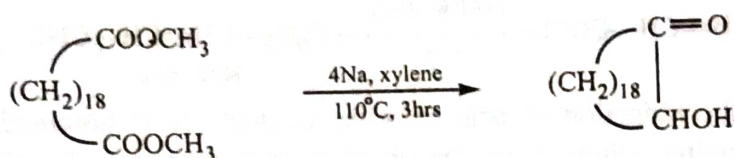


Reduction of lactones to aldehyde-hemiacetals is of the utmost importance in carbohydrate chemistry. The old method of converting aldolactones to aldose by means of sodium amalgam gives very poor yield but this reagent gives very good yield.

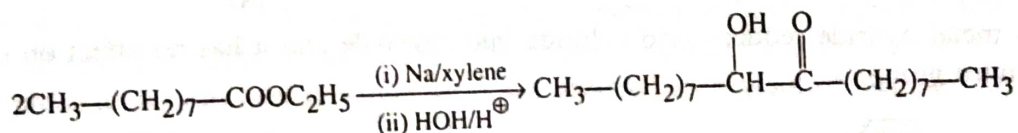
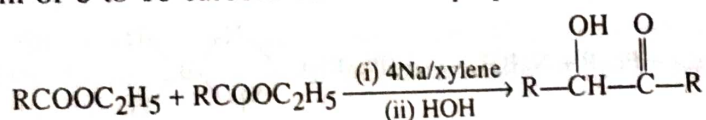


Esters can also be reduced by the use of **acyloin method** and **Bouveault Blanc** method.

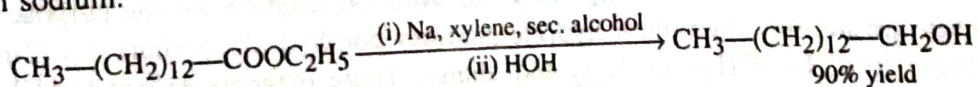
In acyloin method esters are treated with sodium in aprotic solvents. The initially formed radical anion dimerises and ultimately forms an α -hydroxy ketone, an acyloin. Such acyloin condensation of esters is especially useful with esters of α, ω -dicarboxylic acids of at least six carbons in the chain for cyclic acyloin are formed in very good yields.



Open chain acyloin of 8 to 18 carbons can also be prepared by this method.



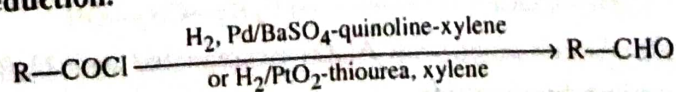
Bouveault-Blanc method is one of the oldest methods of reduction. In this method reduction is carried out by adding sodium into a solution of an ester in ethanol. This method does not give very high yields, possibly because of side reactions like Claisen condensation. The yield of the reaction is improved when reaction is carried out in the presence of inert solvents such as toluene or xylene and secondary alcohol (4-methyl-2-pentanol) which is acidic enough to decompose sodium containing intermediate but does not react too rapidly with sodium.



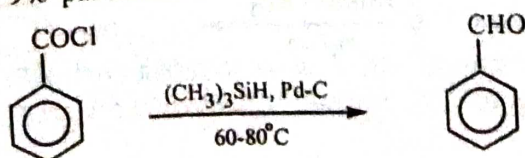
3.5 REDUCTION OF ACID CHLORIDES

Reduction of acid chloride is exceptionally easy. Depending on the reagents and reaction conditions it can lead to aldehydes or to alcohols.

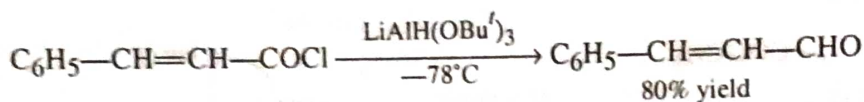
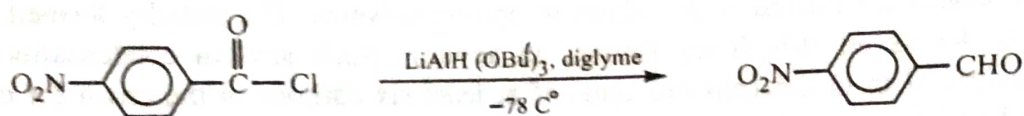
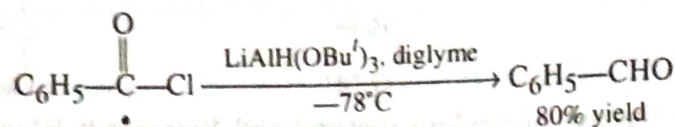
Catalytic hydrogenation of acid chloride is carried out in the presence of poisoned catalyst. The reaction is known as **Rosenmund reduction**.



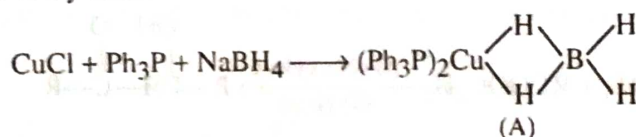
A variation of the Rosenmund reduction is heating of an acyl chloride at 50°C with an equivalent of trimethylsilane in the presence of 9% palladium on charcoal.



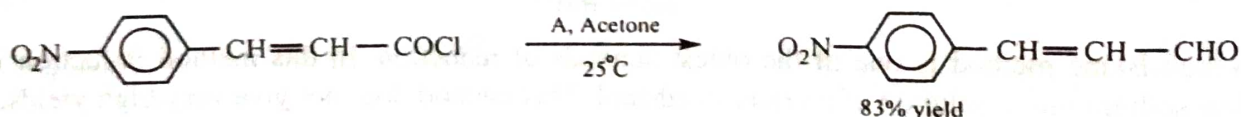
Acid chloride can also be converted to aldehyde by the use of metal hydride. The best result is obtained with lithium tri-*t*-butoxy aluminium hydride. It is prepared from lithium aluminium hydride and *t*-butanol in ether. It is less reactive than lithium aluminium hydride because of the presence of electron withdrawing alkoxy group which stabilises the negatively charged aluminium ion. It is also less reactive because of its bulkiness. The reagent converts acid chlorides into aldehydes at low temperature. Because of its low reactivity, it does not react with aldehydes formed by the reduction. The reagent has no effect on carbon-carbon double bonds.



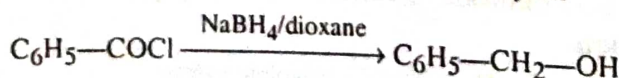
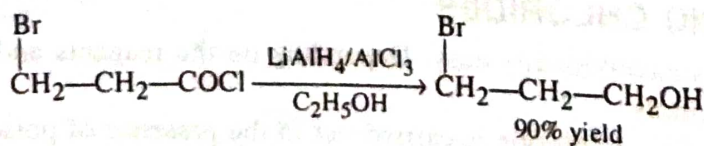
Another hydride for the reduction of acid chloride to aldehyde is obtained by treating a mixture of cuprous chloride and triphenylphosphine, trimethyl phosphite or triisopropyl phosphite in chloroform with an ethanolic solution of sodium borohydride



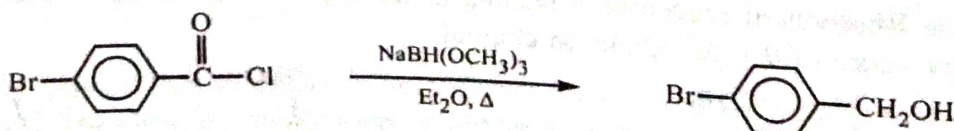
This metal hydride reduces acid chloride into aldehyde and it has no effect on carbon-carbon multiple bond and nitro group.

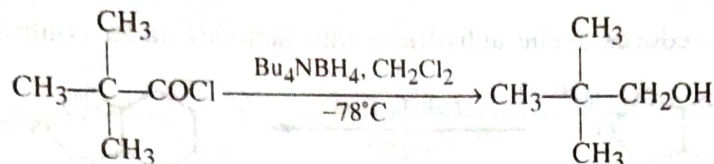
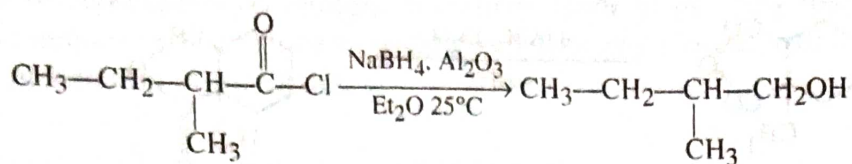


Complete reduction of acid chlorides to primary alcohols is not as important as the reduction to aldehydes since alcohols are readily obtained by reduction of more common compounds such as aldehydes, carboxylic acids or their esters. Because aldehydes are the primary reduction products of acid chlorides strong reducing agents convert acid chlorides directly to alcohols. The most common reagents for the purpose are hydrides or complex hydrides. They are lithium aluminium hydride, sodium borohydride, sodium bis (2-methoxyethoxy) aluminium hydride $\text{NaAlH}(\text{OCH}_2\text{CH}_2\text{OCH}_3)_2$ and alanes. These reagents except LiAlH_4 are especially suitable for reduction of halogenated acid chlorides



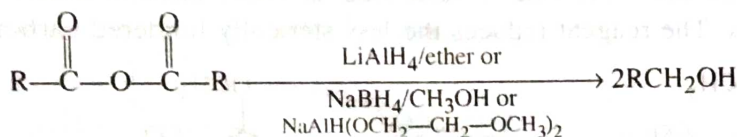
High yields of alcohols are also obtained with Al_2O_3 impregnated with NaBH_4 , sodium trimethoxyborohydride or with tetrabutyl aluminium borohydride.





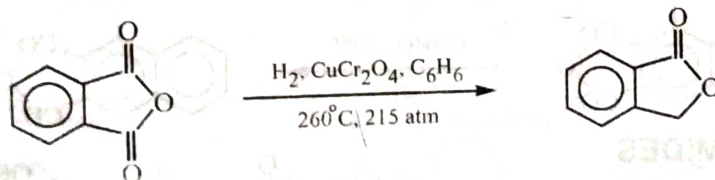
3.6 REDUCTION OF ANHYDRIDES

Reductions of anhydrides of monocarboxylic acids to alcohols are very rare but can be accomplished by complex hydrides.

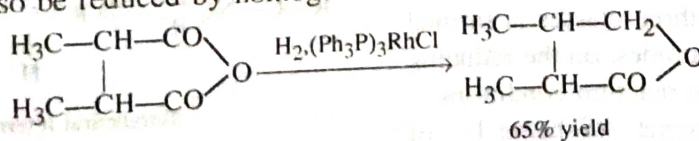


More frequent are the reduction of cyclic anhydrides of dicarboxylic acids. Cyclic anhydrides can be reduced to lactones or diols. Nature of reduction product depends on the nature of reducing agents and reaction conditions.

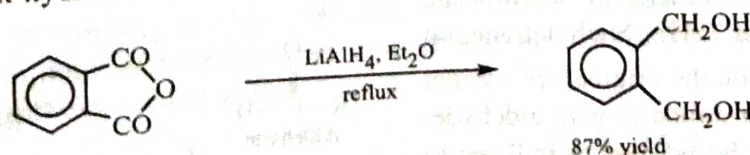
The important reduction reaction of cyclic anhydrides are the reduction of these compounds into lactones. Such reductions are carried out by catalytic hydrogenation, by complex hydrides and by metals. Hydrogenation of phthalic anhydride over copper chromite afforded 82% yield of lactone.



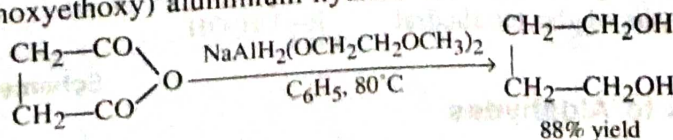
Anhydrides can also be reduced by homogeneous reduction using Wilkinson catalyst.



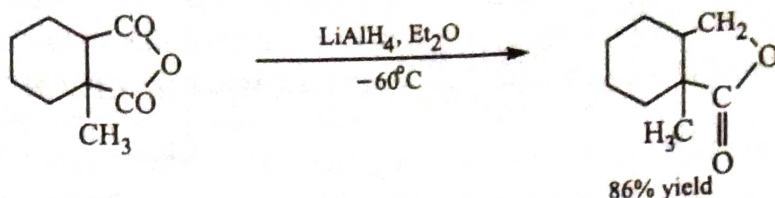
Powerful complex hydrides like lithium aluminium hydride reduces cyclic anhydrides to diols.



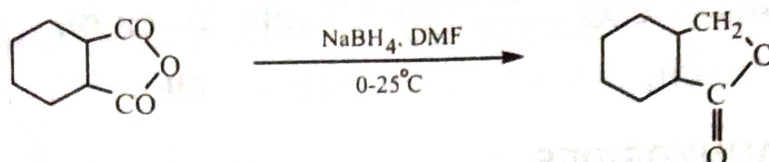
Sodium bis (2-methoxyethoxy) aluminium hydride also reduces cyclic anhydrides to diols.



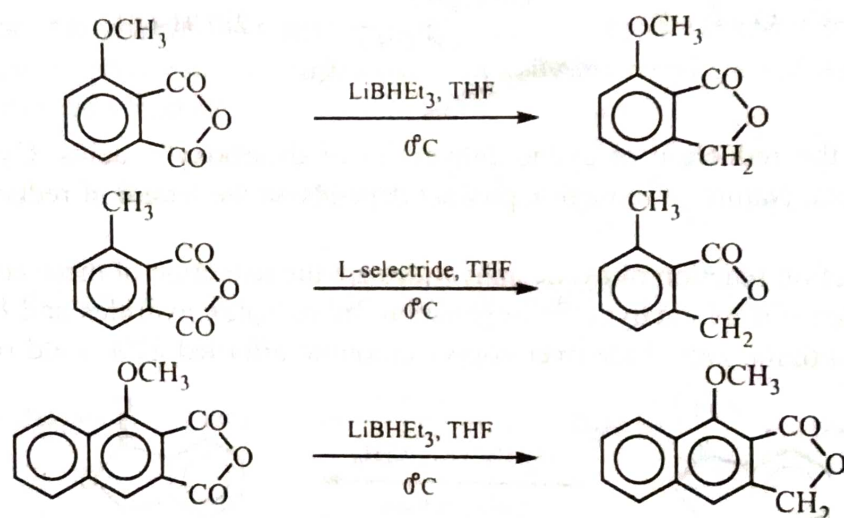
Under controlled conditions, especially avoiding an excess of lithium aluminium hydride and performing the reaction at -60°C , cyclic anhydrides are converted to lactones in high yields.



Sodium borohydride also reduces cyclic anhydrides into lactones under controlled conditions.



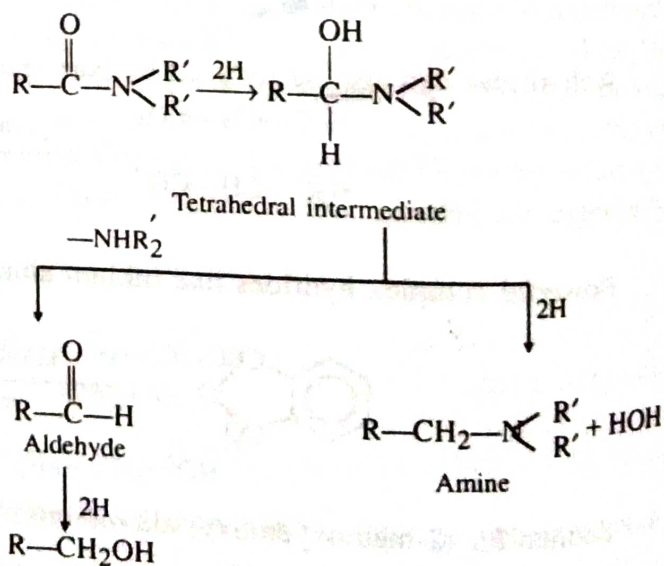
Other reagents used for the preparation of lactones from acid anhydrides are lithium borohydride, lithium triethyl borohydride (known as super hydride) and lithium *tris* (sec-butyl) borohydride (known as L-selectride). Of these three complex borohydrides, the one L-selectride is most stereoselective in the reduction of 3-substituted phthalic anhydrides. The reagent reduces the less sterically hindered carbonyl group.



3.7 REDUCTION OF AMIDES

Reduction of amides may yield aldehydes, alcohols or amines. Which of these three classes is formed depends on the structure of the amides, on the reducing agent, and to a certain extent on reaction conditions.

From a simplified scheme (Scheme-1) of reduction of the amide function it can be seen that the first stage is the formation of tetrahedral intermediate by the addition of hydrogen (2H). Such tetrahedral intermediate tends to regenerate the original sp^2 system by elimination of ammonia or amine to give aldehyde. The aldehyde so formed may be isolated or reduced to an alcohol. Alternatively the product is an amine resulting from direct hydrogenolysis of the tetrahedral intermediate.

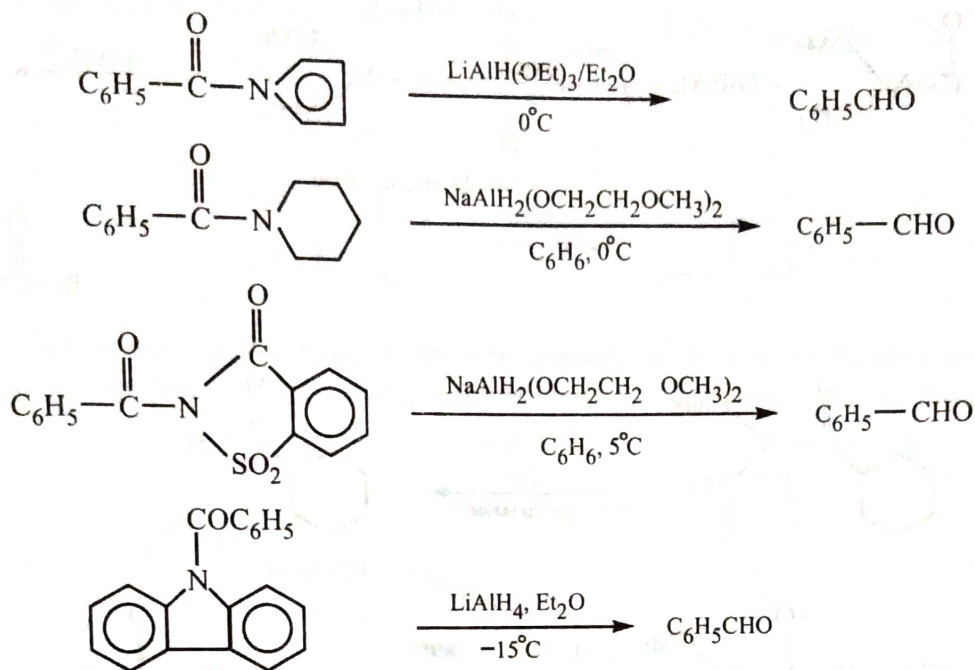


Scheme-1

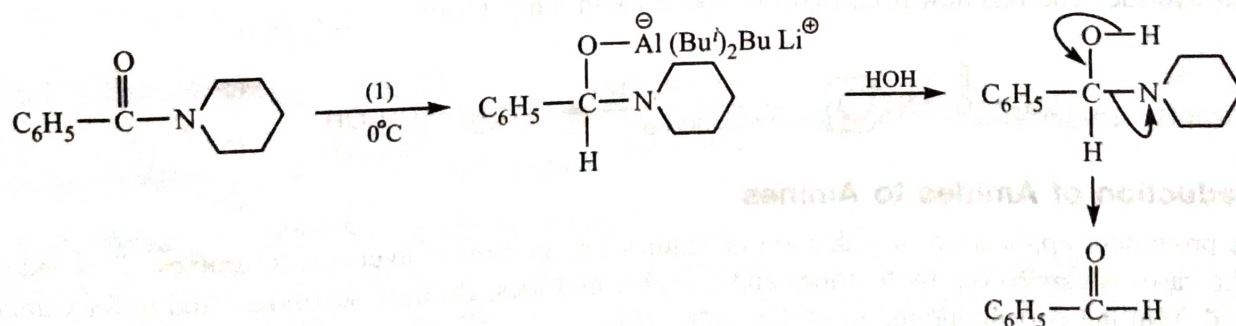
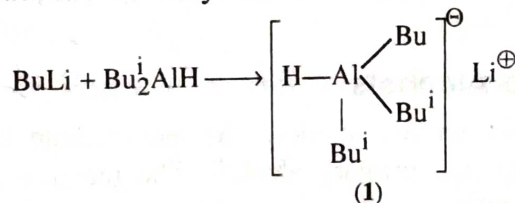
3.7.1 Reduction of Amides to Aldehydes

Tertiary amides on reduction with lithium aluminium hydride, lithium triethoxy aluminium hydride and sodium *bis* (2-methoxyethoxy) aluminium hydride give aldehydes. Primary and secondary amides do not give

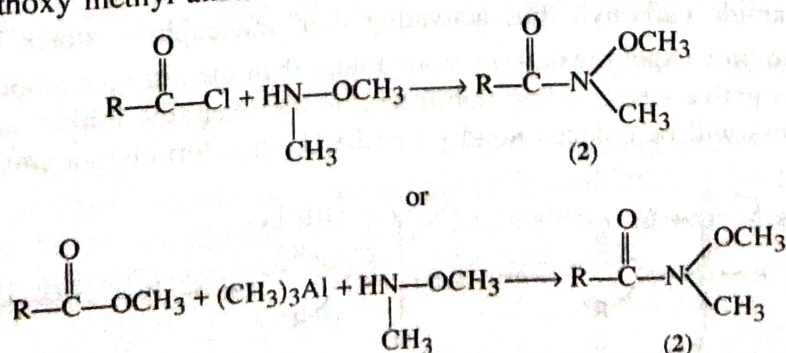
aldehydes. The nature of substituents on nitrogen of tertiary amide plays a key role in this reduction. Amide derived from aromatic amines such as N-methylaniline and specially pyrrole, indole and carbazole are found most suitable for the preparation of aldehydes.



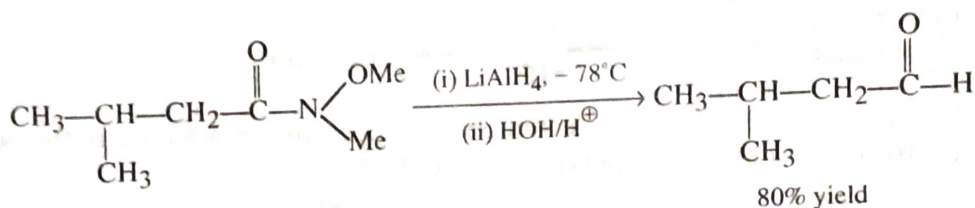
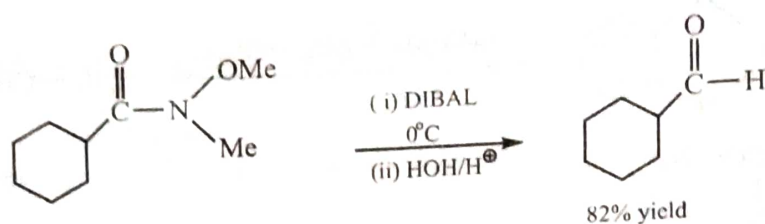
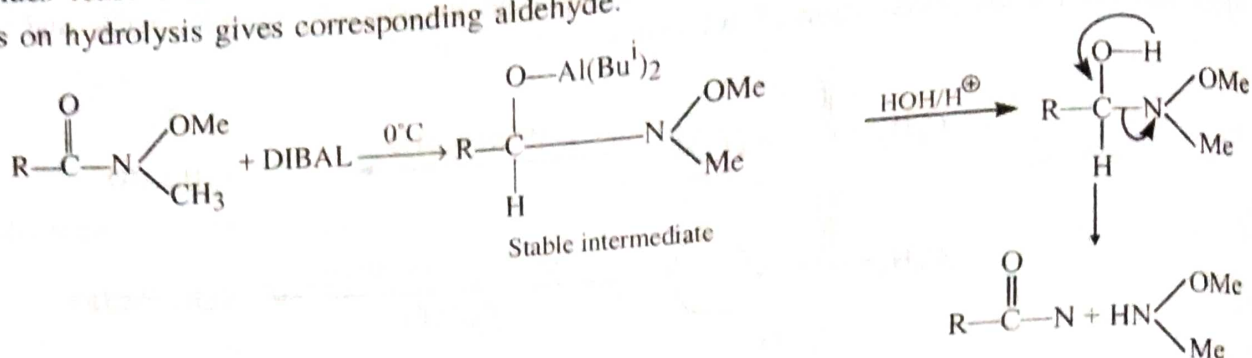
Perhaps the best reagent available for the reduction of amides into aldehydes is the ATE complex (1). This complex is derived from the addition of butyl lithium to DIBAL.



One good way of reducing amides selectively involves the formation of Weinreb amide (2). This amide may be prepared from the corresponding acid chloride and methoxy methyl amine or by reaction of an ester with $(\text{CH}_3)_3\text{Al}$ and methoxy methyl amine.

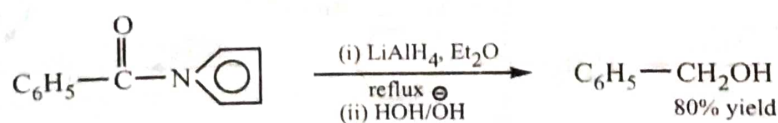


Weinreb amides react with either LiAlH_4 or DIBAL at low temperature and form stable, chelated intermediates. This on hydrolysis gives corresponding aldehyde.



3.7.2 Reduction of Amides to Alcohols

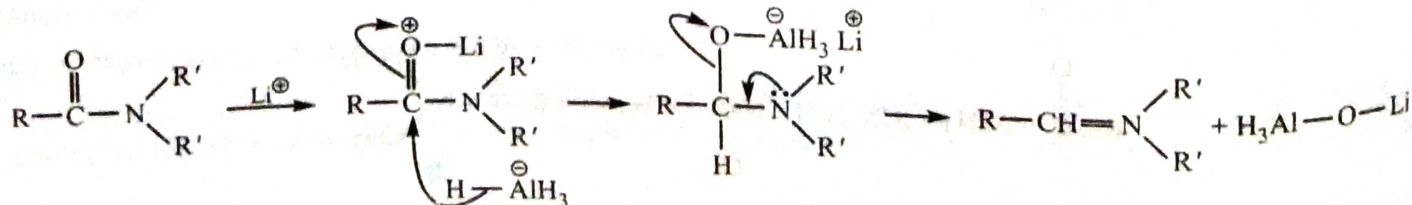
This reduction is given only by tertiary amides. The intermediate product of the reaction is aldehyde which on further reduction converts into primary alcohol. The reaction is not very important and is only exceptionally used for preparative purposes. Tertiary amides are reduced to alcohols generally by lithium aluminium hydride. The reaction is carried out above room temperature.



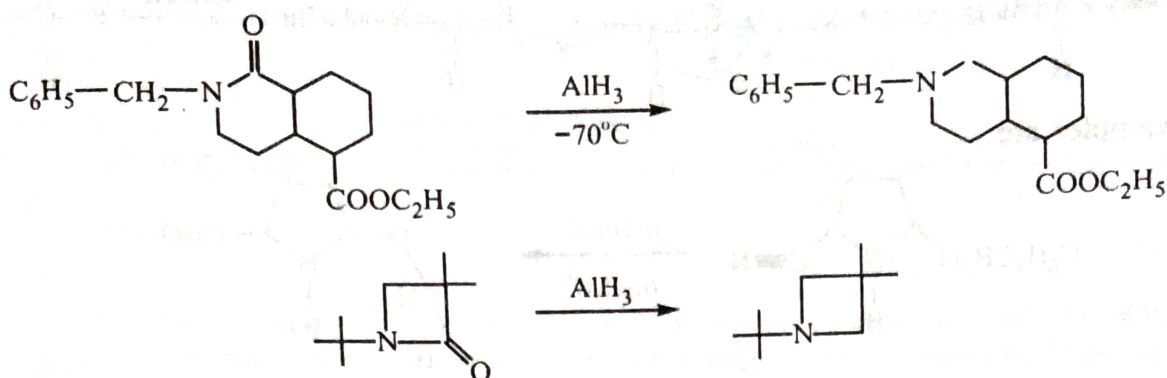
3.7.3 Reduction of Amides to Amines

The prominent application of reduction of amides lies in their conversion to amines. This reduction in most of the cases is carried out by hydrides and complex hydrides. Primary secondary and tertiary amines can be prepared from the corresponding amides in high yields.

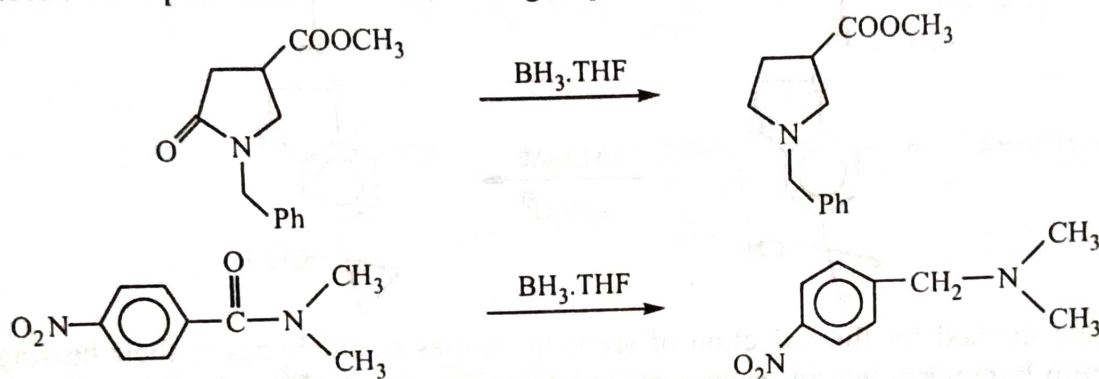
The reduction of amides with LiAlH_4 does not follow the same pattern as that observed for esters and acids. In this reduction LiAlH_4 deoxygenated amides. The mechanism of this reduction involves coordination of lithium cation to the amide carbonyl, thus activating it to nucleophilic attack by AlH_4^- . The resulting tetrahedral intermediate can now expel the oxygen atom, rather than the nitrogen atom which is a poor leaving group, with the incipient negative charge being stabilised by the oxophilic lithium and Al. The iminium ion that results from this process will be reduced rapidly by LiAlH_4 thus forming an amine (Scheme-2).



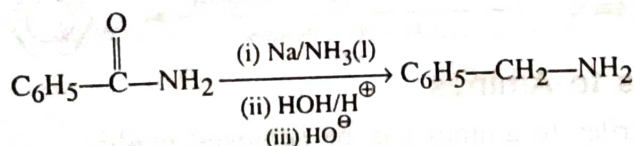
Alane is also a useful reagent which reduces amides into amines in the presence of ester groups.



Borane is also a very good reagent for deoxygenating amides to furnish amines. This reagent is selective because in the presence of amide, ester group does not undergo reduction.



Sodium and sodium amalgam may also be used for the reduction of amides to amines.

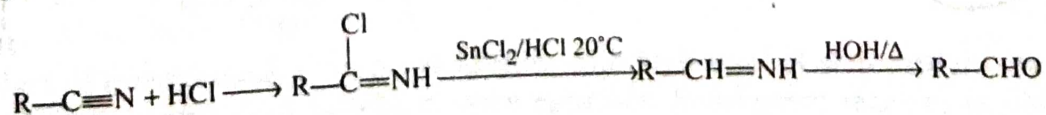


3.8 REDUCTION OF NITRILES

Nitriles are important source of amines which are produced by many reducing agents. However, a few reagents effect partial reduction to aldehydes.

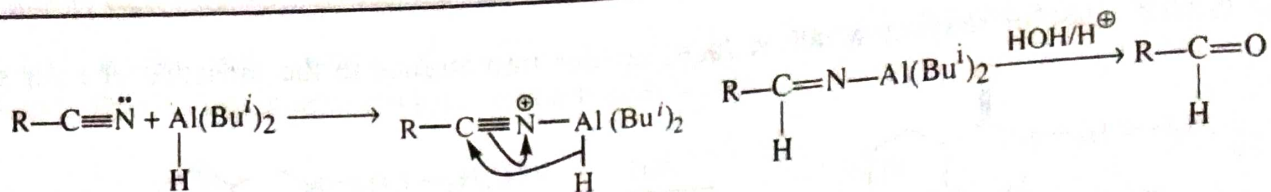
3.8.1 Reduction of nitriles to aldehydes

The most classical method for the reduction of nitriles to aldehydes is **Stephen reduction** which consists of treatment of a nitrile with anhydrous stannous chloride and gaseous hydrogen chloride in ether or diethylene glycol. This leads to the formation of imine which, on hydrolysis, gives aldehyde.

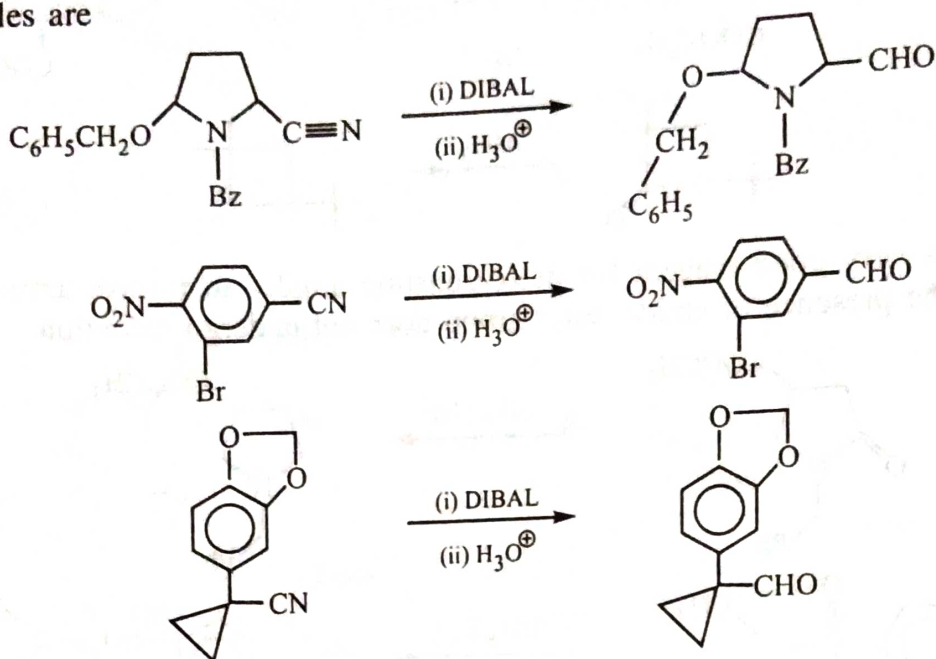


An advantage of the Stephen method is its applicability to polyfunctional compounds containing reducible groups such as carbonyl, nitro carbonyl, nitro carboxylic, ester amide, etc.

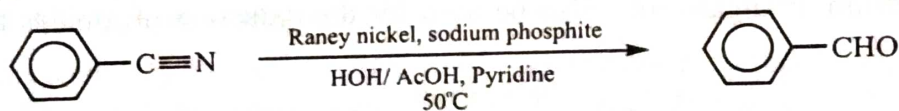
Nitriles can also be reduced to aldehydes by hydride reducing agents. The reagent used for this purpose are DIBAL, sodium triethoxy aluminium hydride and lithium triethoxy aluminium hydride. Among these reagents the most common one is DIBAL. Nitriles on reduction at low temperature give aldimines which are readily converted into aldehydes by hydrolysis.



Some examples are

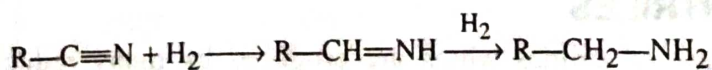


An alternate method for the reduction of aromatic nitriles to aldehydes is their heating with Raney nickel and sodium hypophosphite in water-acetic acid-pyridine (1 : 1 : 2) at 50°C.

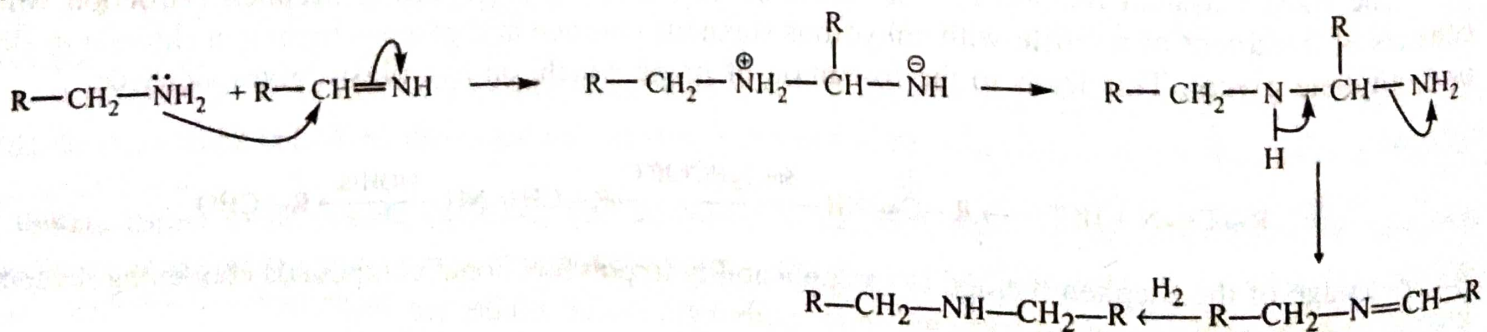


3.8.2 Reduction of Nitriles to Amines

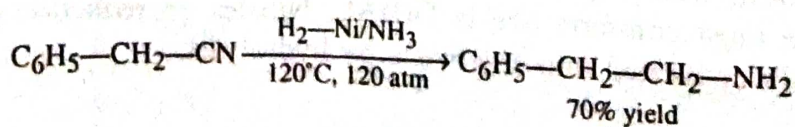
Complete reduction of nitriles to amines can be achieved readily with a powerful reducing agent. Catalytic hydrogenation converts nitriles to amines in good to excellent yields.

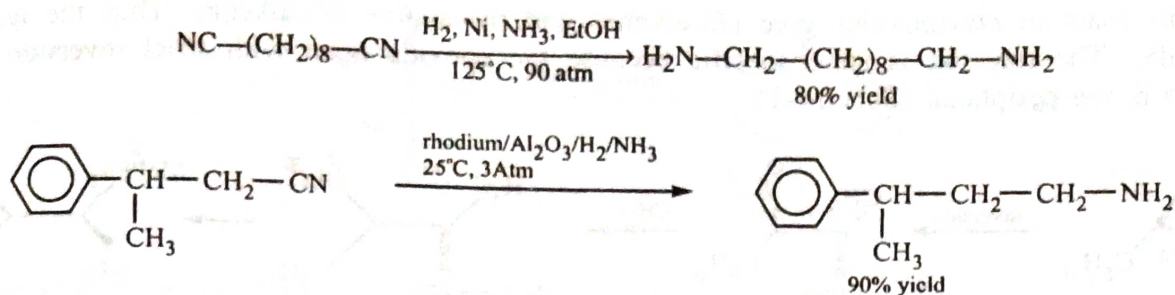


When reduction is carried out in the presence of ammonia, the product is always primary amine. In the absence of added ammonia considerable quantity of secondary amines are formed since the primary amine can add to the imino intermediate.

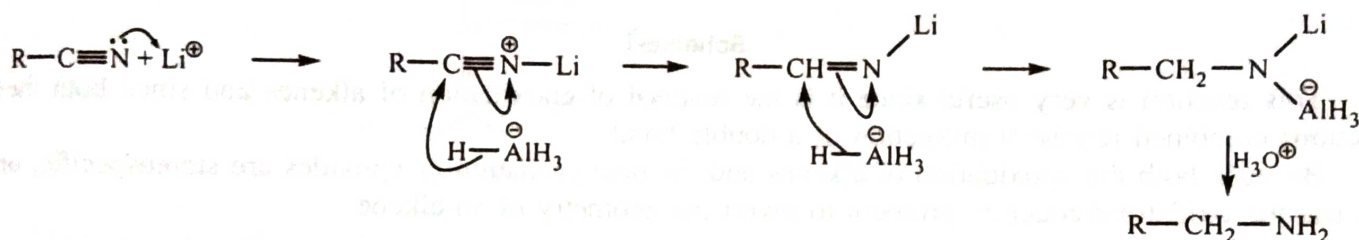
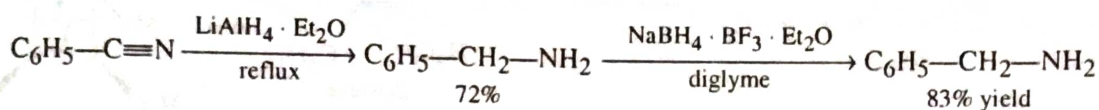


This is circumvented by the addition of an excess ammonia which assumes the role of nucleophile in place of the primary amine and yields are then high.

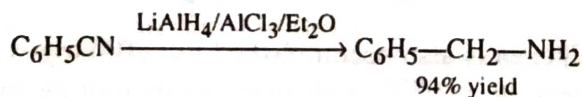




Complete reduction of nitriles to amines can also be achieved by hydride reducing agents. The most important of these are lithium aluminium hydride, lithium trimethoxy aluminium hydride and mixture of $\text{NaBH}_4/\text{BF}_3$. The yield with these reagents is 40-90%.



Nitriles are also obtained with alanes produced *in situ* from lithium aluminium hydride aluminium chloride in ether.



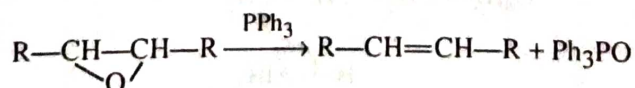
3.9 REDUCTION OF EPOXIDES

Epoxides can be reduced in two different ways:

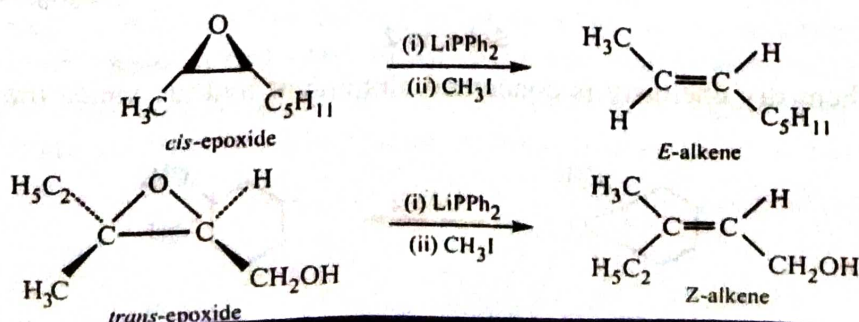
- (i) Deoxygenation of epoxides to alkenes and
- (ii) Reductive cleavage of epoxides to alcohols

3.9.1 Deoxygenation of Epoxides to Alkenes

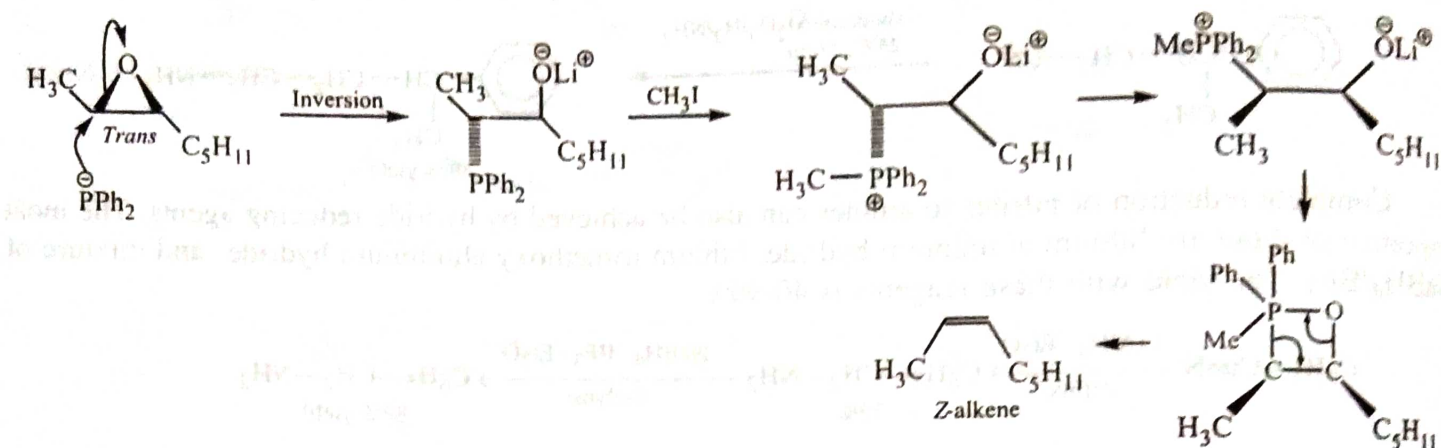
Alkenes are produced from epoxides *via* a complete deoxygenation process. Phosphorus reagents are particularly effective for this purpose. The best reagent is Ph_3P and $(\text{EtO})_3\text{P}$. Phosphorus reagents are effective because phosphorus has strong affinity with oxygen.



A nice method of transforming epoxides to alkenes with high level of stereospecificity was reported in the 1970s by E. Vedejs who used LiPPh_2 to open epoxides. Subsequent reaction *in situ* with methyl iodide forms a betaine. This betaine on *syn* elimination gives alkene.

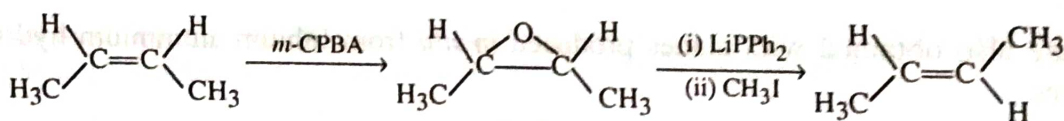


In this reaction *cis*-epoxides give (*E*)-alkenes and *trans* give (*Z*)-alkenes. Thus the reaction is stereospecific. The reaction is stereospecific because the epoxide opens with strict inversion and the elimination is *syn* periplanar (Scheme-1).



This reaction is very useful since it is the reversal of epoxidation of alkenes and since both these reactions combined represent protection of a double bond.

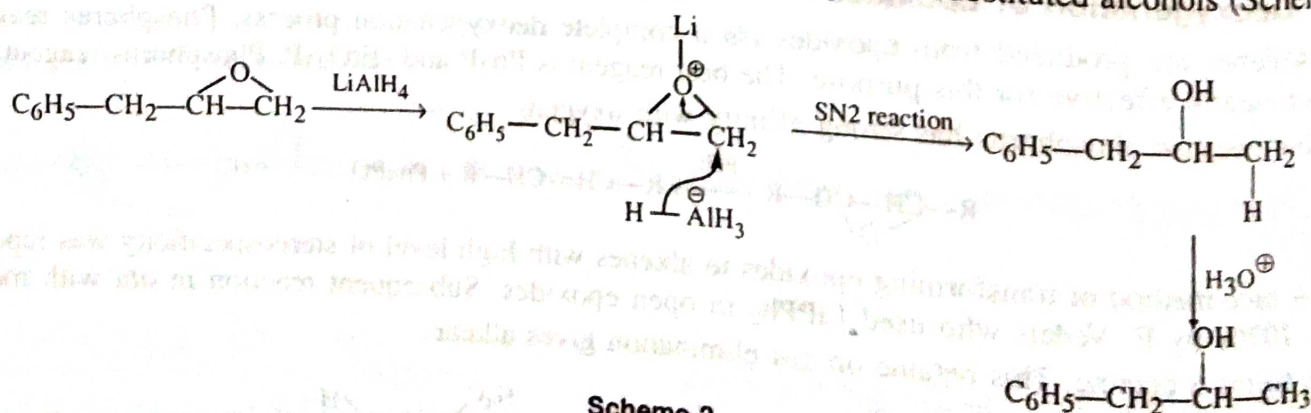
Because both the epoxidation of alkenes and the deoxygenation of epoxides are stereospecific, one can use the oxidation/reduction protocol to invert the geometry of an alkene



Reduction of epoxides to alkenes is also accomplished by refluxing with Zn dust/acetic acid or with Zn—Cu couple in ethanol, by heating at 65°C with titanium dichloride prepared *in situ* from titanium trichloride and LiAlH₄ and by treating with chromous chloride-ethylenediamine complex in DMF.

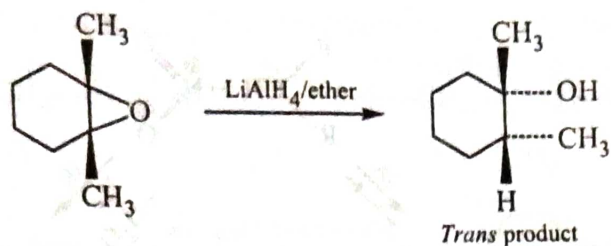
3.9.2 Reductive Cleavage of Epoxides to Alcohols

Reagents of choice for reduction of epoxides to alcohols are hydrides and complex hydrides. A general rule of regioselectivity is that the nucleophilic complex hydrides such as lithium aluminium hydride approach the oxide from the less hindered side thus giving more substituted alcohols (Scheme-2).

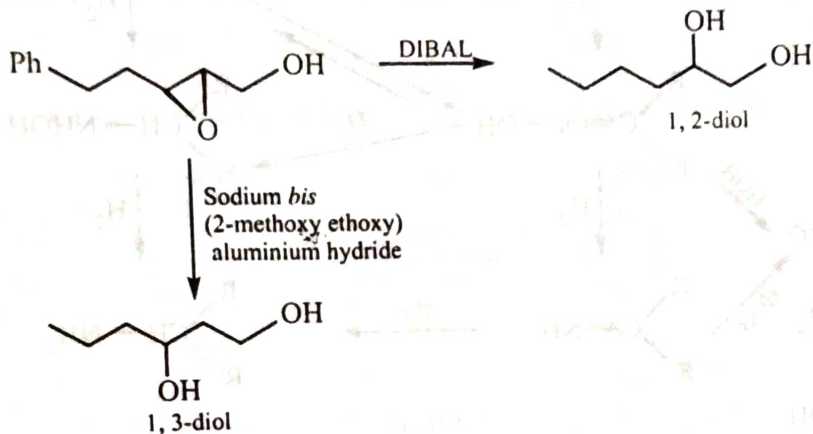


As far as stereochemistry chemistry is concerned aluminium hydride yields *trans* products.

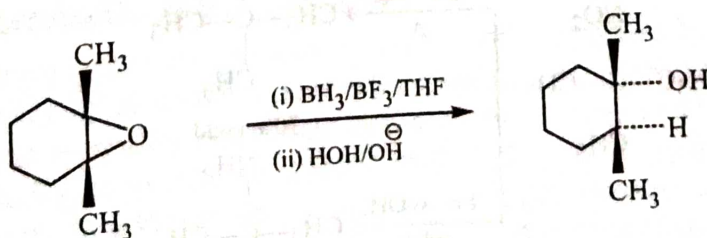
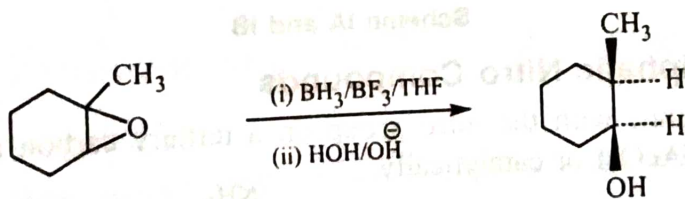
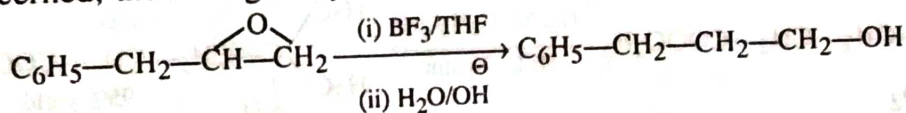




Allyl alcohols on epoxidation give epoxy alcohols. The epoxy alcohols so generated may be reduced selectively to give a range of either 1,2- or 1,3-diols depending on the nature of reducing agents.

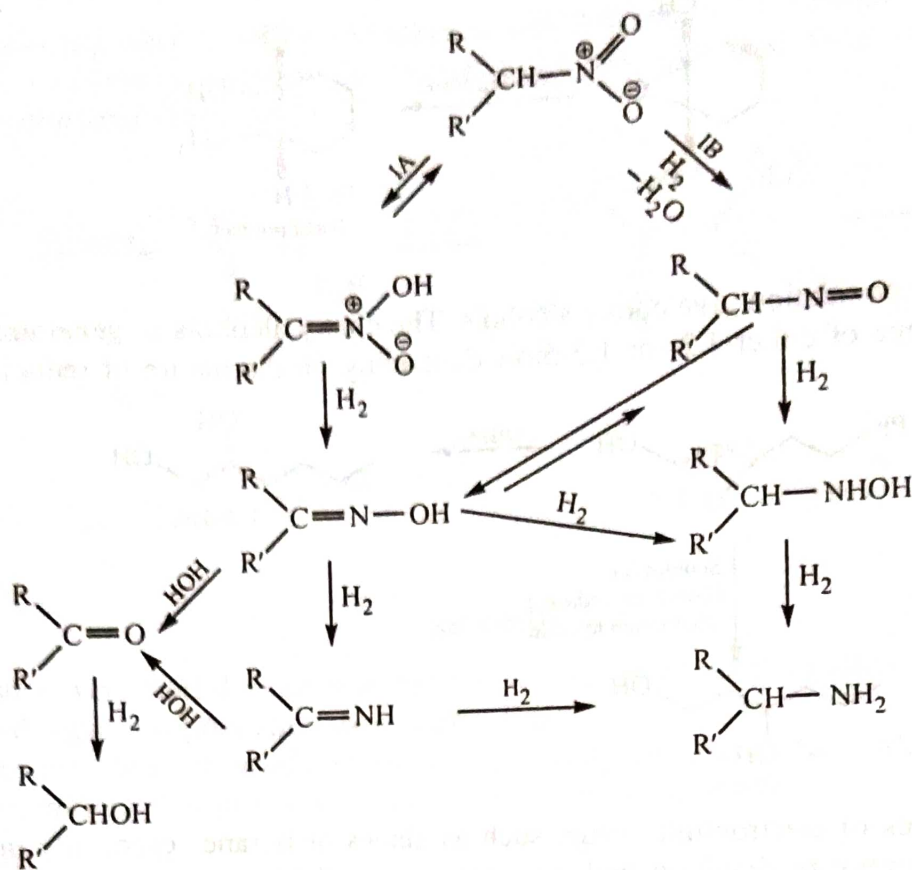


In contrast, hydrides of electrophilic nature such as alanes or boranes especially in the presence of BF_3 , open the ring in opposite direction and give predominantly less substituted alcohols. As far as stereochemistry is concerned, these reagents yield *cis* products.

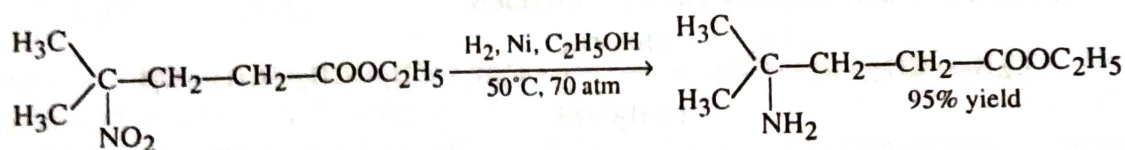


3.10 REDUCTION OF NITRO GROUP

Nitro group undergoes exceedingly easy reduction by many reagents. Both aromatic and aliphatic nitro groups are thus easy to reduce, often without affecting other functional groups. Nitro group behaves differently depending upon whether it is bonded to a carbon having no hydrogen (NO_2 group present on tertiary aliphatic carbon or nitro group present on benzene ring) or bonded to a carbon having hydrogens. In the latter case tautomerism generates *aci* form which is reduced in different ways (Scheme-IA) from those of the nitro group (Scheme IB).



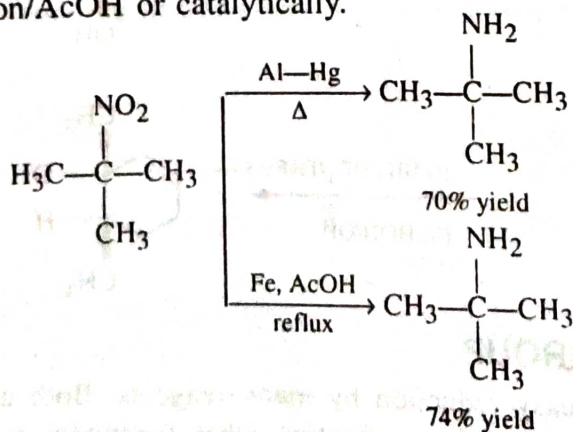
Scheme IA and IB



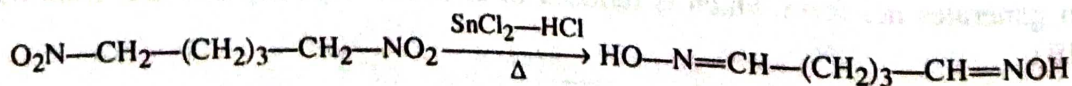
Scheme IA and IB

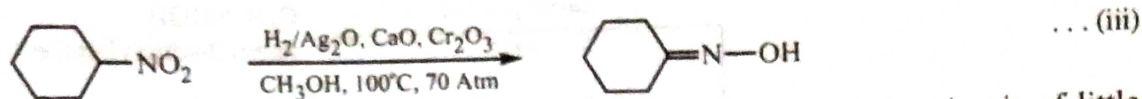
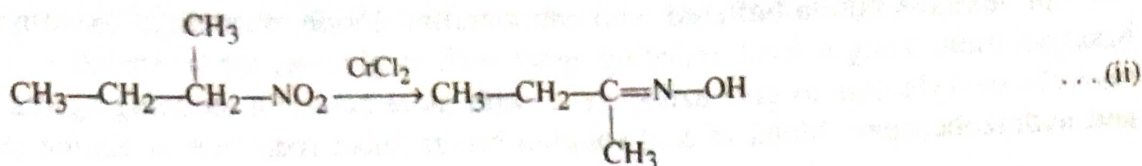
3.10.1 Reduction of Aliphatic Nitro Compounds

Aliphatic nitro compounds with the nitro group on a tertiary carbon are reduced to amines with aluminium amalgam or iron/AcOH or catalytically.

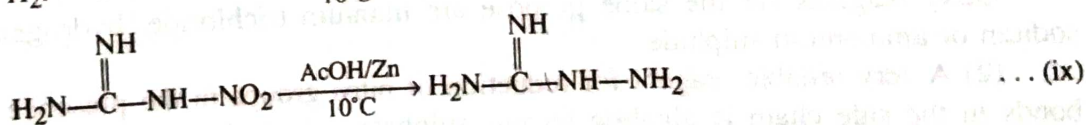
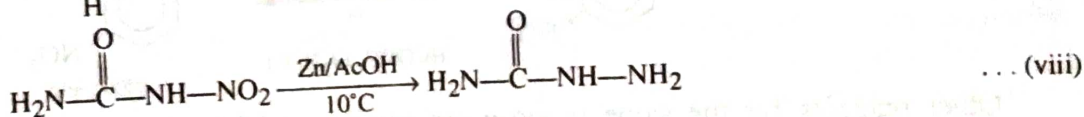
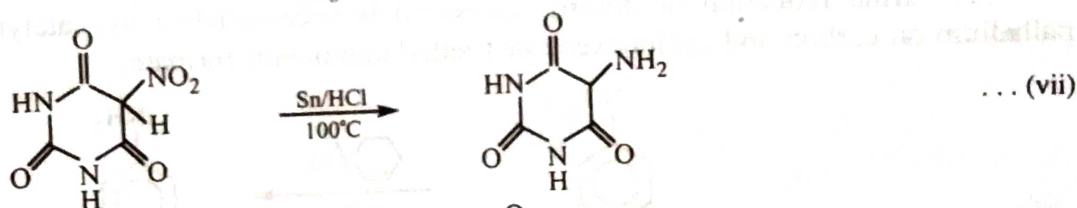
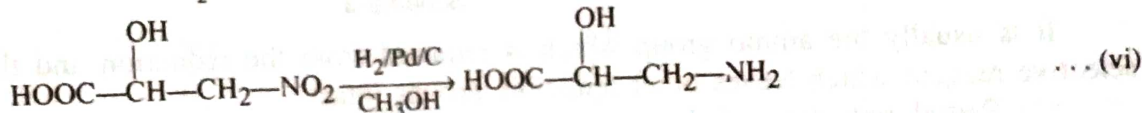
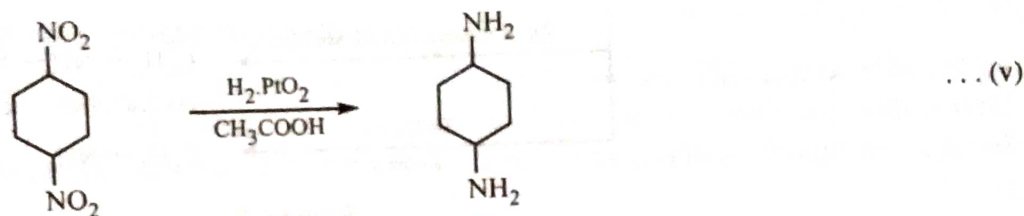
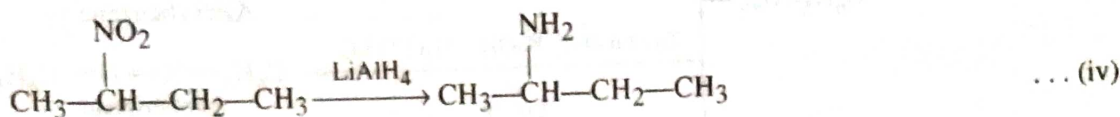


Generally primary nitro compounds are reduced to aldoximes and secondary to ketoximes by metal salts, such as stannous chloride and chromous chloride. The same result is also obtained by hydrogenation in the presence of catalyst.



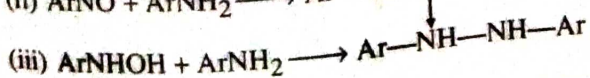
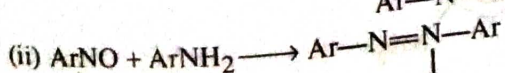
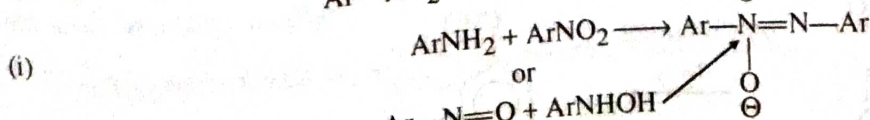
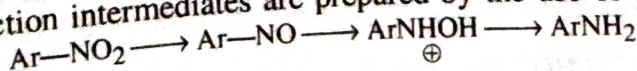


Aliphatic nitro compounds on complete reduction give primary amines. But this reaction is of little importance because the amino group is easily introduced in a number of other ways. Lithium aluminium hydride and catalytic reduction with a transition metal catalyst are suitable methods.

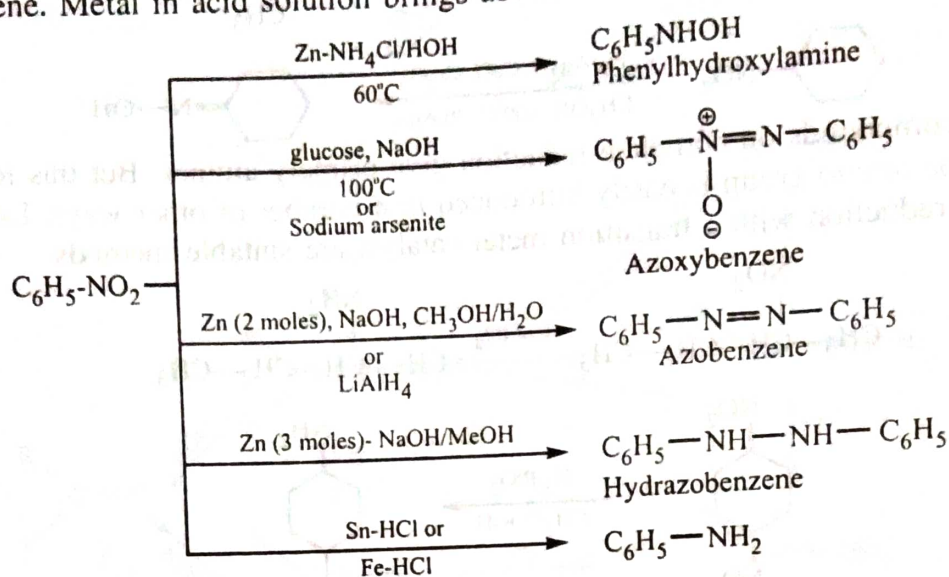


3.10.2 Reduction of Aromatic Nitro Compounds

The reduction of aromatic nitro compounds is much more important because the nitro group can be introduced into a wide variety of aromatic systems by nitration. It is because nitro group is very strong electrophile. The nitro group is readily converted into a series of functional groups of various degree of reduction: very exceptionally to a nitroso group, more often to a hydroxylamino group and most frequently to the amino group. In addition azoxy, azo and hydrazo compounds are formed by combination of two molecules of the reduction intermediates (Scheme-2). With the exception of the nitroso stage, all the intermediate stages of the reduction of nitro compounds can be obtained by controlled catalytic hydrogenation. All the reduction intermediates are prepared by the use of suitable reducing agents.



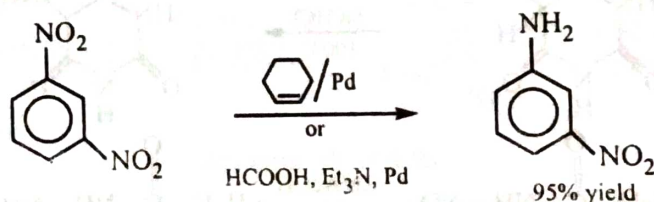
In neutral solution buffered with ammonium chloride, phenylhydroxylamine is the main product. In basic solution, using a weak reducing agent such as glucose, the intermediate nitrosobenzene reacts with phenylhydroxylamine to give azobenzene, with more powerful reducing agents converts into azobenzene and hydrazobenzene. Metal in acid solution brings about reduction to aniline (Scheme-3).



Scheme-3

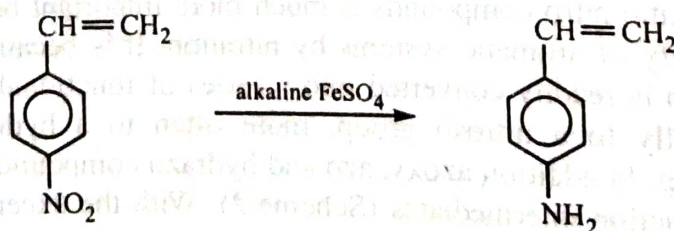
It is usually the amino group which is required from the reduction and the problem is to find a selective reagent which leaves other reducible groups intact.

(1) Partial reduction of dinitro compound is accomplished by catalytic hydrogen transfer using palladium on carbon and cyclohexene or triethylammonium formate.

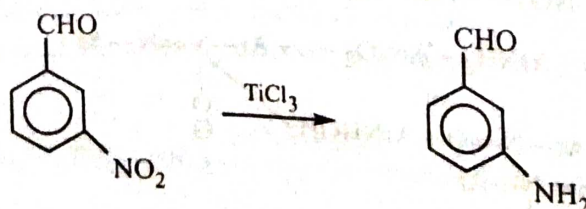


Other reagents for the same purpose are titanium trichloride, hydrogen sulphide in pyridine and sodium or ammonium sulphide.

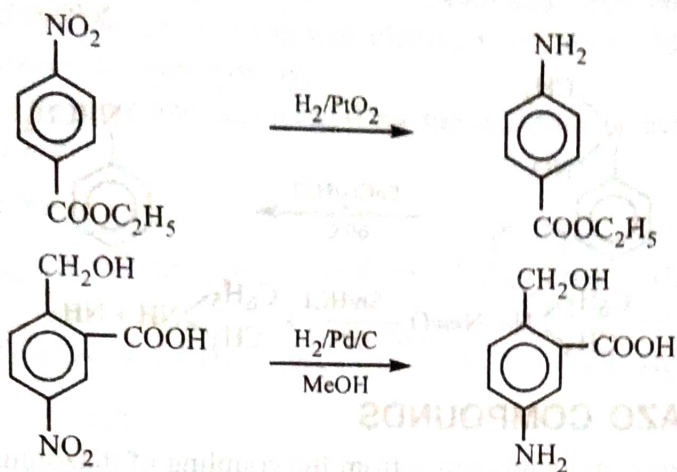
(2) A very reliable reagent for reduction of nitro groups in the presence of carbon-carbon multiple bonds in the side chain is alkaline ferrous sulphate, which does not affect the carbon-carbon multiple bonds.



(3) Titanium trichloride is a very good reducing agent for nitro in the presence of aldehydic group. $SnCl_2-HCl$ can also be used.

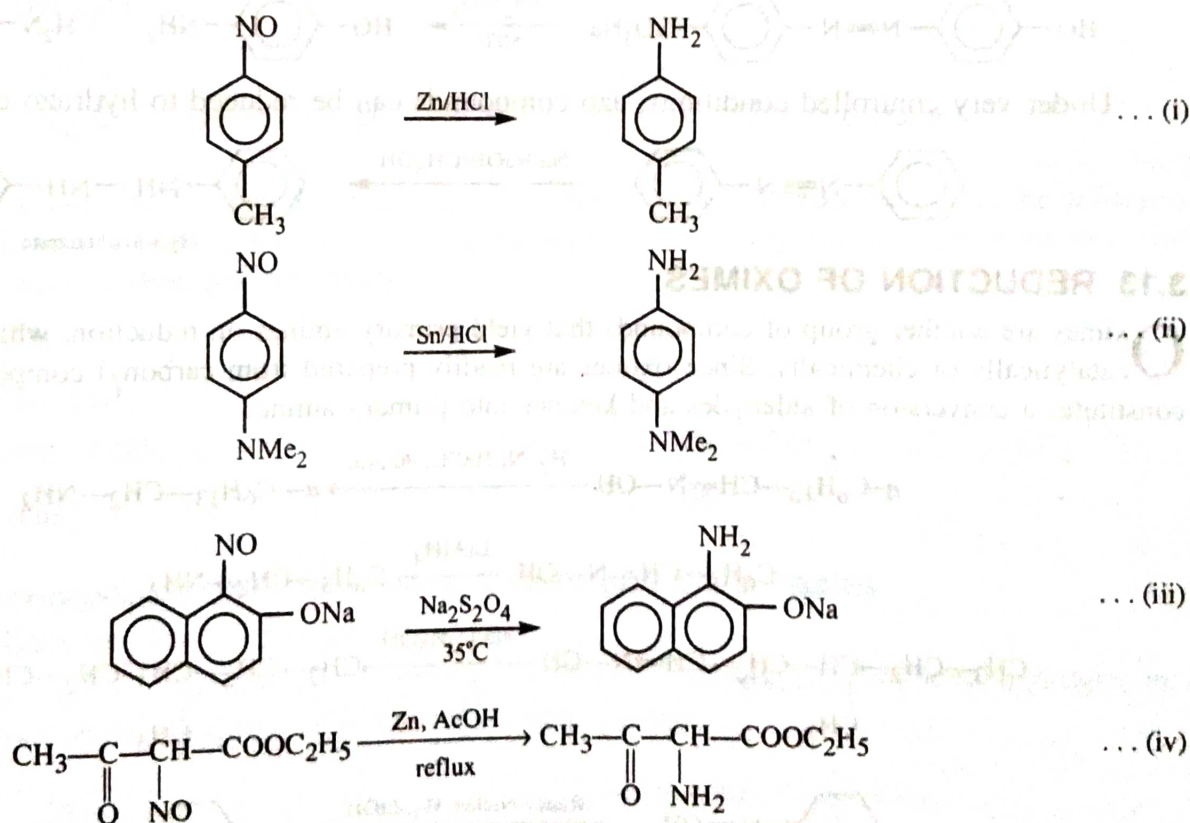


(4) Hydrogenation in the presence of metal catalyst reduces only nitro group and has no effect on ester or carboxylic or hydroxy groups.

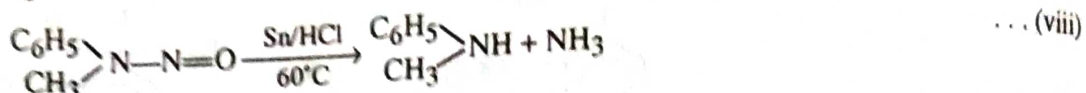
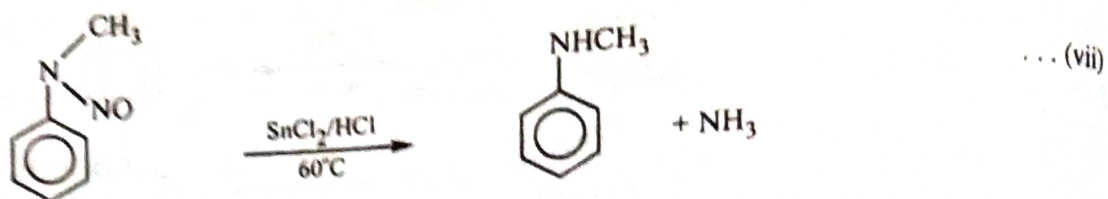
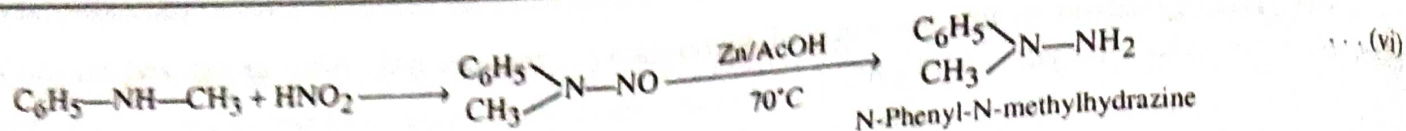


3.11 REDUCTION OF NITROSO COMPOUNDS

Like nitro groups, nitroso groups are readily reduced to the corresponding amines. This can be effected by vigorous reagents such as zinc-acid or Sn—HCl, but more often the reaction is carried out with a mild reducing agent, specially sodium hydrosulphite. Not only aromatic but also aliphatic nitroso groups are reduced to amines.

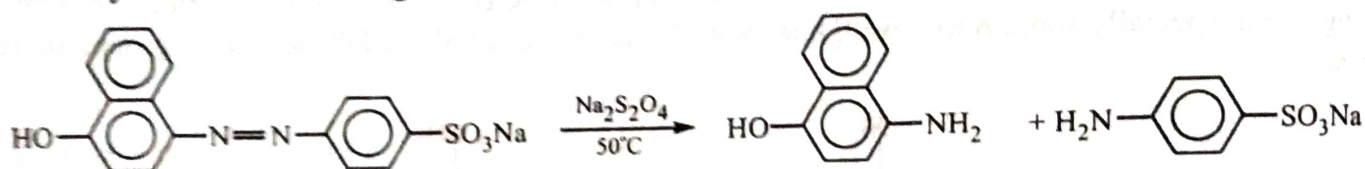


N-nitroso groups, prepared from alkylamines and nitrous acid, are reduced to unsymmetrical hydrazines by Zn and acetic acid, but more vigorous reagents, such as stannous chloride give cleavage to the amine with aromatic amines.

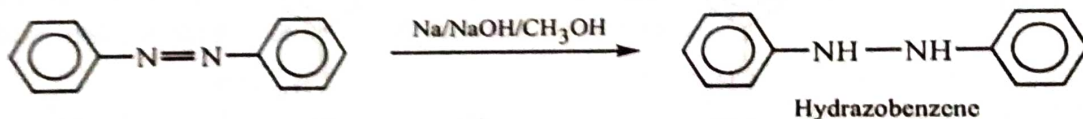


3.12 REDUCTION OF AZO COMPOUNDS

Unsymmetrical aromatic azo compounds result from the coupling of diazonium salts with phenols or tertiary aromatic amines. Symmetrical azo derivatives can be prepared from controlled reduction of nitro compounds. Azo compounds behave like nitroso compounds in that they can be reduced to primary amines under relatively mild conditions, e.g. with sodium hydrosulphide.

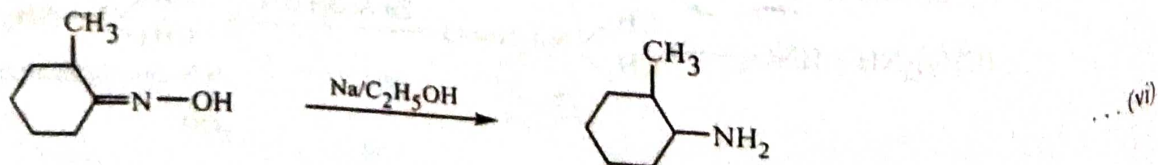
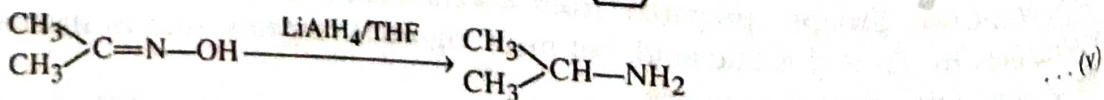
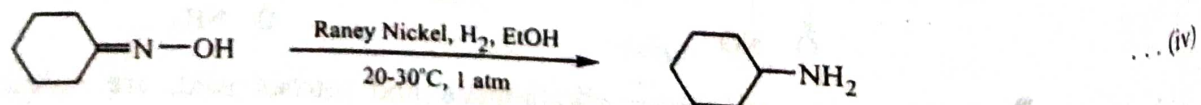
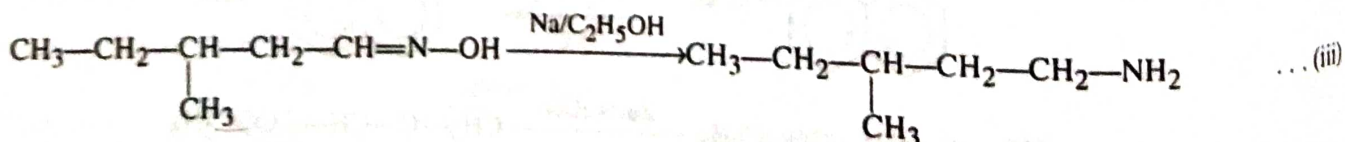
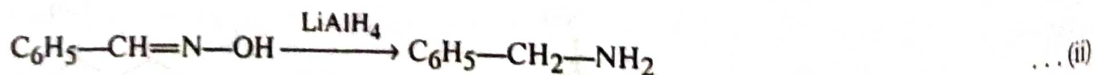
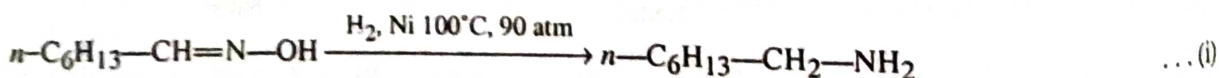


Under very controlled conditions, azo compounds can be reduced to hydrazo compounds.



3.13 REDUCTION OF OXIMES

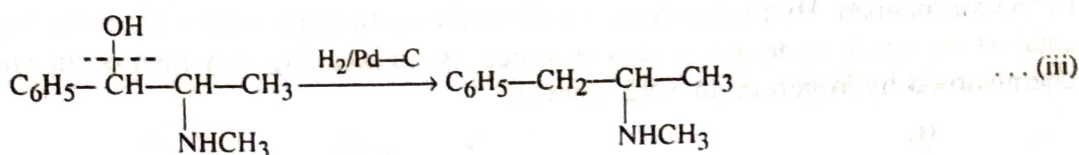
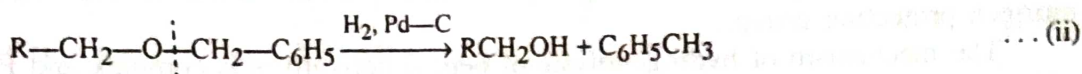
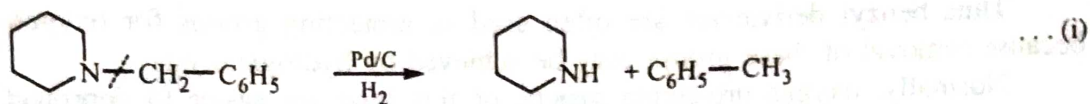
Oximes are another group of compounds that yield primary amines on reduction, which can be carried out catalytically or chemically. Since oximes are readily prepared from carbonyl compounds, their reduction constitutes a conversion of aldehydes and ketones into primary amines.



3.14 HYDROGENOLYSIS

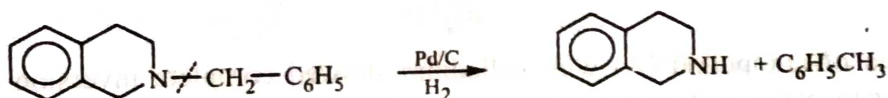
Reactions which completely cleave the bonds between carbon and electronegative elements, replacing them with bonds to hydrogen are known as reductive cleavage reactions. Reductive cleavage reaction using hydrogen and a catalyst is known as hydrogenolysis.

Most hydrogenolysis reactions are accelerated by the addition of acid, generally acetic acid, to the reaction mixture. Examples are:

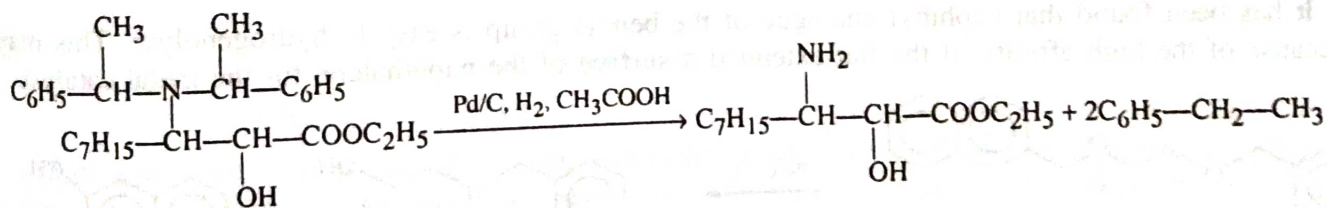


3.14.1 Hydrogenolysis of Amines (Reduction of C—N, σ bonds)

Amines that are substituted with a benzyl group (Bn) may be broken by reduction with hydrogen and a transition metal catalyst.

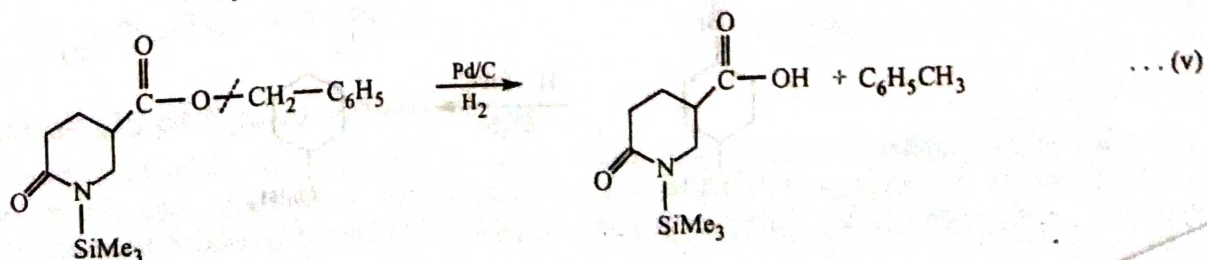
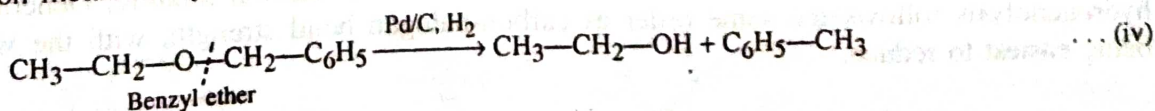


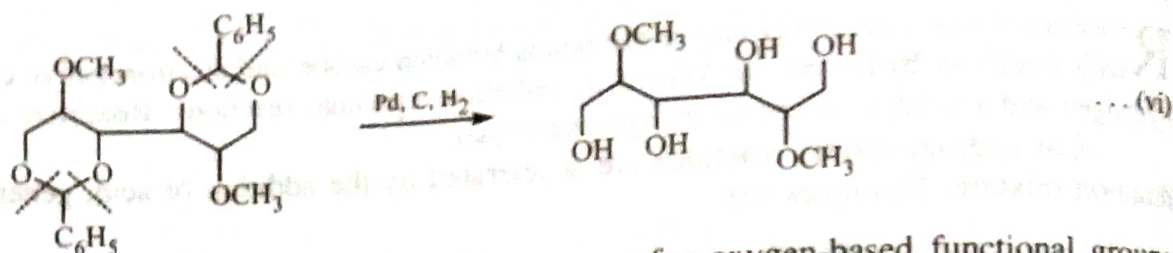
Thus benzyl group can be used as protecting group for amines and deprotection can be achieved by hydrogenolysis. Generally tertiary amines are easier to deprotect this way than secondary amines, which, in turn, are more reactive than primary amines.



3.14.2 Hydrogenolysis of Benzyl Ethers, Esters and Carbamates (Reduction of C—O, σ bond)

Benzyl ethers, esters and carbamates undergo reductive cleavage reaction with hydrogen in the presence of transition metal catalysts. The reaction is very smooth.





Thus benzyl derivatives are often used as protecting groups for oxygen-based functional groups because removal of these groups may be achieved by hydrogenolysis.

Normally, oxygen-protecting groups of this kind are easier to deprotect than the corresponding nitrogen protecting groups.

The mechanism of hydrogenolysis of benzyl derivatives is complex and Fig. 1 provides an outline of the mechanism. Hydrogenolysis is preceded by adsorption of the aromatic ring on to the surface of the catalyst on which hydrogen is also absorbed. Bond breaking may then occur *via* nucleophilic attack of a chemisorbed hydrogen in an S_N2 manner.

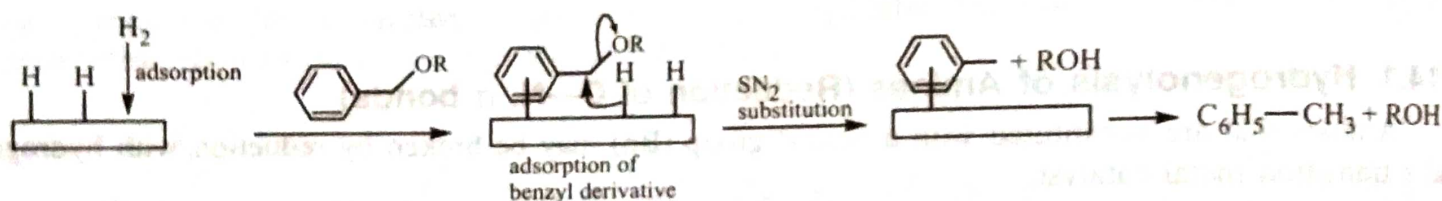
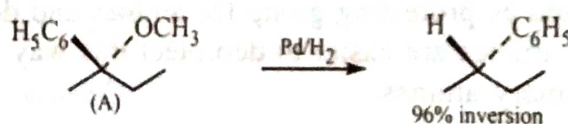
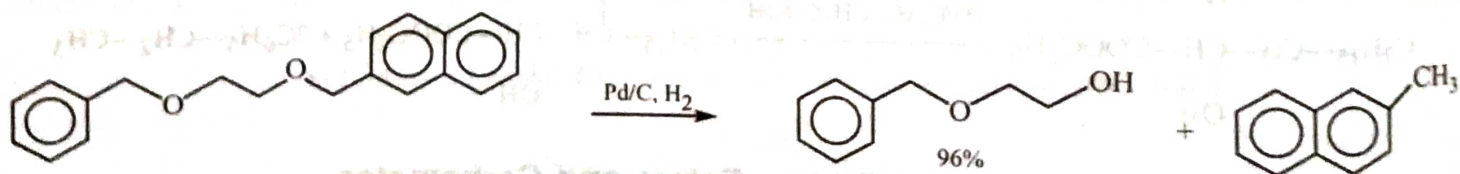


Fig. 1

Hydrogenolysis of compound (A) with palladium showed complete inversion during C—O bond cleavage. This experimental result supports the proposed mechanism.

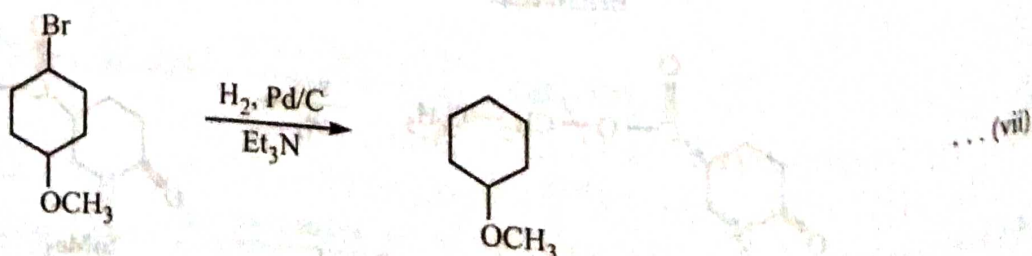


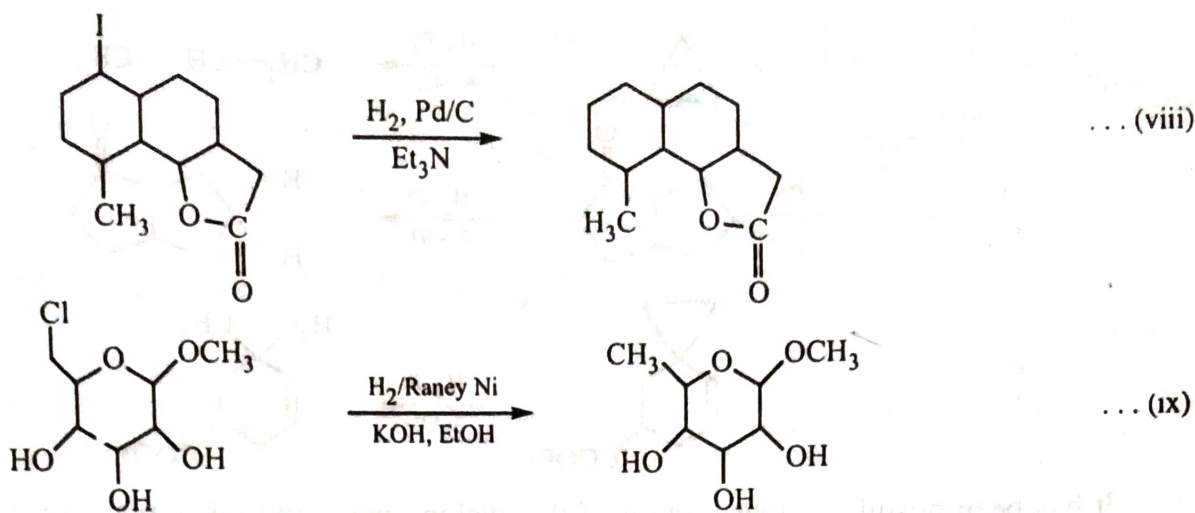
It has been found that naphthyl analogue of the benzyl group is easy to hydrogenolyse. This may be because of the high affinity of the flat extended π -surface of the naphthalene for the metal catalyst.



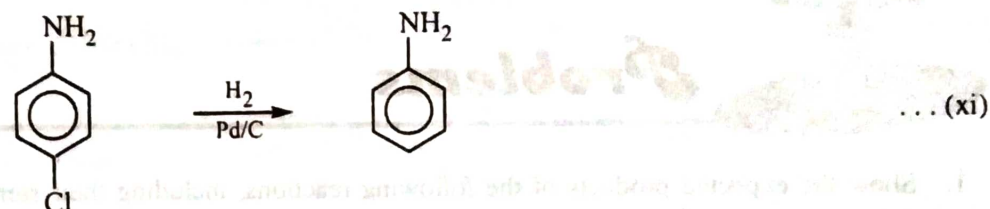
3.14.3 Hydrogenolysis of the C—X bond

Halogens can normally be reductively cleaved by hydrogen and a metal catalyst, *i.e.*, hydrogenolysis. Palladium is perhaps the best metal for this purpose. By-product of the reaction is HX which reduces the rate of the reaction. Due to this reason base is added in the reaction mixture. Generally, the ease of the hydrogenolysis follows the same order as carbon-halogen bond strength, with the weakest bond, C—I being easiest to reduce.

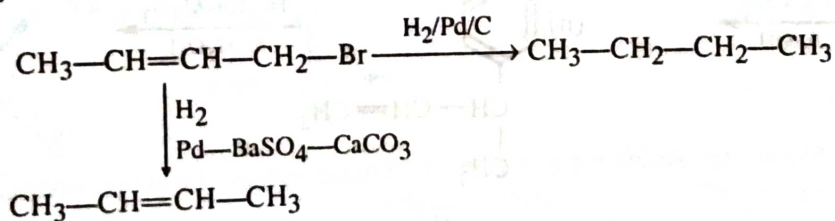




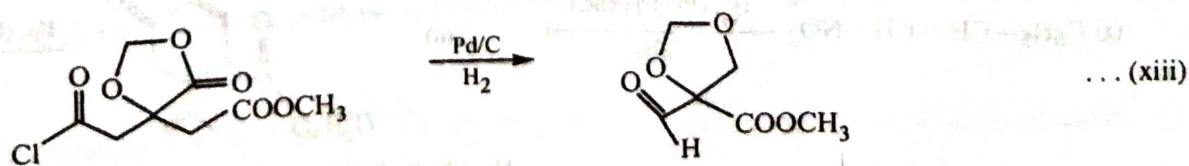
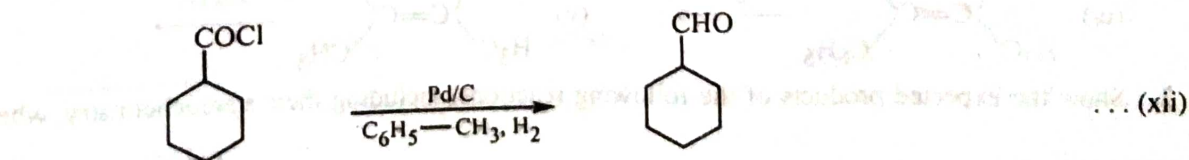
All types of halides may be reduced, including those bound to sp^2 hybridised carbon.



Hydrogenolysis of vinyl halides can also lead to reduction of carbon-carbon double bond. Successful hydrogenolysis of vinyl halides can be achieved in the presence of Lindlar catalyst.

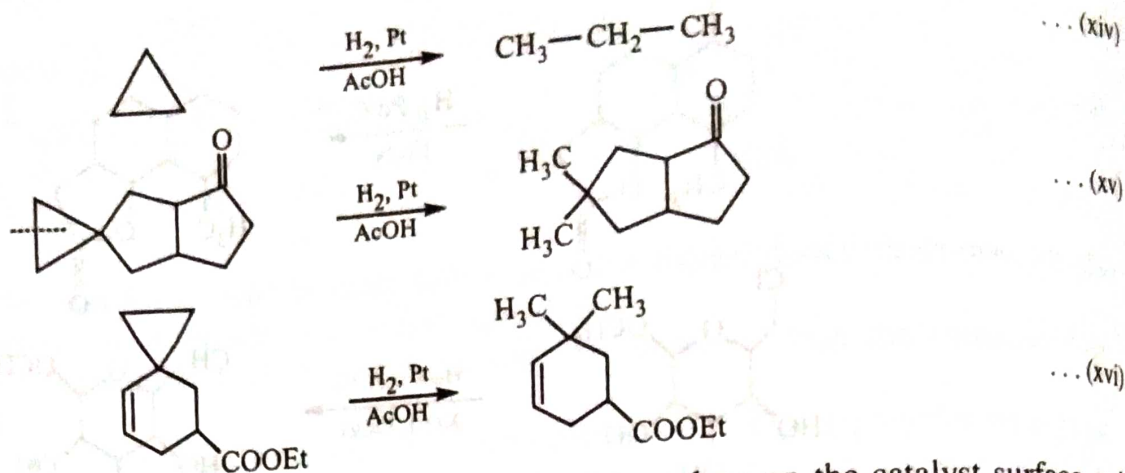


Hydrogenolysis of acid chlorides yields aldehydes and is known as the Rosenmund reduction. In this case also palladium is the metal of choice and this catalyst usually needs deactivation prior to reduction.



3.14.4 Hydrogenolysis of Cyclopropane Rings

The partial π -character of C—C bonds within cyclopropane rings means that they may be cleaved by hydrogenolysis. In this case platinum is the metal of choice. With alkyl substituents present on the ring, it tends to be the least hindered bond that is broken. This regioselectivity can be used to prepare geminal dimethyl groups.

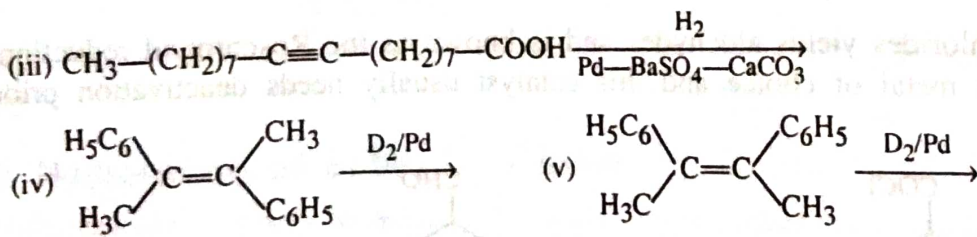
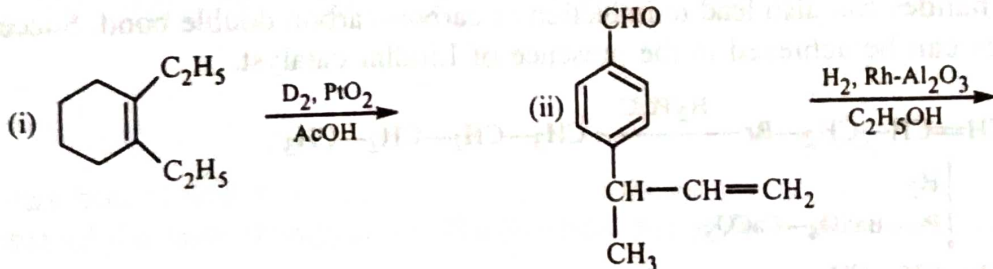


It has been postulated that rupture of the cyclopropane ring takes place on the catalyst surface and a doubly adsorbed species is formed. Presumably, transfer of hydrogen from the metal to the carbon ensues to form the geminal dimethyl group.

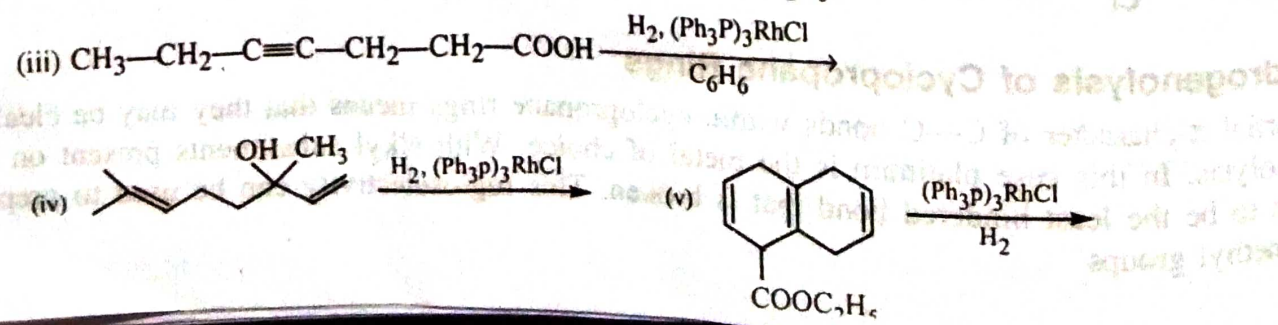
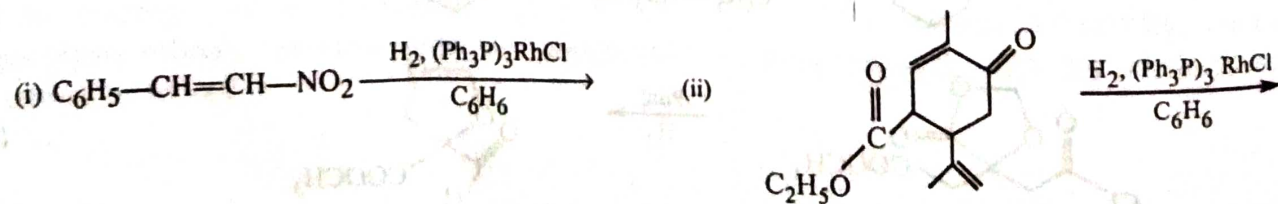


Problems

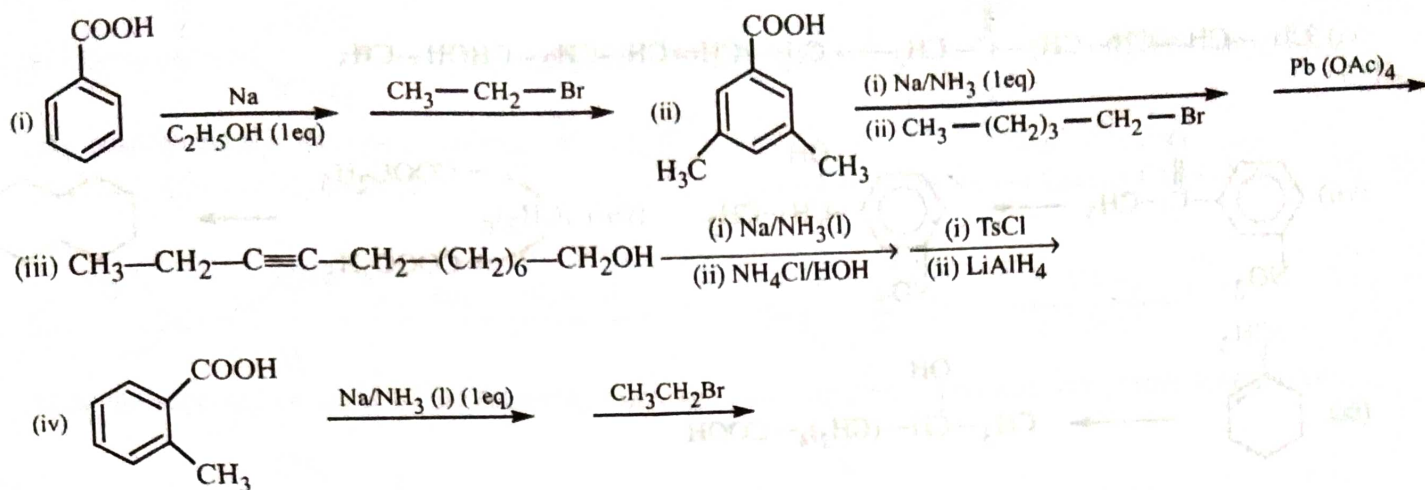
1. Show the expected products of the following reactions, including their stereochemistry, where appropriate.



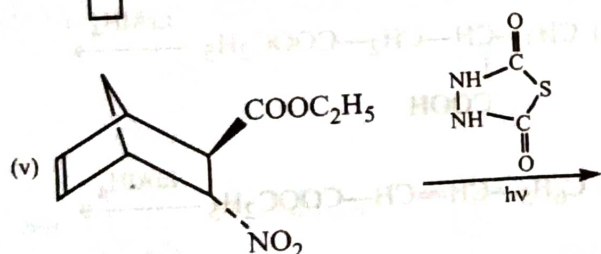
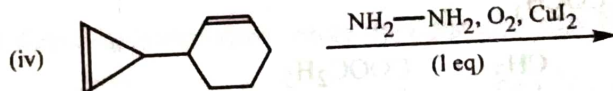
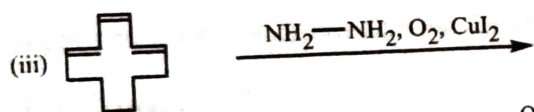
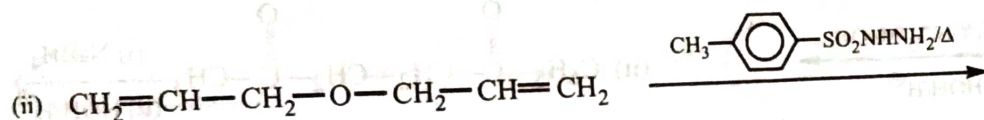
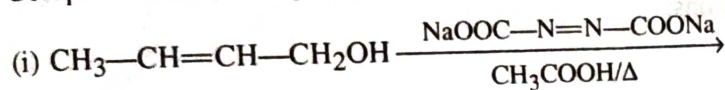
2. Show the expected products of the following reactions, including their stereochemistry, where appropriate.



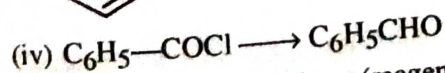
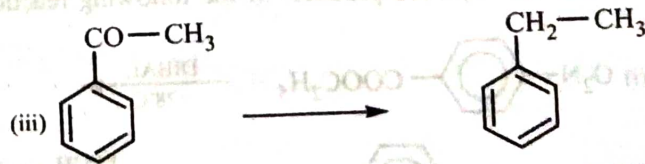
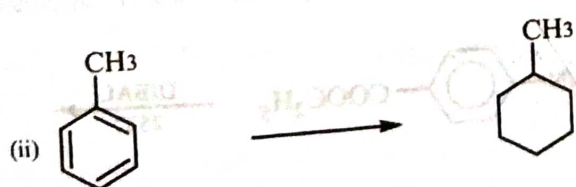
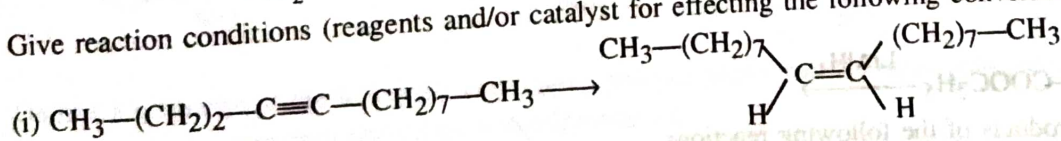
3. Complete the following reactions:



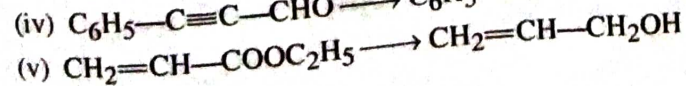
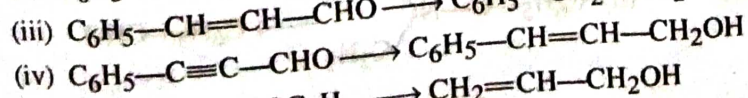
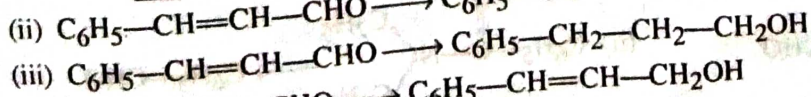
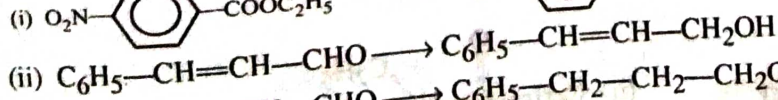
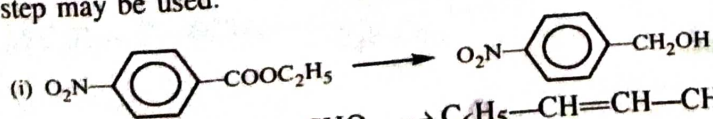
4. Complete the following reduction reactions and indicate the reducing agents in these cases:

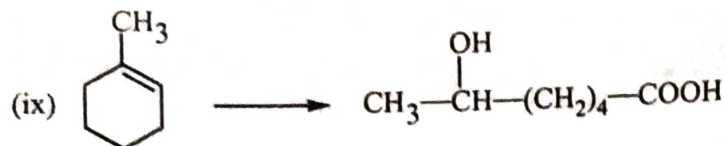
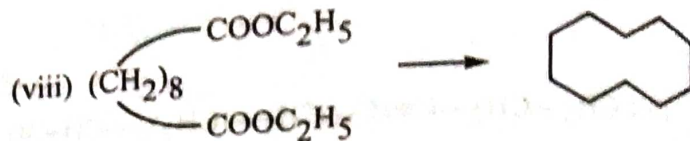
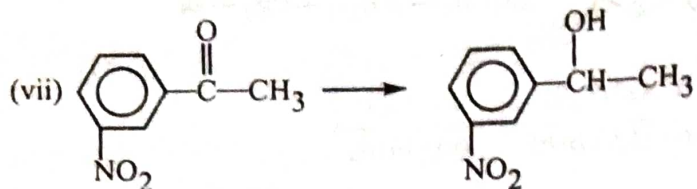
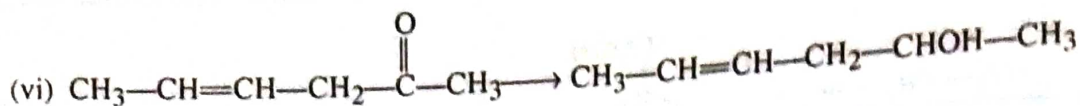


5. Give reaction conditions (reagents and/or catalyst for effecting the following conversions:

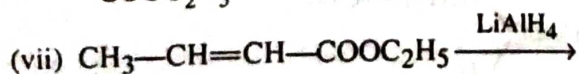
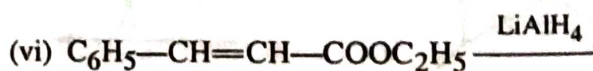
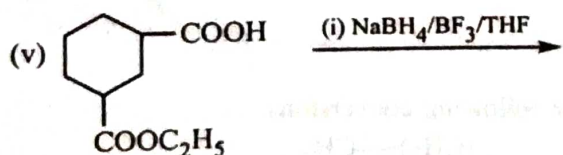
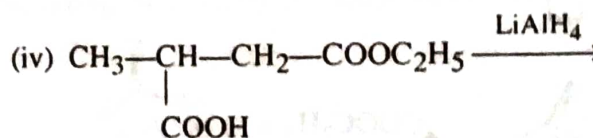
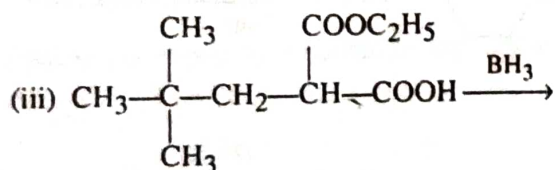
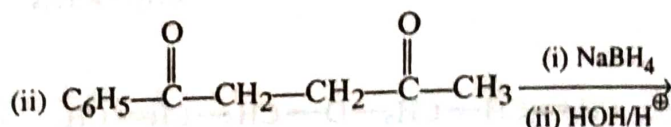
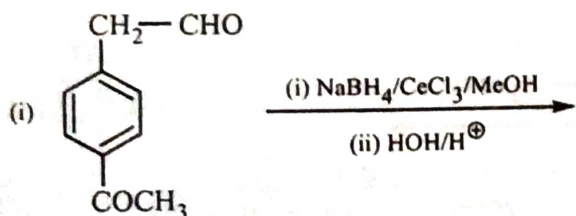


6. Suggest reaction conditions (reagents, catalysts, etc.) suitable for effecting the following conversions. More than one step may be used.

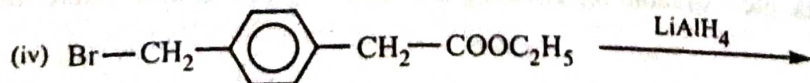
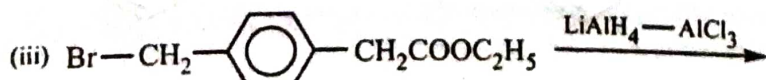
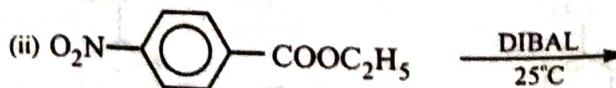




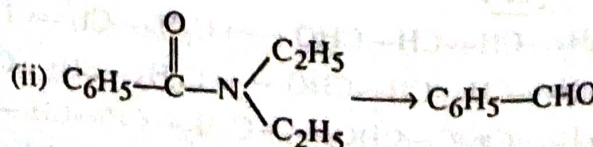
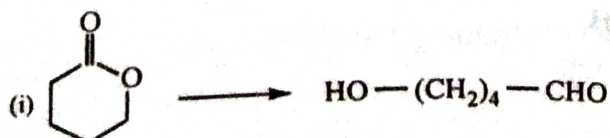
7. Indicate the expected products of the following reactions:

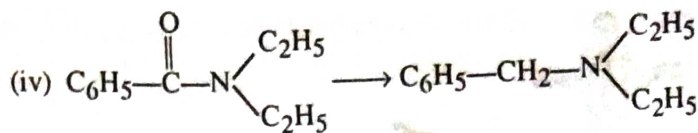
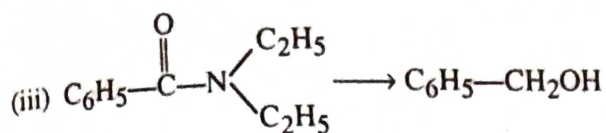


8. Indicate the expected products of the following reactions:

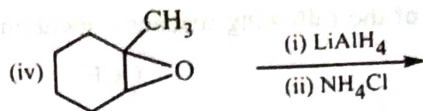
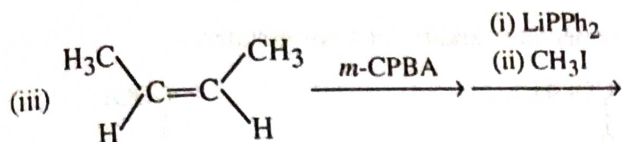
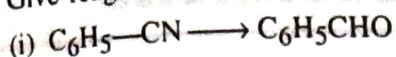


9. Give reagents for effecting the following conversions:

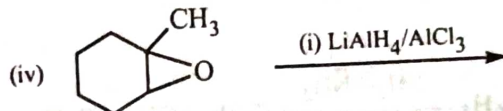
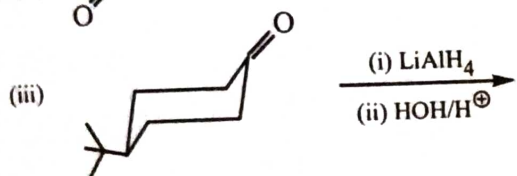
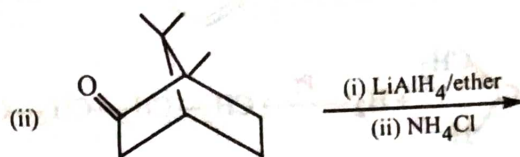
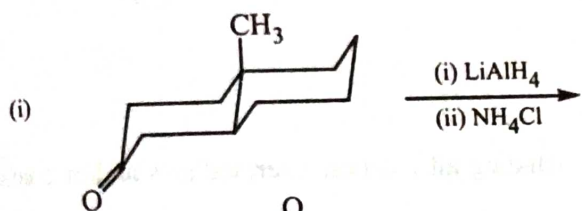




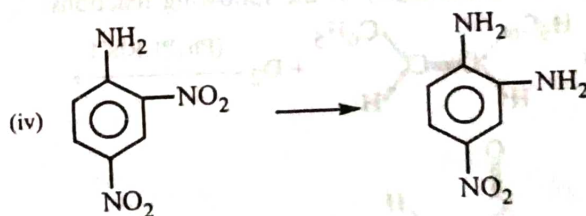
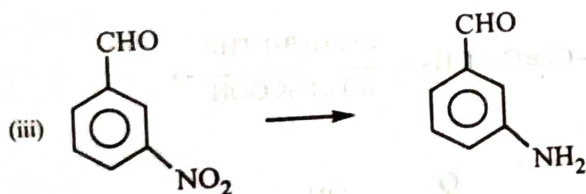
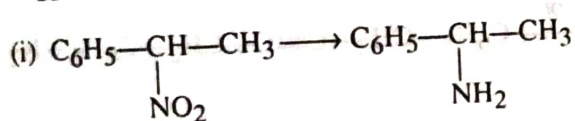
10. Give reagents for the following conversions:



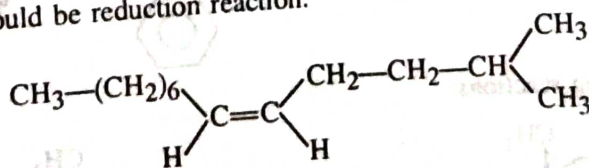
11. Show the expected products of the following reactions, including their stereochemistry, where appropriate.



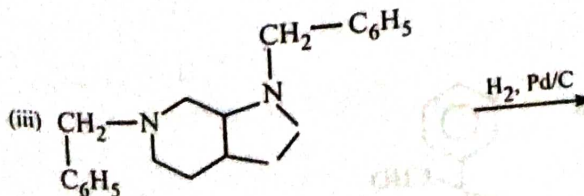
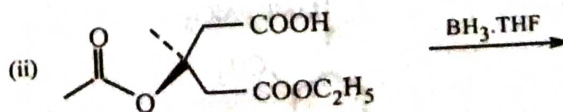
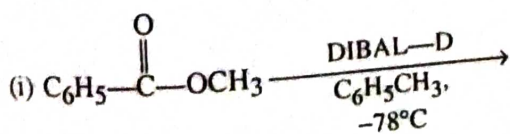
12. Suggest reaction conditions suitable for effecting the following conversions. More than one step may be required.



13. Outline a synthesis of the following compound from acetylene and any other compound containing no more than five carbons. At least one step should be reduction reaction.



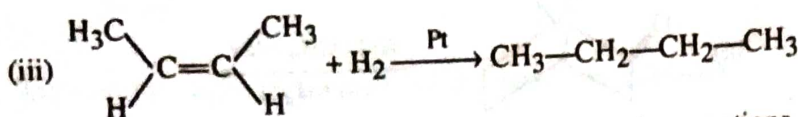
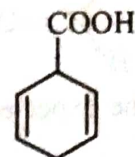
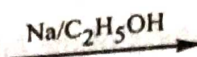
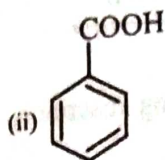
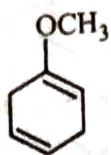
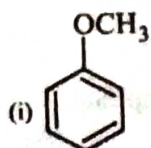
14. Complete the following reactions:



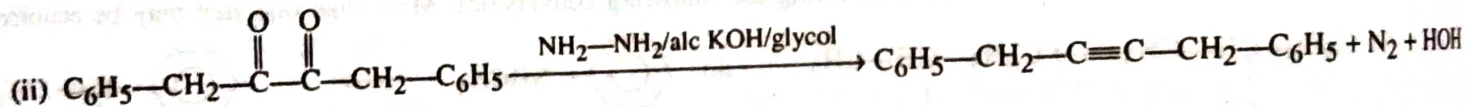
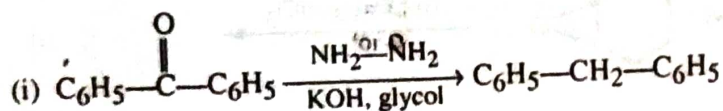


Problems for Self Assessment

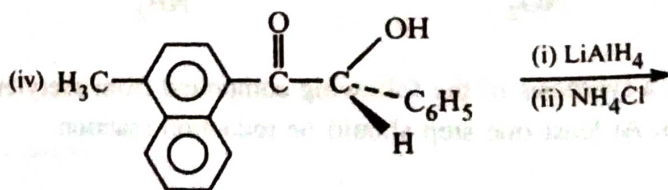
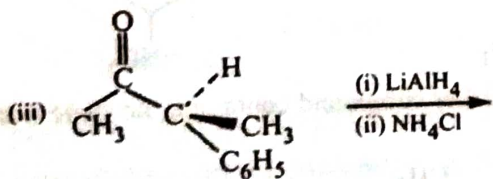
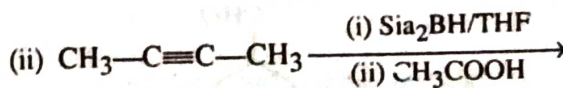
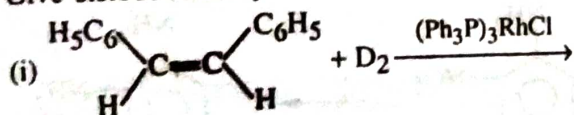
1. Write mechanism of the following reactions, including all intermediates and/or transition states.



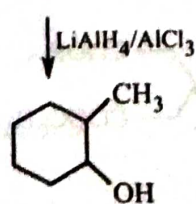
2. Write a detailed mechanism for each of the following reactions, including all reaction intermediates and/or transition states.



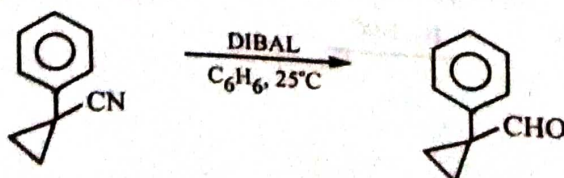
3. Give stereochemistry of the following reactions:



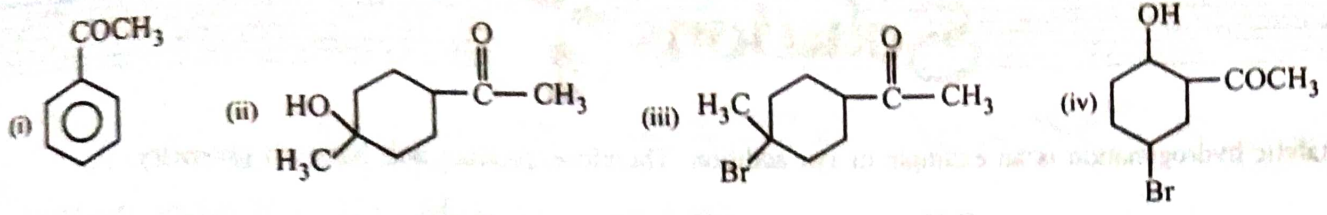
4. Give mechanism of the following reactions:



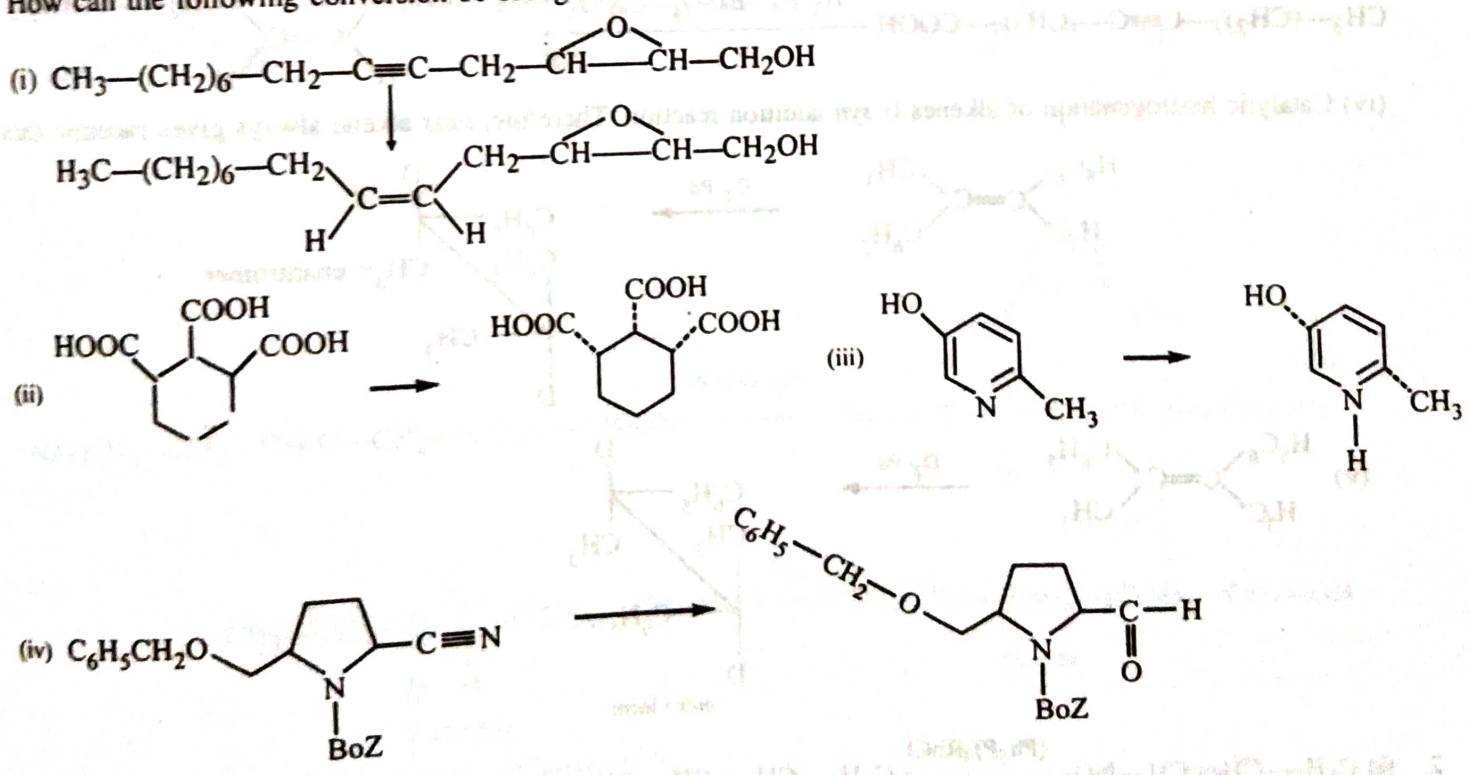
5. Give mechanism of the given reaction:



6. What reducing agents can be used for the conversion of a ketonic group into methylene group in the given compounds:

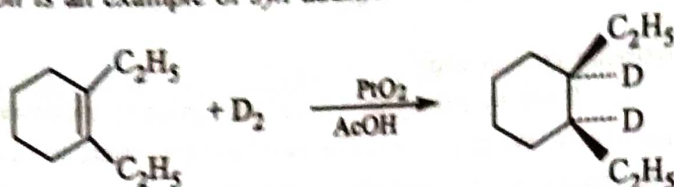


7. How will you bring about the following conversions?
 (i) Acid chloride to aldehyde (ii) Ester to aldehyde (iii) Cyanide to aldehyde (iv) Amide to aldehyde.
8. Define hydrogenation and hydrogenolysis. What is the difference between reductive cleavage and hydrogenolysis?
9. Compare stereochemistry of the the reduction of epoxides using lithium aluminium hydride and alanes.
10. NaBH_4 reduces aldehydic group more readily than the keto group, but in the presence of CeCl_3 it reduces keto group. Explain.
11. Compare the reductions using LiAlH_4 and sodium borohydride.
12. Discuss the application of boranes as reducing agent in organic synthesis.
13. Discuss the application and importance of DIBAL in organic synthesis.
14. What is homogeneous hydrogenation? What are its special uses compared to heterogeneous hydrogenation? Discuss stereochemistry of homogeneous hydrogenation with *cis*-2-butene.
15. Give the mechanism of the reduction of ketones into secondary alcohols in the presence of aluminium alkoxide.
16. Give methods of generation of diimide *in situ*. Discuss its application in organic synthesis. Also give mechanism of the reaction.
17. How can the following conversion be brought about?

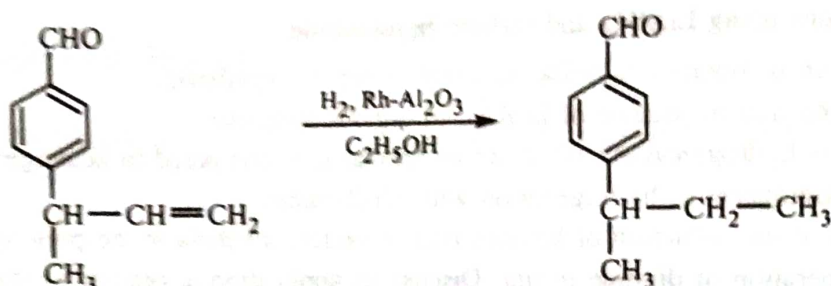


Solutions

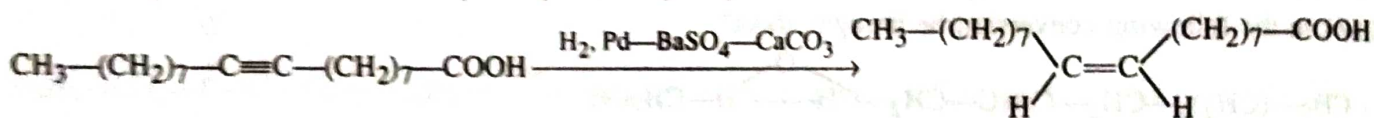
1. (i) Catalytic hydrogenation is an example of *syn* addition. Therefore, product will have *cis* geometry.



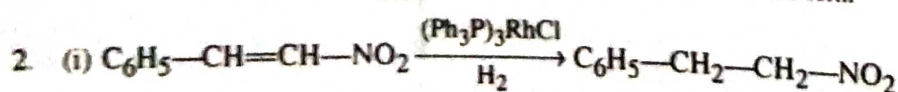
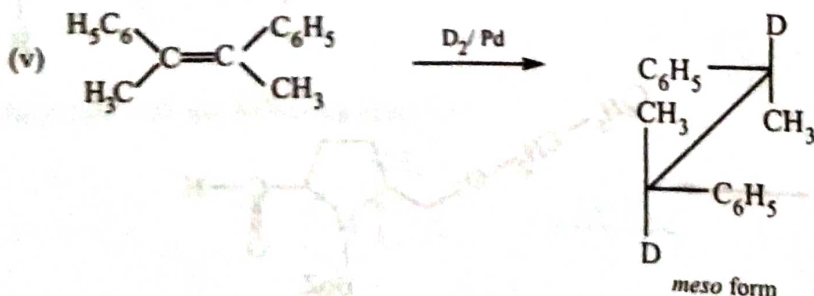
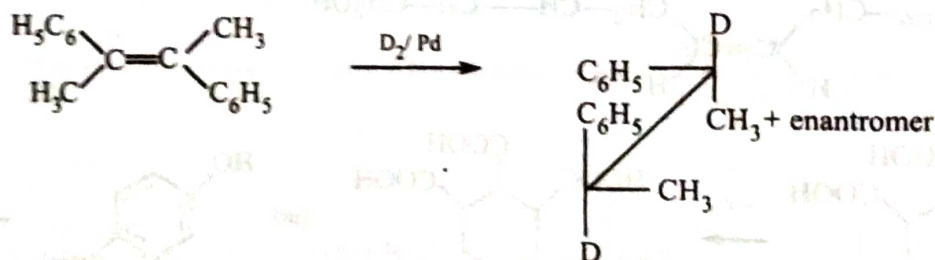
(ii) $Rh-Al_2O_3$ is selective reducing agent and it has no effect on carbonyl group, it only reduces carbon-carbon double bond.



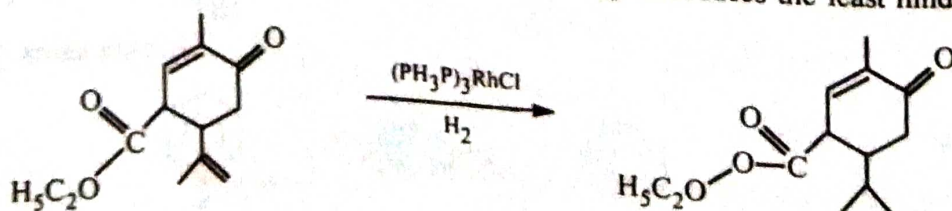
(iii) In the presence of Lindlar catalyst alkyne undergoes partial reduction to give *cis* alkene.

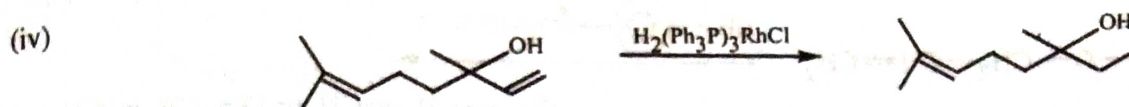
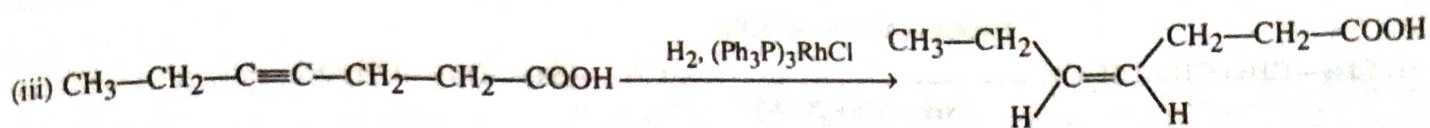


(iv) Catalytic hydrogenation of alkenes is *syn* addition reaction. Therefore, *trans* alkene always gives racemic mixture.

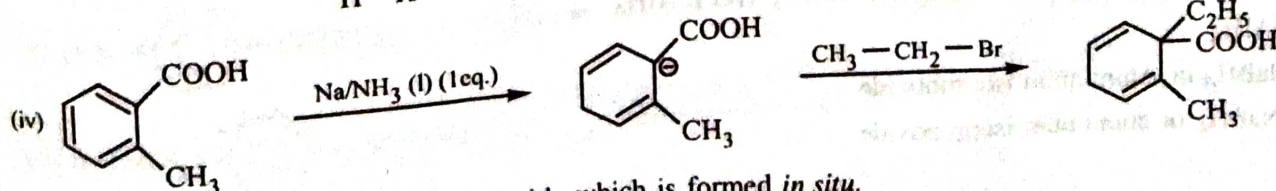
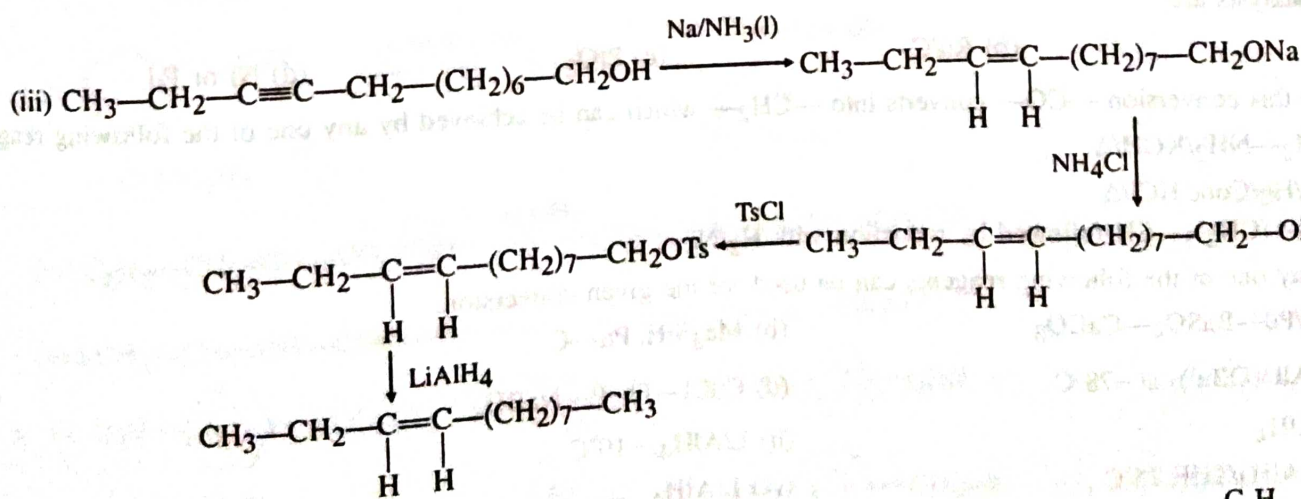
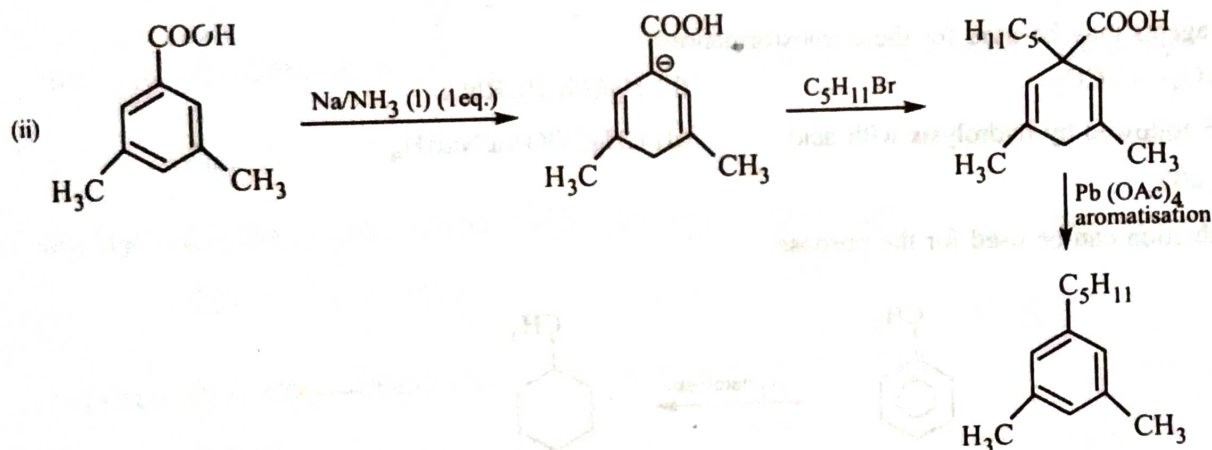
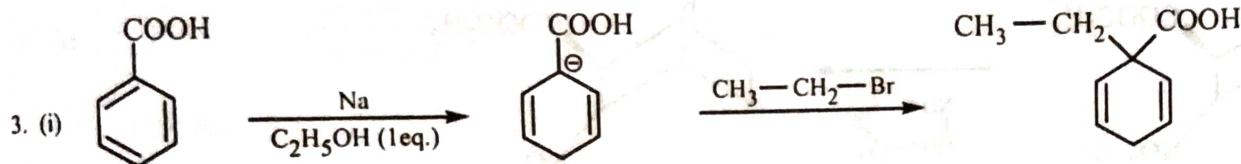
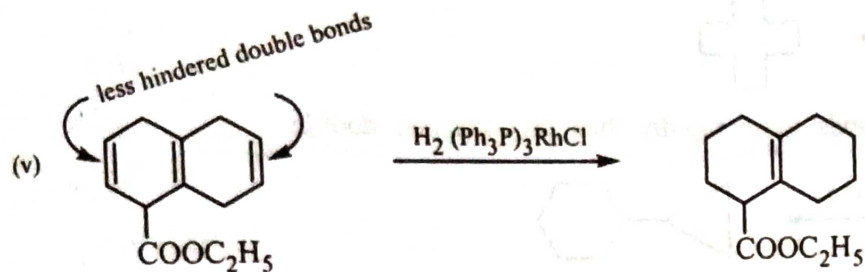


(ii) Where compound contains more than one double bond, the reagent reduces the least hindered one.

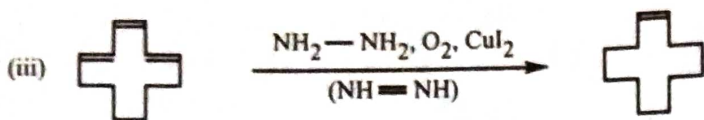
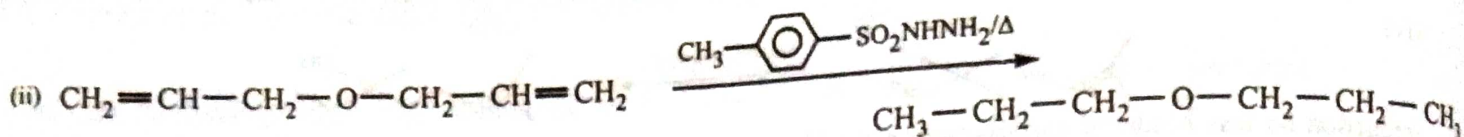
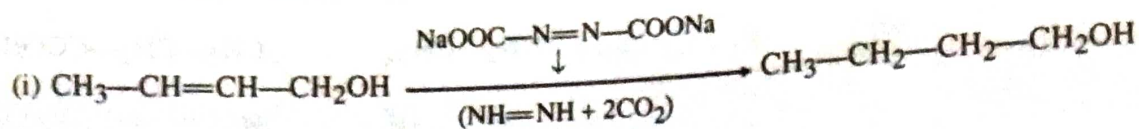




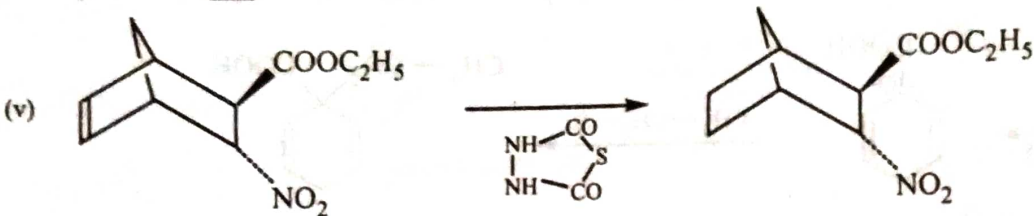
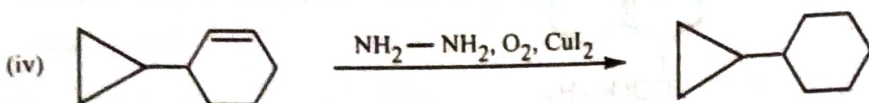
(reduction on less hindered carbon-carbon double bond)



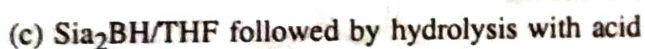
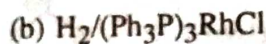
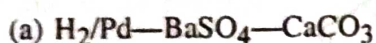
4. In all cases reactive reducing agent is diimide which is formed *in situ*.



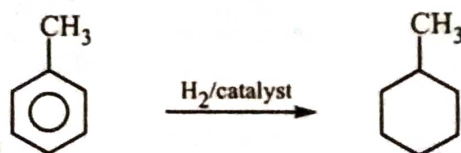
Diimide reduces more strained double bonds more rapidly than less strained double



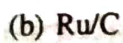
5. (i) Following reagents may be used for these transformations



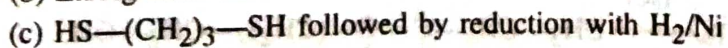
(ii) Catalytic reduction can be used for the purpose



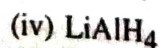
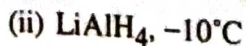
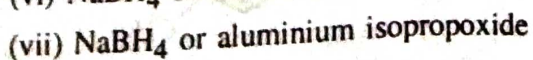
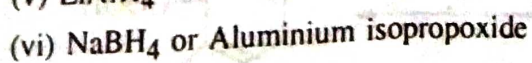
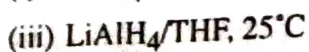
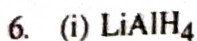
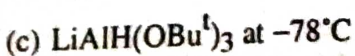
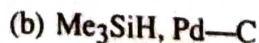
The catalysts are:

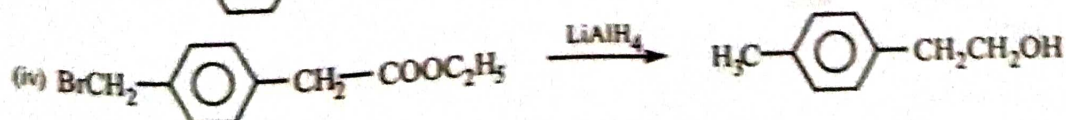
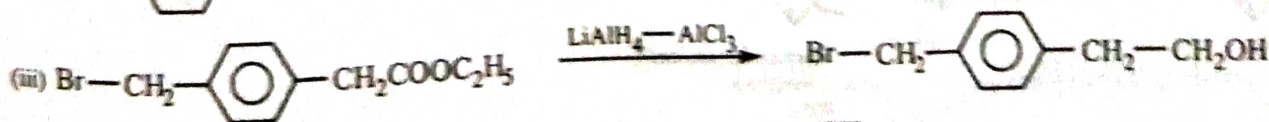
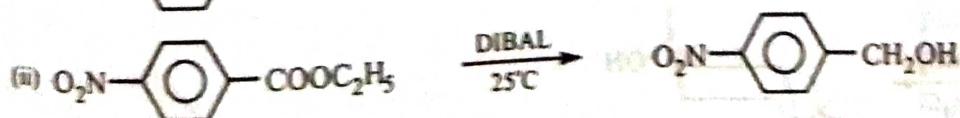
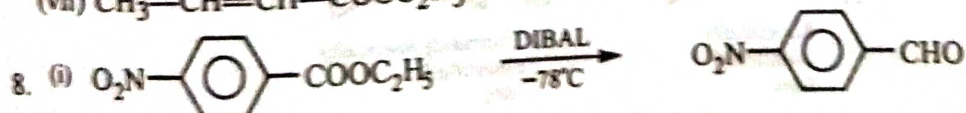
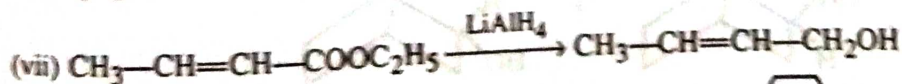
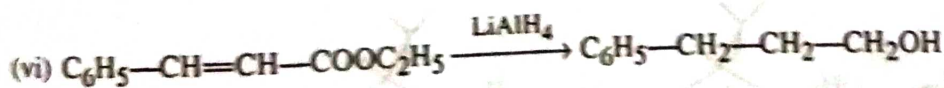
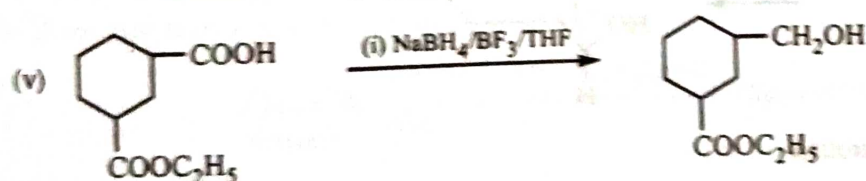
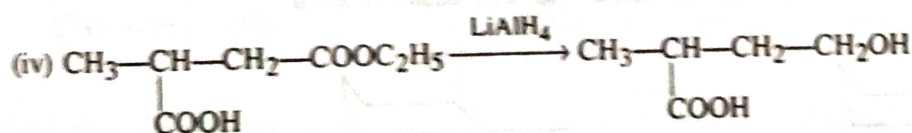
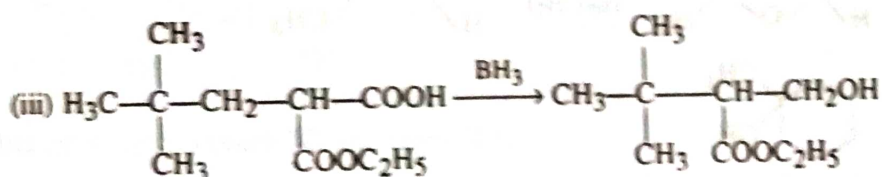
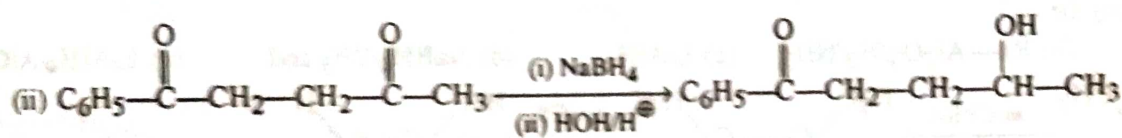
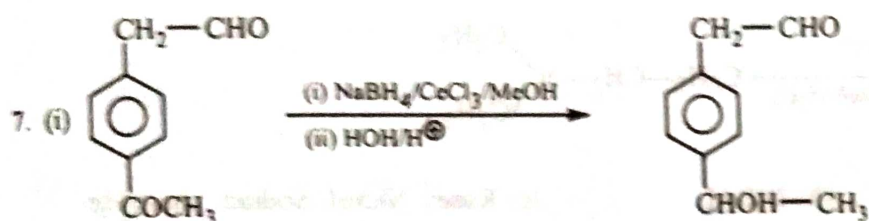
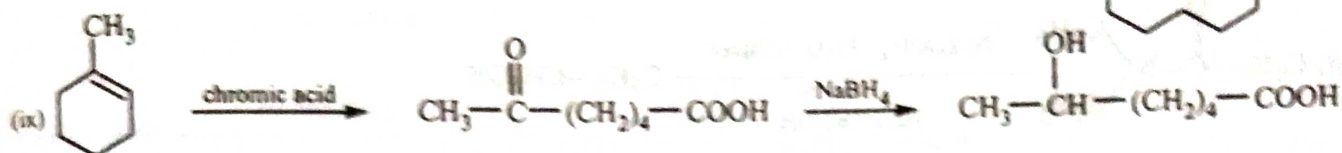
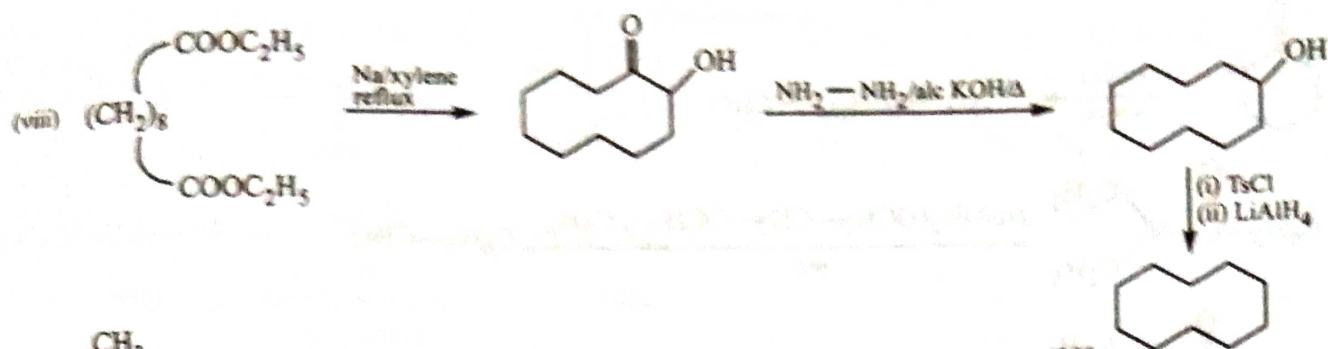


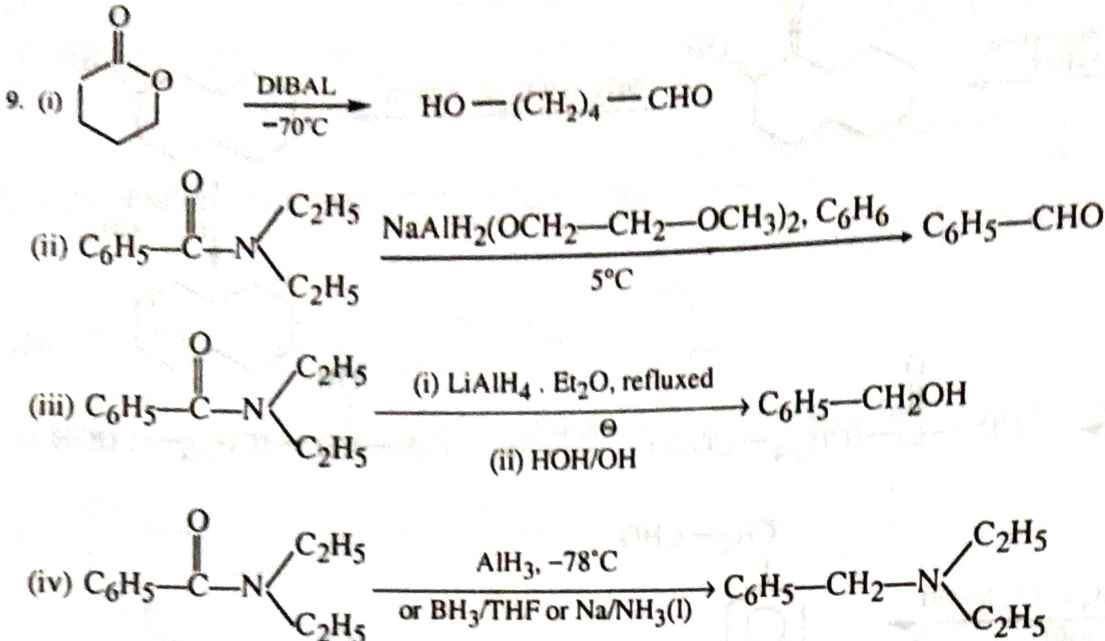
(iii) In this conversion —CO— converts into $\text{—CH}_2\text{—}$ which can be achieved by any one of the following reagents



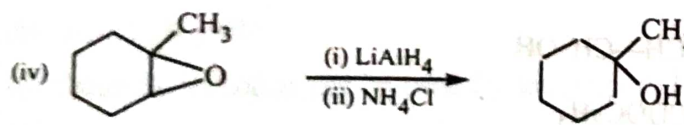
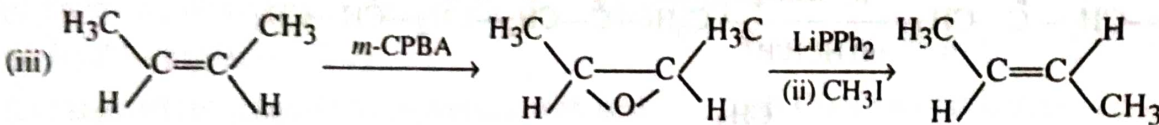
(iv) Any one of the following reagents can be used for the given conversion:



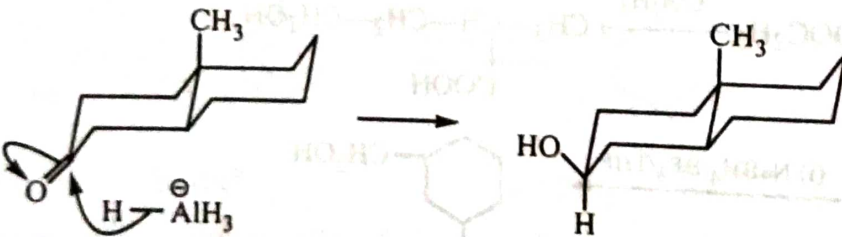




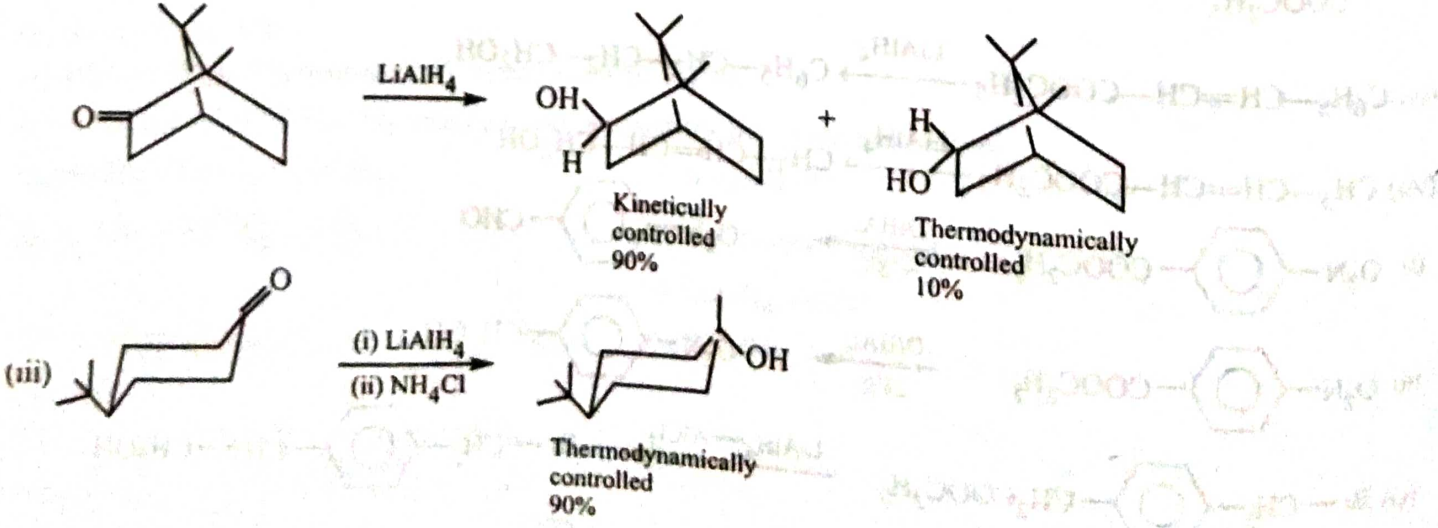
10. (i) Reagents in these reactions may be:
 (a) SnCl2/HCl followed by hydrolysis (b) DIBAL (c) Raney Nickel, Sodium phosphite
- (ii) The reagents may be
 (a) H2, Ni, NH3 (b) Rh-Al2O3/H2/NH3 (c) LiAlH4 (d) NaBH4/BF3 and (e) LiAlH4/AlCl3

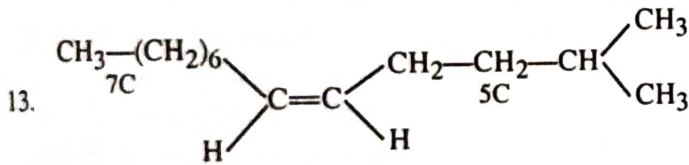
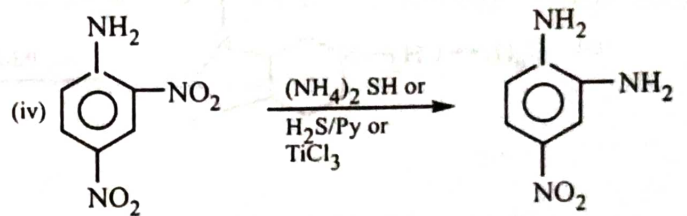
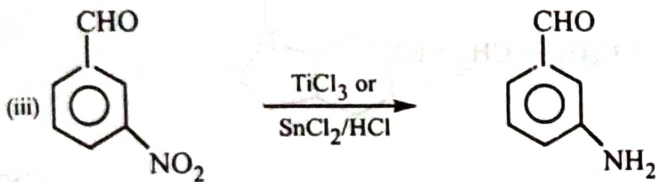
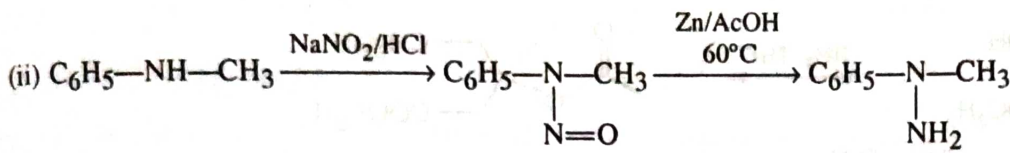
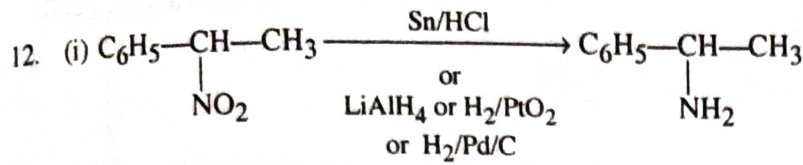
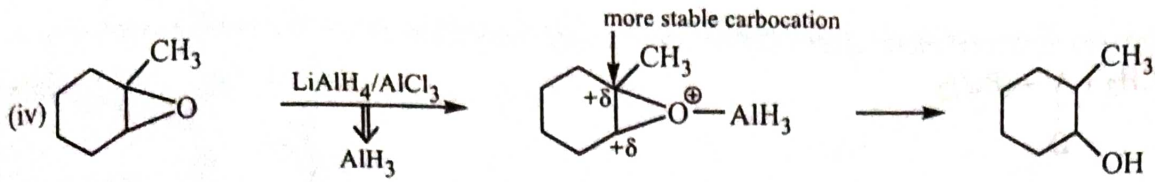


11. (i) LiAlH4 in this compound approaches from the less hindered side, i.e., attack is axial.

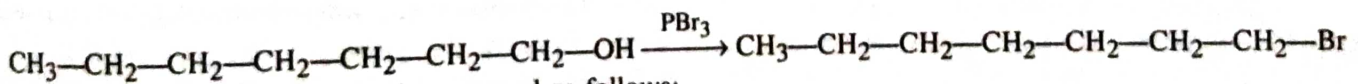
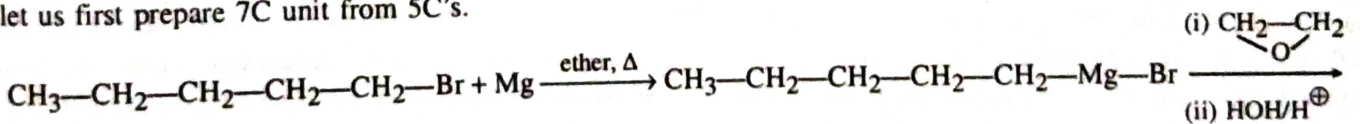


(ii) In this case product is kinetically controlled

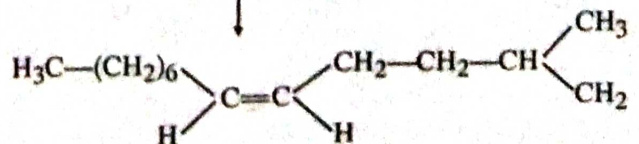
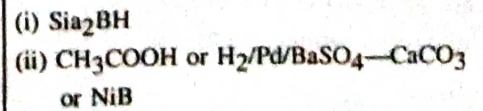
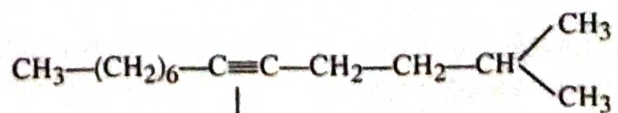
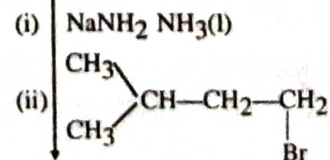
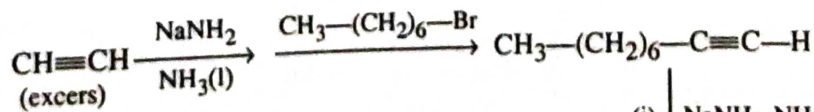


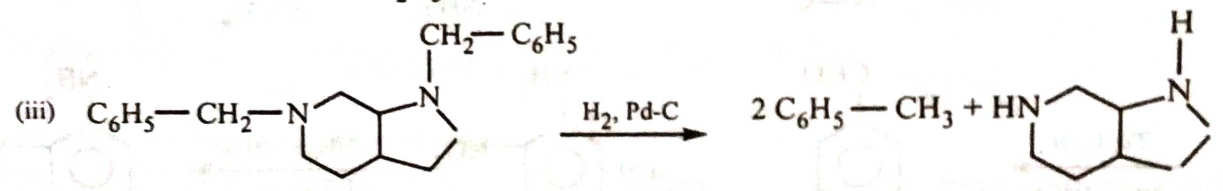
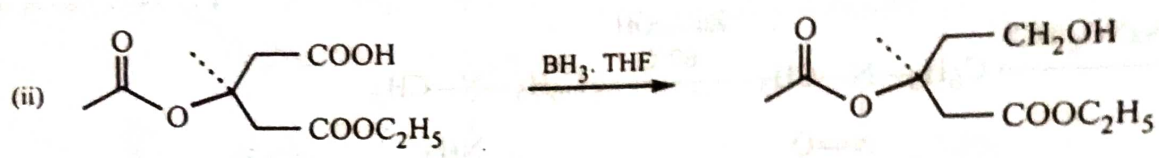
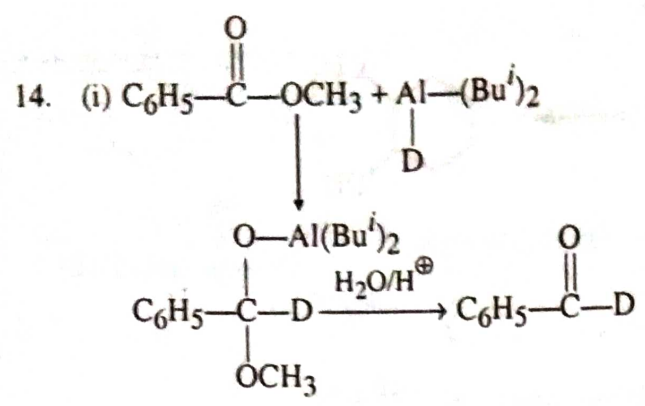


Thus let us first prepare 7C unit from 5C's.



The given compound now can be prepared as follows:





3. REDUCTION

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