

M.Sc. II Sem. REDUCTION. 15-4-20 4-4013

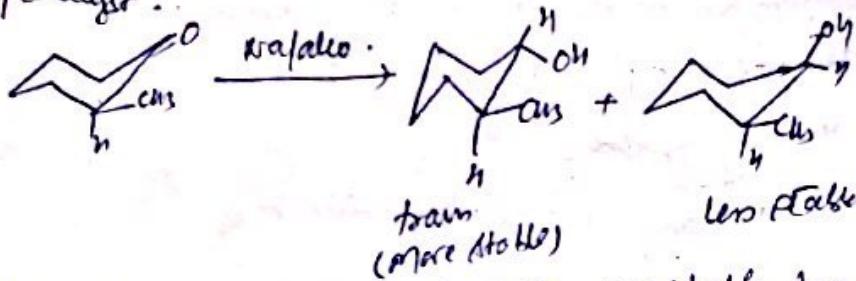
Reduction of Carbonyl Compounds

Distr. by P.K. Sharma (6)

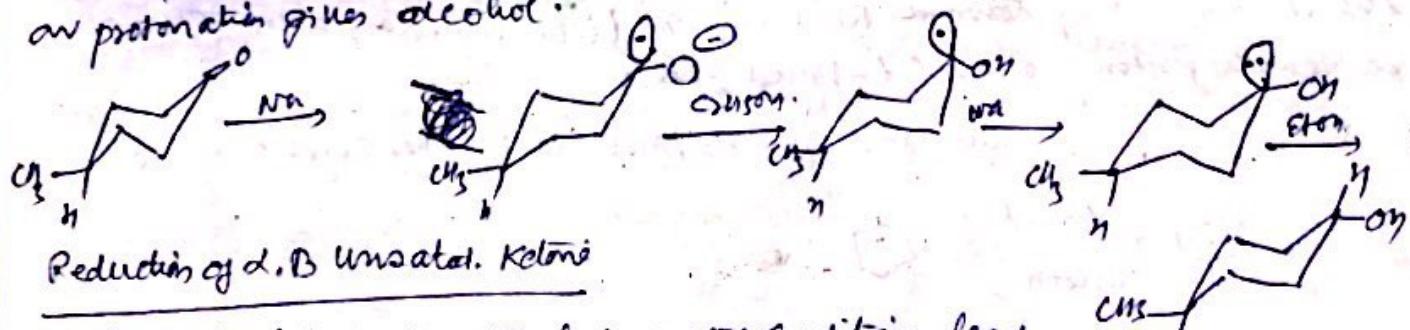
Ketones can be reduced to secondary alcohols by following methods-

- ① By catalytic hydrogenation
- ② With complex hydride
- ③ By reduction by dissolving metals

When cyclic ketones are reduced by Na/alc., the exclusive formation of thermodynamically stable alcohol takes place e.g. on reducing 2-methylcyclohexanone on reduction with Na/alc. gives the more stable trans alcohol in 99% yield. The percentage of trans alcohol decreases sharply on reduction with LiAlH₄ (82%), NaBH₄ (69%) and 7-3% when reduced with H/Catalyst.



Although no mech is universally acceptable, two suggestions are generally given. According to Barton and Robinson (1957) a tetrahedral dianion is formed initially, which adopts equatorial configuration with oxygen and then on protonation gives alcohol.

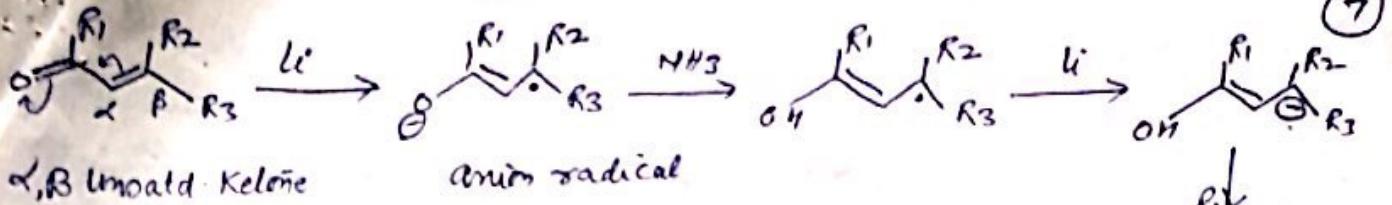


Reduction of d,β Unsaturated Ketone

The reduction under dissolving metal conditions, leads to the enolate of corresponding saturated ketone. Mech. involves following steps -

- ① Formation of anion radical after uptake of one electron
- ② Anion radical abstracts a proton from ammonia or added alcohol
- ③ The addition of another electron leads to the enolate anion
- ④ When a stronger acid is not present, this anion retains its -ve charge and keeps adding another electron and thus no further red "can occur".

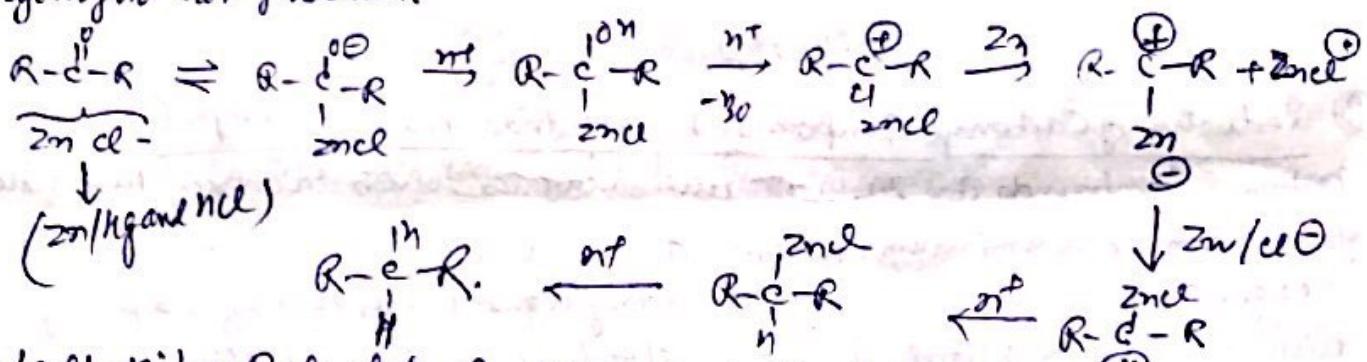
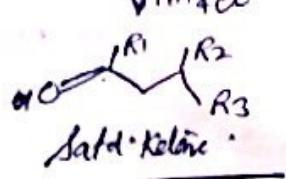
Acidification with NH₄Cl, gives the saturated ketone.



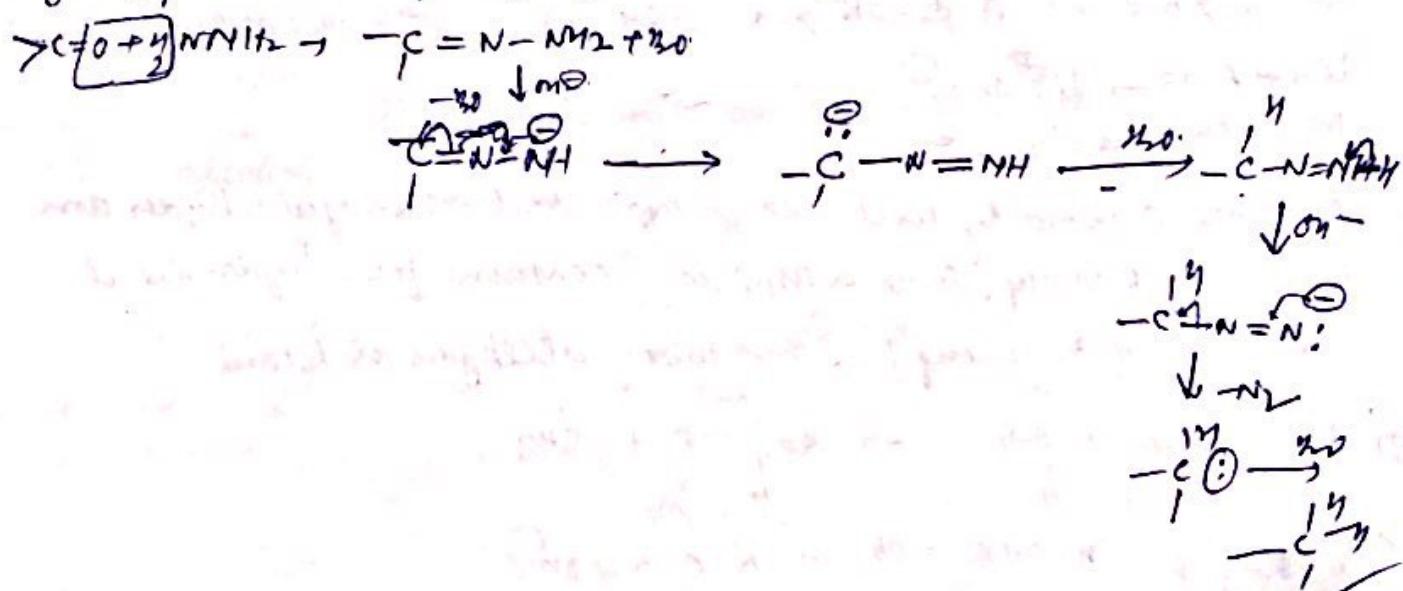
Reductive deoxygenation of carbonyl groups

Various Carbonyl Compounds are reduced to methylene Compounds by a no. of methods. Some of them are -

(1) Clemmensen's method. Zn-Hg / HCl, Amalgamated zinc and HCl is a classical reagent for conversion of carbonyl groups to methylene group. mech may involve carbon-zinc bond at the metal surface. Transfer of electrons from metal surface to carbonyl carbon atom has been suggested. Conc acid helps about initial protonation. Amalgamated zinc reacts w/ hydrogen over voltage so that molecular hydrogen not generated.

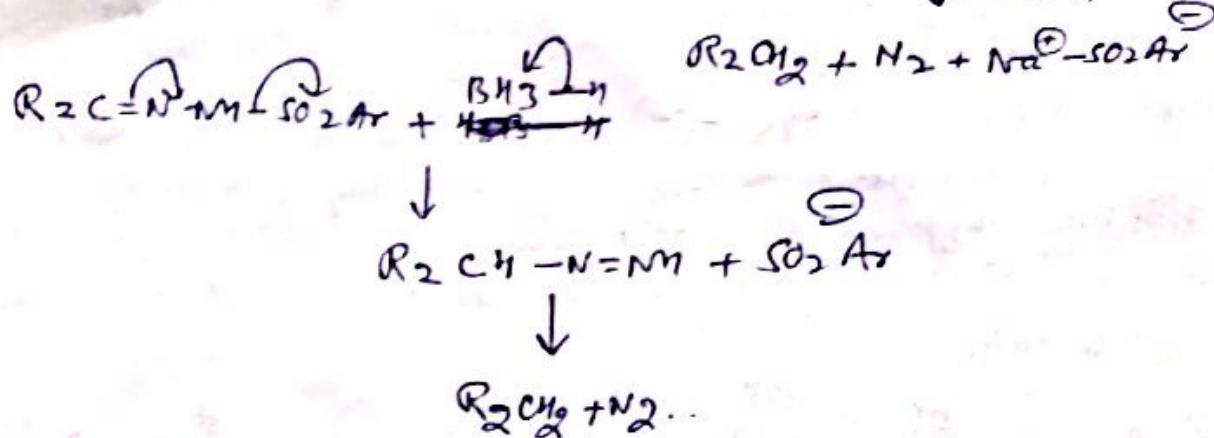


(2) Wolff-Kishner Reduction: In this method the substrate is heated with hydrazine hydrate and a base (NaOH or KOH). The Huang-Minlon-modification in which the reaction is carried out in refluxing diethylene glycol has completely replaced the original procedure.



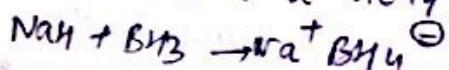
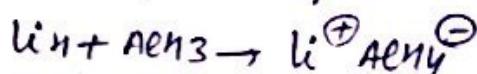
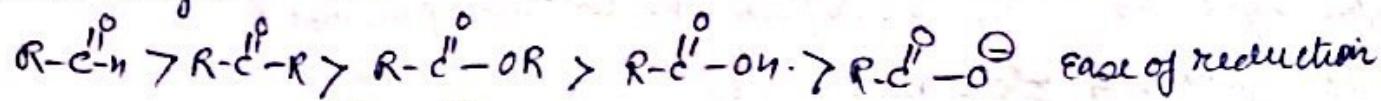
③ Tolyl-hydrazone method

A carbonyl compound reacts with Toluene-p-sulphoxide hydrazone to give corresponding Tolyl-hydrazone, which on reduction with NaBH₄ converts the carbonyl group to methylene group. The mech. in vitro, formation of diimide as in Wolff-Kishner method.

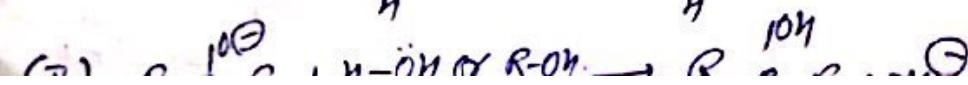
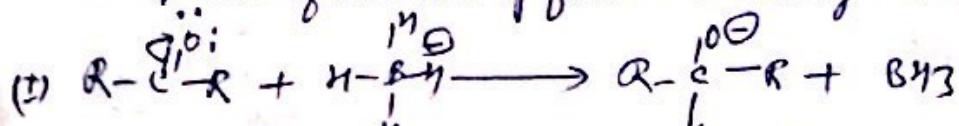


④ Reduction of Carbonyl Compounds by Hydride Transfer reagents

Carbonyl Compounds are reduced with reagents which transfer hydride from boron or aluminium. NaBH₄ and LiAlH₄ are most widely used reagents. NaBH₄ is a mild reducing agent which reacts rapidly with aldehydes or ketones, but only slowly with esters. LiAlH₄ is a more powerful hydride donor reagent, which reduces esters, acids, amides and nitriles along with aldehydes and ketones. But none of these reagents react with carbon-carbon double bonds.

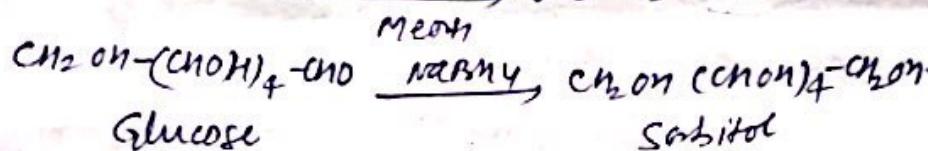
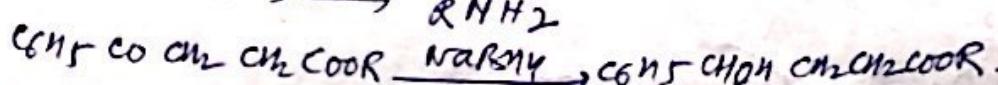
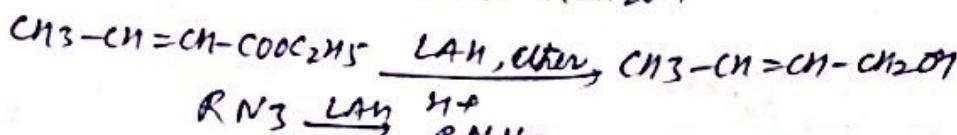
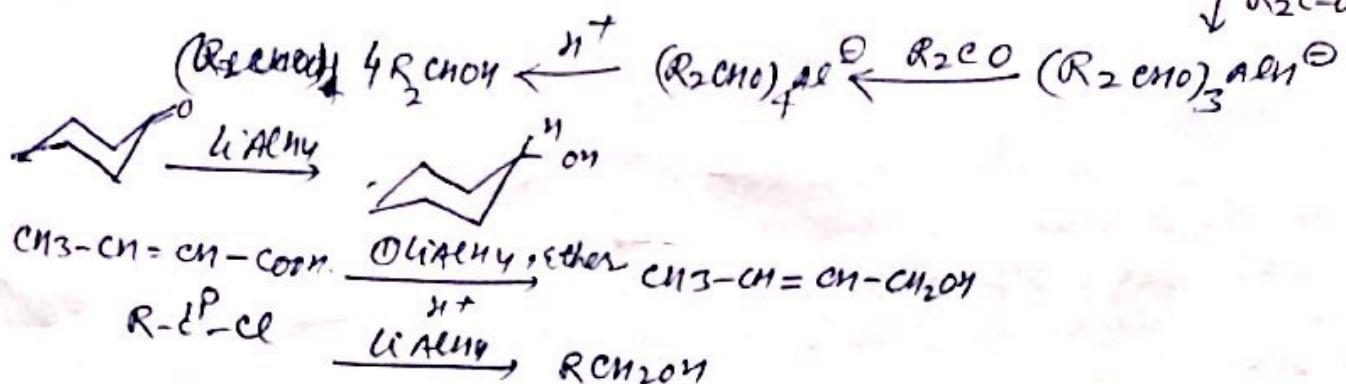
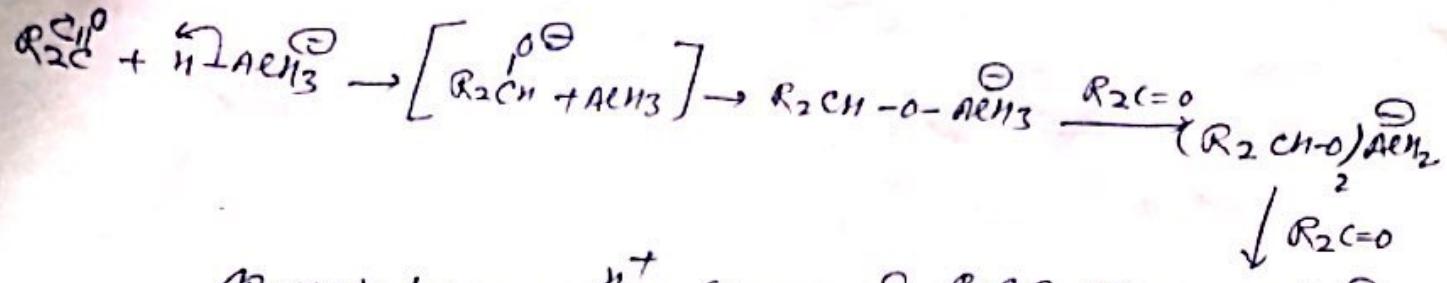


The most commonly used reagent for reduction of aldehydes and ketones is NaBH₄. Since a BH₄⁻ ion contains four hydrides it is capable of reducing four molecules of aldehydes or ketones.



(9)

LiAlH_4 reduction are carried out in a protic solvent, as it reacts violently with water. NaBH_4 reactions can be carried out in water or alcohol solution.



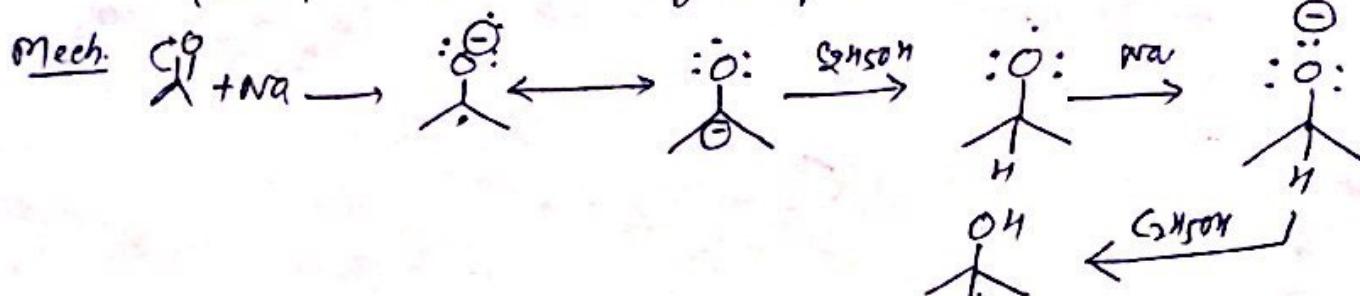
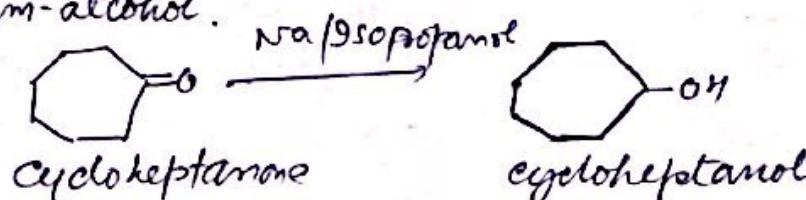
Sorbitol

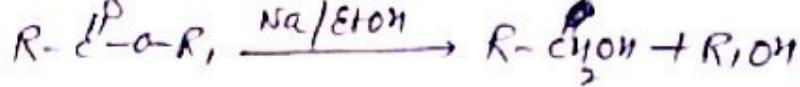
Reduction by dissolving metals.

These reductions take place by ~~diffusing~~ transfer of electrons from the metal and a proton donor which may be water, alcohol or an acid. 1st group metals such as Li or Na give up their outer shell electron easily and dissolve in solvents such as NH_3 (liq.) or alcohol.

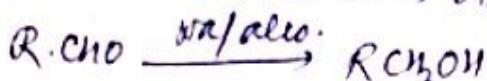
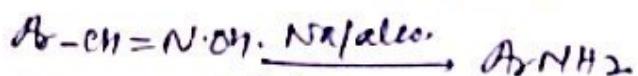
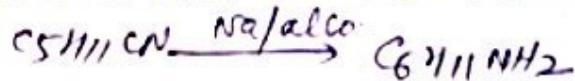
Sodium - alcohol.

The easiest method of reducing ketones is with Sodium-alcohol.

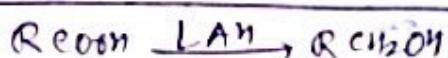




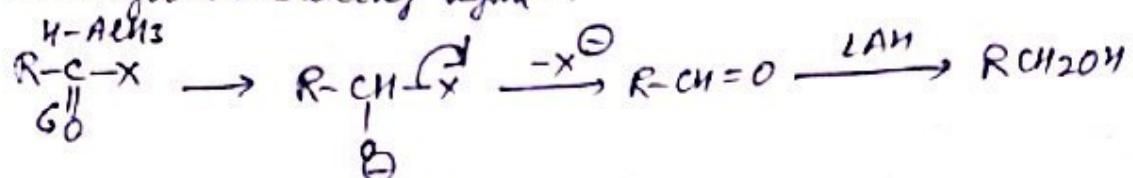
Na/alcohol also reduces nitriles oximes and aldehydes.



Reduction of acids and their derivatives.

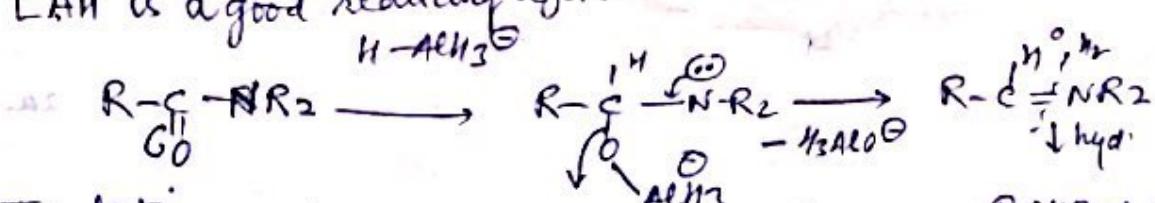


Carboxylic acids are easily reduced by LiAlH₄ to primary alcohol. The reaction does not stop at the aldehyde stage. Other hydrides have also been used but not NaBH₄. Catalytic hydrogenation is not effective. Borane is also good reducing agent.



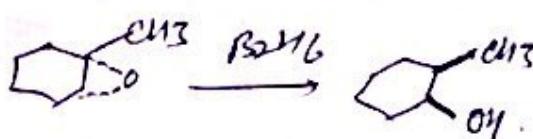
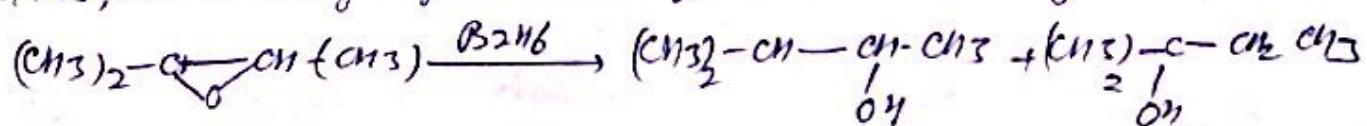
(X = OH, OR, OCOR or halogen)

Reduction of Amides. Amides, however, give amines, since NR₂ is not a good leaving group. The reaction involves an aldehyde-ammonia derivative. LAH is a good reducing agent.



The tertiary amides are also reduced to aldehydes with LiAlH₄ at low temperature.

Reduction of nitiles. Reduction of epoxides with Borane is important. Reduction gives mainly less substituted alcohol, in contrast to reduction with LiAlH₄. During the redn of 1-alkyl cycloalkene epoxides, the 2-alkyl cycloalkans formed, are mainly cis-alcohols.



75%

25%