Study Material
M.Sc. Sem IV

Prof. Abha Bishnoi

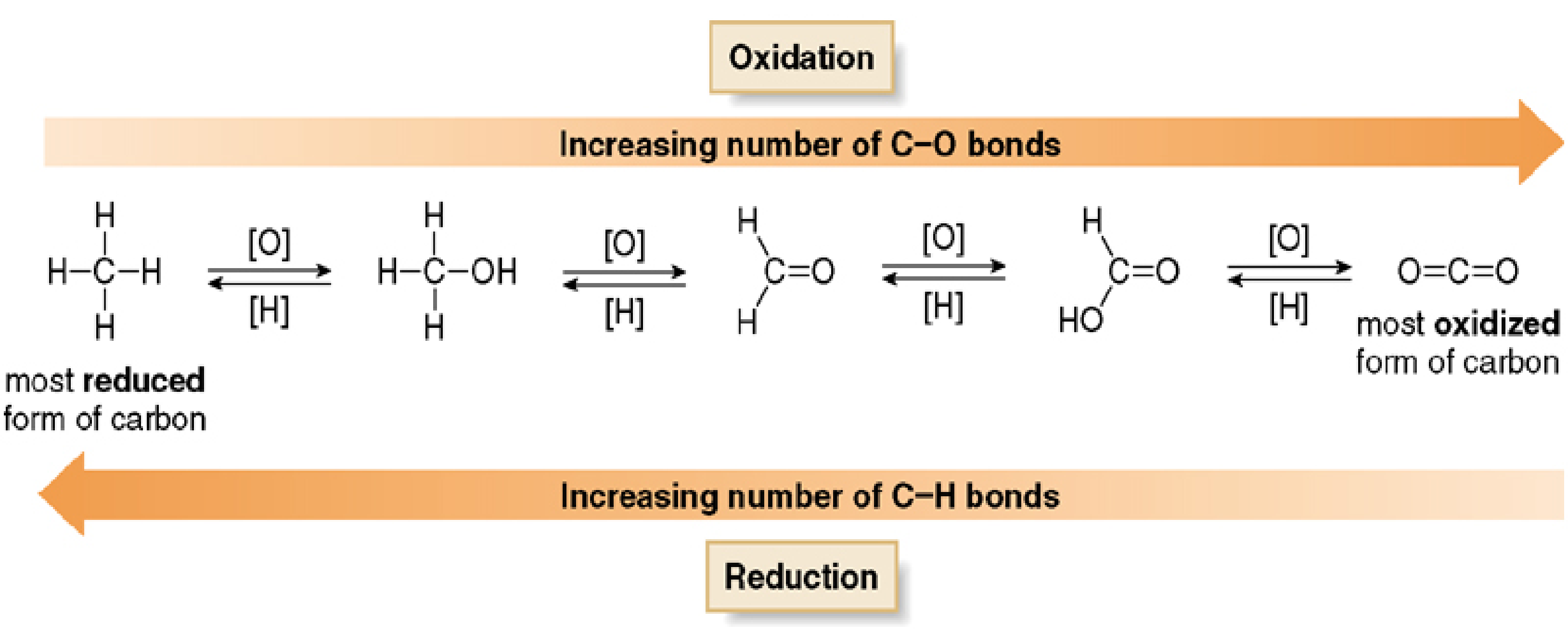
Reduction

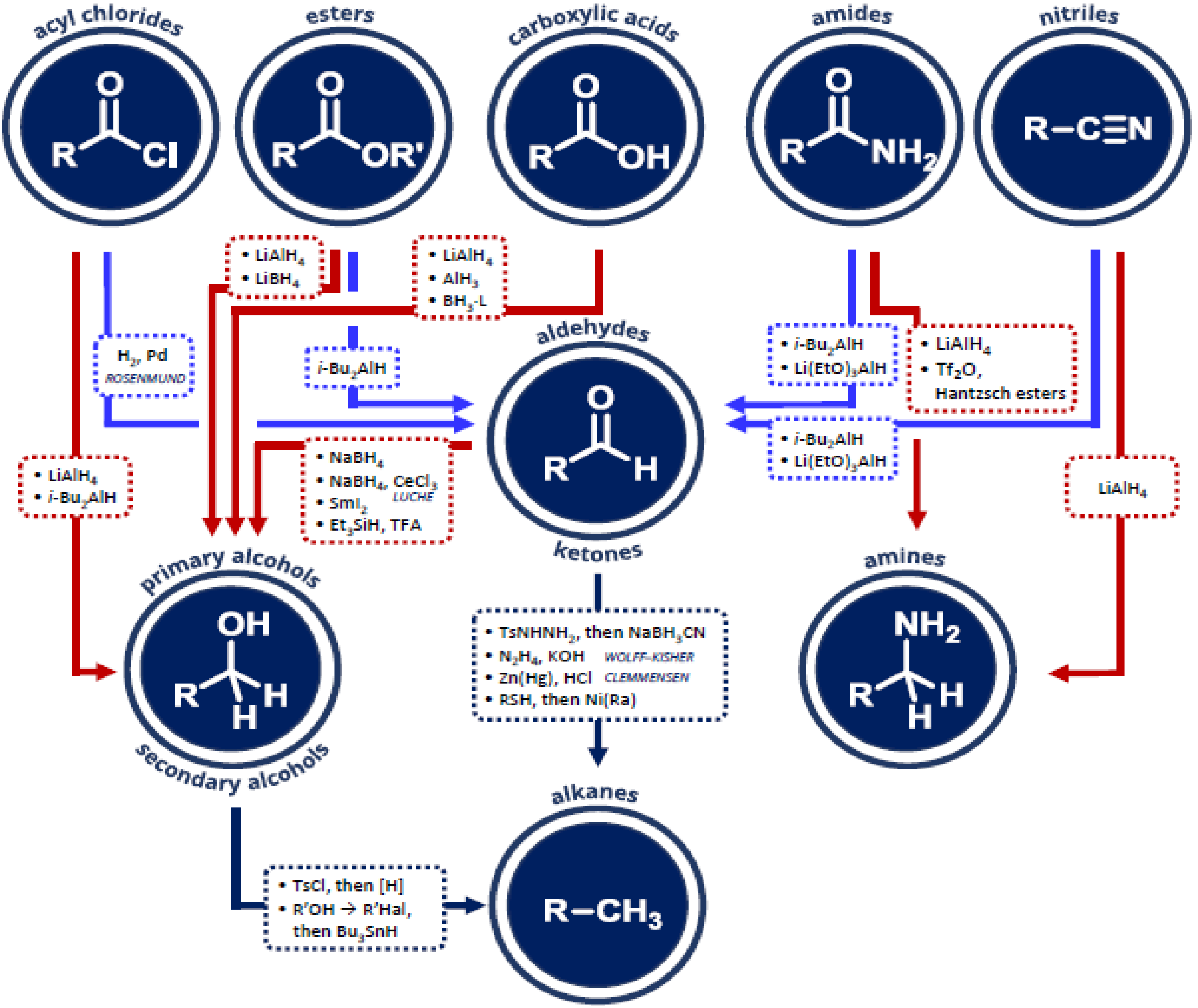
Oxidation and Reduction

Introduction

- oxidation results in an increase in the number of C—Z bonds (usually C—O bonds) or a decrease in the number of C—H bonds.
- reduction results in a decrease in the number of C—Z bonds (usually C—O bonds) or an increase in the number of C—H bonds.

A general scheme for the oxidation and reduction of a carbon compound





acyl chlorides

esters

carboxylic acids

amides

nitriles

- H_2, Pd
  ROSENMUND

- LiAlH$_4$
- LiBH$_4$

- LiAlH$_4$
- AlH$_3$
- BH$_3$·L

- *i*-Bu$_2$AlH

- *i*-Bu$_2$AlH
- Li(EtO)$_3$AlH

- LiAlH$_4$
- Tf$_2$O, Hantzsch esters

- *i*-Bu$_2$AlH
- Li(EtO)$_3$AlH

aldehydes

ketones

- LiAlH$_4$
- *i*-Bu$_2$AlH

- NaBH$_4$
- NaBH$_4$, CeCl$_3$ LUCHE
- SmI$_2$
- Et$_3$SiH, TFA

LiAlH$_4$

primary alcohols

secondary alcohols

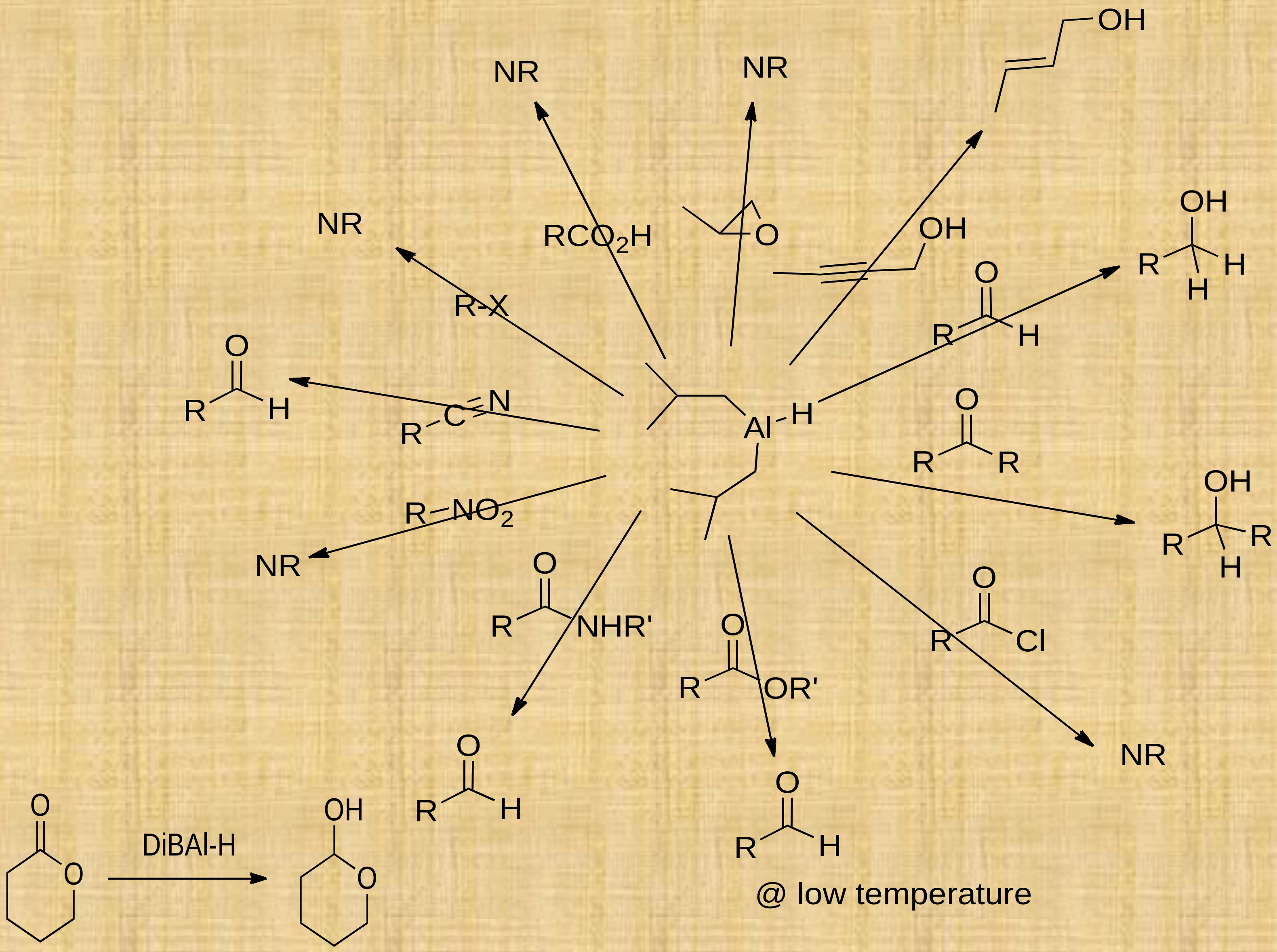
amines

- TsNHNH$_2$, then NaBH$_3$CN
- N$_2$H$_4$, KOH WOLFF-KISHER
- Zn(Hg), HCl CLEMMENSEN
- RSH, then Ni(Ra)

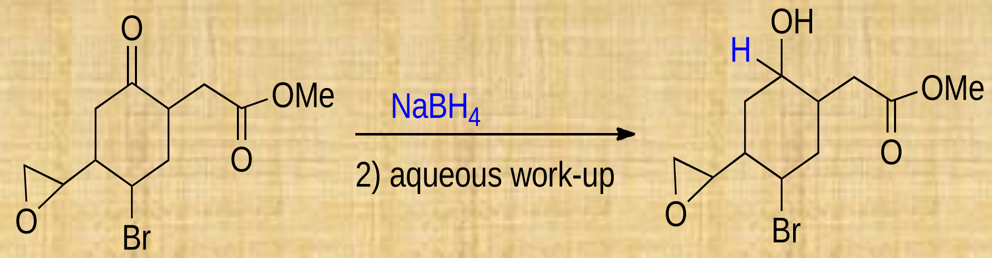
alkanes

- TsCl, then [H]
- R'OH → R'Hal, then Bu$_3$SnH

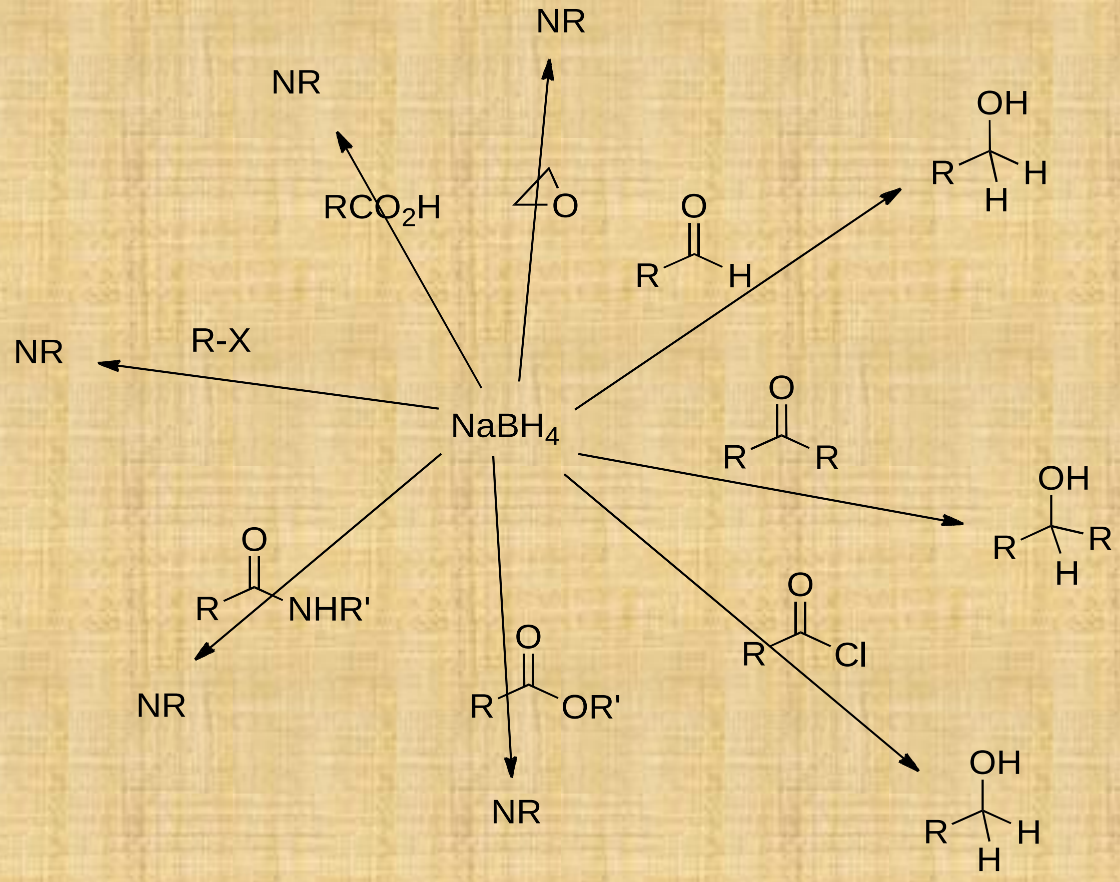
Reductions with DiBAL-H



Sodium Borohydride Reductions in Synthesis

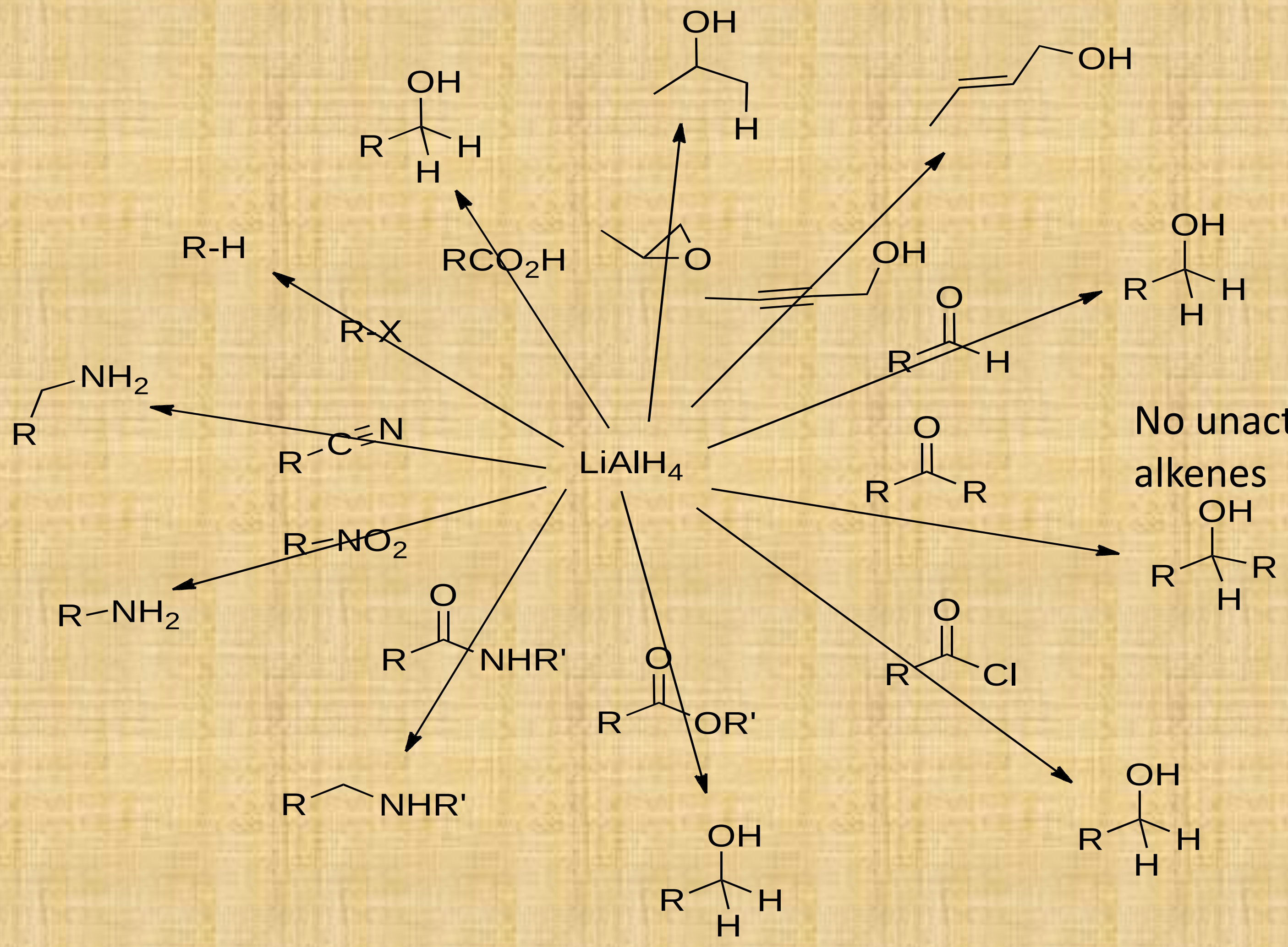


Less reactive;
More selective
Than LiAlH$_4$



Won't reduce esters, amides, halides, epoxides, carboxylic acids

Lithium Aluminum Hydride



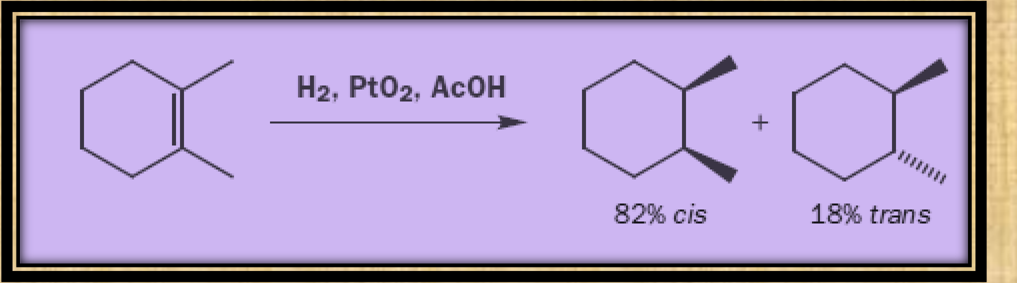
No unactivated alkenes

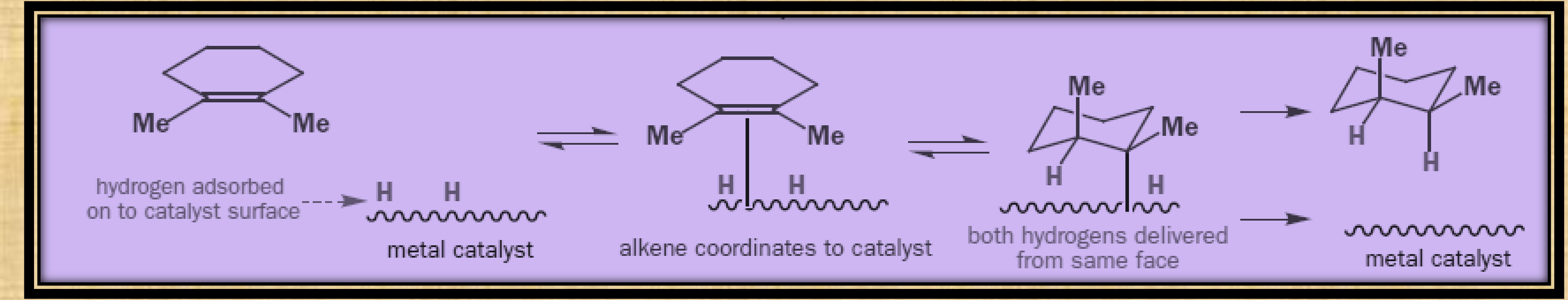
Strong reducing agent. Not very selective

Reduction of hydrocarbon(reduction of alkenes)

(1)Catalytic Hydrogenation

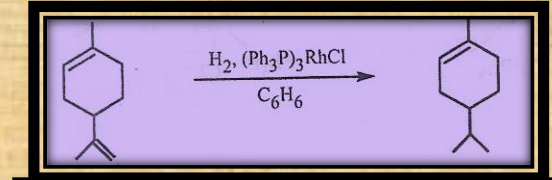
(a) Heterogeneous hydrogenation

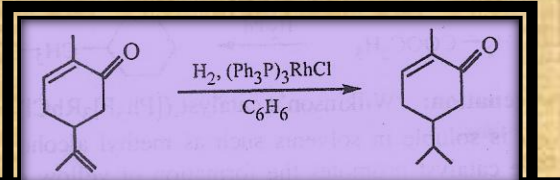


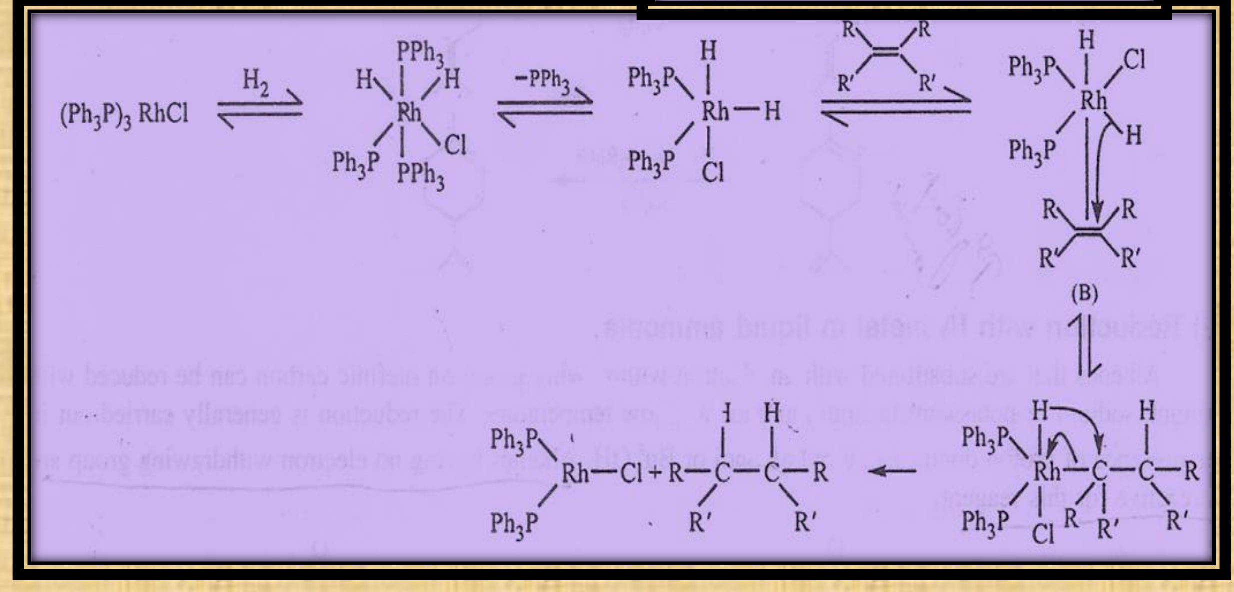


Homogeneous hydrogenation

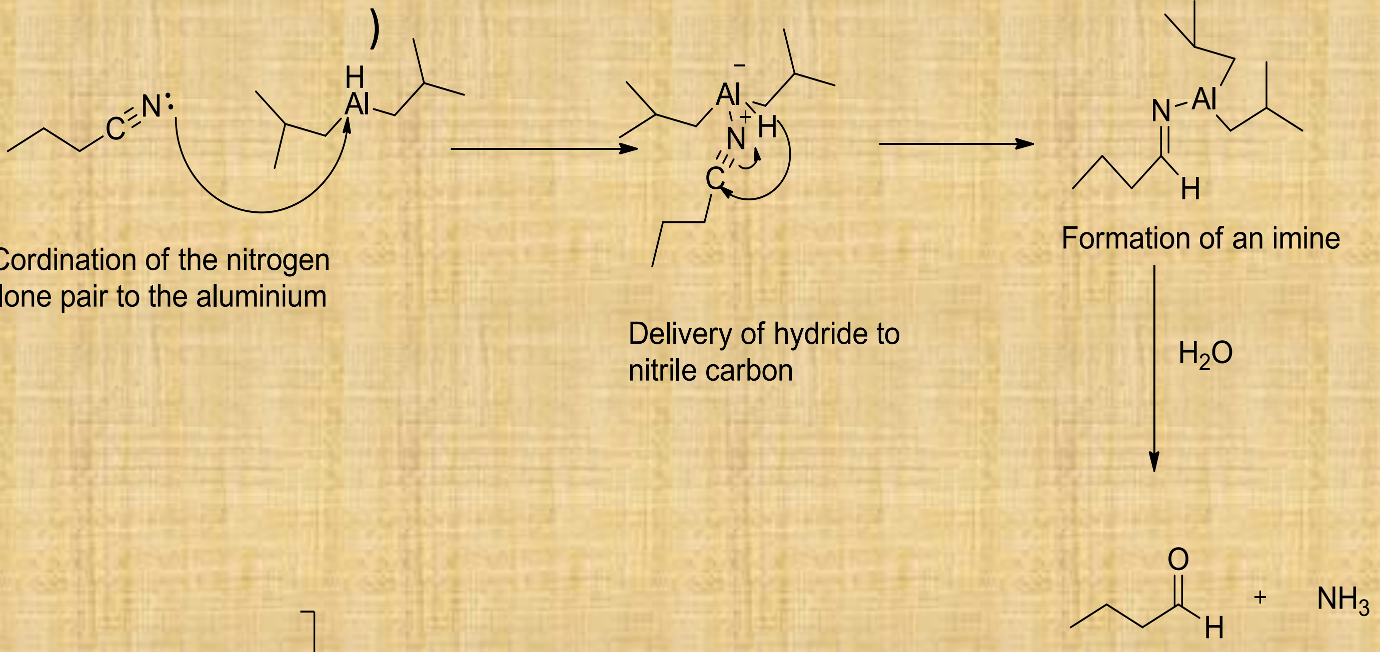
- Wilkinson's catalyst is useful homogeneous catalyst of alkene.
- Mono-and disubstituted double bonds are reduced much more rapidly than tri- and tetrasubstituted one, permitting the partial hydrogenation of compounds.







Reduction of nitriles to aldehyde



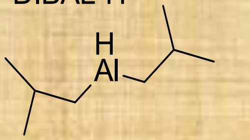
Cordination of the nitrogen lone pair to the aluminium

Delivery of hydride to nitrile carbon

Formation of an imine

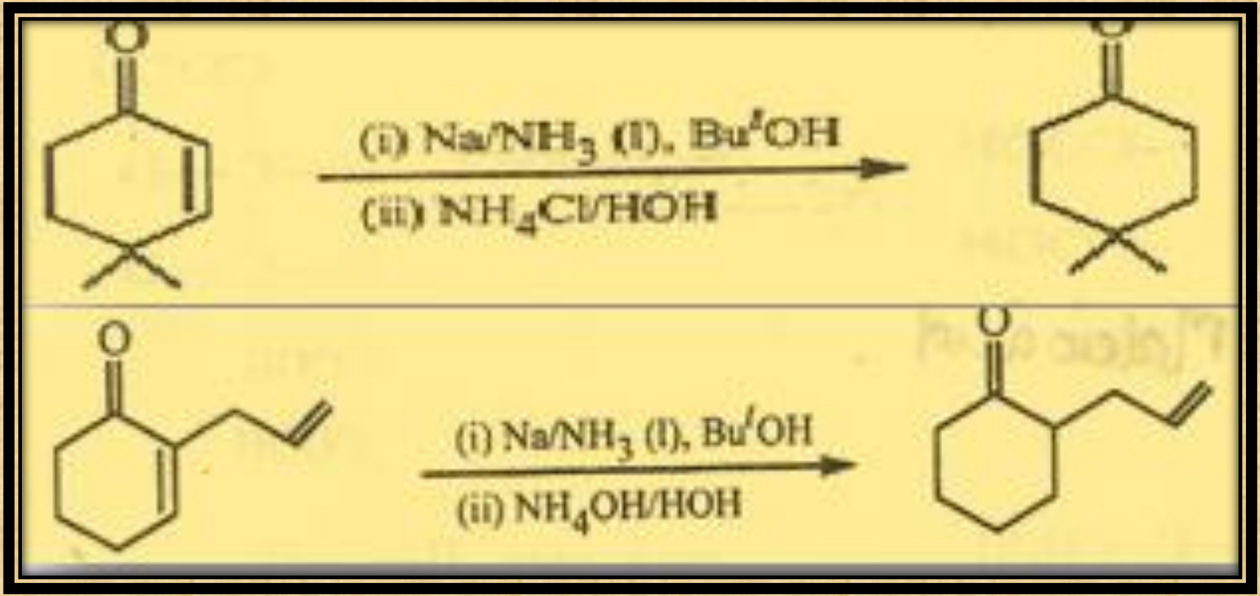
Hydrolysis gives an aldehyde

Diisobutylaluminum hydride
DIBAL-H

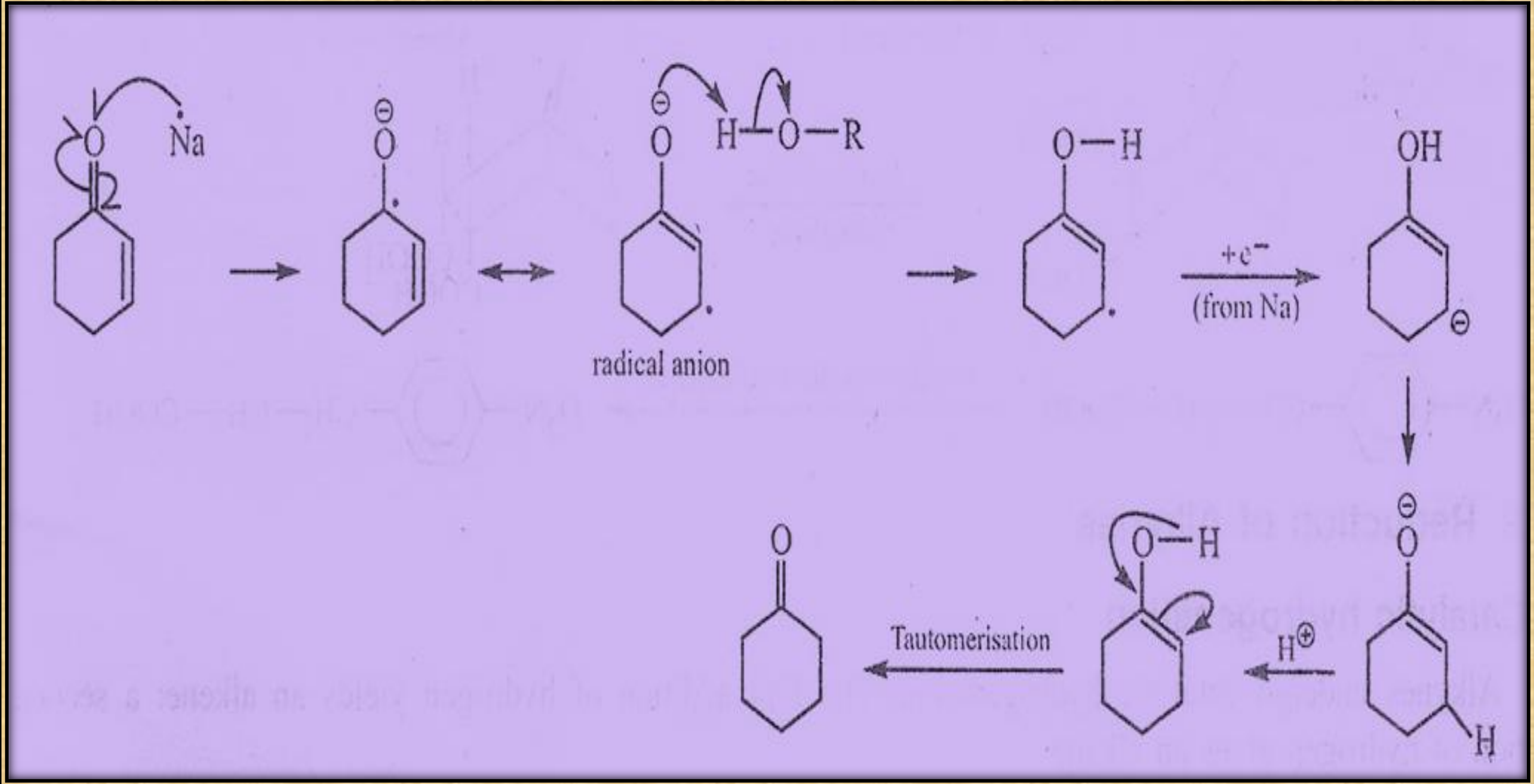


Reduction with IA metal in liquid ammonia

- Alkenes substituted with electron withdrawing group on olefinic carbon reduced with sodium in liquid ammonia.

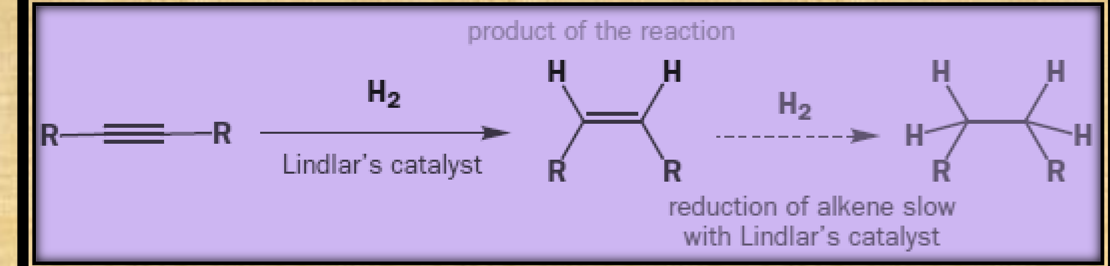


Mechanism for reduction with IA metal in liquid ammonia

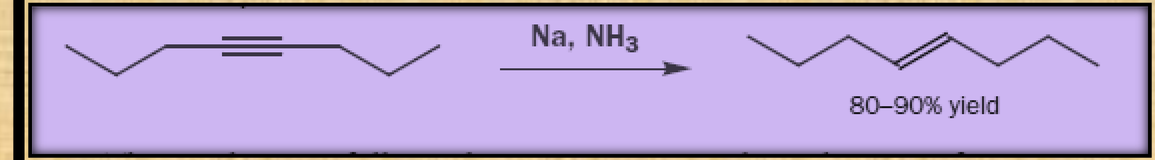


Reduction of alkyne

- Alkyne undergo catalytic hydrogenation to give alkane.
- Non termial alkyne in the presence of Lindlar’s catalyst is converted into cis alkene

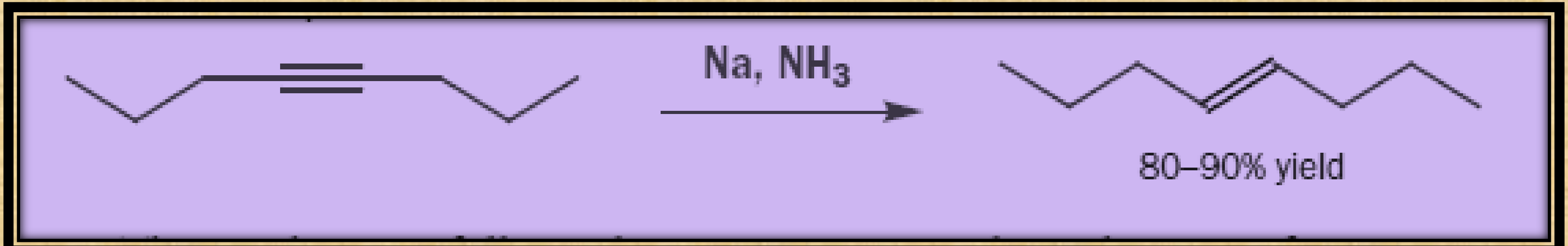


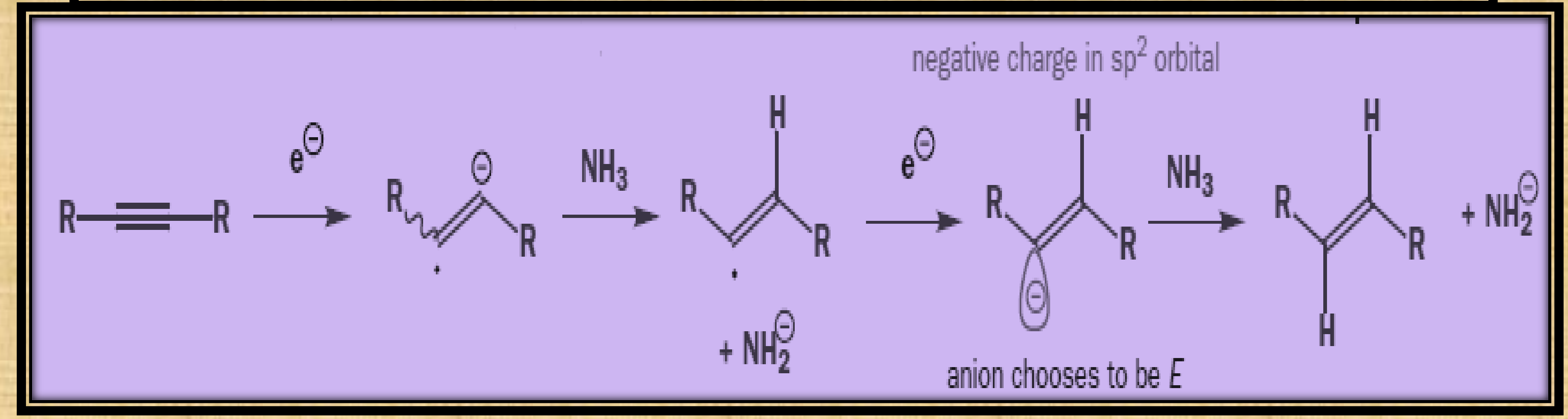
Lindlar’s catalyst =
Pd, $CaCO_3$, $Pb(OAc)_2$



Reduction of alkyne with IA metal in liquid ammonia

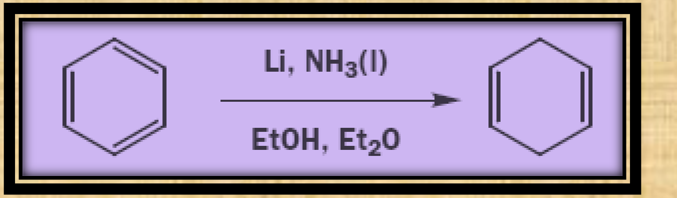
- Nonterminal alkyne is convertedinto trans alkene with a solution of an alkali metal in liquid ammonia.



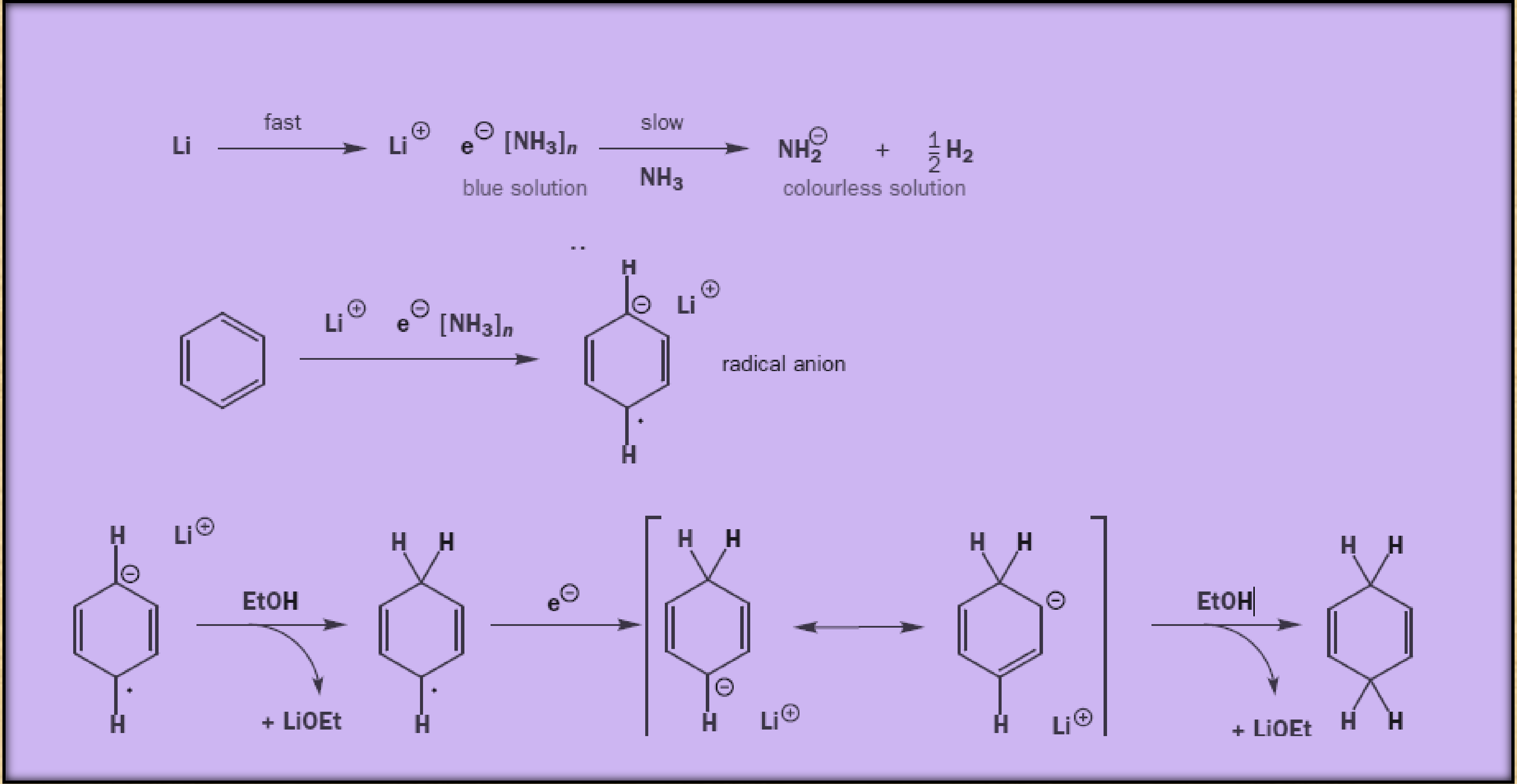


Reduction of aromatic ring “Birch reduction”

- Birch reduction is partial reduction of aromatic ring.
- Aromatic rings are reduced by Li in liq ammonia in alcohol.
- 1,4- addition of hydrogen takes place.
- Product is non-conjugated cyclohexadienes.

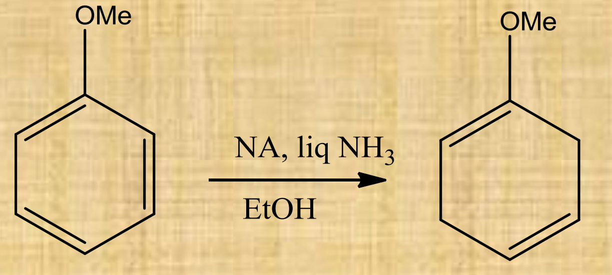


Mechanism


Li
fast
Li⊕ e⊖ [NH3]n
blue solution
slow
NH3
NH2⊖ + ½H2
colourless solution
Li⊕ e⊖ [NH3]n
radical anion
Li⊕
EtOH
+ LiOEt
e⊖
Li⊕
Li⊕
EtOH
+ LiOEt

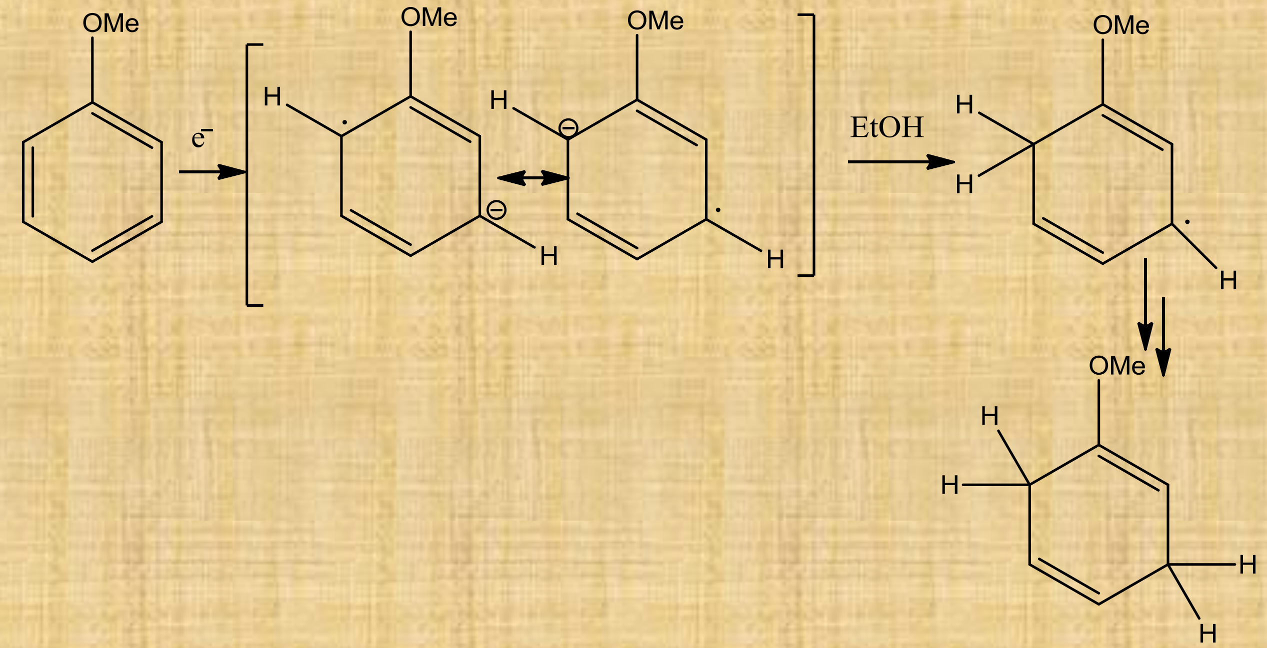
Reduction of substituted aromatic compounds with IA metal in liquid ammonia

- The birch reduction of a benzenoid comp. having an electron donating group (eg-methoxy), should lead, as it indeed does, to the 1-substituted 2, 5-dihydrobenzenes. (ortho, meta reduction) because it stabilise electron density at ortho and meta position.

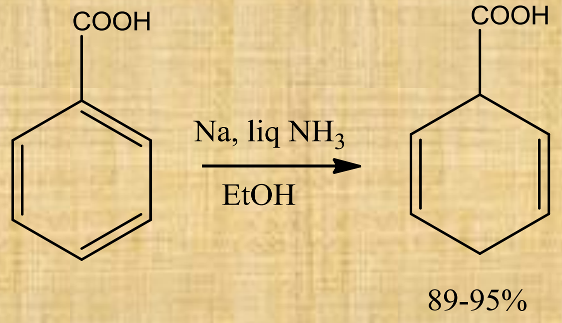


major product

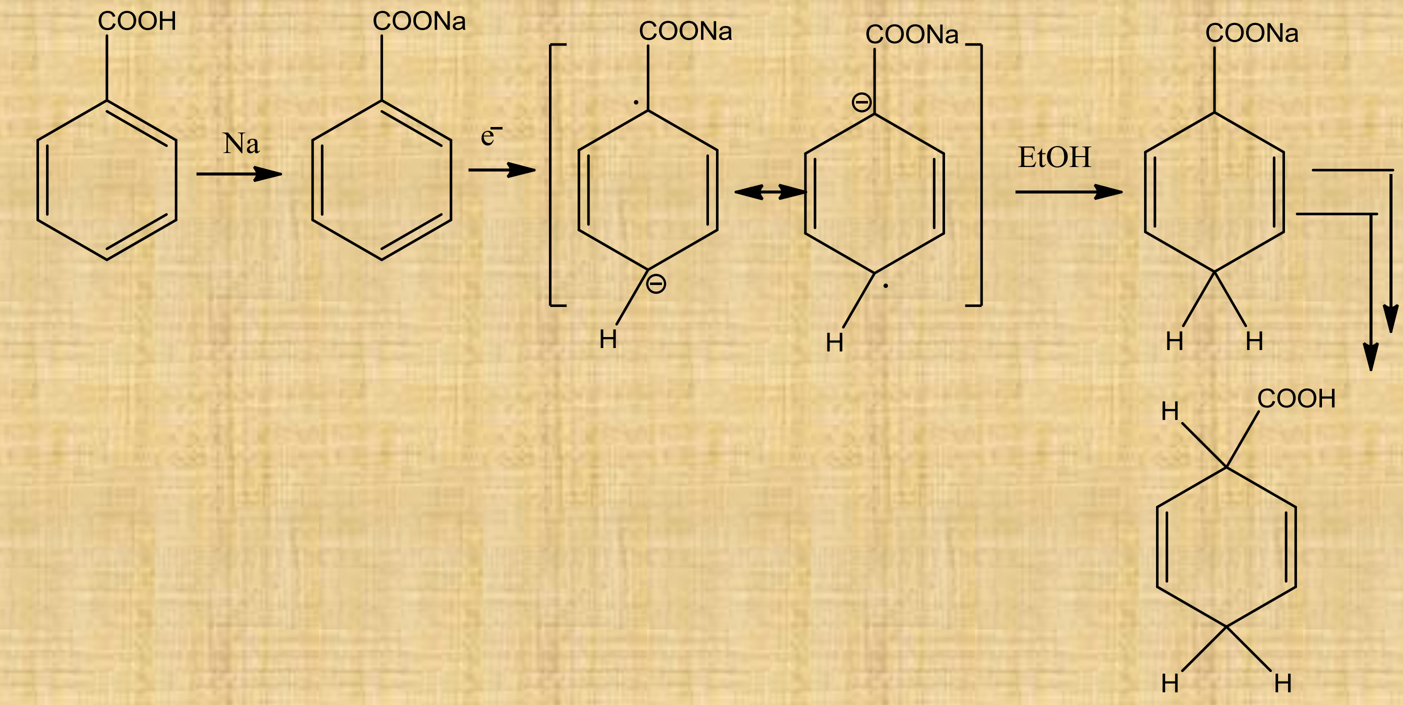
Mechanism-



- Electron withdrawing group(eg- carboxylic acid) gives 1-substituted 1, 4-dihydro benzenes (ipso, para reduction) because it stabilise electron density at ipso position.

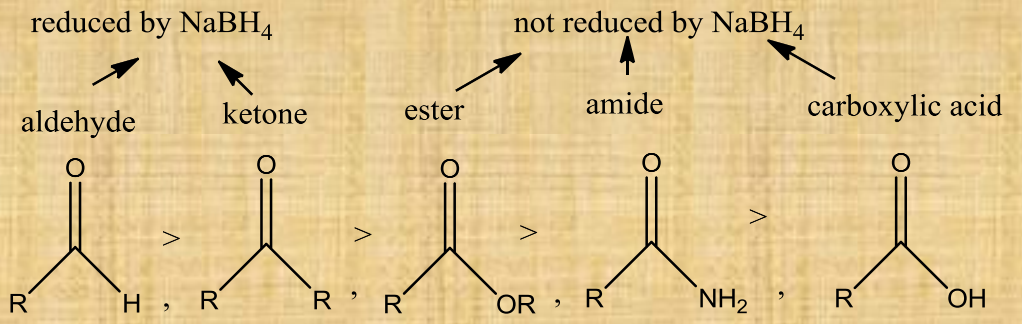


Mechanism -



Reduction of aldehydes and ketones

- Sodium borohydride reduces aldehydes and ketones to alcohols.
- It reduces the compounds only in protic solvents.
- It is a more selective reducing agent as it reduces the nitroketones to nitroalcohols whereas $LiAlH_4$ reduces the nitro group as well.



reduced by $NaBH_4$

not reduced by $NaBH_4$

aldehyde

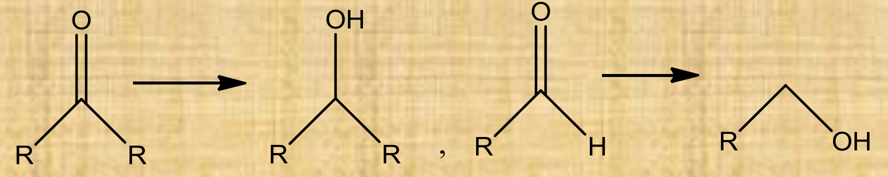
ketone

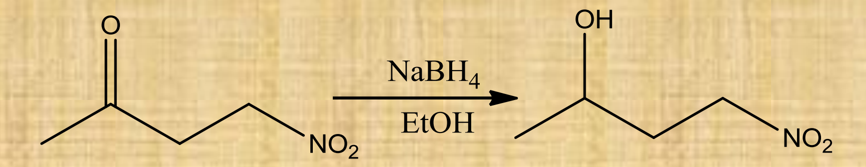
ester

amide

carboxylic acid

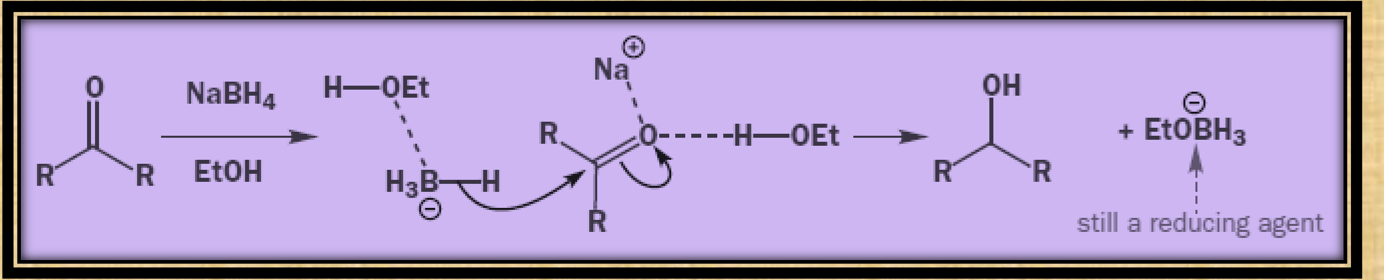
all can be reduced by $LiAlH_4$





Mechanism

- Importance of the reaction is transfer of hydrogen atom with two electrons (hydride transfer without involving hydride ion.



Reduction of α,β-unsaturated carbonyl compound

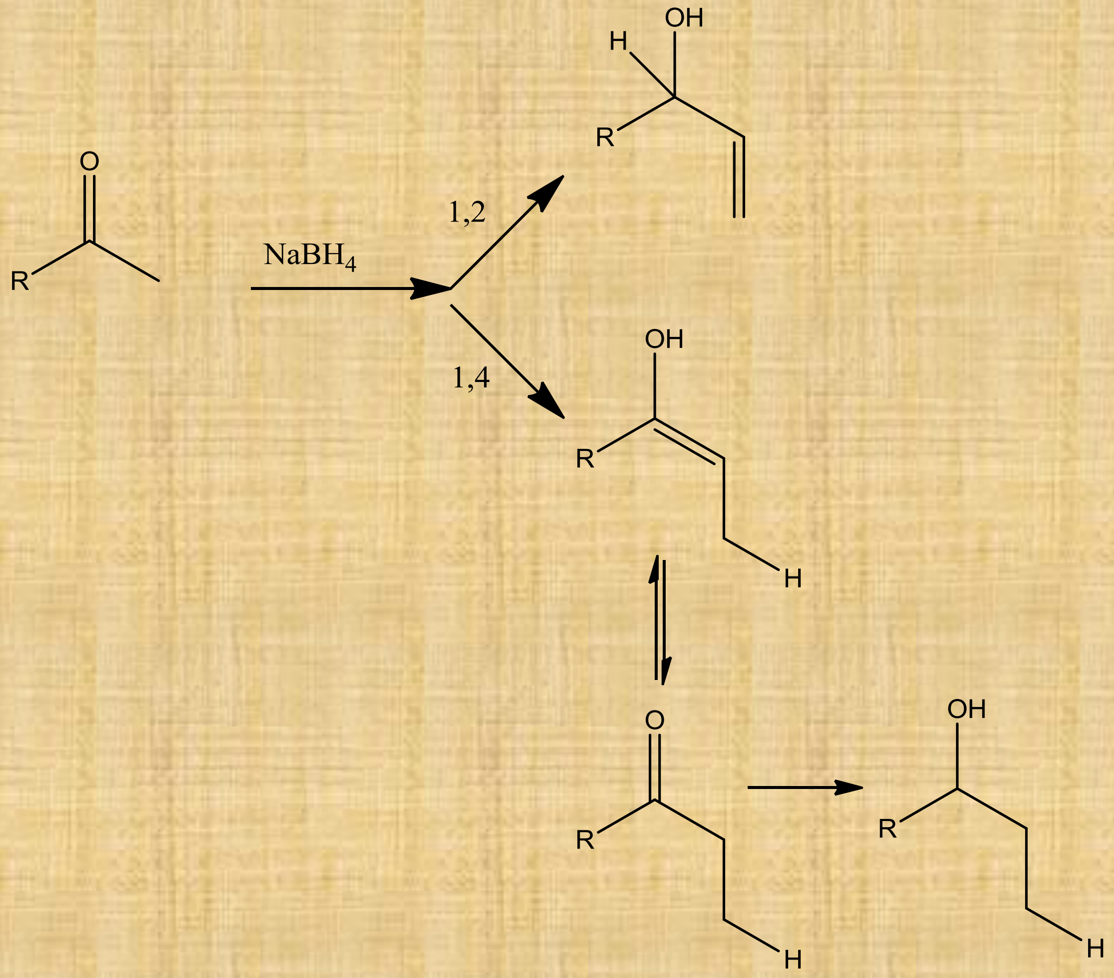
Red of cyclopentanone by $NaBH_4$ can lead to two products A and B. The allylic alcohol A derives from 1,2-attack of hydride onto ketone. While fully reduced comp originates from 1,4-attack tautomerism of the enol and further red of the ketone product.

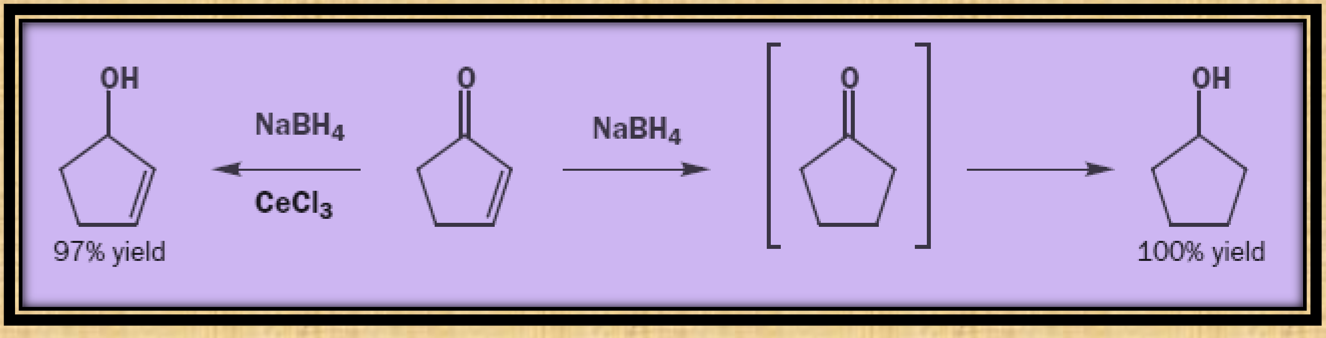
Reduction of cyclopenten-3-one with sodium borohydride in alcohol produces cyclopentanol.

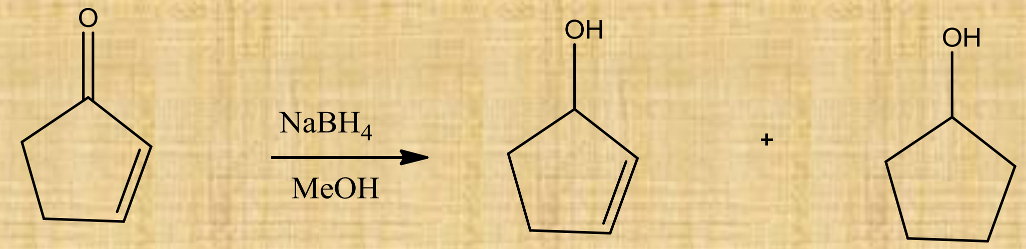
Product is formed by the initial conjugate addition of hydride to the β –carbon atom, followed by ketonization of the enol product and reduction of the resulting saturated ketone.

Luche reduction- Reduction of cyclopenten-3-one in the presence of cerric chloride yields the unsaturated alcohol.

Mechanism



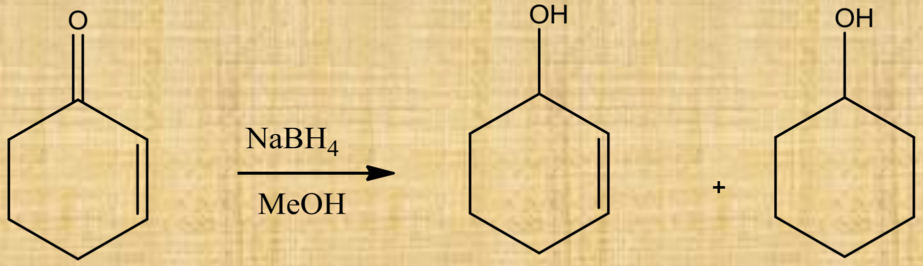




A
allylic alcohol
1,2-attack

B
1,4-attack

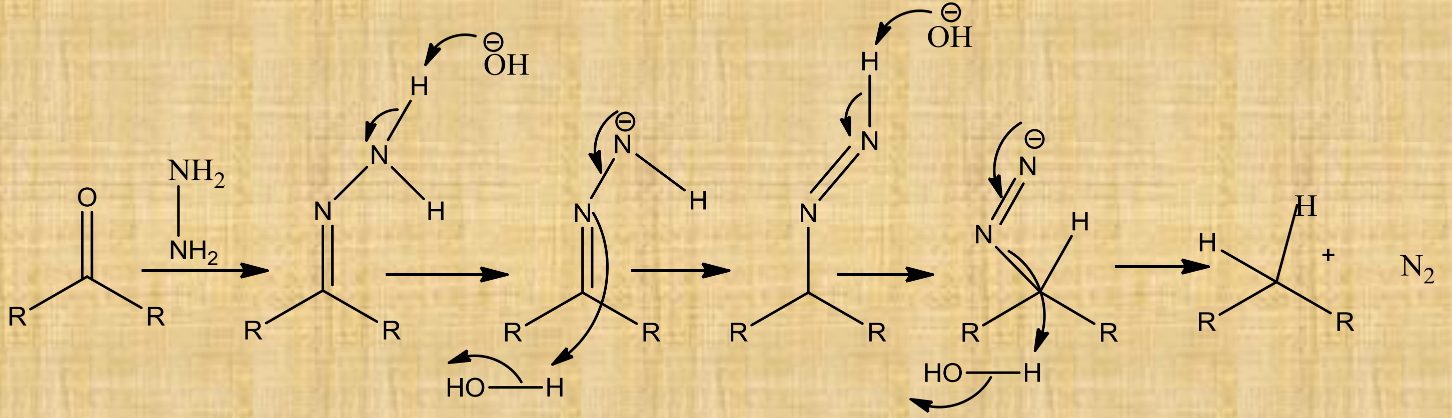
0:100 No $CeCl_3$
97:3 with $CeCl_3$

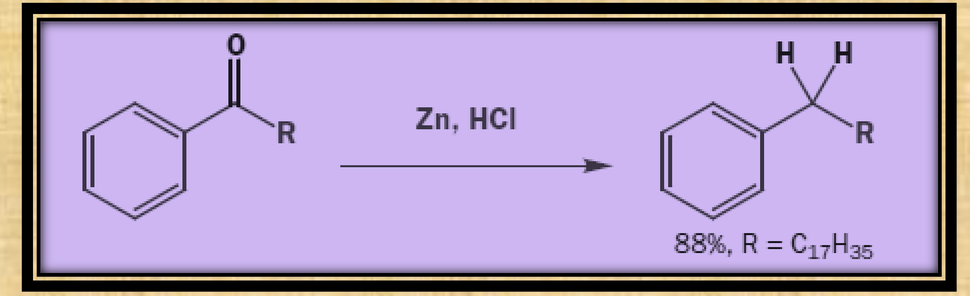


59:41 no CeCl
99:1 with$CeCl_3$

Wolf Kishner reduction and Clemmensen reduction

- Wolf kishner reduction and clemmensen reduction involves the reduction of ketone to alkane.

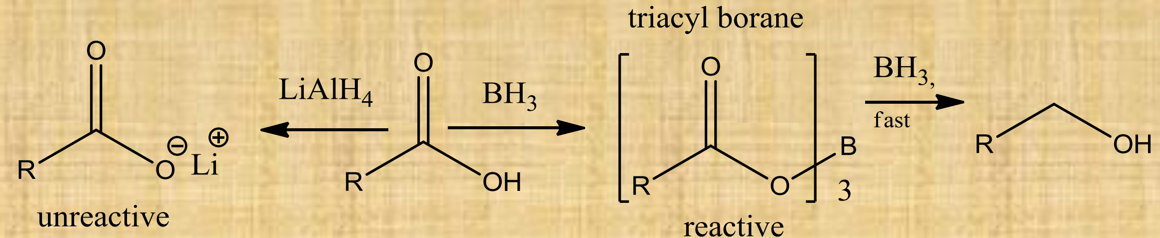


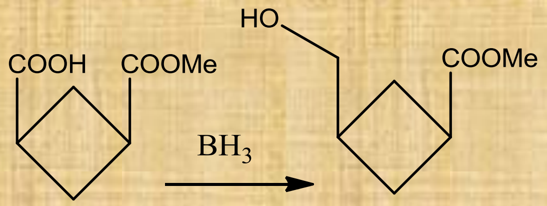


88%, R = $C_{17}H_{35}$

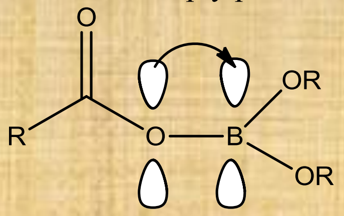
Reduction of carboxylic acid

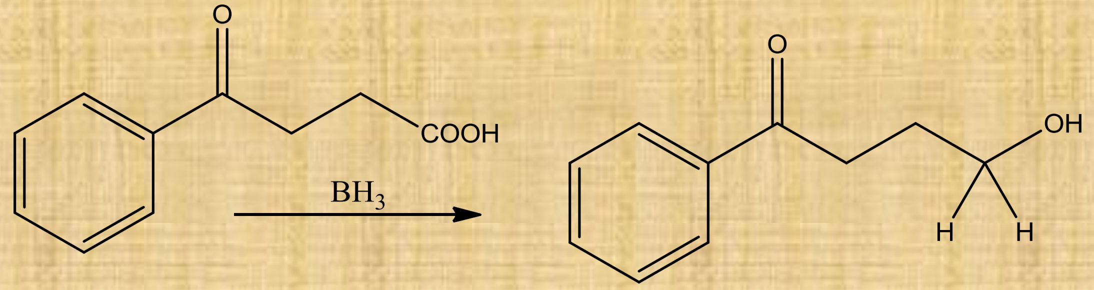
- Borane is an chemoselective reagent for the reduction of carboxylic acid in the presence of other reducible functional groups such as esters and even ketones.





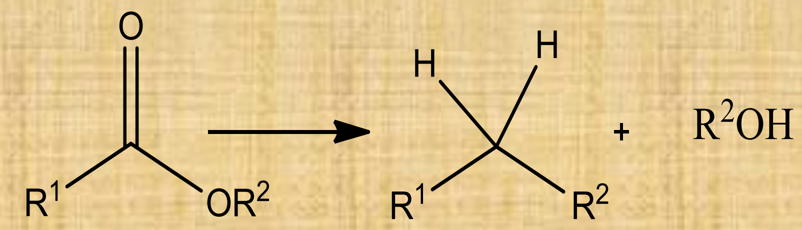
oxygen donates lone pair of electrons into borbn's empty p orbital

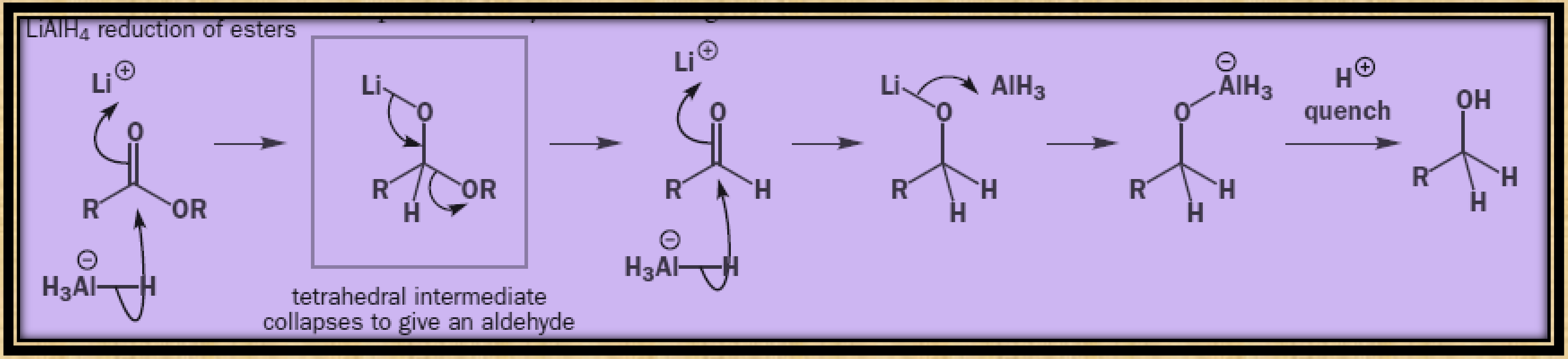




Reduction of esters to alcohol

Esters reduces to alcohol by $LiAlH_4$

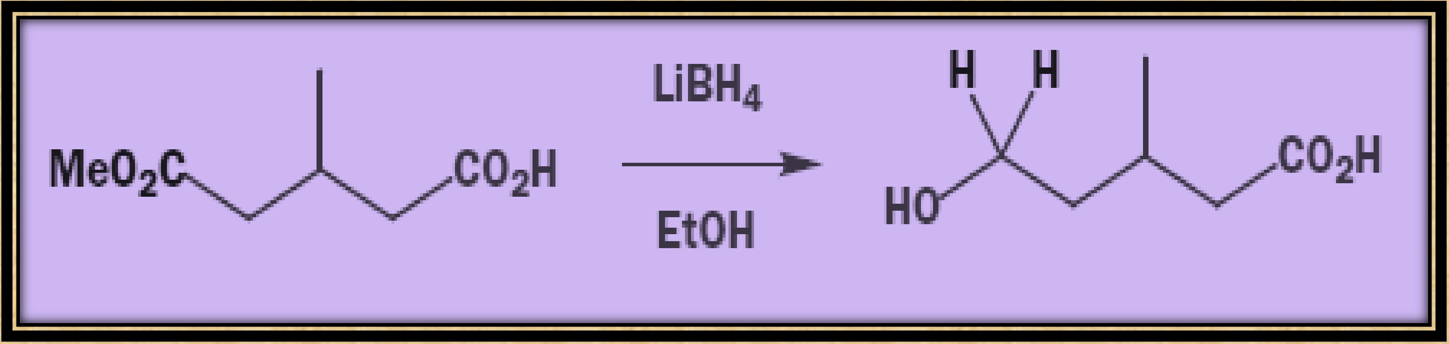



$LiAlH_4$ reduction of esters

tetrahedral intermediate collapses to give an aldehyde

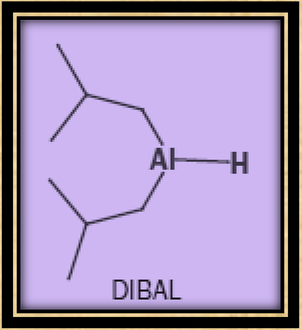
Selective reduction of esters to alcohol

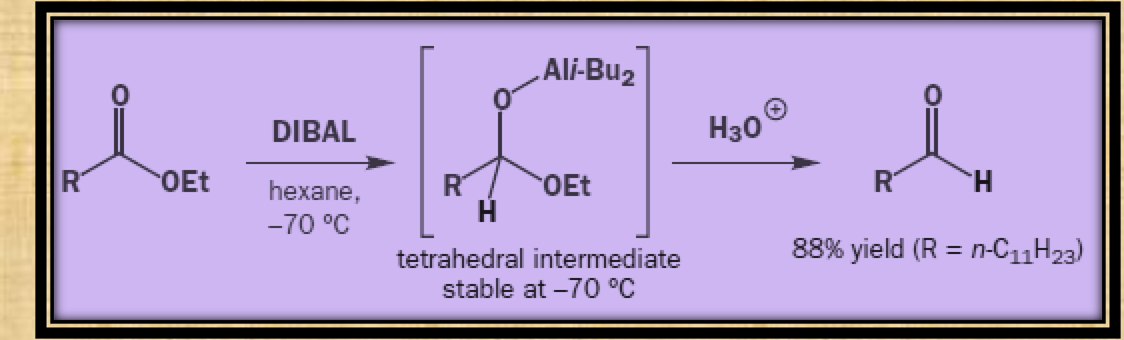
Lithium borohydride in alcoholic solution reduces esters.It has selectivity for esters over acids or amides that $LiAlH_4$ does not have.



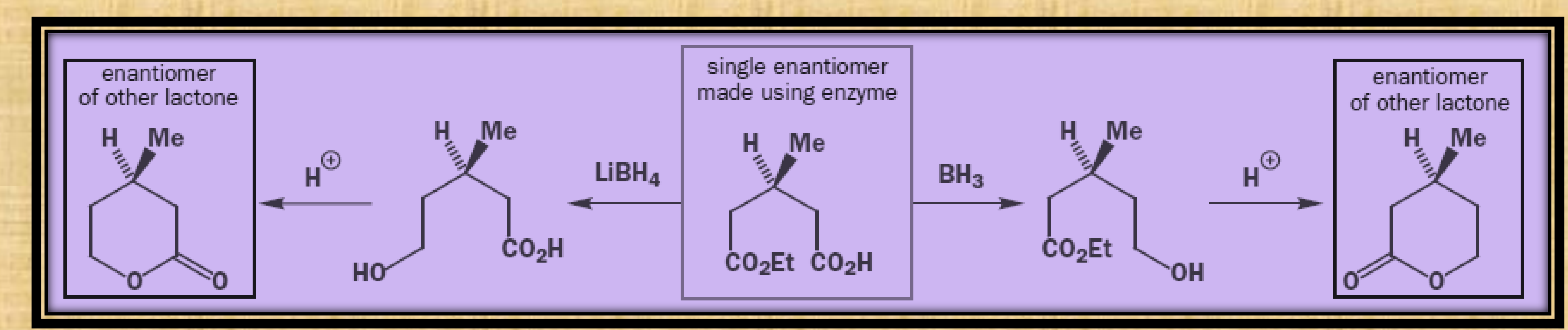
Reduction of esters to aldehyde

- DIBAL reduces esters to aldehyde at -70°C. At this temperature tetrahedral intermediate is stable.

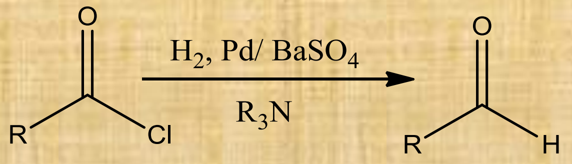




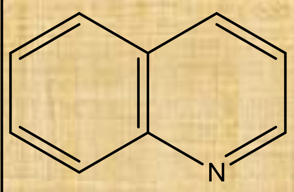
Chemoselective reduction



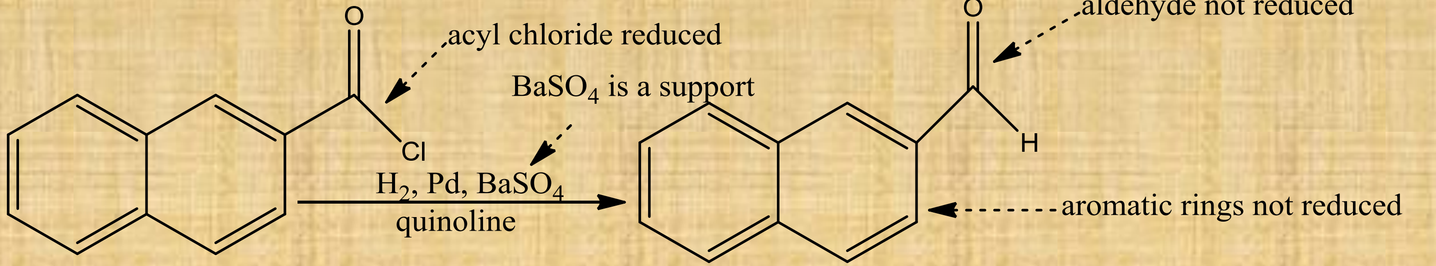
Reduction of acid chloride to aldehyde



the tertiary amine



Quinoline



acyl chloride reduced

$BaSO_4$ is a support

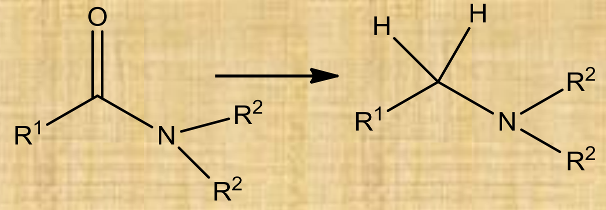
aldehyde not reduced

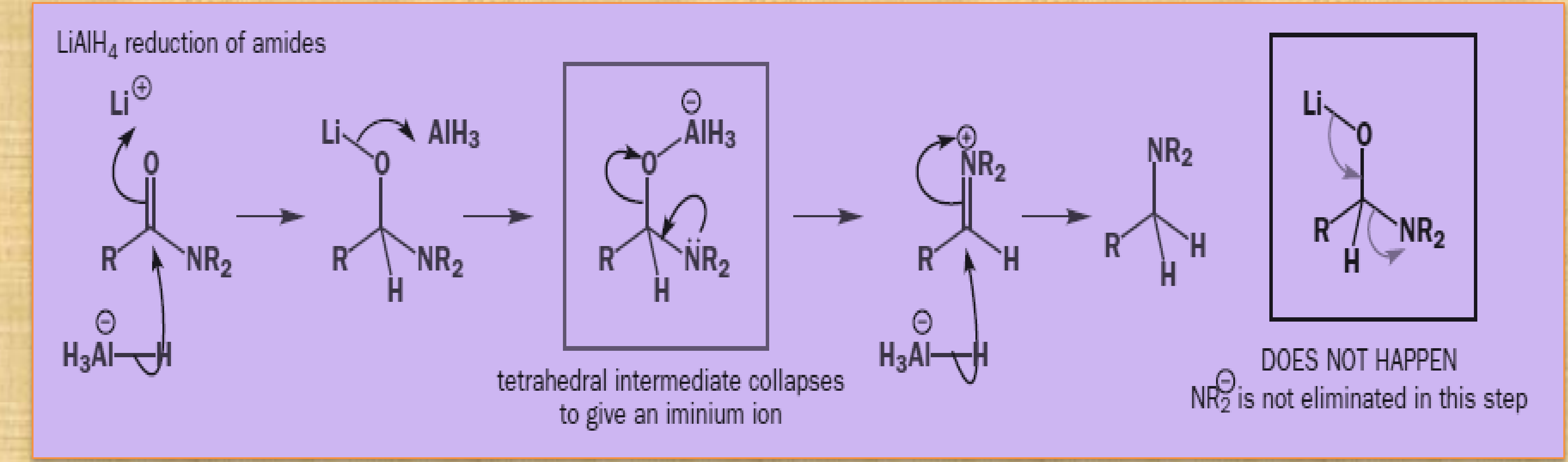
aromatic rings not reduced

74-81%

Reduction of amide to amines

- $LiAlH_4$ reduces amide to amine.



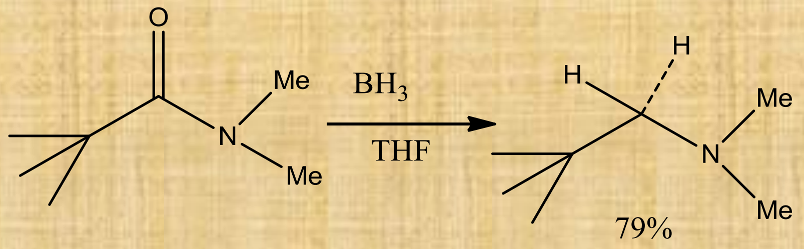

LiAlH4 reduction of amides

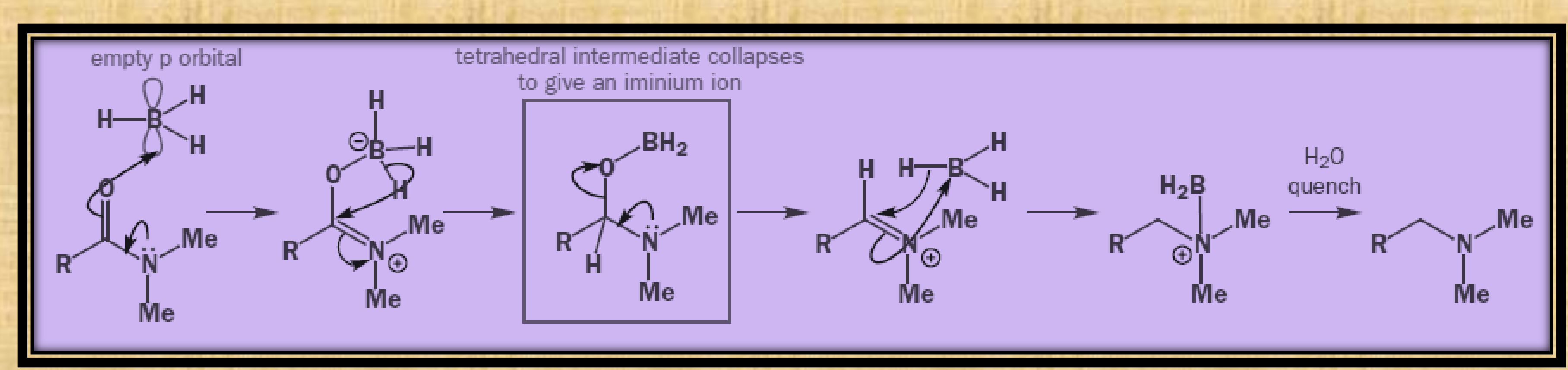
tetrahedral intermediate collapses to give an iminium ion

DOES NOT HAPPEN

NR2⊖ is not eliminated in this step

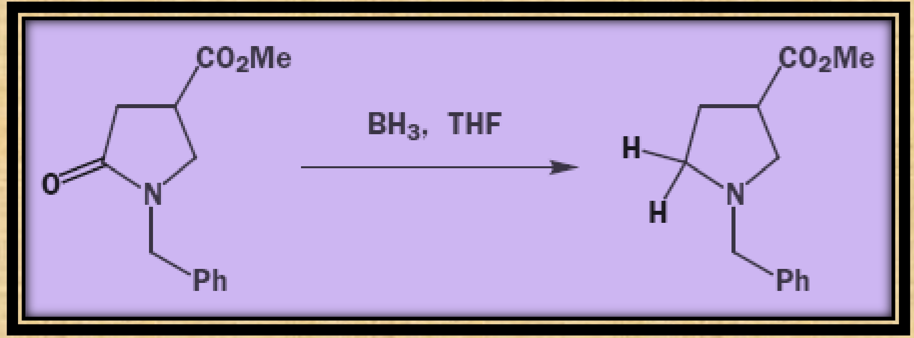
Reduction of amide to amine with borane





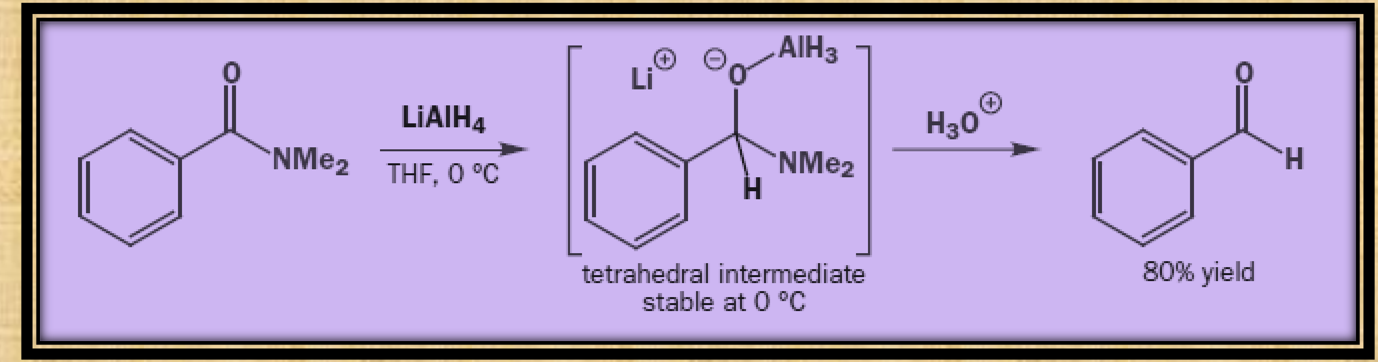
Chemoselective Reduction

- Borane reduces amide to amine in the presence of an ester

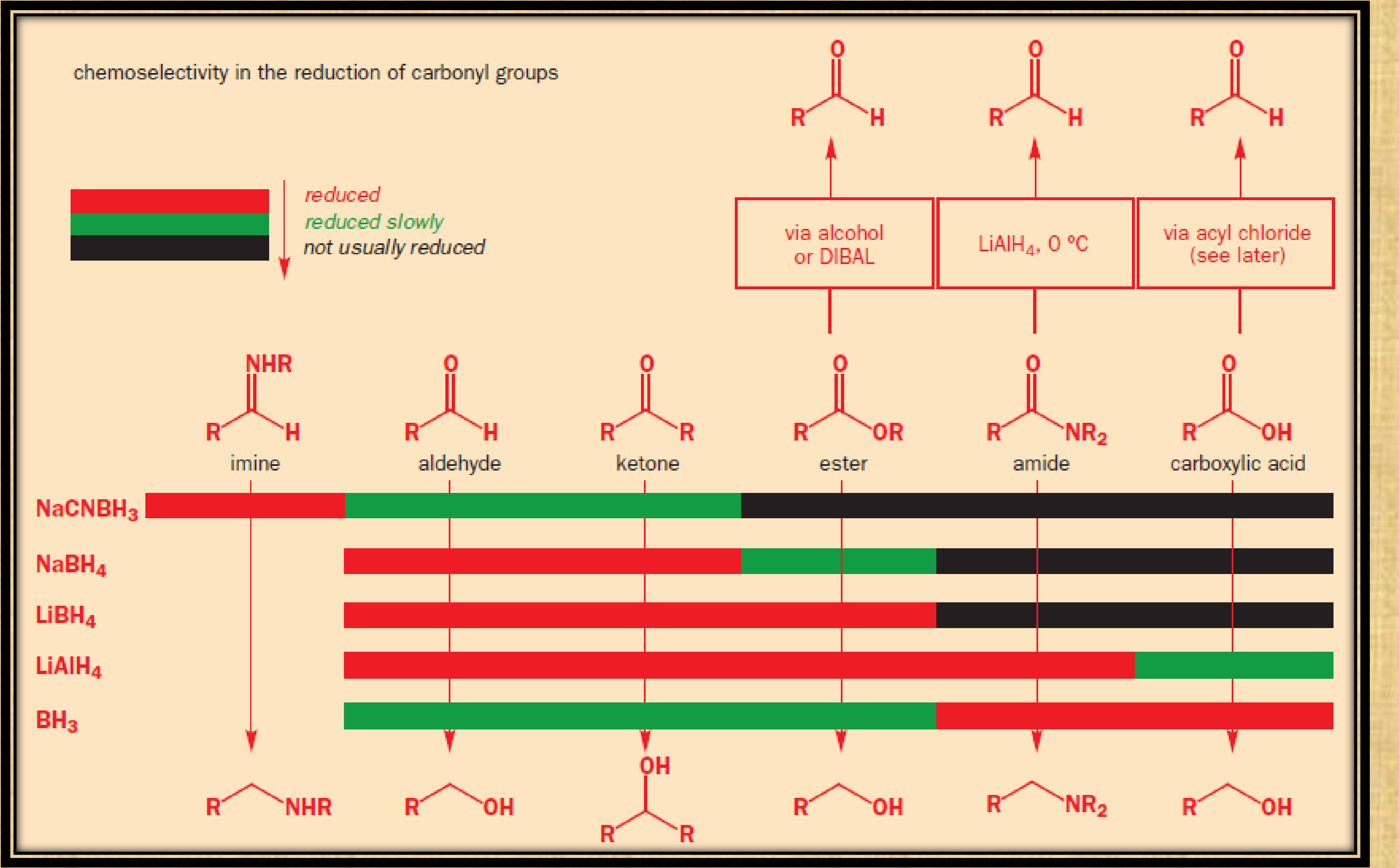


Reduction of amide to aldehyde

- Lithium aluminium hydride at 0°C reduces amide to aldehyde.



Carbonyl reduction using hydride reducing agent

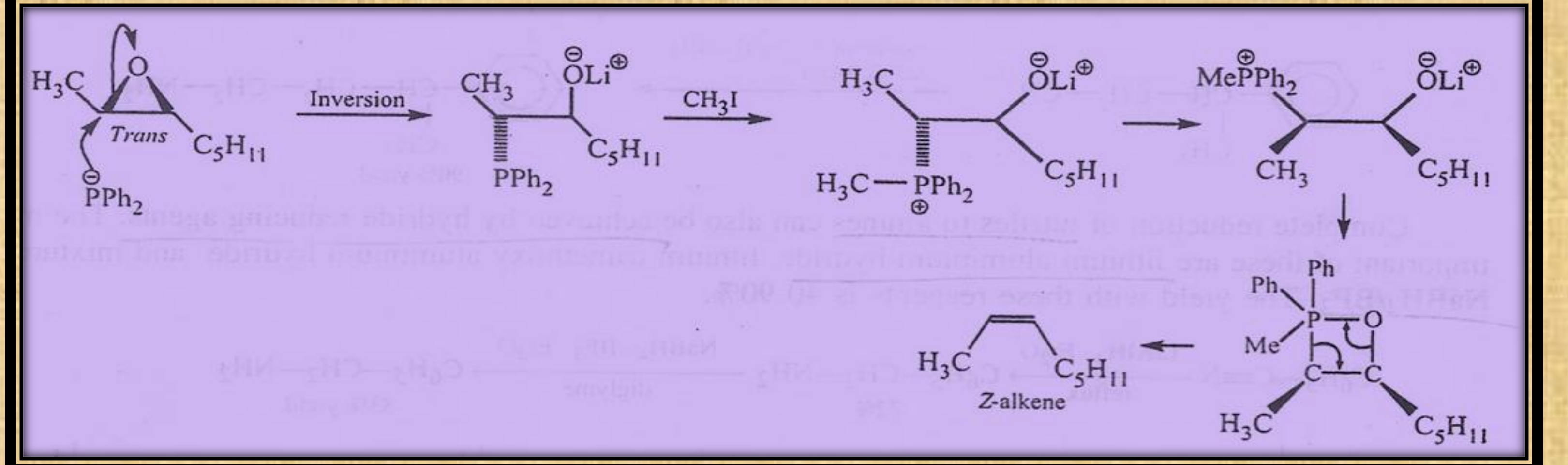


- 🟥 reduced
- 🟩 reduced slowly
- ⬛ not usually reduced

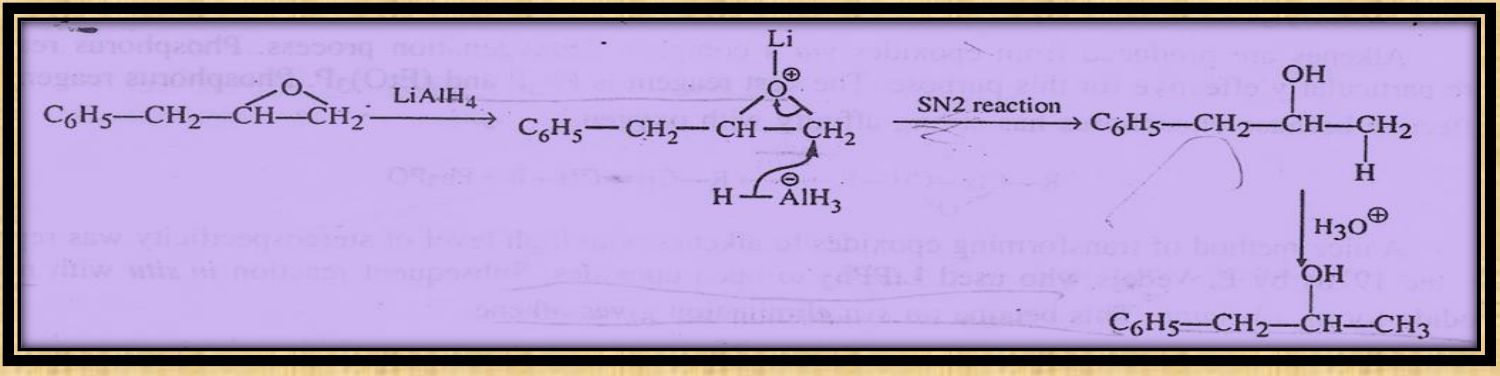
	imine	aldehyde	ketone	ester	amide	carboxylic acid
NaCNBH$_3$	🟥	🟩	🟩	⬛	⬛	⬛
NaBH$_4$		🟥	🟥	🟩	⬛	⬛
LiBH$_4$		🟥	🟥	🟥	⬛	⬛
LiAlH$_4$		🟥	🟥	🟥	🟥	🟩
BH$_3$		🟩	🟩	🟩	🟥	🟥

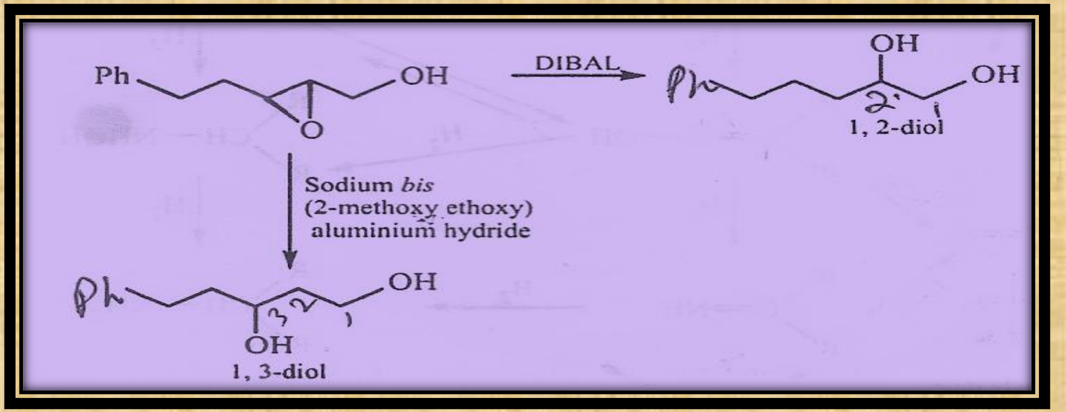
Reduction of epoxide to alkene

- First step is the reaction of epoxide with $LiPPh_2$ which opens the epoxide ring.
- Second step is the subsequent reaction *in situ* with methyl iodide which gives betaine.
- Betaine on *syn* elimination gives alkene.



Reduction of epoxide to alcohol



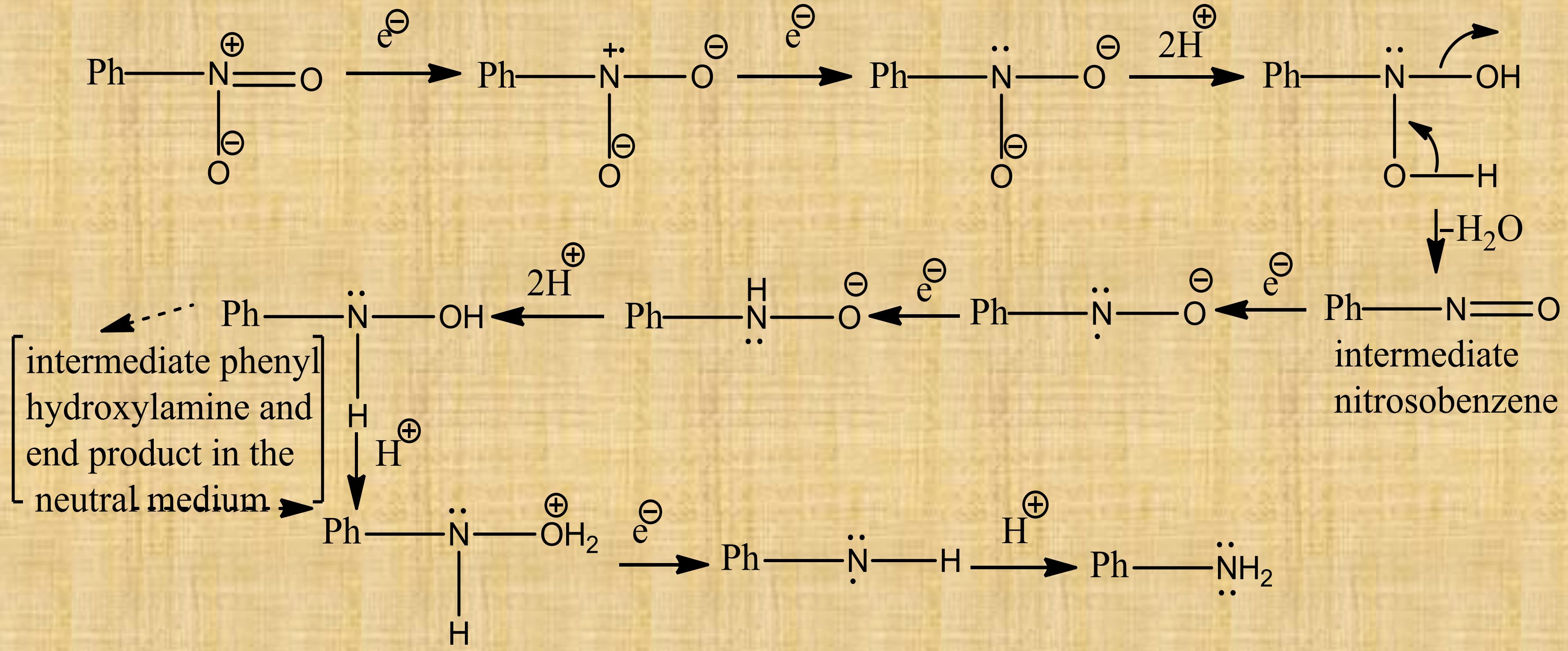


Reduction of nitro group

- Amino gp. can not be introduced into benzene ring directly, nitro gp. Is initially introduced and then it is reduced to get aromatic amine.
- Different types of reduced products are obtained under different conditions and under different pH.
- Exact order of addition of electrons and protons depends on source of electrons and pH of the medium.

Mechanism-

In the acid and neutral medium-



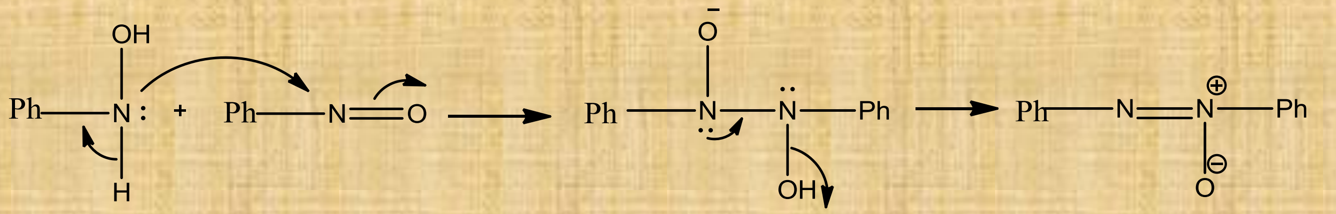
intermediate nitrosobenzene

intermediate phenyl hydroxylamine and end product in the neutral medium

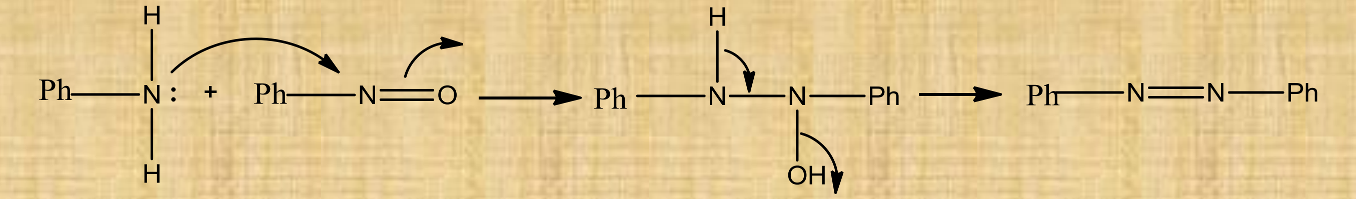
Mechanism-

In the alkaline medium-

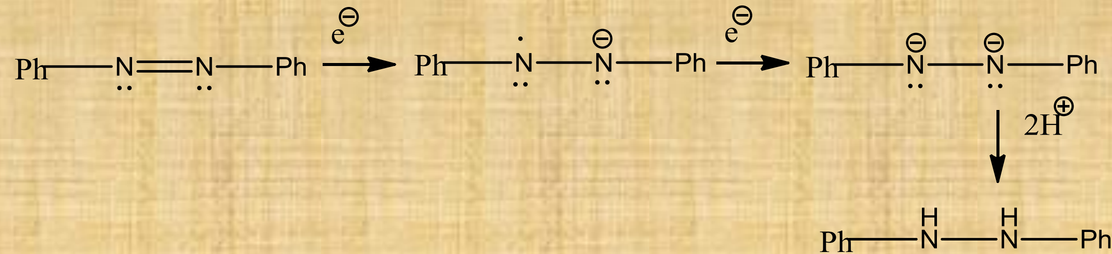
-in the alkaline medium and in presence of sodium arsenite (which is an electron source: $AsO_3^{-3} \longrightarrow AsO_3^{-4} + 2e^-$,), the final product azoxybenzenen is formed by condensation of intermediates phenyl hydroxylamine with nitrosobenzene.



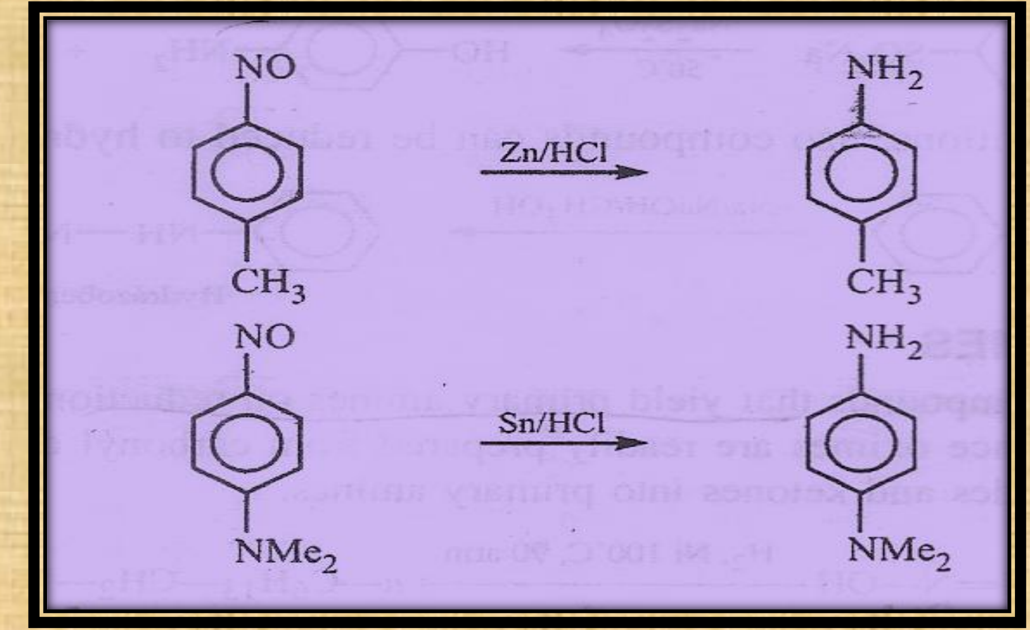
in the alkaline medium and in presence of iron, azobenzene is obtained probably by the condensation of aniline with intermediate nitrosobenzene .



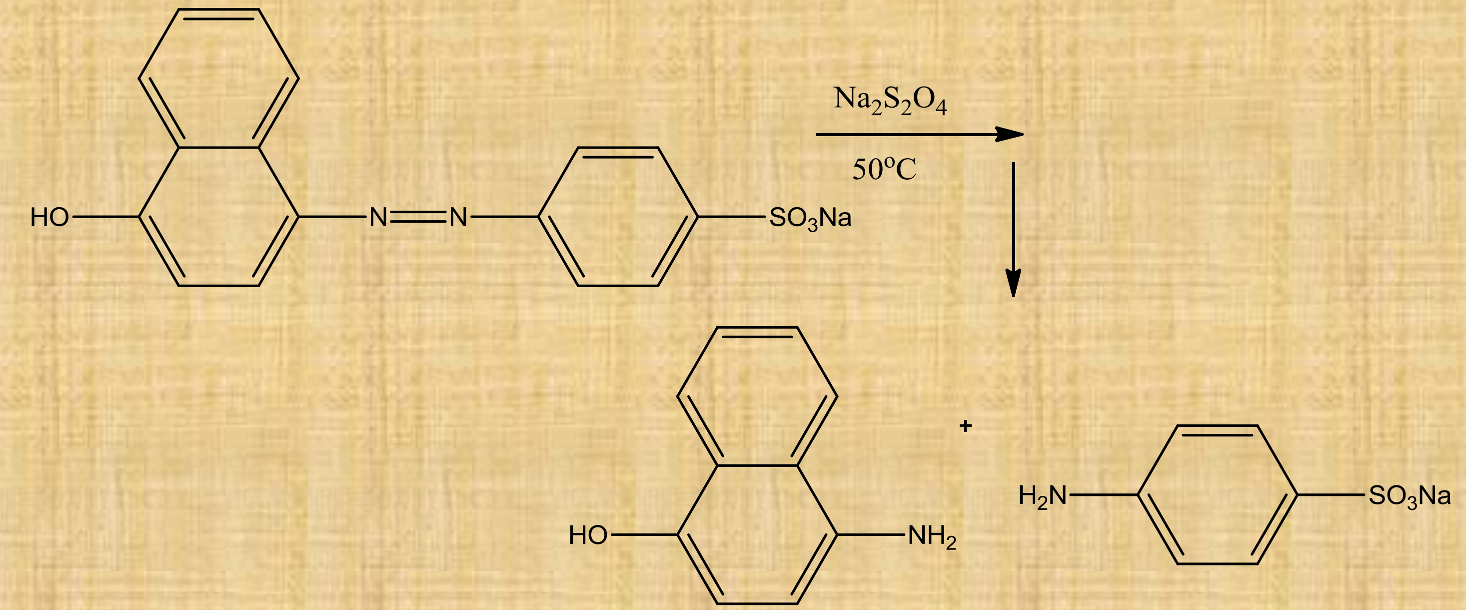
in the alkaline medium and in presence of zinc, hydrazobenzene is obtained by the reduction of azobenzene.



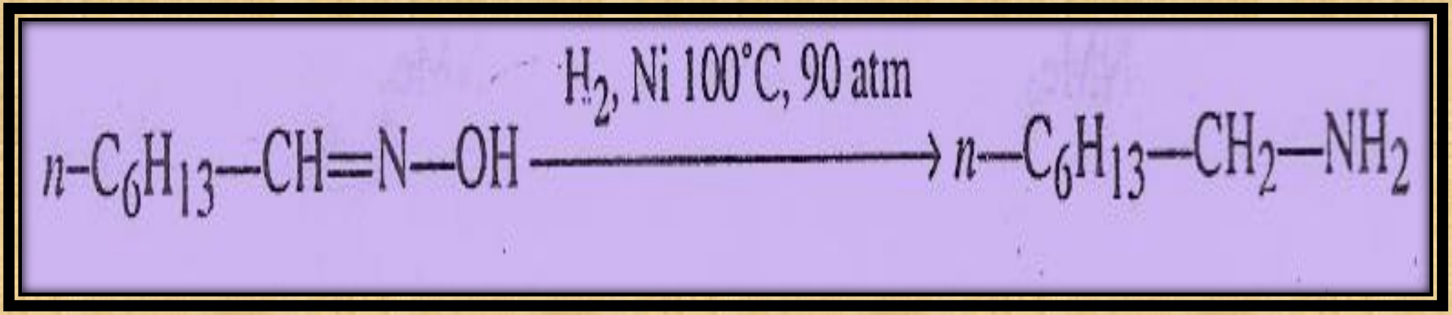
Reduction of nitroso compound with metal and acid



Reduction of azo compounds



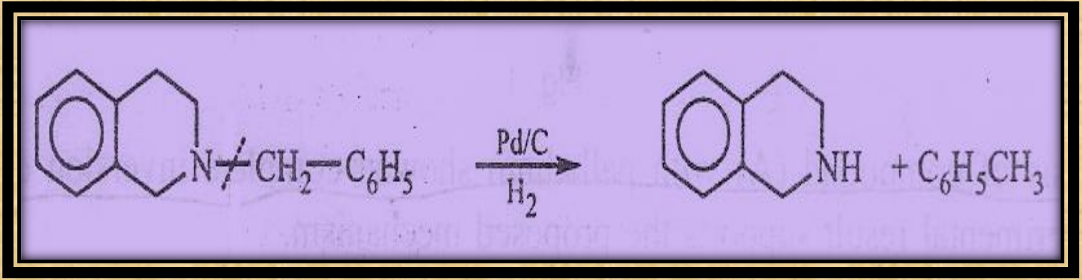
Reduction of oximes



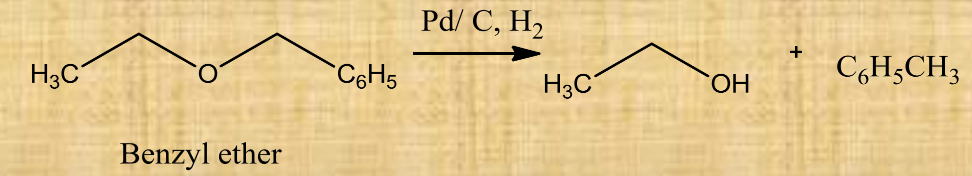
$$n\text{-}C_6H_{13}\text{—}CH{=}N\text{—}OH \xrightarrow{H_2,\ Ni\ 100^\circ C,\ 90\ atm} n\text{—}C_6H_{13}\text{—}CH_2\text{—}NH_2$$

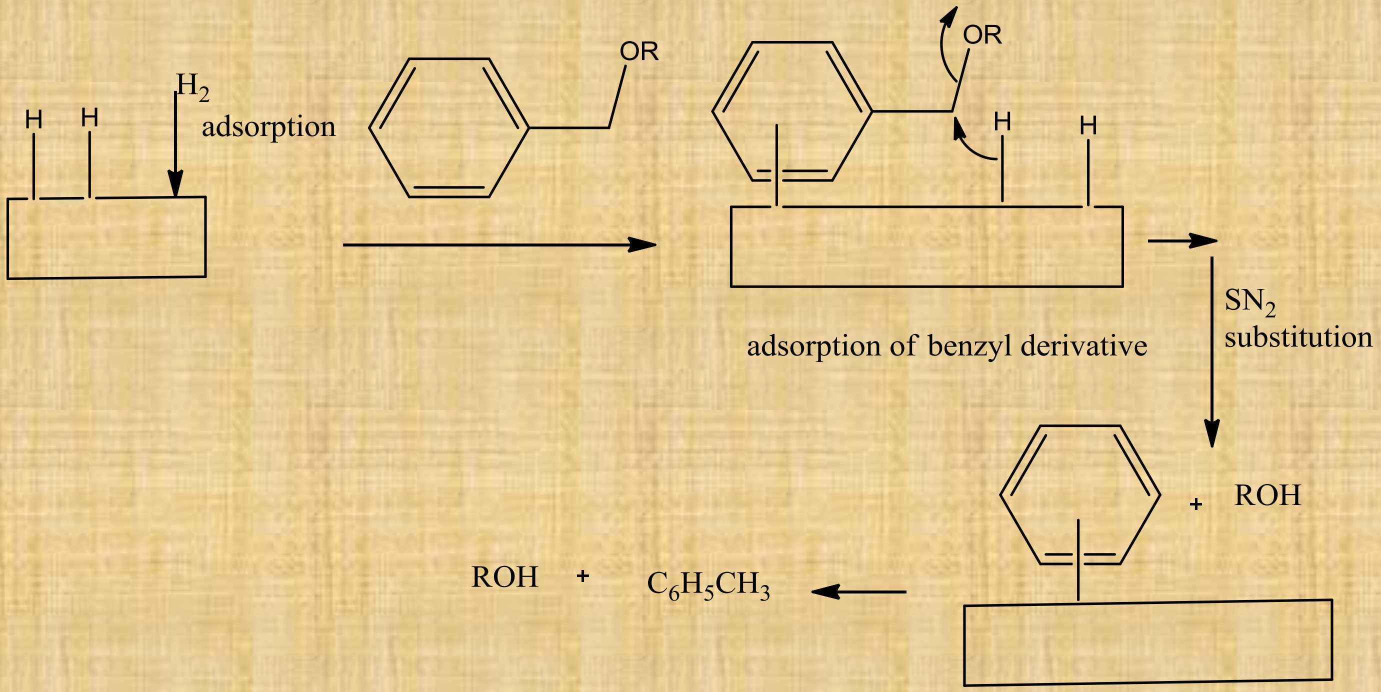
Hydrogenolysis of amines

- Reductive cleavage reaction:
- Reaction which completely cleaves the bonds between carbon and electronegative elements,replacing them with bonds to hydrogen are known as reductive cleavage.
- Reductive cleavage when carried out with hydrogen and catalyst is known as hydrogenolysis.

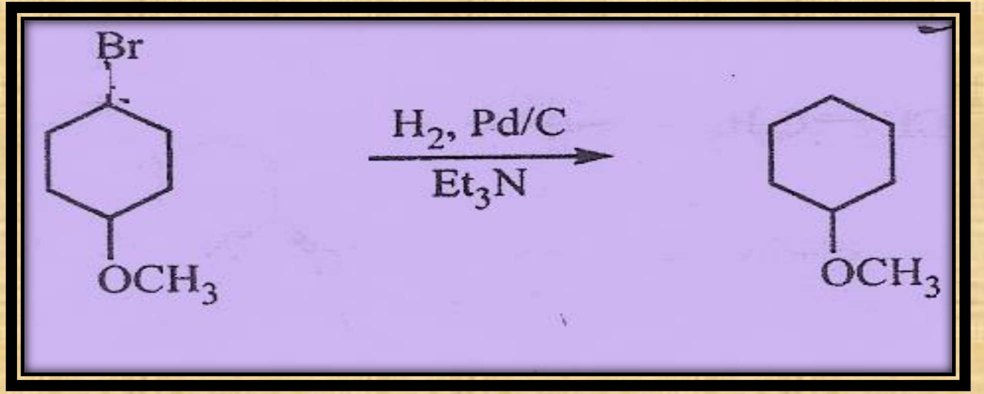


Hydrogenolysis of benzyl ethers





Hydrogenolysis of C-X bonds



Hydrogenolysis of cyclopropane ring