ORGANIC SYNTHESIS REAGENTS

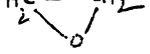
* ORGANO SYNTHETIC REAGENTS *

28/04/08
26/10/2016

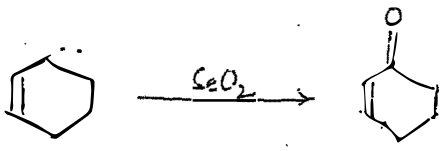
⇒ oxidation :—

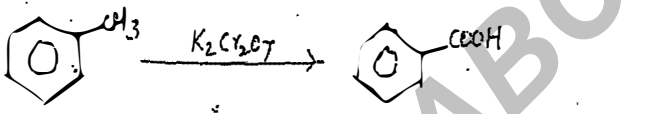
Addⁿ of O_2 or removal of H_2 in chemical change — 'oxidation'.

eg :—

$CH_2=CH_2 \xrightarrow{m\text{-}CPBA}$ 

$H_2C=CH_2 \xrightarrow[-H_2]{Cat}$ $H-C\equiv C-H$





$-CH_3 \longrightarrow -CH_2-OH \longrightarrow -CHO \longrightarrow CO_2H$

oxidation

⇒ Reductions :—

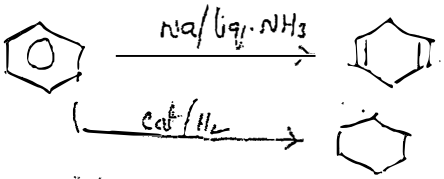
Addition of Hydrogen, removal of oxygen.

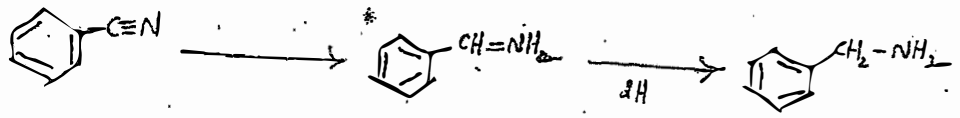
$CH_2=CH_2 \xrightarrow{Cat/H_2} CH_3-CH_3$

$H_3C-C\equiv N \xrightarrow{H_2} H_3C-CH_2-NH_2$

$H_3C-COOH \xrightarrow{LAH} CH_3-CH_2-OH$

$ph-CHO \xrightarrow{Zn/Hg/HCl} ph-CH_3$



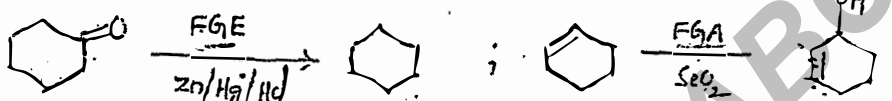


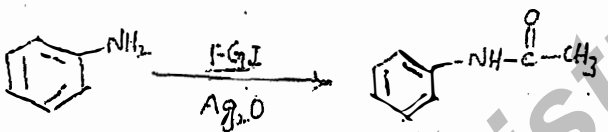
* Synthetic compounds :-

laboratory prepared compounds.

→ Reagents prepared in laboratory - "Synthetic reagents."

* organic chemical changes usually involves functional group elimination (FGE) / addition (FGA) / interconvertion (FGI) with 'c-c' bond or without 'c-c' bond formations.





* Any chemical substance used to FGE / FGA / FGI in organic reax called "Reagent."

* Reagent will do oxidation / Reduction.

⇒ oxidant / oxidising agent :-

→ chemical which is bringing about oxidation is "oxidising agent."

⇒ Reductant / Reducing agent :-

chemical which is bringing about reduction is "reducing agent."

O.A ⇒ Adds oxygen (or) removes hydrogens

R.A. ⇒ Adds hydrogens (or) removes oxygens

Oxidising agents :—

eg:- 1) $KMnO_4$. 7) NBS . 13) Cr^{VI} – oxidants.

2) $K_2Cr_2O_7$. 8) O_2/O_3 . 14) $RCOOAg/I_2$

3) DDQ . 9) LTA : $Pb(OAc)_4$.

4) chloranil . 10) HIO_4 .

5) SeO_2 . 11) DMSO .

6) OsO_4 . 12) I_2 .

Reducing agents :—

1) Cat/H_2 7) Metal/acid Clemensen

2) $LAH = LiAlH_4$ 8) Metal/basic (Birch redn)

3) $NaBH_4$ 9) Di Imide : N_2H_2

4) complexometric Hydrides 10) DIBAL

5) Boranes 11) Alane : AlH_3

6) $NaBH_3CN$

⇒ ORGANO – METALLIC REAGENTS :—

→ "Functional group interconversion with "C-C bond formation".

eg:- 1) ORGANO LITHIUM REAGENTS

1) ORGANO LITHIUM REAGENTS
2) ORGANO COPPER REAGENTS
3) ORGANO MAGNESIUM REAGENTS
4) " PALLADIUM "
5) " TIN "
6) " ZINC "
7) " SILICON "
8) " MERCURY "

Synthetic Reagents

- oxidn reagents — 'Do oxidn'
- Reducing reagents — 'do reduction'
- 'Organometallic reagents' — Do FGI-interconversion with C-C bond formn.

Oxidizing Agents :-

oxidations

1) oxidn of active CH-function
   - Allylic CH- ; $CH_2=CH-\underline{CH}-$
   - benzylic CH- ; $ph-\underline{CH_2}-$
   - α-position of withdrawing gp
   - $-\underline{CH_2}-W$ (withdrawing gp)

2) oxidn of olefine into epoxide

3) oxidn of olefine into 1,2 diols

4) oxidn of 1,2-diols into carbonyl compounds
   'cleavage of glycols'

5) oxidn of simple alcohols into carbonyl compds.

6) oxidn of alcohols / carbonyl compds into acids

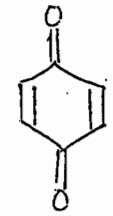
7) oxidn of active positions into carbonyl / acid functions.

1) oxidn of active –CH function :–

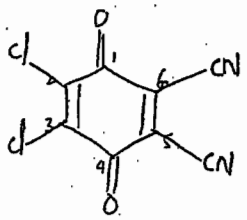
"Allylic / benzylic / α-position of withdrawing gps."

eg:– DDQ, chloranil, SeO_2, Cr^{VI} – oxidns.

1) DDQ :– 2,3-dichloro, 5,6-dicyano benzoquinone



quinone



DDQ

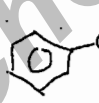
→ yellowish solid

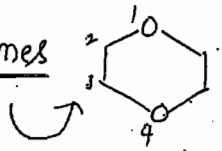
→ mp – 213 – 214°C.

→ Readily soluble in organic solvents

eg:– solvents :

1) Aromatic hydrocarbons (Benzene, o-xylene, toulene etc)

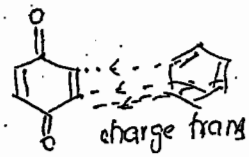
2) Halobenzene  , 

3) cyclic ethers : THF,  1,4-dioxanes 

4) Alcohols : MeOH, EtOH

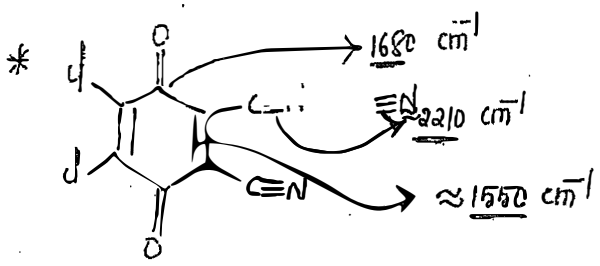
* "Benzene" is widely used solvent for DDQ oxidations.

DDQ + Benzene → red-colour (due to charge transfer phenomenon)

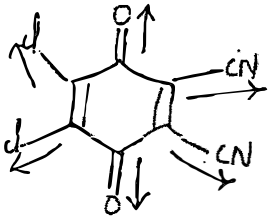


charge transfer

→ "dissolving of DDQ in benzene develops red colour to soln due to formation of charge transfer complex b/w DDQ & benzene.

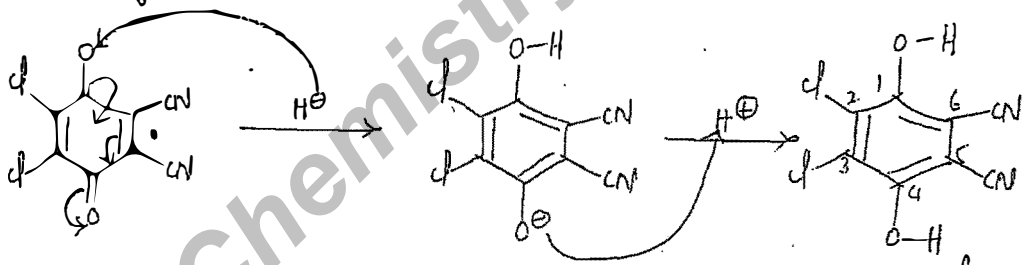


(No H¹-nmr)

→ 

→ "In the presence of :e⊖ withdrawing grp, DDQ is highly e⊖ deficient.

→ It readily approach e⊖ rich species.

→ 

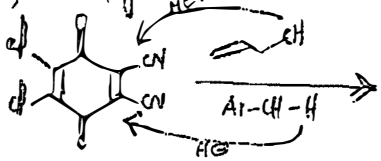
yellow coloured compd

2,3-dichloro, 5-6-dicyano hydroquinone.

DDQ $\xrightarrow{H^{\ominus}}$ HO-Q-O$^{\ominus}$ $\xrightarrow{H^{\oplus}}$ HO-Q-OH

$H^{\ominus}/H^{\oplus} \Rightarrow H_2$

→ DDQ is e⊖ deficient, readily abstracts H⊖ ion from active positions, allylic, benzylic positions

→ 

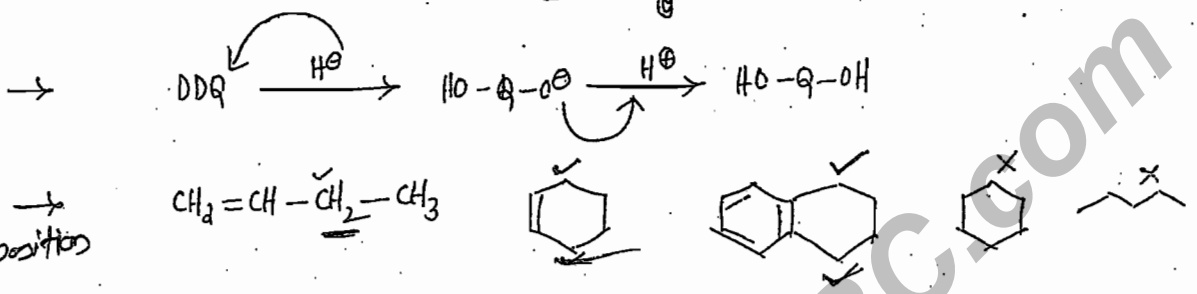
Limitations :-

→ DDQ abstracts $H^{\ominus}$ ion only from allylic & benzylic -CH functions.

∴ DDQ is used for oxidn of only allylic & benzylic positions.

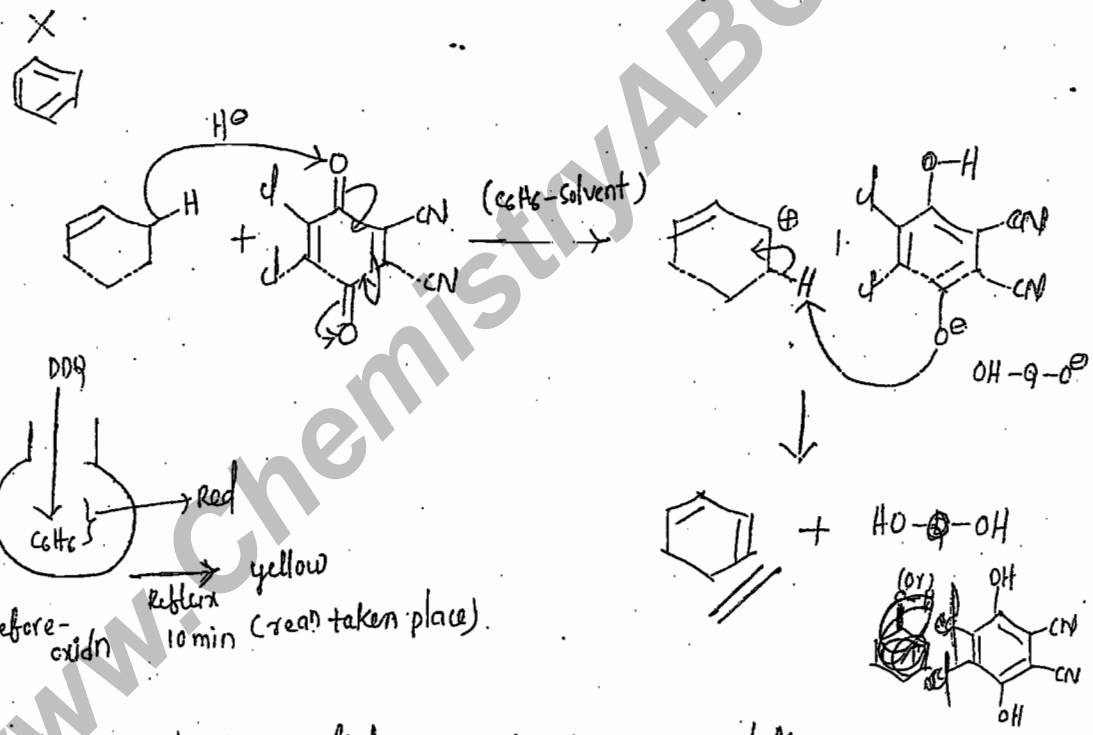
Stoichiometry :-

→ "1 equivalent of DDQ can eliminate one equivalent of Hydrogen."

→ 

Active → C-H position

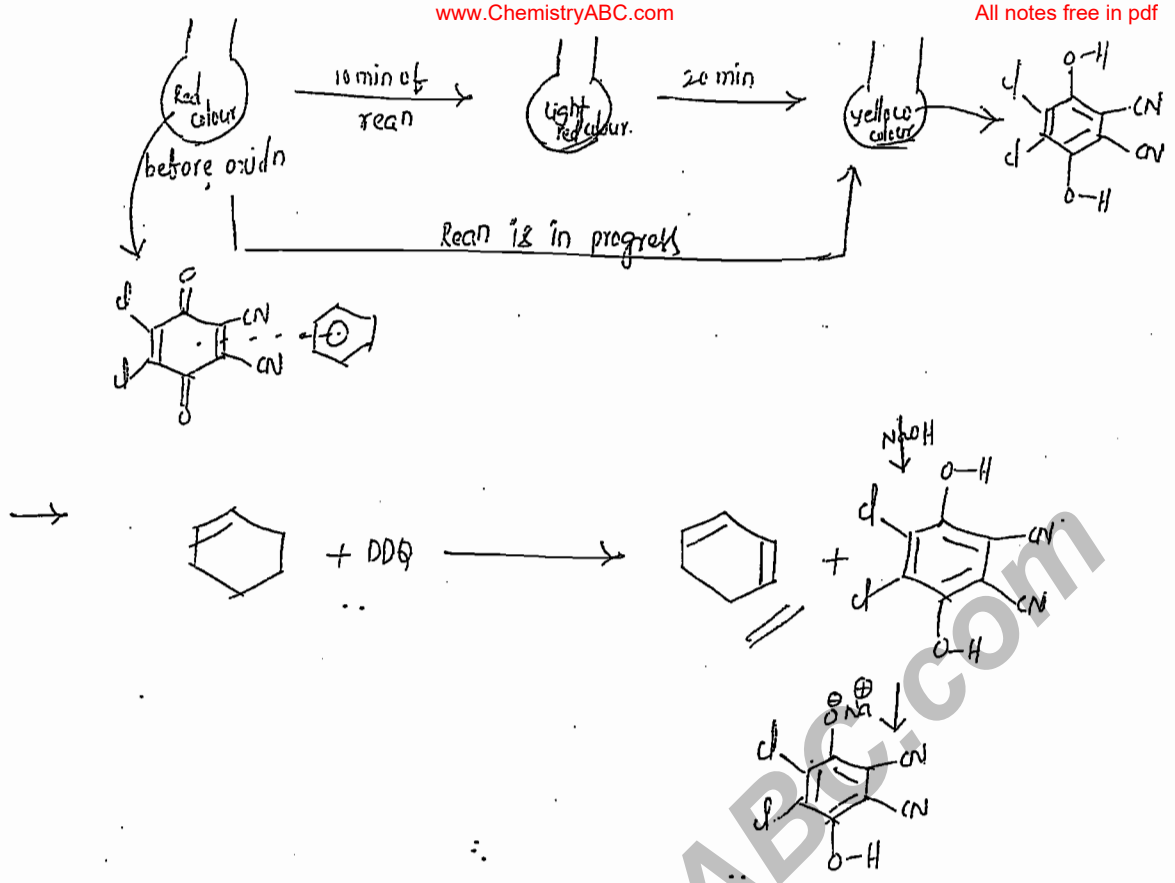
$CH_2=CH-\underset{\checkmark}{CH_2}-CH_3$



→ It is possible to predict progress of DDQ oxidations.

If oxidn takes place, the red colour of DDQ soln disappears due to conversion of DDQ into hydroquinone.

→ Hydroquinone is with yellow colour, after completion of oxidn, soln. gets yellowish colour.

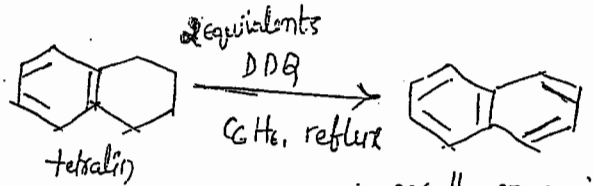


→ In DDQ oxidn, the biproduct 2,3-dichloro, 5-6-dicyano hydroquinone easily removed by treating with NaOH solution.

*** Applications :-**

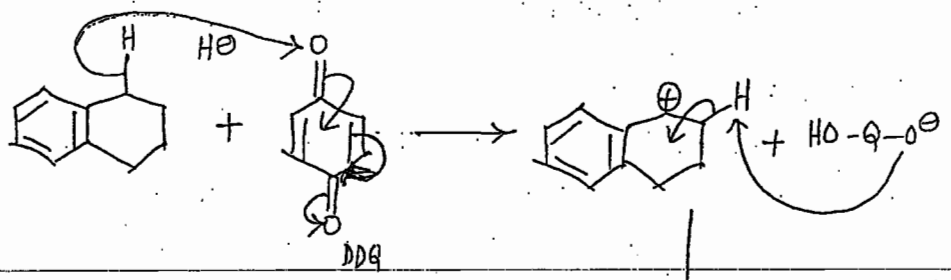
1) Dehydrogenations :-
2) Dehydrogenative cyclizations :-
3) Insertion of oxygens :-
4) Miscellaneous properties. :-

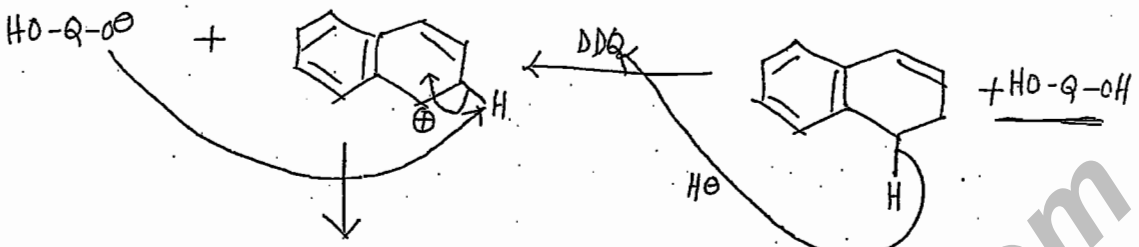
*** Examples :-**

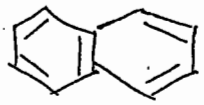
1) 

→ per db, one equivalent of DDQ consumed.

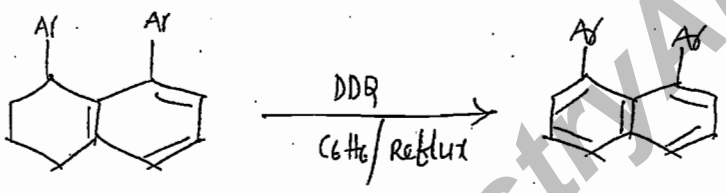
Mech:-





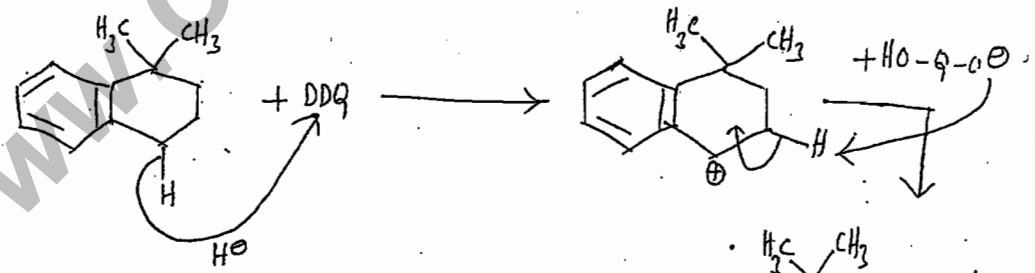
HO-Q-OH + 

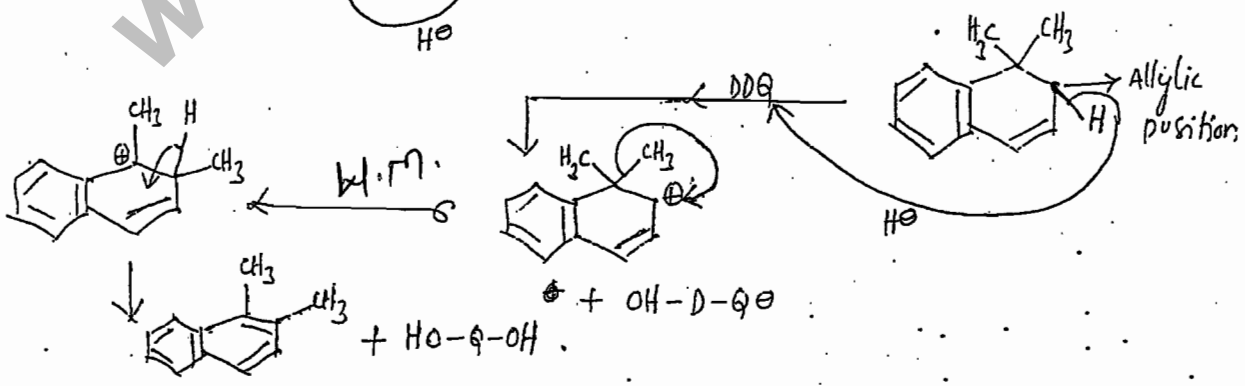
 Naphthalene

2) 

3) 

Mech:-





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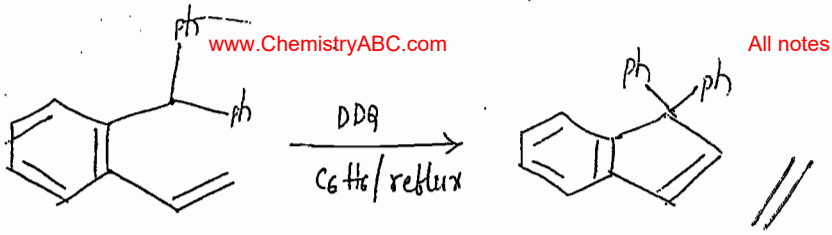

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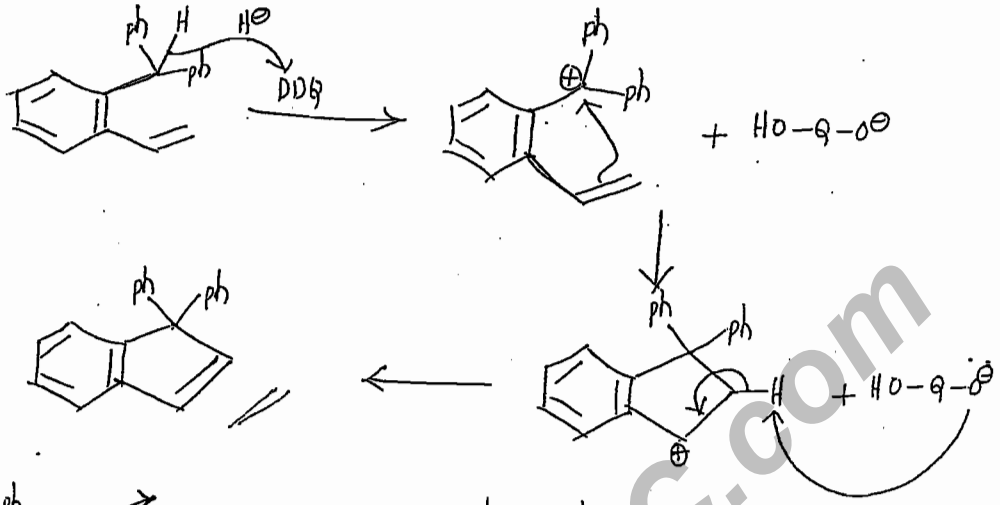

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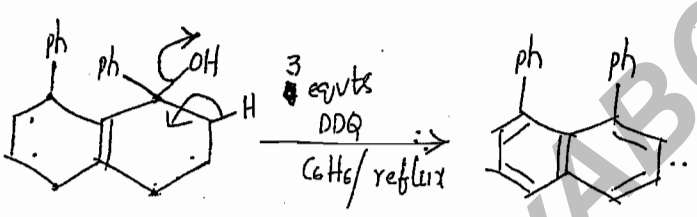
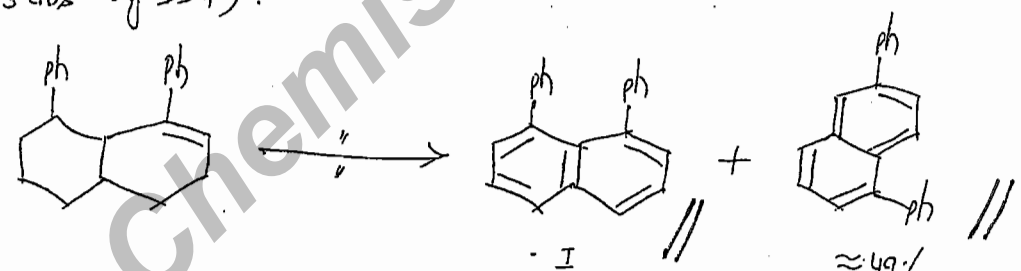


→ 4 db from dehydration but n't by DDQ.

(3 db's by DDQ).

6)



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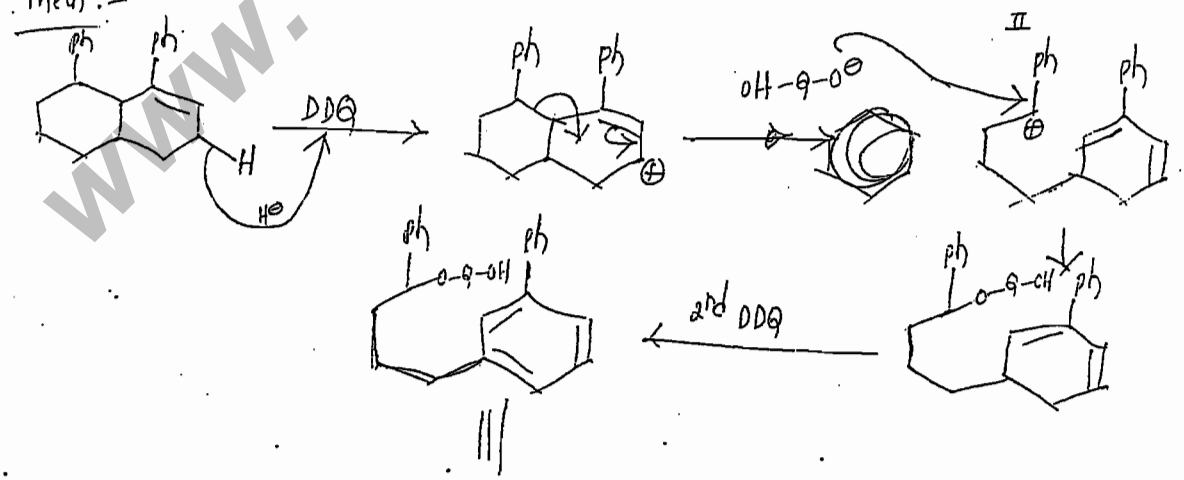
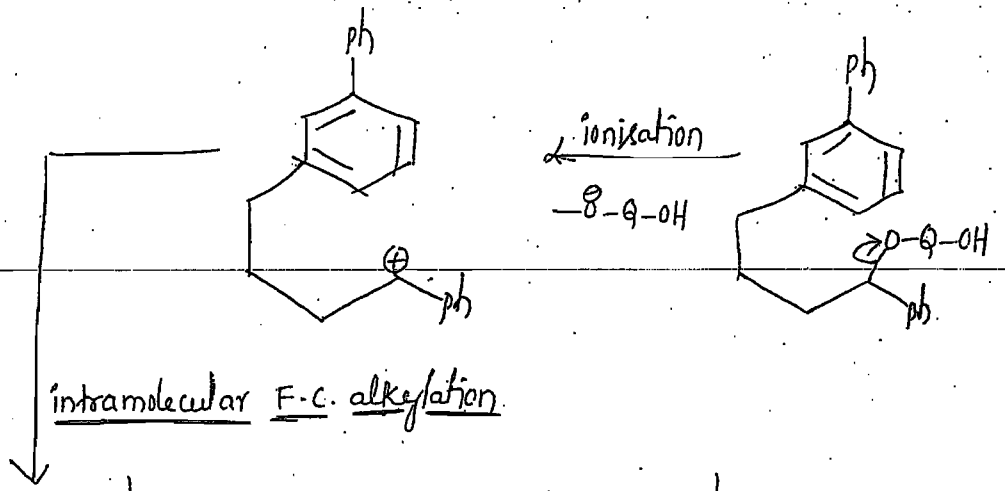
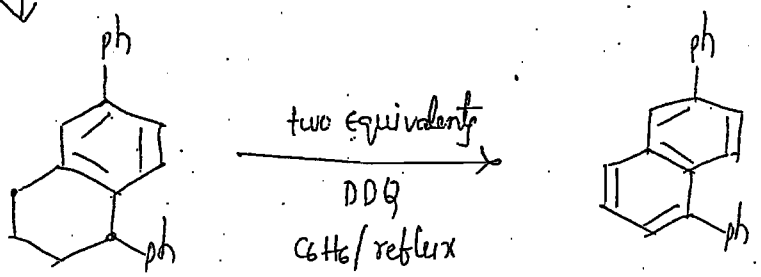




intramolecular F-C. alkylation



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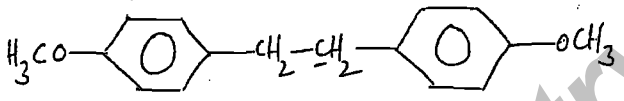

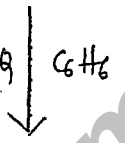

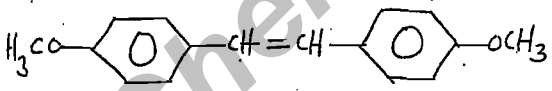

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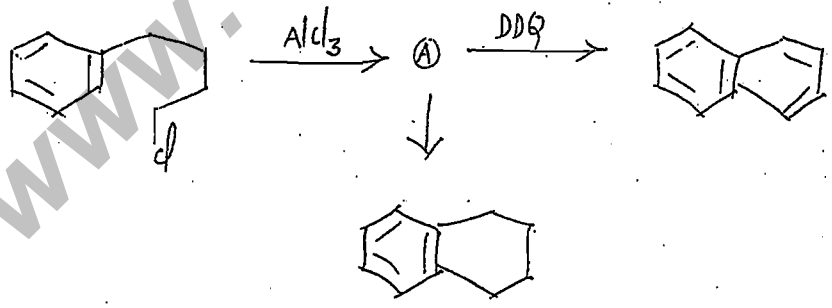

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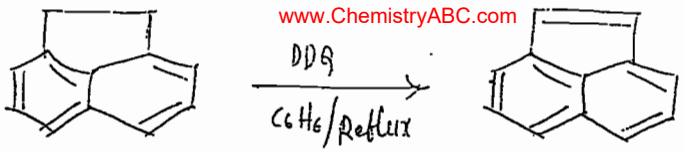

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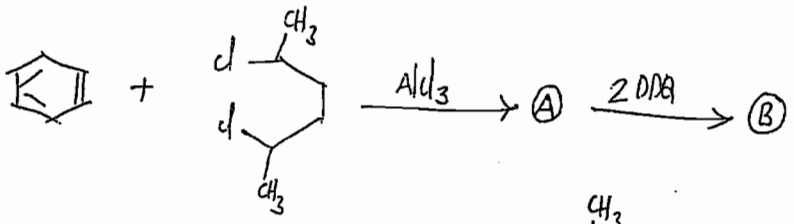
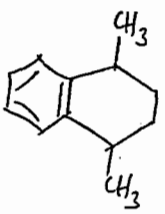
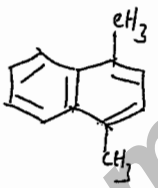




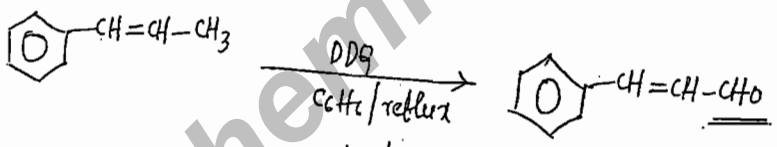


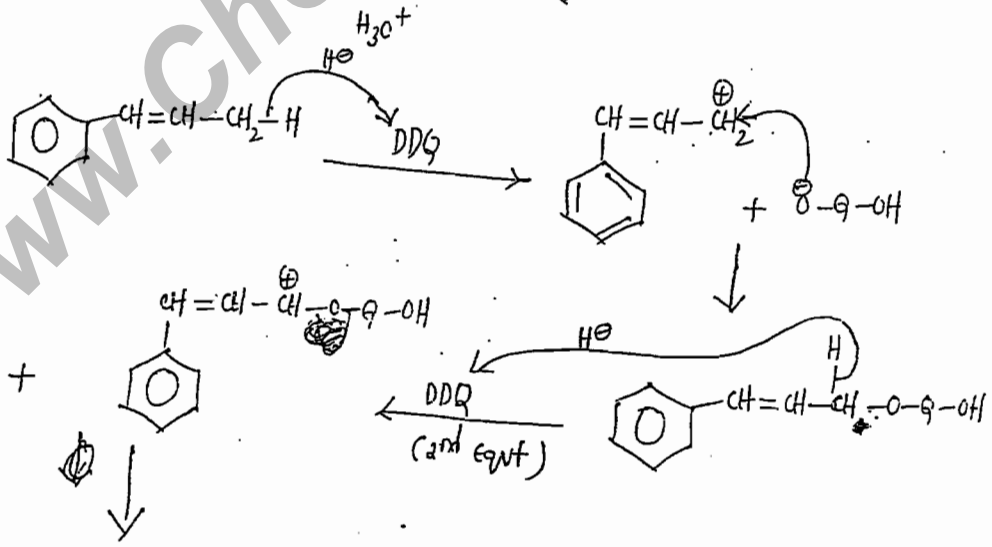
Date : 29/04/08

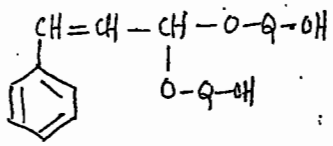
* 8) Insertion of oxygen :—

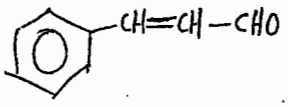
→ $CH_2=CH-CH_3 \xrightarrow[C_6H_6/\text{reflux}]{DDQ} CH_2=CH-\overset{H}{\underset{|}{C}}=O$

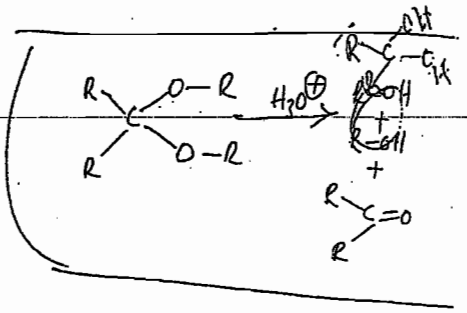
If dehydrogenation not possible on allylic or benzylic positions, oxidises into carbonyl function.

→ 

→ 

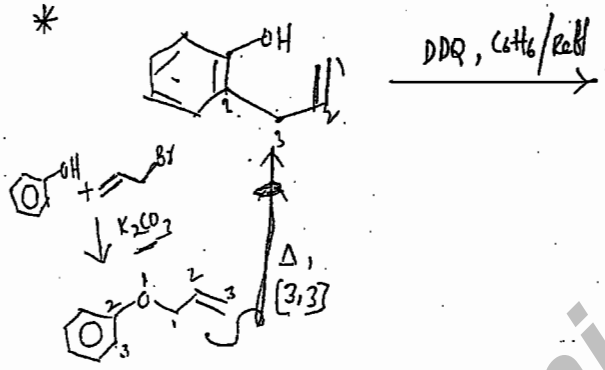






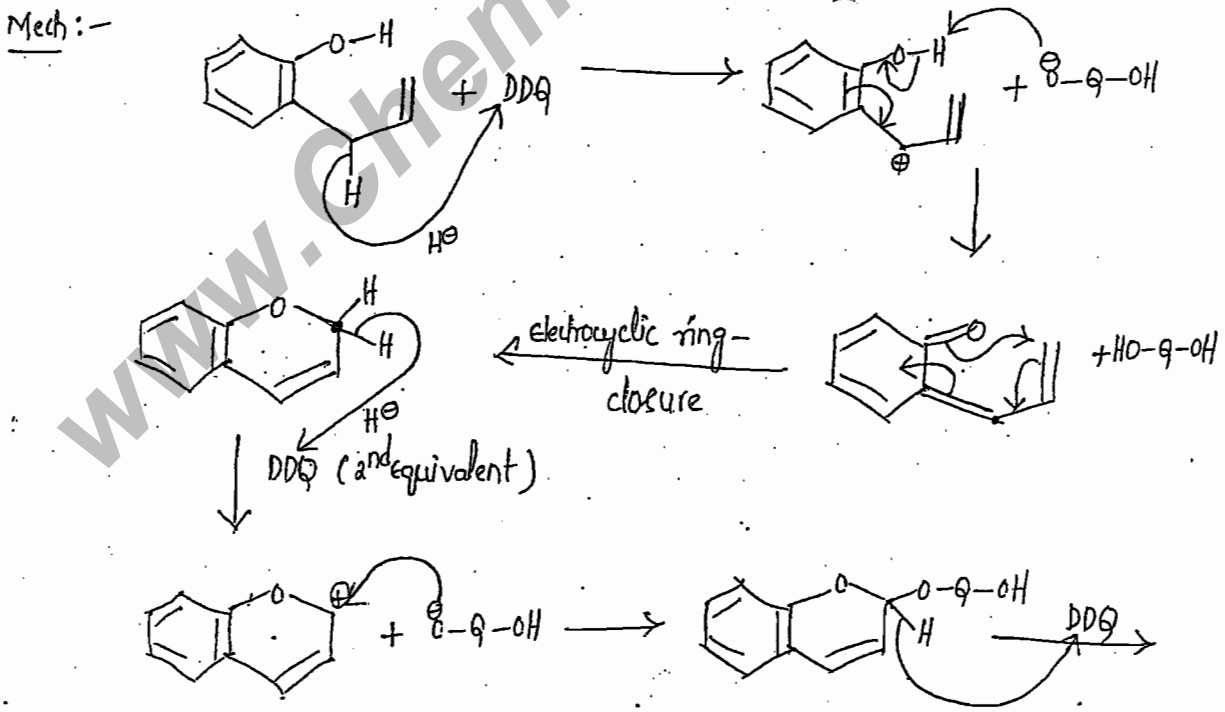
→ "To introduce one carbonyl fn at allylic or benzylic positions, two equivalent of DDQ is required."

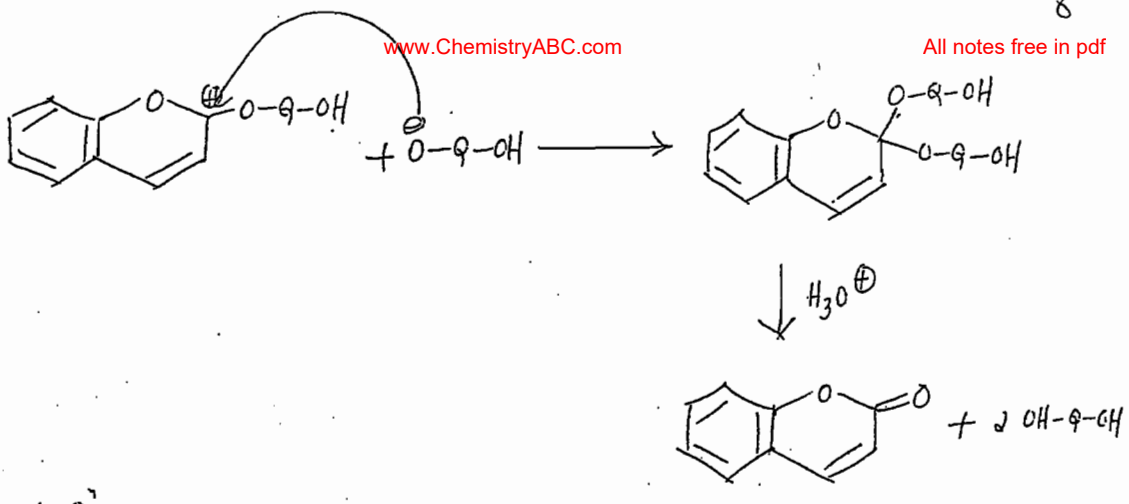
*

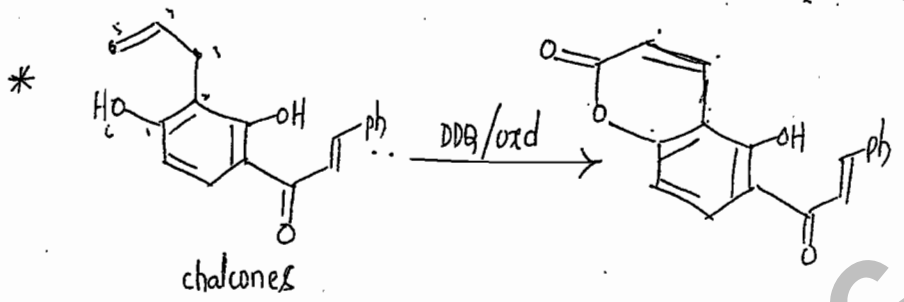


'coumarin'

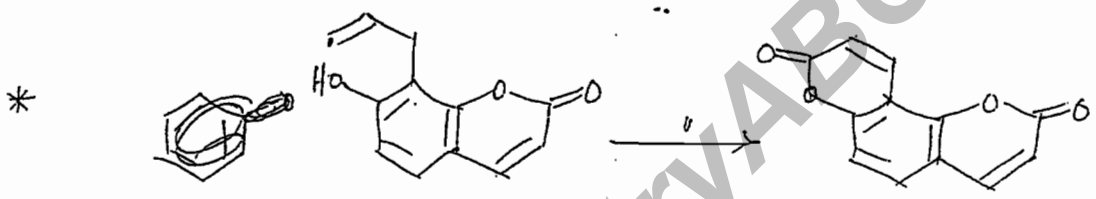
Mech :-

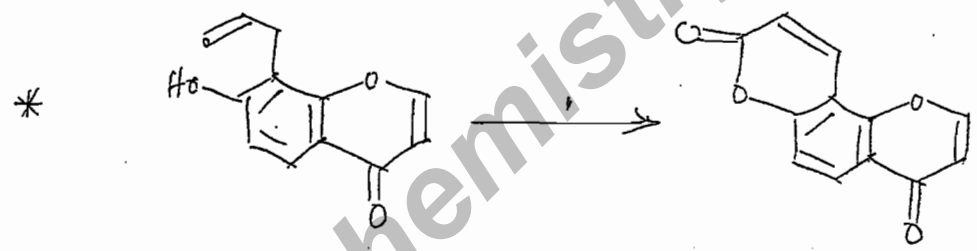


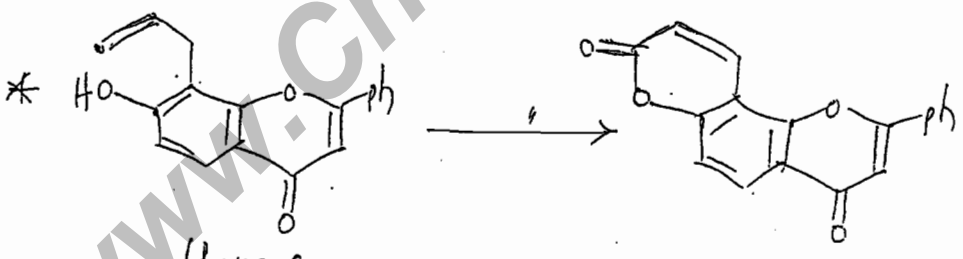




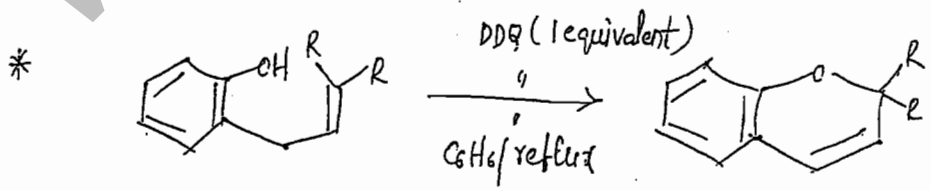
chalcones



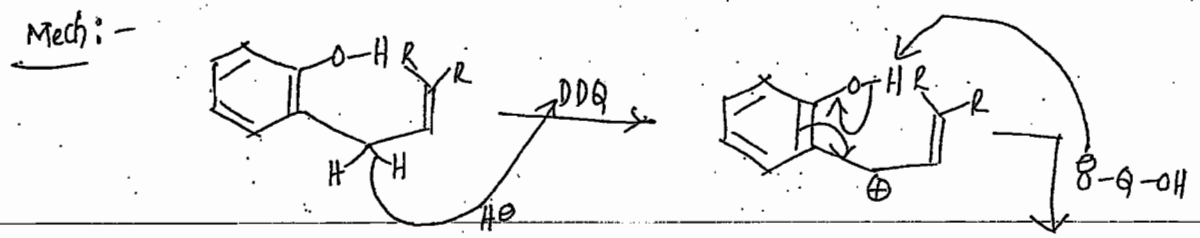


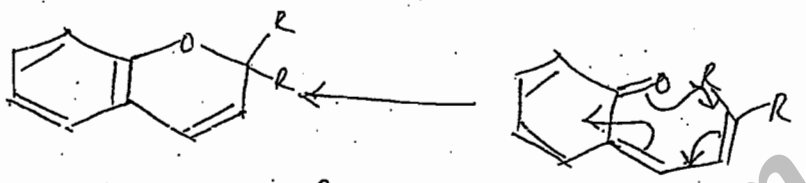


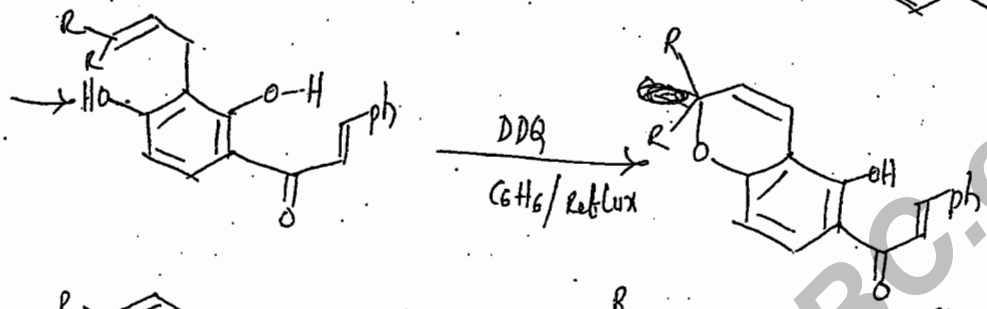
flavones

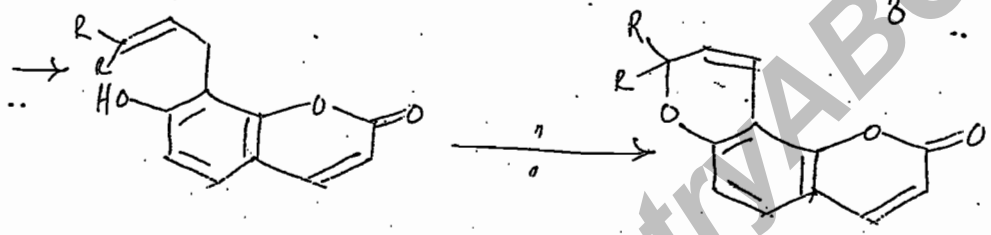


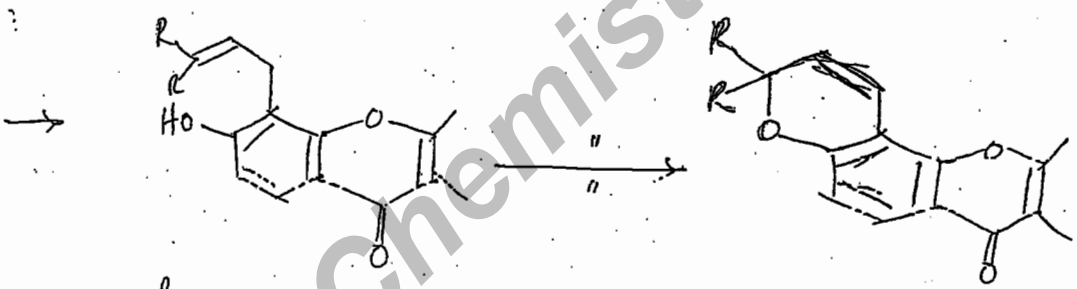
Mech:-

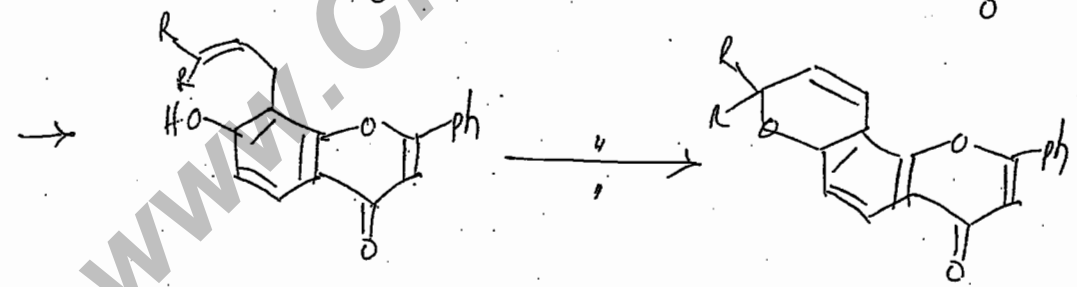


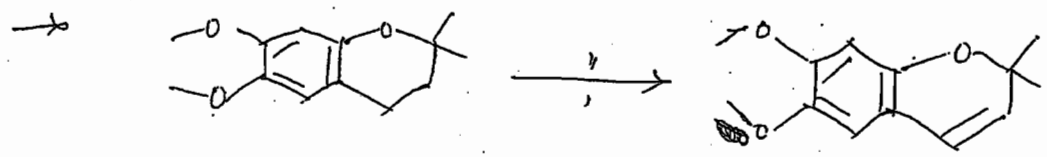


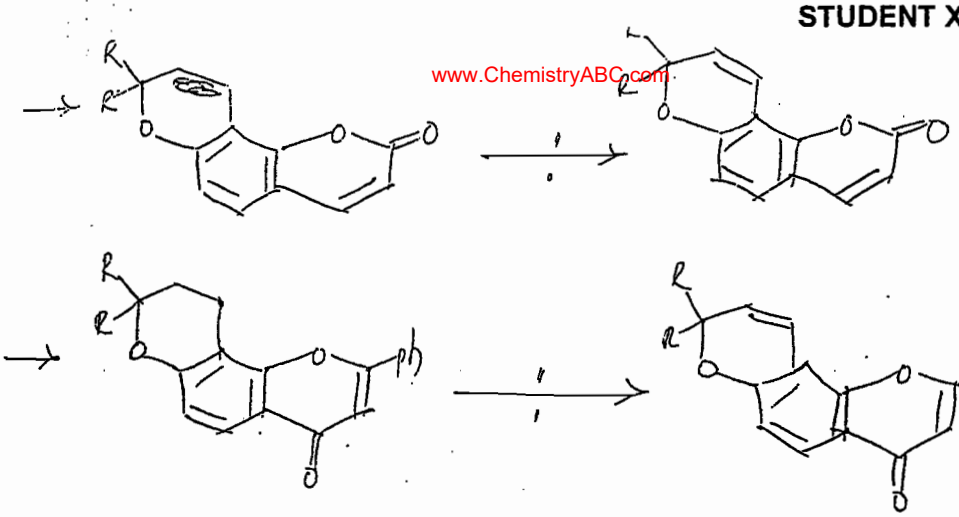


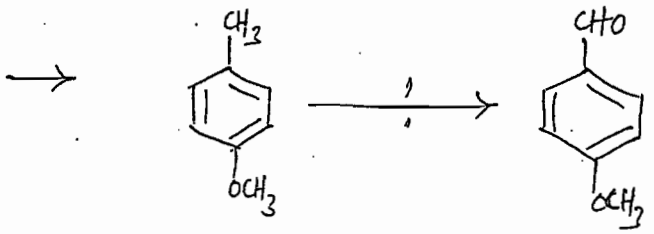


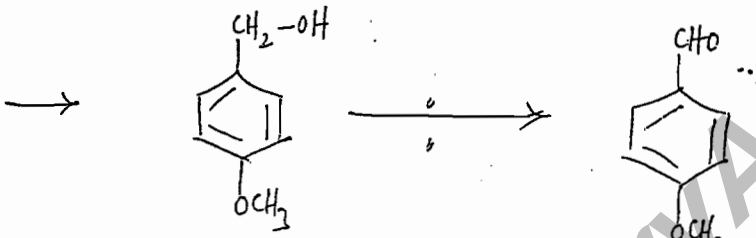


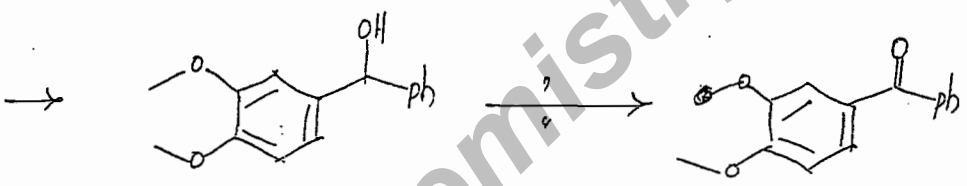






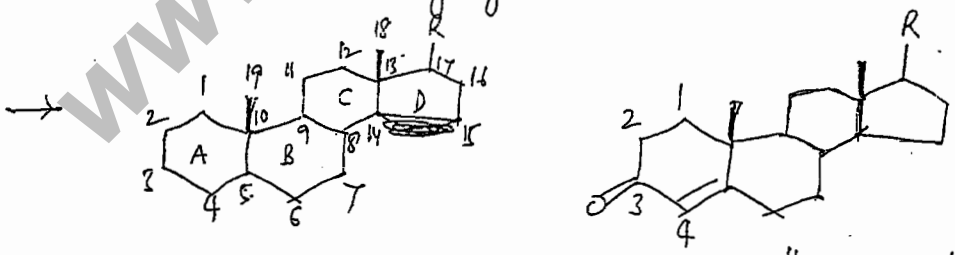




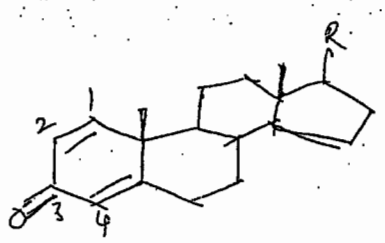


→ Steroidal skeleton synthesis :—

→ DDQ used as oxidising agent.

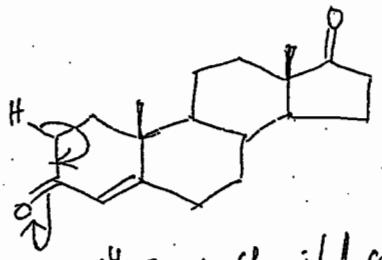


Δ^4-3-oxo-steroidal skeleton

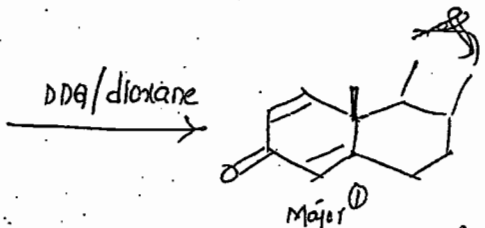


Δ^{4}– 3-oxo-steroidal skeleton

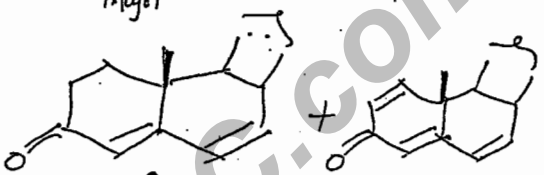
* V.IMP:–



Δ^{4}– 3-oxo steroidal skeleton



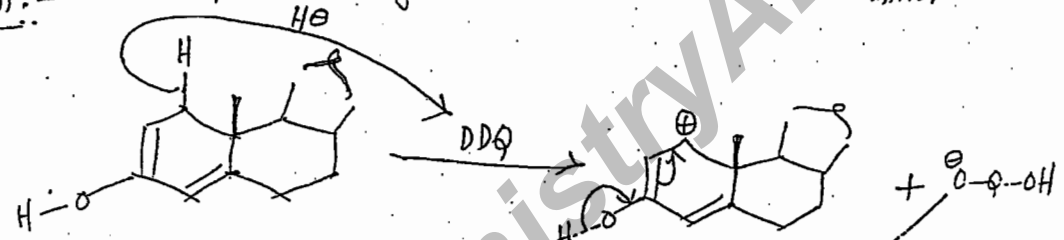
Major ①

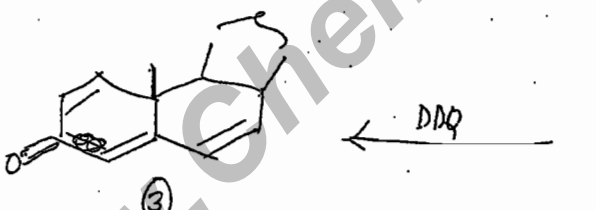


② minor ③

Enolisation
Kinetically controlled

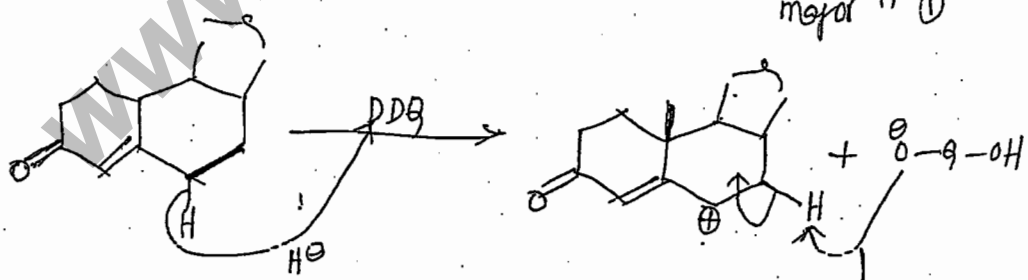
Mech:–

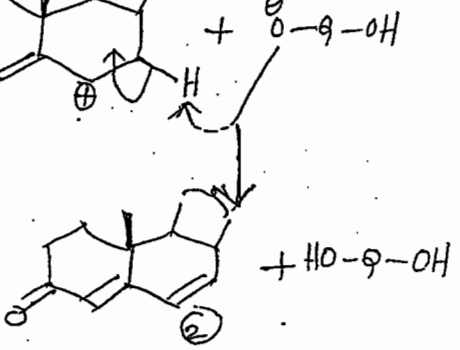




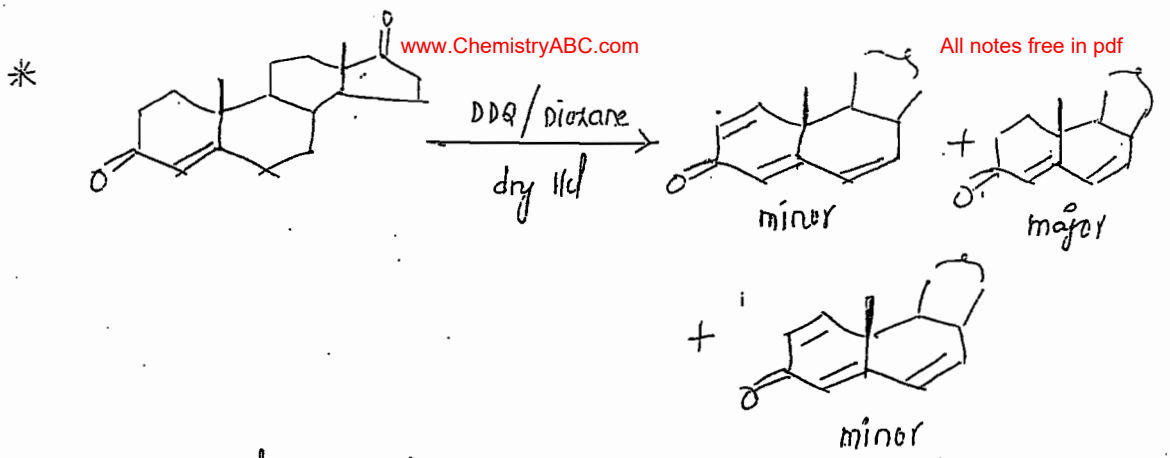
③

major ① H

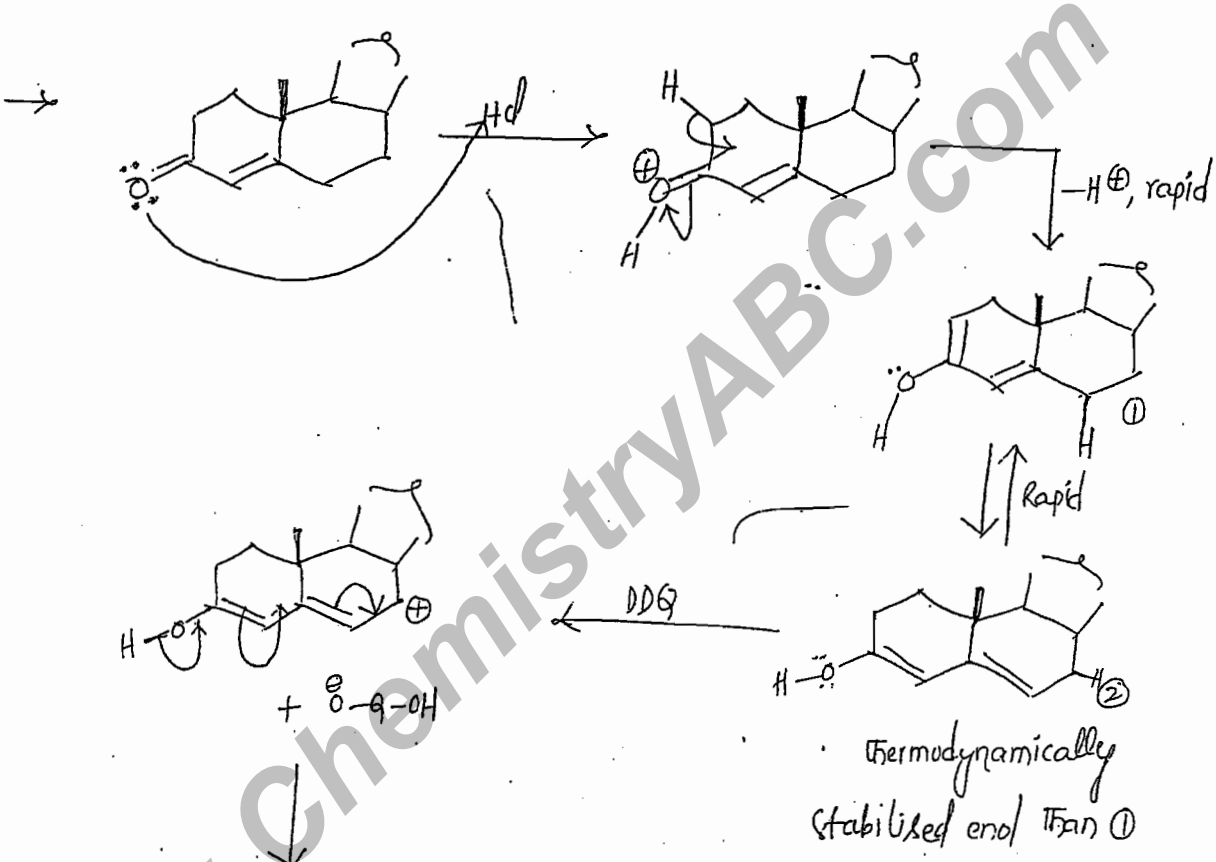


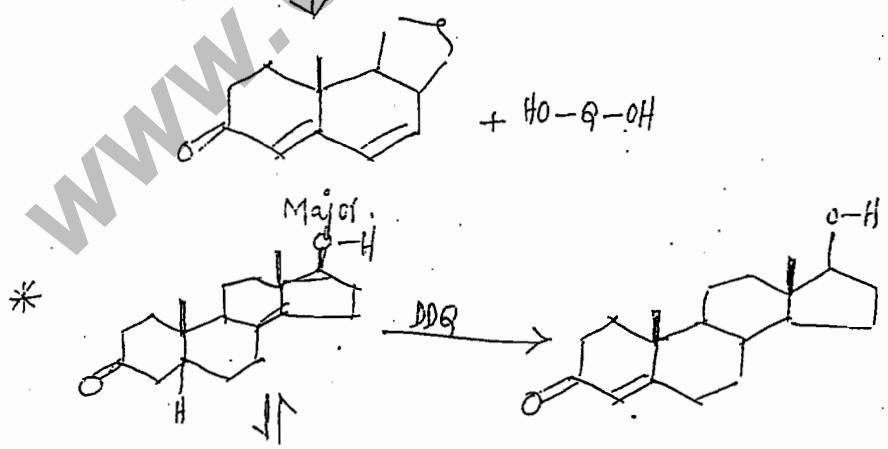


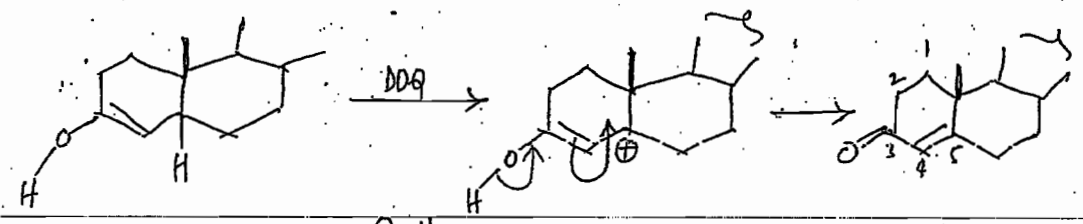
Major

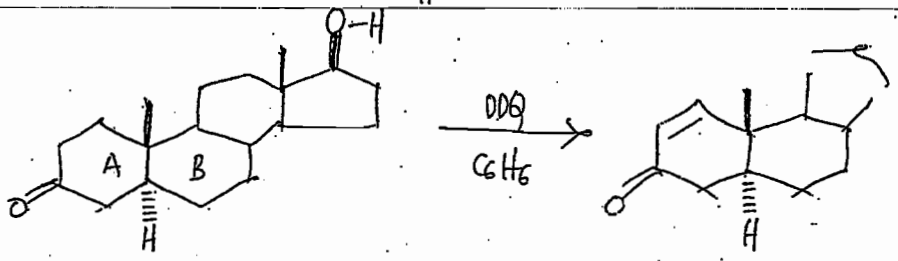


→ In dry Hcl, thermodynamically stable enol is produced.

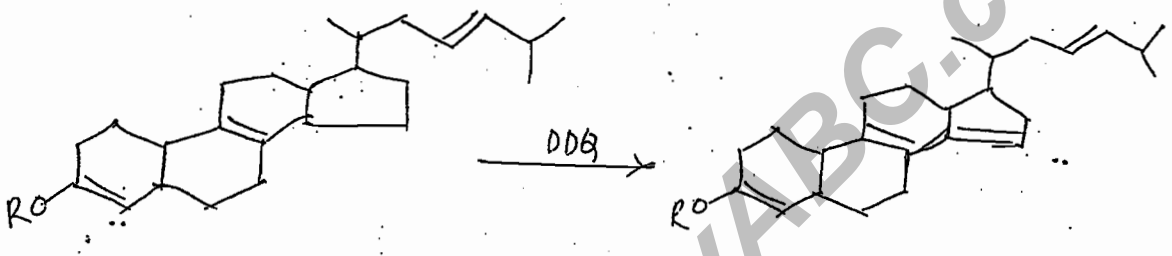




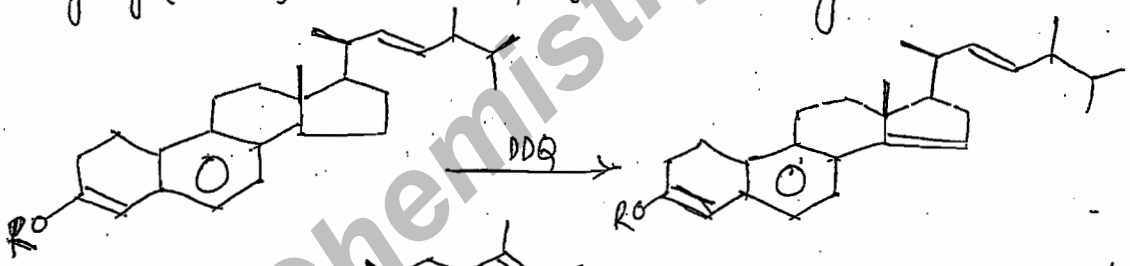


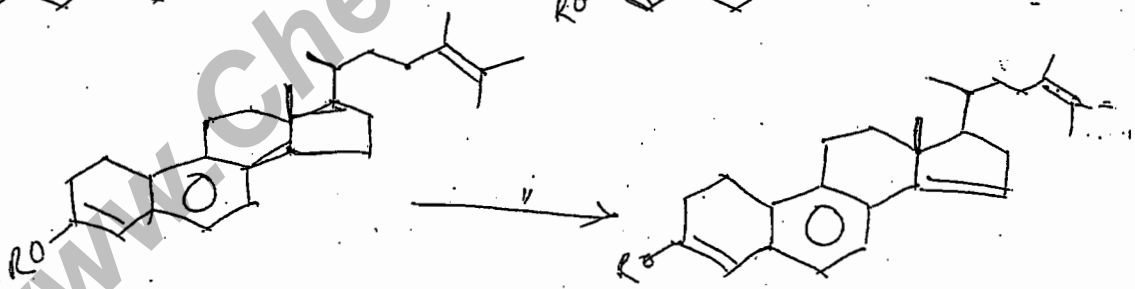


A/B fusion – trans → stable



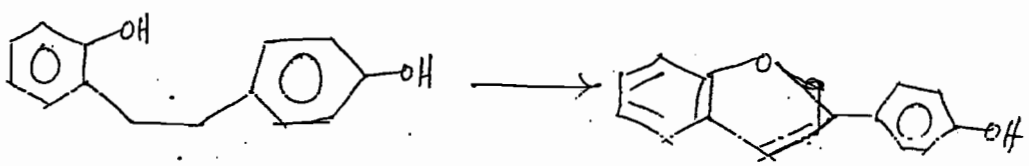
'Dehydrogenation from a strained five membered ring'



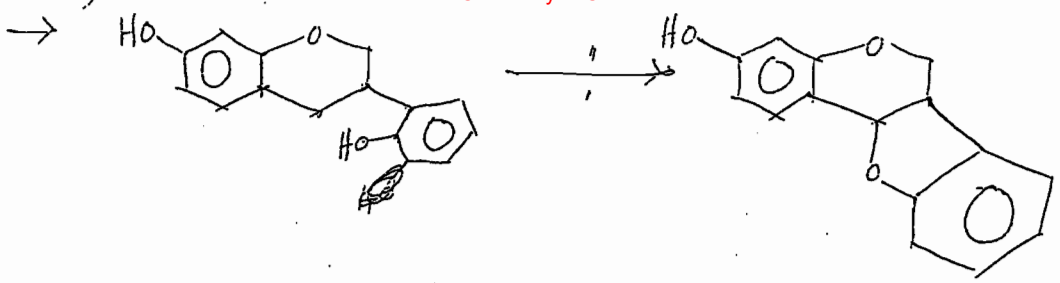


⇒ cyclisation – DDQ oxidn :–

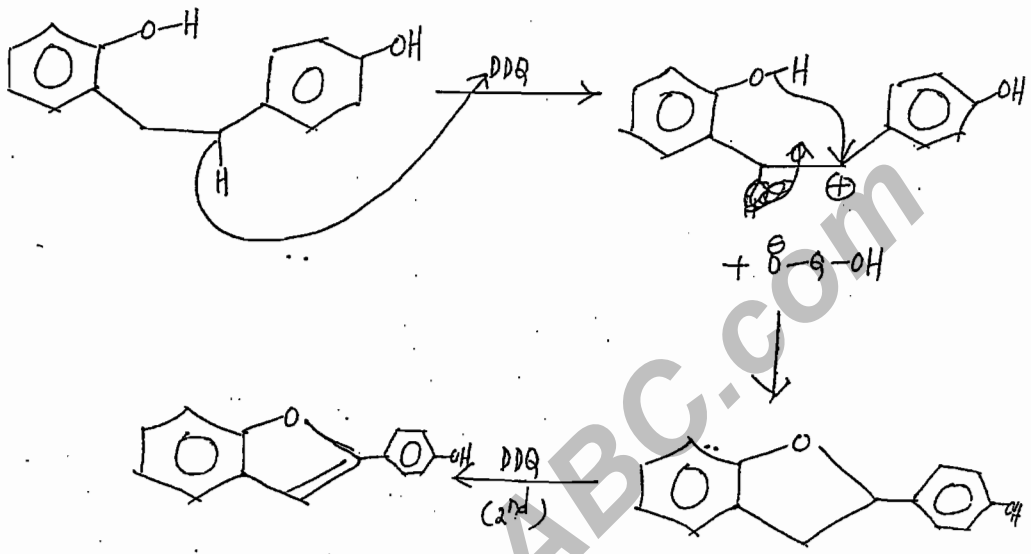
1)



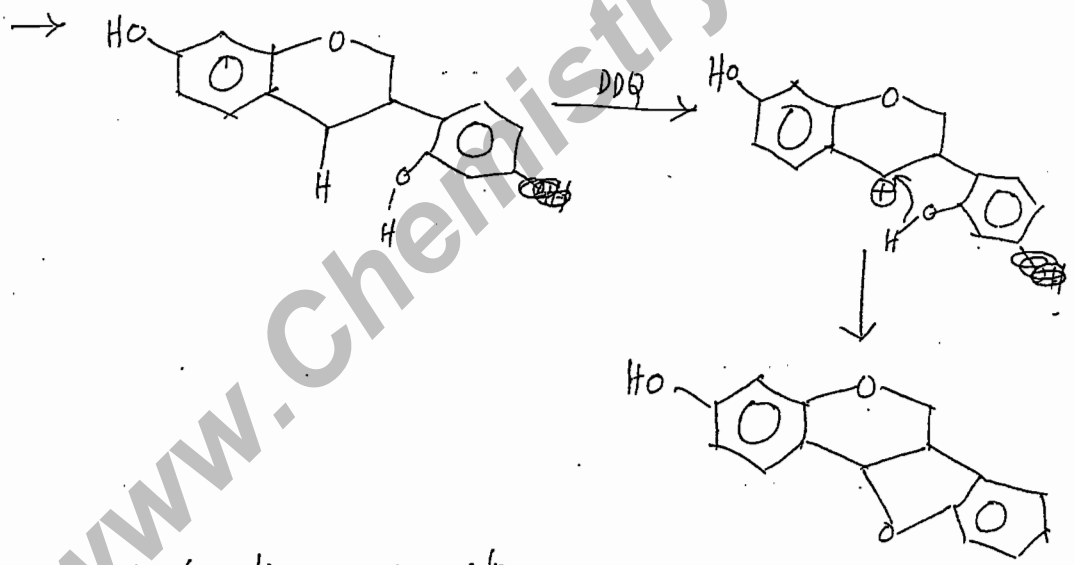
2)



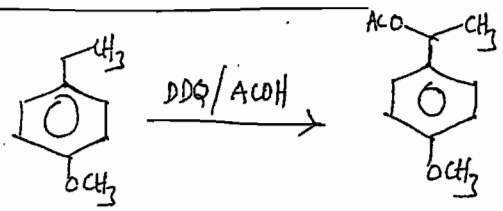
Mech:- 1)



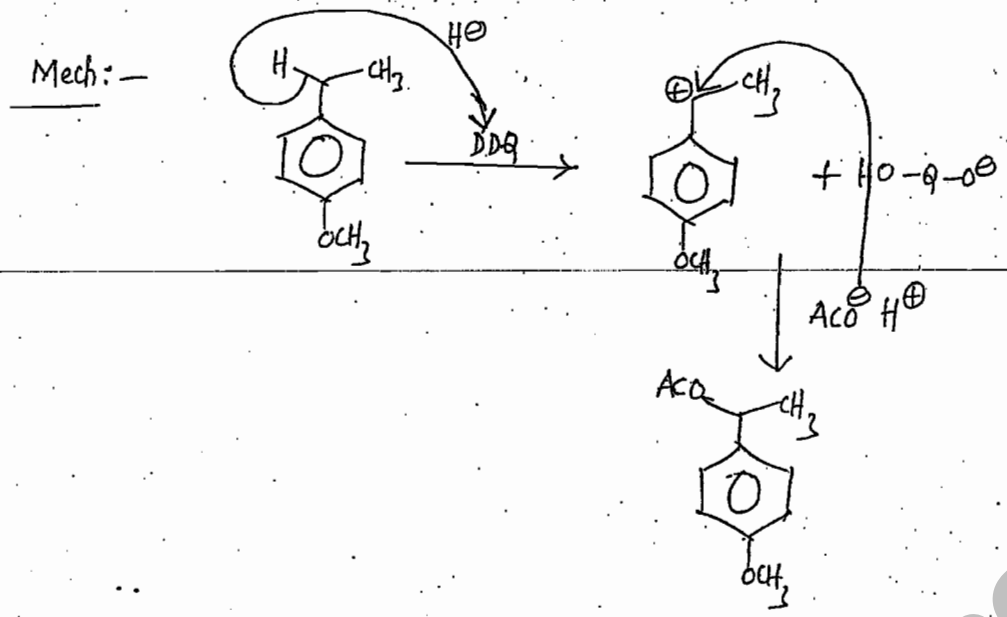
2)

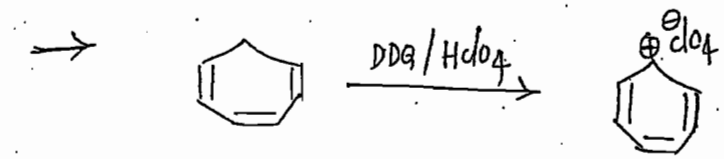


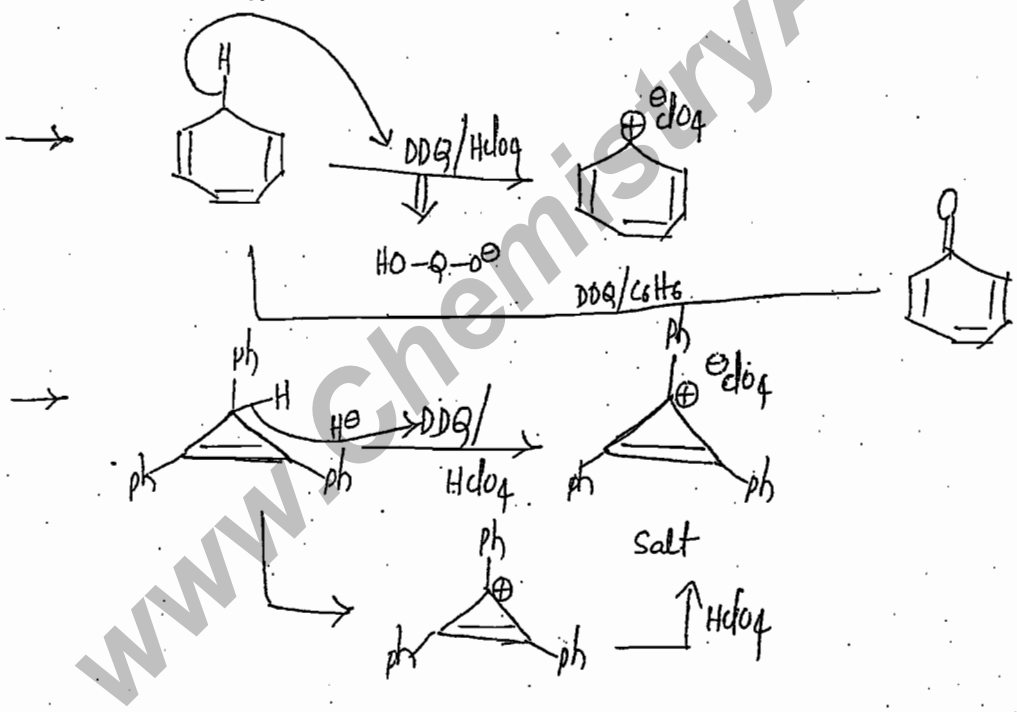
→ Salt formation in DDQ oxidn:-

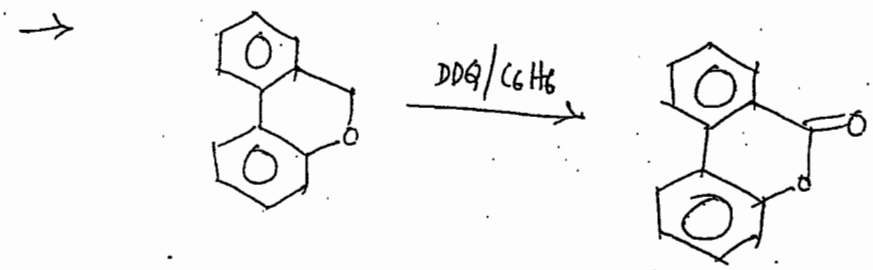


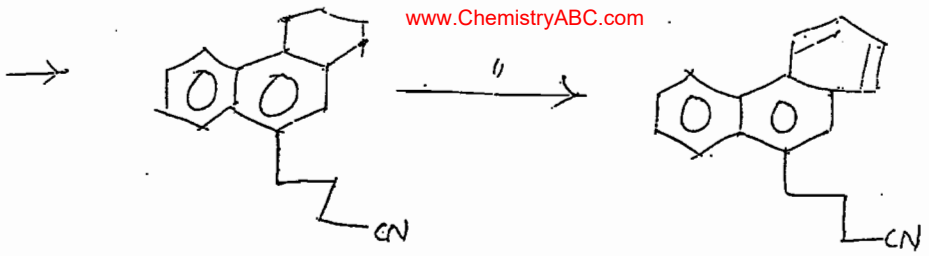
Mech:-

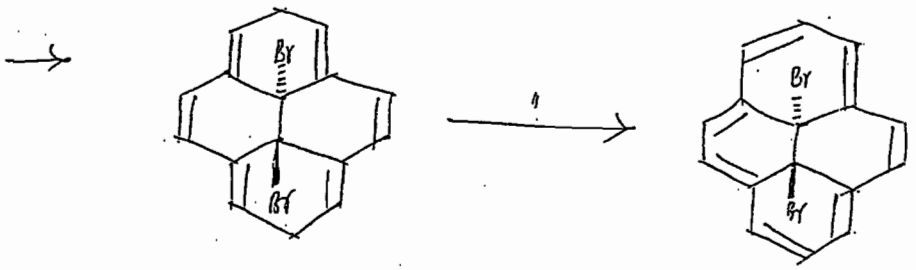


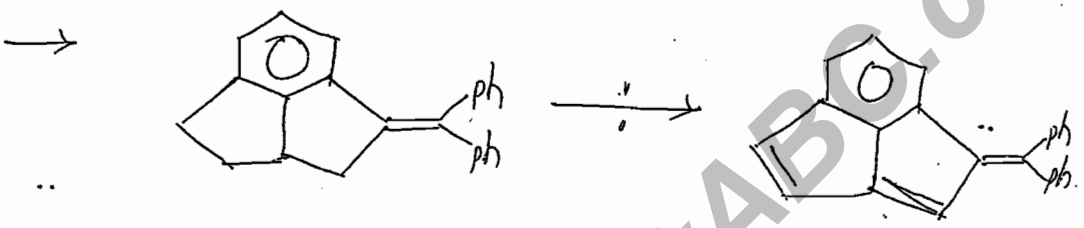


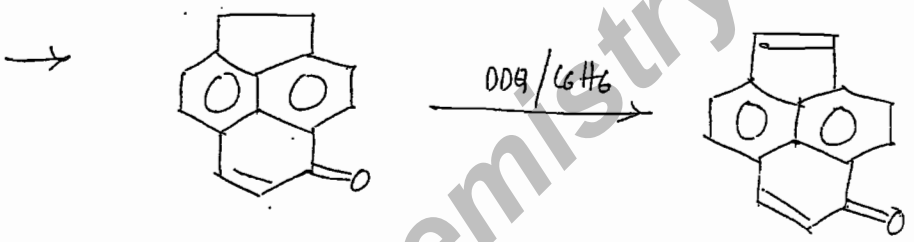


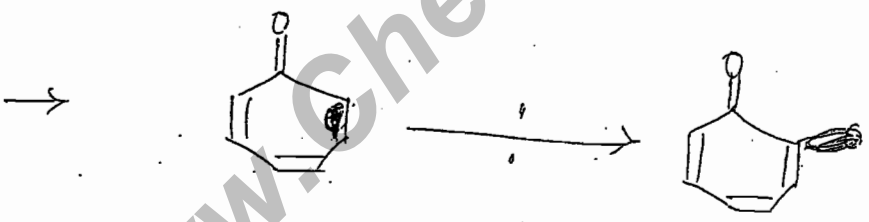




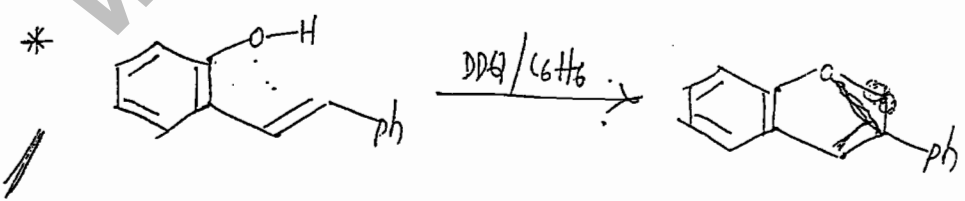


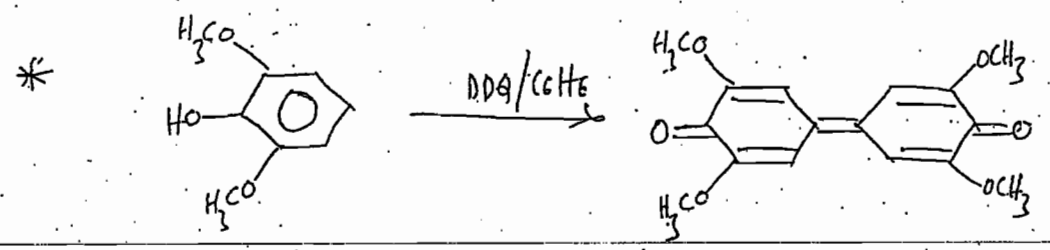


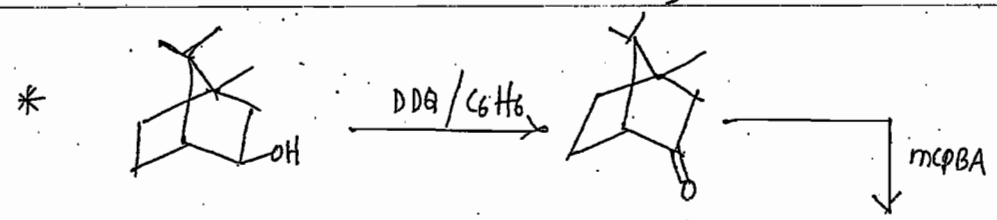




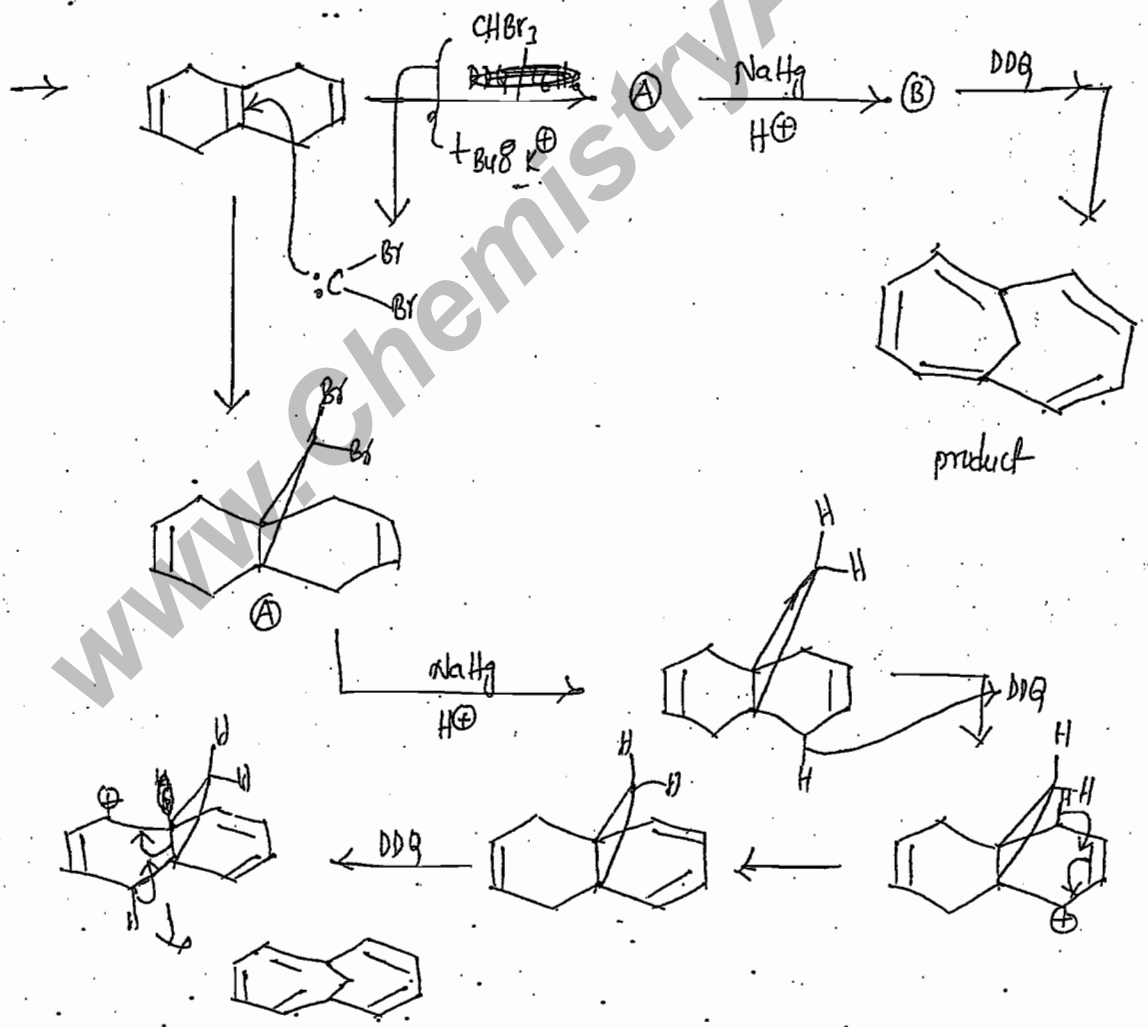
Miscellaneous types :—



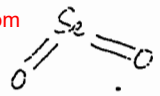




Exercises :—



Selenium – Dioxide (SeO_2)



Date : 30/04/18

→ white crystalline substance

→ Sublimable : purification of SeO_2

→ little toxic

→ $Se + O_2 \xrightarrow{\Delta} SeO_2$

Solvents :–

→ Aromatic hydrocarbons ; Benzene, xylene, toulene

→ Halobenzene , d- 

→ Cyclic Ethers , THF, 1,4-dioxanes

→ Alcohols , MeOH. EtOH

→ AcOH, Ac_2O, water

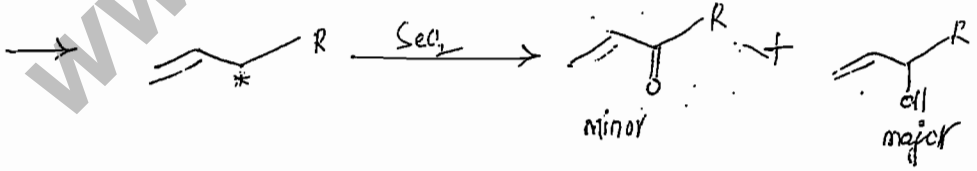
C_6H_6 + SeO_2 ← few drops of water

Applications :–

→ i) oxidation of allylic, benzylic and α-position of withdrawing group.

eg :- $-\overset{\alpha}{C}H_2-W \xrightarrow{SeO_2} -\underset{\underset{O}{\|}}{C}-W$

eg : carbonyl

→ 

→ Ar–CH_2–R $\xrightarrow{SeO_2}$ Ar–$\underset{\underset{O}{\|}}{C}$–R

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2) Dehydrogenation

3) Ac Catalyst

4) Miccellaneous.

⇒ (I) oxidation of α-position of withdrawing group :–

→ oxidises α-position of withdrawing gp into new carbonyl function.

→ Examples :– oxidation of α-position of carbonyl compounds.

→ $R-CH_2-\underset{\underset{O}{\|}}{C}-R \xrightarrow{SeO_2} R-\underset{\underset{O}{\|}}{C}-\underset{\underset{O}{\|}}{C}-R$

1,2-diketo

→ $CH_3-CHO \longrightarrow OHC-CHO$

glyoxal

→ $H_3C-\underset{\underset{O}{\|}}{C}-CH_3 \xrightarrow{SeO_2} H-\underset{\underset{O}{\|}}{C}-\underset{\underset{O}{\|}}{C}-CH_3$

methyl glyoxal

→ $H_3C-\underset{\underset{O}{\|}}{C}-CH_2-CH_3 \xrightarrow{SeO_2} H_3C-\underset{\underset{O}{\|}}{C}-\underset{\underset{O}{\|}}{C}-CH_3 + OHC-\underset{\underset{O}{\|}}{C}-CH_2-CH_3$

dimethyl glyoxal (major) minor

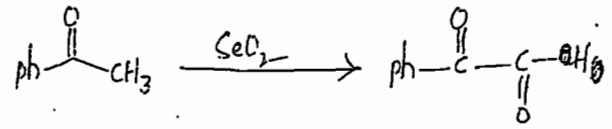
(highly alkylated α-position gets oxidised preferentially in the case of unsym. ketones)

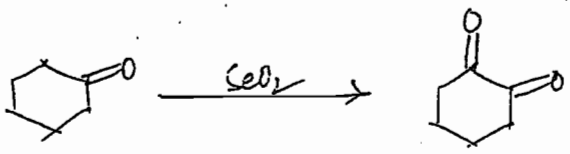
$H_2C=\underset{\underset{OH}{|}}{C}-CH_2-CH_3$ less stable

$H_3C-\underset{\underset{OH}{|}}{C}=CH-CH_3$ stable

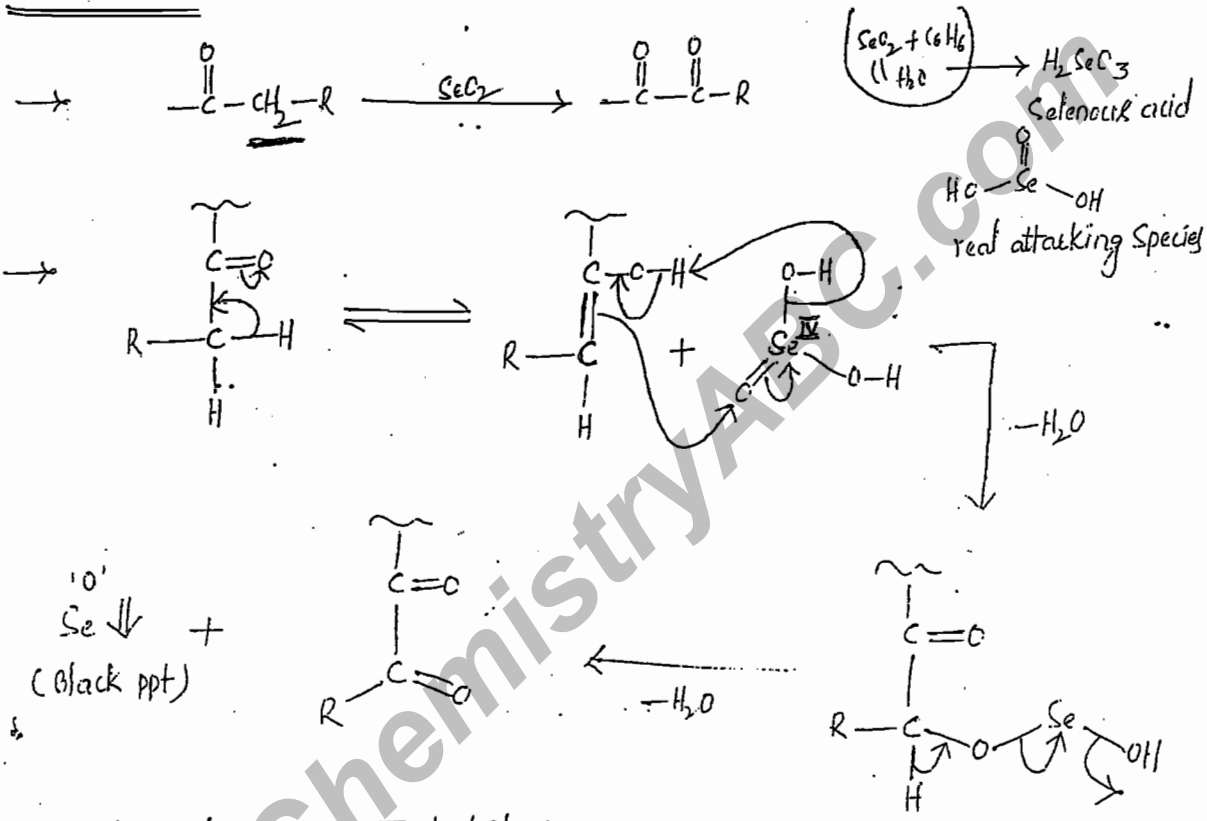
→ whichever position produce the stable enol, will easily get oxidised.

→ VIMP:-

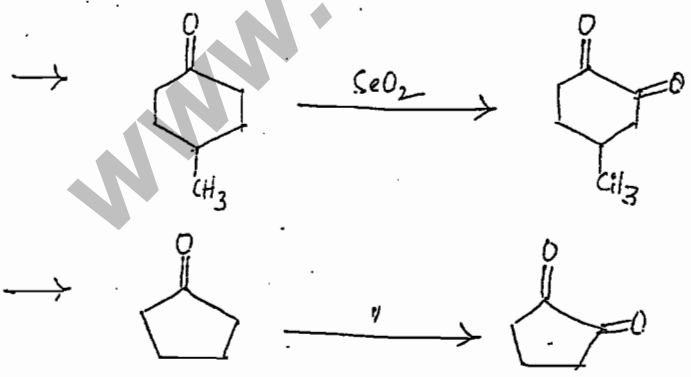


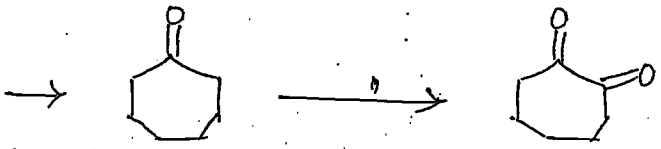


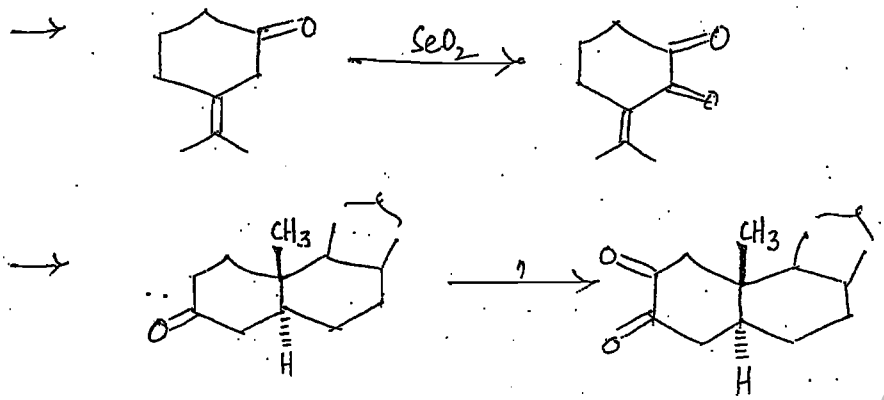
Mechanism :-

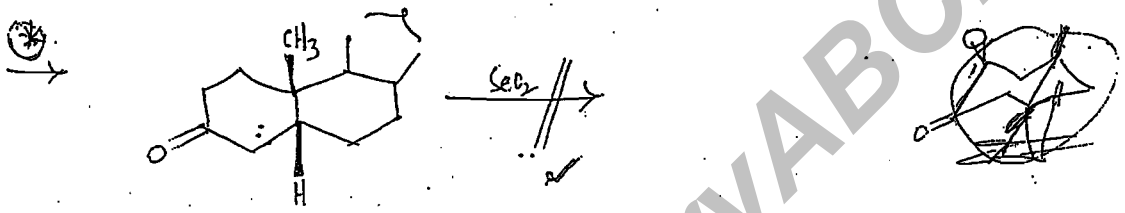


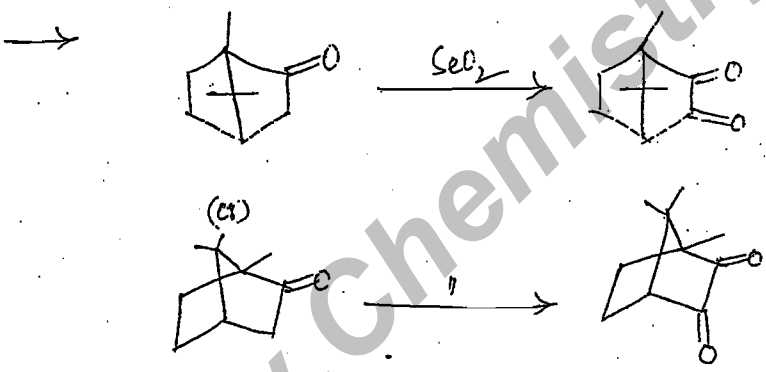
* change in O.S : +IV to '0' :

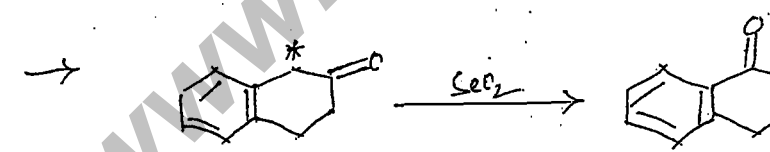


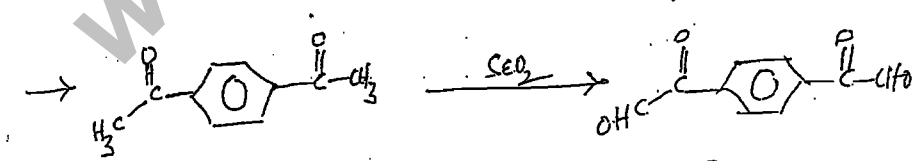


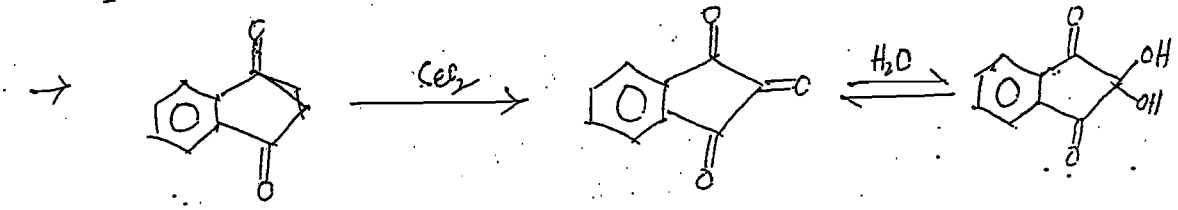


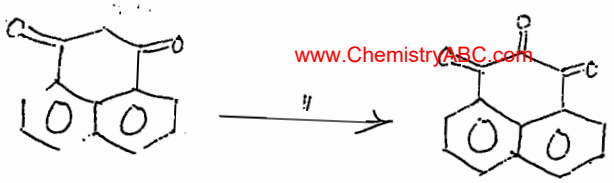


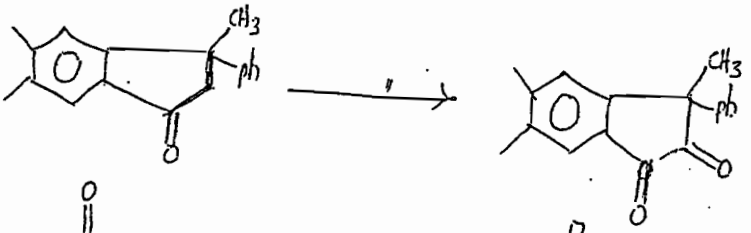


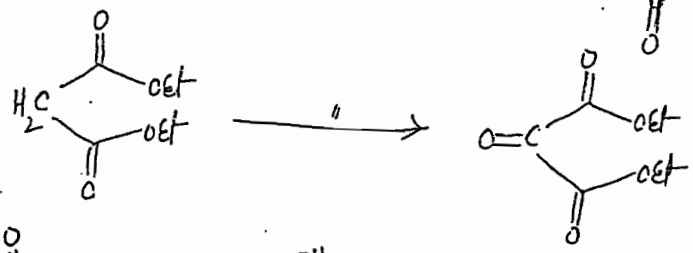


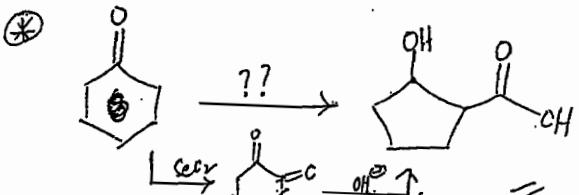








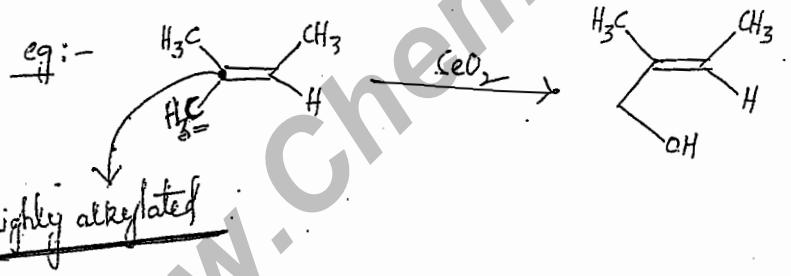




II. oxidn of allylic positions :— **Benzilic acid R.R.**

→ Major product is alcohol

Rules :— 1) "In unsym. alkylated olefines, highly alkylated sp^2 carbon α-positi preferentially get oxidised

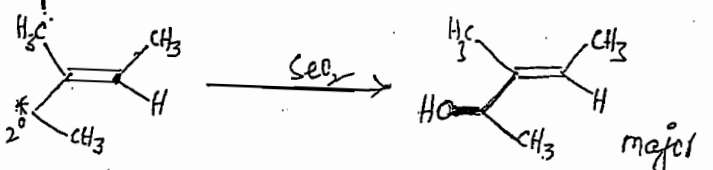


highly alkylated

2) At allylic positions, 1°/2°/3° C–H functions present, reactivity order

3° > 1° > 2°

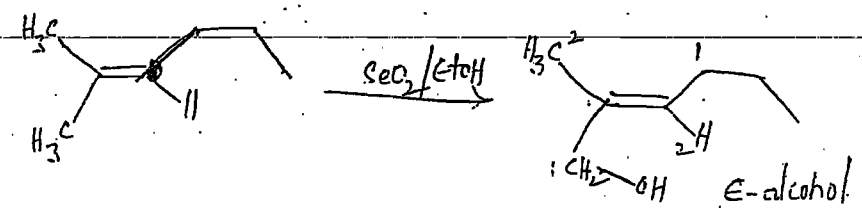
→ eg :-



major

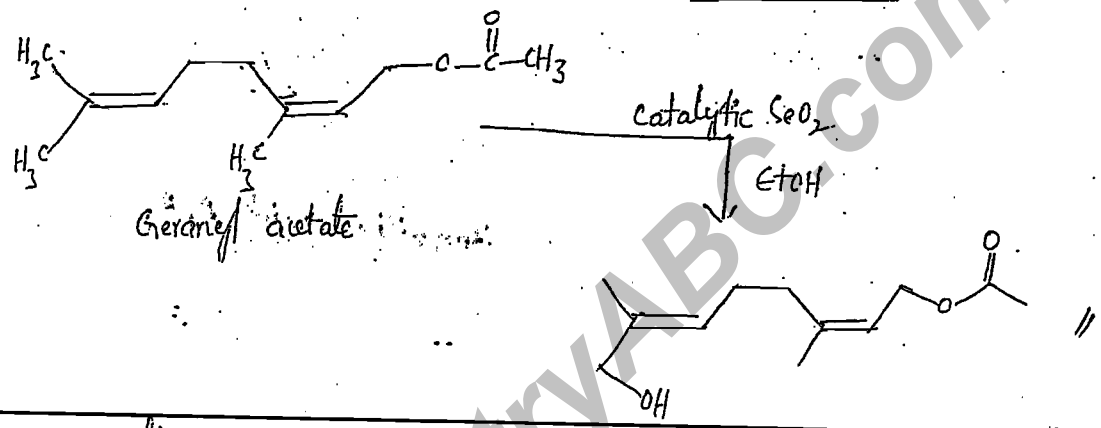
3) If there is a possibility of ∈ & z alcohols formation, ∈-alcohol's formation – major.

→ eg:



✓ If (1) & (2) rules are in competition, (2) rule is preferred.

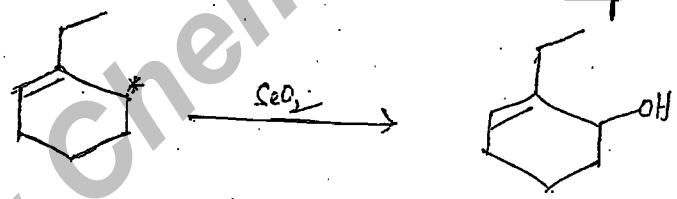
→



Geranyl acetate

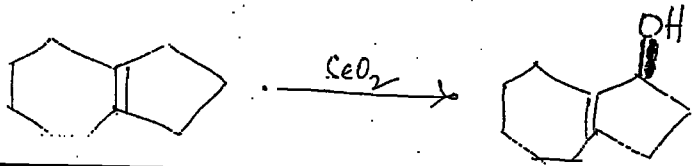
4) In monocyclic systems, if there is a allylic position, part of ring, preferentially get oxidised into alcohol.

→ eg:



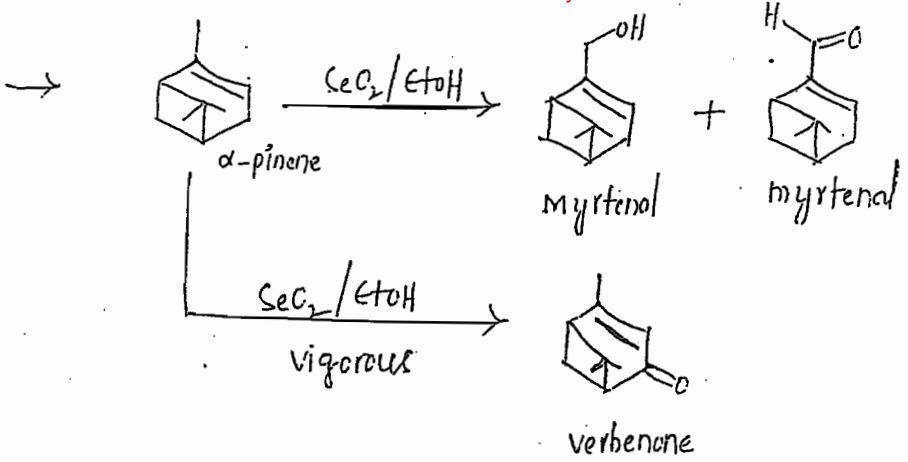
5) In Fused bicyclic systems, if ring size unsymmetrical, strained ring allylic positions predominantly or preferentially oxidised.

→ eg:-



6) In bridged bicyclic systems, oxidation product depends on reaction conditions.

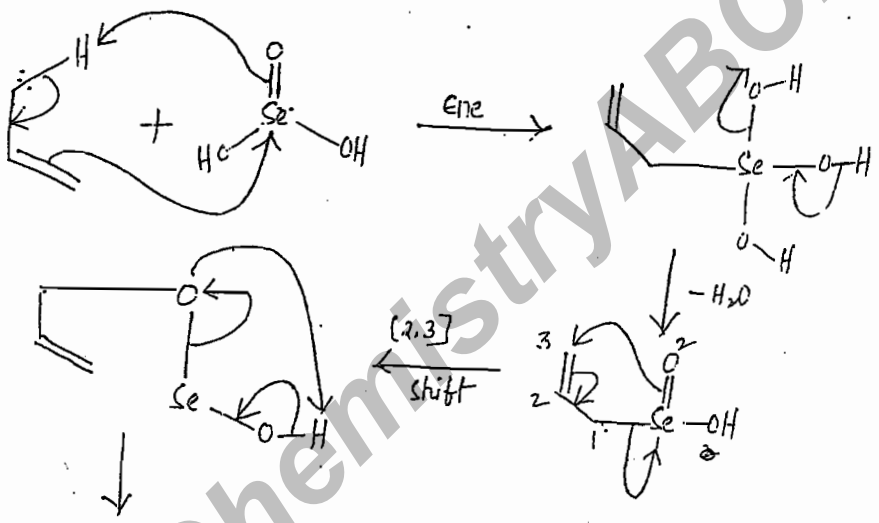
V.IMP :-



Mechanism :- (Alcohol formation)

→ Ene reaⁿ + [2, 3] Sigmatropic shifty } ⇒ V.IMP.

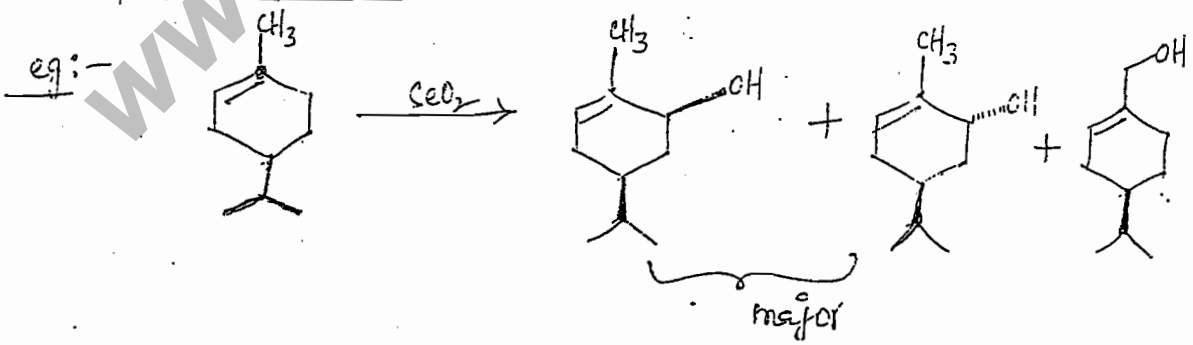
→ $CH_2=CH-CH_3 \xrightarrow{SeO_2} CH_2=CH-\overset{*}{C}H_2-OH$



$CH_2=CH-CH_2-OH + Se=O$ (or) SeO.

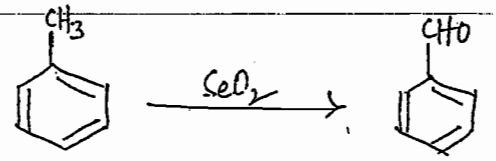
→ i.e. It is one of the method for conversion of olefines into allylic alcohols.

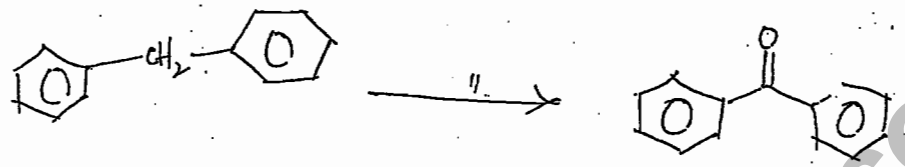
eg:-



III. oxidation of Benzylic positions :—

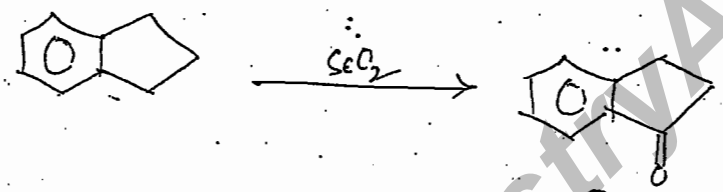
→ Benzylic position get oxidised into carbonyl function.

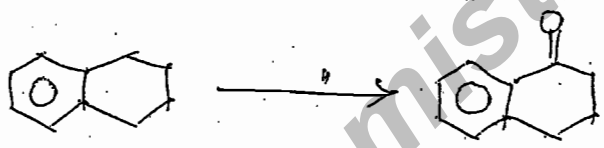
→ 

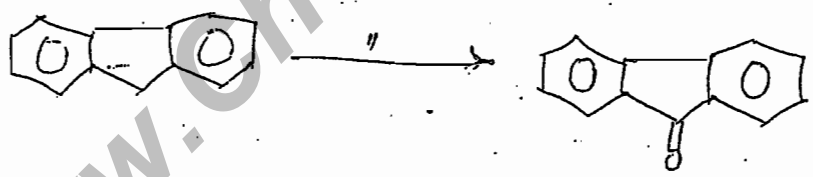
→ 

→ ph–CH_2–CH_2–ph ⟶ ph–C(=O)–C(=O)–ph

Benzil

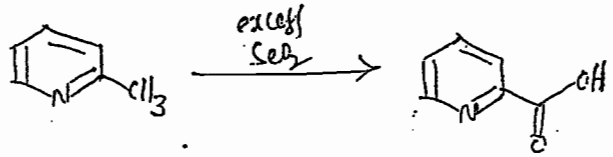
→ 

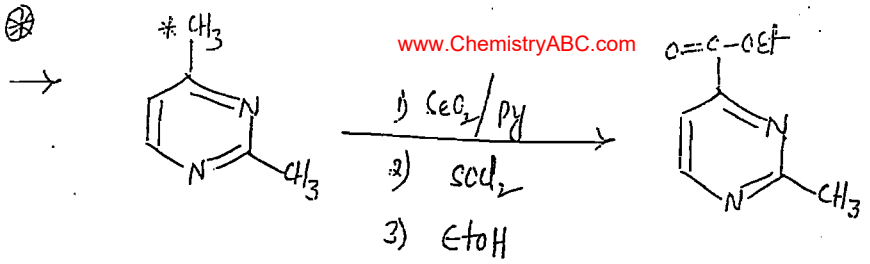
→ 

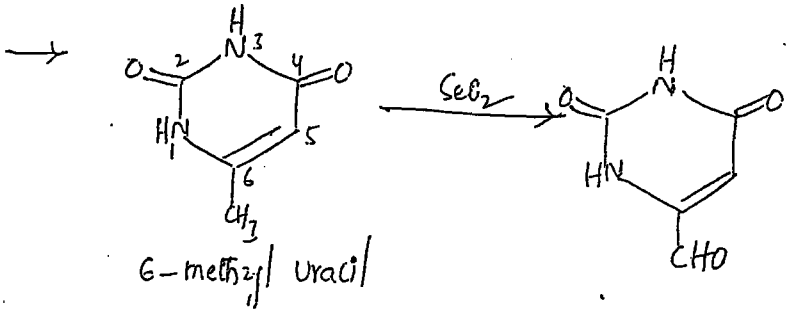
→ 

* Active position of Heterocyclic oxidn of :—

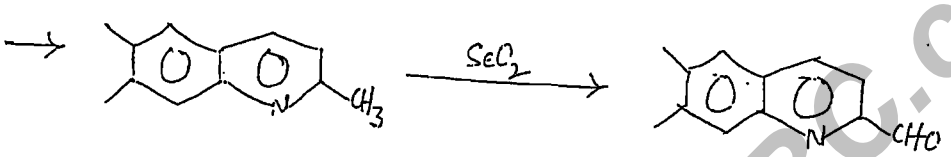
→ oxidn product depends on nature of reactant & reagent conditions.

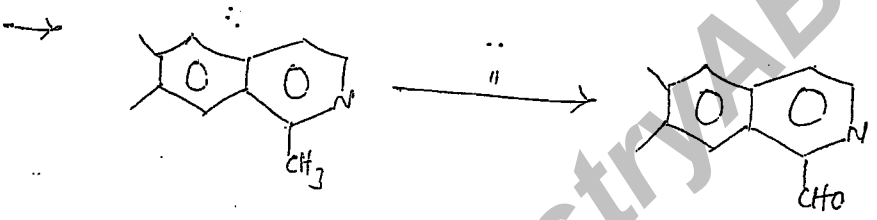
→ 

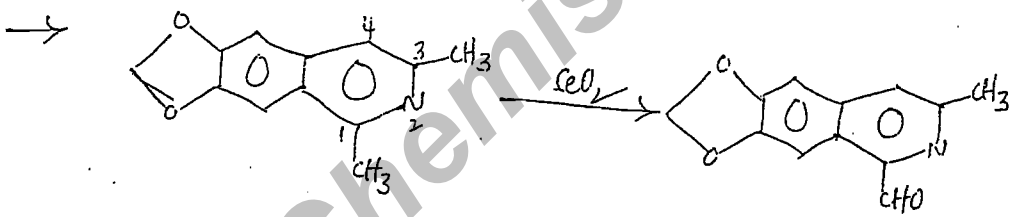


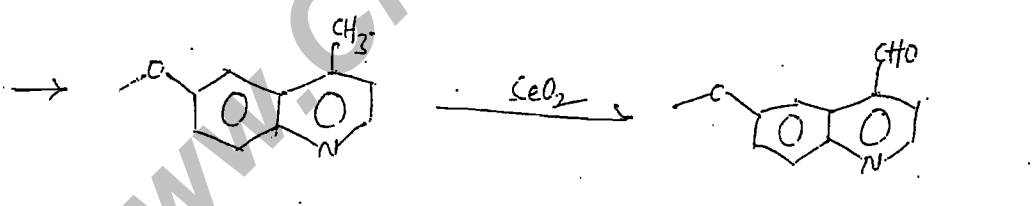


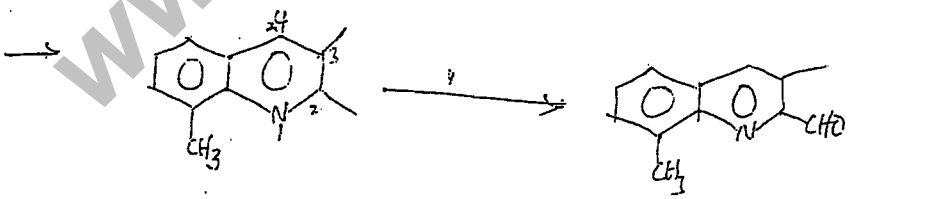
6-methyl uracil

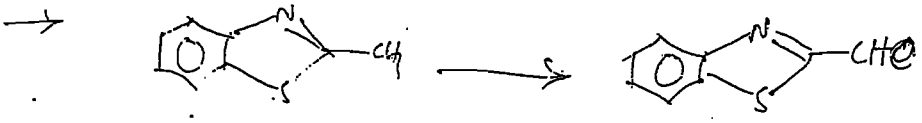




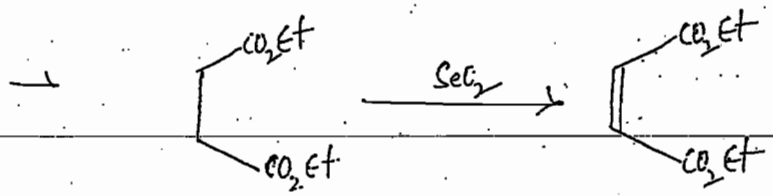




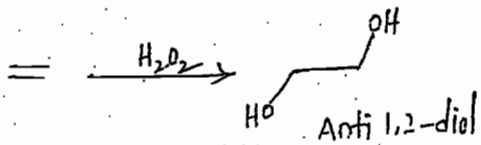




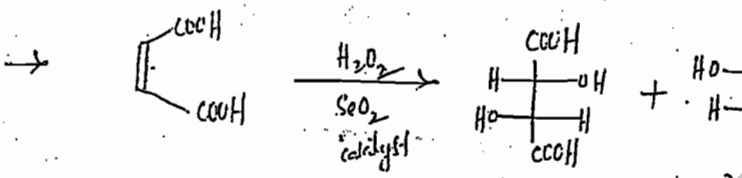
Dehydrogenations :-



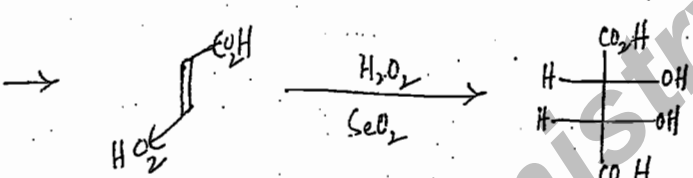
As catalyst :- H_2O_2



Anti 1,2-diol

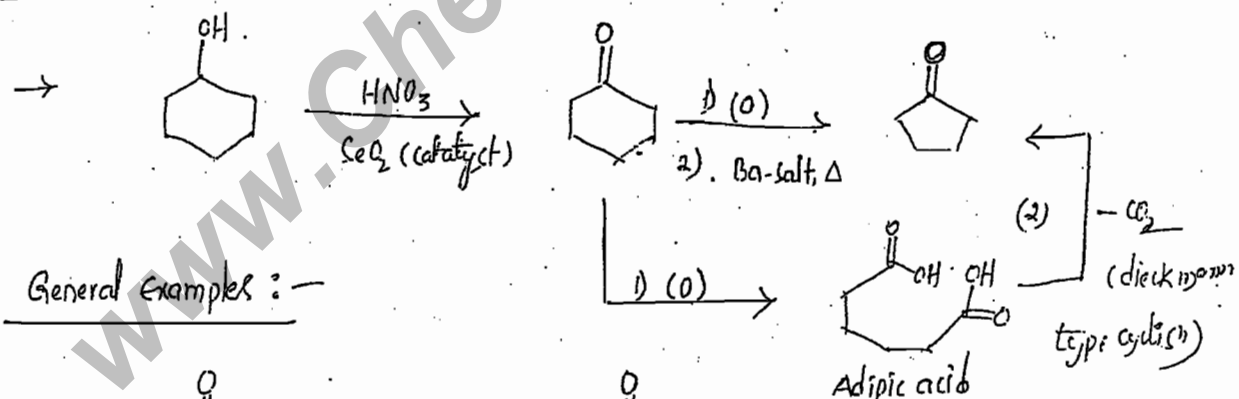


Racemic

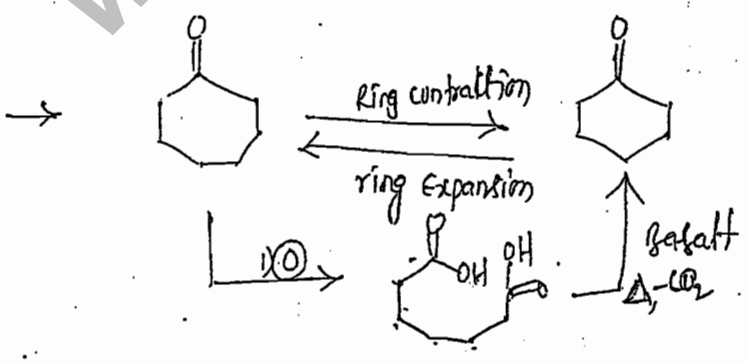


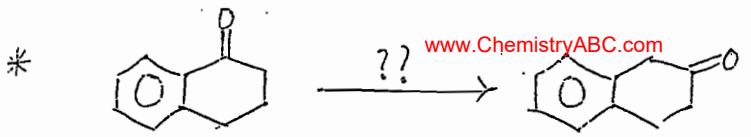
Meso

V.IMP:-



General Examples :-



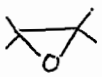


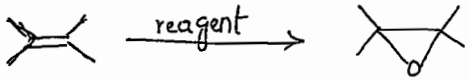
V.V.IMP

Date : 04/05/08

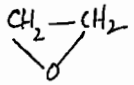
Oxidation of olefines into epoxides ; epoxidation —

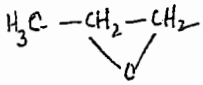
Epoxide :— Three membered 'oxygen heterocyclic'

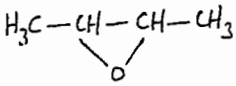
IUPAC – oxirane 

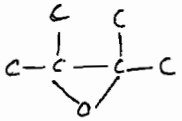
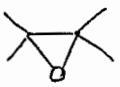


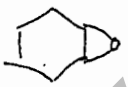
Nomenclature Alkane/ cycloalkanes : —

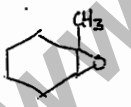
→  1,2 epoxy Ethane epoxy + alkane
epoxy + cycloalkane

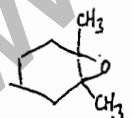
→  1,2 epoxy propane

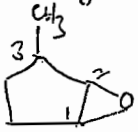
→  2,3 " Butane

→ 2,3 dimethyl 2,3-epoxy butane  

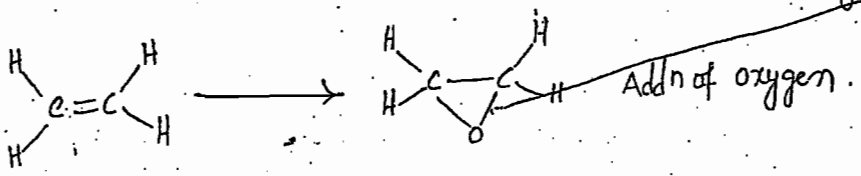
→  1,2 epoxy cyclohexane

→  1-methyl, 1,2-epoxy cyclohexane.

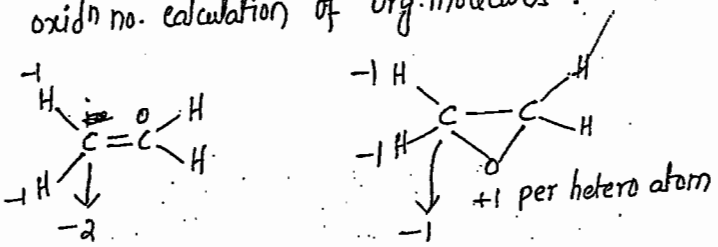
→  1,2-dimethyl " " "

→  3-methyl, 1,2 epoxy cyclopentane.

Epoxidation :- conversion of olefine into oxirane by using oxidising agent.



⇒ oxidn no. calculation of org. molecules :-



$-2 \longrightarrow -1$ ∴ oxidn

In epoxidn of olefine, $1e^{\ominus}$ is lost by 1 'C'.

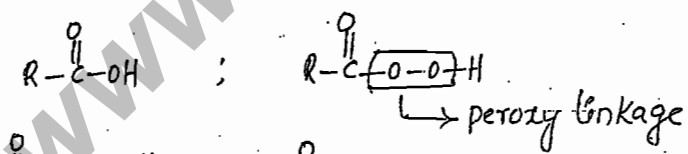
⇒ $2e^{\ominus}$s per molecule 2 C's

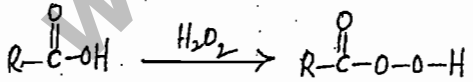
olefine $\xrightarrow{\text{reagent}}$ epoxide ∴

Types of reagents for epoxidation :-

1) per acids / peroxy acids
2) $H_2O_2/OH^{\ominus}$; basic media
3) Alkyl hydro peroxide / metal complexes
4) dioxiranes
5) hypo halous acid
6) Iodine catalysed epoxidn.

I. per acids / peroxy acids :-

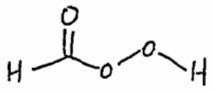




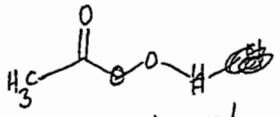
$R-CO_3H$ R = H, alkyl, aryl

$R-CO_3H \xrightarrow{\Delta}$ even at room temp. $RCOOH + (O)$ nascent 'O'.

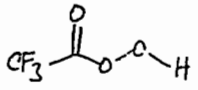
∴ RCO_3H readily releases 'O', ∴ used as reagent for epoxidation.

eg:- 

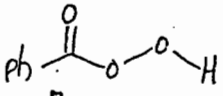
per formic acid / peroxy " PFA.



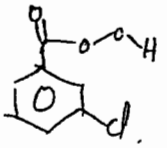
per acetic acid PAA

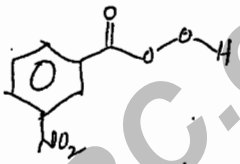


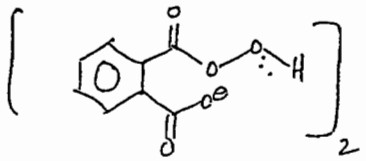
per trifluoro acetic acid PTFAA / PTAA

→ if R = ph : per benzoic acid ; 

→ m-chloro Benzoic acid

" peroxy " mCPBA 

m-nitro " " 

→  Mg^{+2} → Mg Monoperoxy phthalic acid

" mono per " "

" MMPPA.

→ mCPBA widely used laboratory reagent.

→ stable, easy to preserve for long time.

→ cheaper (low cost)

→ In org. solvents, easily soluble

Solvents:— CH_2Cl_2 – DCM – dichloro methane

$CHCl_3$ — chloroform

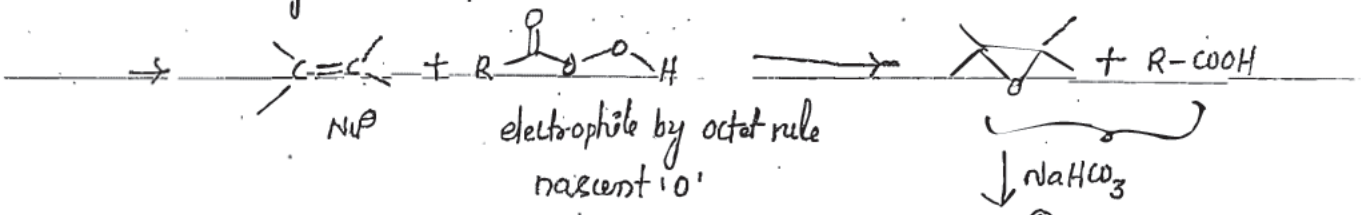
C_6H_6 ⌀, toulene, xylene;, ether, Et_2O, THF.

Alcohols, MeOH, EtOH ; Acids, AcOH, H_2O

Temp:— −10°C to 25°C.

olefin + per acid ⟶ epoxide + carboxylic acid

→ Treating of product mixture with $NaHCO_3$ soln, eliminate by product carboxylic acid.

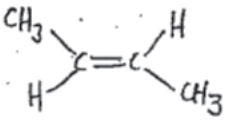


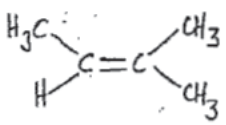
→ In epoxidn, olefin is $Nu^{\ominus}$, per acid - electrophilic agent.

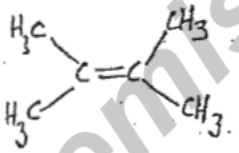
✱ Reactivity of olefines in epoxidation :—

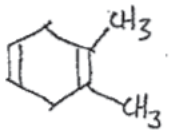
→ $e^{\ominus}$ rich olefins, good $Nu^{\ominus}$, faster in epoxidation.

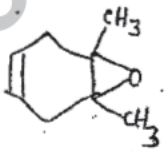
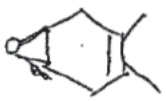
→ In alkylated olefins, with ↑ in alkyl gps at db, reactivity of olefins ↑ in epoxidn, steric crowding ignored.

→ $CH_2=CH_2 < CH_2=CH-CH_3 < CH_2=C(CH_3)_2 <$  <

 <

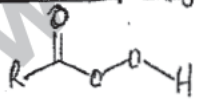


→ 

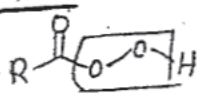
 + 

structural isomers in unequal proportions. (ratio)

→ Electrophilic reagent - reactivity :— ∴ regio selective.

 R = $e^{\ominus}$ withdrawing group

✱"at carbonyl of peracid, presence of $e^{\ominus}$ withdrawing group ↑ reactivity of peracid."

 → makes O–O link weak by $e^{\ominus}$ withdrawing group.

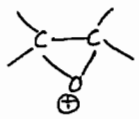
→ CF_3-CO_3H highly reactive in peracids in epoxidation due to

presence of strong $e^{\ominus}$ withdrawing CF_3 gp at carbonyl.

→ CF_3-CO_3H releases (O) readily. ∴ cann't be stored for long time.

→ Although CF_3-CO_3H highly reactive in epoxidation, less commonly used in laboratory synthesis due to

- ✓→ high cost chemical
- ✓→ highly unstable
- ✓→ byproduct CF_3CO_2H (strong acid) opens the epoxide.

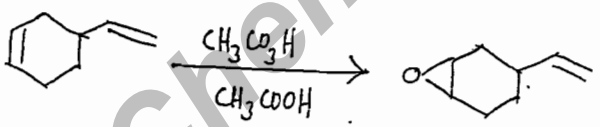
→ 

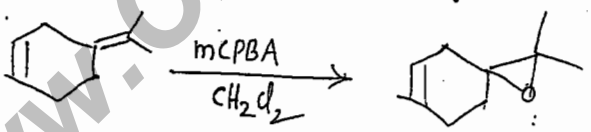
→ Regioselectivity in epoxidation with peracids :—

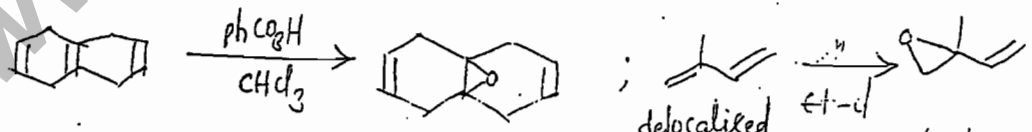
olefinic compound with multiple double bonds, selective epoxidation takes place at "highly alkylated db."

$$CH_2=CH-CH_3 \xrightarrow{HBr} \underset{Br}{CH_2-CH_2}-CH_3 + H_3C-\underset{Br}{CH}-CH_3$$

→ 

→ 

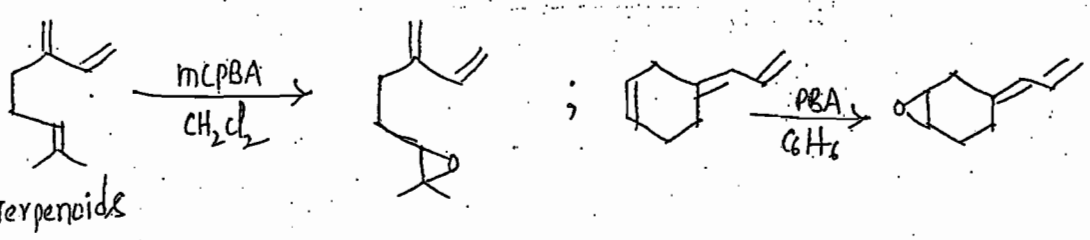
→ 

→ 

∴ less nucleophilicity.

→ conjugated olefins, weak Nu$^{\ominus}$ than isolated olefins

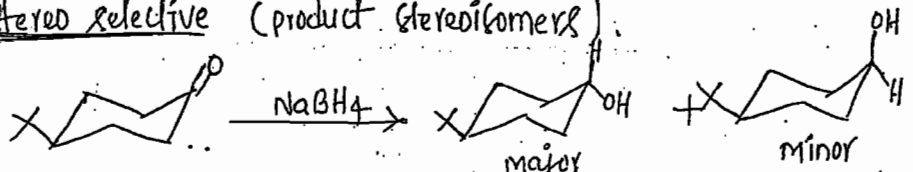
∴ In cmpd, if isolated & conjugated double bonds are present, selective epoxidn at isolated double bond



Terpenoids

Stereo selectivity in epoxidation :—

In chemical rean, stereoisomers produced in unequal amounts, called Stereo selective (product stereoisomers).



major minor

Stereo isomers (selectivity)

→ In epoxidation, stereo selectivity controlled by—

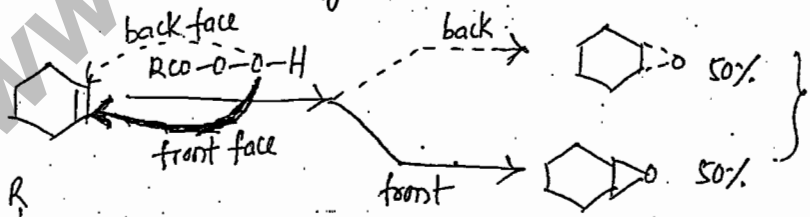
i) steric crowding near to db ii) chelations / H-bonding.

*i) Steric crowding near to db : Stereo selectivity—

→ Epoxidn at olefin is syn-addition (∵ (O) develops two new σ bonds same side).

→ Stereochemistry depends on facial selectivity.

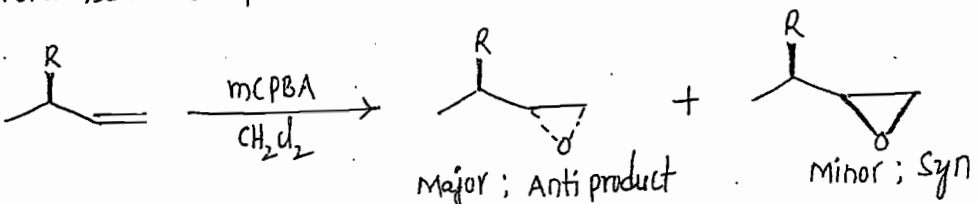
At olefin, if no steric crowding at top or bottom face, epoxidn equally probable at both places, resulting product in equal amounts/ratio. No stereo selectivity in epoxidation.

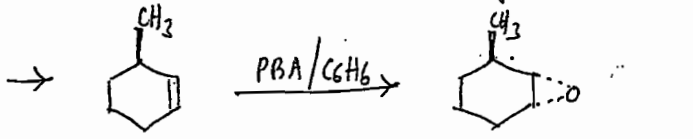


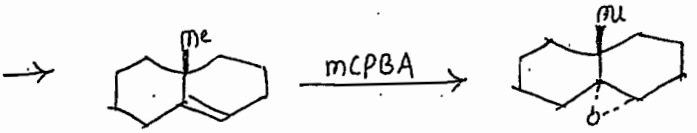
→ near to unsaturation (allylic position) if there is a alkyl substituent at db, one of face suffers from steric crowding, at time of epoxidatn, approaching reagent partiallarly delives 'O' at sterically

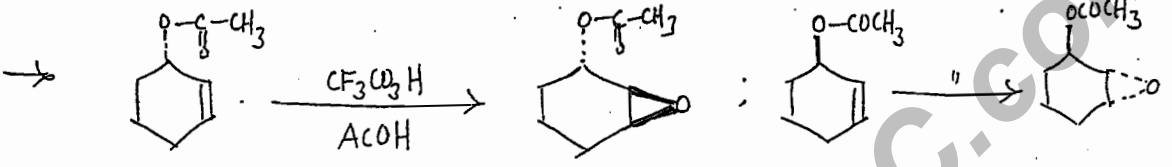
less crowded face, in resulting product, stereo isomers – unequal ratio.

Stereo selective epoxidn.









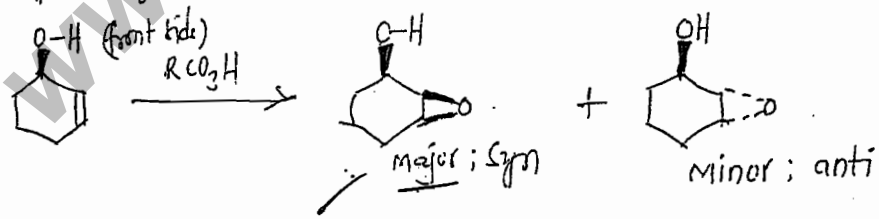
front face crowded due to bulky gp at allylic position.

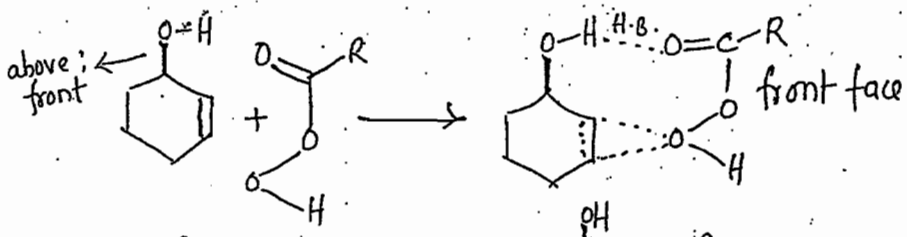
Anti addn :– addn opposite to sterically crowded face.

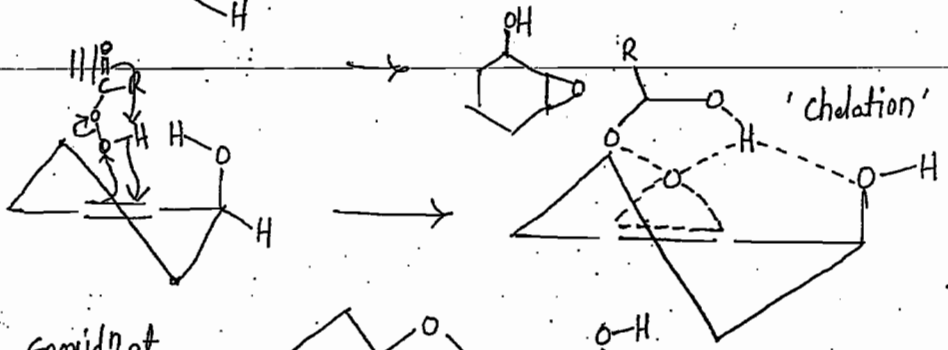
✱ ii) Chelation (H-bonding) :–

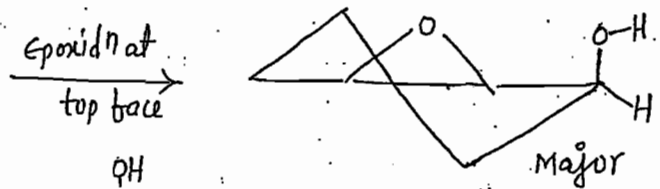
At allylic position, if there is a chelating gp (–OH, $–NH_2$), epoxidn preferentially takes place at the same side of chelating group at allylic position. The steric crowding suppressed by chelation b/w gp at allylic position & approaching reagent. Gp at allylic position develops H-bonding with reagent & holds spatially at one face of olefin unsaturatn.

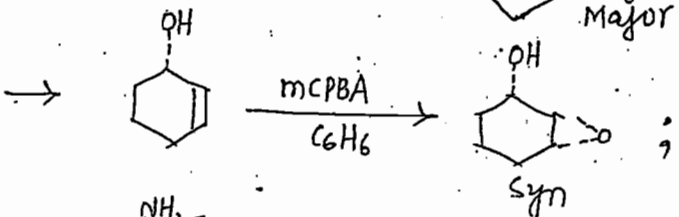
cyclic systems are best ex. for chelatn effect (∵ rigid C–C rotn).

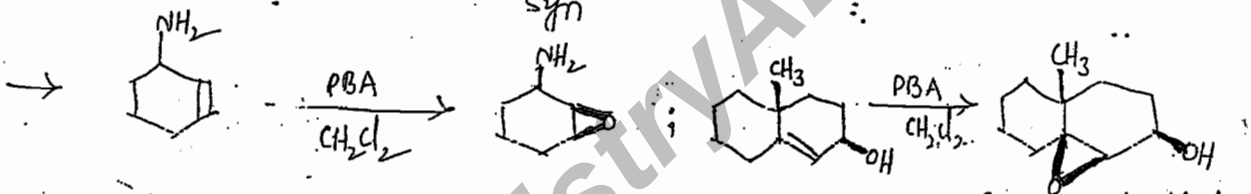






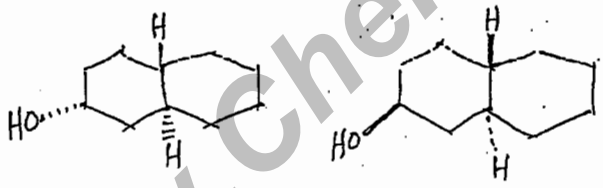




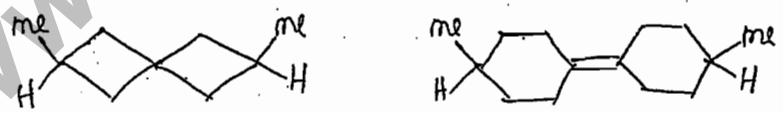


Exercises :-

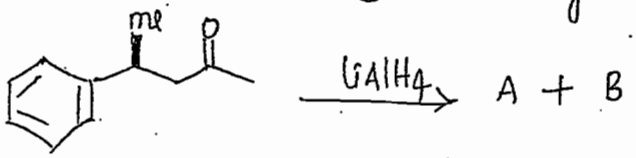
→ write most stable confirmations of following molecules.



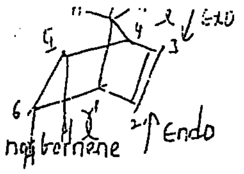
→ Draw 3D structures of following molecule, which of two is chiral.



→ write down possible products in following reacn with stereochemical specifications.

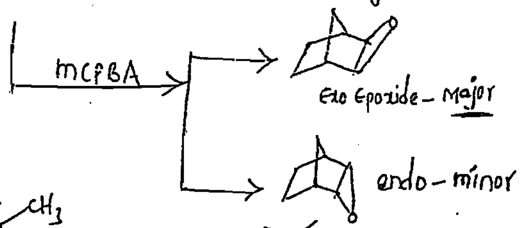


02/05/08

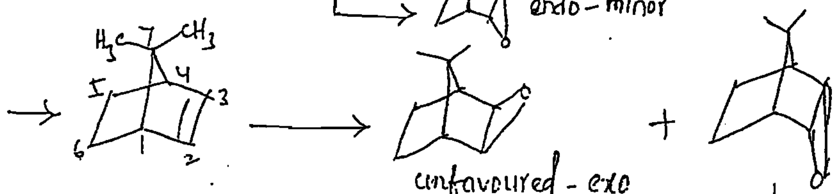
→ 

exo ... upper favoured

Endo sterically crowded by 5,6th C's H's (lower) unfavoured.



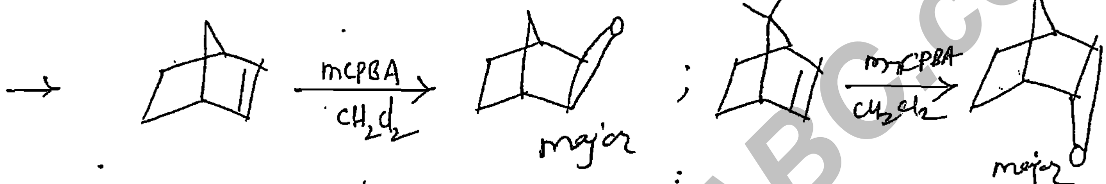
Stereo selective

→ 

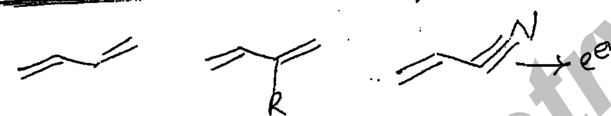
endo - selective, favoured.

→ exo, endo diastereomers

∴ Reaⁿ is diastereoselective reaⁿ.

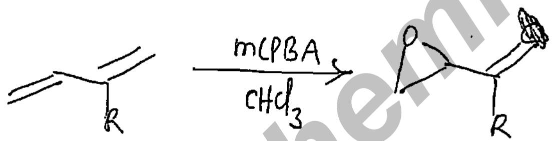
→ 

Limitations of Epoxidation :—



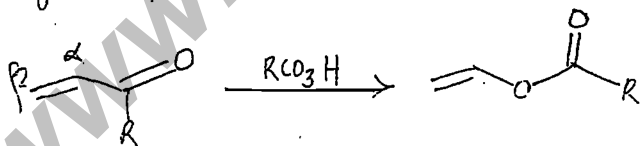
→ e⁻ withdrawing group

→ peracids insufficient in epoxidⁿ of conjugated olefins.



5-10% yield

→ In some of α, β unsaturated olefins, epoxidⁿ with peracids, Baeyer-villiger oxidⁿ side reaⁿ (competetive reaⁿ).

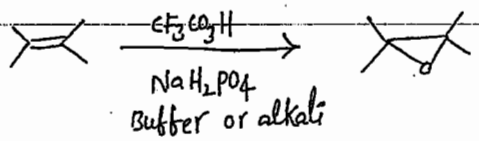


→ peracids also insufficient in epoxidⁿ of terminal alkenes, because of low nucleophilicity of these olefines.

R–C–C–C=C , R–C–C=C–C

terminal olefin

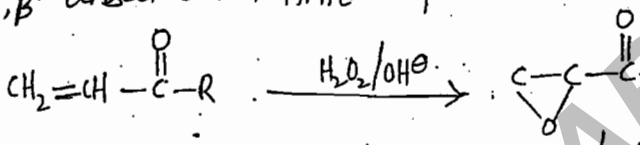
→ In CF_3CO_3H epoxidn, to prevent opening of epoxide by CF_3CO_2H basic buffer salts or simple bases used in combination with CF_3CO_3H.
(NaH_2PO_4, NaOH, KOH etc used).

→ 

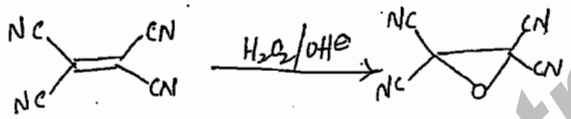
ii) $H_2O_2/OH^\ominus$:— H_2O_2 in alkali ; Alternative to peracids in epoxidn

$H_2O_2/OH^\ominus$ mainly used in epoxidn of conjugated olefins.

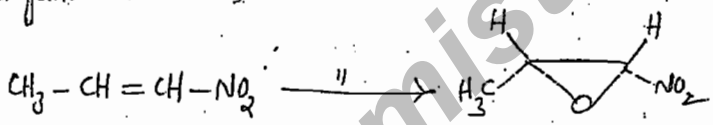
eg :— α,β- unsaturated carbonyl compound.
α,β- unsaturated nitriles compound
α,β- unsaturated nitro compounds.

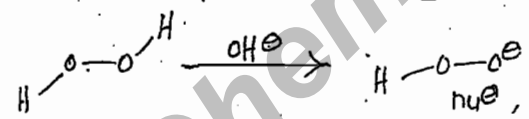
→ 

good % yield ∴

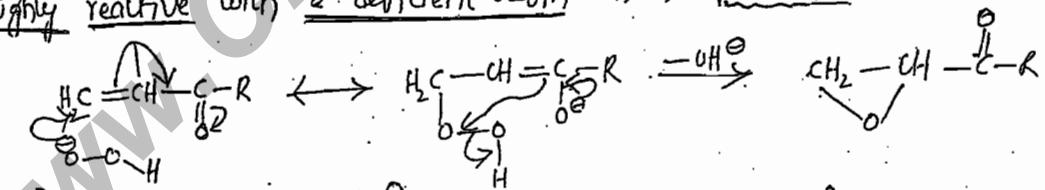
→ 

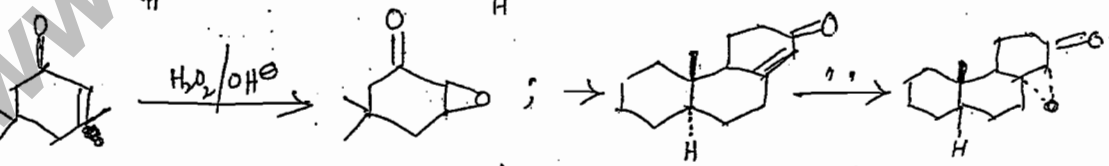
Tetracyano Ethene

→ 

Mech :— 

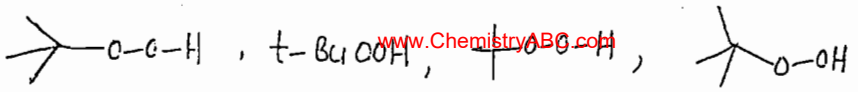
"highly reactive with $e^\ominus$ deficient olefin than peracids."

→ 

→ 

(iii) "Alkyl hydro peroxides in metal complexes" :—

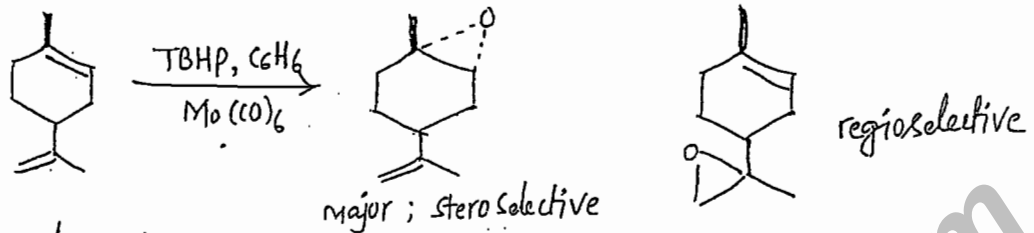
used for stereoselective epoxidn (importance) .. common alkyl hydro peroxide is 3°-butyl hydro peroxide.

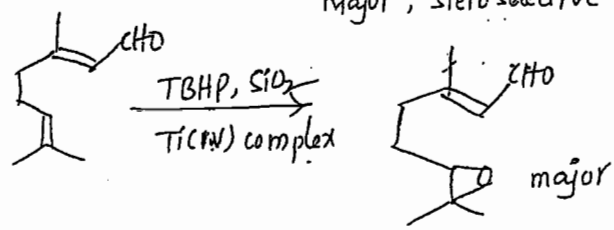


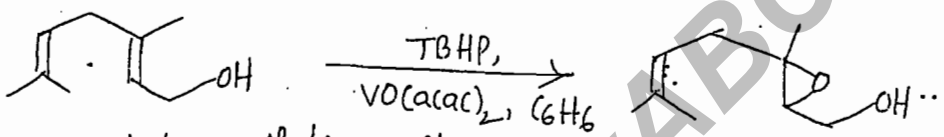
→ following metal complexes are common.

Mo, V, Ti ; $Mo(CO)_6$, $VO(acac)_2$, $VO(acac)_3$, $Ti(iopr)_4$ tetra isopropoxide

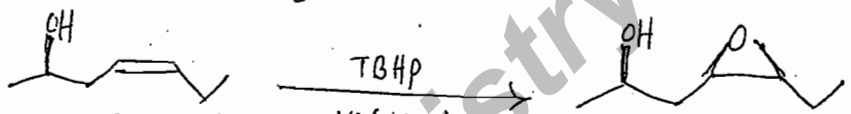
$MnCl_2$, $MnCl_4$

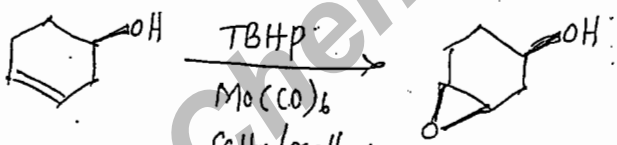
→ 

→ 

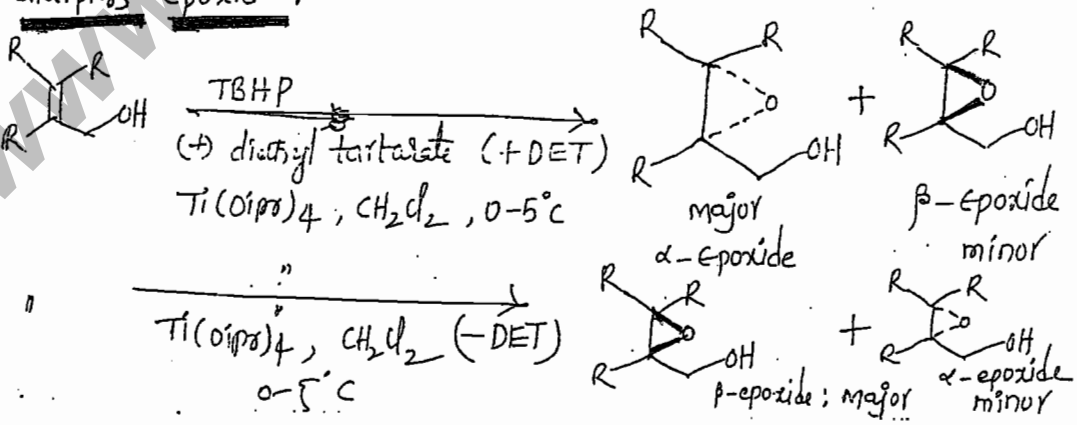
→ 

–OH at homo allylic position

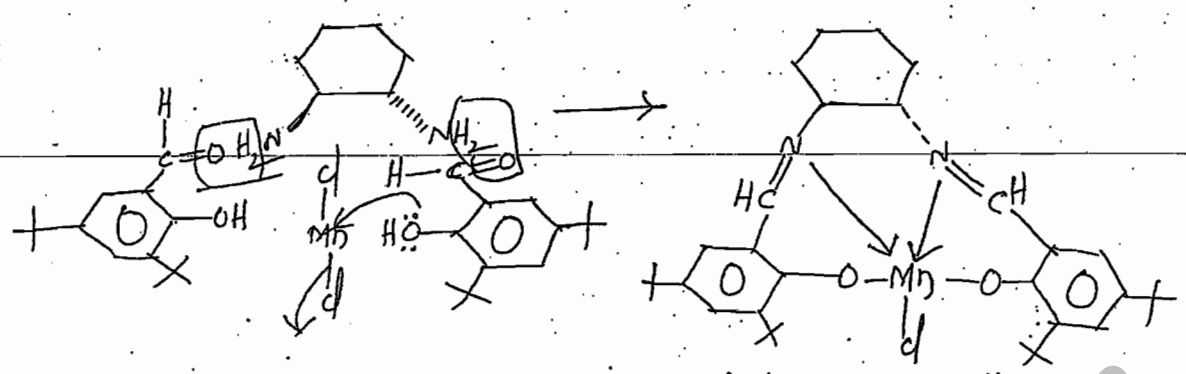
→ 

→ 

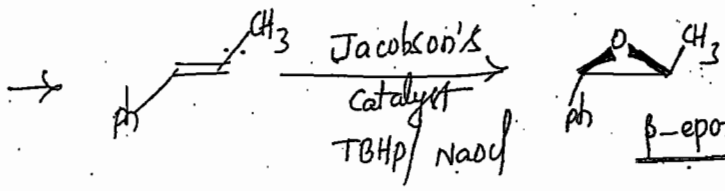
→ Sharpless Epoxidn :—



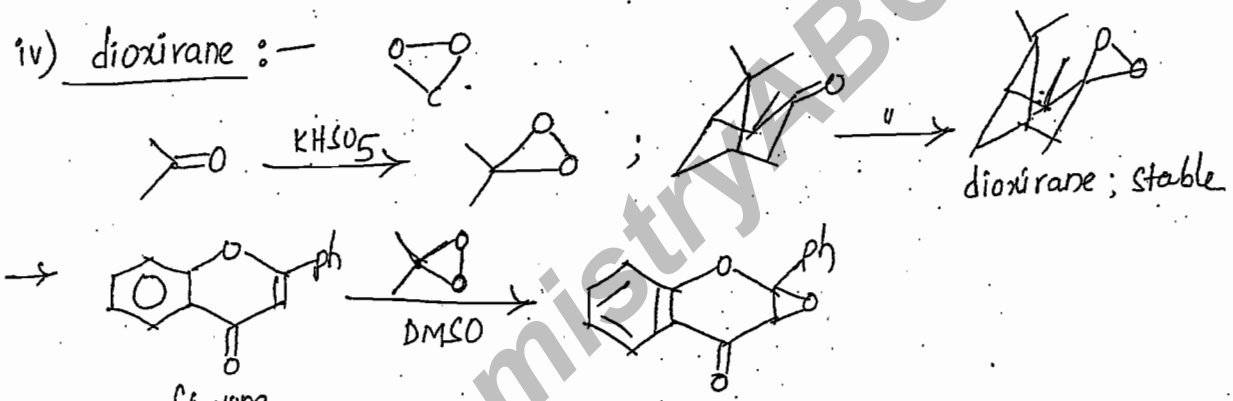
* Jacobson's Epoxidation :—



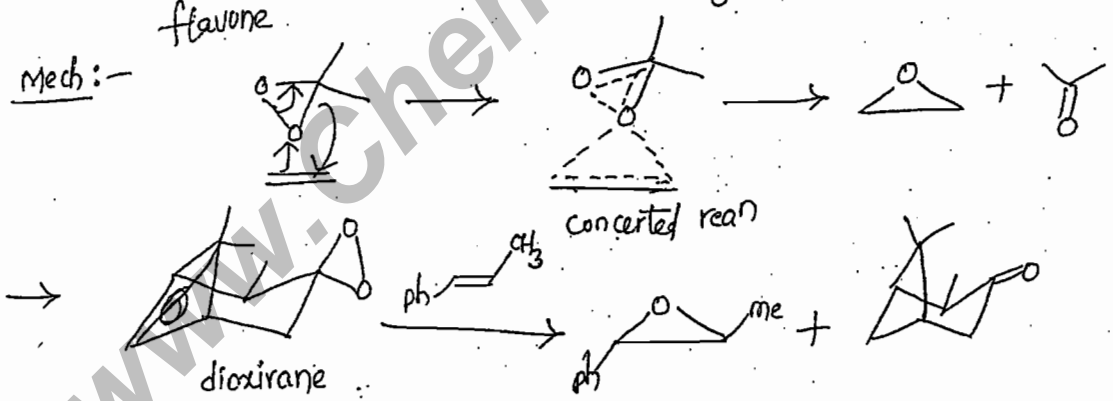
imine schiff's base



iv) dioxirane :—



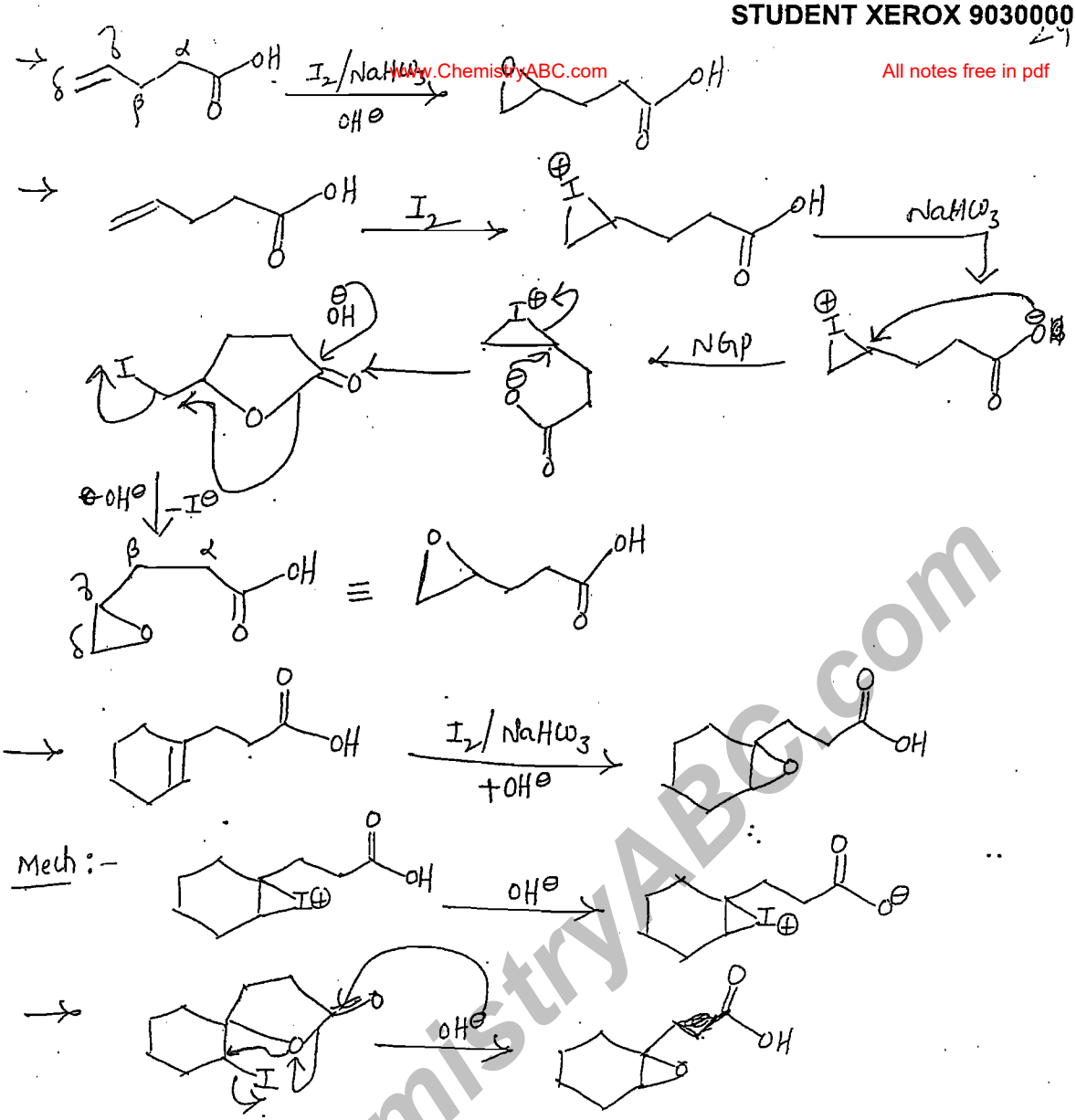
Mech :—



v) Iodine catalysed Epoxidation :—

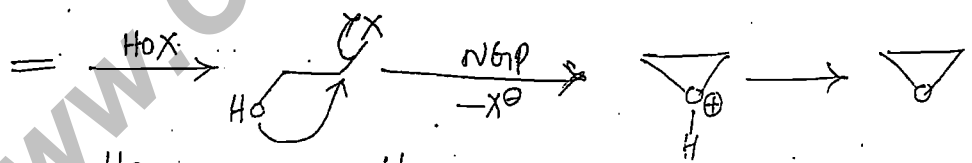
Substrate : unsaturated carboxylic acid

unsatyratn at β, γ, δ & ε are more appropriate for I_2 catalysed Epoxidn.



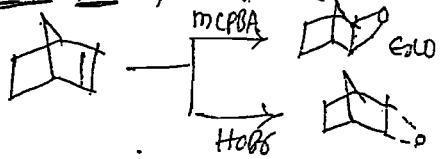
(vi) Hypo halous acid (HOX) :-

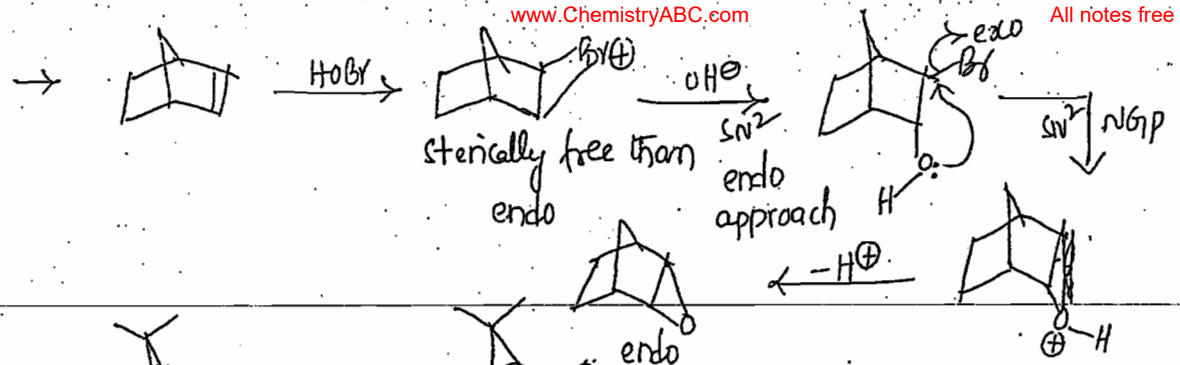
→ HOBr is best for epoxidation.

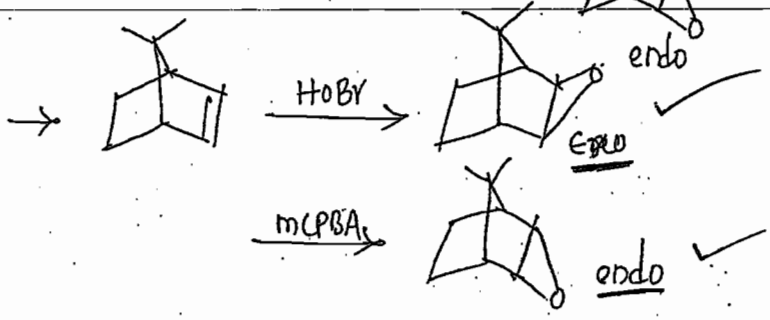


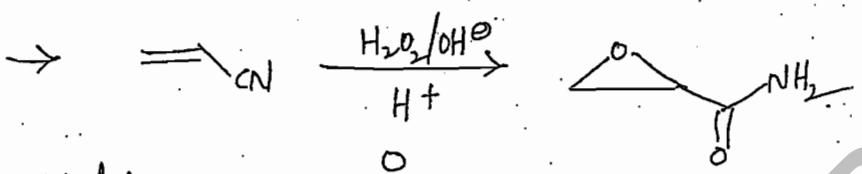
HOX addn are anti addn.

→ Stereo selectivity :- "HOX will do epoxidn preferentially at sterically crowded face of olefin" (reverse to peracids selectivity).

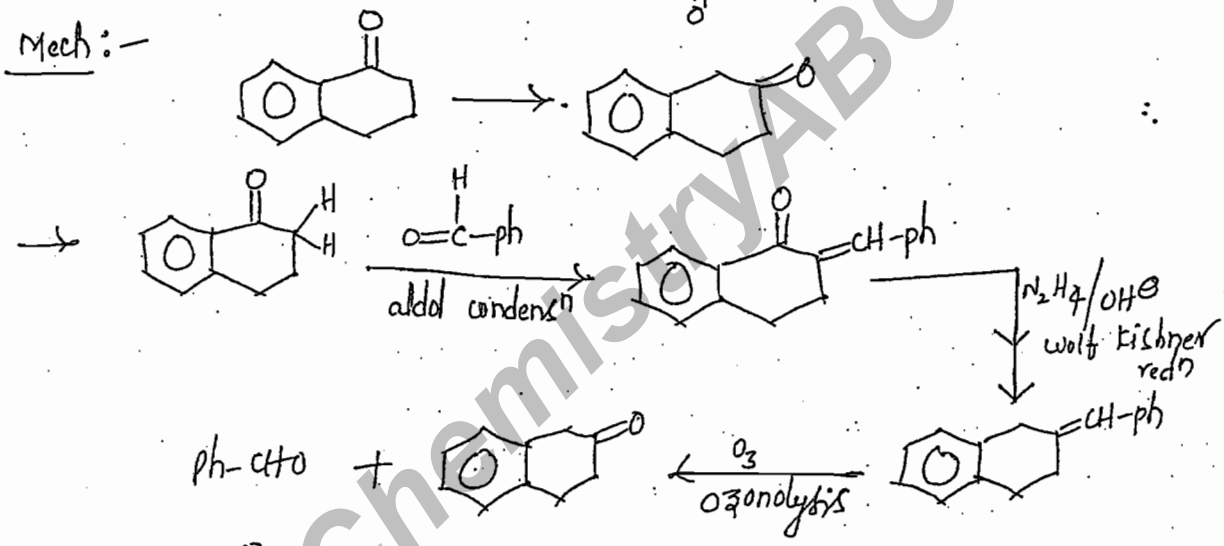


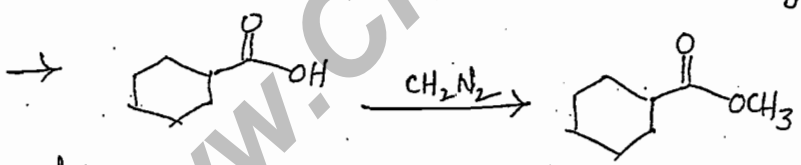






Mech :-





Mech :-

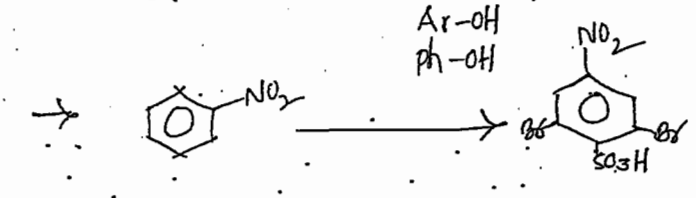
→ CH_2N_2 used for methylation of carboxylic acids, phenols, alcohols.

→ strongly acidic, more reactive in methylatn.

∴ $-COOH > phenol > R-OH$

$Ar-OH$

$ph-OH$



Date: 03/05/08

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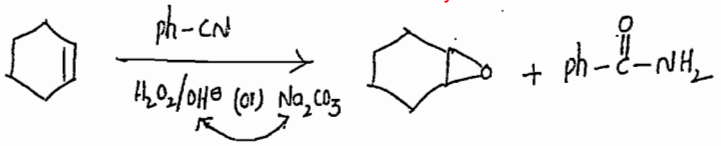

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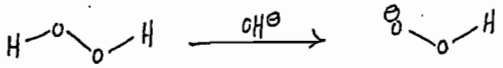
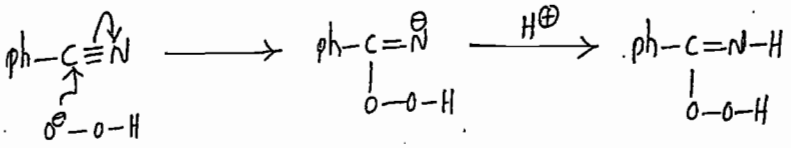
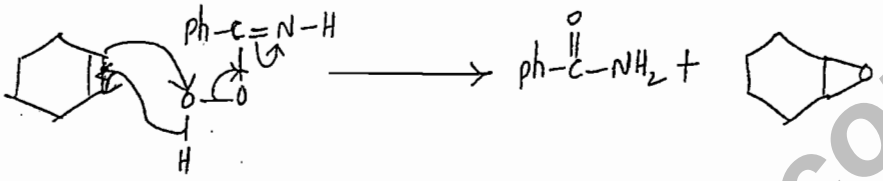
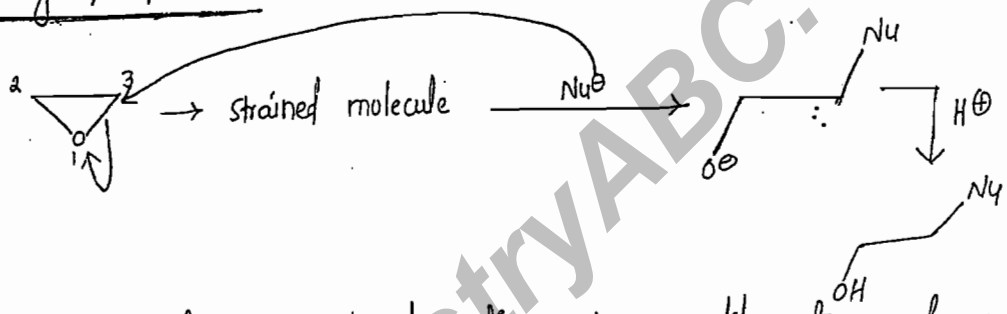




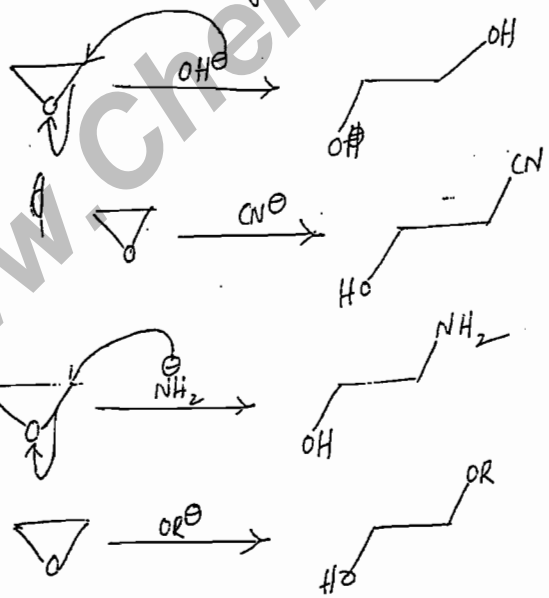


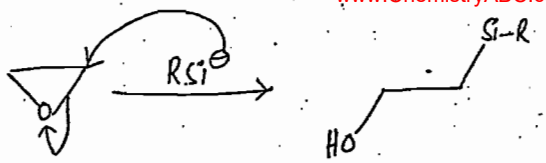
* opening of Epoxide :-



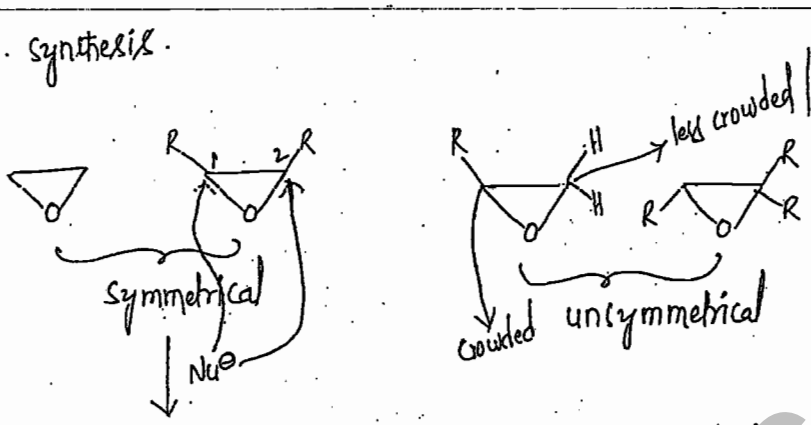
→ Epoxide, strained three membered cyclic system, readily gets opened even with weak nucleophiles – resulting product – alcohols.

→





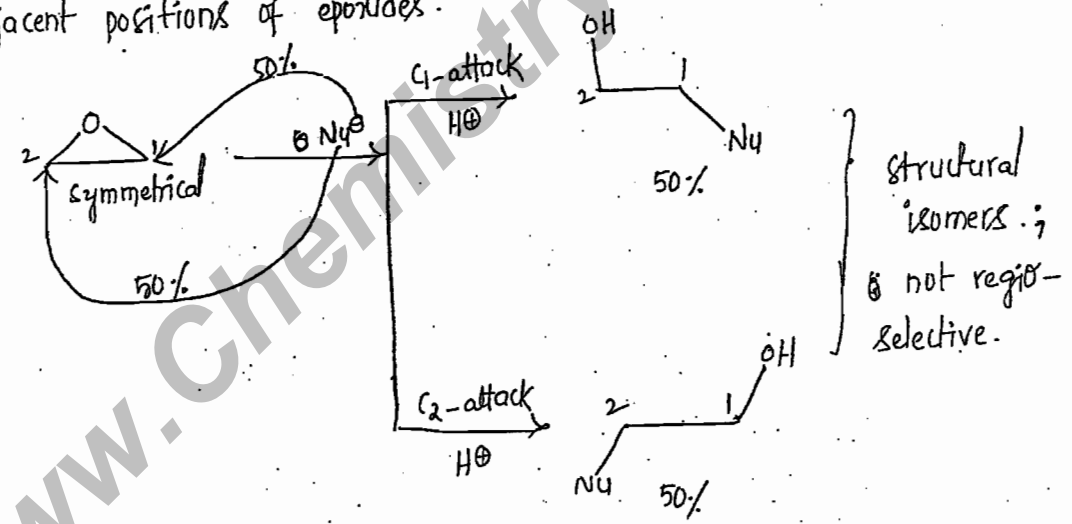
→ Epoxides are versatile intermediates to produce variety of new fns in org. synthesis.



→ Regio selectivity in opening of Epoxides :-

→ opening of Sym. epoxides - not selective, with equal probability Nu⊖ attacks at adjacent positions of epoxides.

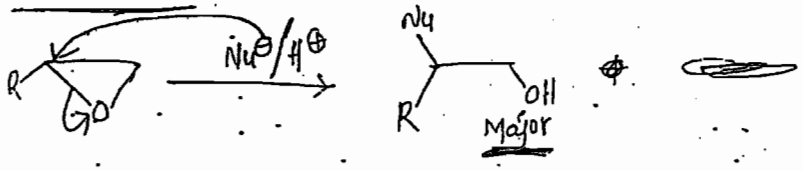
→



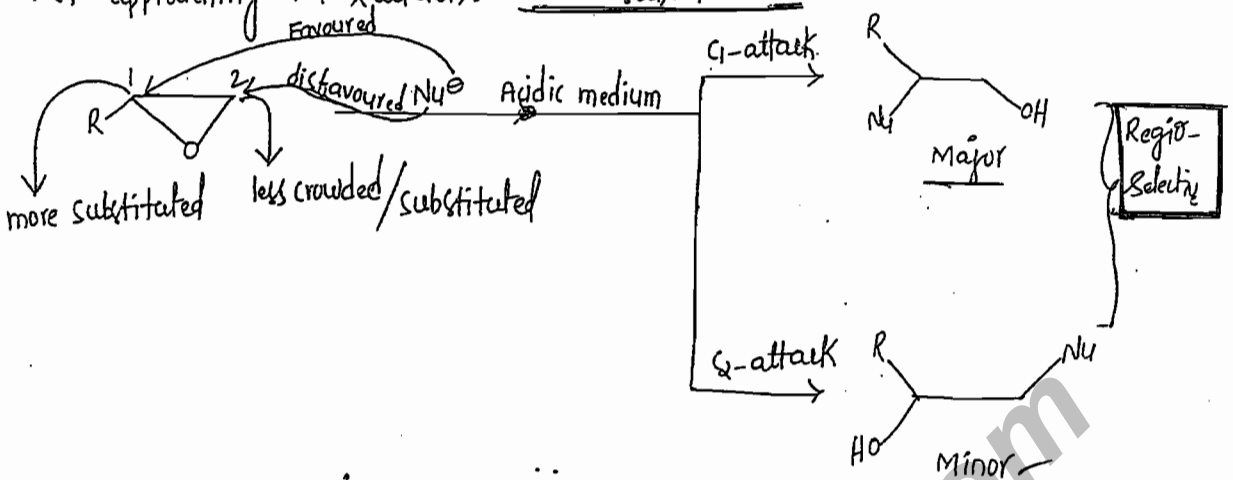
→ opening of unsym. epoxides – regio selective.

selectivity depends on rean conditions.

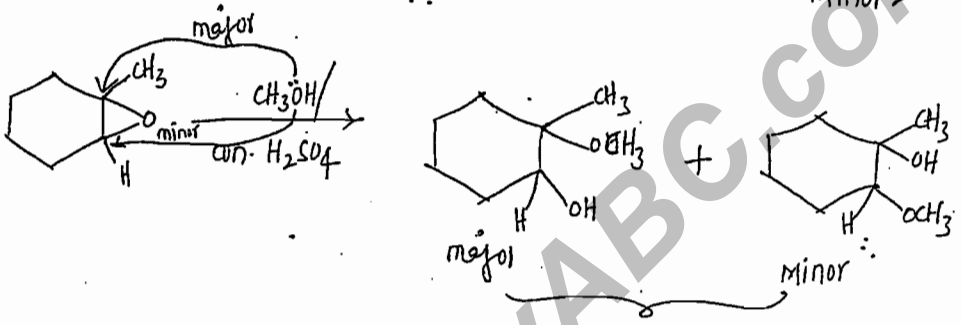
→ In acidic medium :-



→ In acidic medium, opening of epoxide at sterically more crowded position i.e. approaching $Nu^{\ominus}$ selectively attacks more sub. position.

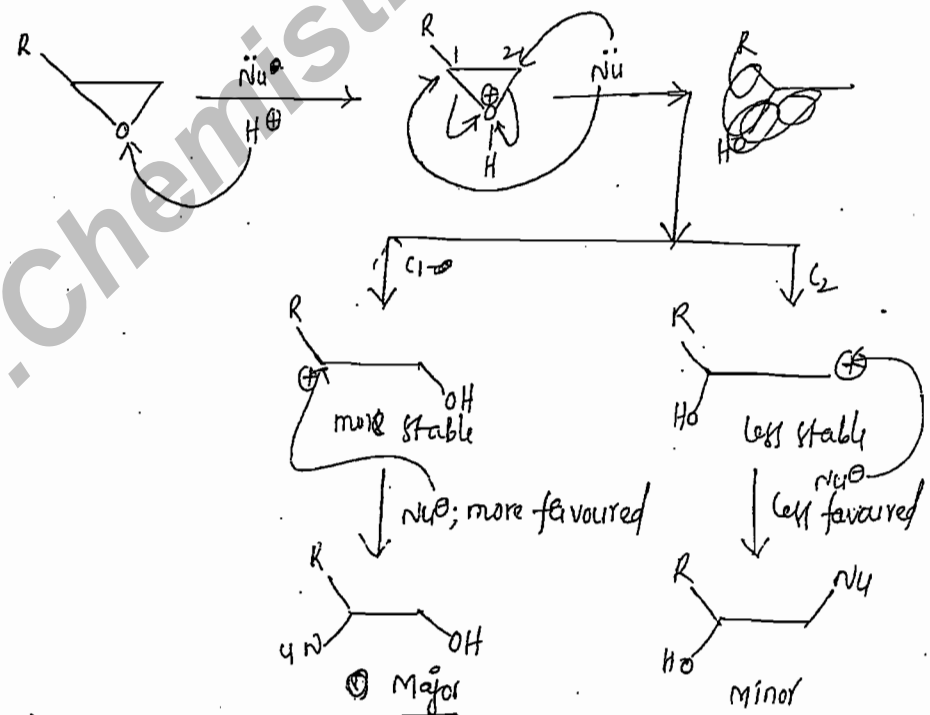


→



Regioselective

→ Reason :-



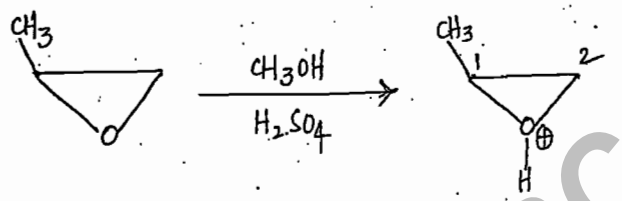
→ In acidic medium, protonation of epoxide oxygen, resulting oxonium ion.

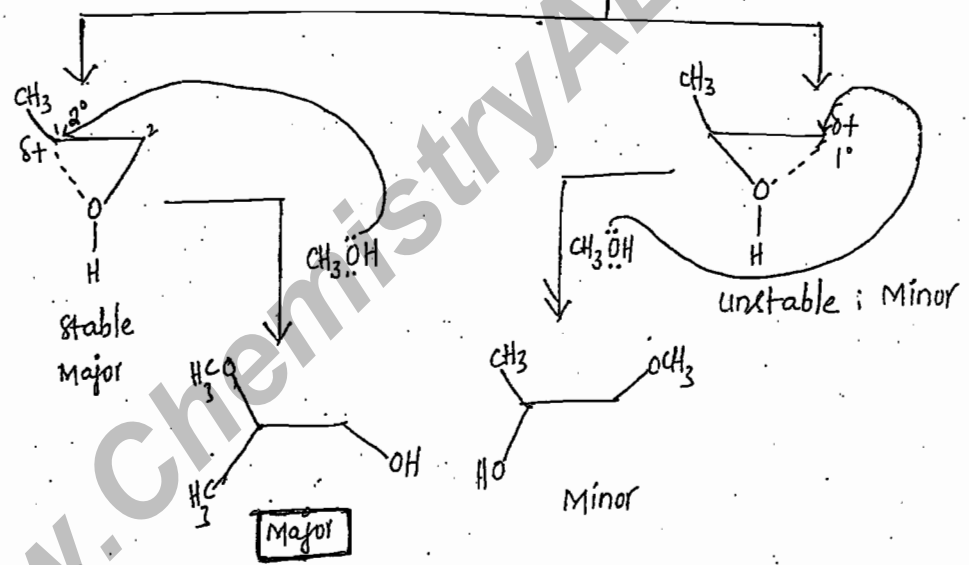
develops carbocation T.S/ Intermediates.

"More alkylated/ arylated (substituted) position of epoxide develops stable carbocation T.S or intermediate than less sub. position of epoxide."

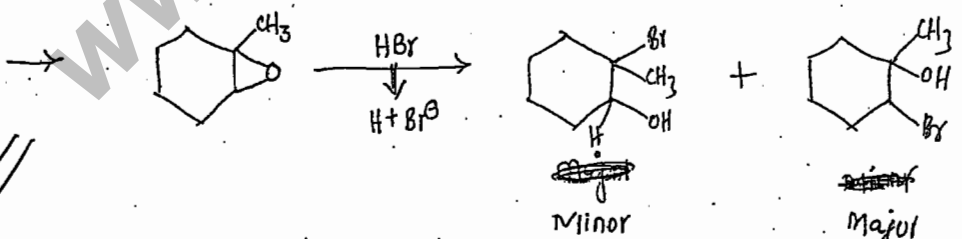
~~less sub position of epoxide~~, In opening of epoxide, nuc⊖ preferentially attacks stabilized c⊕ i.e, more sub. position of epoxide resulting product is major, Regioselectivity.

eg:- 1)





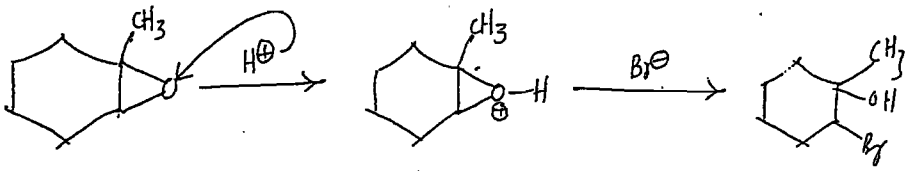
Exceptions :-



Acc. to acidic medium regioselectivity, opening of epoxide preferentially at more sub. position, but experimental result unexpectedly showing.

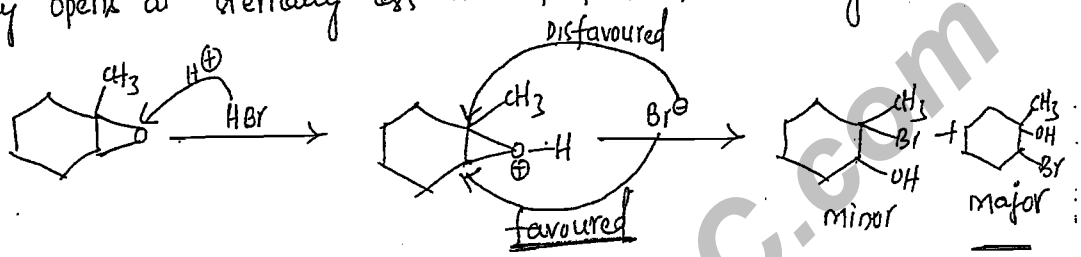
formation of major product which is from opening of epoxide selectively at less sub. position.

Mech:-



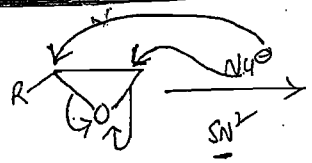
→ "$Br^{\ominus}$ – powerful nu$^{\ominus}$, before formation of carbocation T.S. approaches epoxide, selectively opens at sterically less crowded position – resulting product major"

→



⇒ **In basic medium** –

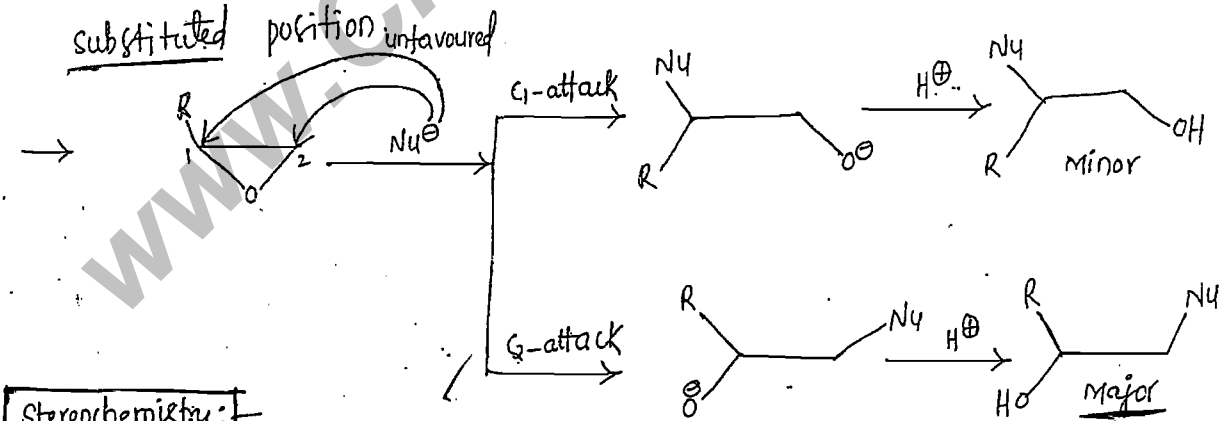
→



→ In basic medium, opening of epoxide acc. to S_N2 pathway. No carbocation/ T.S formations due to absence of acidic medium.

Approaching Nu$^{\ominus}$ preferentially opens sterically less crowded or less substituted position

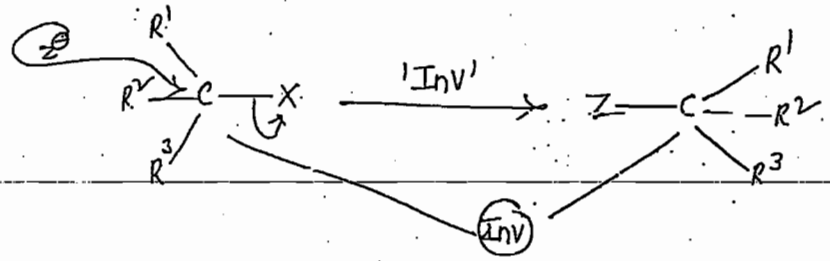
→

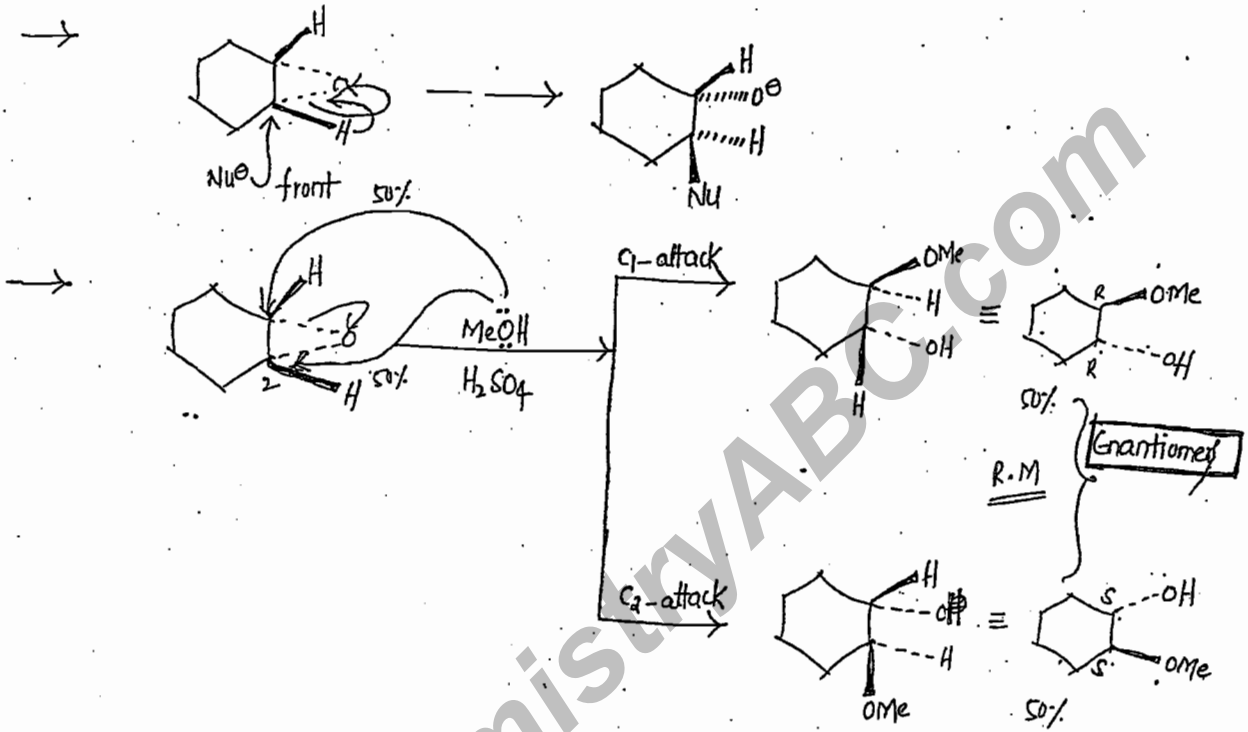


Stereochemistry:-

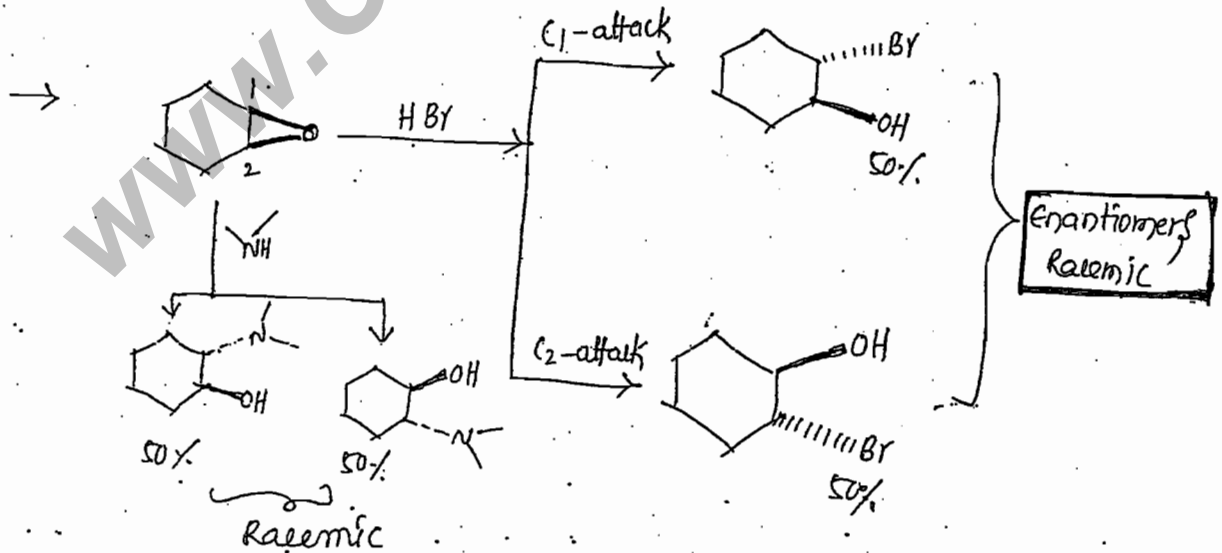
Whether opening of epoxide in basic/acidic medium, S_N2 type

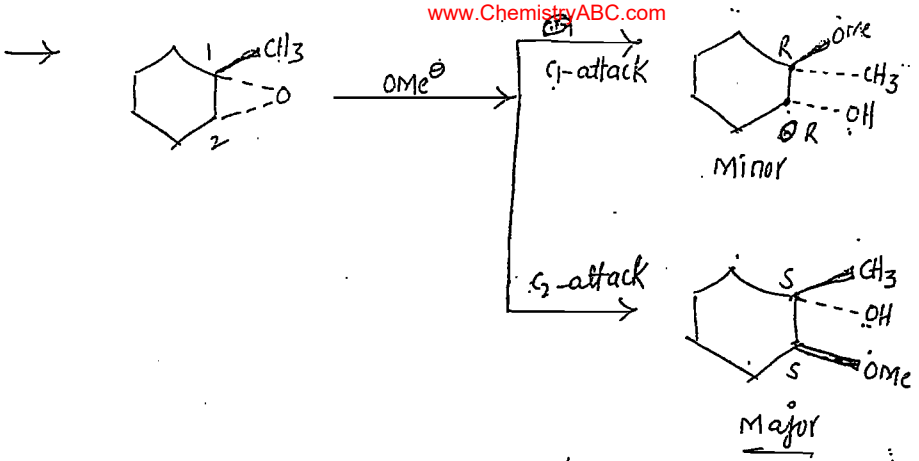
Inversion of configuration.

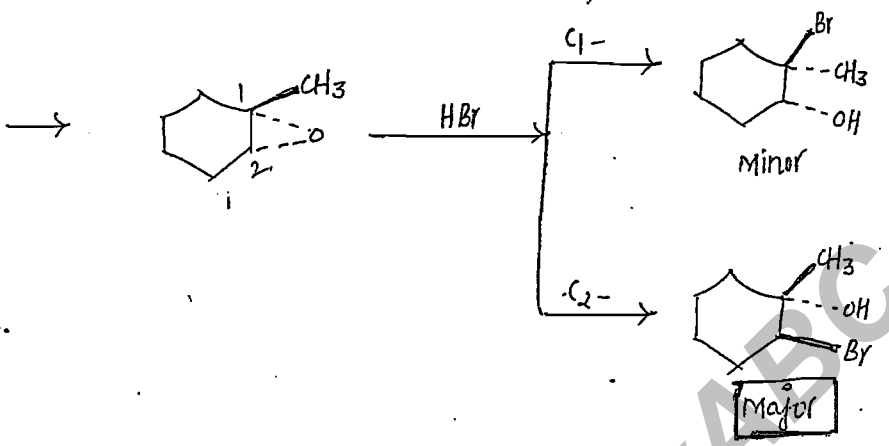




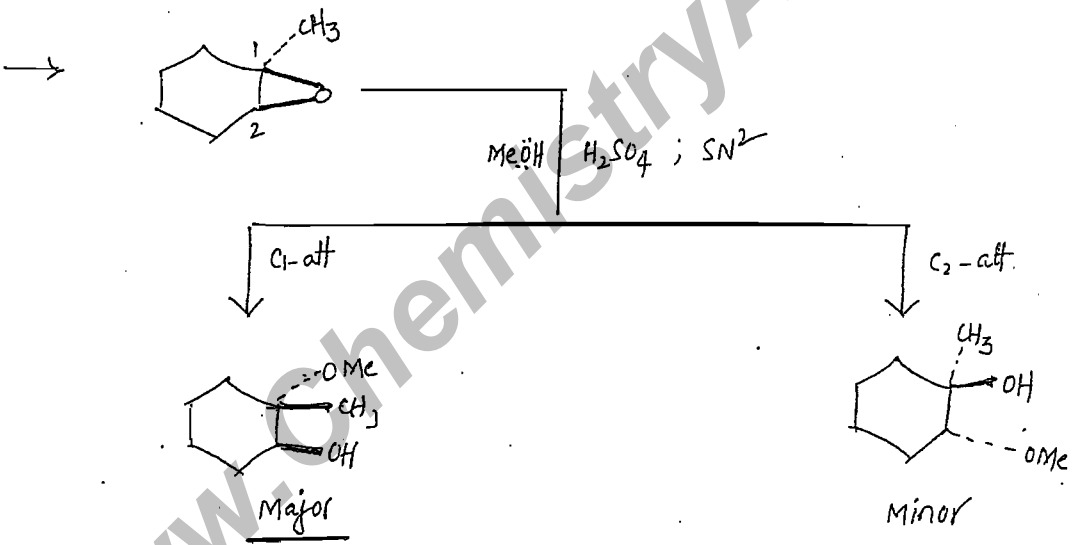
* "opening of sym. epoxide with Nuᵒ produces racemic, 1:1 ratio of enantiomers".



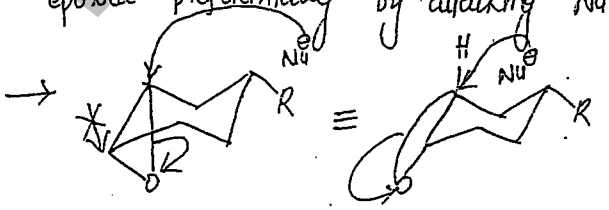




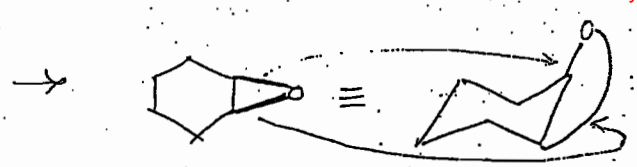
$Br^{\ominus}$ is powerful Nucleophile.

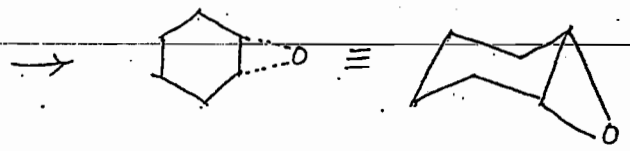


* "In conformationally rigid epoxides of cyclohexane derivatives, opening of epoxide preferentially by attacking $Nu^{\ominus}$ in axial direction."

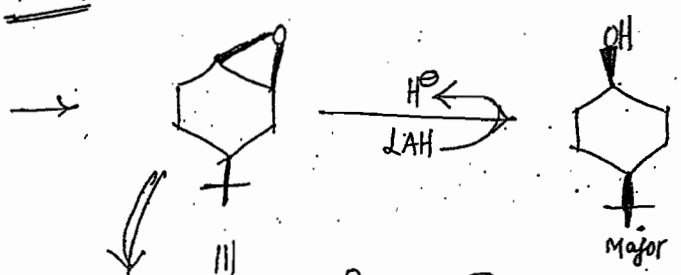


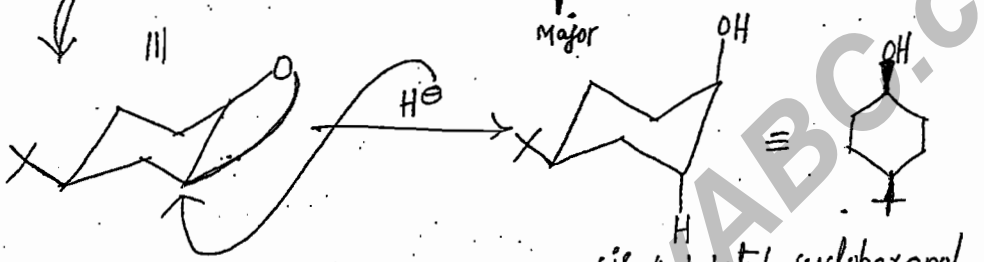
⇒ Resulting product 1,2-diaxial cyclohexane derivatives.



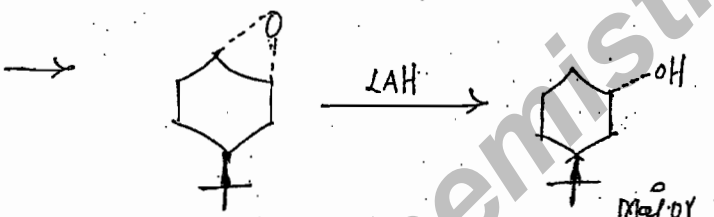


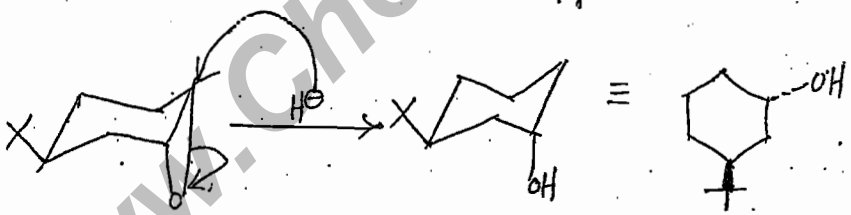
V. IMP :-

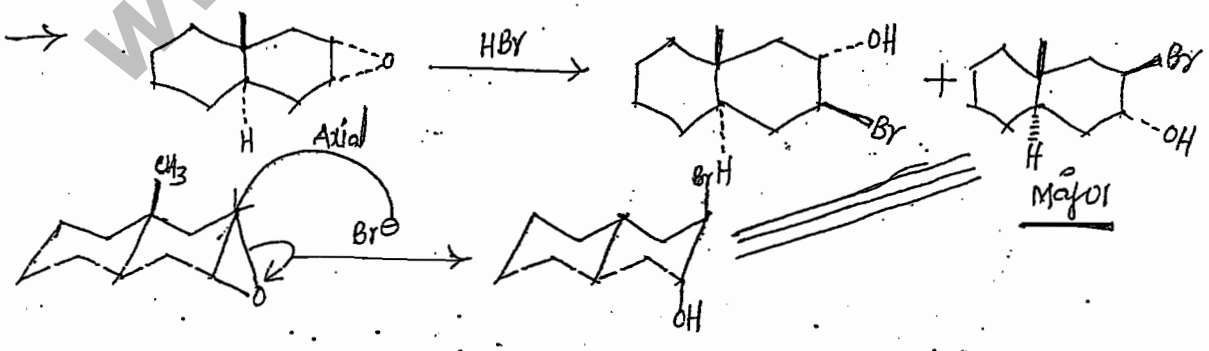


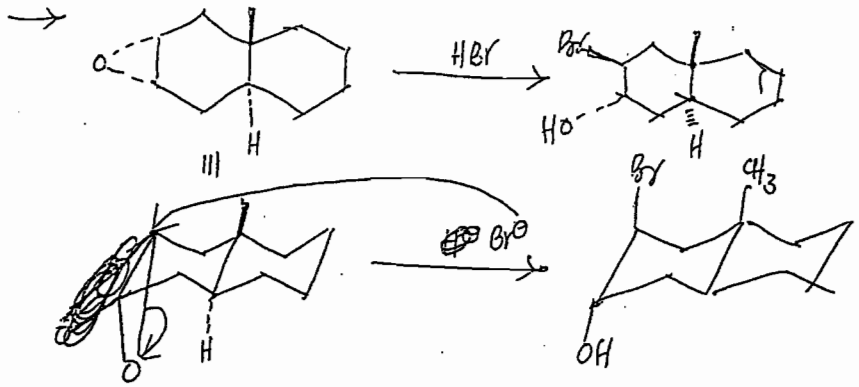


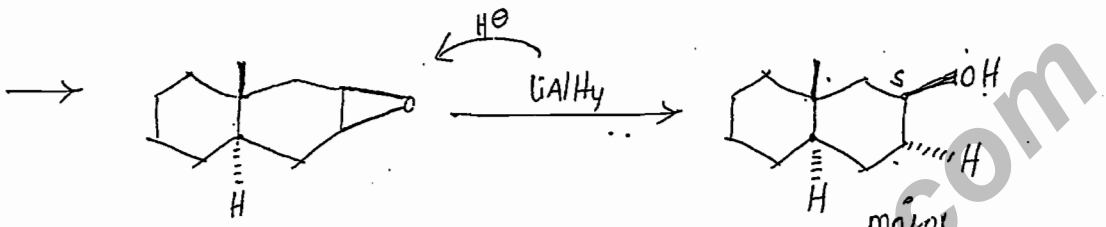
cis 4-t-butyl cyclohexanol.

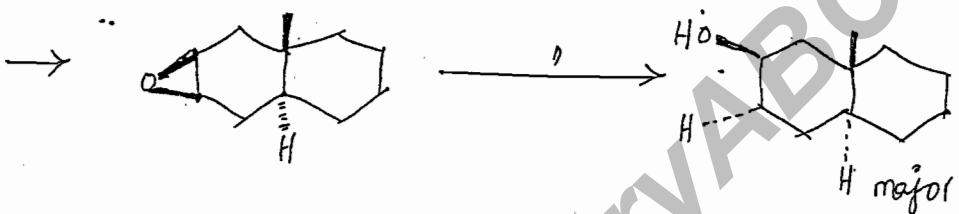








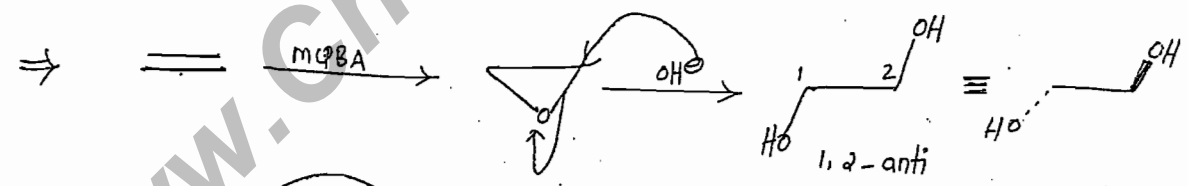


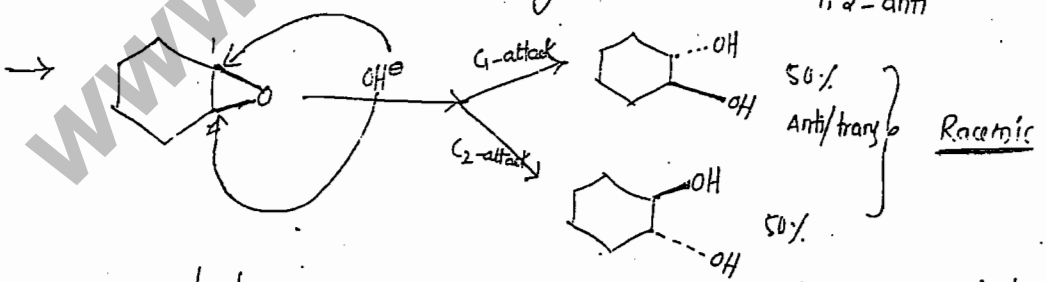


Date : 04/05/08

* opening of Epoxide with $OH^{\ominus}$:-

⇒ olefine $\xrightarrow{mCPBA}$ epoxide $\xrightarrow{OH^{\ominus}}$ Anti 1,2-diol





→ method for conversion of olefines into trans/anti 1,2-diols

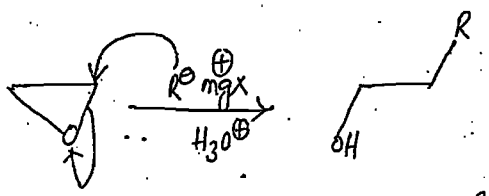
* With Grignard / Gilman's reagent ; S_N2 type :—

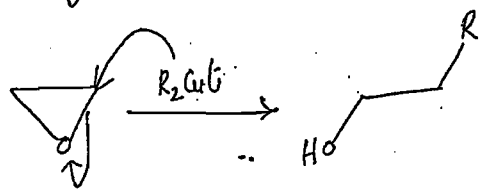
→ S_N2 type

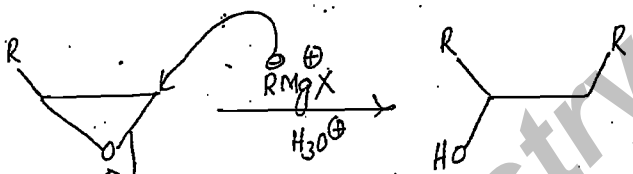
→ opening at sterically less crowded position.

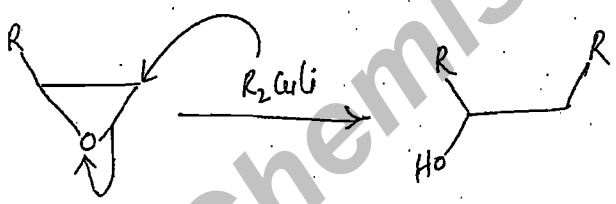
→ $RMgX$ ⇒ Grignard

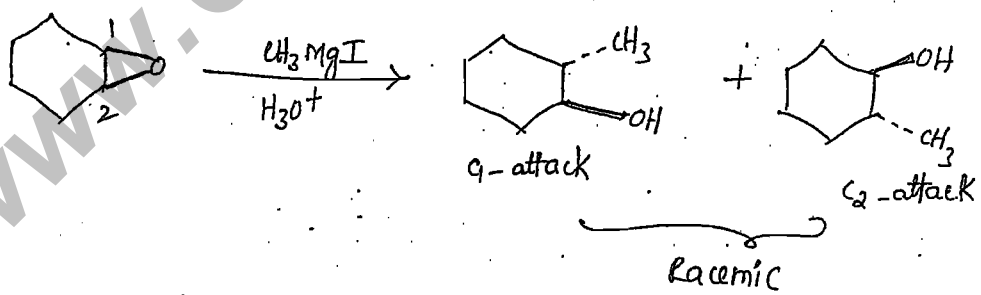
R_2CuLi ⇒ Gilman's reagent

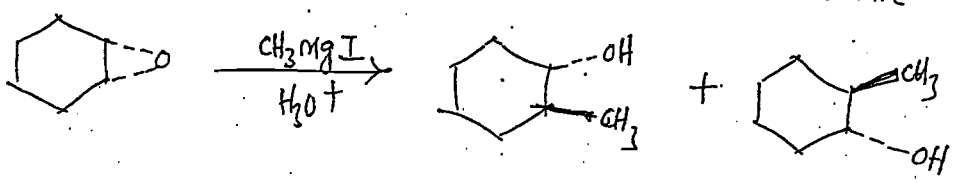
→ 

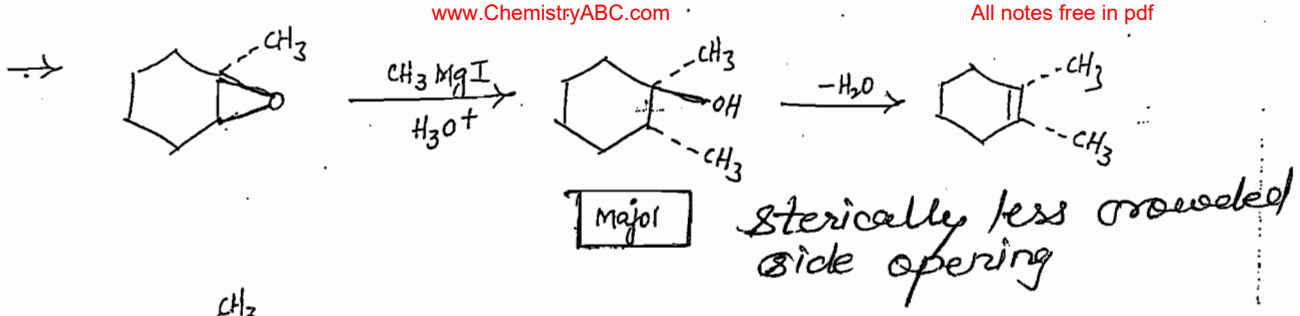






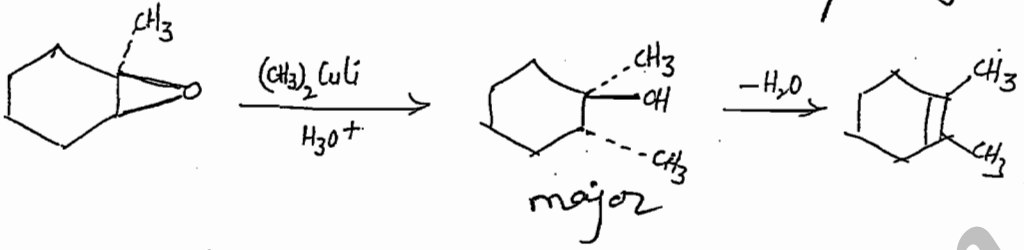




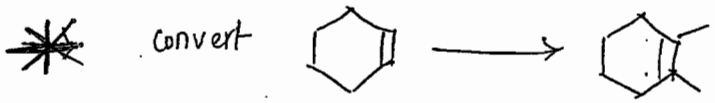


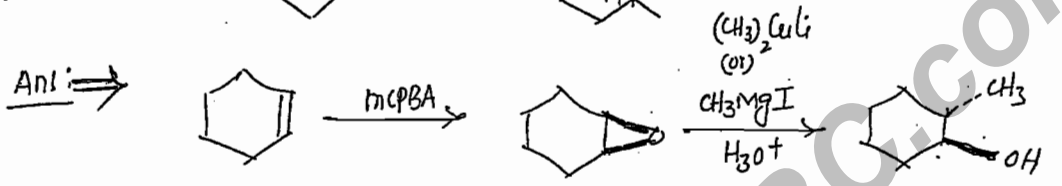
Major

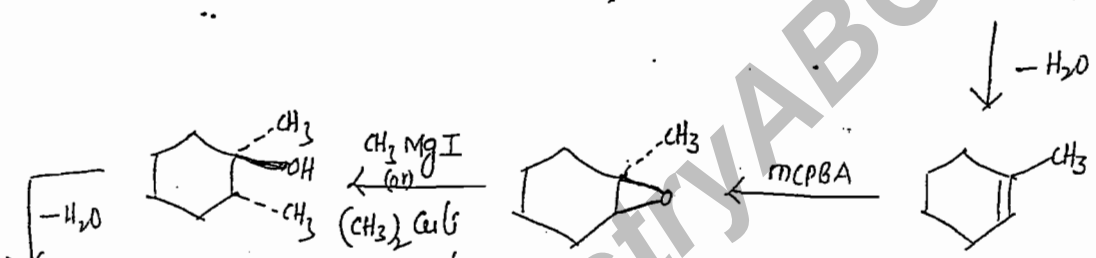
Sterically less crowded side opening



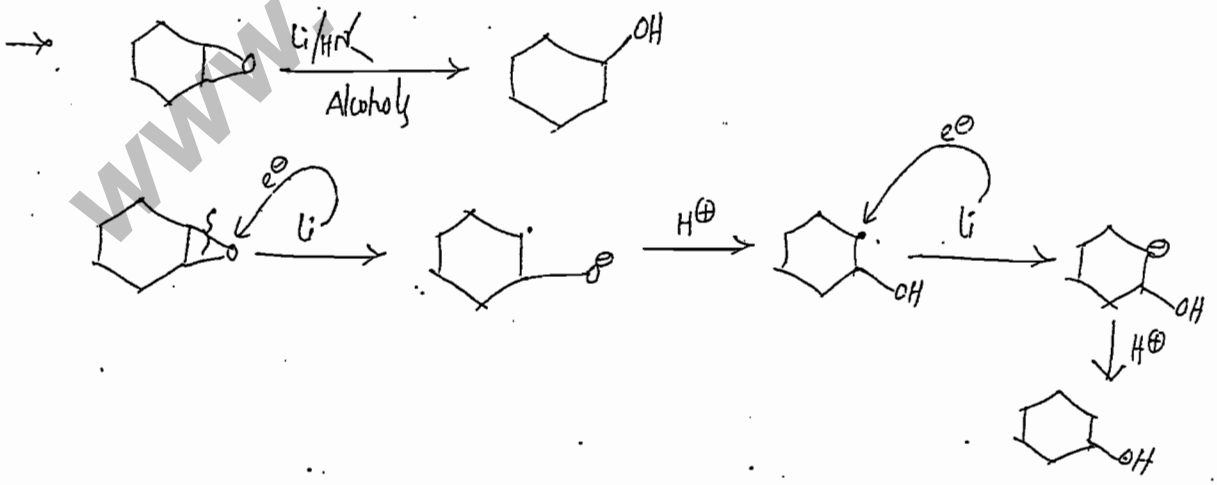
major







* opening of Epoxides with Li/ 2°-amines $\left(\begin{matrix} CH_3 \\ H_3C \end{matrix}\!\!>\!NH\right)$



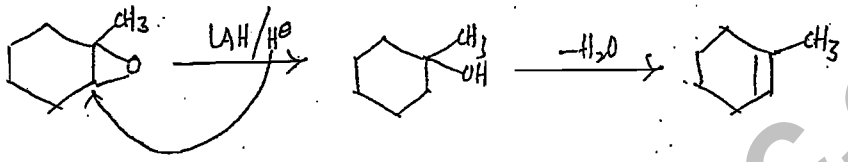
* **opening of Epoxide with LAH :**

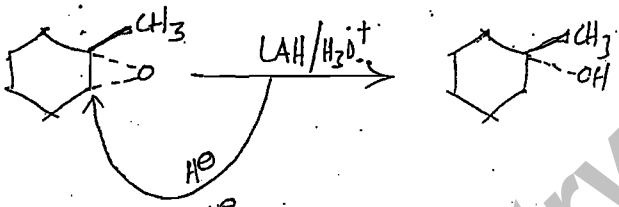
→ $H^{\ominus}$ is attacking $Nu^{\ominus}$.

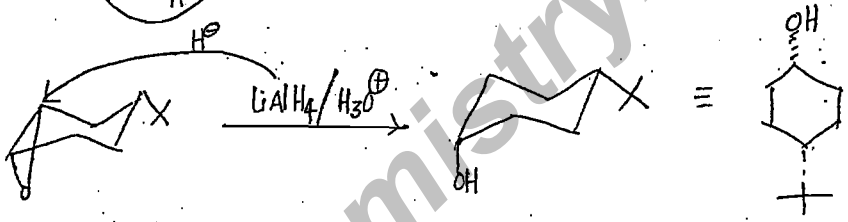
Epoxide $\xrightarrow{LAH/H_3O^{\oplus}}$ Alcohols

→ S_N2 type

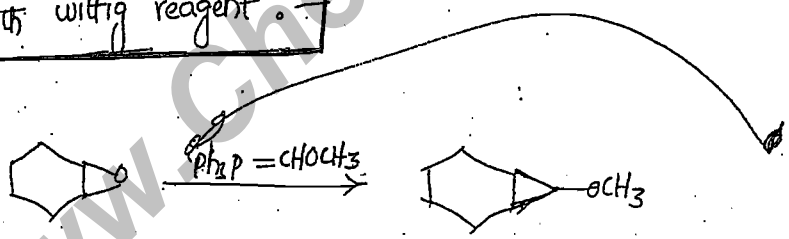
→ Regio selectivity at sterically less crowded position.

→ 

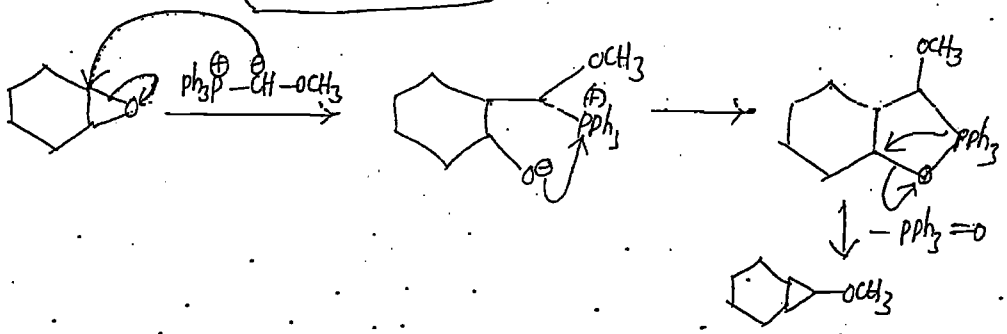
→ 

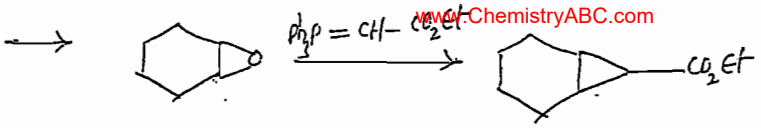
→ 

* **with wittig reagent :**

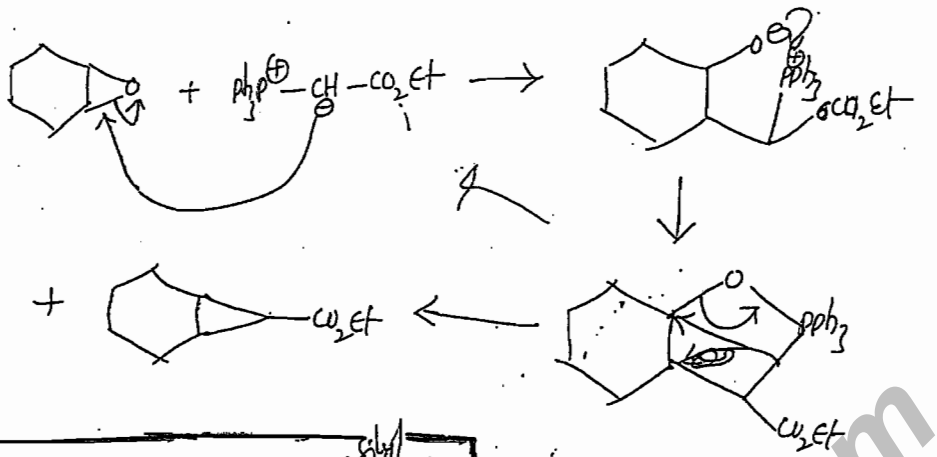
→ 

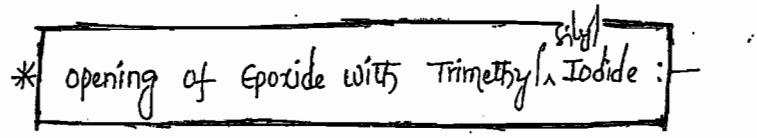
→ $Ph_3P{=}CH{-}OCH_3 \equiv Ph_3P^{\oplus}{-}\overset{\ominus}{C}H{-}OCH_3$

→ 



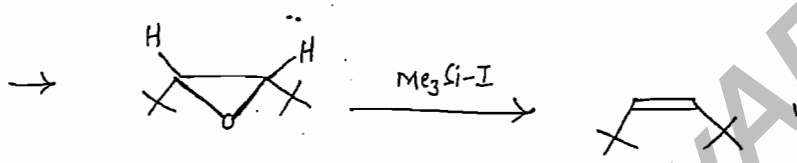
Mech :-

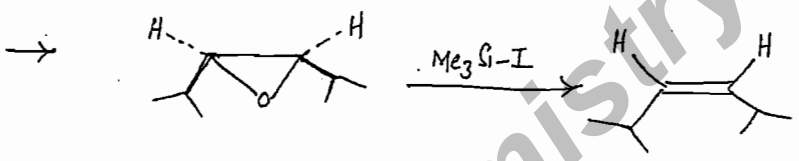


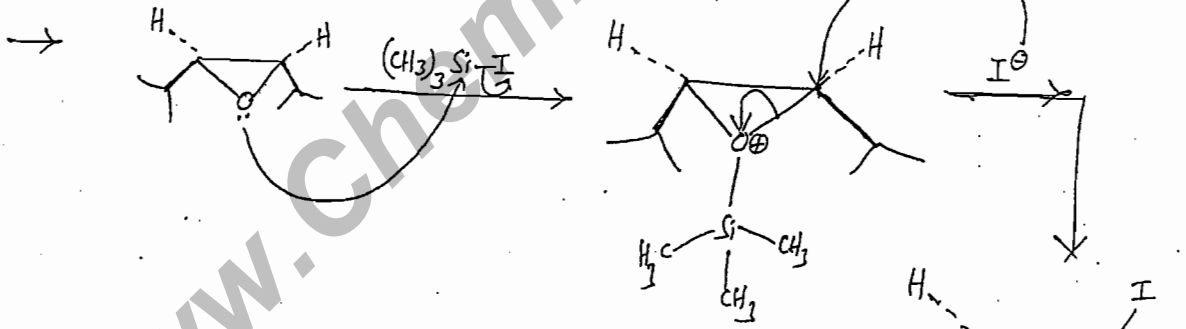


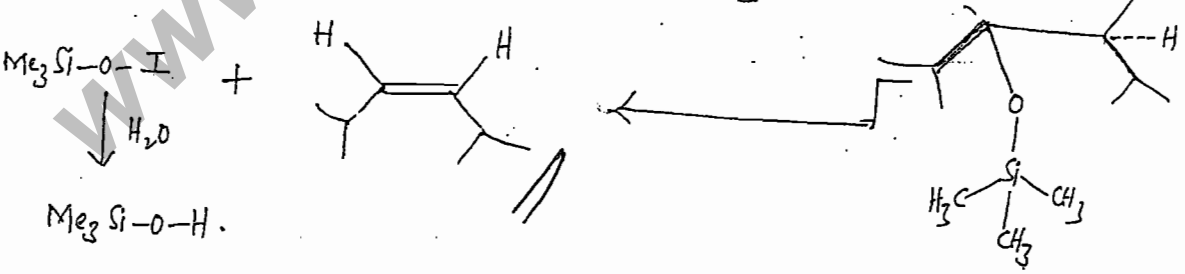
* opening of Epoxide with Trimethyl silyl Iodide :-

→ Epoxide Me_3SiI → olefines



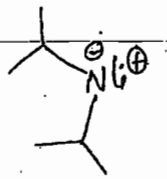




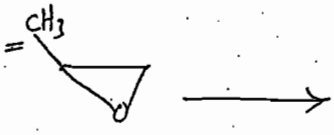


* with strong bases; LDA / $t_{BuO}^{\ominus}K^{\oplus}$:

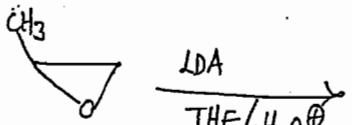
LDA = Lithium diisopropyl amide



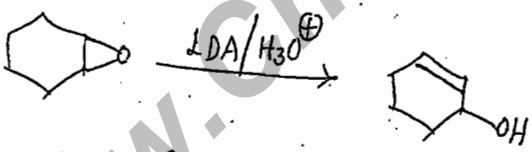
→ Epoxide —LDA→ Allyl alcohol

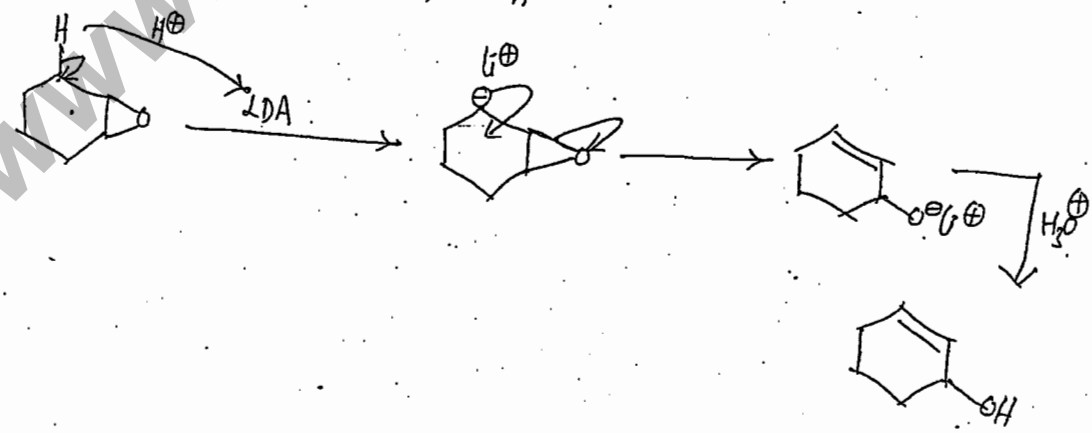
→ 

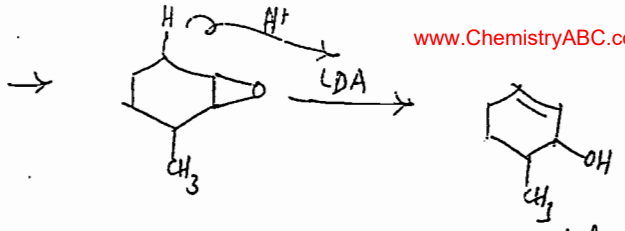
At α-position of epoxide, —CH fn must be present.

→ 

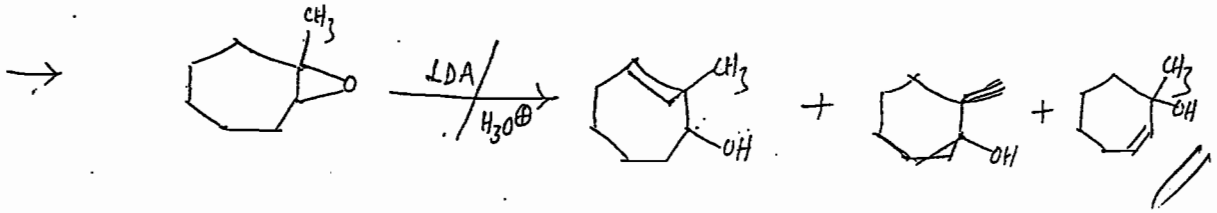
Mech:-

→ 





LDA prefers $H^{\oplus}$ from less crowded position.

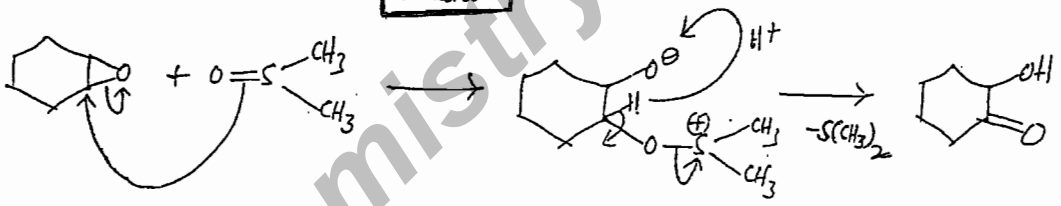


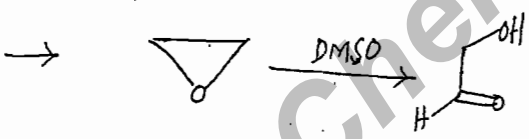
*** with DMSO :-**

→ Epoxide $\xrightarrow[BF_3 \cdot Et_2O]{DMSO}$ **α - Ketals.**

V.IMP :-

Mech :-





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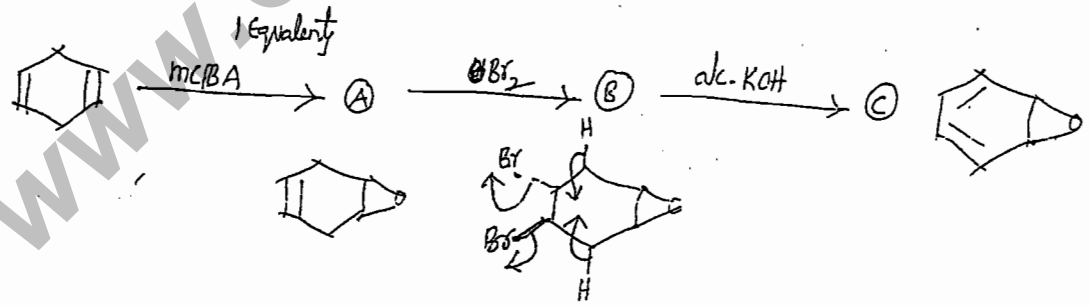
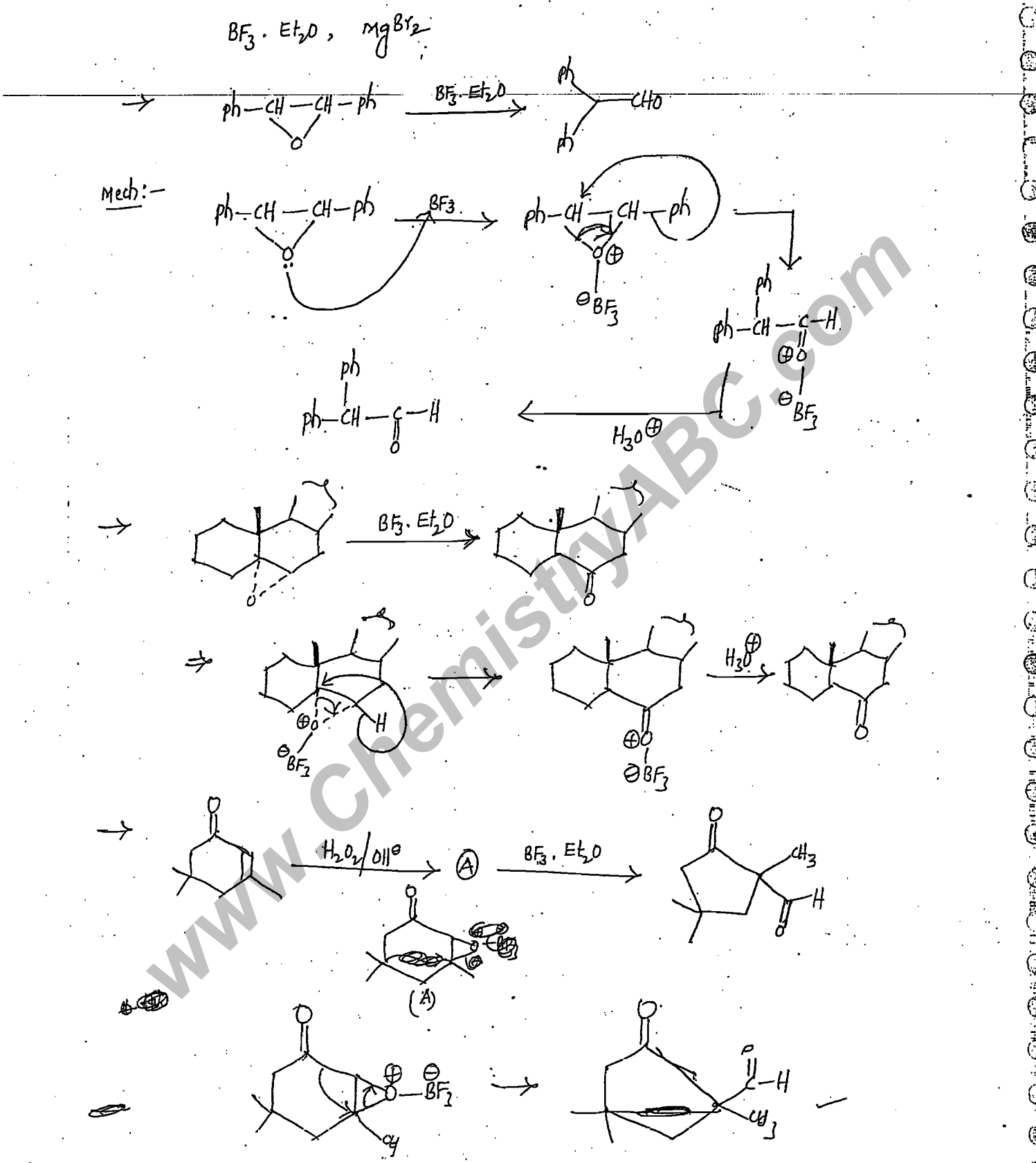
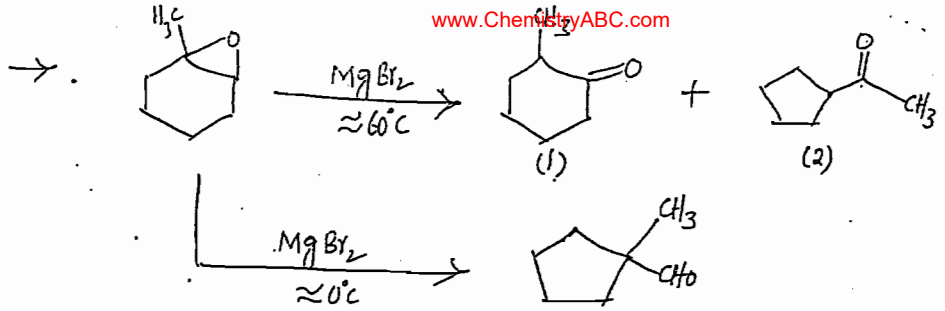


* Rearrangement of epoxide with lewis acid





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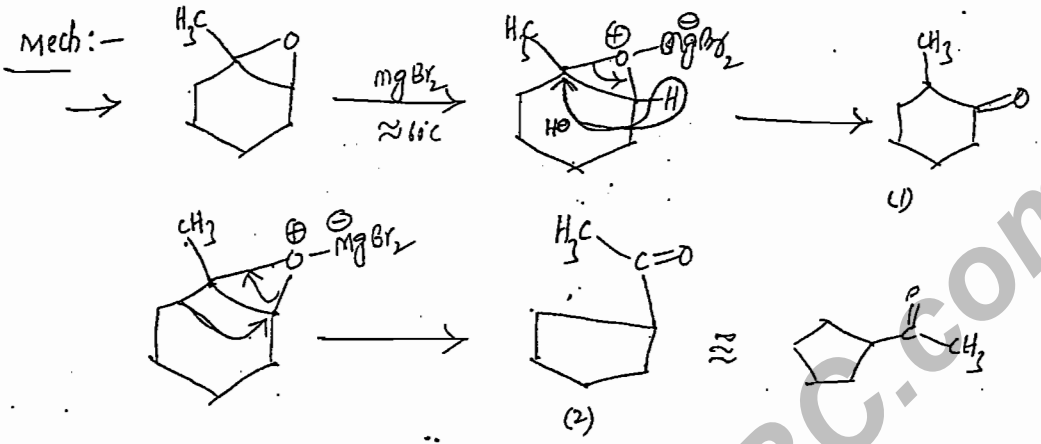
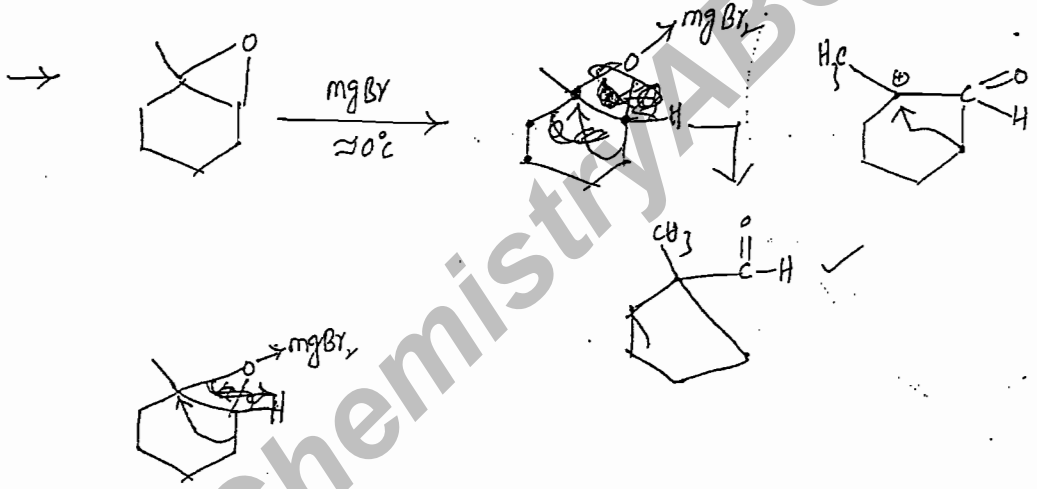
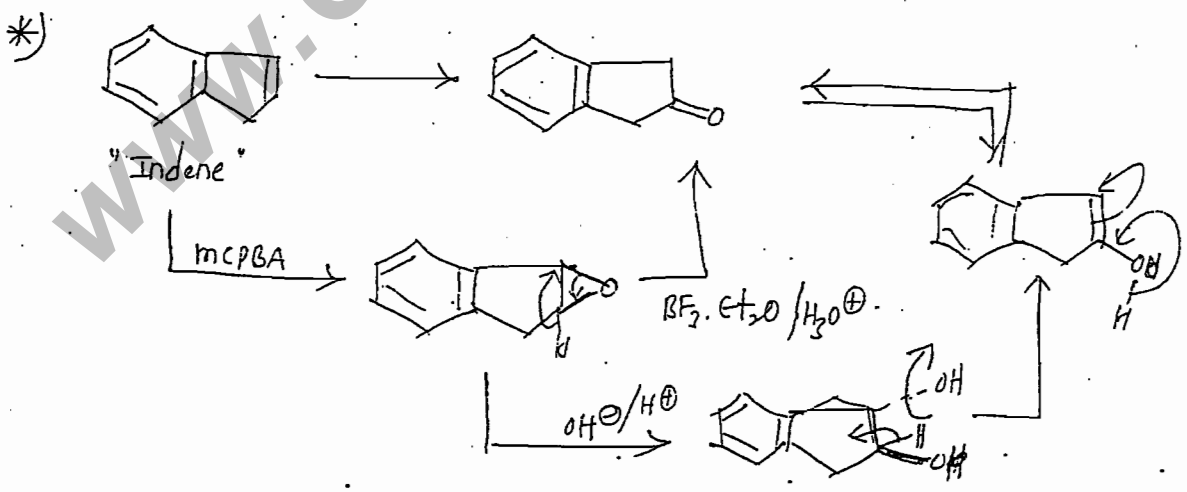
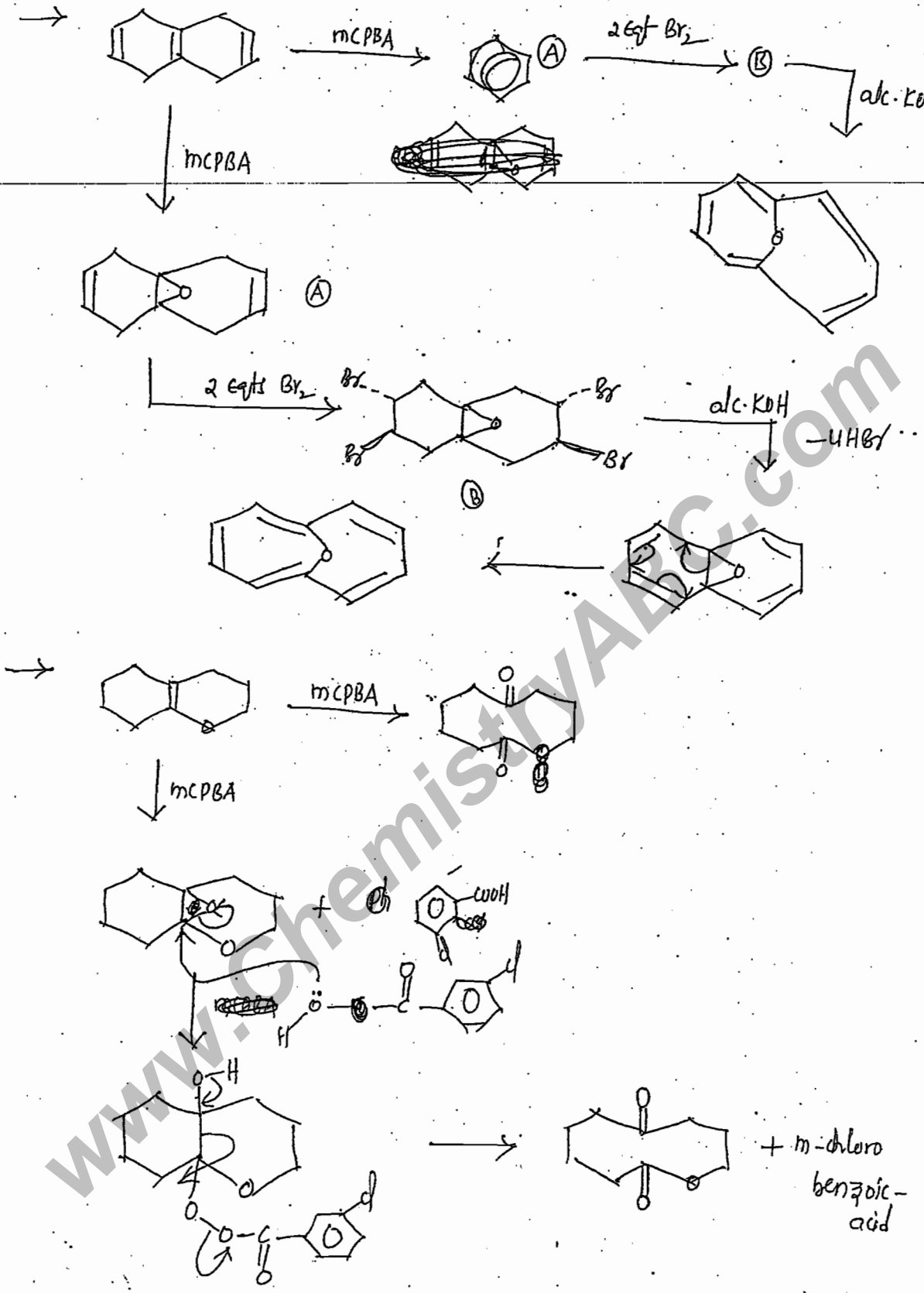
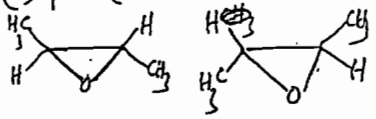








* cis-2-butene $\xrightarrow{mCPBA}$ meso-product + stereochemical product
* Trans-2-butene $\xrightarrow{}$ (±) pair (or) R.M.
* propene $\xrightarrow{}$?

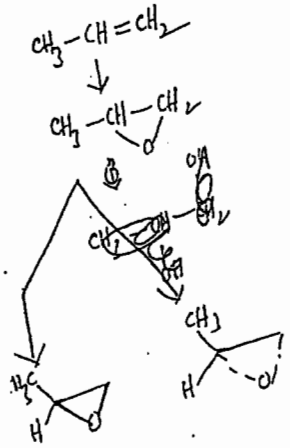


a) Racemic

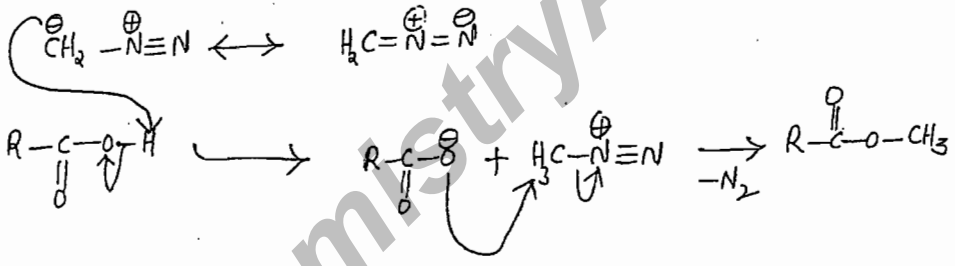
b) R-enantiomer

c) S-enantiomer

d) unequal amount of enantiomers



* $R-C(=O)-OH \xrightarrow{CH_2N_2} R-C(=O)-O-CH_3$



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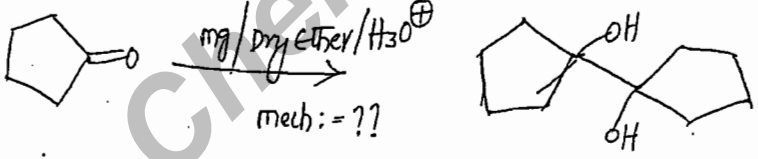
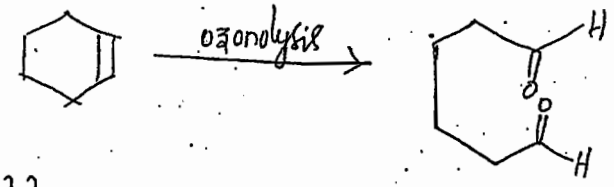


mech: = ??

→ 

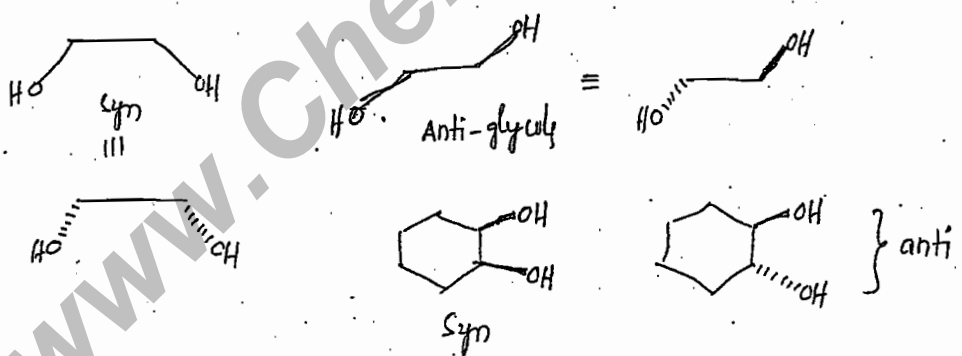
→ mech ??

→ pericyclic reaction steps

Date : 05/05/08

→ **oxidn of Alkenes into 1,2-Diols :—**

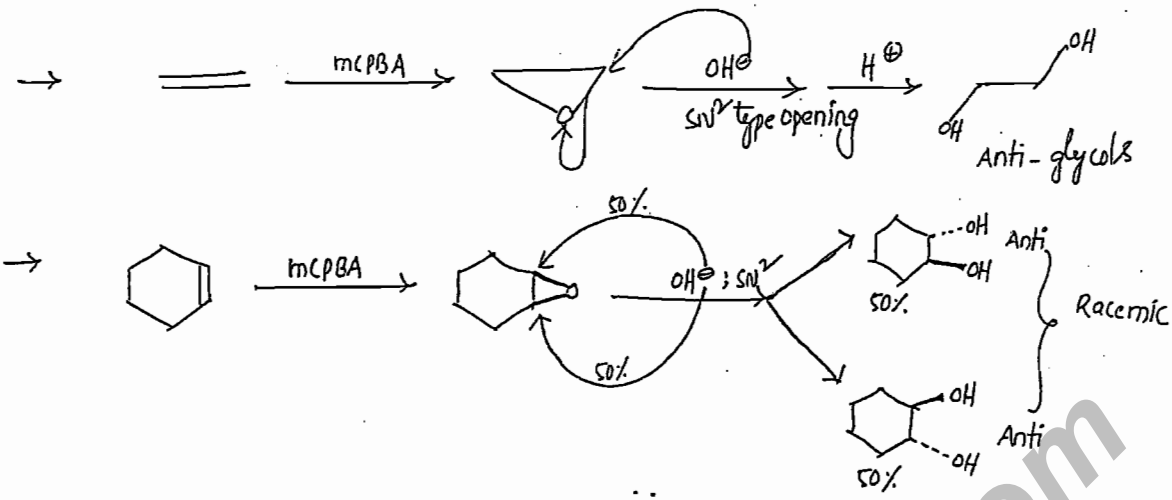
Alkene $\xrightarrow[\text{agent}]{\text{oxidising}}$ 1,2-diols (glycols)



* **Reagents:—**

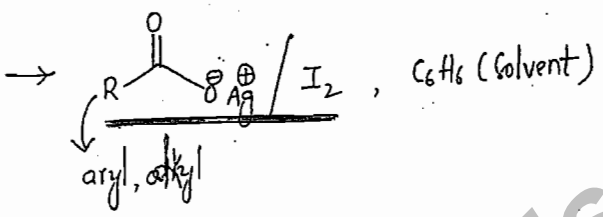
1) $OH^{\ominus}$, opening epoxide
2) Osmium Tetroxide
3) prevost & woodward hydroxylations $RCOOAg/I_2$
4) $KMnO_4$

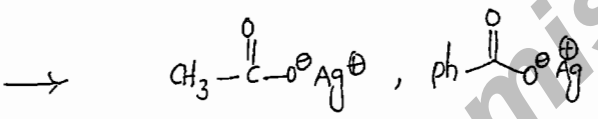
I) **opening of Epoxide with $OH^{\ominus}$: Anti-glycols**

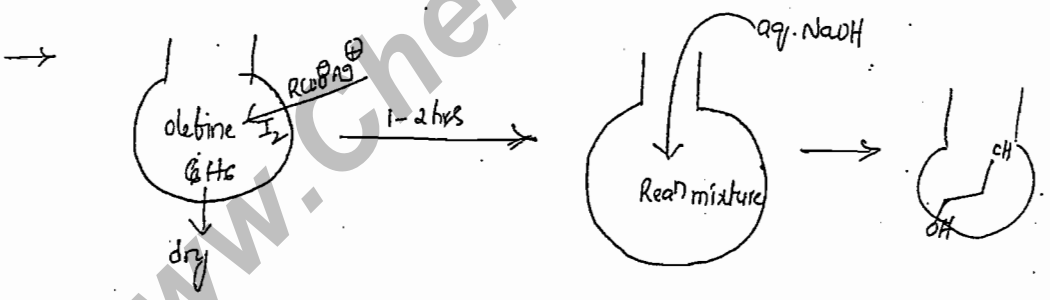


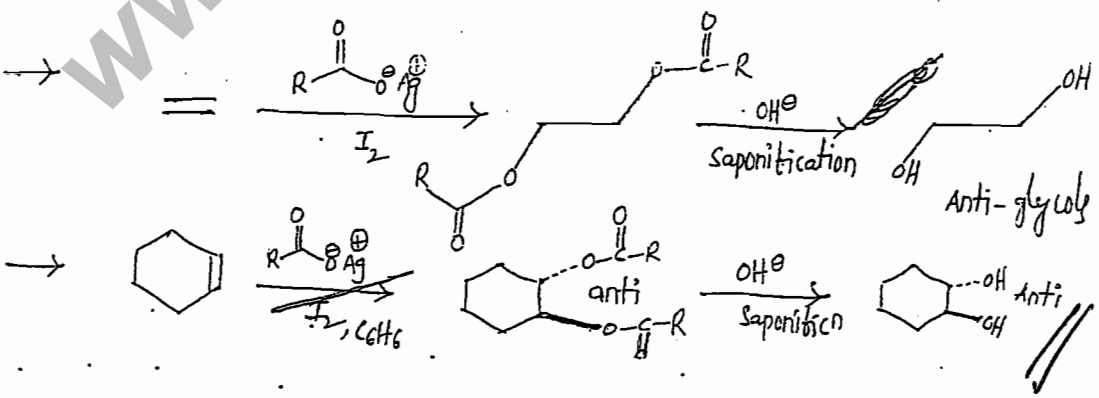
II) **prevost-oxidations : Dry-Hydroxylations :** — Antiglycol

→ Anti-Hydroxylations / Anti-glycols

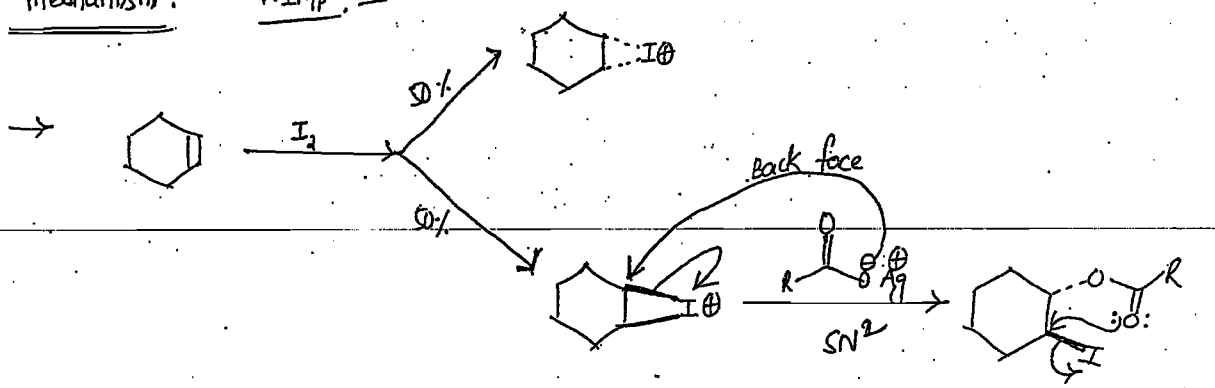


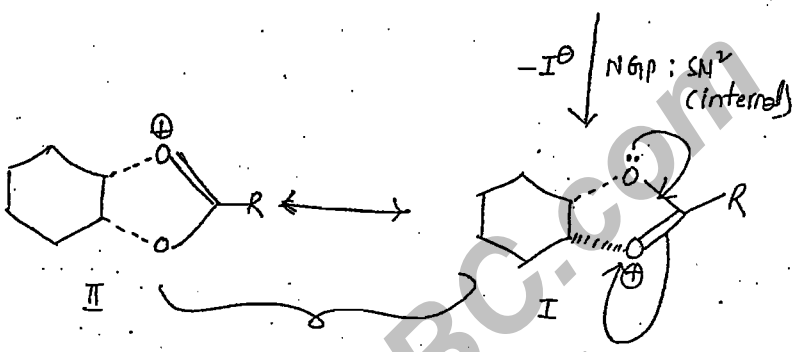


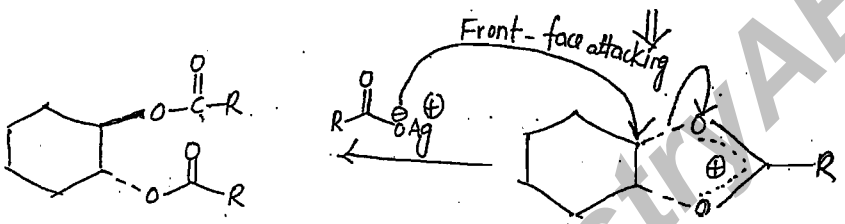




Mechanism :— V.IMP :—

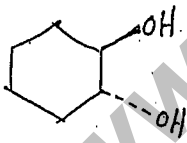




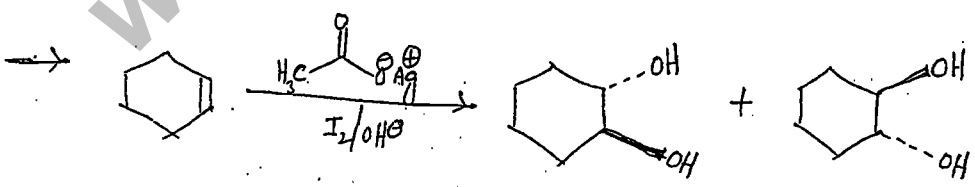


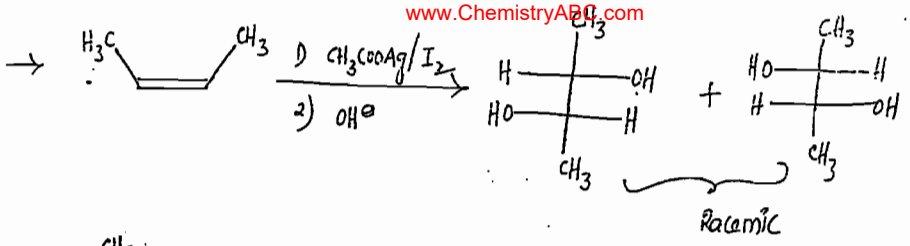
Anti 1,2-diester intermediate Resonance hybrid

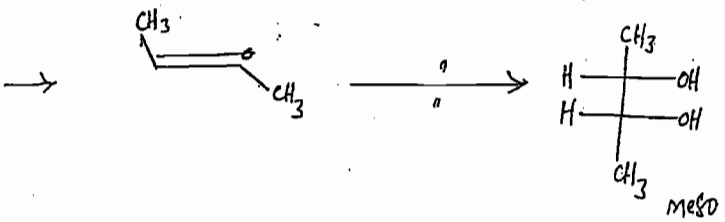
OH⊖/saponification

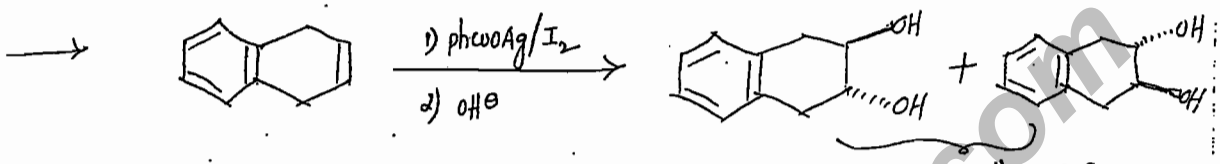


Anti 1,2-diols.



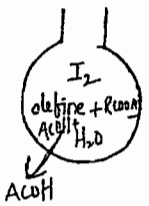




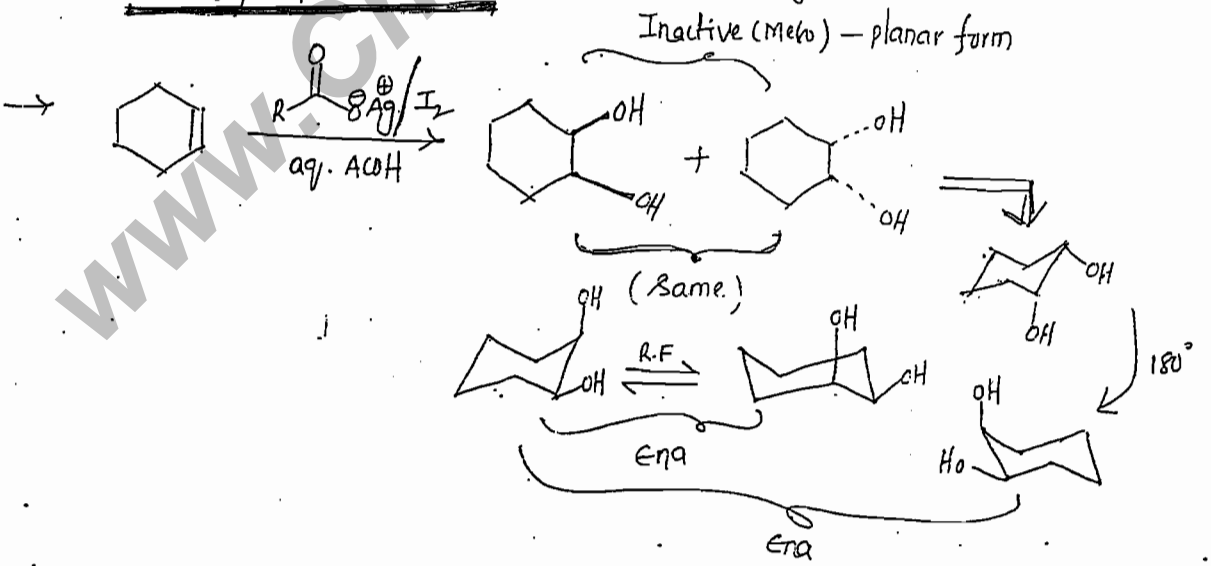


III) **Woodward Hydroxylations / Modifications** :- " wet-oxidations." Syn glycol

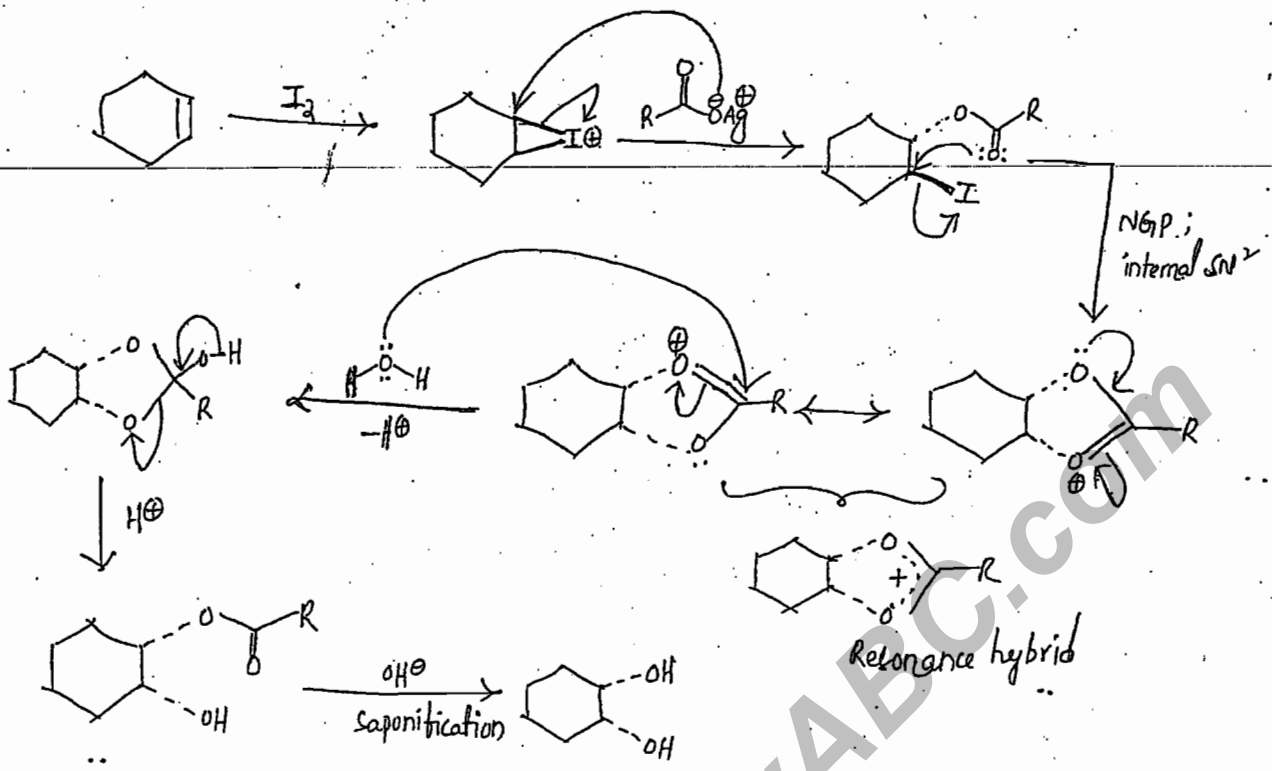
→ Syn glycol / 1,2-diol (Stereochem. of the product opposite to prevost).



→ $RCOO^\ominus Ag^\oplus / I_2$ / aq. AcOH. → woodward reagent.



→ Mechanism :-

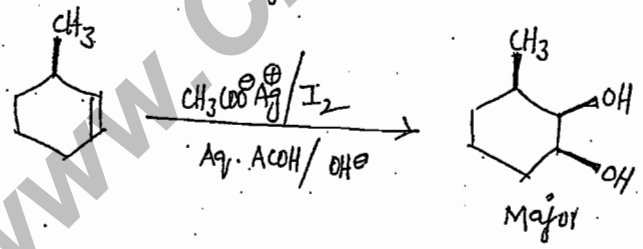


⇒ Even no. of S_N2 — Syn

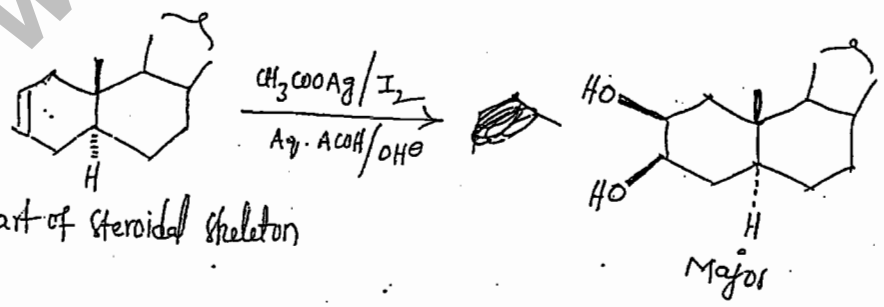
odd " " — Anti .

* "Near to olefine, if there is a subⁿ, woodward hydroxylations preferentially takes place at sterically more crowded side of olefine."

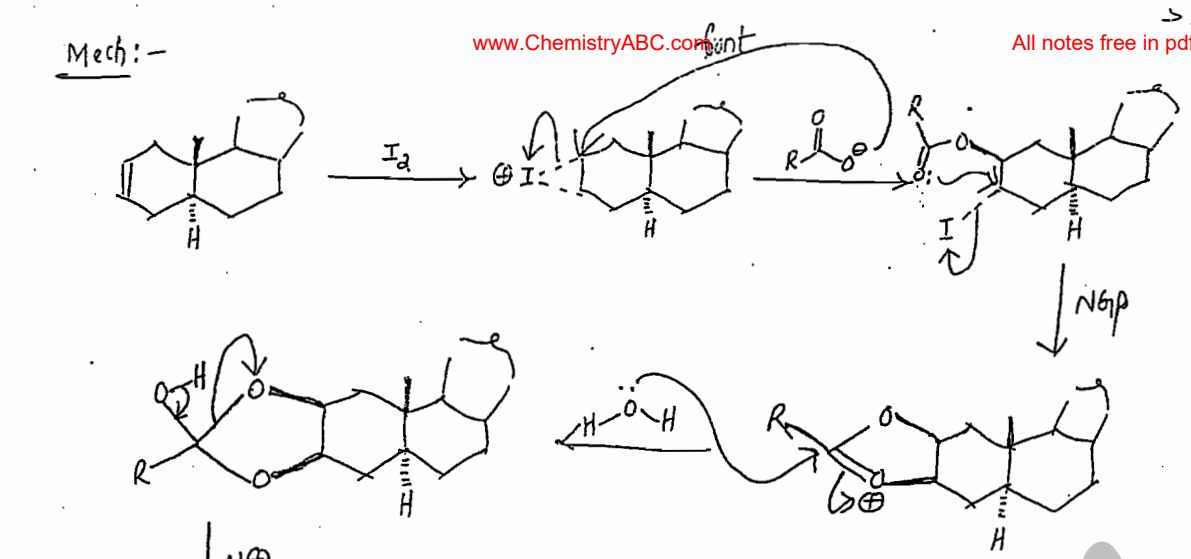
→



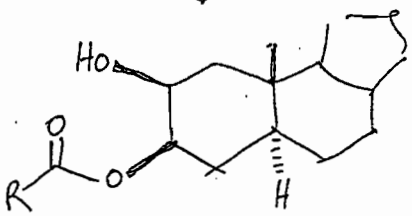
→



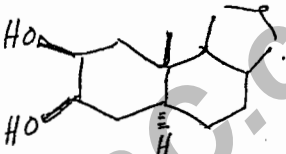
Mech:-



$H^{\oplus}$

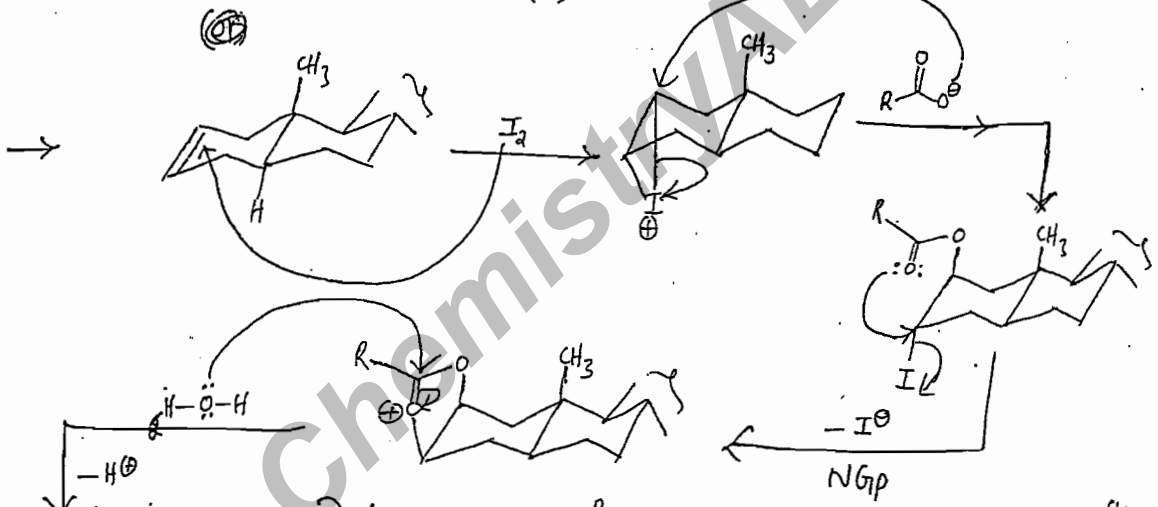


$OH^{\ominus}$/caporiben



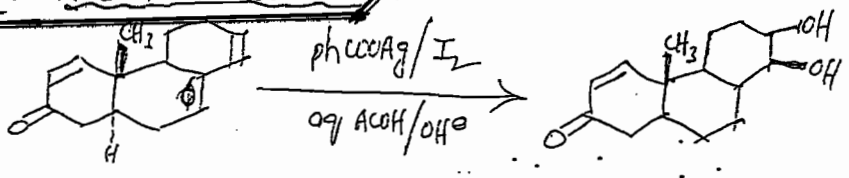
(or)

(or)



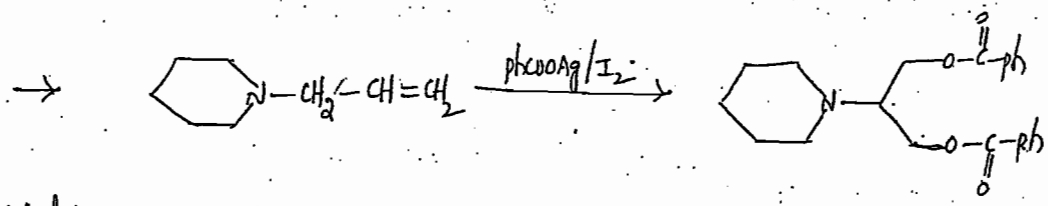
In a molecule if conjugated, isolated olefines present, woodward hydroxyl. takes place at isolated double bond

eg:-

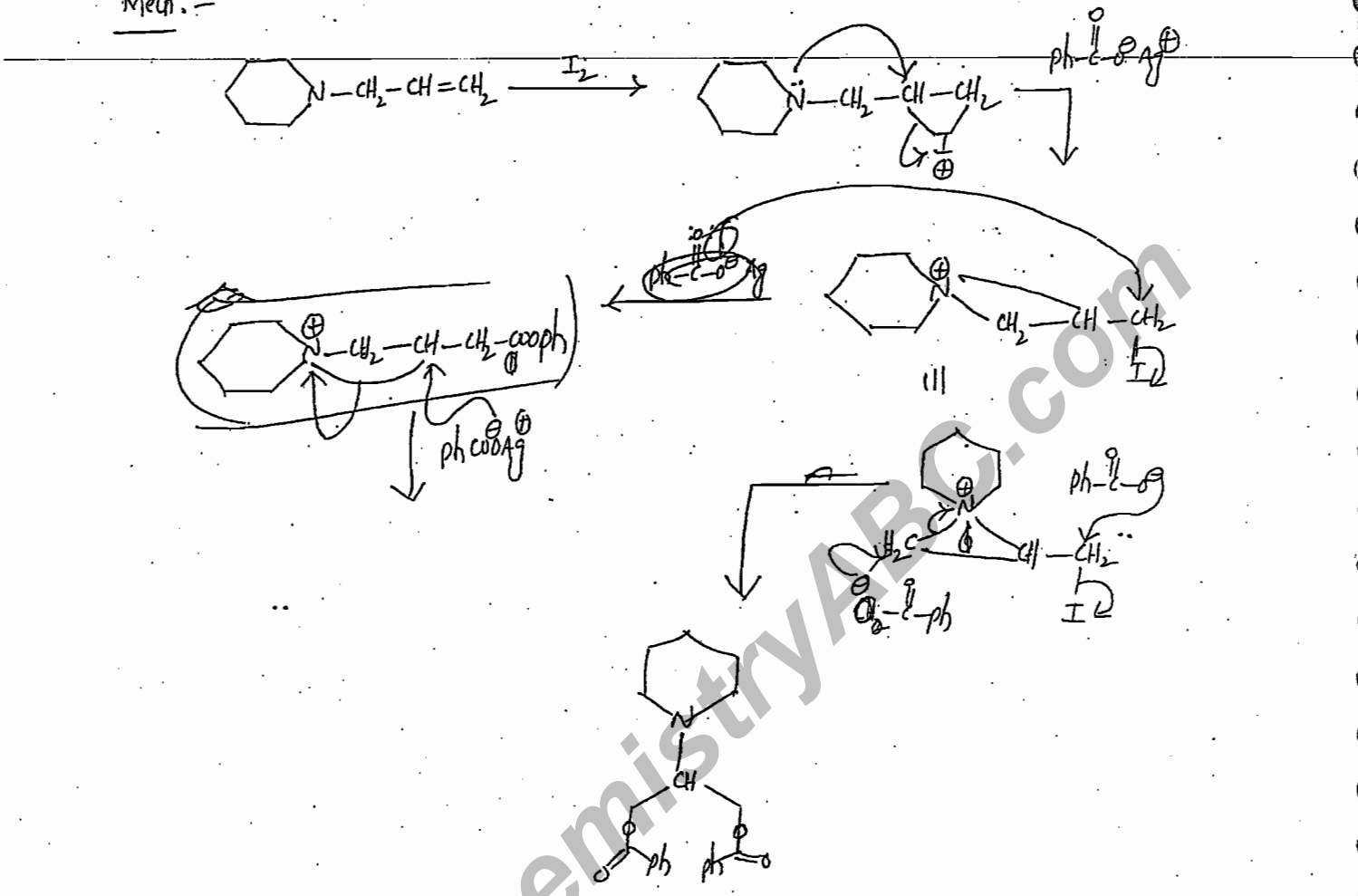


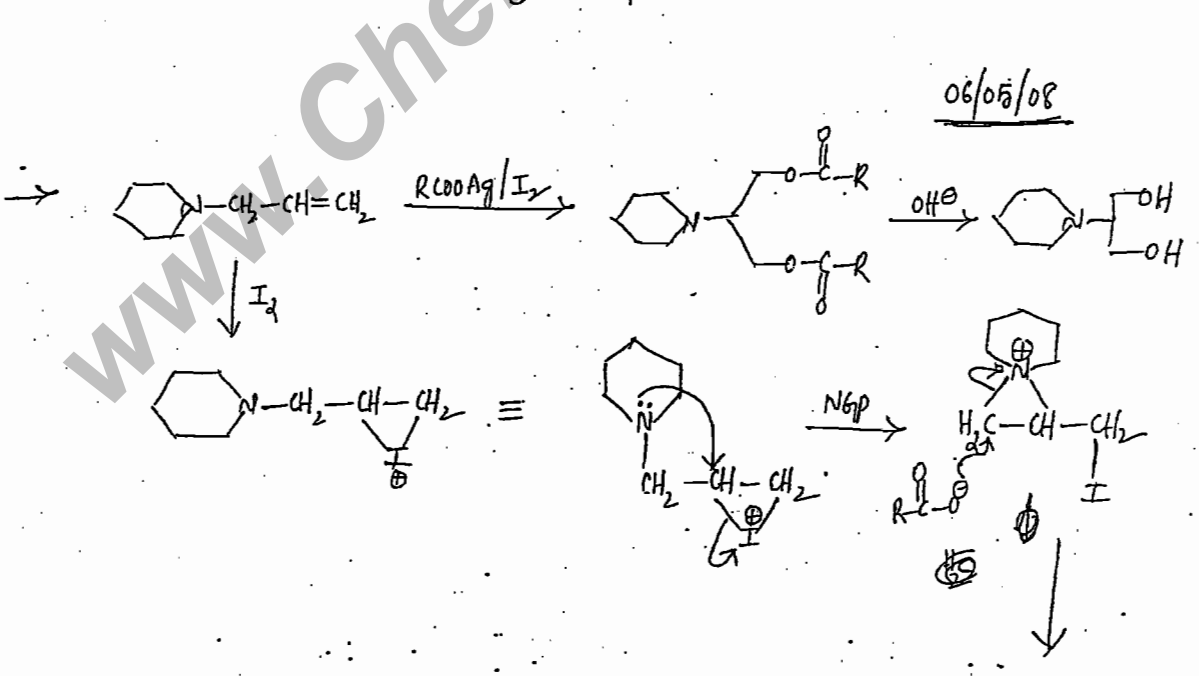
75

STUDENT XEROX 9030000126

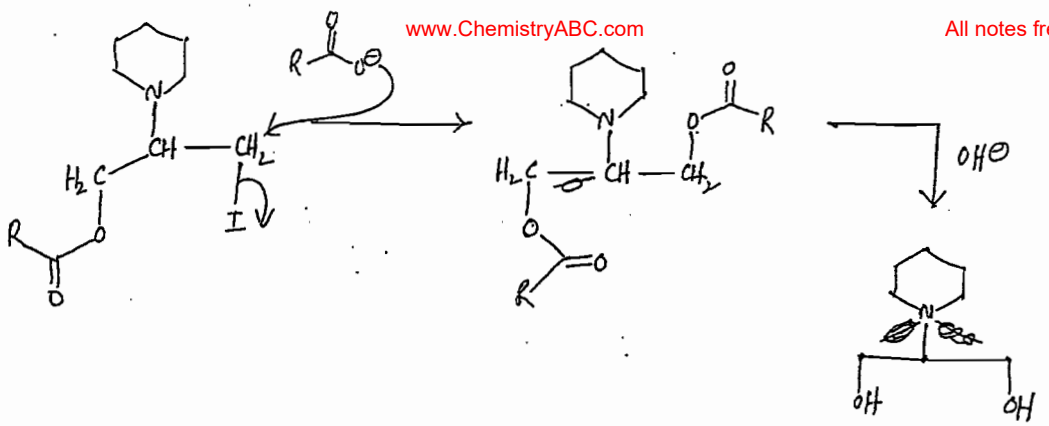


Mech :-

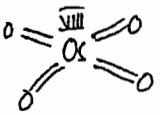


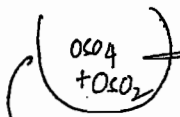


06/05/08



* OSMIUM TETROXIDE :-

OsO_4 :  ; syn-diols : Hydroxyls

* Solid, 100% pure
* colourless
*  Light yellow

usually OsO_4 contaminated with impurity OsO_2, gets light yellow colour.

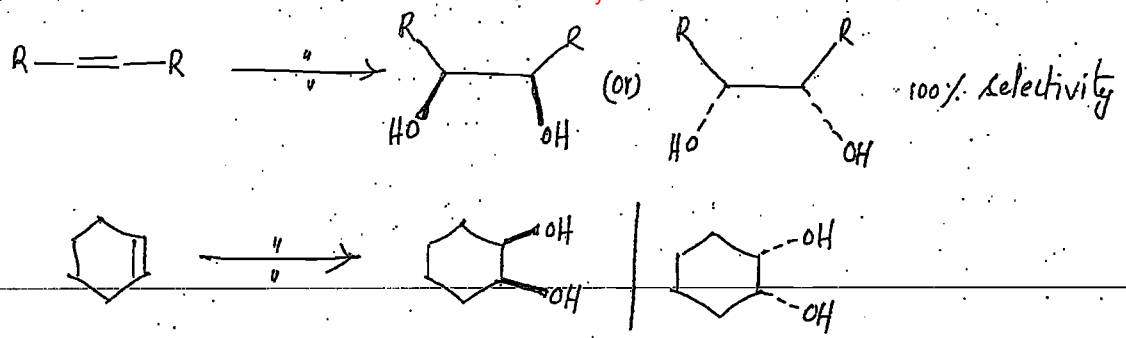
* little Toxic
* Highly expensive.
* Prep^n :- $Os + O_2 \xrightarrow{\Delta} OsO_4$.

Solvents :- Soluble in water/org. solvents.

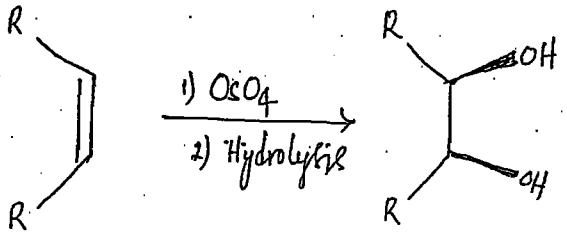
1) water
2) Acetone
3) Alcohols/ tert. Butanol
4) Ethers, Dry ethers, Et_2O, THF, dioxane
5) Benzene

→ preferable : aq. acetone (for majority of OsO_4 oxidations)

Application :- olefins $\xrightarrow[\text{Solvents}]{OsO_4}$ syn 1,2-diols.



Mechanism :-

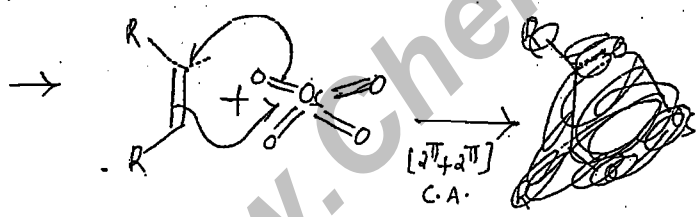


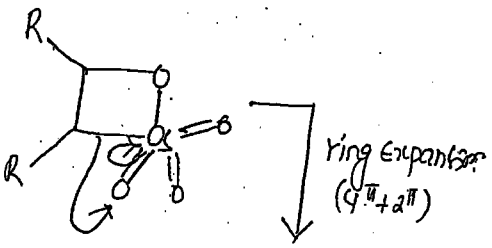
olefin + OsO_4 ⟶ $[2\pi+2\pi]$ (Addition INT) ⟶ (ring expansion) $[4\pi+2\pi]$ (or) osmate ester (Addn int.) intermediate, & isolable

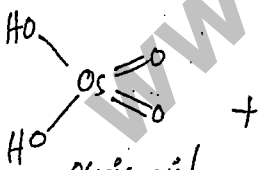
Syn 1,2-diols ⟵ (or) decomposition of osmate ester ⟵ Hydrolysis by using oxidising, reducing agent (widely used- R.A)

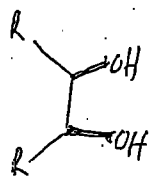
(Simple H_2O hydrolysis is slow)

∴ oxidising or R.A. are used.

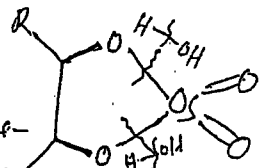








⟵ Hydrolysis / oxidative or reductive- decomposition.



* In hydrolysis, cleavage of Os & O- bonding, bcoz M-O bondings are weaker than C-O bonding. Syn stereochem. at 'C' skeleton retained

→ Some of the R.A's convert Osmic acid into osmium metal.

→ Following are best oxidative, reductive agents in hydrolysis of Os esters.

→ 1) Bisulphite + pyridine

2) Bisulphite or Sulphite + aq. EtOH

3) KOH + Mannitol

4) Metal chlorate / Acid : $KClO_3/H_2SO_4$

5) Sulphide ions' soln

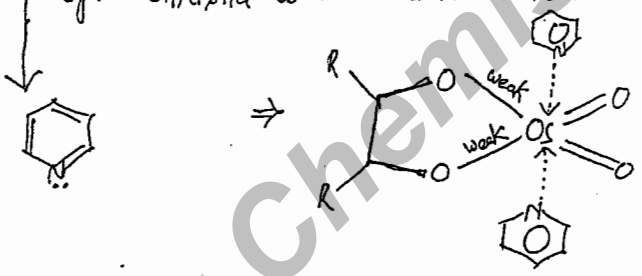
6) $LiAlH_4$

→ presence of 3°-amines, enhances OsO_4 oxidations. 3°-amine co-ordinate with Os metal in Os-ester. As a result, ↓ in strength of M–O bond, ↑ in rate of hydrolysis.

eg:- Pyridine, Quinuclidine →

→ In assymetric hydroxylation, chiral 3°-amines used.

eg: Cinchona alkaloid derivatives.



→ olefin $\xrightarrow[\text{Weak R.A.}]{OsO_4}$ syn 1,2-diol + α-ketol ($-\overset{\alpha}{C}H(OH)-\overset{\alpha}{C}(=O)-$)

→ Some of the OsO_4 oxidn produces, over oxidn product – α-ketol.

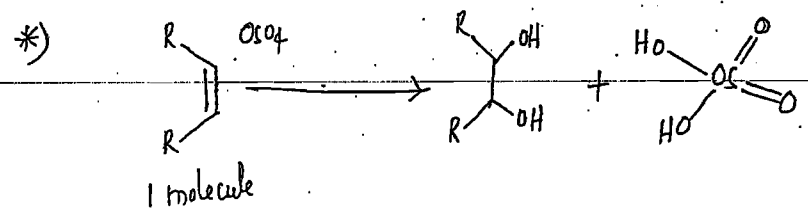
→ olefin $\xrightarrow{OsO_4}$ syn 1,2-diol + α-ketal

↳ over oxidn bipnduct

→ Inorder to prevent formation of over oxidation product, α-ketal in

combination with OsO_4, some other weak R.A's are used.

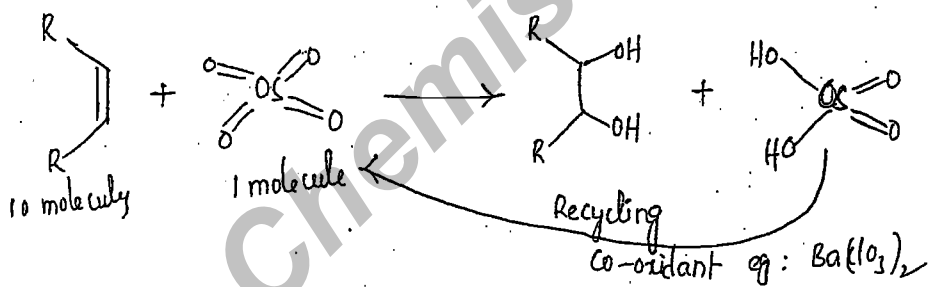
eg:- weak R.A. 1) Na_2SO_3 2) Alk. HCHO 3) Ascorbic acid

*) 

→ OsO_4 is the expensive agent, in oxidn of olefins, 1:1 ratio of olefin & OsO_4 is required. Inorder to lessen the quantity of OsO_4, other oxidising agents are used, which converts the biproduct osmic acid into OsO_4. i.e, in the presence of other oxidising agents, recycling of OsO_4 oxidn takes place.

∴

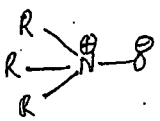
→ whichever added O.A. used for regeneration of OsO_4 from osmic acid called "co-oxidants"

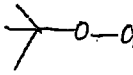
→ 

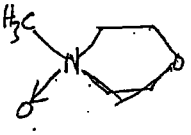
* Co-oxidants :- cheaper than OsO_4.

* Metal chlorate $KClO_3$/ $Ba(ClO_3)_2$

* H_2O_2

* 3°-amine oxide ; 

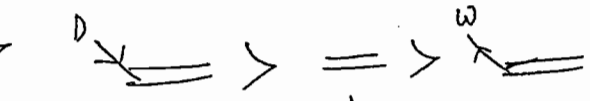
* Alkyl hydroperoxide ; TBHP, 

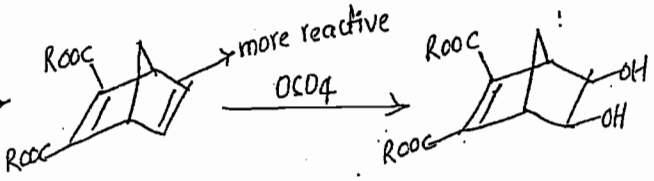
* N-methyl morpholine-N-oxide ; NMO ; 

* Reactivity of olefin

→ presence of donating gp's at olefin ↑es reactivity of olefin in OsO_4 oxidations.

→ (In OsO_4 oxidn, olefin nucleophile
OsO_4 electrophile)

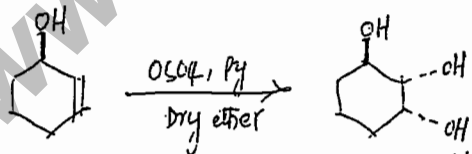
→ 

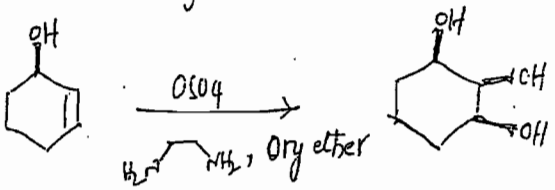
→ 

→ Selectivity :- preferentially oxidises sterically less crowded face of olefin.

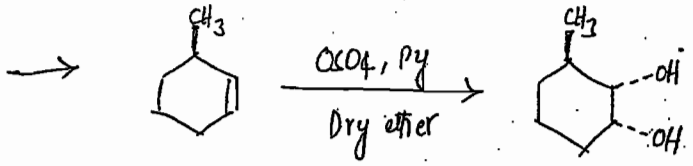
→ Simple OsO_4 oxidations willn't involve in chelation or H-bonding, but in the presence of diamino ethane, involve in chelation with allylic alcohols or amines, preferentially do oxidn at sterically more crowded side, i.e, hydroxylation at the same side of allylic alcohol/amine gps.

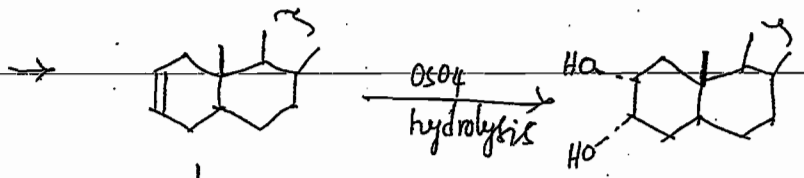
→ do oxidn at the same side of allylic alcohol/amine gps.

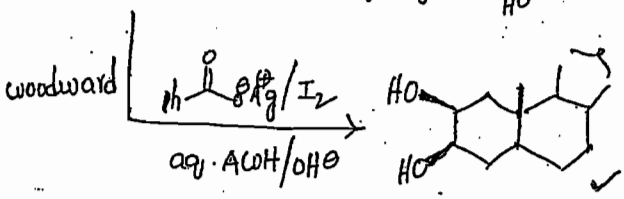
→ 

→ 

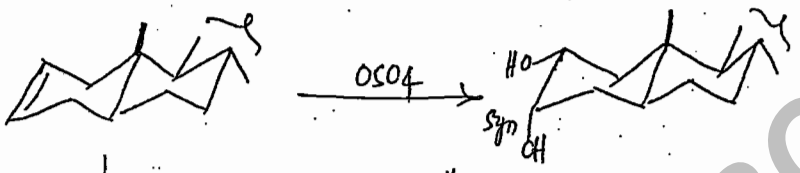
→ OsO_4 is one of the best reagent to convert allylic alcohols into 1,2,3-triols

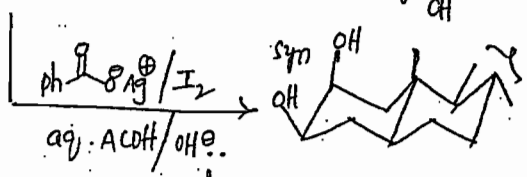


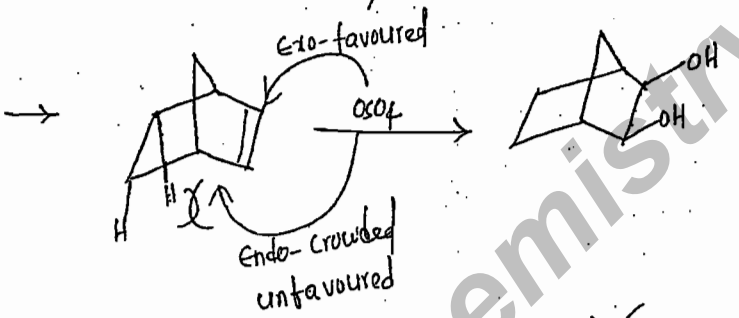


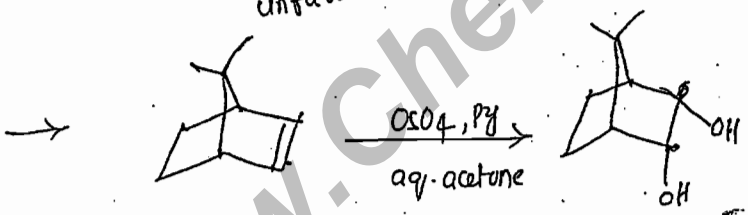


(or)





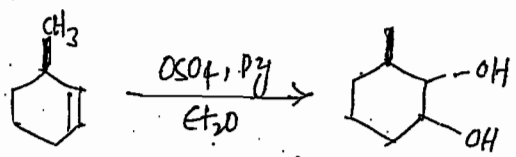


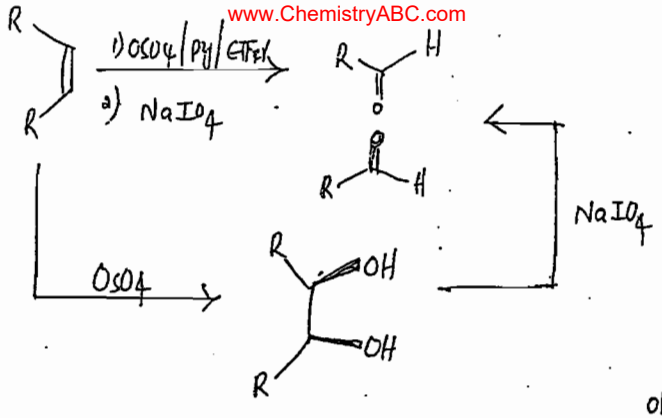


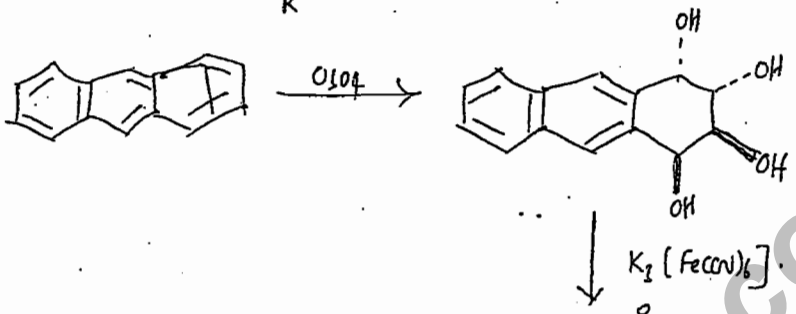
→ whenever OsO_4 used in small quantities by mixing with co-oxidants said to be catalytic amount of OsO_4.

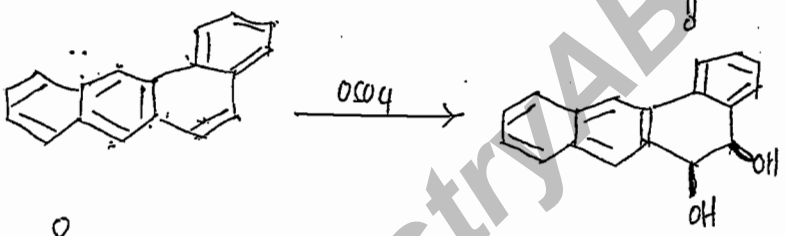
Examples :- without co-oxidant :

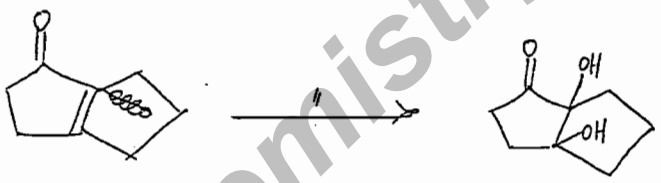
eg: ①



2) 

3) 

4) 

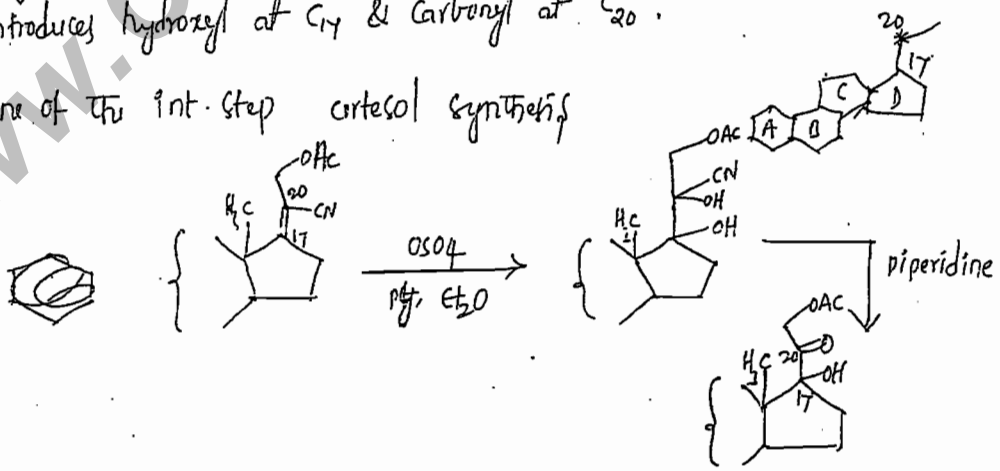
5) 

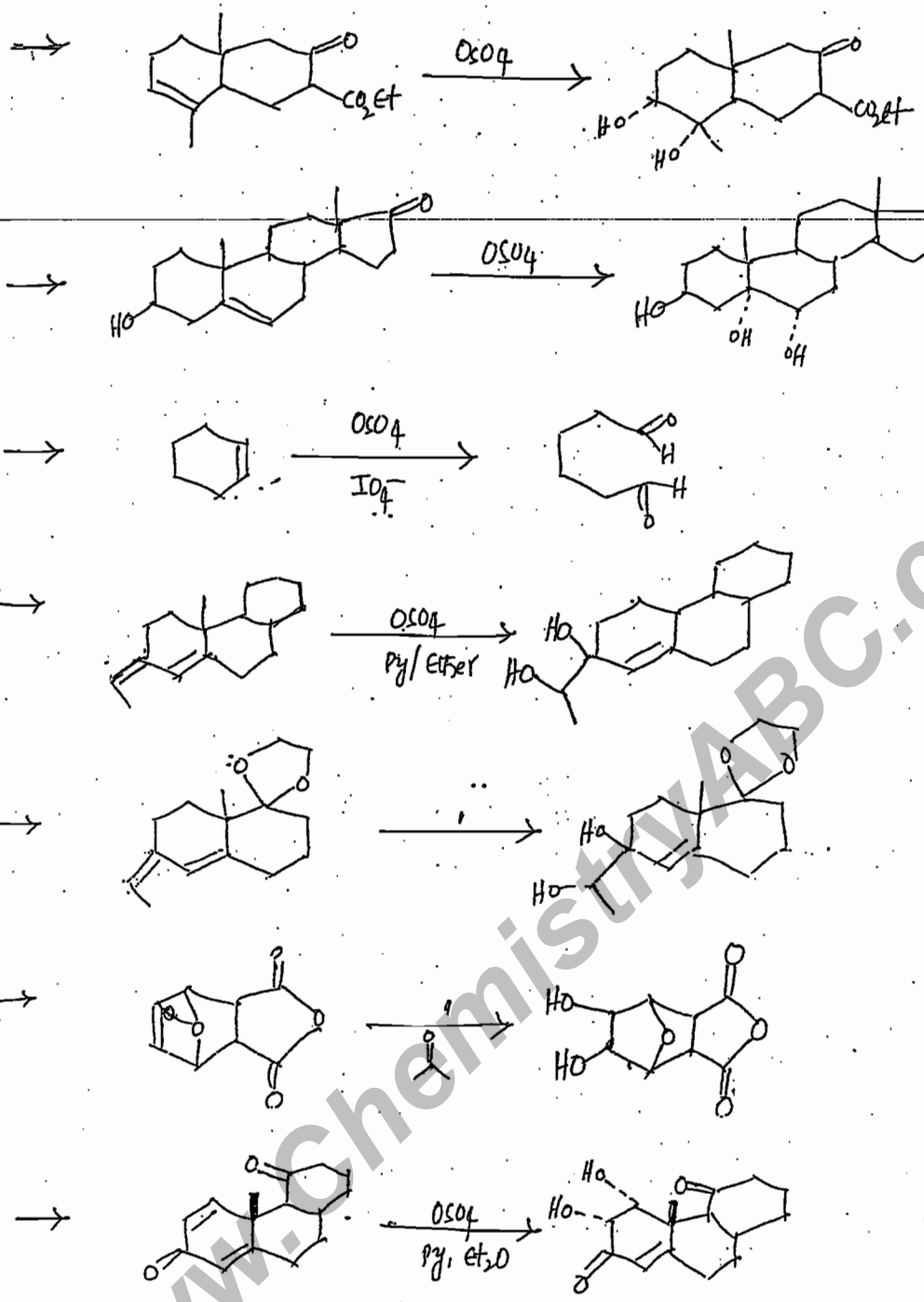
6) OsO_4 used in synthesis of steroidal skeleton

⇓

introduces hydroxyl at C_{17} & carbonyl at C_{20}.

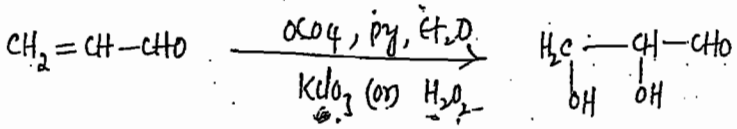
eg:- one of the int. step cortesol synthesis



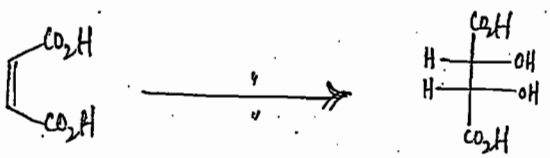


Eg:- catalytic amount of OsO_4 (OsO_4 + co-oxidant) : 07/05/08

1)



2)



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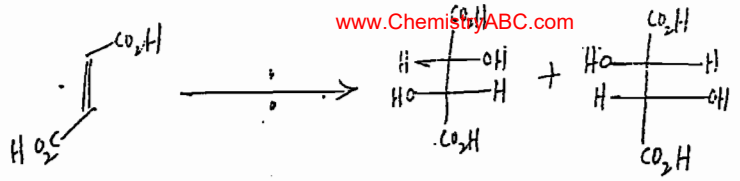

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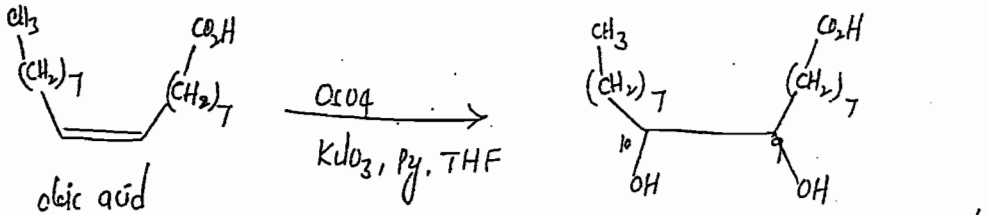


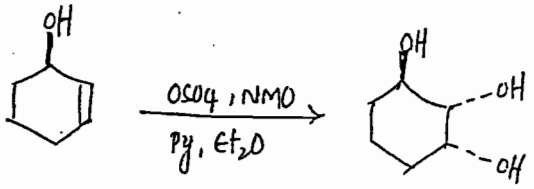
oleic acid

OsO_4

$KClO_3$, Py. THF

9, 10-dihydroxy stearic acid

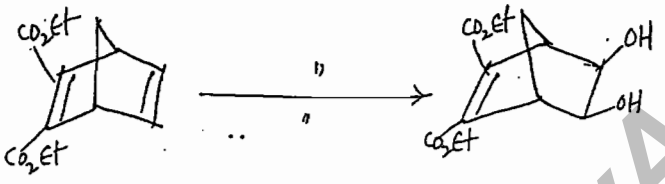
5)



OsO_4, NMO

Py, Et_2O

6)



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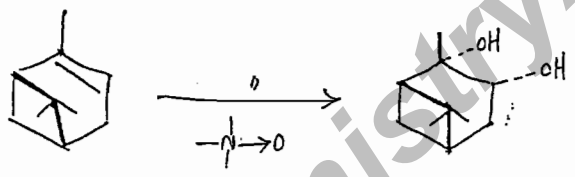
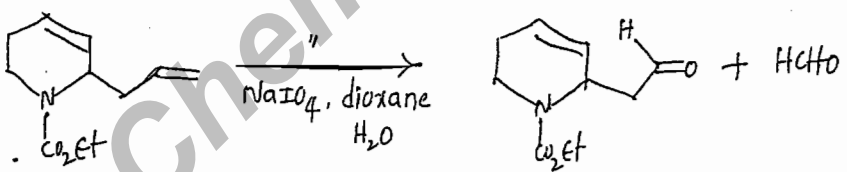


8)

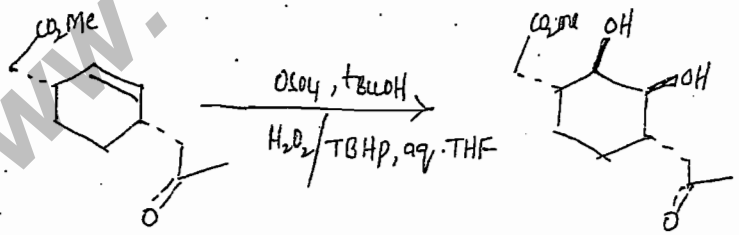


$NaIO_4$, dioxane

H_2O

+ HCHO

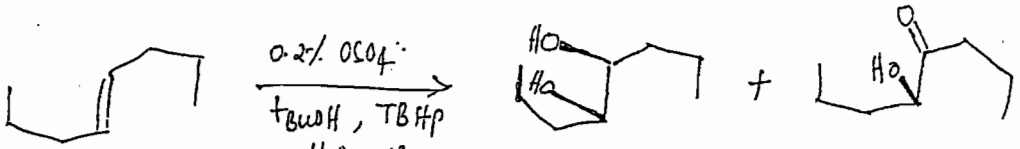
9)



OsO_4, $tBuOH$

H_2O_2/TBHP, aq. THF

10)



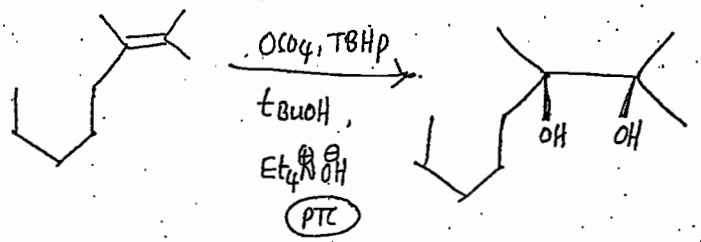
0.2% OsO_4

$tBuOH$, TBHP

H_2O, 0°C

$Et_4\overset{\oplus}{N}\text{-}OH^{\ominus}$ ⇒ phase transfer catalyst (PTC)

→ 11)



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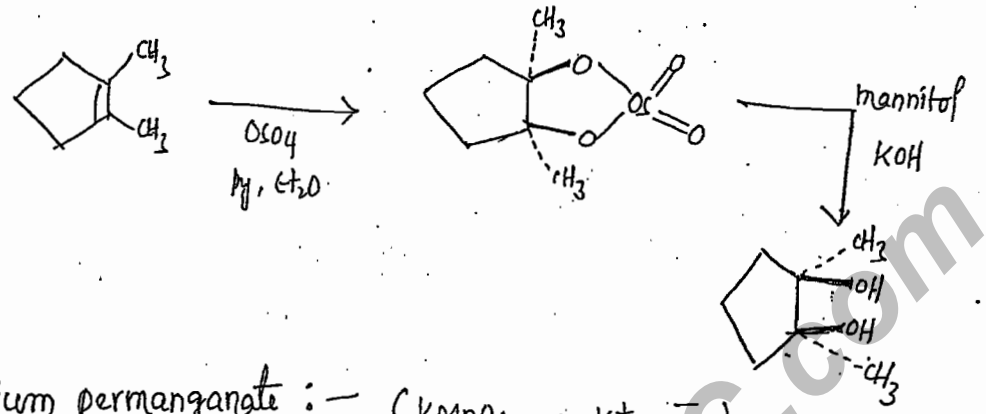
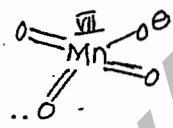


* potassium permanganate :- (KMnO4 or K⁺MnO4⁻)



→ 1) cheaper / solid

2) Insoluble in org. solvents

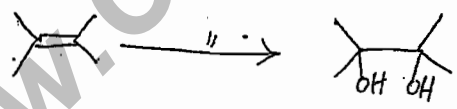
highly soluble in water.

Applications :-

→ syn hydroxylating agent

→ Alkene $\xrightarrow{KMnO_4}$ syn 1,2-diols.

Solvents :-



→ 1) water 2) aq. benzene 3) aq. acetone 4) aq. alcohols

5) aq. AcOH 6) aq. Et_2O

Limitations :- 1) Insoluble in org. solvents

2) Useful for org. compds which are soluble in water.

eg :- unsaturated carboxylic acids, unsaturated sulphonic acids, oleic acid /  etc

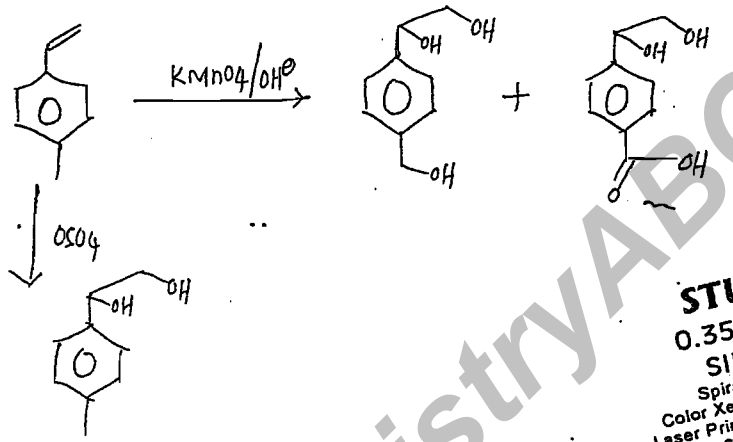
3) $KMnO_4$ oxidn product depends on nature of reaction conditions.

In neutral / acidic medium, over-oxidn (acid) product produced.

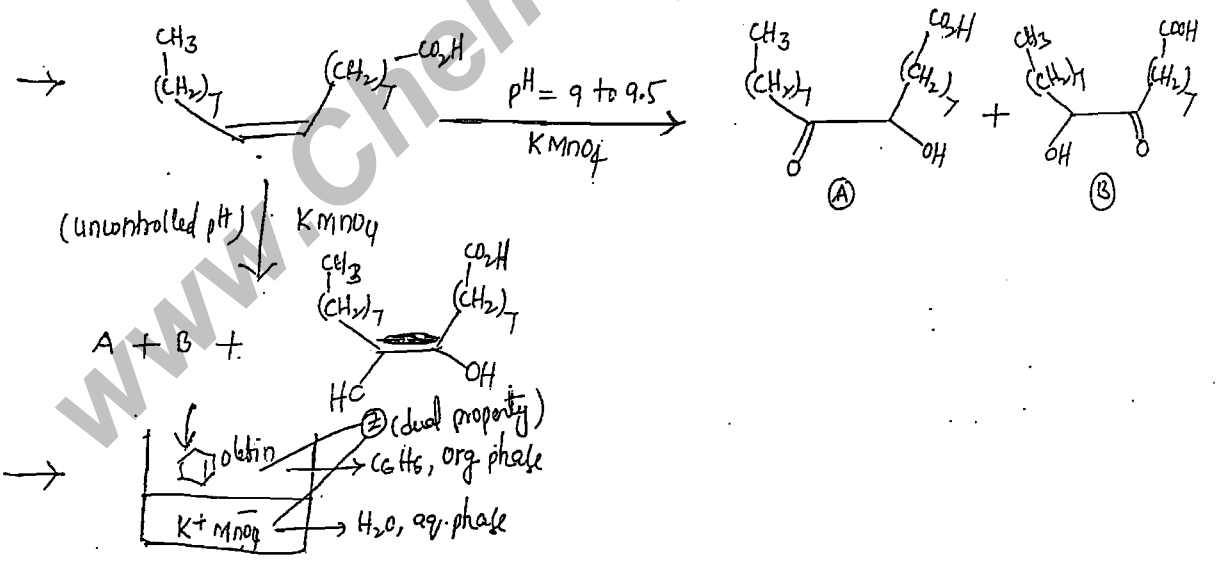
In basic medium, usually "1,2-diol". over-oxidn product formn almost negligible.

∴ For 1,2-diol formation from olefins, most suitable medium - alkaline or basic.

4) If olefin having other oxidizable gp, selectivity poor in oxidn of olefins.

→ 

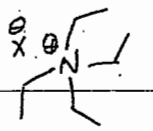
5) oxidn product depends on pH of reaction medium.

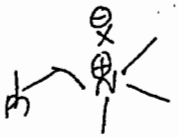
→ 

→ Any substance which transfers ions or groups from one phase to other

phase / org. phase to aq. phase or vice-versa called PTC. (phase transfer catalyst).

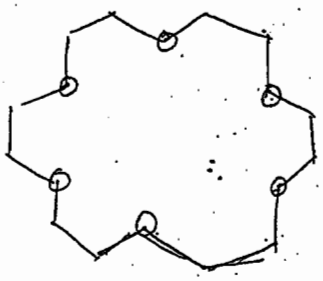
eg: → 1) Quaternary amm. salts; $Q^{\oplus}X^{\ominus}$

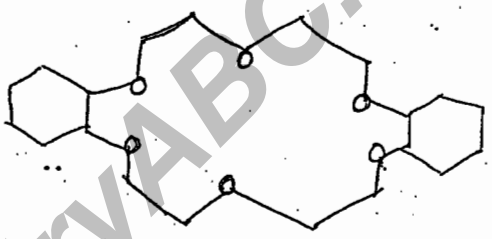


→ benzyl trimethyl amm. salt 

2) Crown Ethers ;

→ 18-crown-6

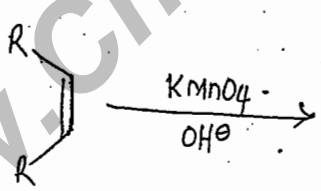




~~dicyclohexano~~ 18-crown-6 dicyclohexano – 18-crown-6

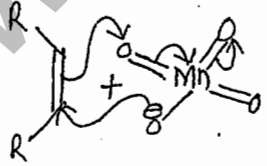
→ simple olefins' oxidn with $KMnO_4$ under PTC conditions readily take place.

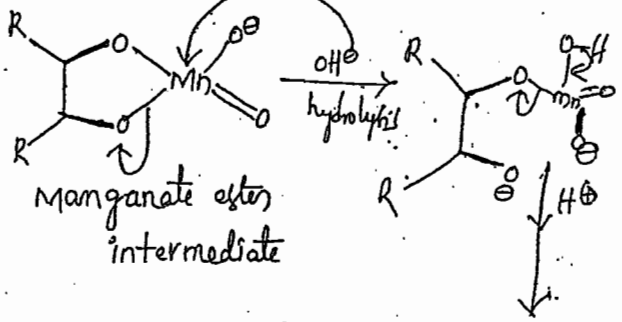
Mechanism :-



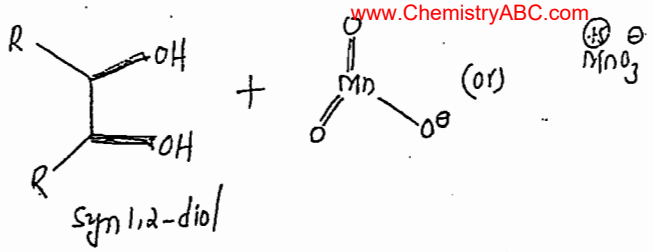
Syn 1,2-diol

→





Manganate ester intermediate



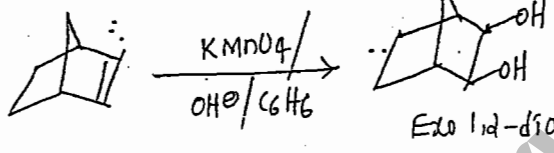
Syn 1,2-diol

→ In hydrolysis, cleavage of Mn–O bonding, not C–O bonding.

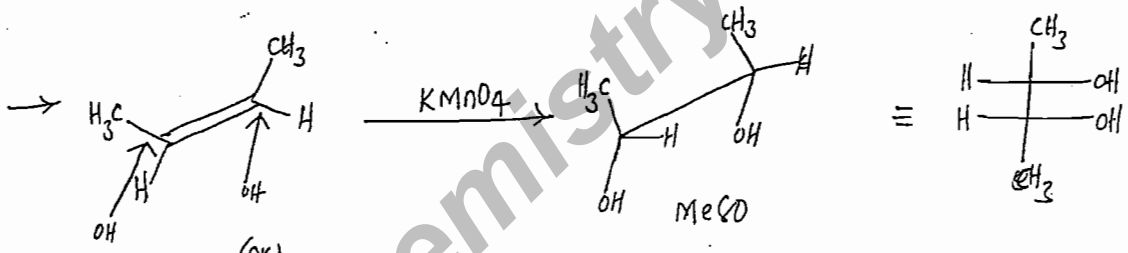
∴ Syn-stereochem. retained / maintained.

eg:- Stereochemistry ; Selectivity :-

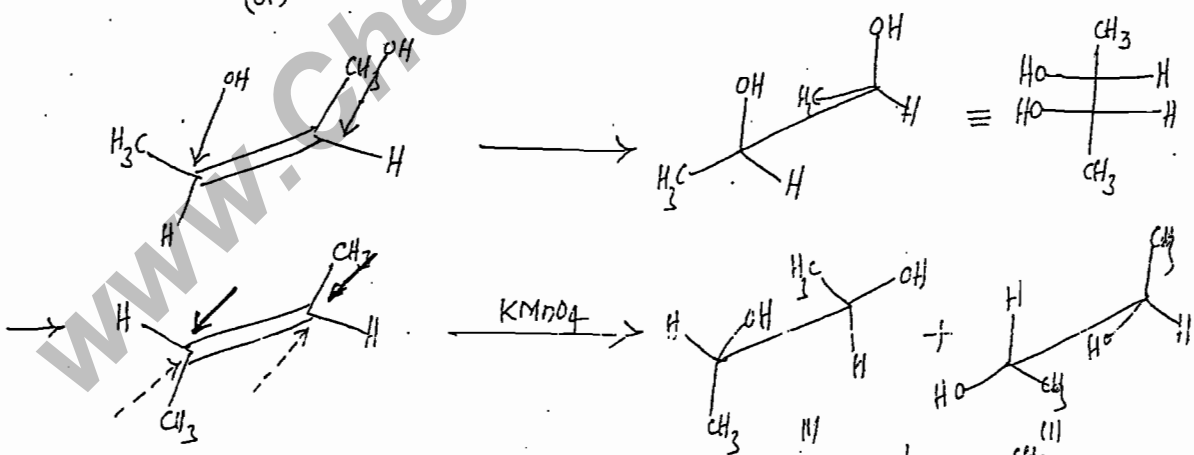
→ similar to OsO_4, selective hydroxylation at sterically less crowded phase of olefin.

→ 

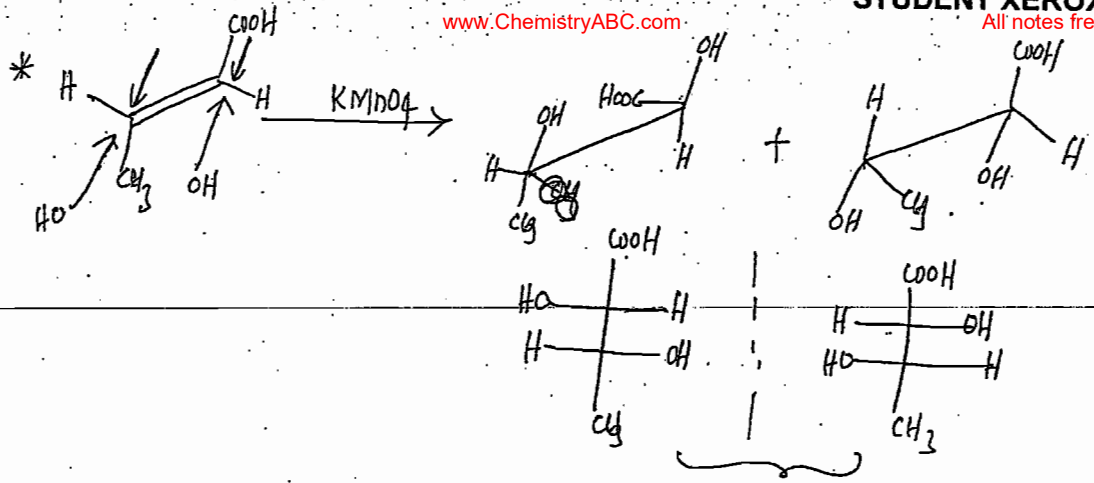
Exo 1,2-diol

→ 

(or)

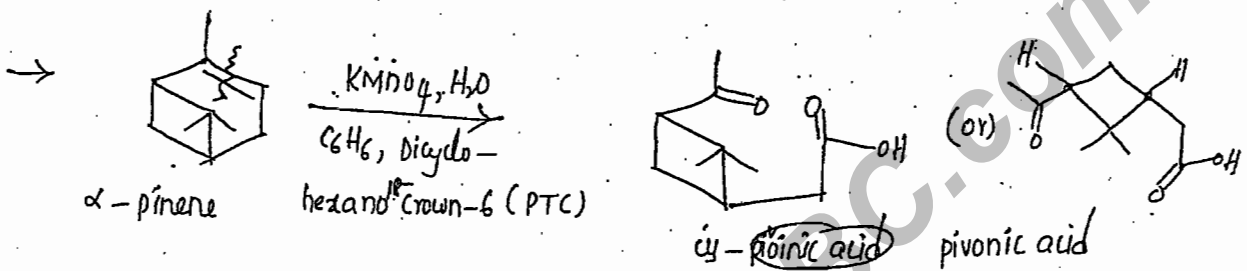


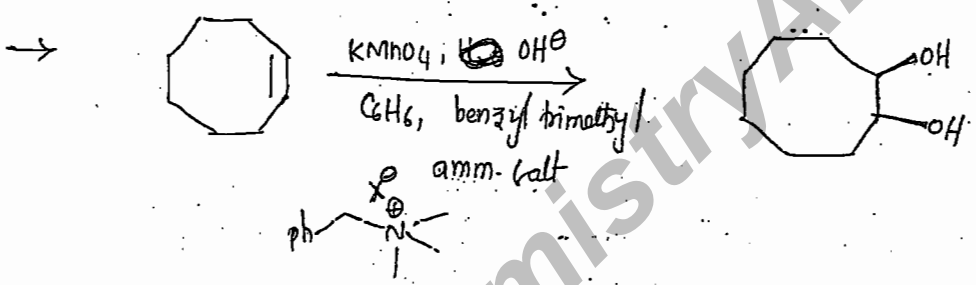
Racemic



threo racemic.

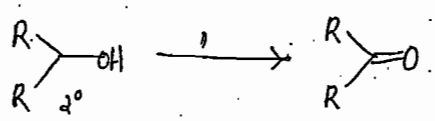
V.IMP:—





Oxidation of simple alcohols into simple carbonyl compounds

eg: $R-CH_2OH \xrightarrow{\text{reagent}} R-CHO$ (1°)



→ Alcohols $\xrightarrow{\text{oxidising agent}}$ carbonyl compounds.

* Cr^{VI} – oxidants.
* Ag_2CO_3.
* NBS.
* DMSO – " .
* oppenaur oxidations.
* MnO_2 – " .
* HgO.

* Chromium - VI - oxidations :-

1) H_2CrO_4 ,

2) CrO_3 + Acetone + H_2SO_4 (Jones oxidations)

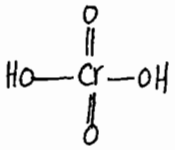
3) CrO_3 + Pyridine (Sarett's oxidations)

4) CrO_3 + Pyridine + CH_2Cl_2 : collin's Oxidations

5) PCC : pyridinium chloro chromate } corey's Reagents

6) PDC : " dichromate

Chromic acid :- H_2CrO_4.



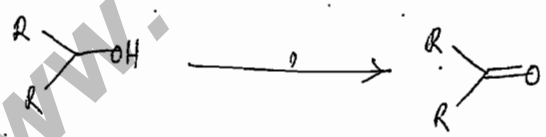
* $(CrO_3)_n + H_2O \longrightarrow H_2CrO_4$

* $Na_2Cr_2O_7$ (or) $K_2Cr_2O_7$ } $\xrightarrow{conc.\ H_2SO_4}$ H_2CrO_4

* Applications :-

→ 1°/2° alcohols $\xrightarrow{H_2CrO_4}$ Carbonyl compounds

$R-CH_2OH \xrightarrow{[O]} R-CHO$

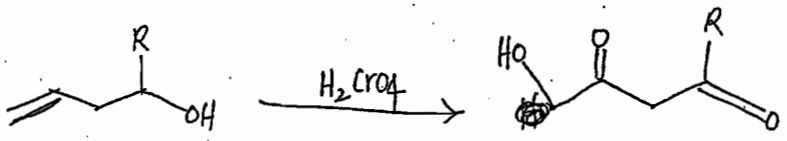


* Limitations :-

1) with H_2CrO_4, 1° alcohols usually produces over oxidn products - carboxylic acids, ∴ not suitable for 1° alcohols' oxidation.

$R-CH_2OH \xrightarrow{H_2CrO_4} R-CHO + R-COOH$ (over oxidn product)

2) If alcohols having other oxidisable groups, these also get oxidised.

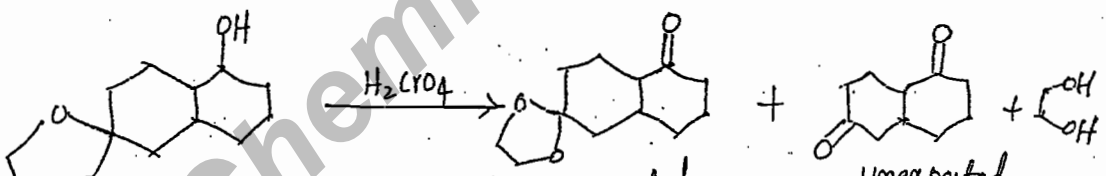
→ 

DB/TB's gets oxidised.

3) Acid-labile gps get opened in chromic acid oxidations.

Acid-labile gps :— Groups or frs which readily gets opened/disturbed in acidic medium called "acid-labile groups".

eg: epoxides, acetals, ketals, β-lactums, lactones, some of the simple ethers, amides ().

→ 

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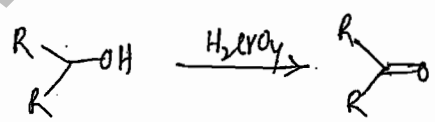

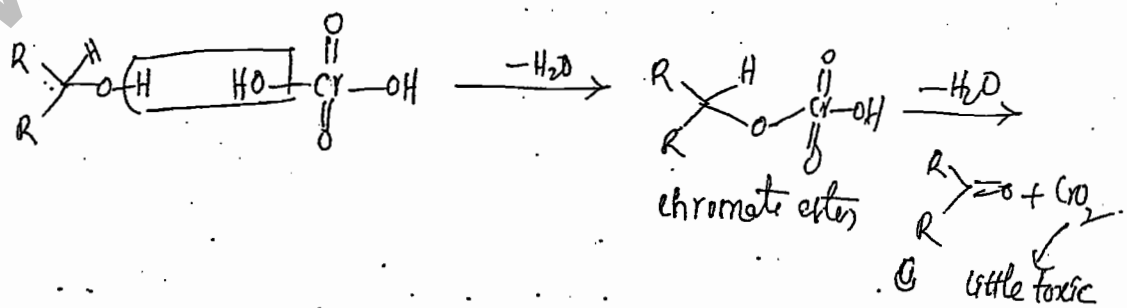

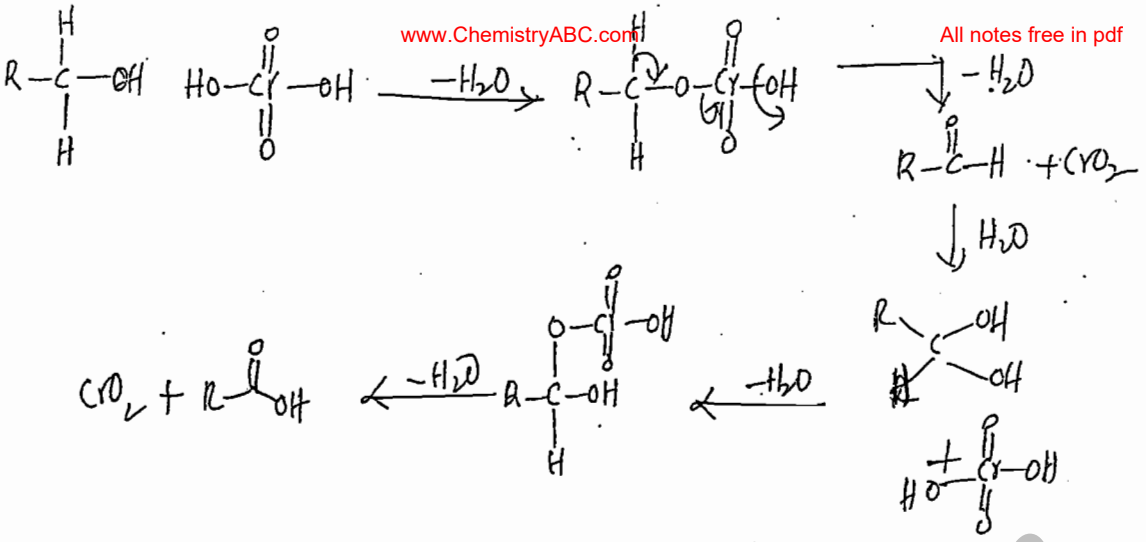

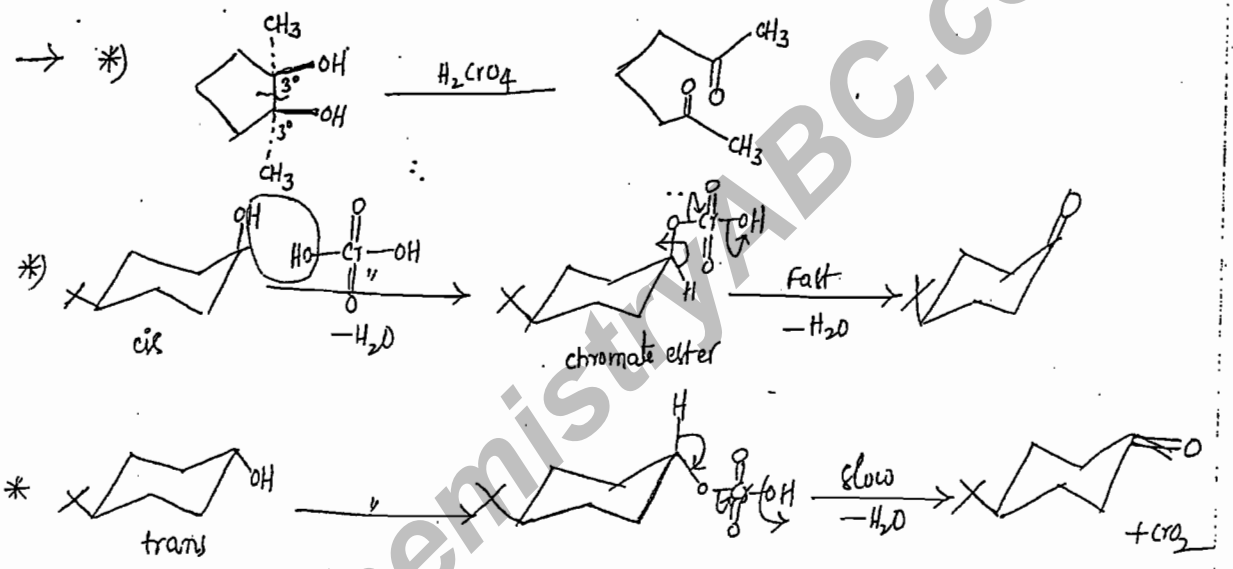

→ chromate esters at G.S. sterically crowded, to get relief from crowding, undergo fast oxidn (steric assistance) in the case of 3°.

→ In trans, sterically free, slow oxidn.

Jones oxidations:— (CrO_3 + aq. H_2SO_4 + Acetone)

* presence of acetone brings about the changes in oxidations.
* over oxidations reduced. i.e, acid formations even from 1°-alcohols will be prevented.

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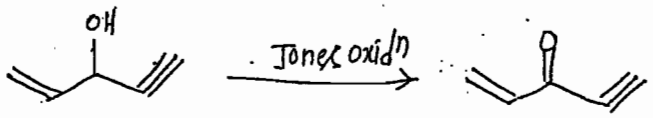
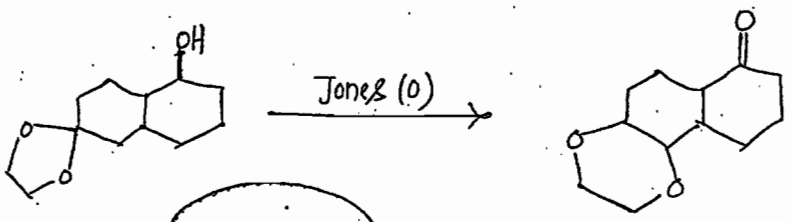
* unsaturated groups (db/tb) uneffected.

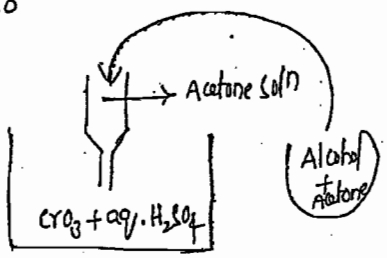
→ 

∴ can be used for oxidn of allylic, benzylic, propargylic alcohols.

→ In general, acid labile gps uneffected.

But there few examples in which acid labile gps effected.

→ 

→ 

* experiment is carried out by titrating alcoholic soln with CrO_3, aq. H_2SO_4 soln.

* LIMITATION :-

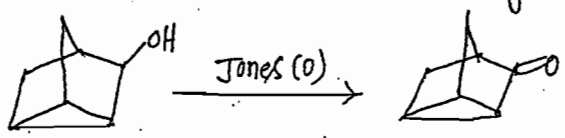
1) 1:1 ratio of CrO_3 - aq. H_2SO_4 and alcoholic soln must be taken.

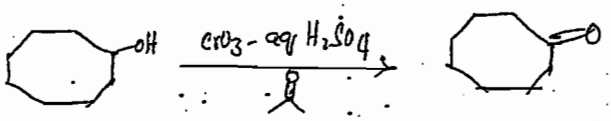
2) * If not maintains stoichiometric ratio, over oxidn products produced.

2) Acid-labile groups may get effected.

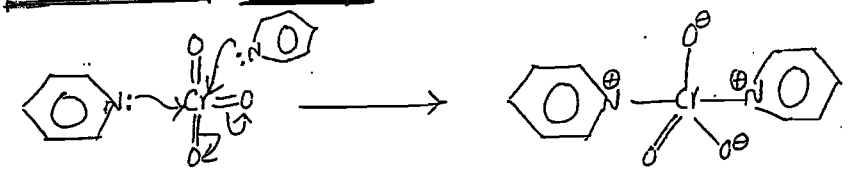
3) Byproducts toxic.

4) Random combination of components may lead to explosion.

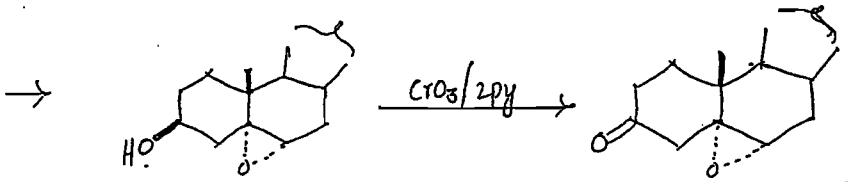
eg:- 



* Sarett's oxidn : CrO_3. 2py (Basic)



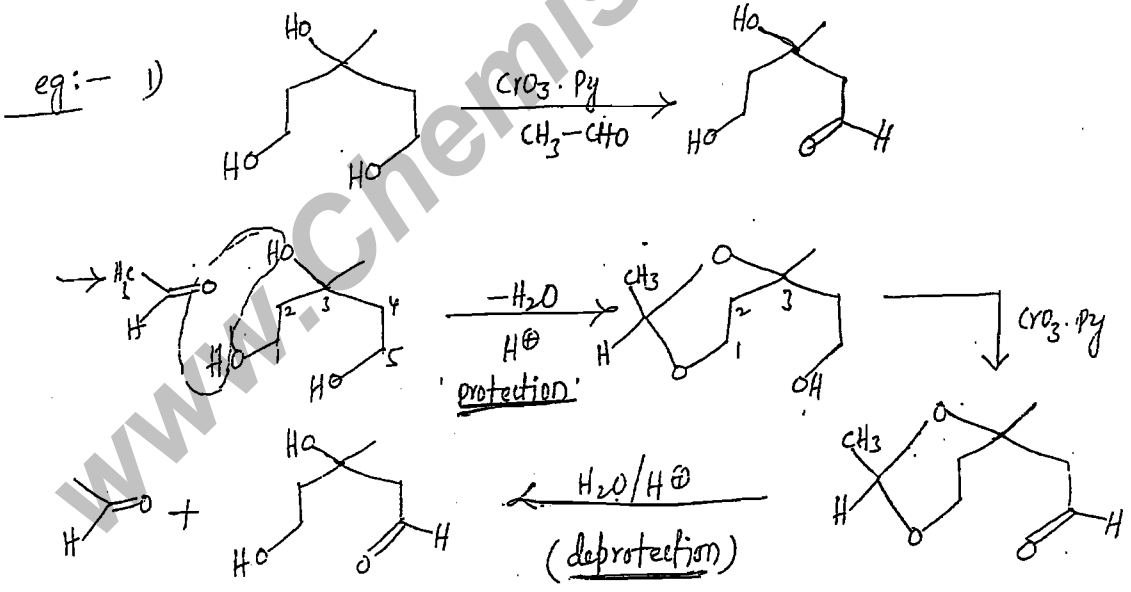
* oxidises 1°, 2°-alcohols
* no over oxidn products
* no effect of unsaturation (db/tb)
* acid labile gpf uneffected.

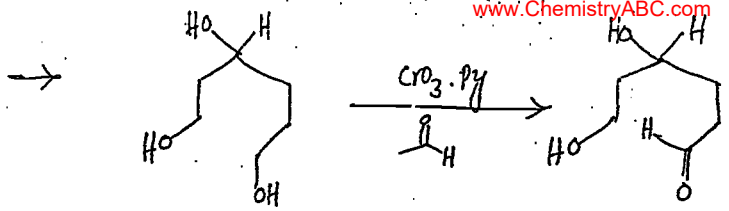


* Limitations :—

1) By product toxic
2) After oxidn, isolating carbonyl compd in pure form from pyridine difficult.
3) little expensive.

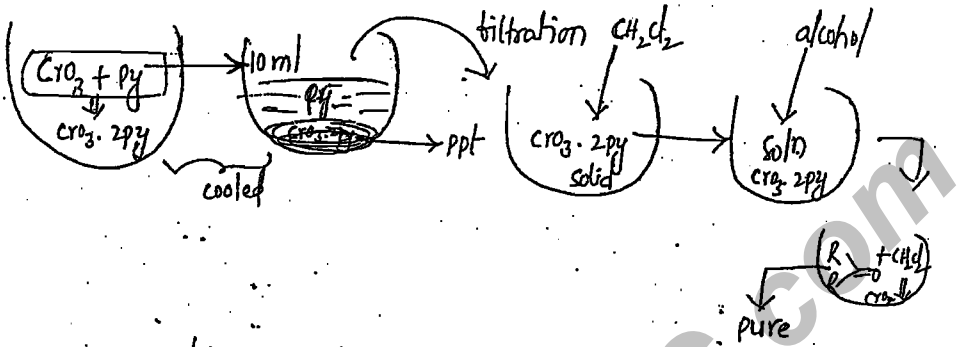
eg:— 1)





→ Collins oxidations :— ($CrO_3 - py + CH_2Cl_2$)

(DCM)



→ presence of DCM modifies oxidation

→ After oxidations, removal of DCM easier.

∴ carbonyl compd in pure form – easy to isolate. ~~no overoxid~~

→ No over oxidatns, unsat. frs unaffected.

→ Acid-labile gps unaffected.

* Newer Reagents :— EJ Corey & [redacted] etal

PCC, PDC → pyridinium dichromate.

↓

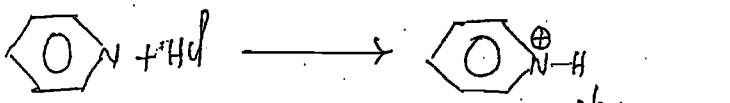
pyridinium chloro chromate

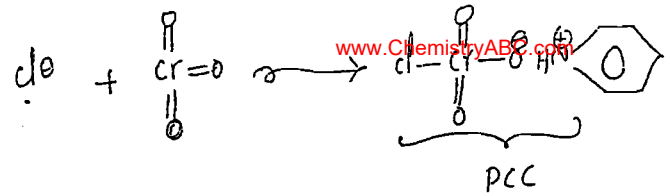
PCC : $CrO_3 + py + aq.\ HCl$

↓

aq. HCl

→ addn of $CrO_3 \cdot py$ to aq. HCl produces PCC.

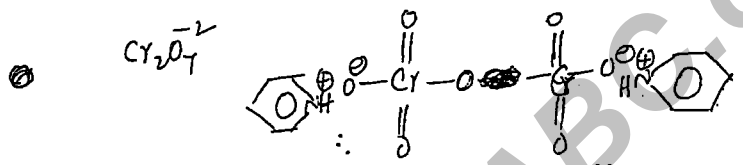
→  pyridinium ion



PCC

* Easy to carry out the experiment.
* No over oxidations.
* Unsat. gps db/tb uneffected.
* High yields.
* Acidic medium oxidn ; Acid-labile gp may get effected.
* Byproducts CrO_2 etc toxic.

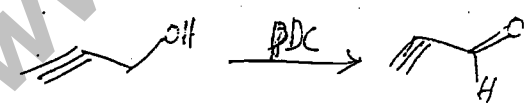
PDC :-

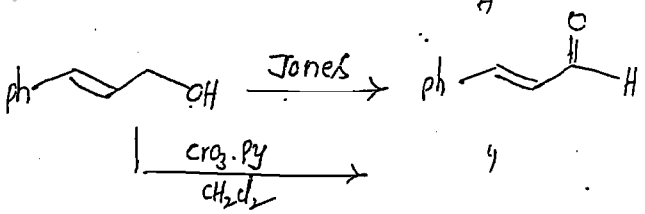


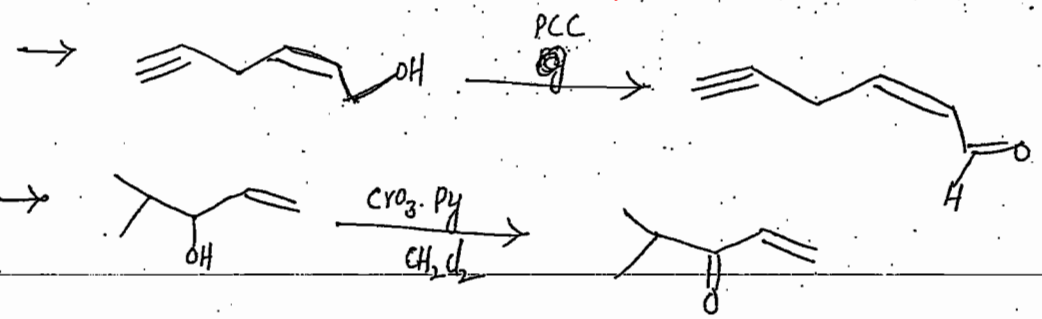
PDC

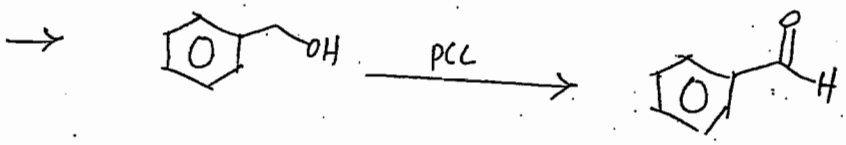
→ not acidic medium oxidation.
→ no over oxidations
→ excellent reagent for oxidn of allylic / benzylic alcohols.
→ No effect on acid labile groups.
→ Unsaturation uneffected.
→ Easy to handle in laboratory.
→ high % of yields.
→ biproducts are toxic.

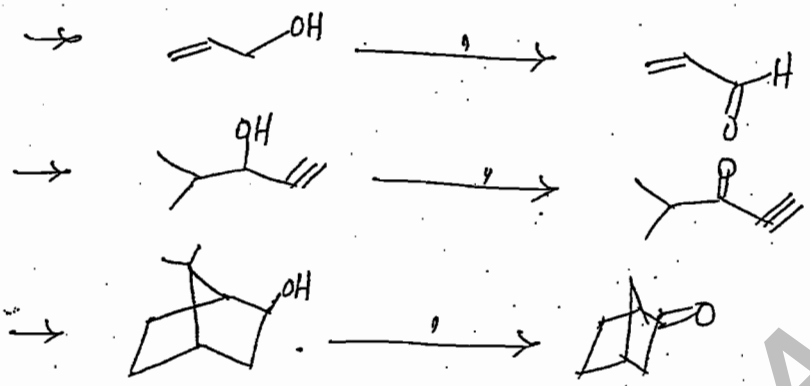
eg:

→ 

→ 







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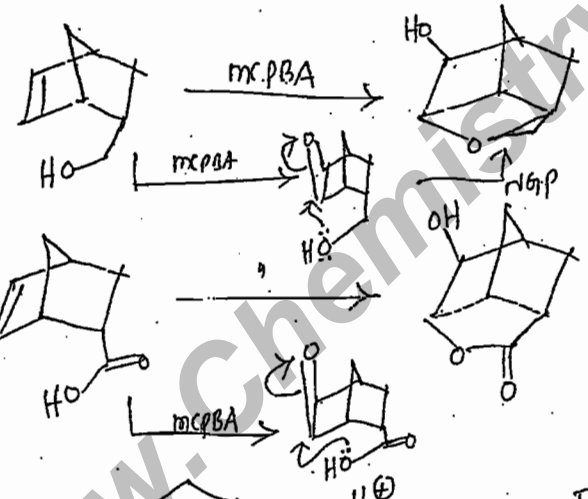

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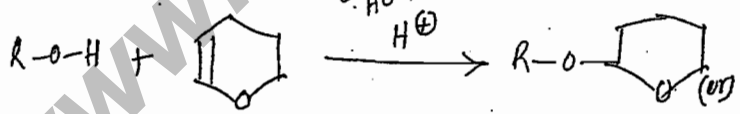
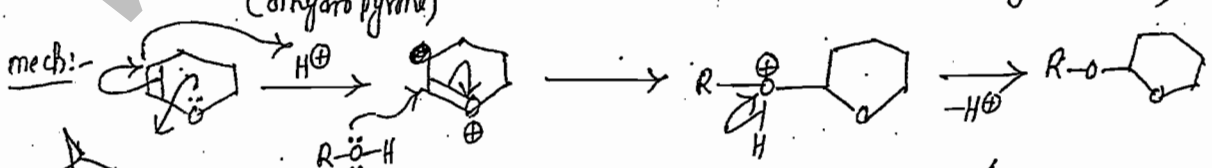
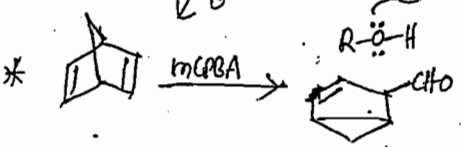


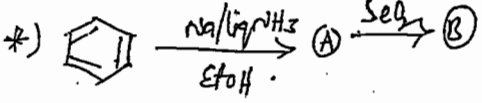
(dihydro pyrone)

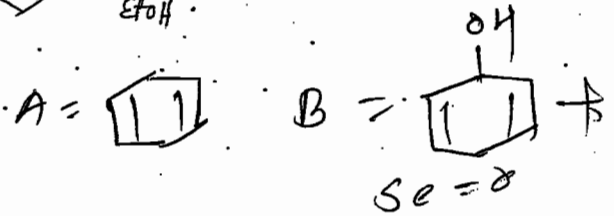
mech ?

(tetrahydro pyrone)









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or see

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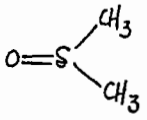
* DMSO – oxidants :–

① DMSO – Dimethyl Sulphoxide ;

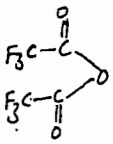


→ DMSO alone cannot oxidise alcohols, requires activators.

a) alcohols $\xrightarrow[\text{activator}]{\text{DMSO +}}$ C.C.

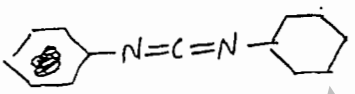
I) DMSO + DCC (or) DCCD + Acid medium (H_3PO_4, Cl_2CHCO_2H) ; Moffat's oxidation

II) DMSO + Ac_2O

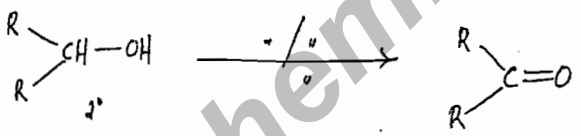
III) DMSO +  (or) $[cod]_2$ + triethyl amine ; V.IMP swern oxidations.

I) DMSO + DCC/DCCD + H_3PO_4 / Cl_2CHCO_2H ; Moffat's oxidn :

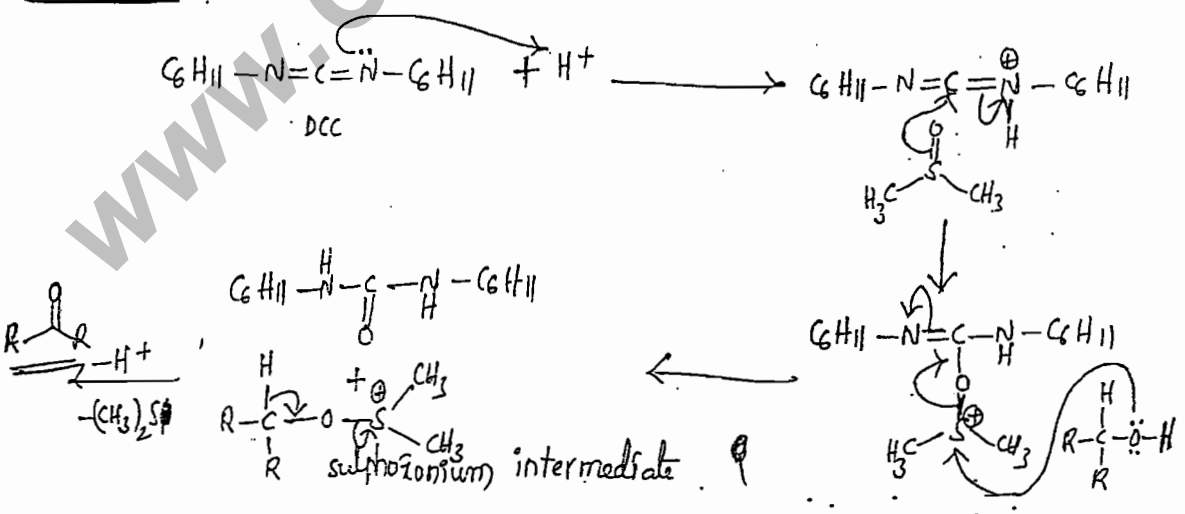
⇒ DCC (or) DCCD : Dicyclohexyl Carbodiimide.

 (or) $C_6H_{11}-N=C=N-C_6H_{11}$

→ $R-CH_2-OH \xrightarrow[H^\oplus]{DMSO/DCC} R-C(=O)-H$ (1°)

→  (2°)

Mechanism :–



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byproduct : N, N'-dicyclohexyl urea.

LIMITATIONS :—

* After oxidation, isolating carbonyl compd in pure form not easier, because byproduct N,N'-dicyclohexyl urea, removal is difficult.

*) DCC is weak base, for protonation, large quantity should be taken. Rean becomes expensive or costlier.

* No over oxidation product
* Unsaturations unaffected.
* Acid-labile groups unaffected.

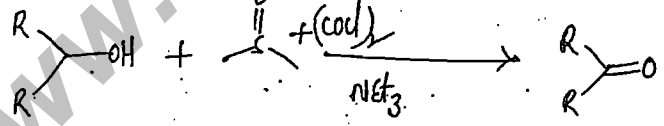
II DMSO + Ac_2O :—

→ usage is less common.

v.IMP
III → Swern oxidations : (Industrially imp for oxidn of 2° alcohols)

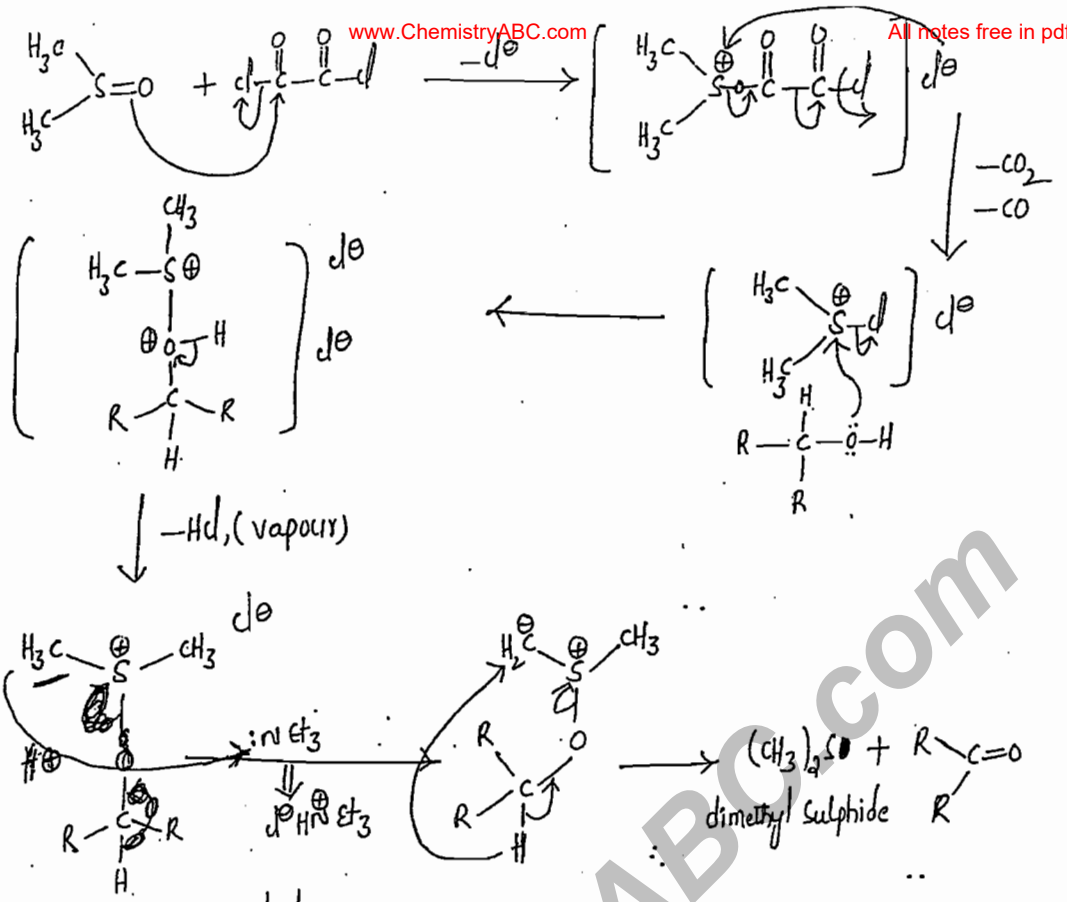
⇒ Industrially viable.

→ DMSO + $F_3C-C(=O)-O-C(=O)-CF_3$ (or) $(COCl)_2$ + NEt_3 } Swern-reagent.
oxalyl chloride

→ 

v.IMP *
Mechanism :— → oxalyl chloride widely used activator for DMSO in swern oxidn.

$O=C(Cl)-C(Cl)=O$ (or) $[COCl]_2$
oxalyl chloride

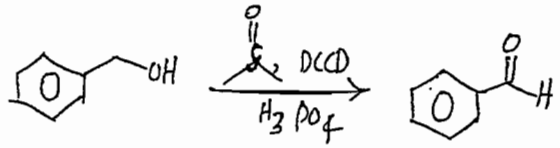


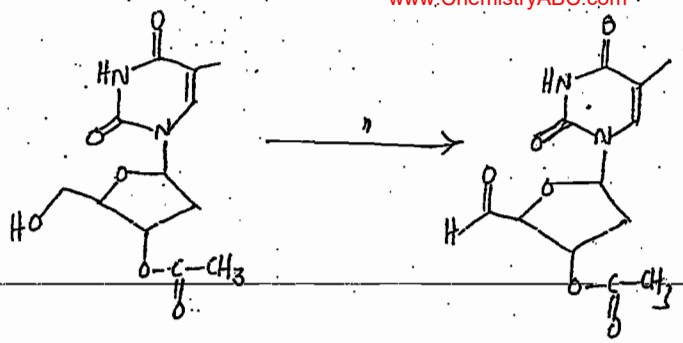
Limitations :—

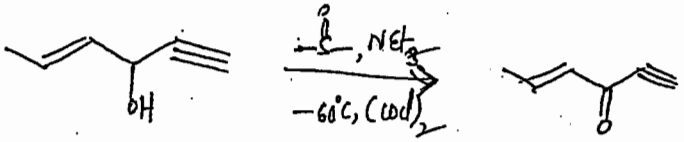
→ Rean has to be performed at lower temp. approximately −60°C, at higher temp. rean explosive.

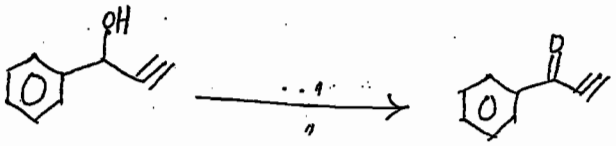
* Removal of biproduct is simple in Swern oxidations.
* High % yields of the products.
* No over oxidations ; unsaturations unaffected ;
* Acid labile gps unaffected.

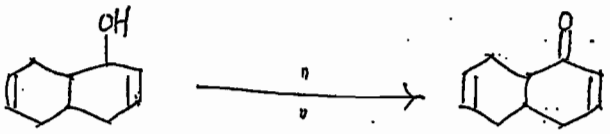
* Some examples for DMSO oxidations :—

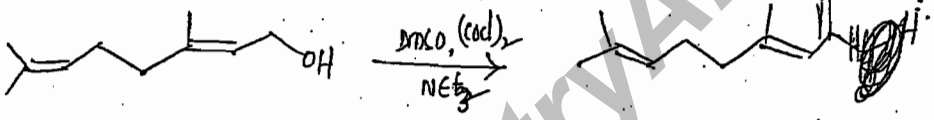
1) 

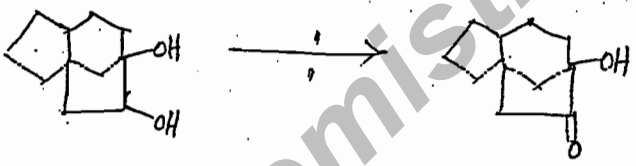
2) 

3) 

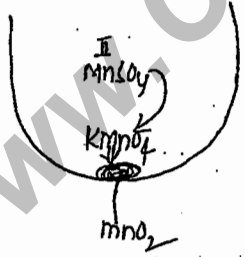
4) 

5) 

6) 

7) 

* Manganese Dioxide :— MnO_2



→ Dissolving of $MnSO_4$ in $KMnO_4$, pptate MnO_2.

$MnO_2 \xrightarrow{Heat} MnO_2$ (pure)
(activated MnO_2)

· initially prepared MnO_2 contaminated with volatile impurities & moisture.

∴ MnO_2 subjected to heating to remove impurities and moisture resulting pure MnO_2 called "activated MnO_2".

* $O=\overset{IV}{Mn}=O$, solid, mild-oxidizing agent ; neutral oxidations.

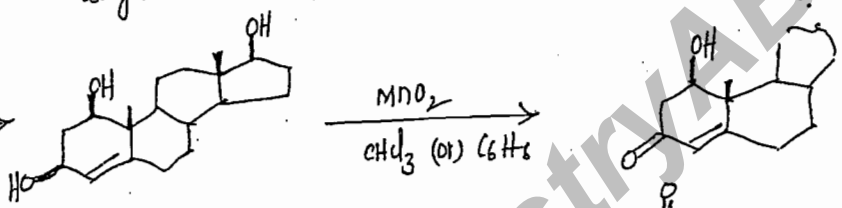
* Solvents : C_6H_6, CH_2Cl_2, $CHCl_3$, alcohols, ethers

* Applications :-

→ oxidn of 1°/2°/allylic/benzylic alcohols.

→ If molecule having 1°/2°/allylic/benzylic alcohols, selectively oxidises "allylic & benzylic alcohols".

→ benzylic, allylic } alcohols > 1°/2° alcohols

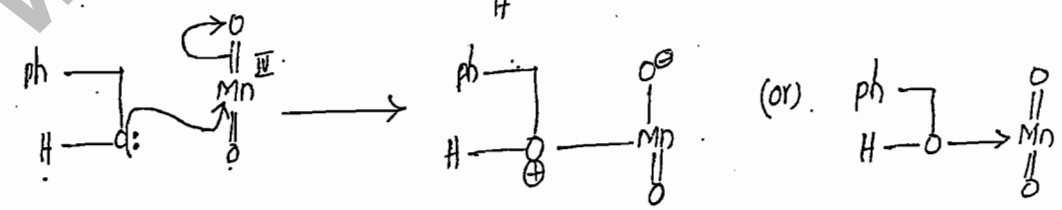
→ 

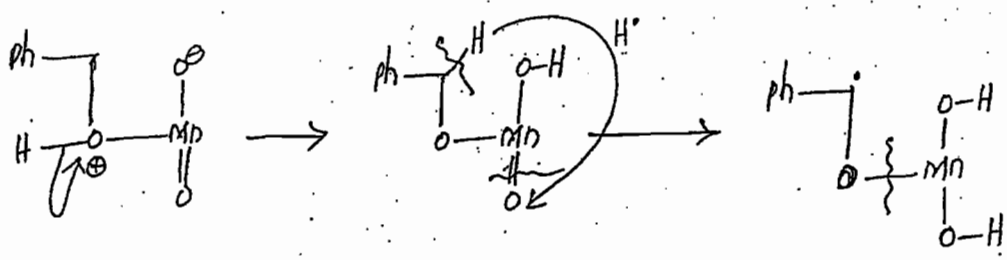
→ 

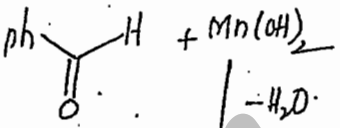
* Mechanism :- V.IMP (Not for NET)

→ ADSORPTION of alcohol on MnO_2 (solid)

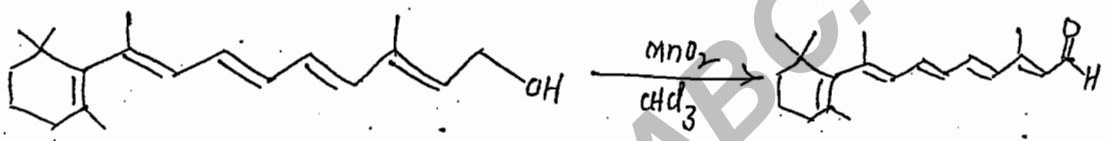
→ $ph-CH_2-OH \xrightarrow{MnO_2} ph-\underset{H}{\overset{O}{C}}$

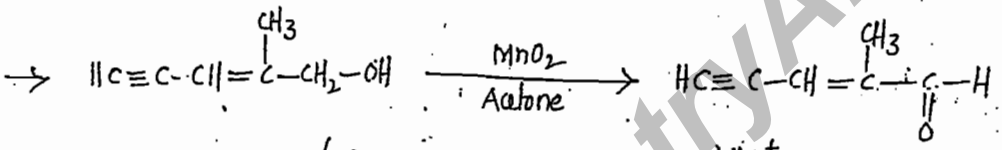


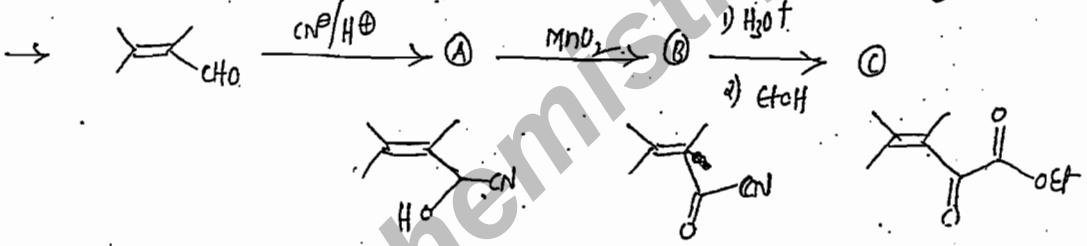




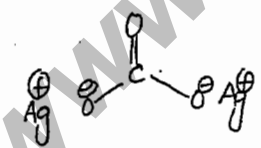
* Some more examples :—







* Silver Carbonate (Ag_2CO_3) :—



→ oxidation properties similar to MnO_2.

→ mild oxidising agent

→ Neutral medium oxidations

→ Solvent ; C_6H_6, CH_2Cl_2, $CHCl_3$

Applications :-

→ oxidises 1°/2°/allylic/benzylic alcohols into carbonyl compounds.

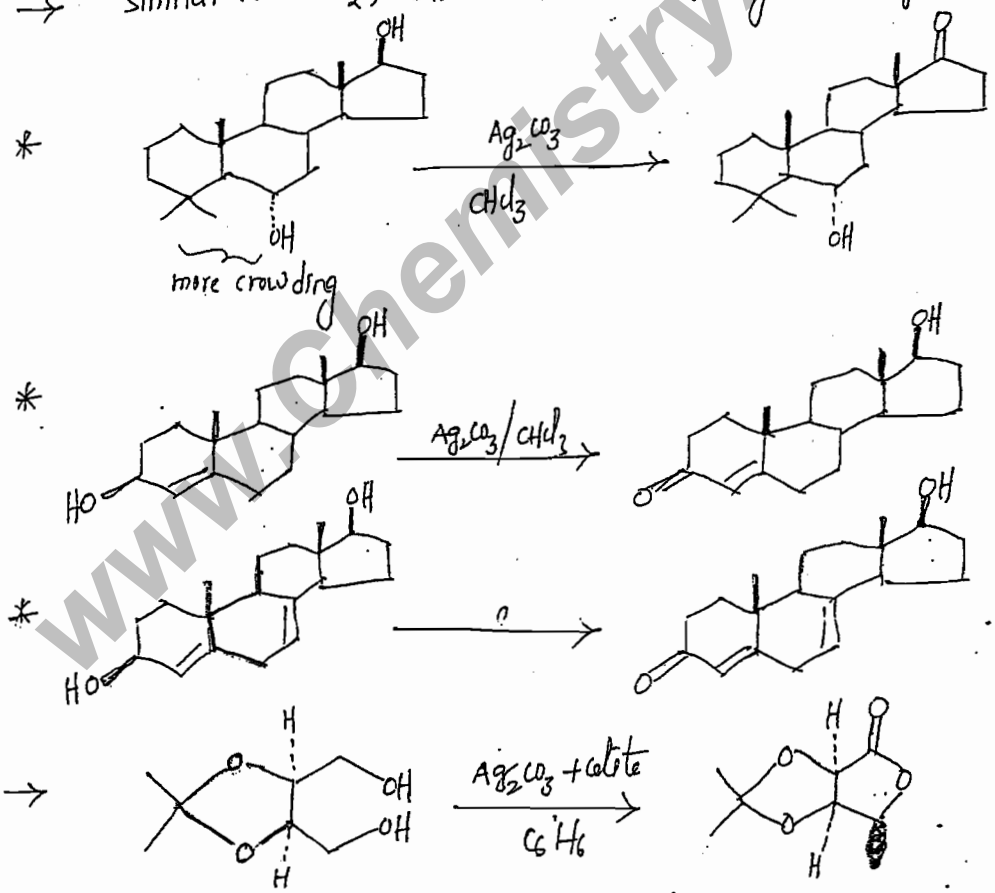
Ag_2CO_3 oxidn in presence of celite (sand type material) called "Fetizon's oxidations".

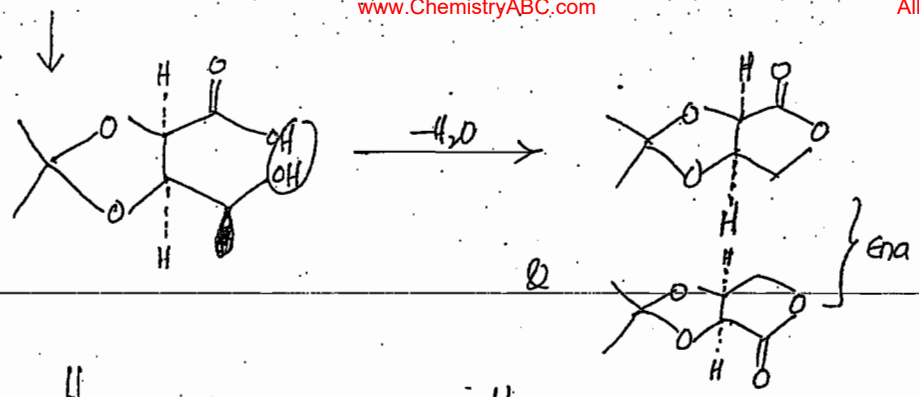
→ In 1° & 2° alcohols, Fetizon's oxidn selectively oxidises 2° alcohol.

→ 1,4/1,5 diols oxidises into cyclic esters.

→ In a molecule, hindered / unhindered alcoholic gps present, selectively oxidises unhindered alcohols..

→ Similar to MnO_2, selective in oxidn of allylic, benzylic alcohols.





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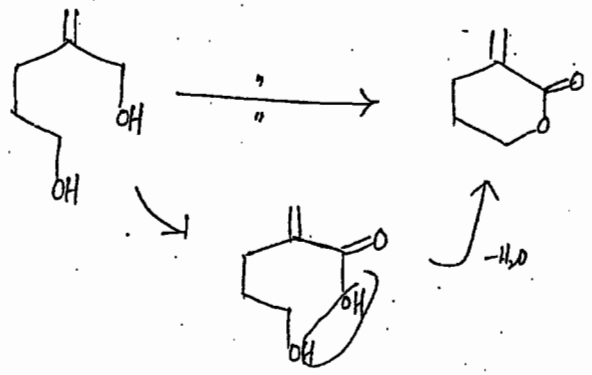

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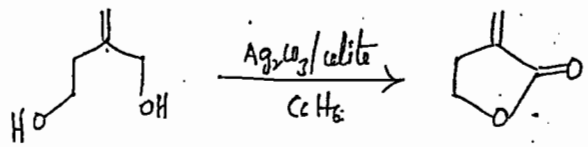

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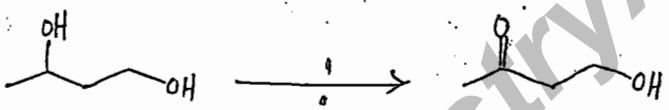
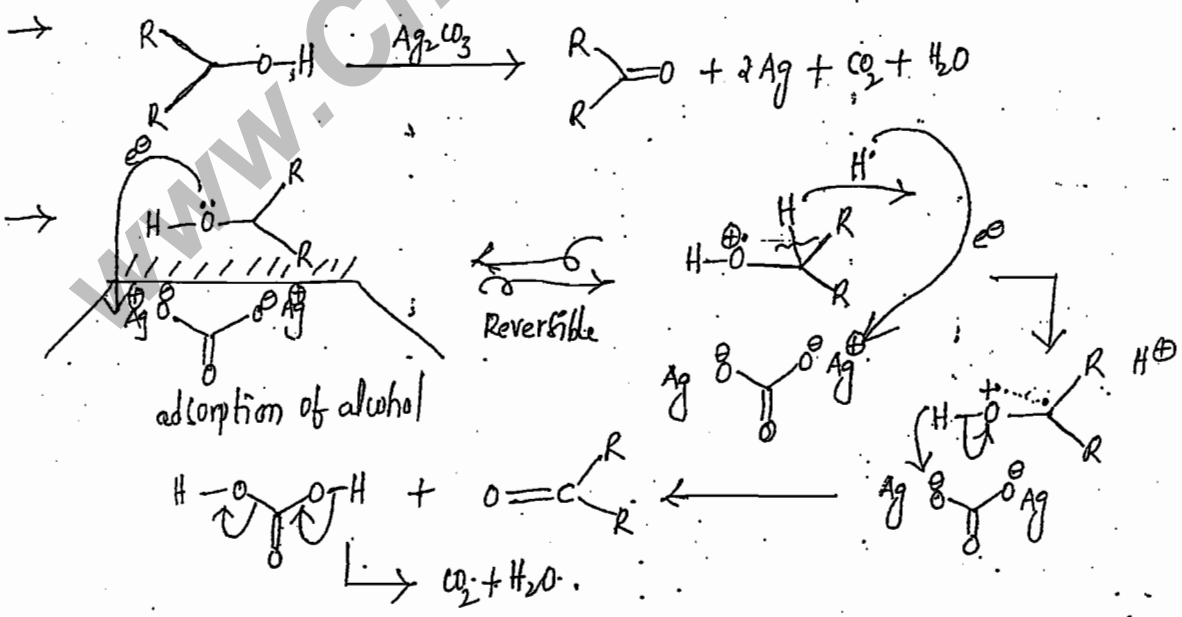
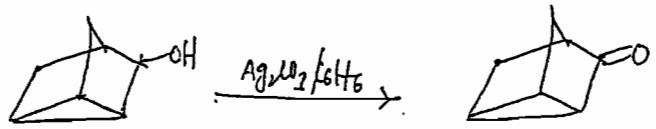


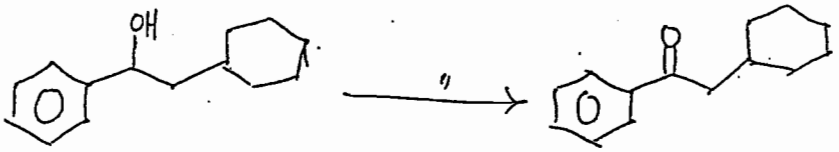
Mechanism :— v.imp (not for NET)

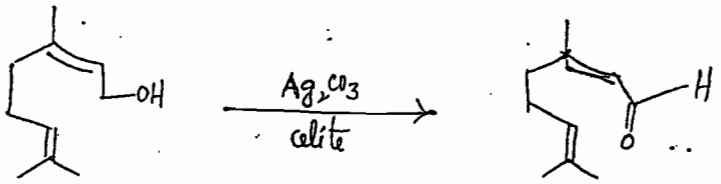
→ alcohol gets adsorbed on Ag_2CO_3. Then undergo oxidn with $e^\ominus$ transfer.



* Some more examples :-

1) 

2) 

3) 

→ oppenauer-oxidations; reversible of MPV-reductions.

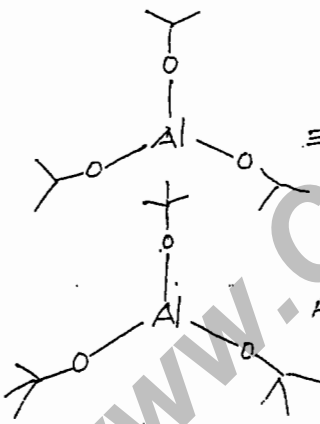
Applications :-

→ oxidises alcohols into carbonyl compounds.

→ Reagent :- Aluminium alkoxide

eg : AIP : Aluminium isopropoxide → "common"

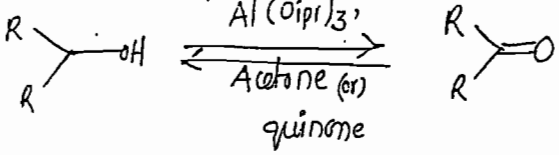
ATB : " tert. butoxide



$\equiv Al(OiPr)_3$ (or) $Al(O_iC_3H_7)_3$

ATB : $Al(OtBu)_3$ (or) $Al(O_tC_4H_9)_3$

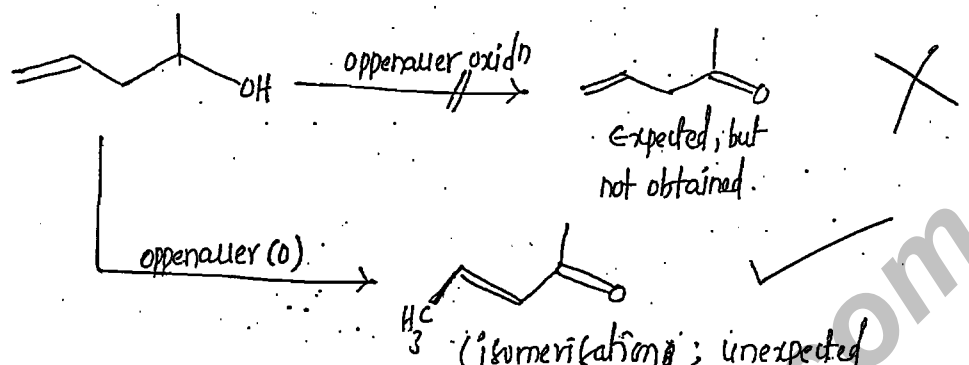
Solvent : Benzene

Reagent :- 

LIMITATIONS :—

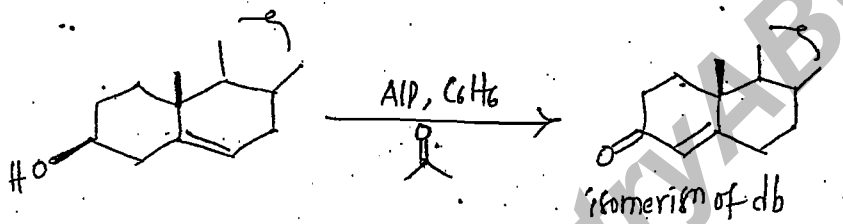
1) Because of reversibility, complete oxidn of alcohol (100%) not possible.

2) Isomerisation of double bonds may takes place.



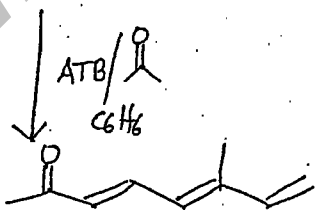
(isomerisation ; unexpected of db taken place)

→ oppenauer oxidn also common in steroidal chem.



Mechanism :—

*) $CH_3-CH(OH)-CH=CH-CH=C(CH_3)-CH=CH_2$



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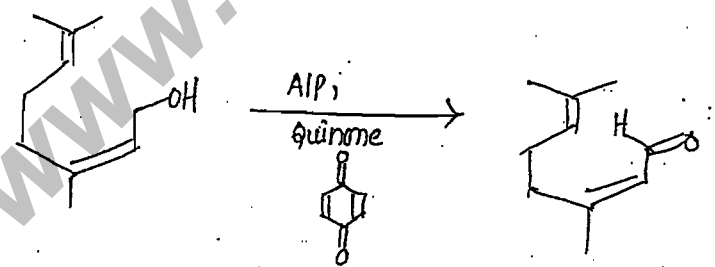

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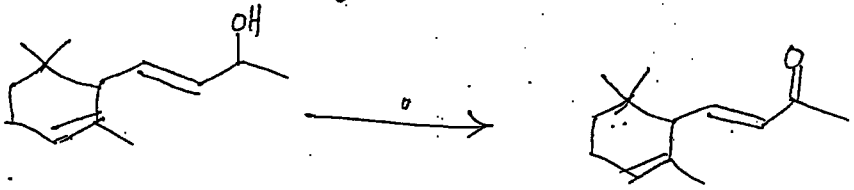
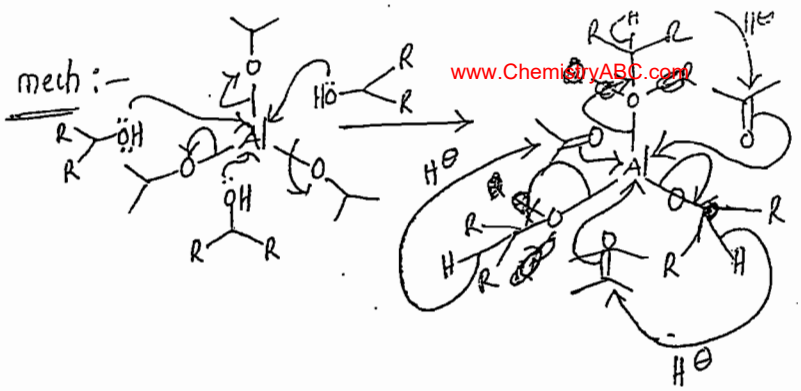
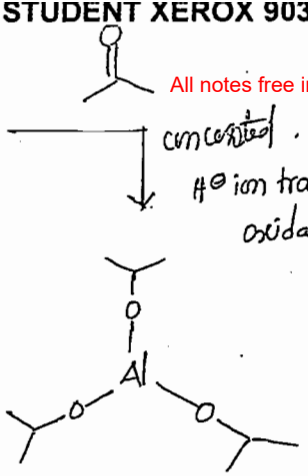
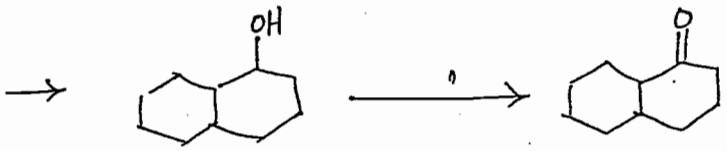
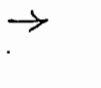






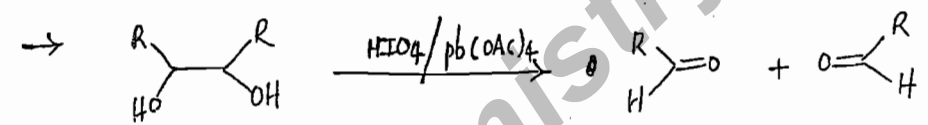
+ 3 eqts of $R{=}O{-}R$





11/05/08

* OXIDATION OF 1,2-DIOLS INTO CARBONYL COMPOUNDS ; GLYCOL-CLEAVAGE



oxidizing agent : HIO_4, $Pb(OAc)_4$.

→ periodic acid HIO_4 (meta per-iodic acid) :-

→ $HIO_4 + 2H_2O \longrightarrow HIO_4 \cdot 2H_2O$ (or) H_5IO_6 . ; ortho per-iodic acid.
(same)

→ In aq. medium HIO_4 exist in ionic form.

$HIO_4 \xrightarrow{H_2O} H^+ + IO_4^-$

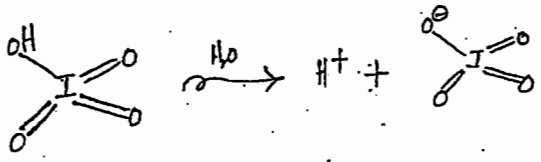
$H_5IO_6 \longrightarrow H^+ + H_4IO_6^-$

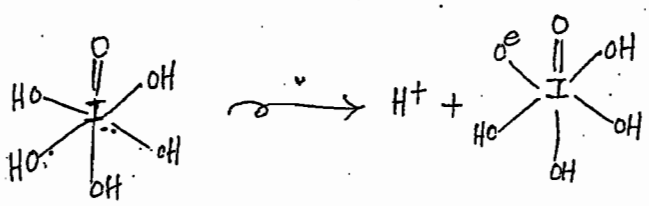
→ Not only HIO_4, even salts of periodic acid also used as oxidizing agents for glycol cleavages.

$NaIO_4$ ⟶ Sod. meta periodate (or) Sodium periodate.

KIO_4 ⟶ pot. meta " (or) pot. "

→ a these salts also exist in ionic form. $Na^+ IO_4^-$.

→ 



→ Solvents :-

→ Readily soluble in water

∴ HIO_4 is the best reagent for the cleavage of glycols of water-soluble org. compds.

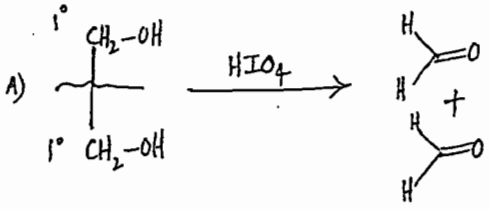
eg:- Carbohydrates.

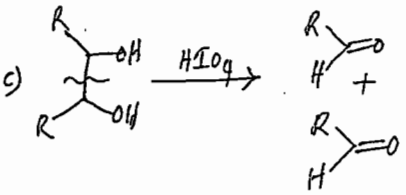
∴ HIO_4 widely used in Carbohydrate chemistry.

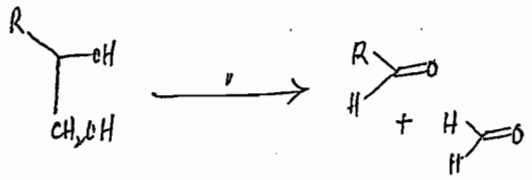
* Applications :-

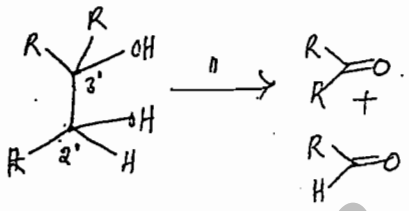
1) Glycols / 1,2-diols cleavage
2) cleavage of α-amino alcohols.
3) 1,2-diamino cleavages
4) α-hydroxy carbonyl cleavages
5) α-amino carbonyl cleavages.

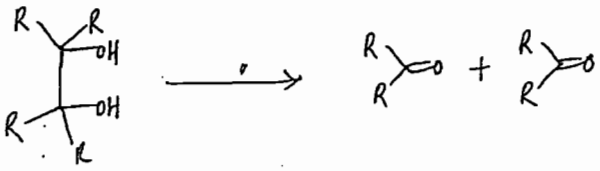
I) Glycol - cleavage :—

A) 

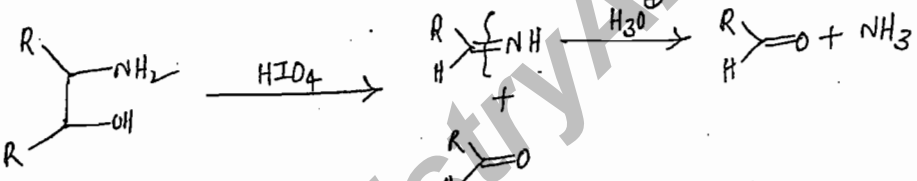
C) 

B) 

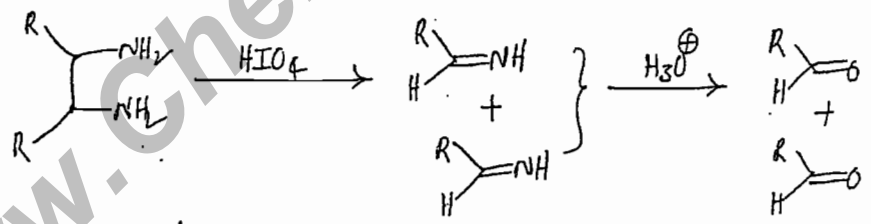
D) 

E) 

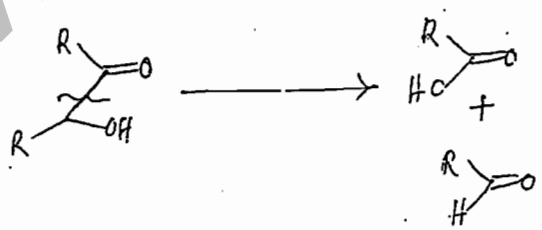
II) α-amino alcohol



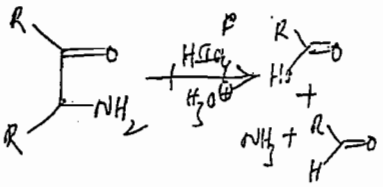
III) * 1,2-diamino cleavage :—



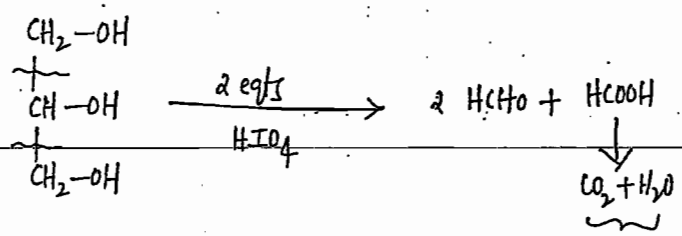
IV) α-hydroxy carbonyl :

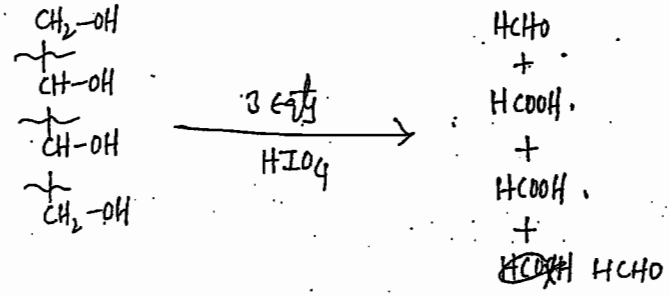


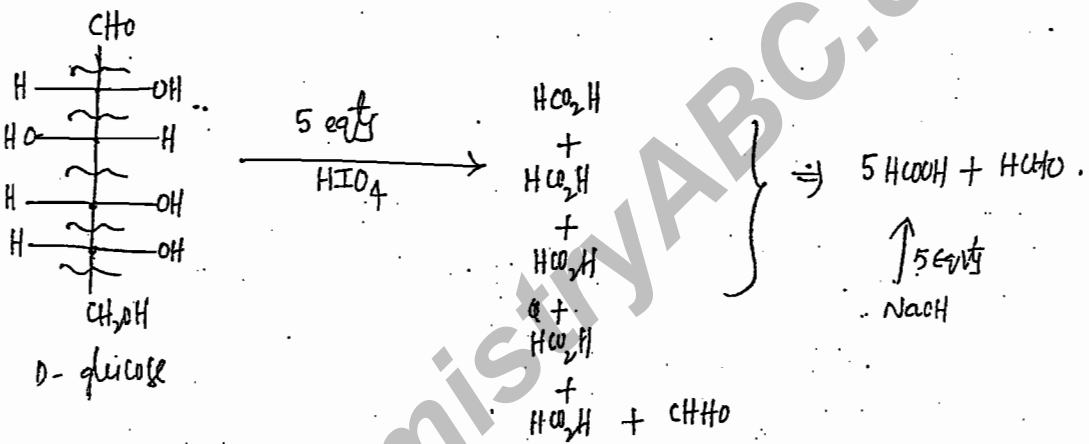
V) α-amino carbonyl compd

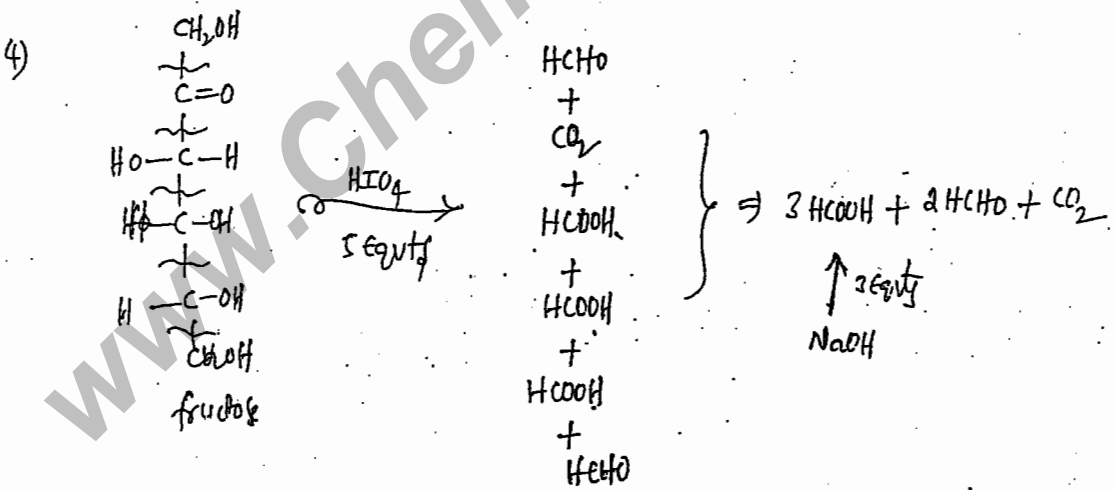


* cleavages in polyhydroxy compounds :—

1) 

2) 

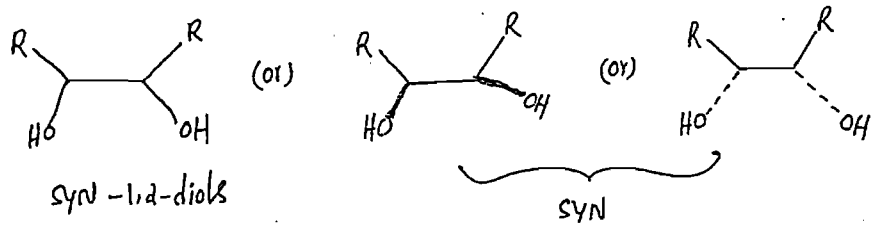
3) 

4) 

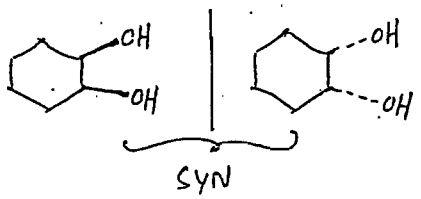
→ 5 eqts of HCO_2H from glucose, 3 eqts of HCO_2H from from fructose.

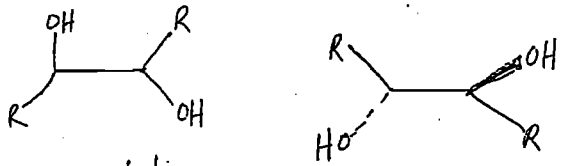
→ " NaOH ~~for~~ required for glucose, 3 eqts of NaOH required to neutralise formic acid formed from fructose.

Mechanism :— with H_5IO_6 : $H^+ + H_4IO_6^-$

→ 

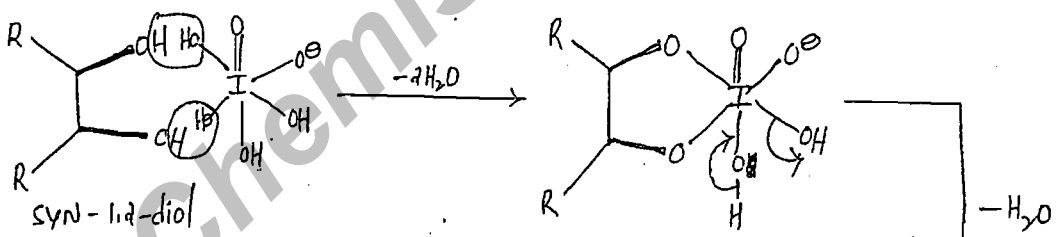
syn-1,2-diols

→ 

→ 

Anti 1,2-diols Anti-1,2-diols Anti

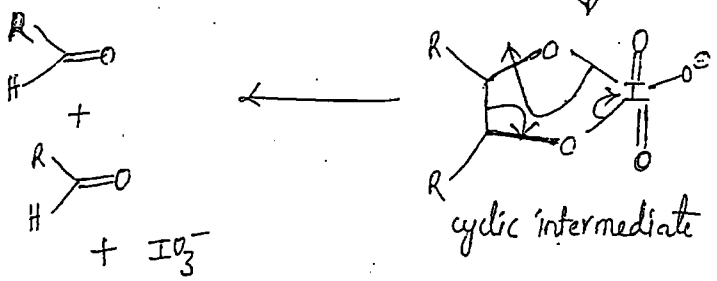
→ HIO_4 fast in oxidn of syn-1,2-diols. Anti-1,2-diols slow or inert in HIO_4 oxidations.

→ 

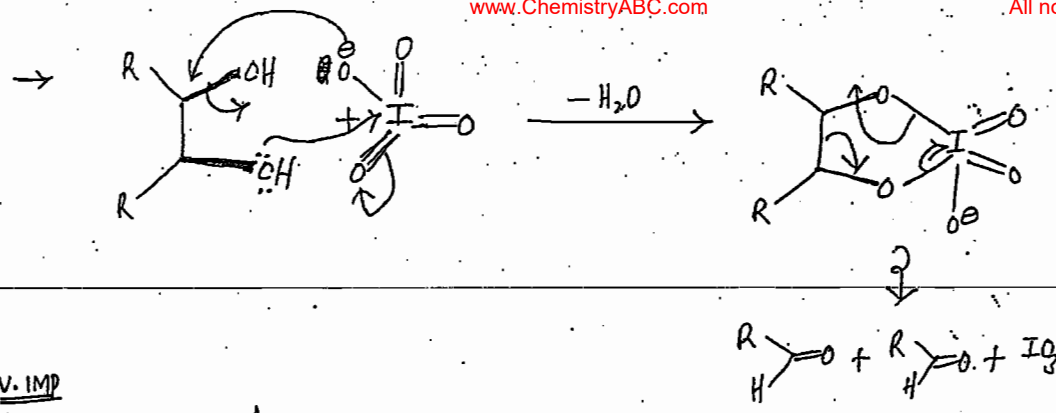
syn-1,2-diol

syn-1,2-diols readily forms cyclic intermediate with per-iodic acids.

∴ fast in oxidations.



cyclic intermediate

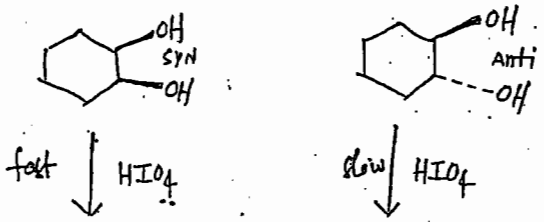


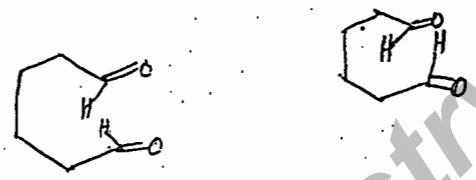
V. IMP

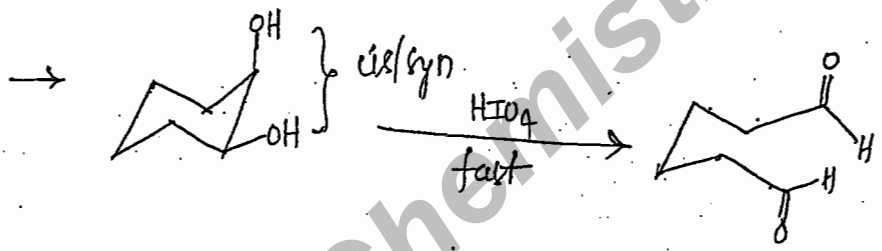
* Stereo chemical aspects :-

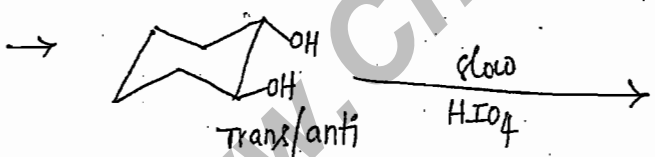
→ SYN is preferred over Anti.

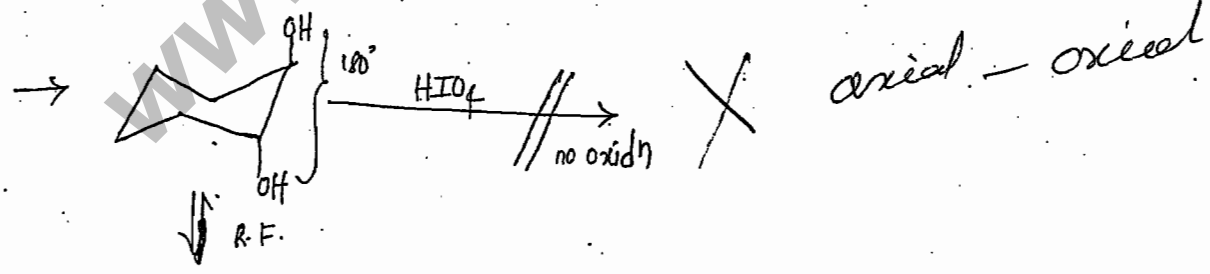
eg :- I)

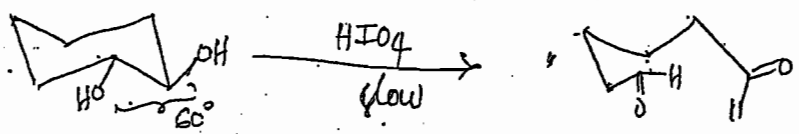










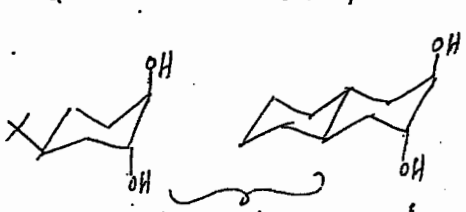


→ 1,2-cis (a,e) diols fast in HIO_4 oxidations.

→ 1,2-diequitorial trans (diol) slow in HIO_4 oxidn.

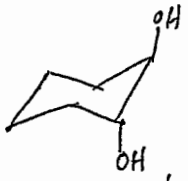
→ 1,2-di axial " " (rigid) inert.

→ 1,2-diaxial trans, flexible diols slow in HIO_4 oxidations.

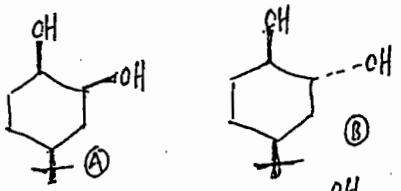
⇒ 

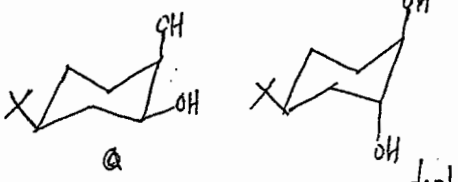
rigid, don't undergo HIO_4 oxidn

cannot undergo R.F.

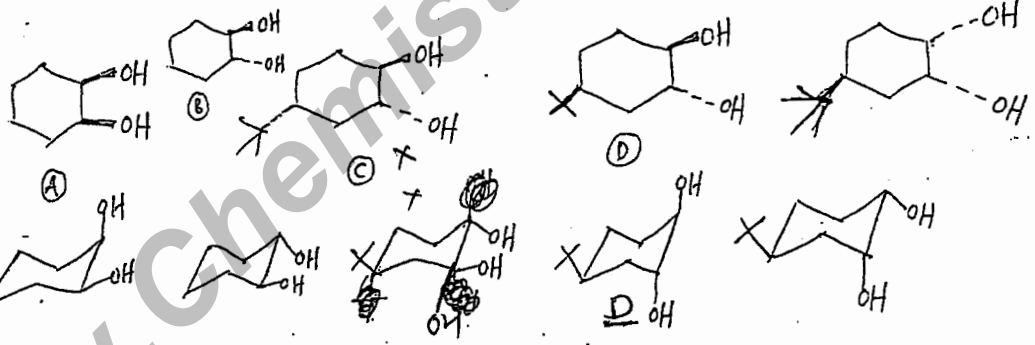


can undergo R.F.

⇒ 

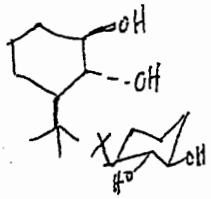


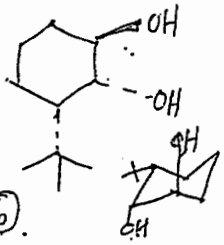
⇒ ⑧ don't undergo HIO_4 oxidn.

⇒ 

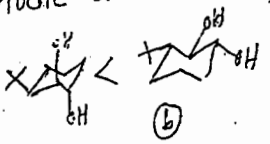
∴ ⑩ cannot undergo HIO_4 oxidn.

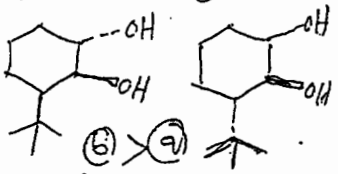
⇒ which of each pair diols cleaved more rapidly by periodic acid. (HIO_4).

I) a) 

b) 

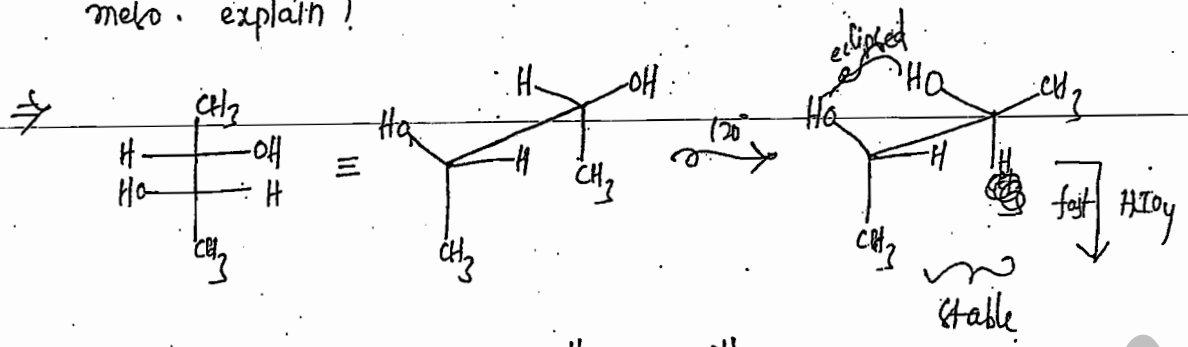
⑧ > ⑥

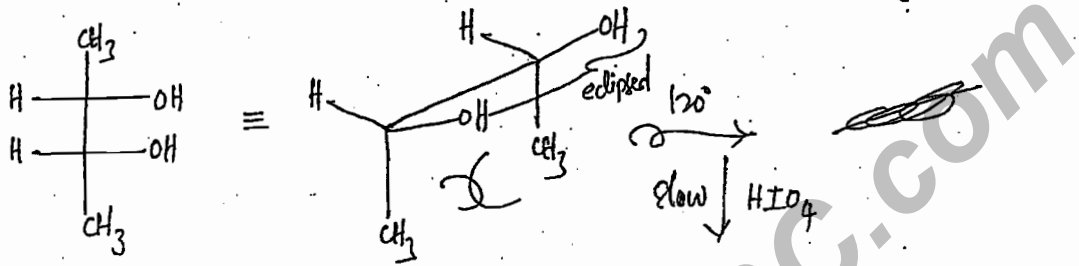
II) a) 



⑥ > ⑨

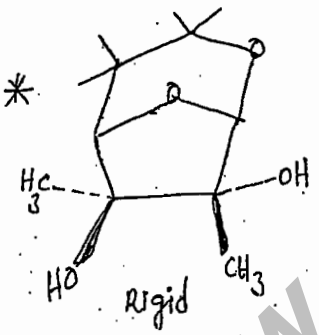
* $CH_3-CH(OH)-CH(OH)-CH_3$, active diastereomer fast in HIO_4 cleavage than meso. explain ?





unstable (CH_3, CH_3 interaction).

→ conformations which are keeping –OH gps eclipsed involve in HIO_4 oxidation, stable eclipsed faster in oxidn.



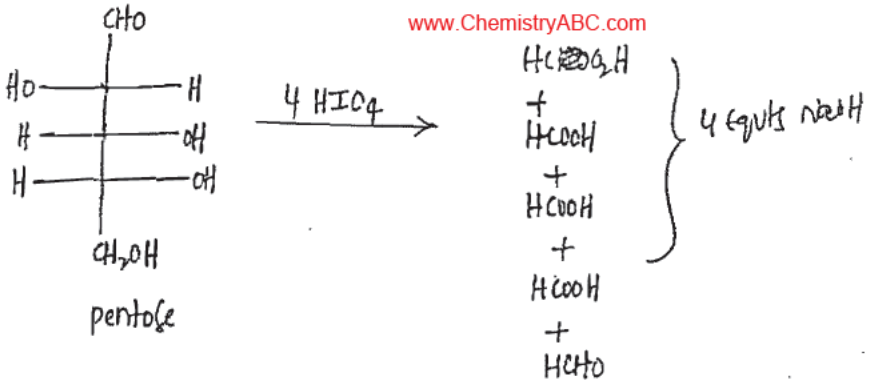
Rigid

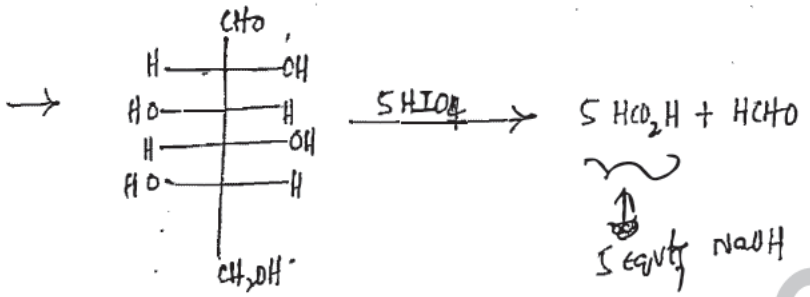
∴ will not undergo oxidn with HIO_4

* Some more applications :—

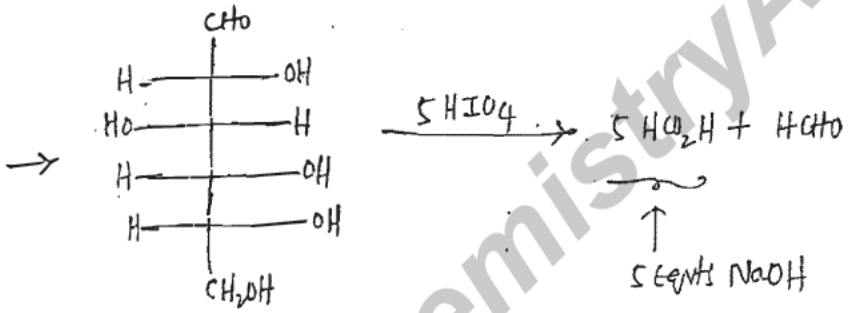
* widely used in carbohydrate chemistry.

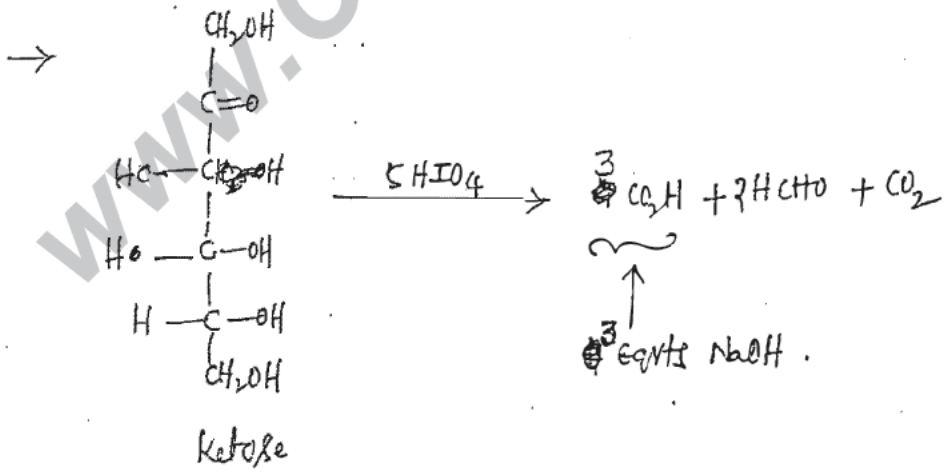
1) To distinguish pentoses, hexoses.





2) To distinguish aldoses/ ketoses :





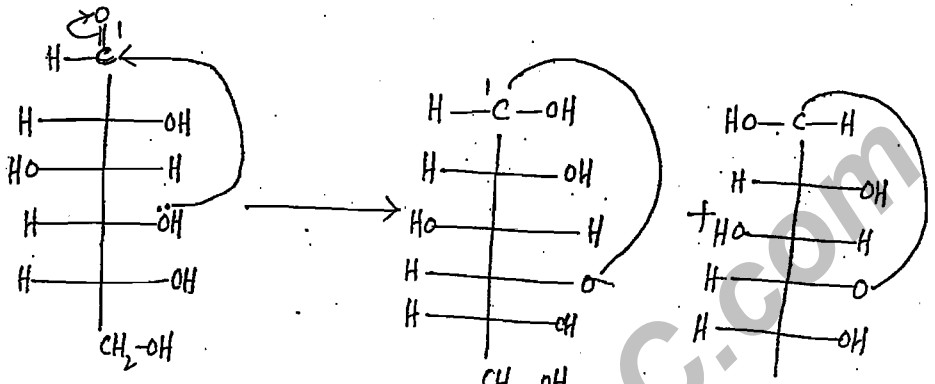
→ Glucose liberates 5 HCO_2H, in titration consumes 5 equivs of NaOH.

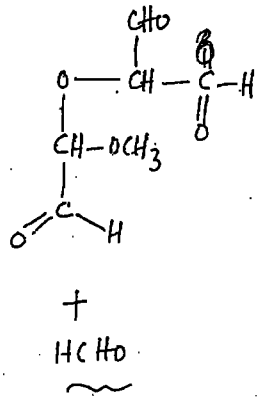
But Fructose " 4 " " " 3 equivs of NaOH.

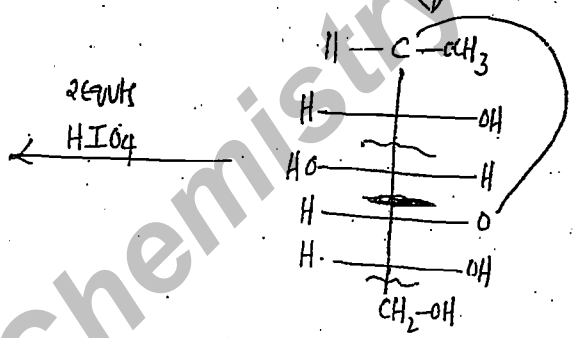
Date : 12/05/08

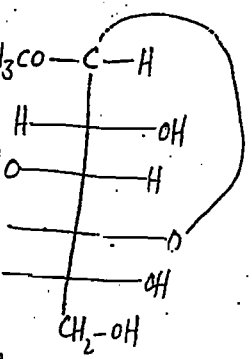
* Determination of Ring size in carbohydrates :-

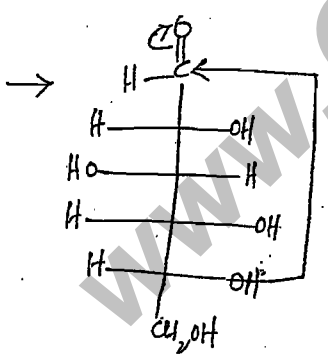
Glucose :-

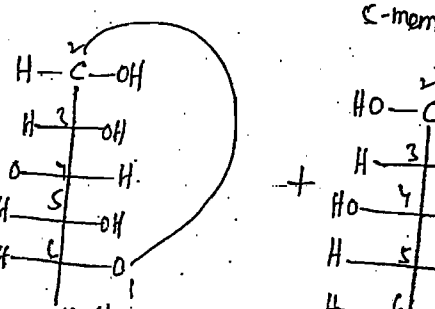


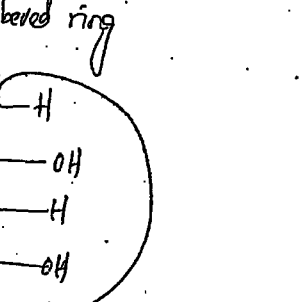


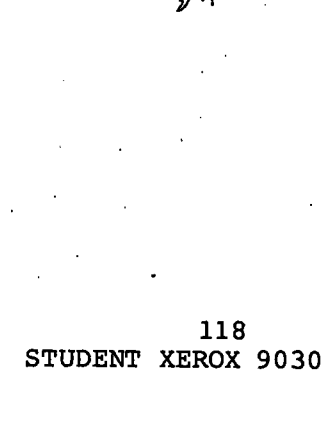


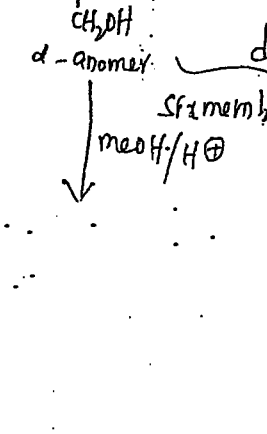


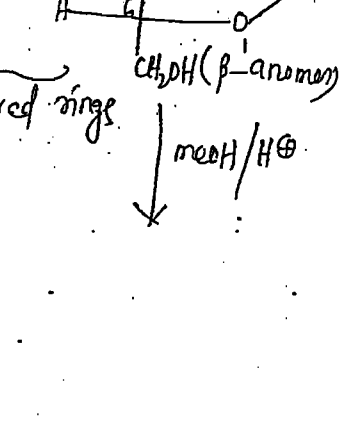


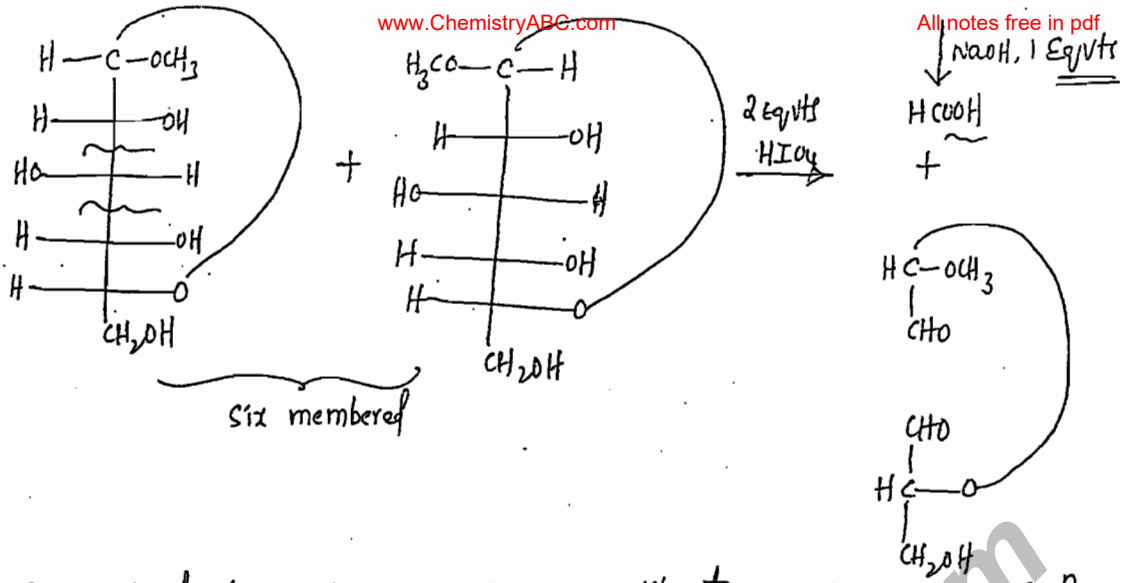






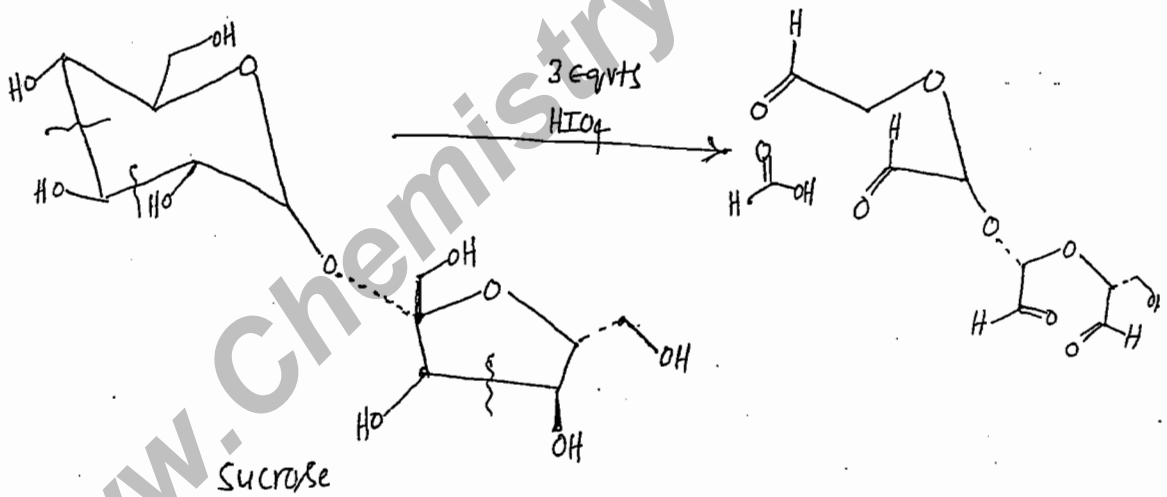






→ Five membered ring consumes 2 eqvts HIO_4, liberate 1 eqvt HCHO, no reaction with NaOH. But Six membered ring consumes 2 eqvts HIO_4, liberate 1 eqvt formic acid(HCO_2H), in titration reacts with 1 eqvt NaOH.

* Sucrose, HIO_4-cleavage :— sucrose = Glucose + fructose



Sucrose

→ consumes 3 eqvts of HIO_4, liberate 1 eqvt HCOOH.

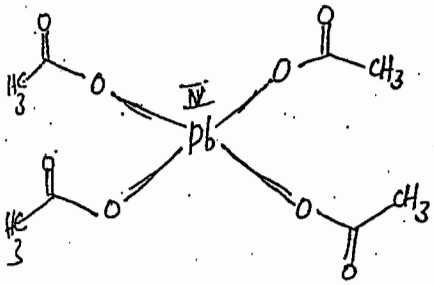
2)

*) LEAD TETRA ACETATE (LTA) :- $Pb(OAc)_4$

→ white crystalline substance.

→ $Pb_3O_4 \xrightarrow[\text{Reflux}]{AcOH} Pb(OAc)_4 + Pb(OAc)_2 + H_2O$

litsar



Solvents :- C_6H_6, AcOH

* LTA soluble in org. solvents, can be used as oxidising agents for oxidn of diols which are soluble in org. solvents.

But HIO_4 soluble only in H_2O, used as oxidising agents for H_2O soluble org. compds only.

* Applications :- 1) glycol cleavages

2) α-hydroxy carbonyl compds' cleavages.

3) α-Keto carboxylic acid

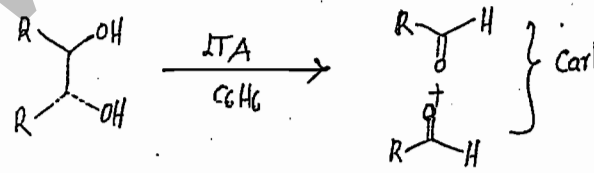
4) 1,2-diamino cleavages

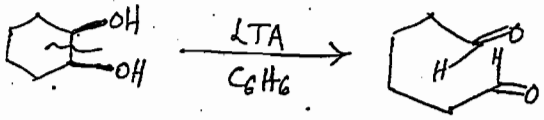
V.Imp 5) Bis-decarboxylation.

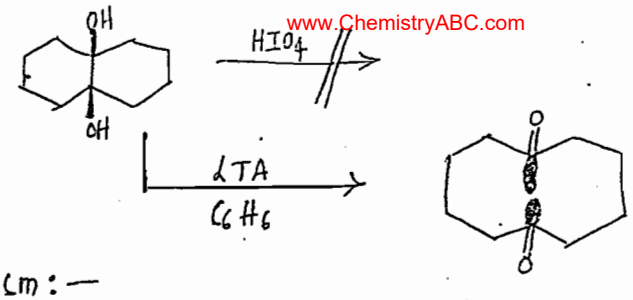
6) Simple alcohols into carbonyl compds

7) As methylating, acetoxylating agent.

1) LTA used for cleavage of 1,2-diol's which are soluble in org. solvents. Carbohydrates insoluble in org. solvents, LTA not useful.

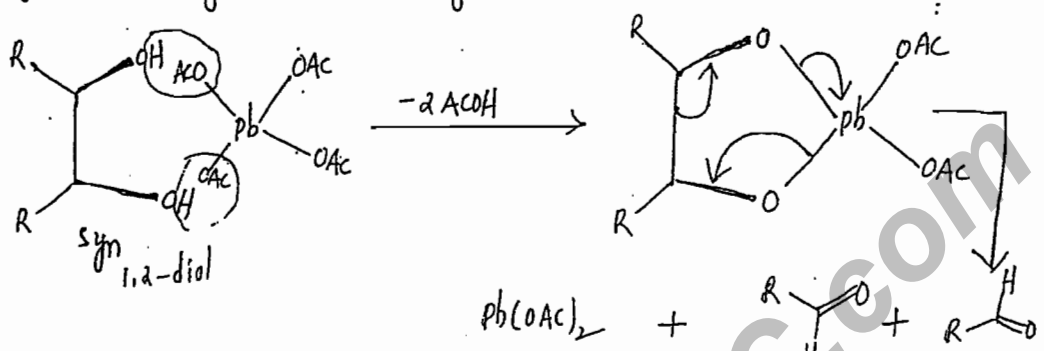




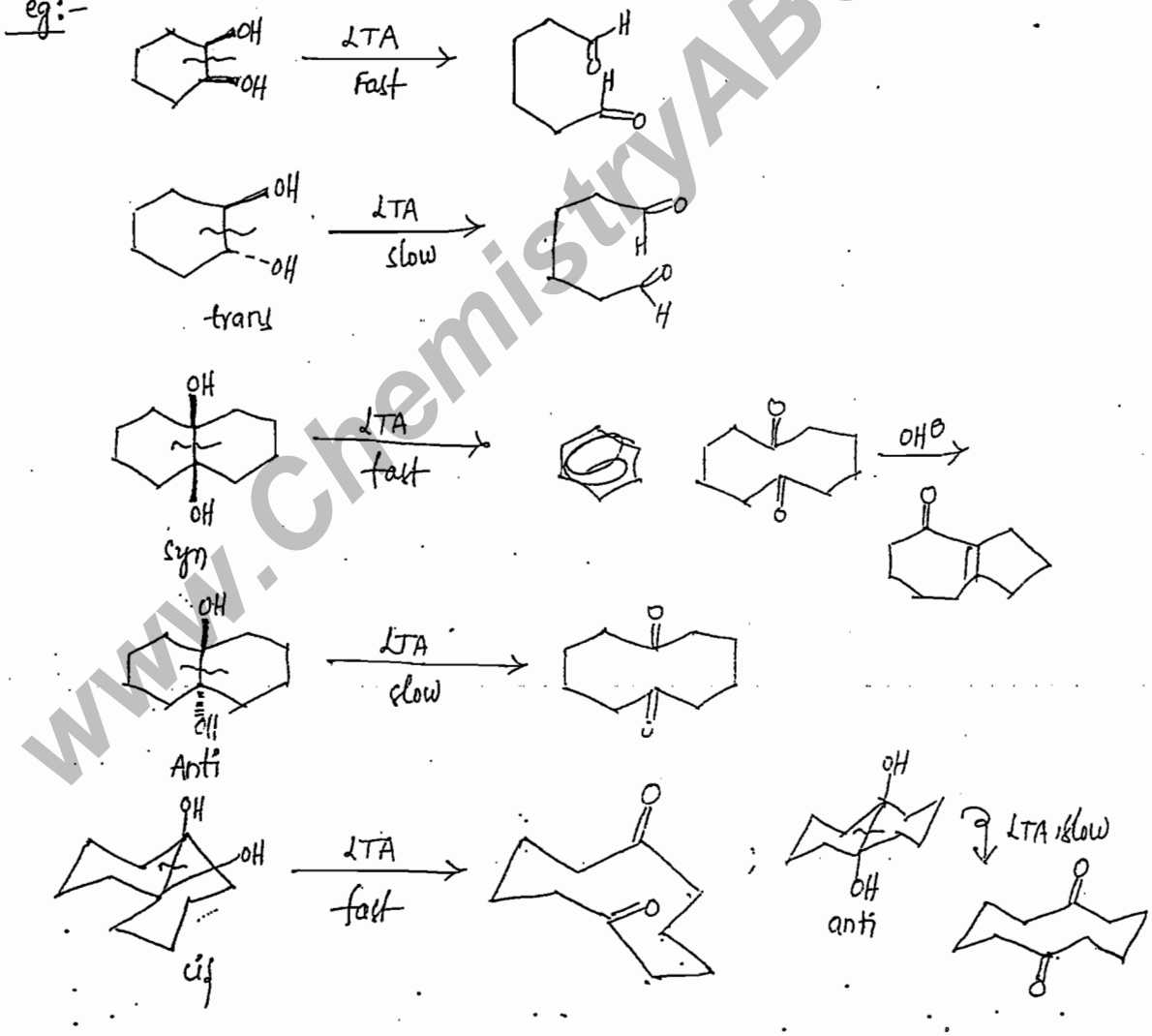


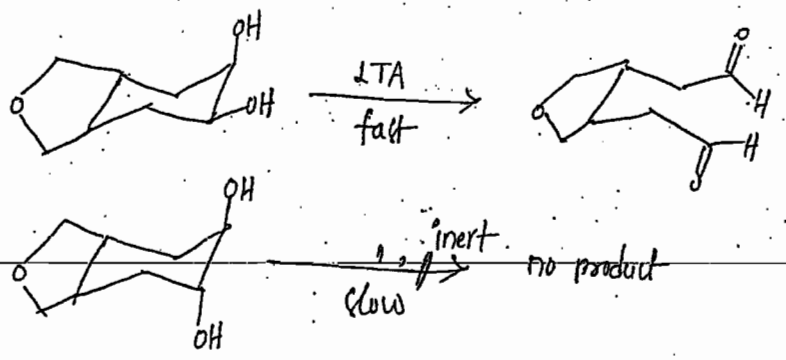
Mechanism :—

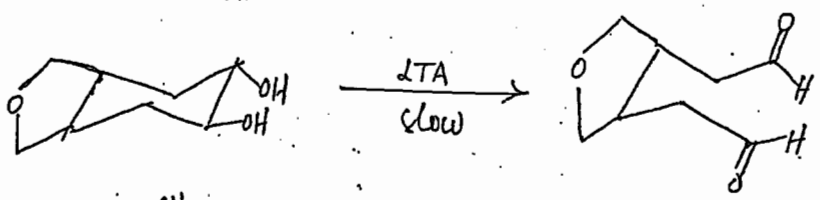
→ Syn diol readily gets oxidised by LTA .

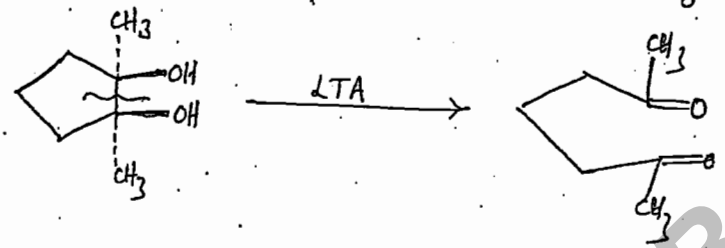


eg:—

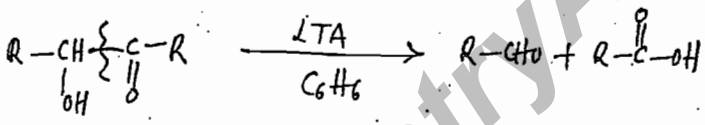








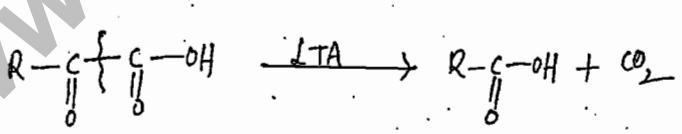
* 2) α-hydroxy carbonyl compds' cleavage



V. IMP

*)

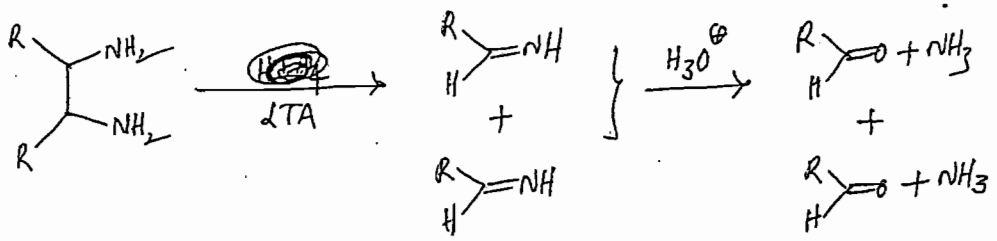
3) α-keto carboxylic compds' cleavages :



α-keto carboxylic acids oxidises into CO_2 & acid.

e.g. $CH_3-\overset{O}{\overset{\|}{C}}-CO_2H \xrightarrow{LTA} CH_3COOH + CO_2$

* 4) cleavage of 1,2-diamino compounds :



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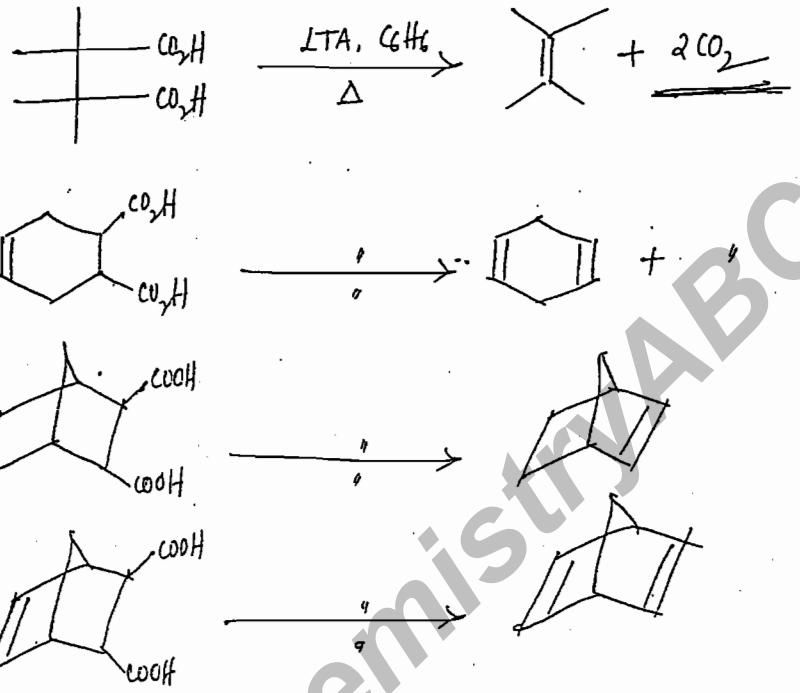
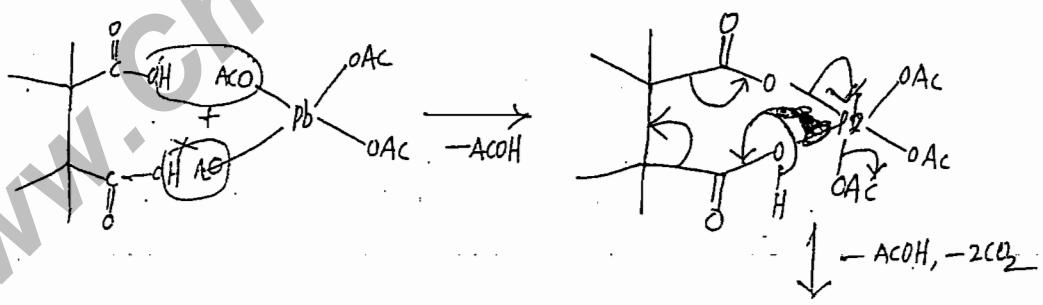
* 5) Bis-Decarboxylations :—

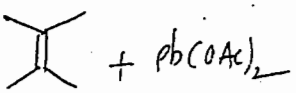
(Loss of two equts of CO_2 at one time – bis decarboxylations).

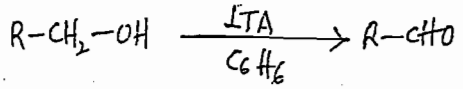


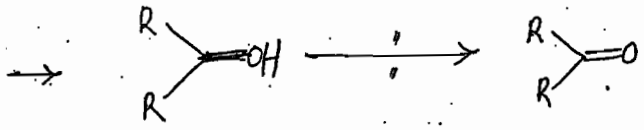
Mech :—

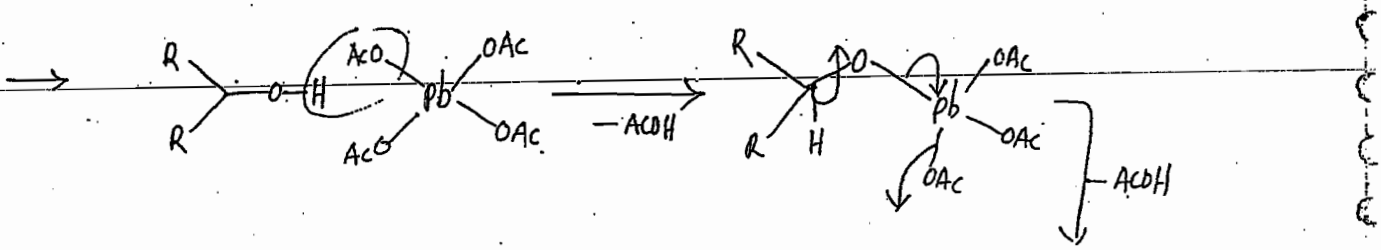


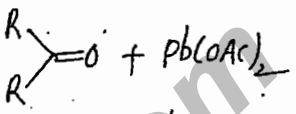
6) oxidn of simple alcohols into carbonyl compds



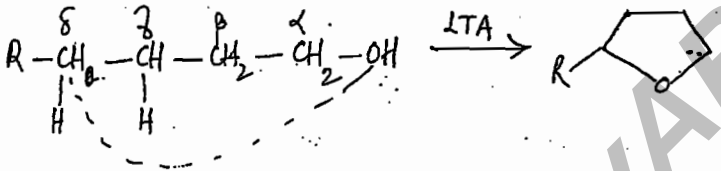






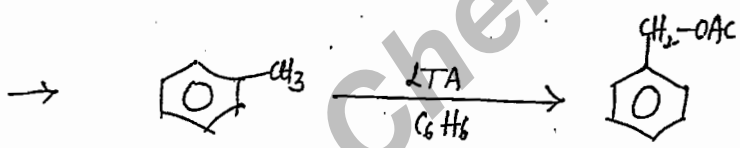


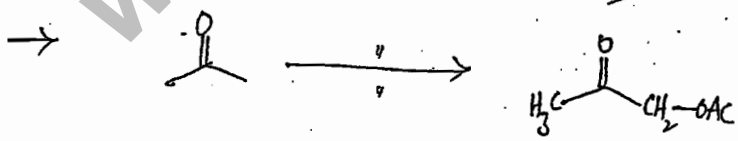
→ In alcohol, at β or δ positions, –OH fn is present, LTA oxidises alcohol into cyclic ether.



F) As methylating & acetoxylating agent :–

→ LTA introduces methyl or OAc at allylic, benzylic, α-position of withdrawing group.





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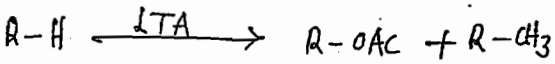
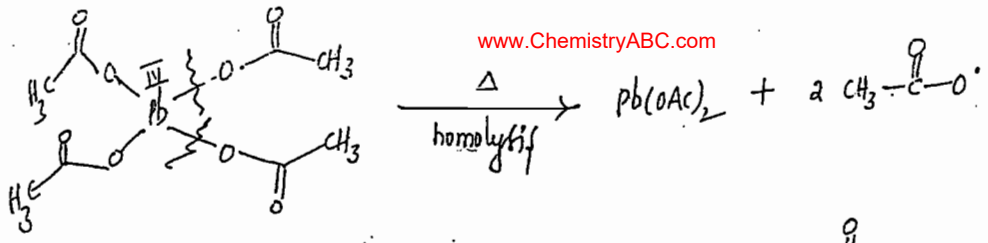


→ mech. involves free radicals' intermediate.



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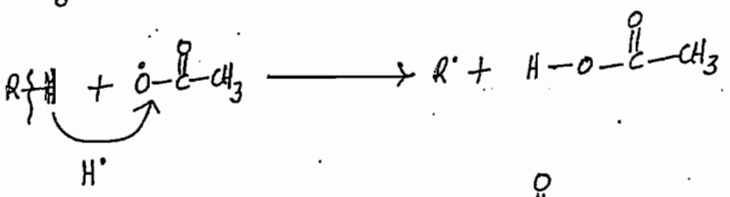

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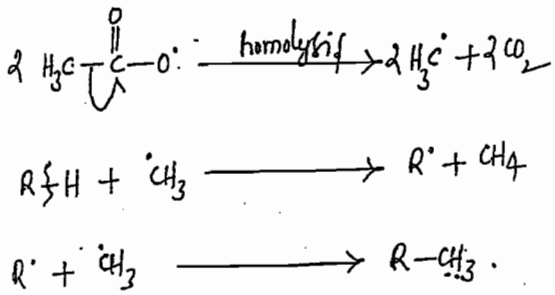

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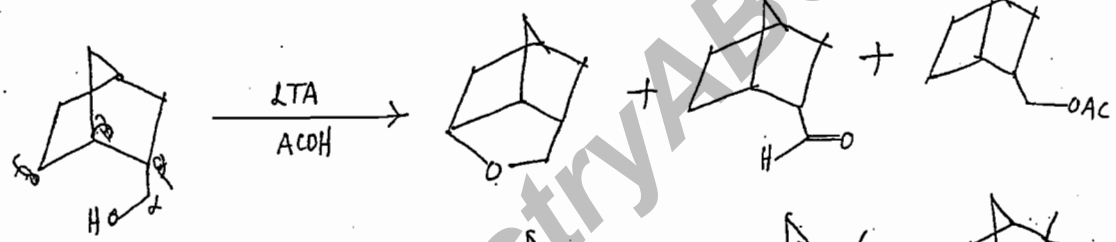

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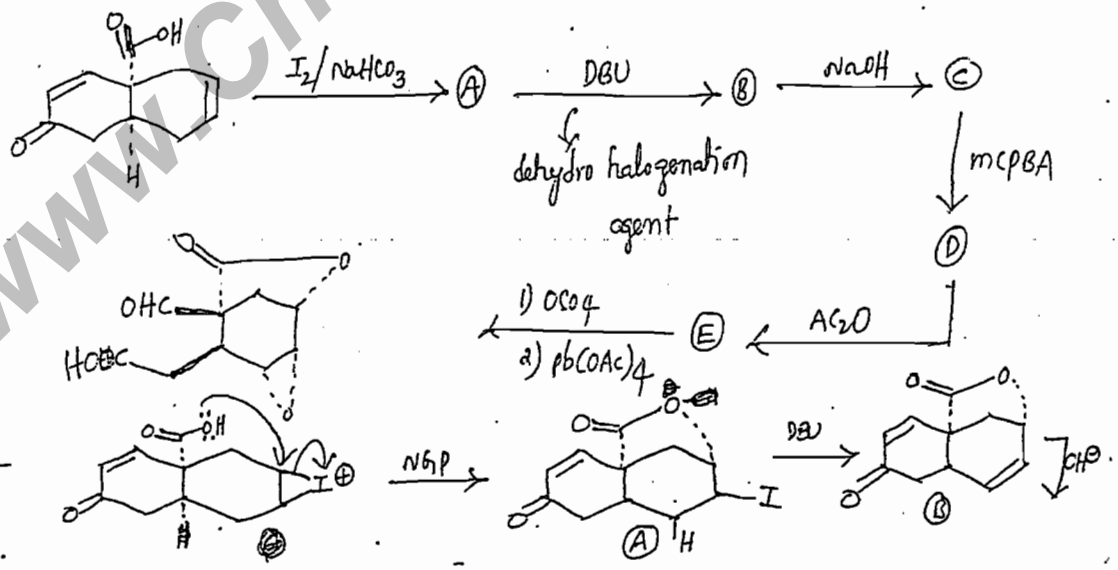
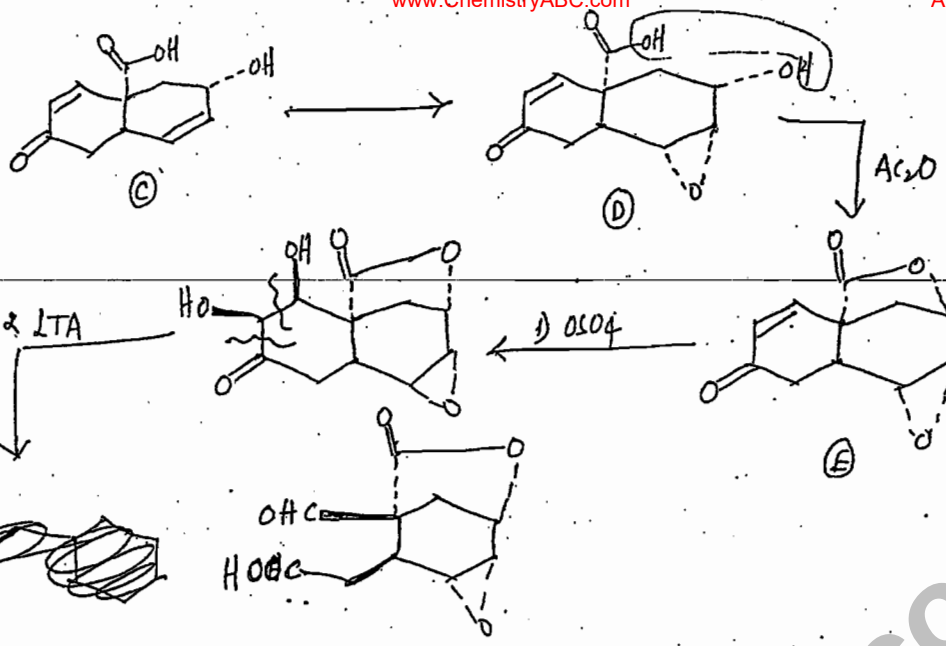
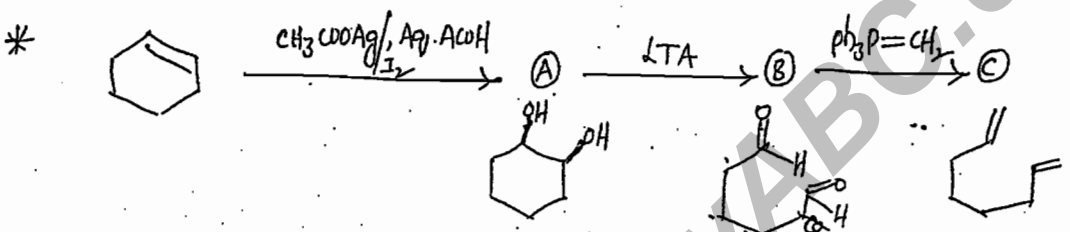
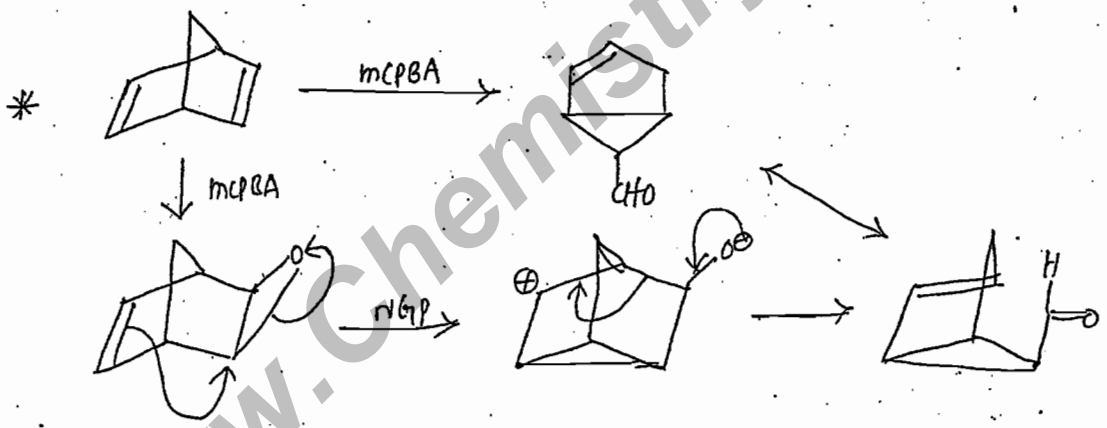
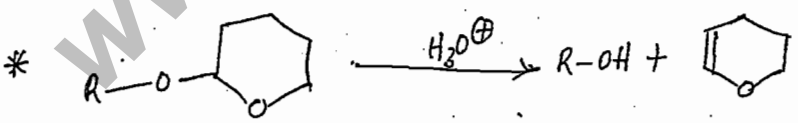
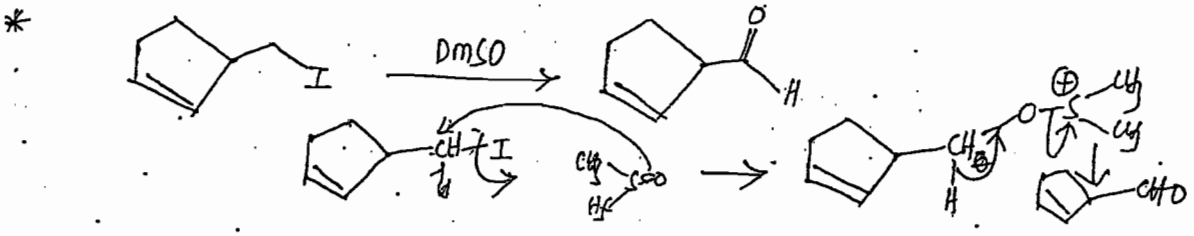


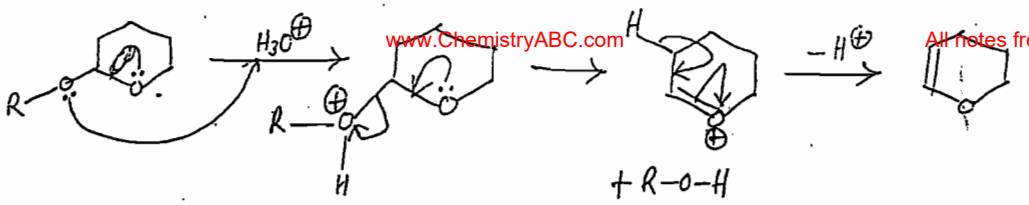


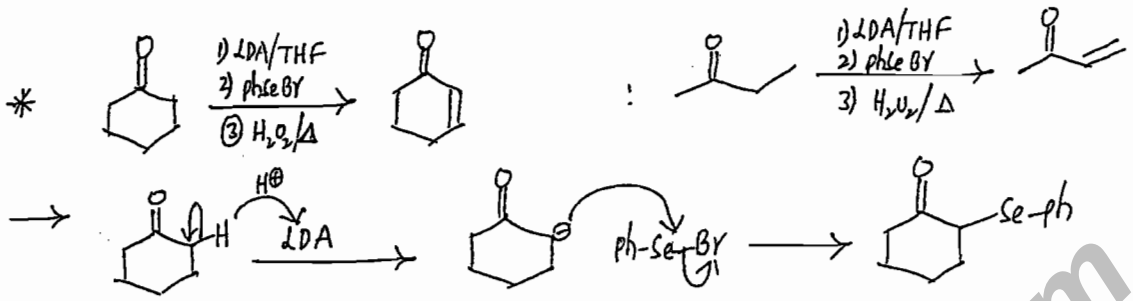


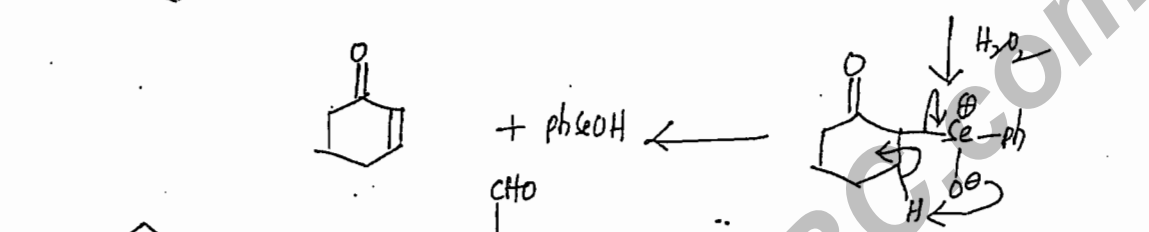


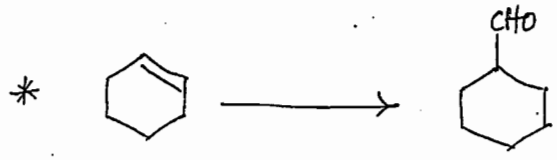


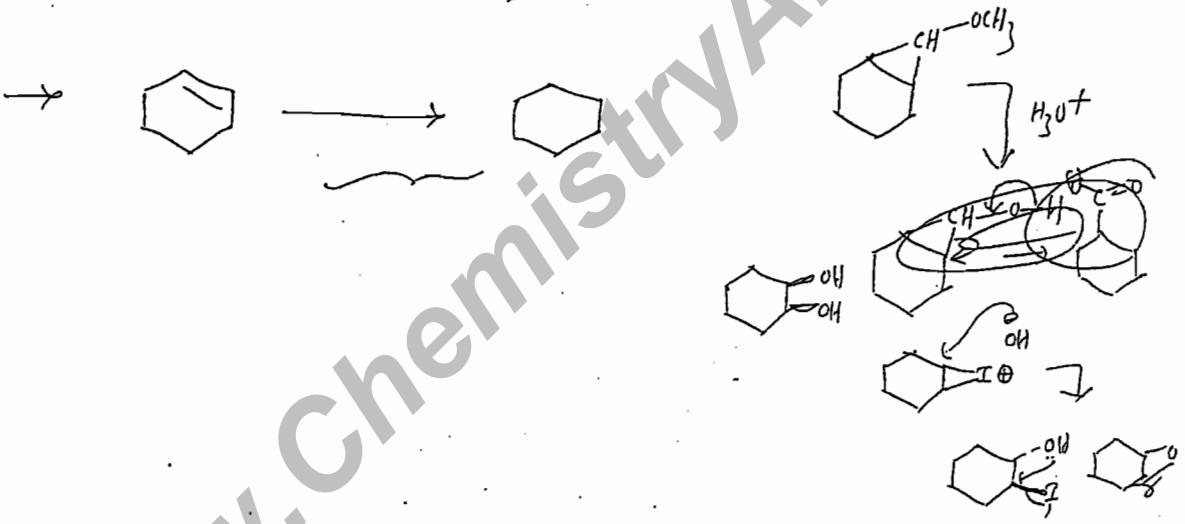












Reductions: Reducing agents :—

Date : 13/05/08

→ . Addn of hydrogens/ removal of oxygens to substrate.

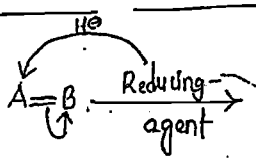
Reductions

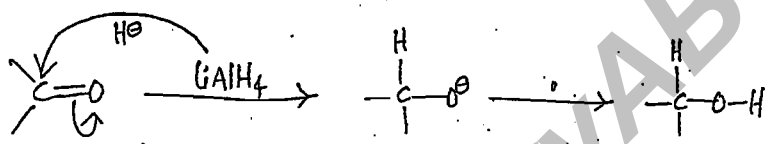
I. Hydride ion transfer reductions

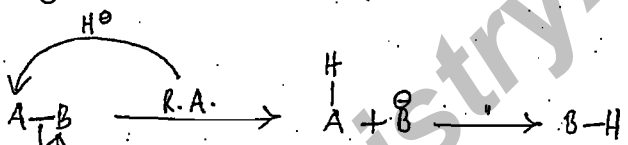
II : $e^{\ominus}$ transfer reductions

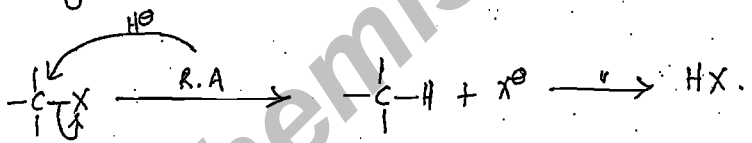
III. concerted reductions

I) Hydride ion transfer reductions :—

* 

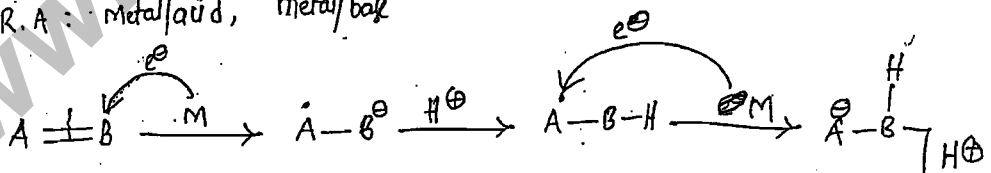
* 

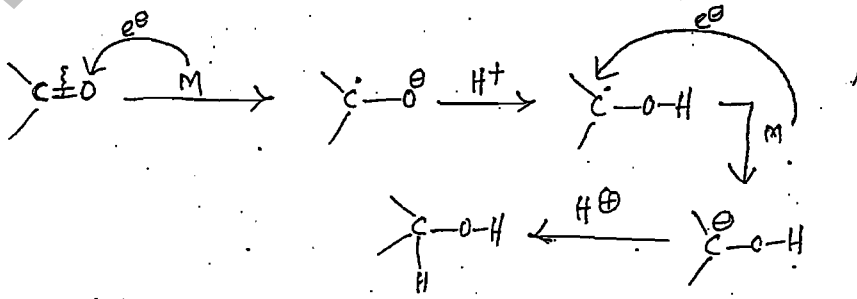
* 

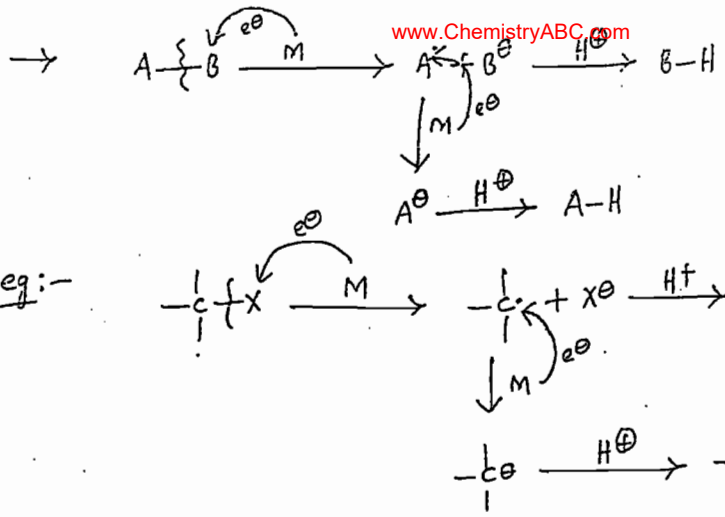
* 

II. $e^{\ominus}$ transfer reductions :—

eg: R.A : Metal/acid, metal/base



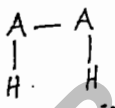
→ 



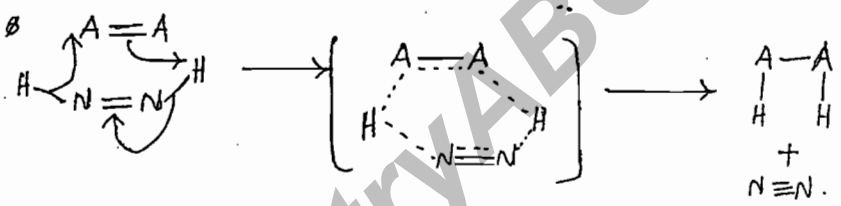
eg:-

III concerted reductions :- (less-common)

→ Diimide - reductions.

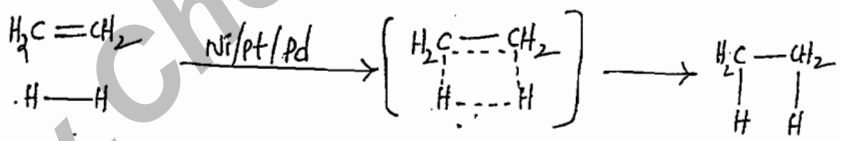
N_2H_2 ; $A=A \xrightarrow{N_2H_2}$ 

Mech:



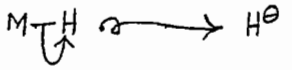
Catalytic - Hydrogenations :-

$H_2C=CH_2 \xrightarrow[Ni/Pt/Pd]{H_2} H_3C-CH_3$

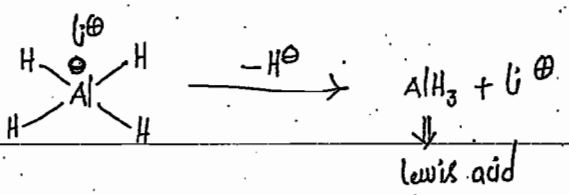


I. Hydride ion transfer Reducing agents :-

→ Metal - Hydride complexes



1) Lithium Aluminium Hydride (LAH) :—



→ white crystalline substance, unstable..

→ violent in water. ∴ Anhydrous / inert conditions has to be maintained.

$$LiAlH_4 \xrightarrow{H_2O} Li(OH) + Al(OH)_3 + H_2$$

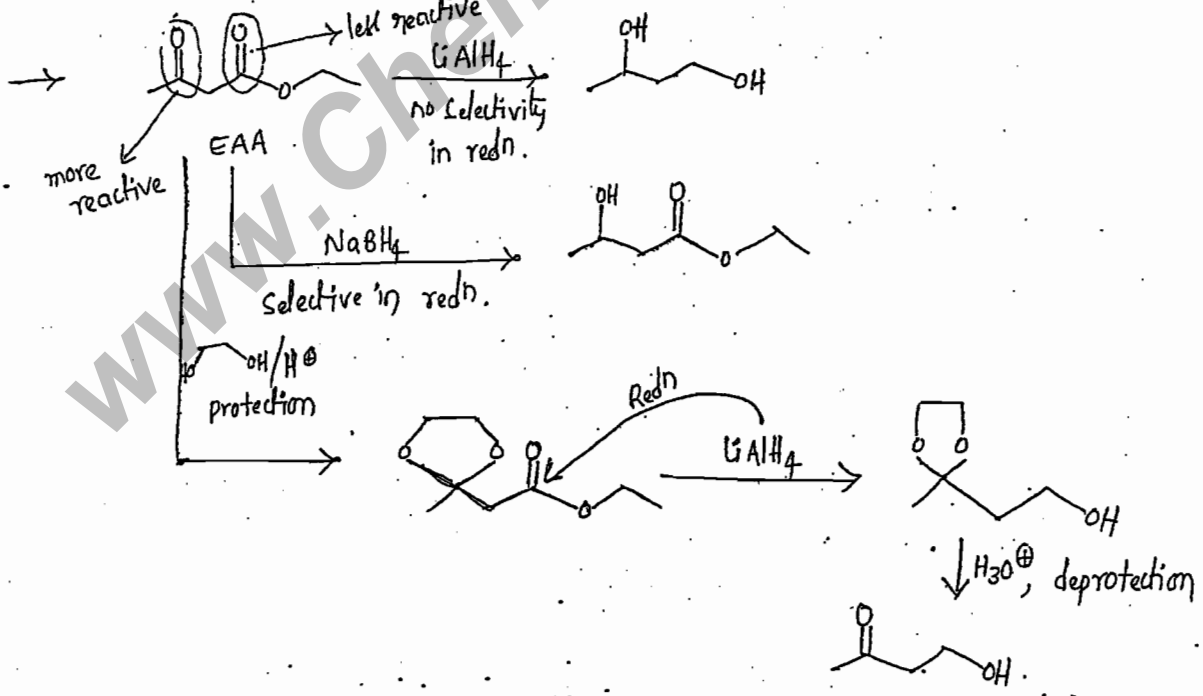
preparation :— $LiH + AlCl_3 \longrightarrow LiAlH_4$

solvents :— Dry ethers, Et_2O, THF ()

Functions/applications :— LAH, highly reactive, versatile reducing agents.

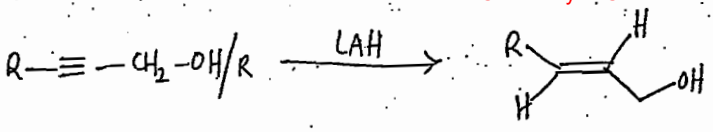
A Reagent which reduces wide range of functional groups called as "versatile agent".

→ LAH is powerful, non-selective reagent.



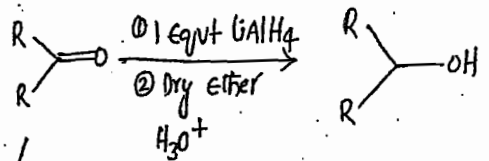
* Almost all the org. fn reduced by LAH.

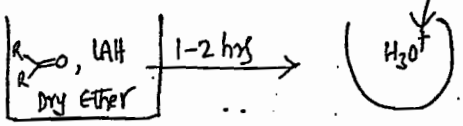
organic function	LAH	New function
Carbonyl C=O	→	Alcohols
Acid C=O, OH	→	Alcohols
ester C=O, OR	→	Alcohols
Acid halide C=O, X	→	Alcohols
cyclic ester (lactone)	→	Alcohols
epoxide	→	Alcohols
Amide	LAH →	Amines.
nitrile.	LAH →	Amines.
Imine	LAH →	Amines.
azide	LAH →	Amines.
oxime	LAH →	Amines.
Nitro	LAH →	Amines.
Halo compounds	LAH →	hydrocarbons.
Alkyl sulphonate ($R-O-\overset{O}{\overset{\|\|}{S}}-R$)	LAH →	hydrocarbons.
propargyl alcohol (ethers)	→	trans olefins



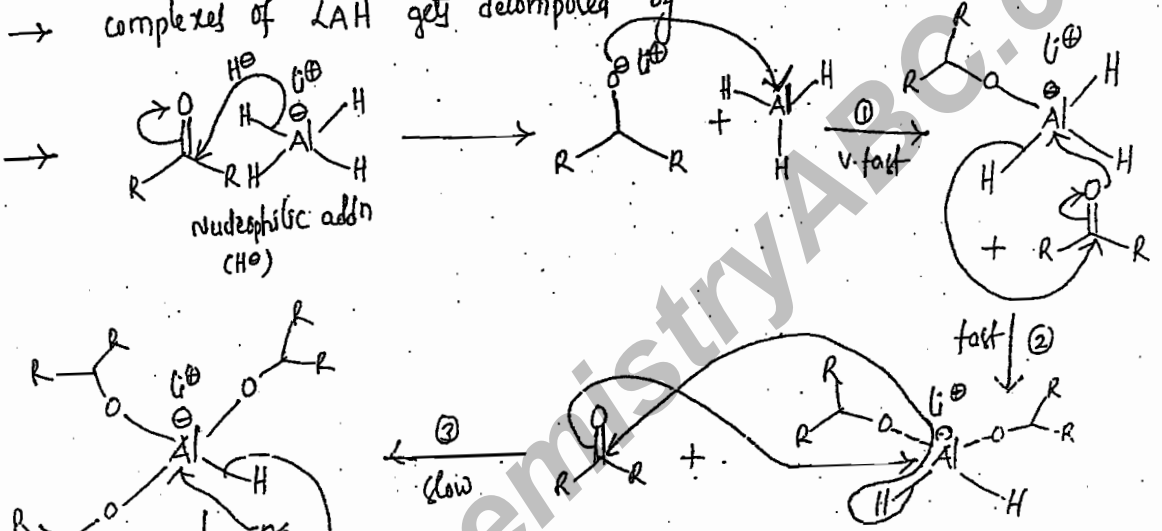
* simple isolated dbs, tbs, ethers (=, ≡, C–O–C) won't get reduced by LAH.

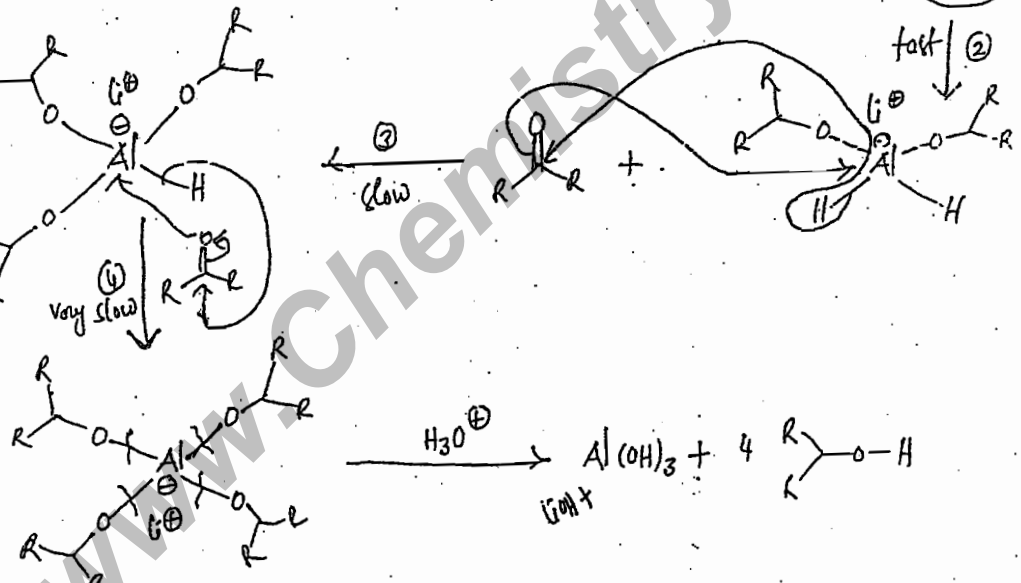
* **Mechanisms:-** - 4 eqvts





→ complexes of LAH gets decomposed by "acidic water".





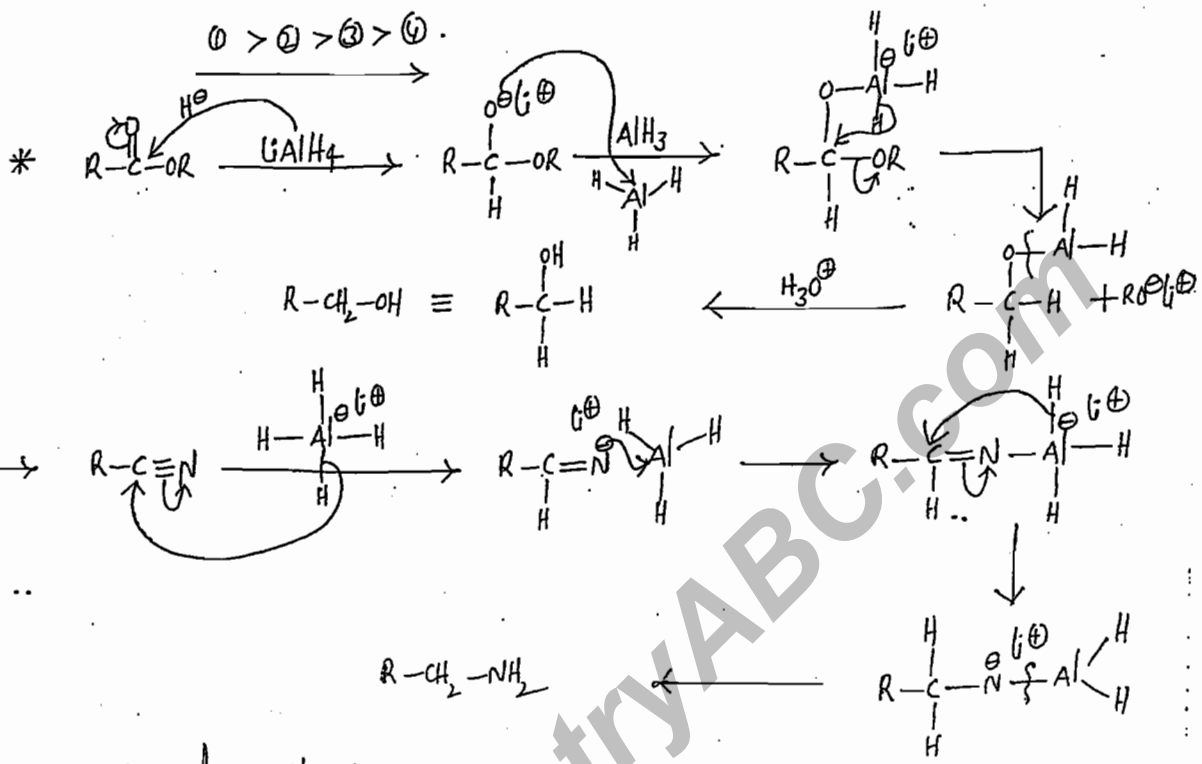
→ Alkoxy gps exerts –I.E. on 'Al', with ↑ in no. of alkoxy gps, –I.E. becomes stronger on Aluminium hydride, reactivity of $LiAlH_4$ ↓es, more alkoxy, less reactive, slow in releasing $H^{\ominus}$.

→ Alkoxy aluminate - weak reducing agent than LAH.

$LiAl(OR)_3H < LiAl(OR)_2H_2 < LiAl(OR)_1H_3 < LiAlH_4$

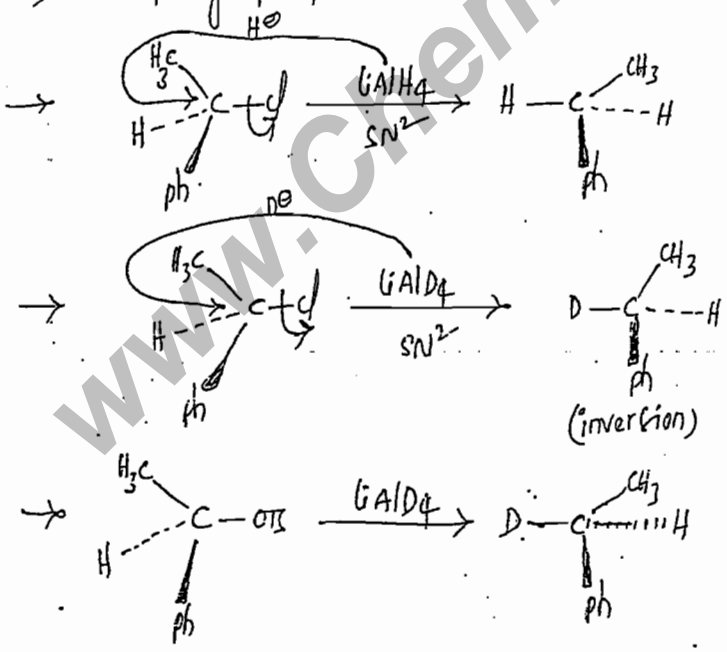
Reactivity order ⟶

① > ② > ③ > ④.

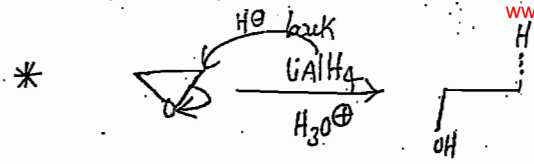


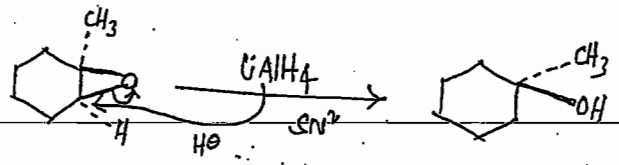
* Stereo chemical aspects :-

→ In opening of epoxide and reduction of halo compounds, tosylates, S_N2 (inversion of stereochemistry)

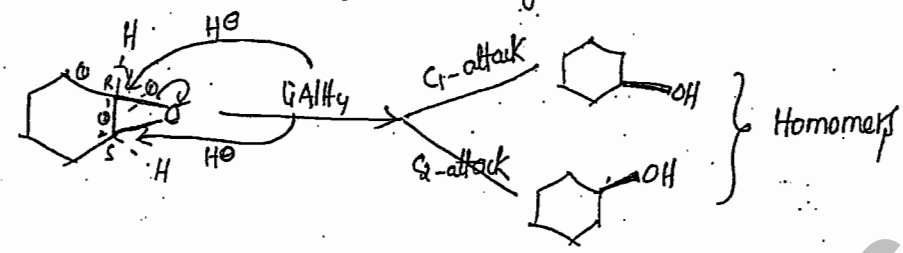


(inversion)

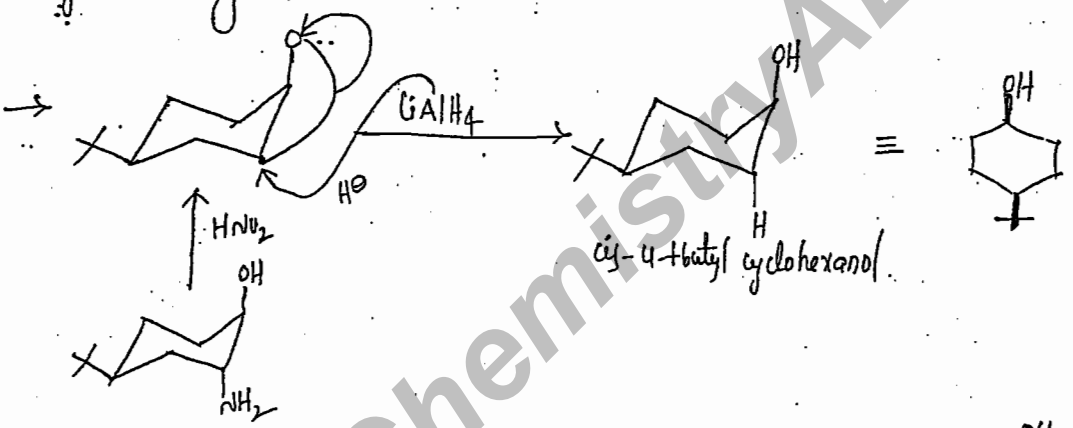


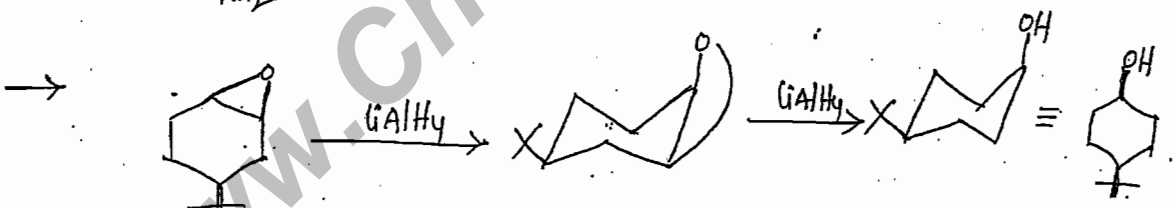


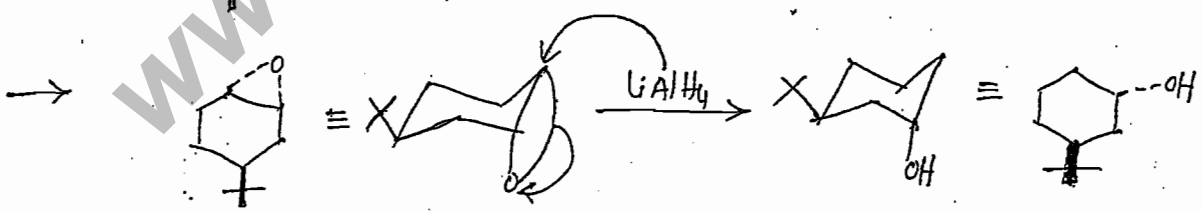
Regioselectivity at sterically less crowded.

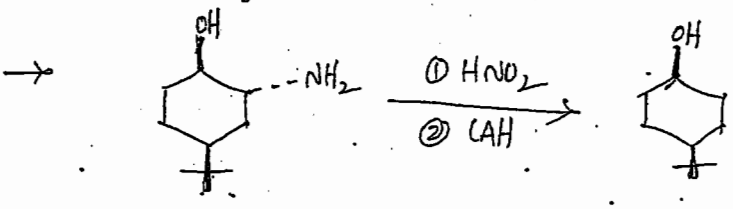


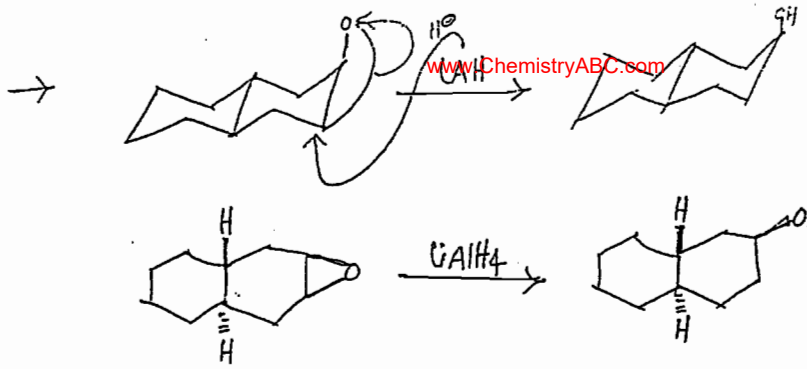
* In conformationally rigid molecules, opening of epoxide (epoxides) with LiAlH4 by attacking in axial direction.



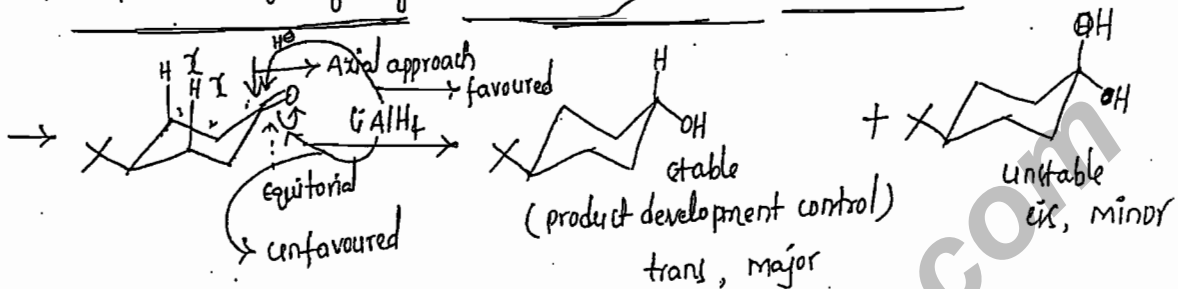






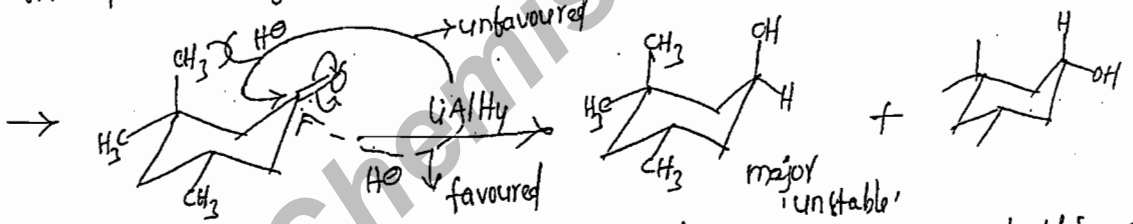


→ Reduction of rigid cyclohexanone derivatives with $LiAlH_4$:—



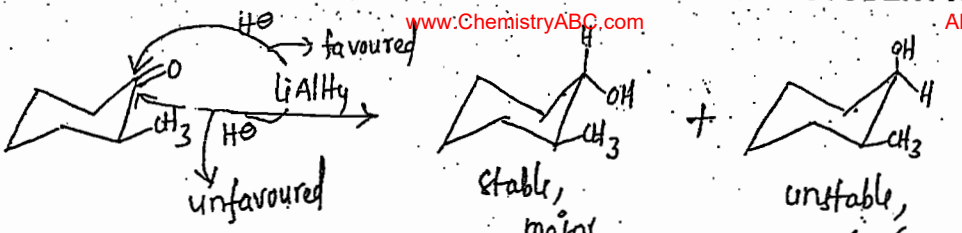
→ Axial, equitorial approach free from steric crowding, selectivity controlled by stability of the product.

whenever resulting products' stability controls selectivity in addn of nucleophile at cyclohexanone carbonyl, phenomenon called "PDC".

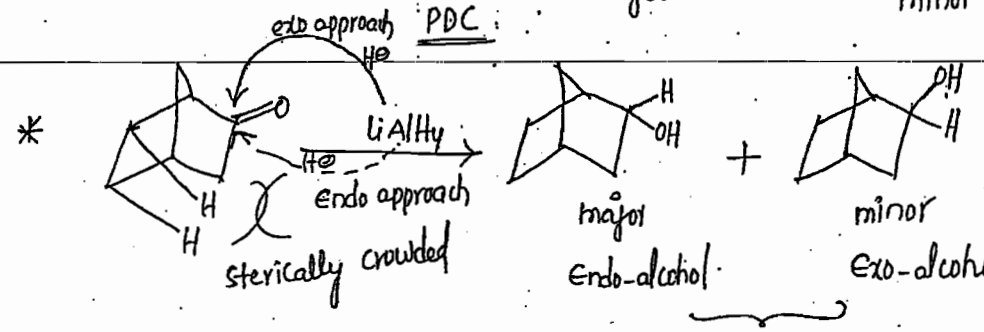


axial approach is sterically crowded due to presence of bulkier gp at C_3-axial position, equitorial direction of attack preferred, axial alcohol is the major.

→ whenever steric crowding controls selectivity in addn of nuc$^{\ominus}$ at cyclohexanone carbonyl referred as "steric approach control".

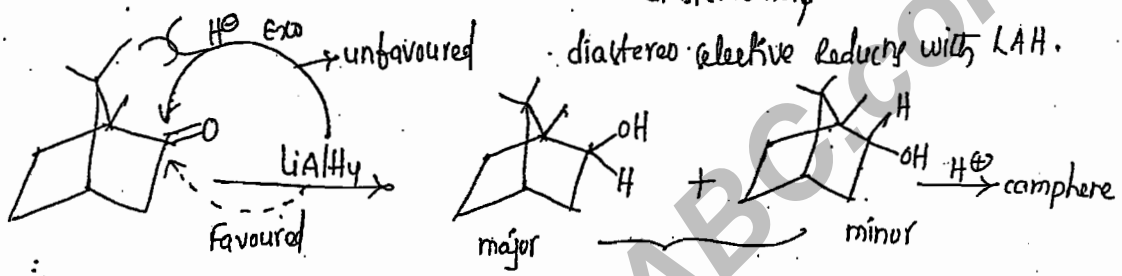


PDC :

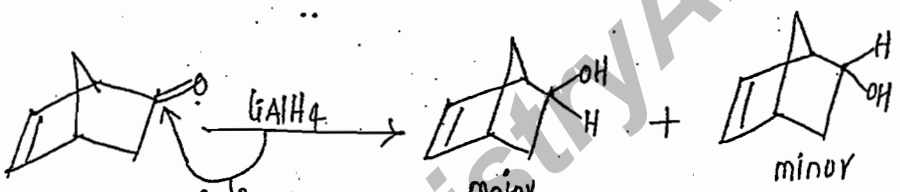


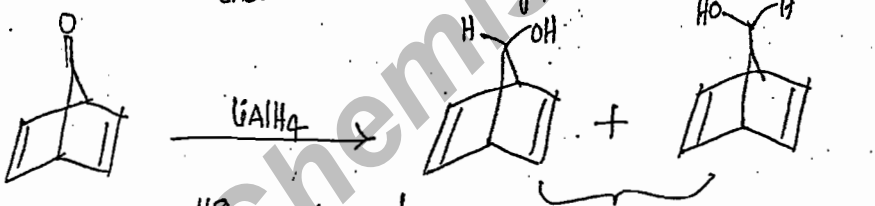
Endo-alcohol. Exo-alcohol.

diastereomers

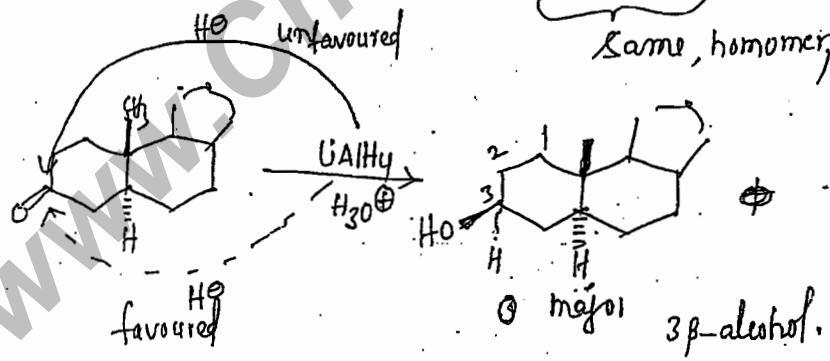


diastereo selective reducing with LAH.



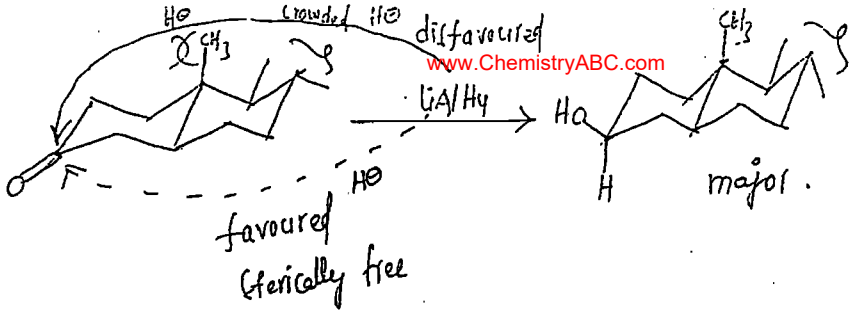


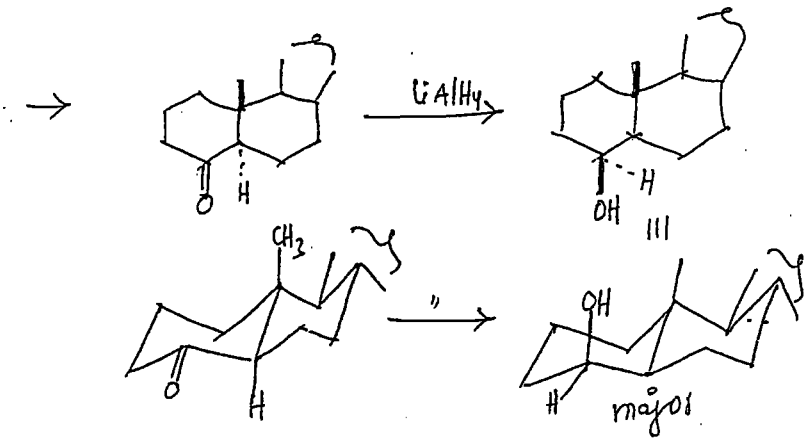
Same, homomers

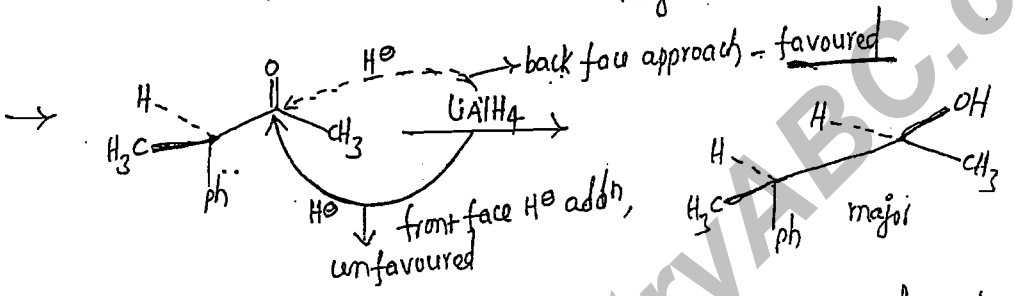


3β-alcohol.

front face addn sterically crowded, becuz of presence of Me at angular position.







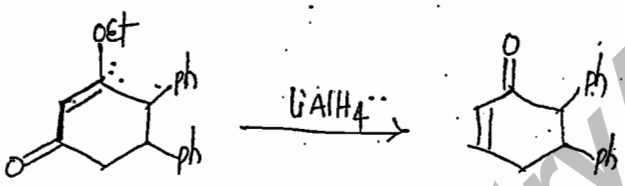
→ due to presence of bulkier $-CH_3$ gp at α-chiral centre of carbonyl, front face addn - sterically crowded, selective nucleophilic addn at back face, resulting product major.

* In the case of aromatic α,β-unsaturated aldehydes, degree of redn depends on reaction conditions. At lower temp. selectively reduces aldehyde, at room temp or little higher temperatures, reduces both unsaturation, carbonyl.

→ $ph-CH=CH-CHO$ (cinnamaldehyde) —
- $LiAlH_4, Et_2O$, 35°C → $ph-CH_2-CH_2-CH_2-OH$. (mechanism) ??
- 0-5°C → $ph-CH=CH-CH_2-OH$

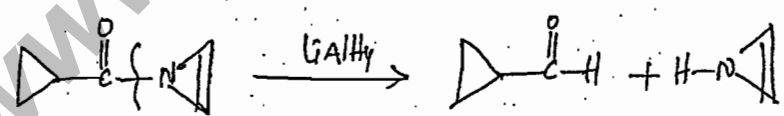
* Mech :-

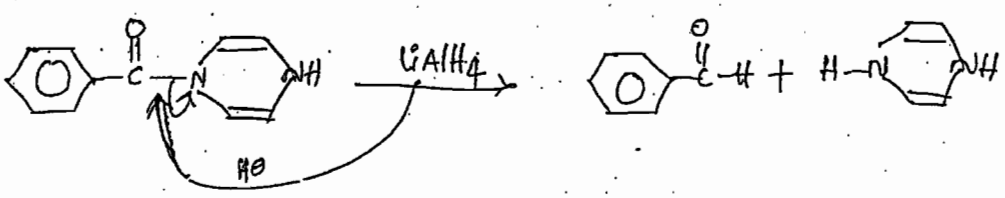
* Examples :-

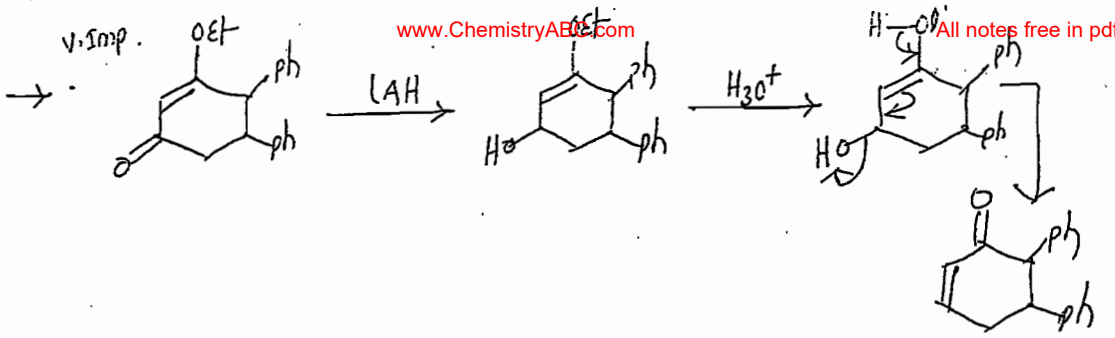
→ 1) 

→ 2) 

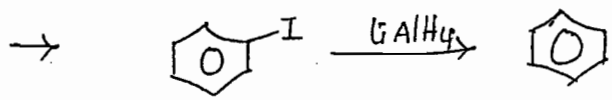
→ In amides 'N' is part of heterocyclic ring, in CAH redn, products aldehydes/ amines.

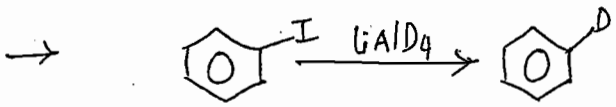
→ 

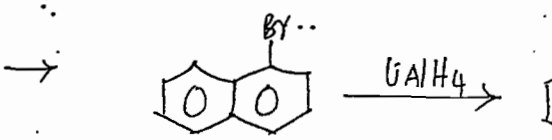
→ 

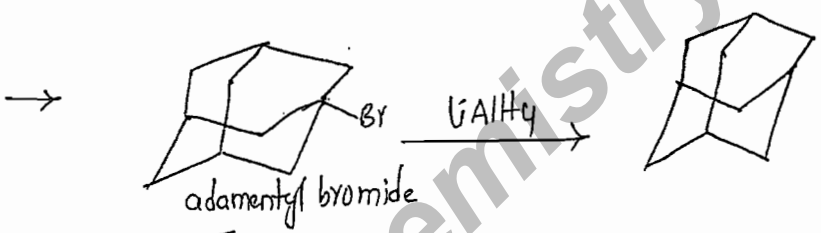


* If molecule having different halogroups, selective displacement of less e.n. halogroup by $LiAlH_4$.

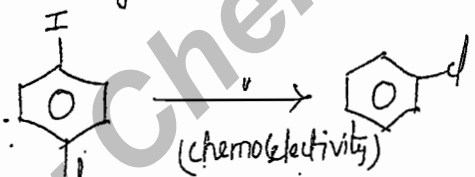




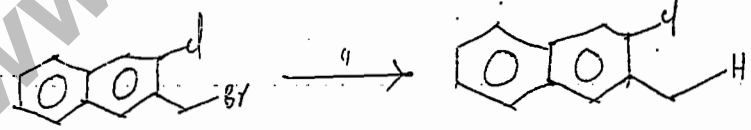




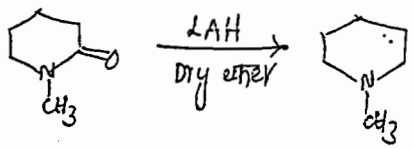
adamantyl bromide



(In a molecule if two potential gps are present, attacking reagent prefers one over other called chemoselectivity).



Dt: 14/05/08

1) 

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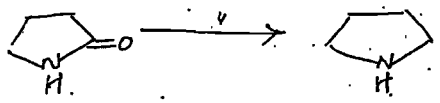

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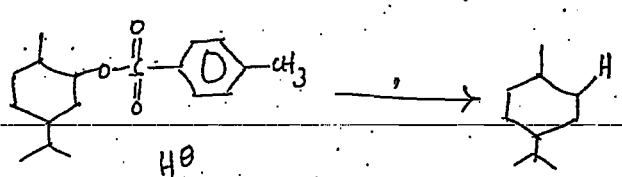

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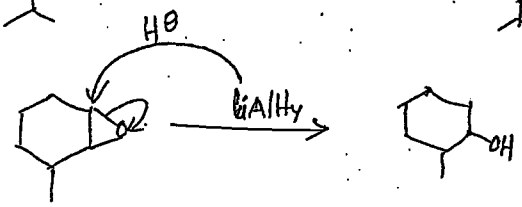

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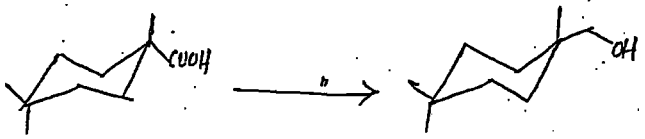

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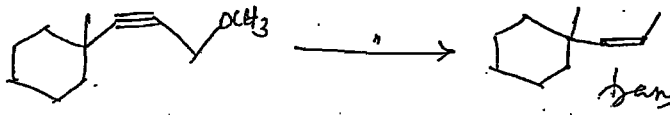

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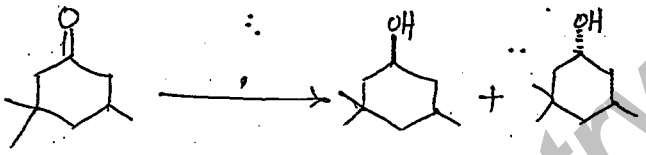

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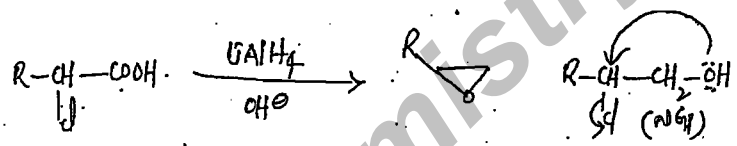

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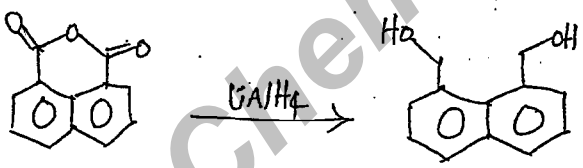

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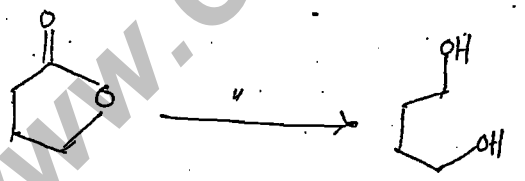

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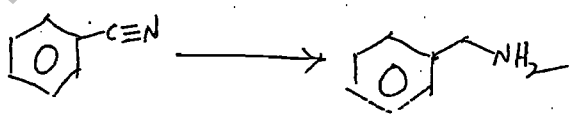

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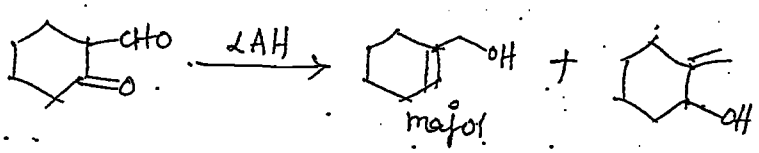
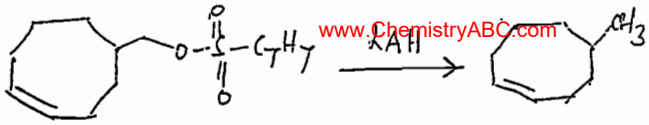
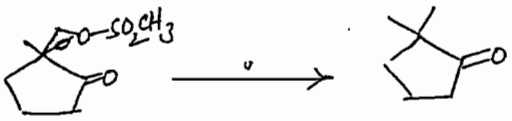
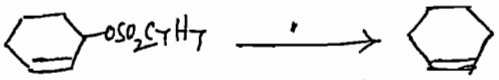
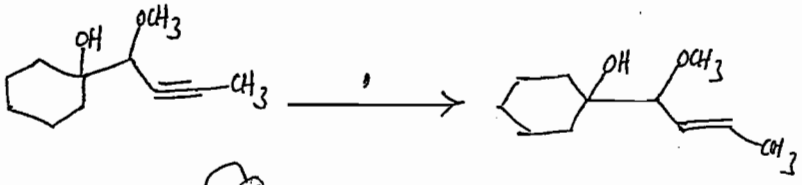


13) 

14) 

15) 

16) 

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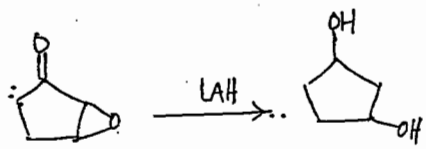
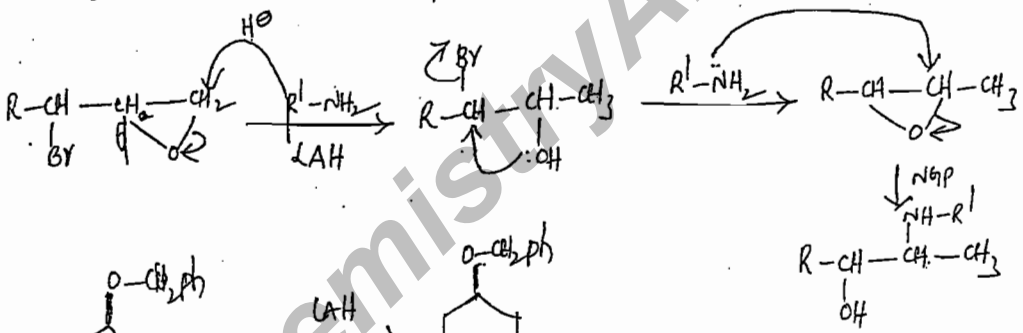
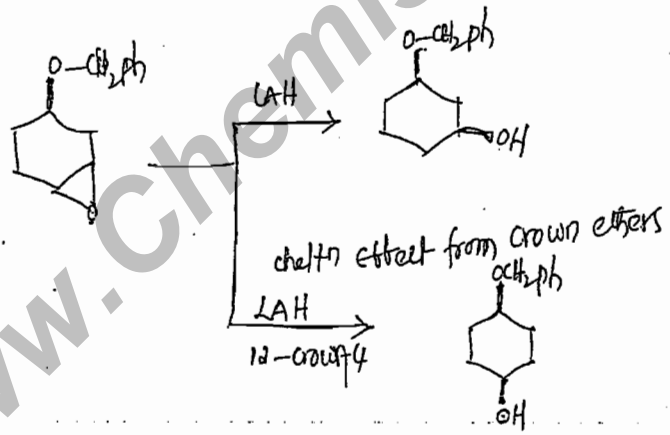
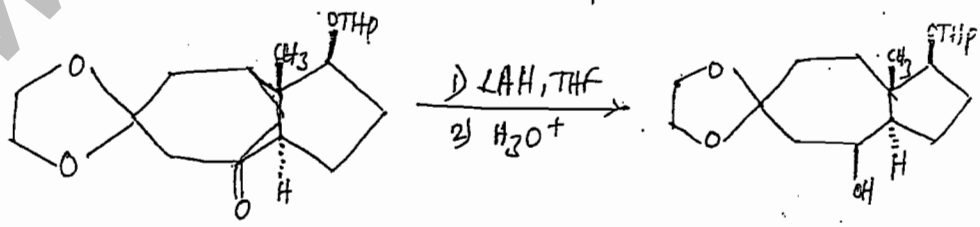
18) 

19) 

20) 

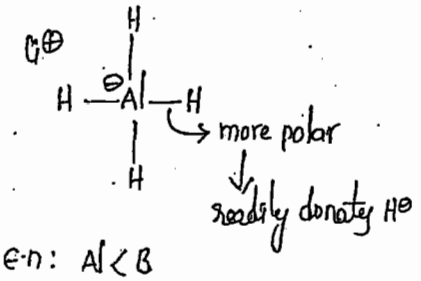
21) 

SODIUM – BOROHYDRIDE :– $NaBH_4$

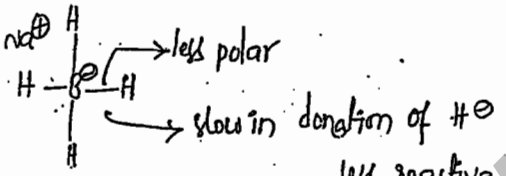
→ white crystalline solid.

→ In aq. state. ∴ Even in water solvent can be used as R.A.

Solvents :– water, alcohol, MeOH, EtOH, iproH, $t_{Bu}OH$.

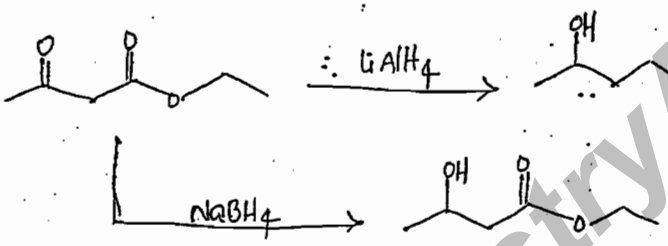


E.n: Al < B



e.n. diff B, H small
Al, H more.

→ $NaBH_4$ less reactive, more selective



→ $NaBH_4$ less reactive ∴ Select more reactive FG.

→ $NaBH_4$ reductions are chemoselective.

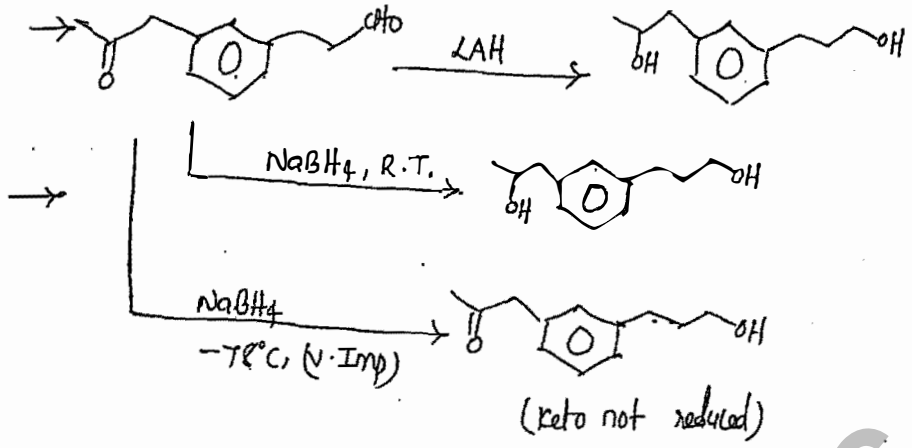
Functions / applications :–

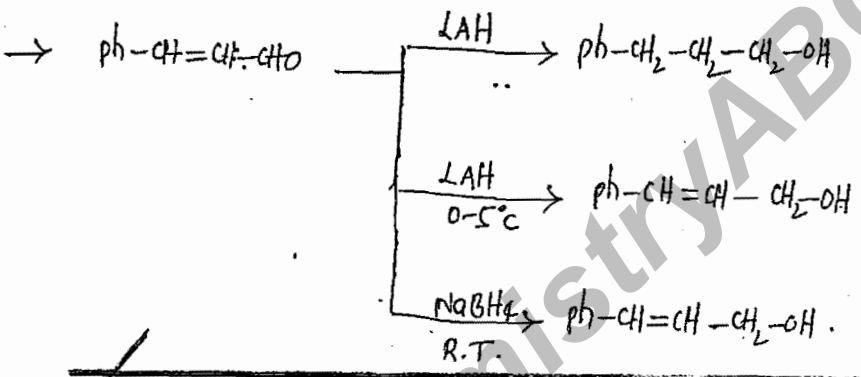
Functions	$NaBH_4$	Product
→ Carbonyl compd		alcohol
→ Esters (specific conditions) i.e., addnl additives must be present.. eg: I_2		"
→ Imine		Amine
→ Iminium salts		

→ If in molecule, aldehyde, keto functions present at lower temp (−78°C)

$NaBH_4$ selectively reduces aldehyde into alcohol.

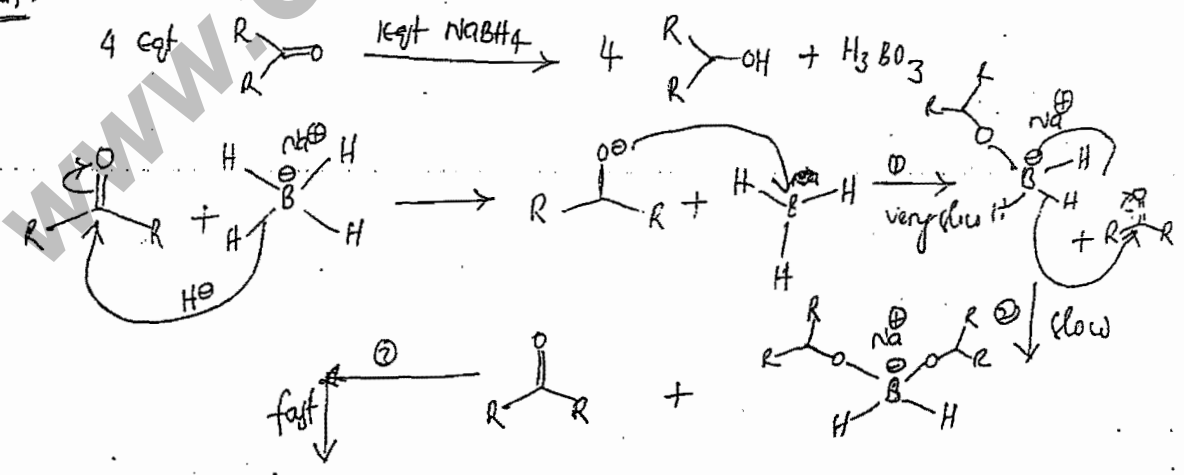
At room temp. both will be reduced.

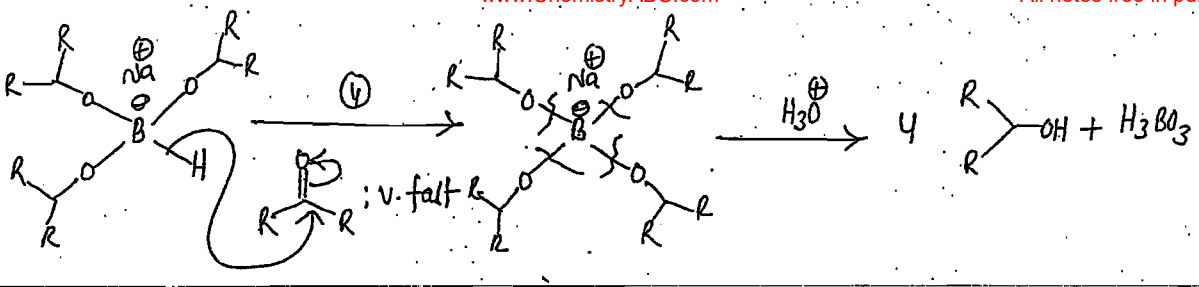




→ In the case of aromatic α,β unsat. carbonyl compds, even at higher temp. $NaBH_4$ reduces only carbonyl fn into alcohol, unsaturatn unaffected.

Mech:





→ $NaBH_4$ complexes decomposed by mineral acids (HCl, HNO_3, H_2SO_4) (or) aq. NH_4Cl (or) aq. AcOH.

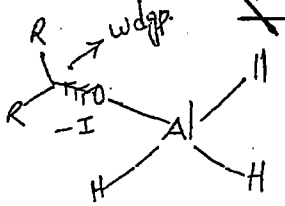
Reactivity : ④ > ③ > ② > ①

→ Reactivity of $NaBH_4$ in reductions reverse to LAH.

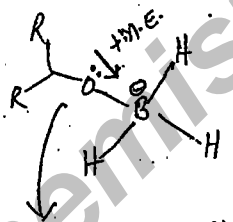
→ with ↑ in no. of alkoxy gps on B, reactivity of $NaBH_4$ ↑s in reduction.

∴ Reactivity : $NaBH_4$ < Alkoxy borohydrides

$LiAlH_4$ > " aluminium "



stable, less reactive

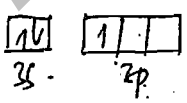


donating gp

o-donor
B-acceptor

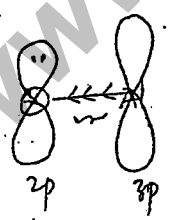
unstable, highly reactive

Al (z=13) – $1s^2 2s^2 2p^6 3s^2 3p^1$

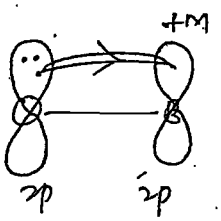


O (z=8) – $1s^2 2s^2 2p^4$

B (z=5) – $1s^2 2s^2 2p^1$



energy gap more, poor overlapping



Energy gap less

→ presence of alkoxy gps on B in borohydrides making borohydrides more reactive due to +M.E from alkoxy gps.

→ $Al-\overset{-I}{O}$; $B-\underset{+M}{\ddot{O}}$

Empty orbitals of B, occupied orbital of 'O' belongs to same shell (2p), energetically closure, allows strong overlapping. Transfer of $e^{\ominus}$ cloud from $O \xrightarrow[to]{} B$, +m.E. hence ↑ in reactivity.

→ Empty orbitals on 'Al', filled orbital on 'O' belongs to different shells

O-2p ; Al-3p

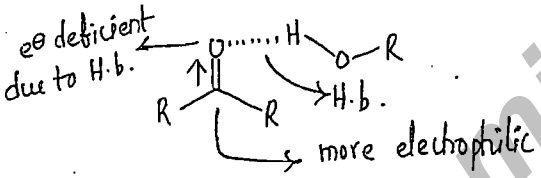
poor overlapping, weak in strength of +M.E.

In preference to +M. alkoxy 'O' exerts −I.E. ↓ in reactivity of alkoxy alluminate.

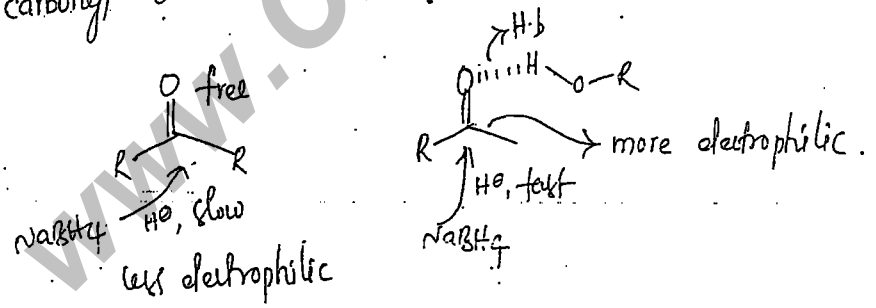
∴

→ Alkoxy borate poor in selectivity than in $NaBH_4$.

Example :- Alcohols as solvents



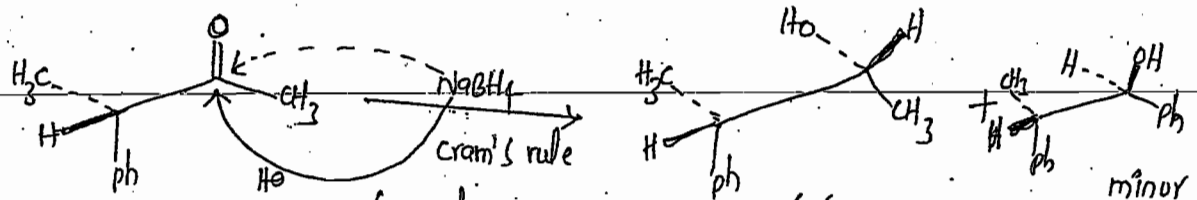
Alcohols little enhances of $NaBH_4$ reduction by establishing H.b. with carbonyl 'O'.

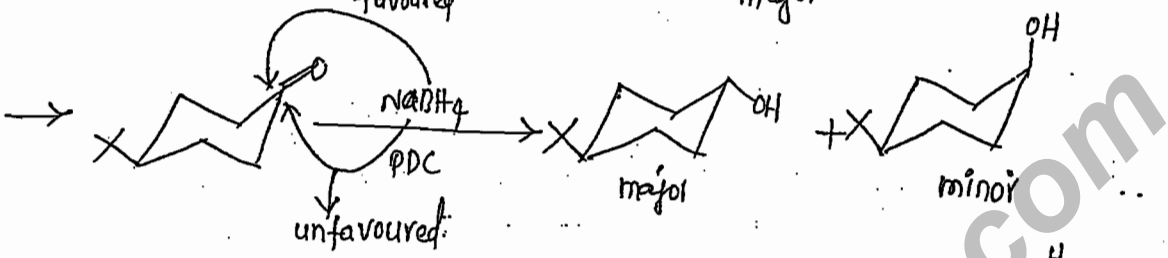


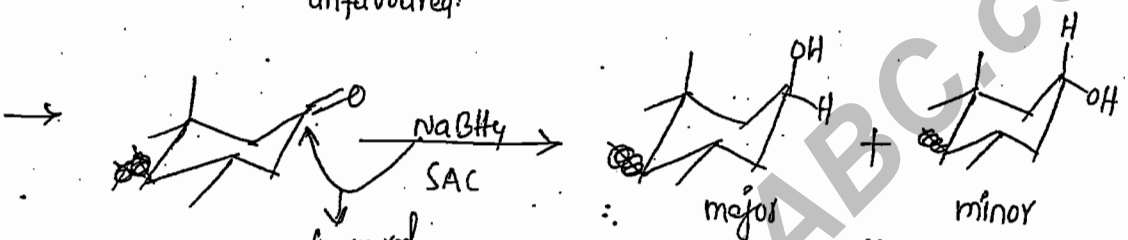
Stereochemical aspects of $NaBH_4$:-

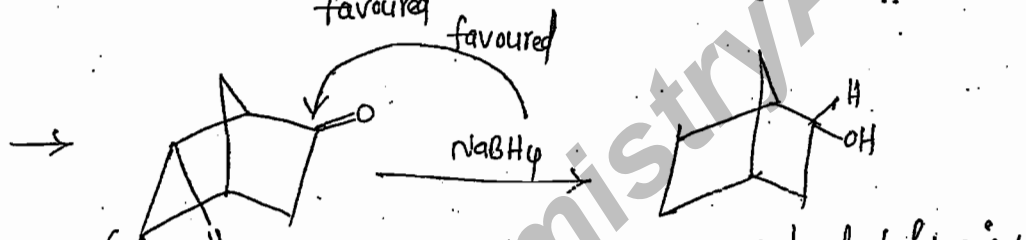
→ Same as $LiAlH_4$

→ $NaBH_4$ delivers hydride ion at sterically less crowded side (or) face of carbonyl.

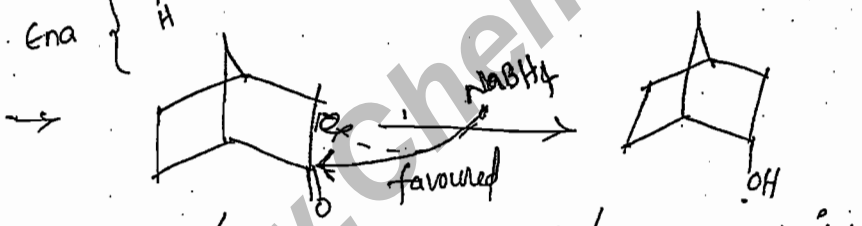


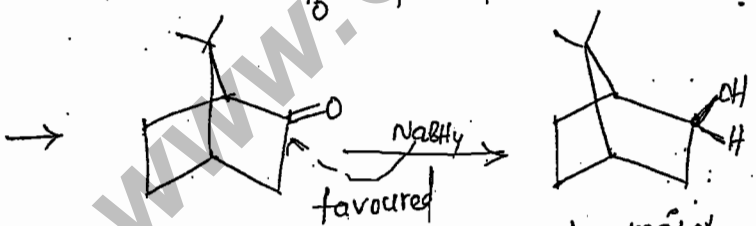


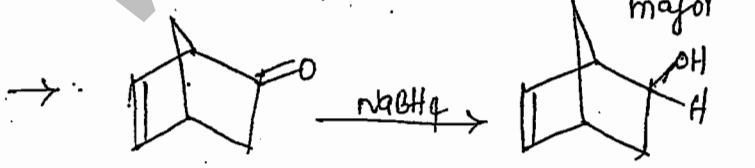


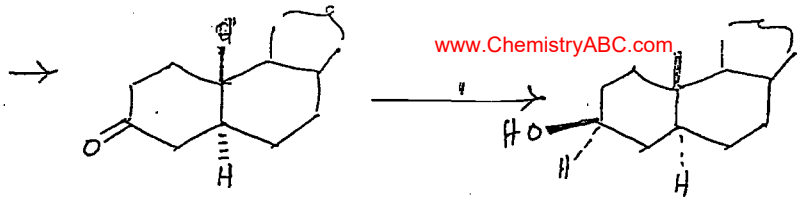


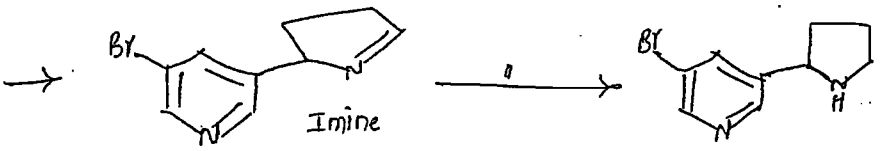
Ena

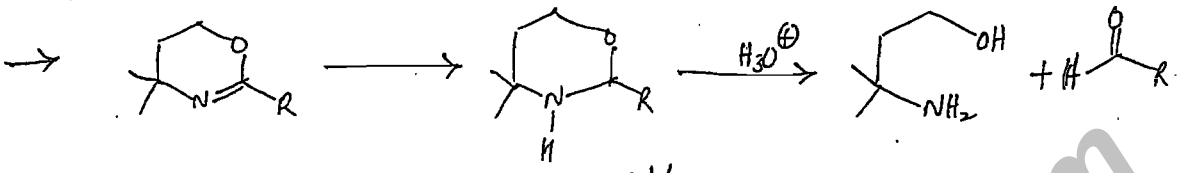




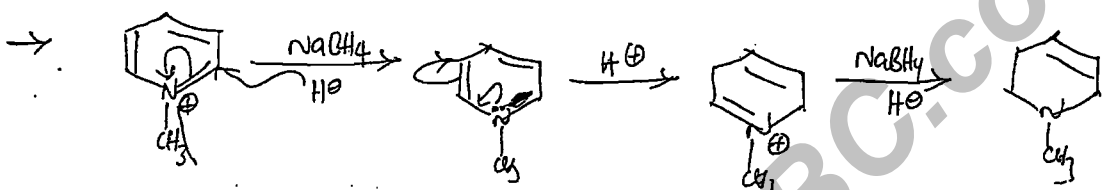


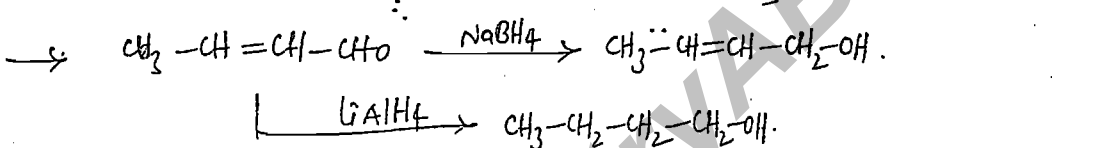


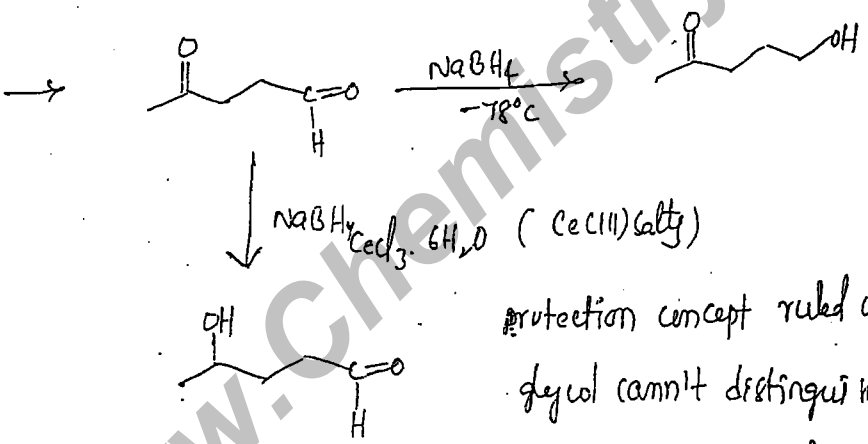




amino acetal/ketal







protection concept ruled out (∵ both are C=O, glycol cannot distinguish)

less reactive carbonyl should reduce over more reactive carbonyl.

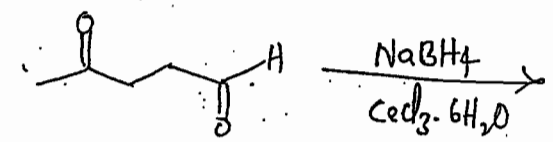
LUCHE'S Reductions :— $NaBH_4 + CeCl_3.6H_2O$

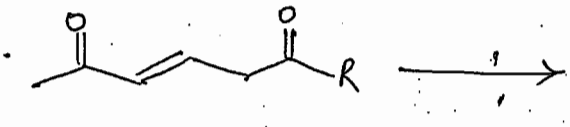
$NaBH_4 + Ce(III)$-salt

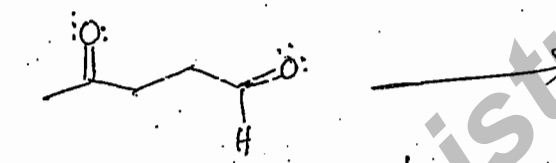
→ $NaBH_4$ in combination with Ce(III) salt selectively reduces "less reactive carbonyl" in carbonyl compds (not ester, others)

→ keto less reactive than aldehyde. → (keto reduction)

→ conjugated carbonyl less reactive than unconjugated or isolated carbonyl ⇒ (unjugated C=O reducth).

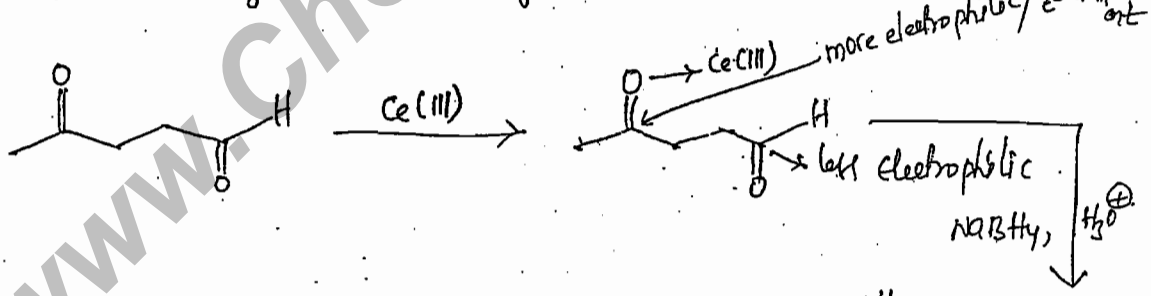
→ 

→ 

→ 

keto carbonyl 'O' good nu$^{\ominus}$ than aldehyde carbonyl oxygen.

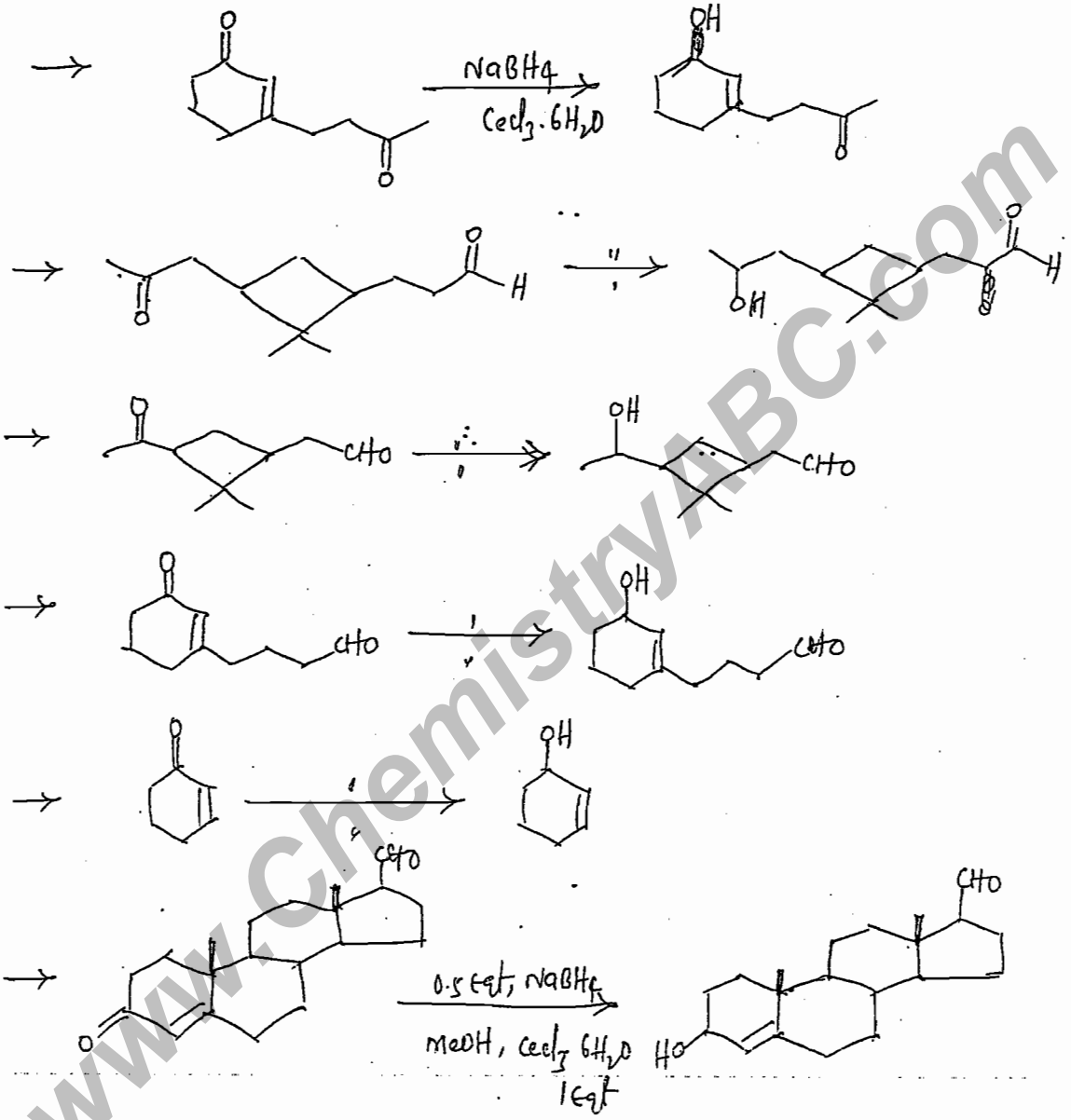
∴ keto is good in reactivity of metal M$^{\oplus}$.



∴ keto carbonyl 'O' preferentially co-ordinate with Ce(III) ion due to its high nucleophilicity, co-ordination of Ce(III) ions with keto carbonyl 'O' makes carbonyl 'C' more e⊖ deficient than competetive

more reactive carbonyl 'C'.

Approaching nuᵉ selectively attacks more eᵉ deficient carbonyl 'C' as a result selective reduction of less reactive carbonyl by leaving behind more reactive carbonyl.



* Alkoxy Aluminates / Lithium Aluminium hydrido alkoxy R.A :-

Alkoxy derivatives of $LiAlH_4$, alkoxy aluminates these are less reactive more selective than LAH.

Solvents :- dry ether

$LiAl(OR)H_3$ $LiAl(OR)_2H_2$ $LiAl(OR)_3H$

$LiAlH_4 + 1Eqt\ R-OH \longrightarrow LiAl(OR)H_3 + H_2$

$" + 2Eqt\ " \longrightarrow LiAl(OR)_2H_2 + 2H_2$

$" + 2Eqt\ " \longrightarrow LiAl(OR)_3H + 3H_2$

eg :- $LiAl(OCH_3)H_3$ $LiAl(OCH_3)_2H_2$ $LiAl(OCH_3)_3H$

$LiAl(OEt)H_3$ $LiAl(OEt)_2H_2$ $LiAl(OEt)_3H$

$LiAl(OiPr)_2H_2$ $LiAl(OiPr)_3H$ } widely used

$LiAl(OtBu)_2H_2$ $LiAl(OtBu)_3H$ }

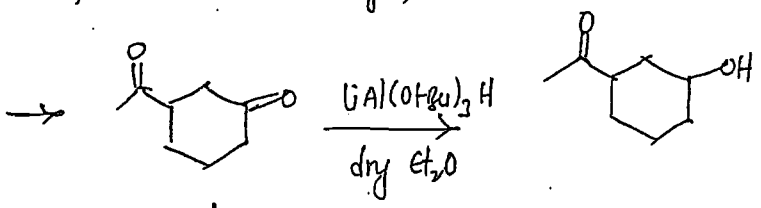
Functions :-

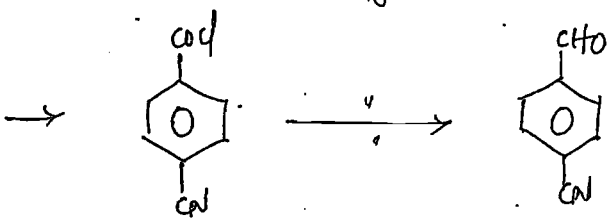
functional gp	alkoxy aluminate	new final gp.
carbonyl	,	alcohol
ester		
acid halide	} ,	→ aldehyde
amide		
nitrile		

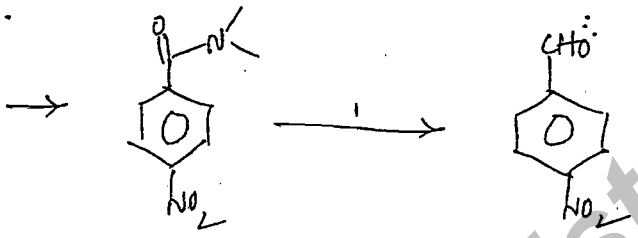
Reactivity :- aldehyde, ketone > ester, acid halide > amide, nitrile

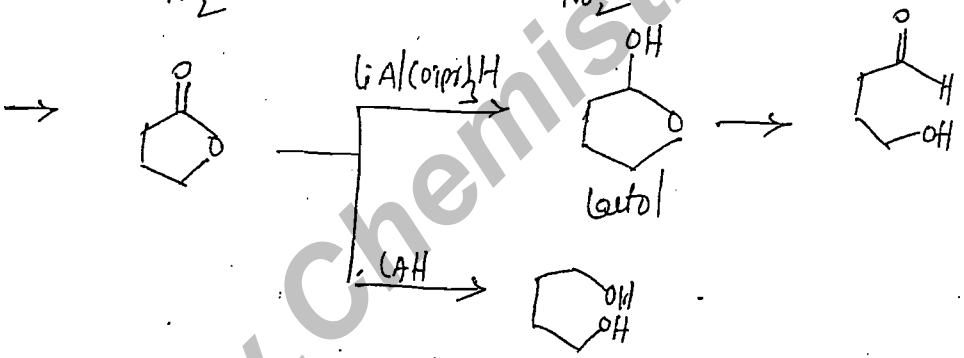
→ Stereochemical aspects similar to $NaBH_4$ & LAH.

→ Selective reduction at sterically less crowded side or face of function (carbonyl)

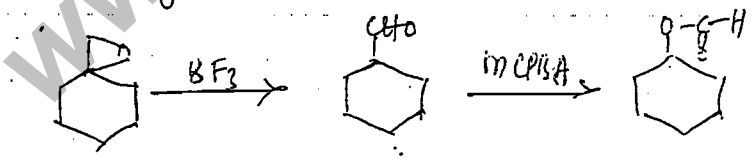


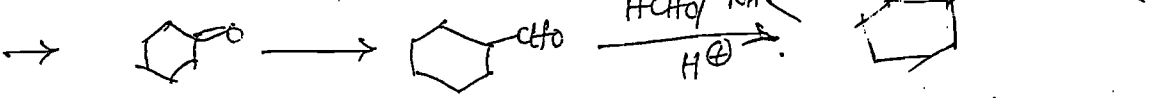






→ alkoxy aluminates reduces cyclic esters (lactones) into lactones

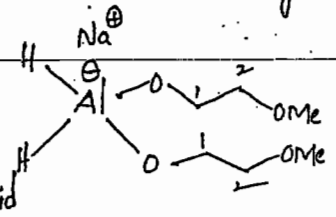




* Red-Aluminium :-

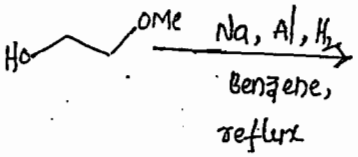
15/05/08

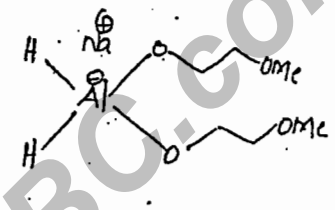
Sodium bis[2-methoxy ethoxy] aluminium hydride



→ Stable, even at high temp, solid.

∴ It can be used for high temp. reductions

* preph :- 2 eqvts 



* Functions :- / Applications :-

Functional gp	Red 'Al'	New functional gp
→ carbonyl (aliphatic)	→	Alcohol
* → carbonyl (aromatic, with ee donating gp's)	→	Hydrocarbon (similar to clemmensons & wolf kishner reductions)
→ geminal dihalo functions	→	Mono-halo functions
→ Epoxides	→	Alcohols
→ Ester, acid halide, amide, nitriles (Red-Al less common for reduction of above fn's)	→	Aldehydes

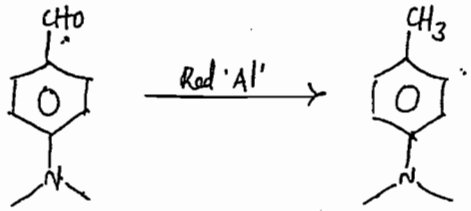
* conjugated carbonyl compd. $\xrightarrow{Red\text{-}Al + CuBr}$ only reduction of unsaturated carbonyl fn uneffected.

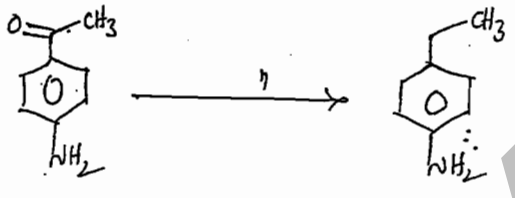
* In some of the R.A. Red 'Al' used as a base.

eg:- Steven's R.A.

examples :-

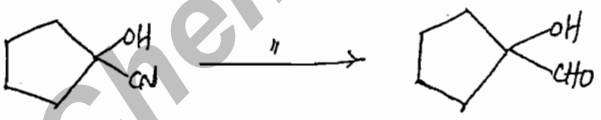
1) $CH_3-(CH_2)_8-CHO \xrightarrow[C_6H_6]{Red\ 'Al'} CH_3-(CH_2)_8-CH_2-OH$

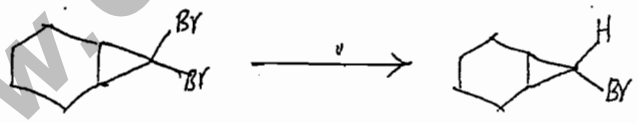
2) 

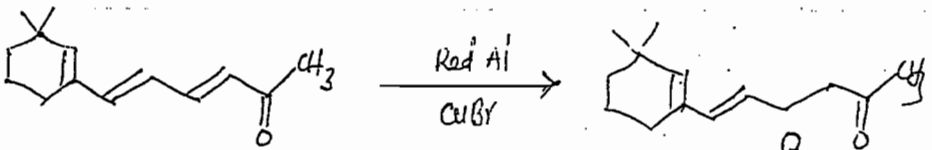
3) 

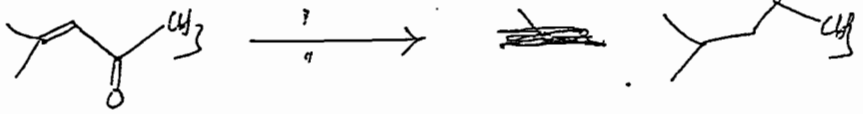
4) 

vanillin

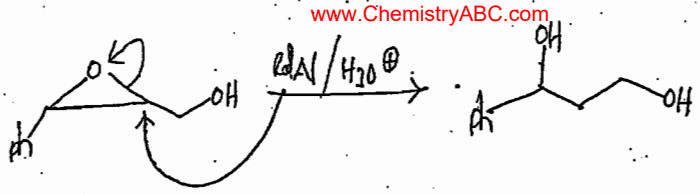
5) 

6) 

7) 

8) 

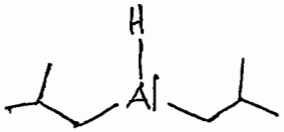
→ g)



(h)

* DIBAL (or) DIBAL-H :- (Di isoButyl Aluminium Hydride)

→ Industrially widely used

→ 

→ gaseous substance : but commercially available in soln form (dissolving in xylene).

Solvents : Toulene, n-hexane (for prepn of DIBAL soln).

⇒ Reaction solvents :- Toulene, xylene, ethers (Et2O, THF & dioxanes etc).

→ Reduction properties of DIBAL-H depends on temp. at which reaⁿ is carried out.

→ At ambient & higher temperatures, DIBAL-H reduction closure to LAH.

→ At low temp. (≈ -78°C) alkoxy aluminate.

→ At high/ambient temp :

Carbonyl —DIBAL-H→ Alcohol

Acid halide, ester, anhydride } ——→ " "

Amide, Nitrile $\xrightarrow{"}$ Amine

Epoxide $\xrightarrow{"}$ Alcohols.

At lower temperatures :

→ Carbonyl $\xrightarrow{DIBAL-H}$ alcohol

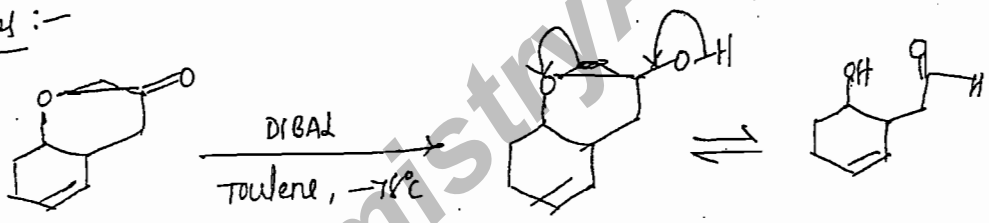
Acid halide, esters, amides, nitriles $\xrightarrow{"}$ Aldehydes

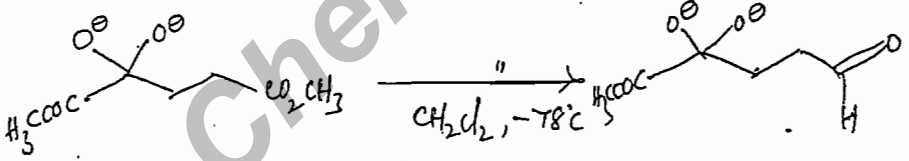
Epoxide $\xrightarrow{"}$ Alcohol.

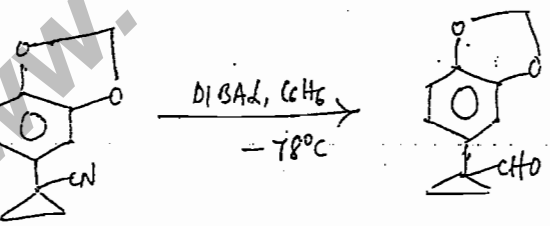
→ In few cases, it reduces alkynes into cis alkenes (only cis)

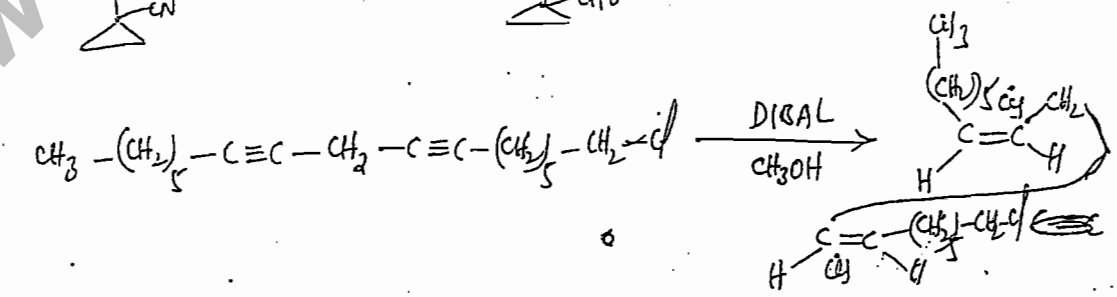
→ In the presence of methyl copper, it selectively reduces only unsat of α,β-unsaturated carbonyl compounds or esters.

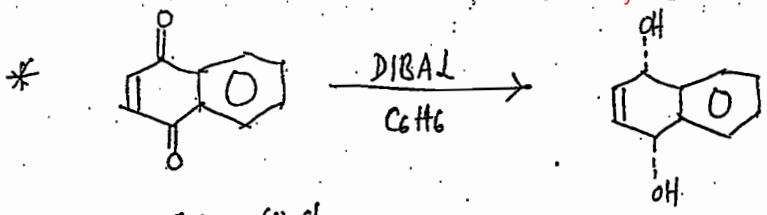
Examples :-

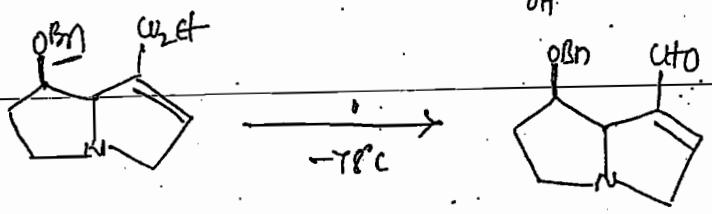
→ 

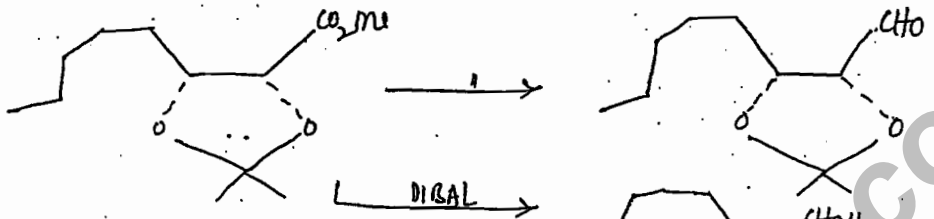
→ 

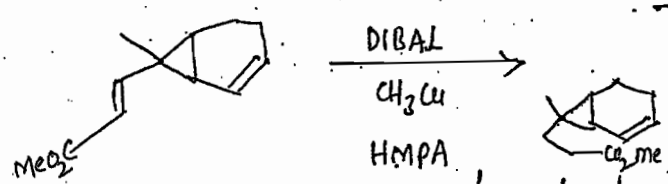
→ 

→ 



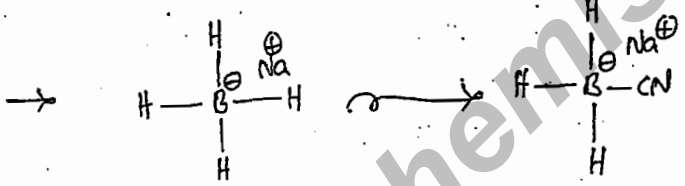






Chexamethylene phosphoramide).

* SODIUM CYANO.BOROHYDRIDE :— $NaBH_3(CN)$

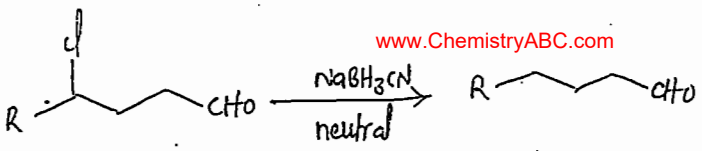


→ 'CN' withdrawing gp, stabilises borohydride

→ compared to $NaBH_4$, less reactive / more selective in reductions.

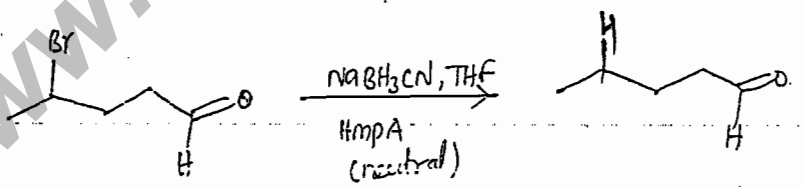
→ Reactivity of $NaBH_3(CN)$ depends on pH of rean medium (neutral, acidic, basic etc).

→ under neutral conditions (pH ≈ 7), selectively displaces halo & tosyloxy groups, any other fns (carbonyl, epoxy etc) unaffected.



* At pH ≈ 2 to 3; reduces carbonyl @ into alcohol.
* At pH ≈ 5 to 6, reduces imines into amines.
* In acidic medium, tosyl hydrazones of alicyclic, acyclic carbonyl compds reduced into hydrocarbons.
* opens epoxy into alcohol. (In acidic medium, opens at sterically more crowded position).

Functions	$NaBH_3CN$	new fn
Carbonyl	$NaBH_3CN$ / pH: 2–3	Alcohols
Halo / tosyloxy displacement	" / pH ≈ 7 / HMPA	hydrocarbon
Imine / Iminium salt	" / pH ≈ 5 to 6	Amines
Tosyloxy hydrazones	" / acidic	Hydrocarbons
Epoxy	"	Alcohol.

*


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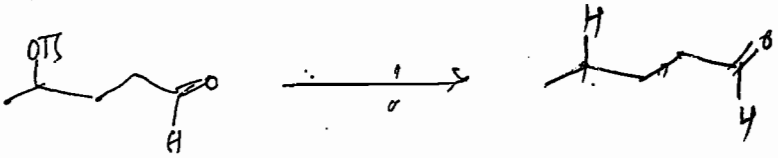
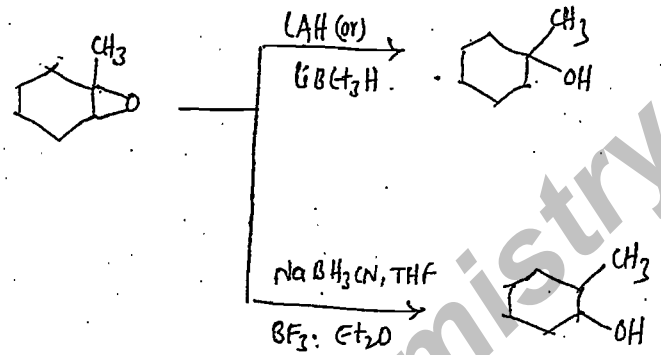


* $(CH_3)-(CH_2)_8-CHO \xrightarrow[pH \approx 2-3]{NaBH_3CN} CH_3-(CH_2)_8-CH_2OH$

* $Ph-\underset{H}{C}=O + H_2N-R \xrightarrow{H^\oplus} Ph-\underset{H}{C}=N-R \xrightarrow[NaBH_3CN;\ H_3O^+]{HCl\ (gas)\ ;\ pH\approx 6} Ph-CH_2-NH-R$

* $Ph-CH_2-\underset{O}{C}-\underset{O}{C}-O^\ominus Na^\oplus \xrightarrow{NH_4Br} Ph-CH_2-\underset{\overset{\oplus}{N}H_2\ Br^\ominus}{C}-\underset{O}{C}-O^\ominus Na^\oplus \xrightarrow[pH\approx 6]{NaBH_3CN,..} Ph-CH_2-\underset{NH_2}{CH}-COOH$

*

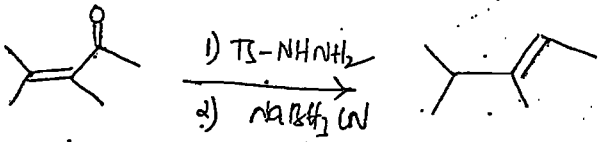


(because of presence of lewis acid BF_3, opening of epoxide at more sterically crowded by $NaBH_3CN$)

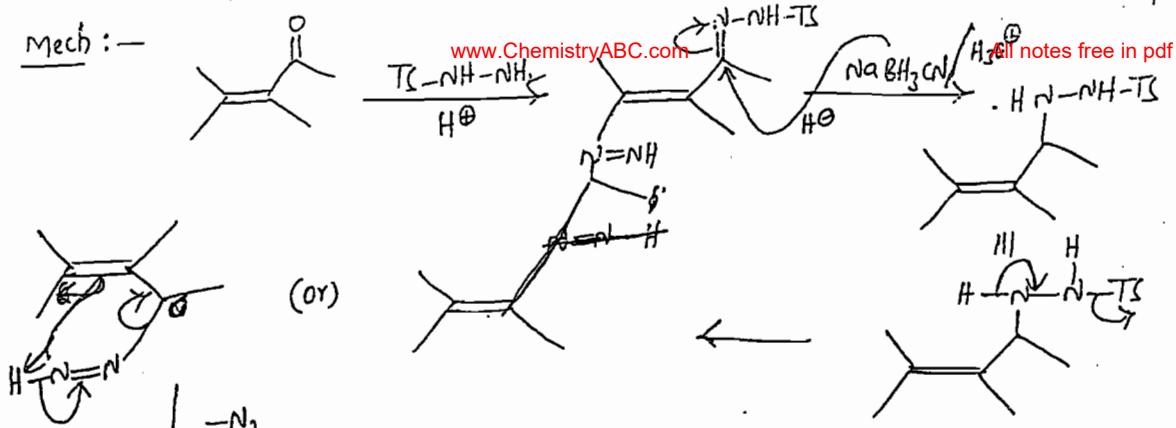
*) $CH_3-(CH_2)_8-CHO \xrightarrow[2)\ NaBH_3CN]{1)\ OTs-NH-NH_2} CH_3-(CH_2)_8-CH_3$

$CH_3-(CH_2)_8-CHO \xrightarrow{1)\ Ts-NH-NH_2} CH_3-(CH_2)_8-CH=N-NH-Ts \xrightarrow{2)\ NaBH_3CN} CH_3-(CH_2)_8-CH_3$

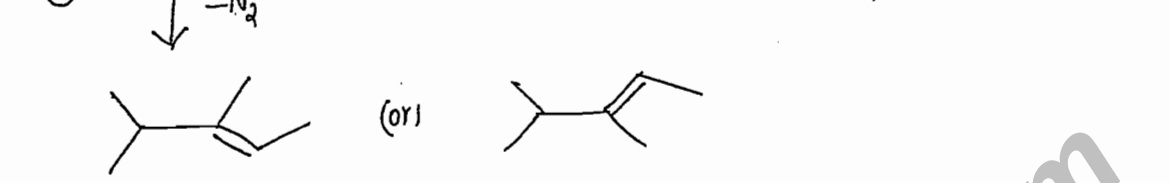
* whenever carbonyl fn in conjugation with α,β-unsaturation, isomerisation of unsaturation takes place.



Mech :—



(or)



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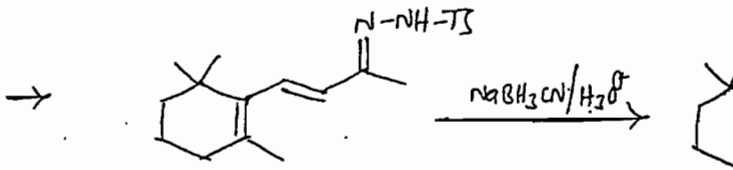
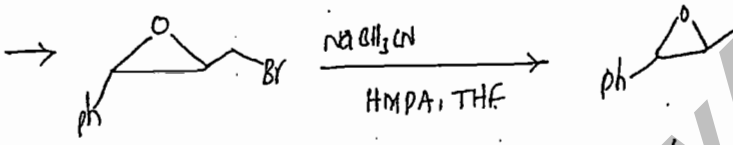
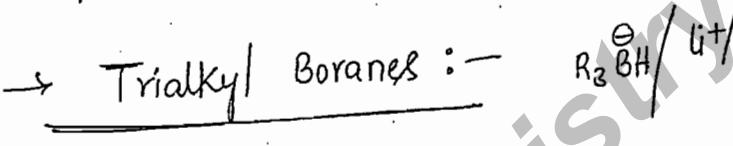
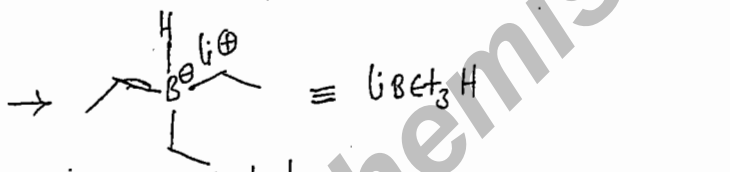


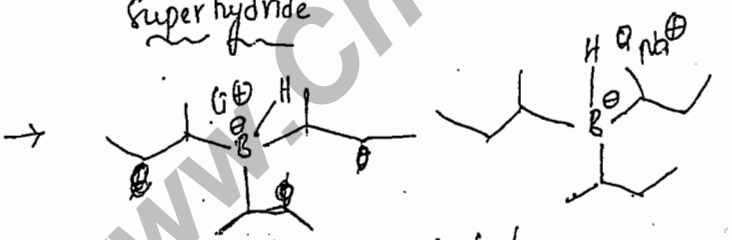




→ Trialkyl Boranes :— $R_3\overset{\ominus}{B}H$ / $Li^+/Na^+/K^+$



Super hydride



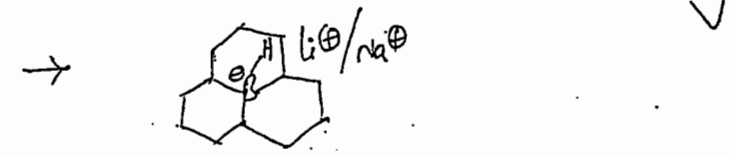
tri sec-butyl Borohydride

$LiB(SC_4H_9)_3H$

Li-selectrides

Na- " "

K- " "

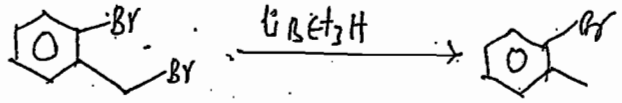


Super hydrides : $Et_3\overset{\ominus}{B}H\ Li^{\oplus}$

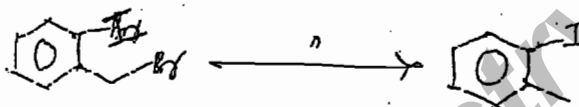
→ Super hydride is powerful in displacement of halo & tosyloxy compared to $NaBH_3CN$, $LiAlH_4$ etc, ∴ called 'Superhydride'.

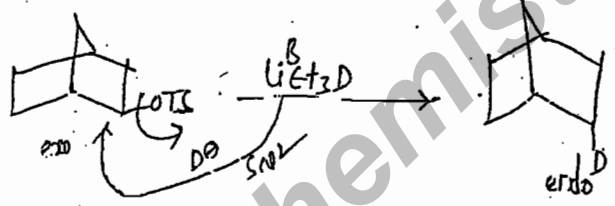
→ In a molecule, if variety of halo positions present, 1°/2°/3°, aryl, vinyl, alkenyl, Superhydrides displaces selectively 1°/2° halo groups only.

→ Displacement of halo & tosyloxy is S_N2 type.

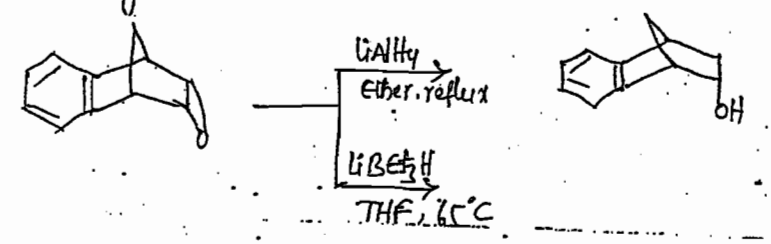
→ 

→ Bromo & Iodo are excellent leaving gps for Superhydride displacement.

→ 

→ 

functions	Superhydride	new function
→ 1°/2° halo, tosyloxy	→	Hydrocarbon
→ Epoxy	→	Alcohol
→ Carbonyl	→	alcohol

→ 

Date : 16/05/08

* Electrophilic Reducing agents :—

→ $H^{\ominus}$ ion transfer reductions.

eg: Alane, Borane

(AlH_3), $(BH_3) \Rightarrow B_2H_6$

Alane :— AlH_3, exists in polymeric form, $(AlH_3)_n$

→ white crystalline solid substance

→ compared to LAH, it is stable

Prepn :— $LiAlH_4 + AlCl_3 \longrightarrow AlH_3 + LiCl$

Reactant $\xrightarrow{LAH/AlCl_3}$ product

$\Downarrow$

AlH_3

* sensitive to air, moisture.

* **Solvents :—** Dry ethers, THF, Et_2O

→ Reduction properties of Alane are closure to LAH.

* powerful in reduction of esters compared to LAH. } IMP.

* Alane can't reduce halo, tosyloxy, nitro functions. } IMP.

* Acid-halide reduction depends on conditions :—

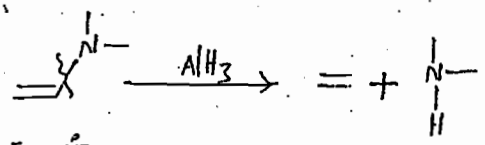
* Alane can open acetals, ketals.

* In α,β-unsaturated carbonyl compds, esters, amides, nitriles, selectively reduces only function, unsaturation unaffected.

$$ph-CH=CH-CHO \xrightarrow{LAH} ph-CH_2-CH_2-CH_2OH.$$

$$\underset{|}{} \xrightarrow{AlH_3} ph-CH=CH-CH_2OH.$$

→ capable in reduction of ENAMINES



Enamine

Functions :-

AlH_3 (or) LAH/$AlCl_3$ → new function.

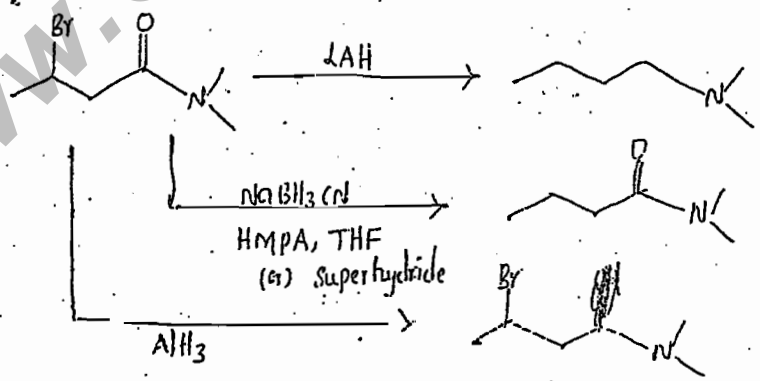
carbonyl
ester (better than LAH)
acid halide
anhydrides
} → Alcohols

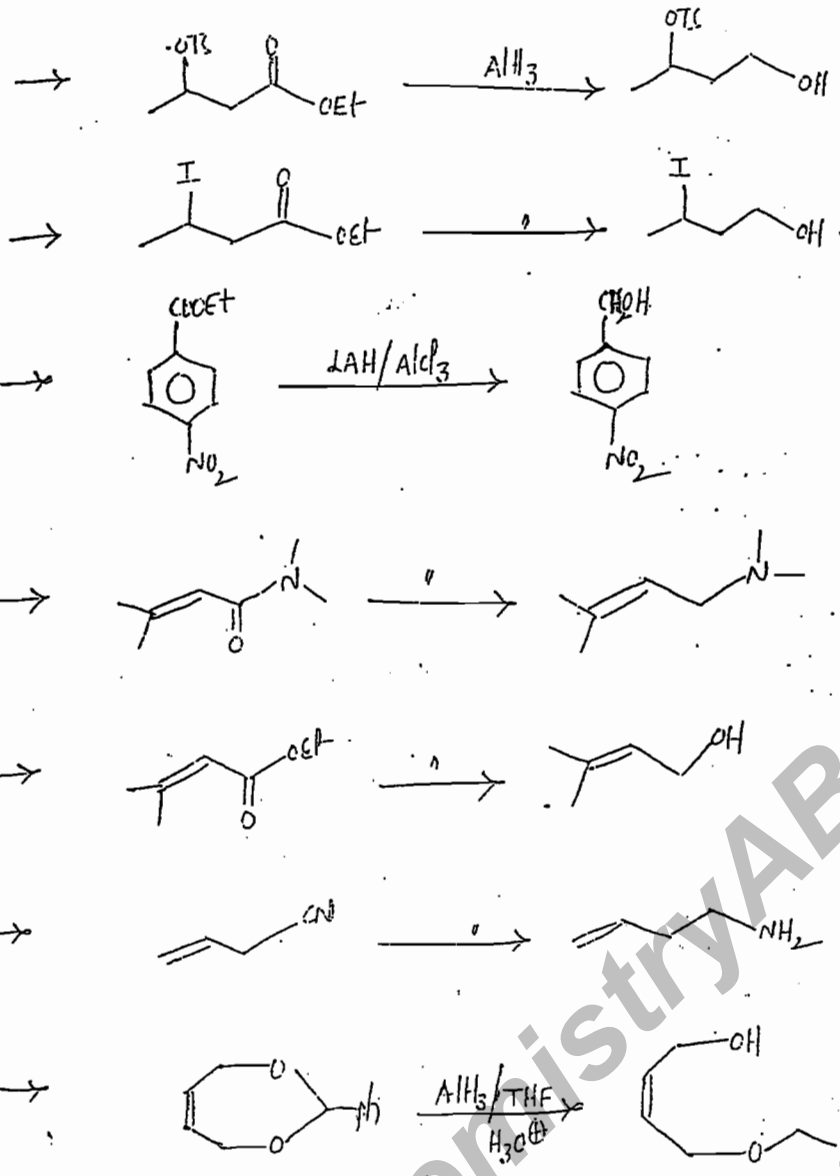
Amide, nitrile
Imine, Iminium ion
Enamine, oxime
} → Amine

Epoxide → Alcohol

* Halo, tosyloxy, nitro → AlH_3 // Inert

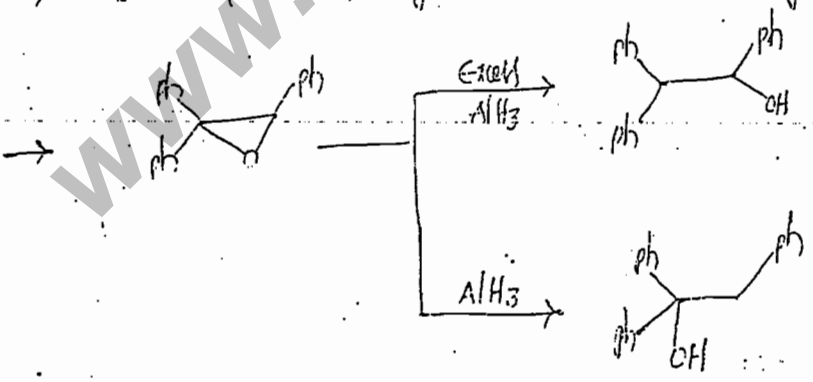
eg:-





* Epoxide opening : S_N^2 type ; In excess alone, sterically crowded position.

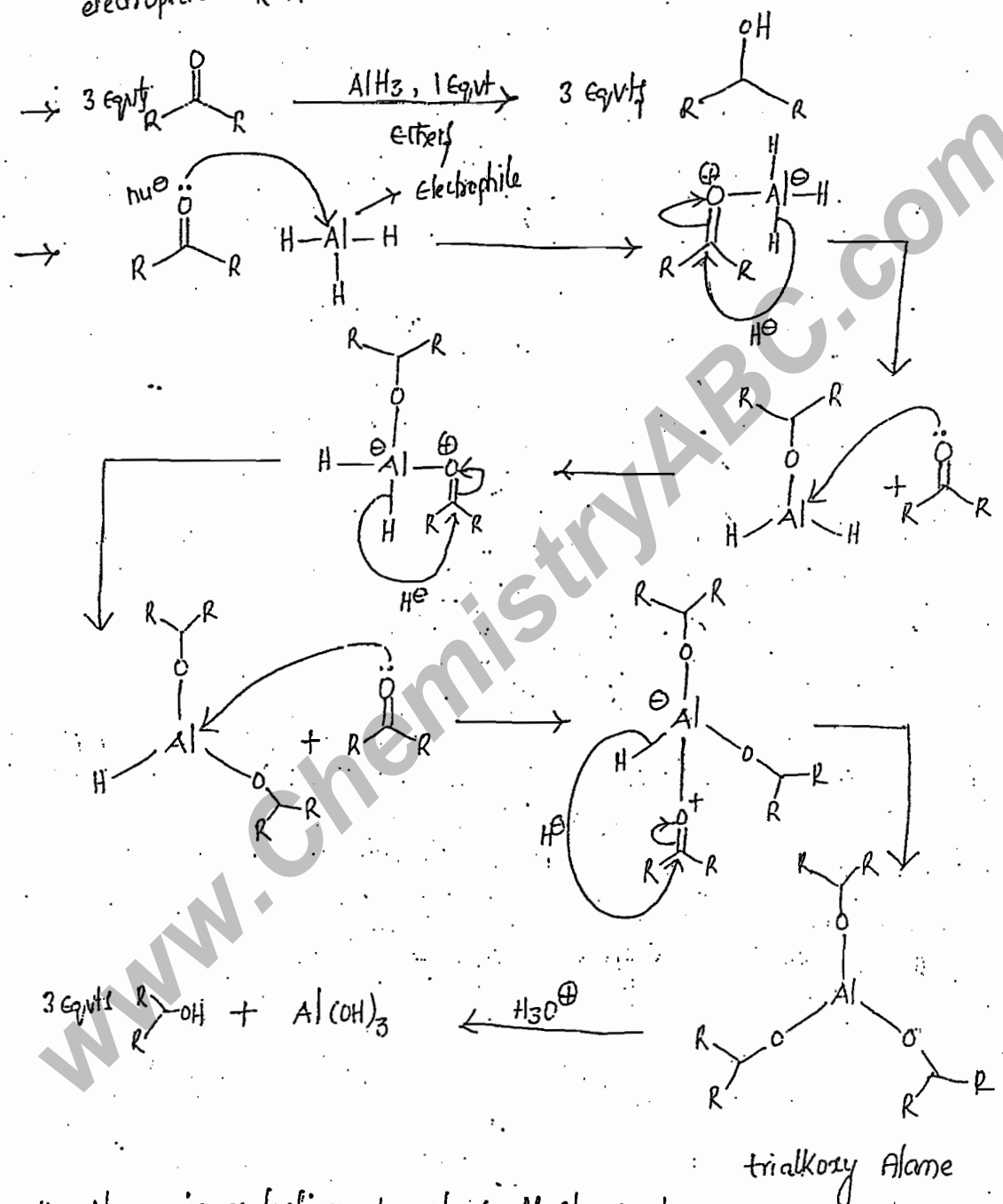
→ Stoichiometric opening of epoxide at sterically less crowded.



Mechanism :— Electrophilic R.A.

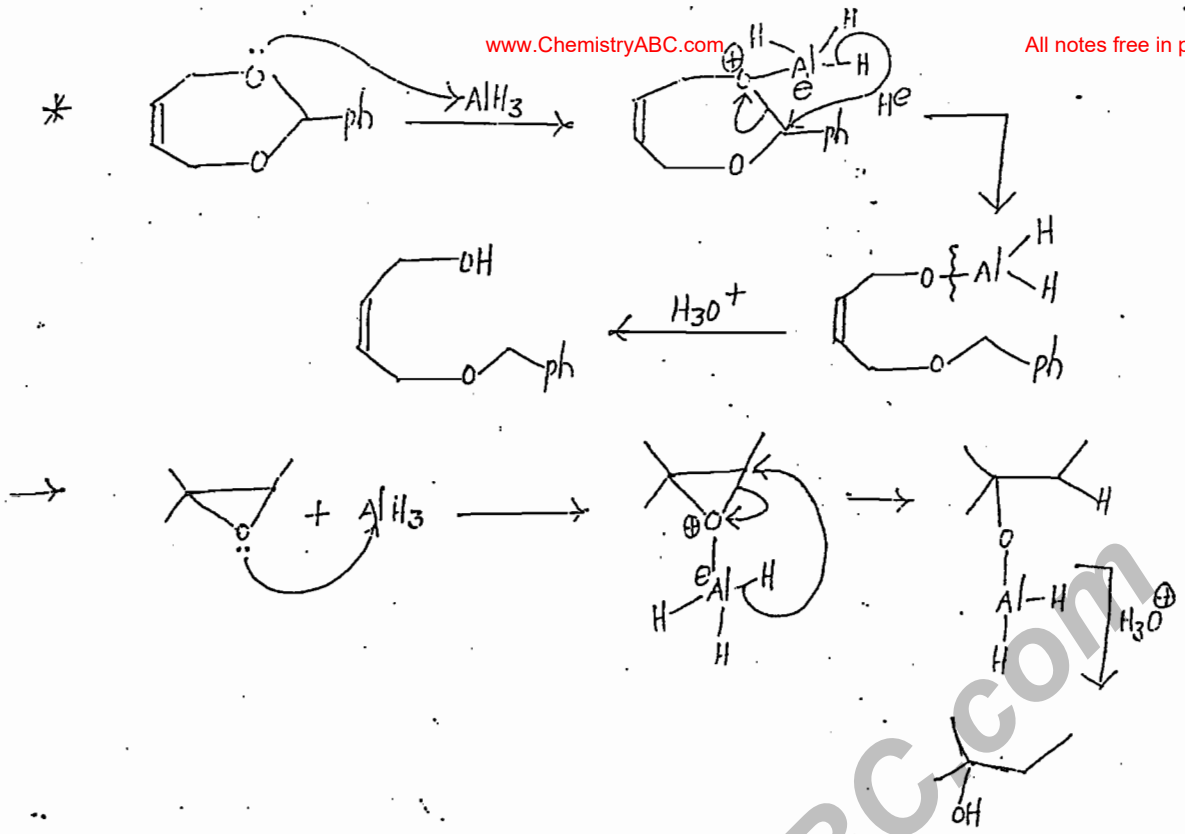
H—Al—H } lewis acid, incomplete octet, acts as electrophile.

→ In reduction of functional group, as ⊕ it approaches called "electrophilic R.A".

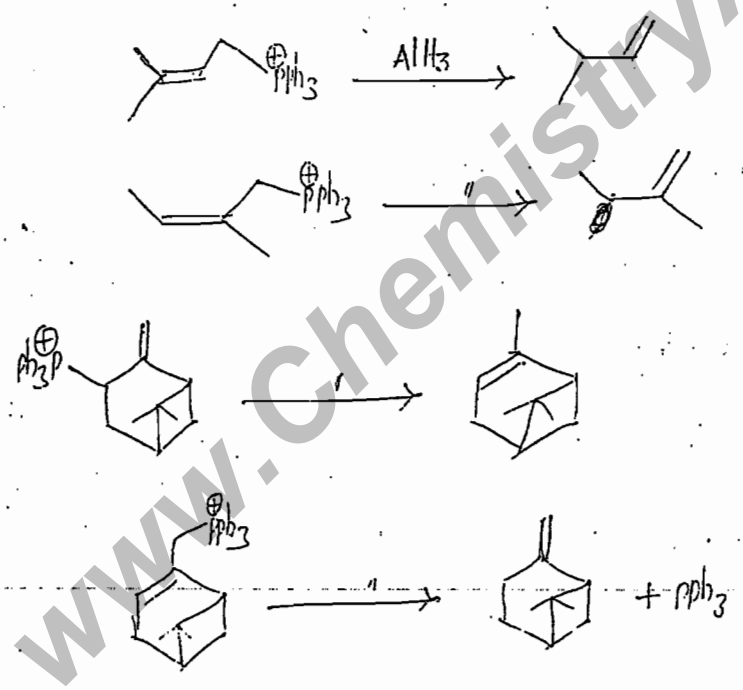


* Alane in reduction transfers all its hydrogens.

∴ Stoichiometry 3:1



* Alane can act as catalytic medium in allylic R.A.



* Borane : BH_3 ;

→ In monomeric form unstable, exists as dimer ; diborane.

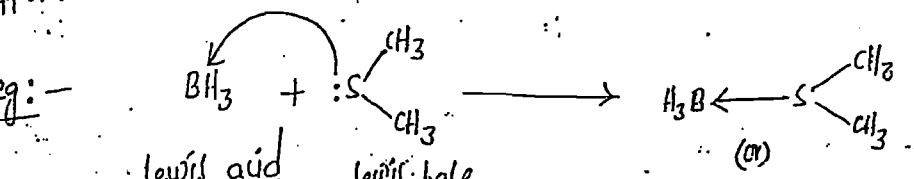
→ Although it exists in dimeric form ; the attacking species is-

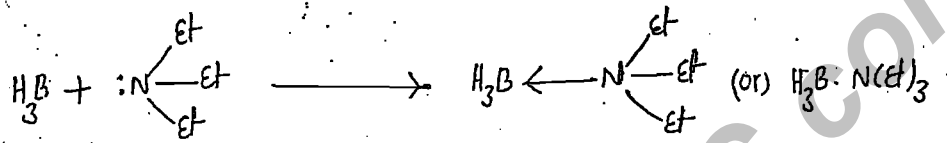
reduction: BH_3, monomer.

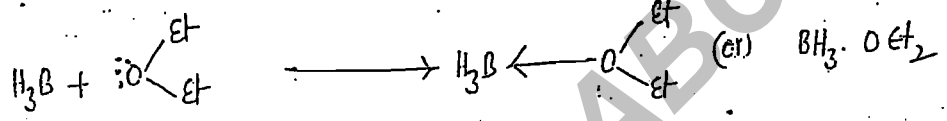
→ BH_3 + support;

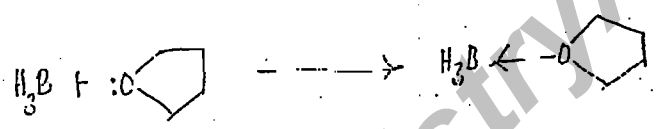
To stabilise in monomeric form, lewis base should be used as support.

eg:-



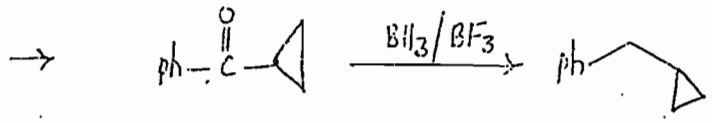




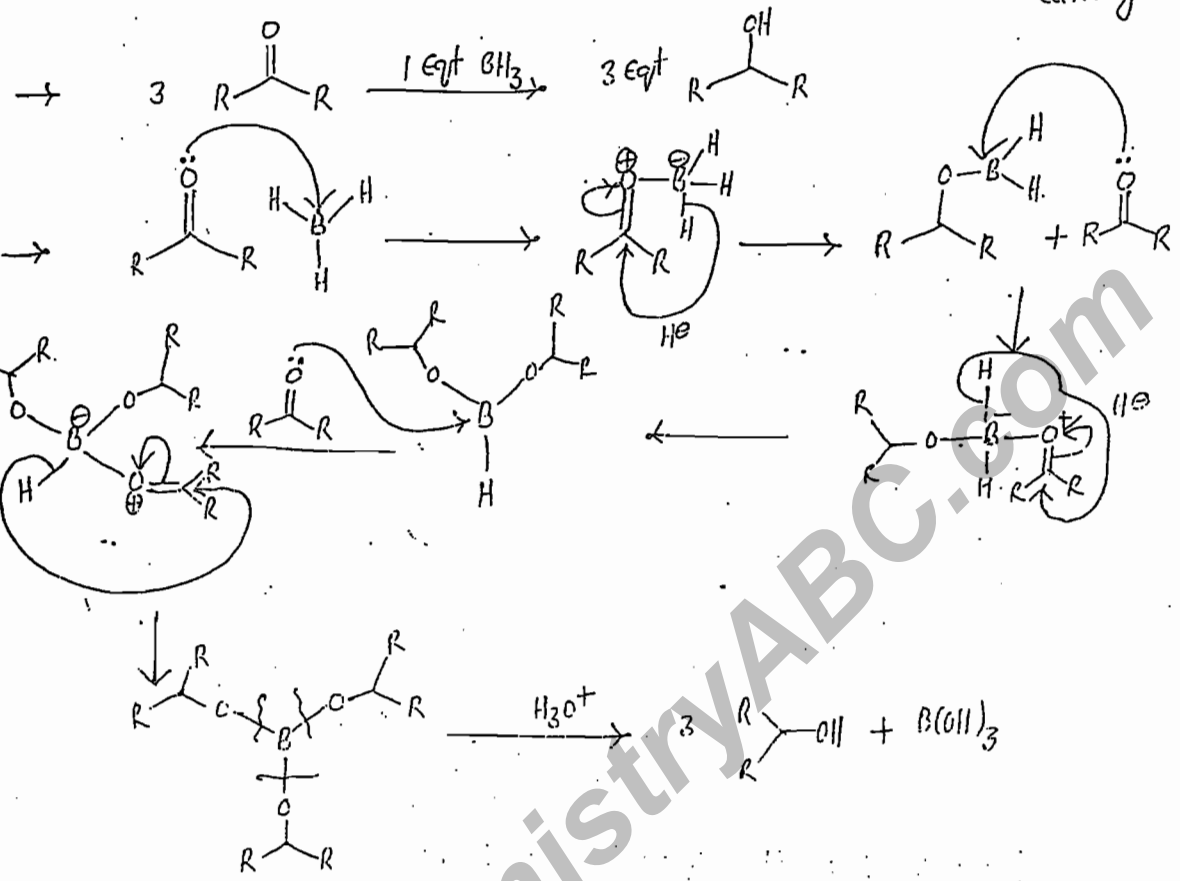


prepn:-

* $NaBH_4 + BF_3.Et_2O \longrightarrow NaBF_4 + B_2H_6$.
* 99% LAH; properties of Boranes are almost same as LAH reduction properties.
* ∴ versatile reducing agent.
* Excellent reagent in reduction of carboxylic acids compared to LAH.
* If molecule having multiple functions, selective in reduction according to their reactivity order.
* Inert in reduction of acid-halides (eg: RCOCl etc)
* In some of the aromatic carbonyl reductions, products are hydro carbons, not alcohols.



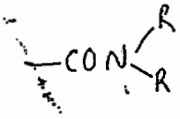
* Mechanism :- (Same as Alane reduction) ; 1Eqvt BH_3 can reduce 3 equiv Carbonyl.

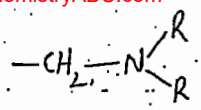


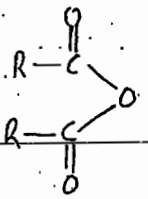
→ Reactivity ↓es with ↑se in no. of alkoxy group.

⇒ Reactivity order in reduction of various functional groups :-

Functional	New functions
$-CO_2H$	$-CH_2OH$
$-CH=CH-$	$-CH_2-CH_2-$
$-CHO$	$-CH_2OH$
$-\overset{\overset{O}{\|}}{C}=O$	$-\underset{\underset{\oplus}{|}}{CH}-OH$
$-C\equiv N$	$-CH_2-NH_2$

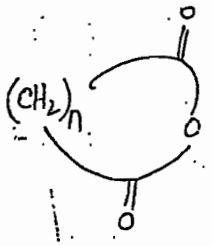


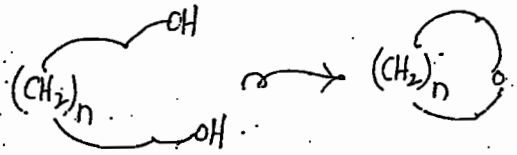


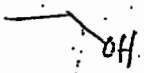


$R-CH_2-OH$

$R-CH_2-OH$







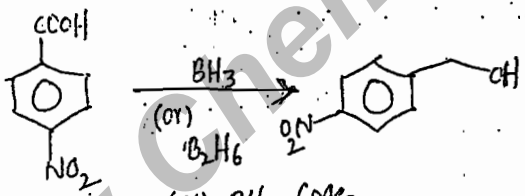
$-CH_2R$

$-CH_2-OH$

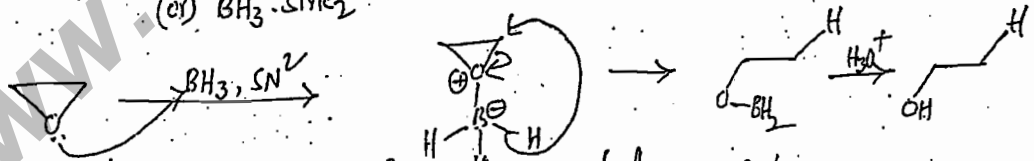
* $-COCl$ ⟶ No reaction. } Inert ;

* $-NO_2$ ⟶ No reaction }

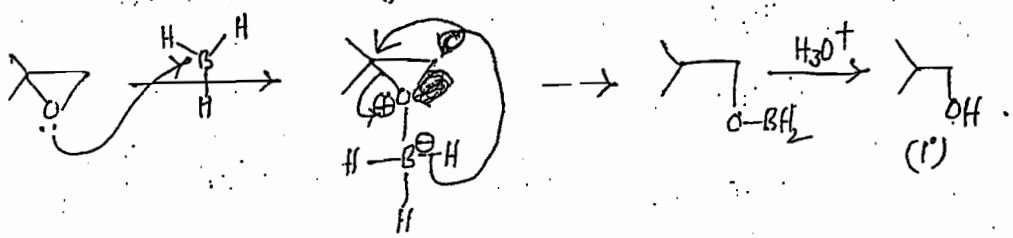
⇒ from top to bottom, reactivity with borane ↓ (e).

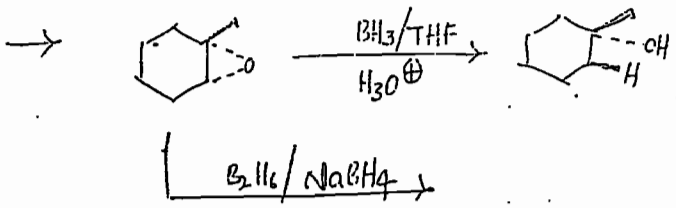
→ 

(or) $BH_3.SMe_2$

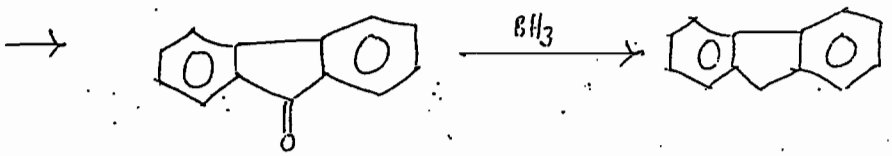
* 

epoxide opens at sterically more crowded — SN^2 type

* 



$B_2H_6/NaBH_4$



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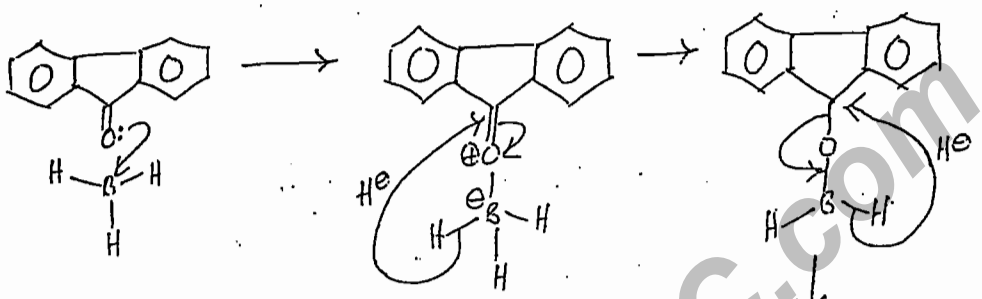
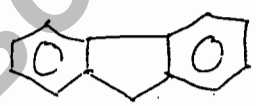
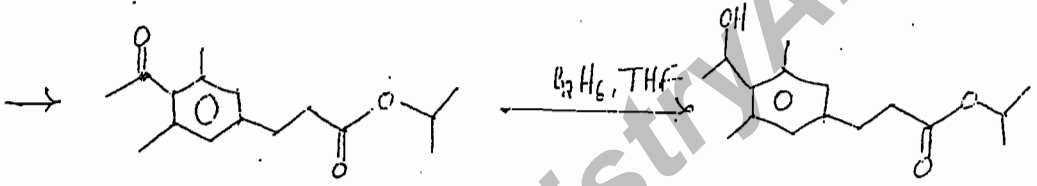
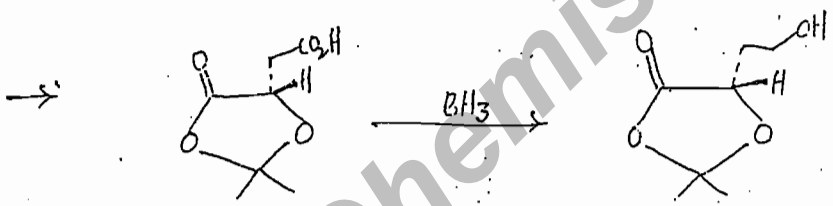


$H_3BO_3 \xleftarrow{H_3O^{\oplus}} H-B=O$ +







→ Electron-Transfer reductions :-

→ Reagents are metal in acid/ metal in base.

Metals: d-block metals Fe, Sn etc

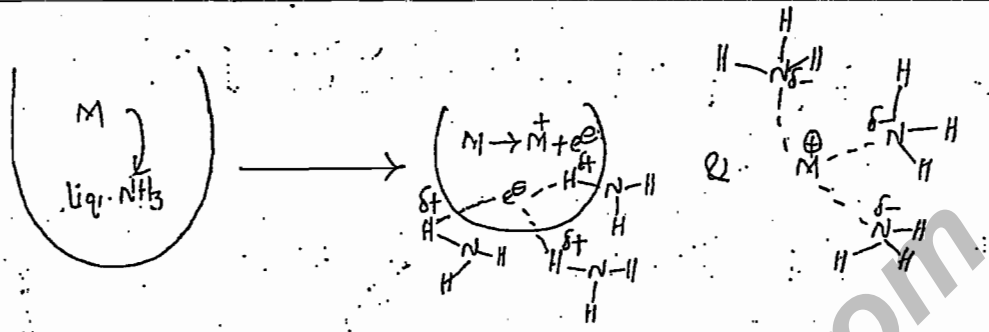
IA group metals Li, Na, K

IIA " Ca, Mg

* Metal – Base medium :— Reductions.

Metals : IA – group : Li/Na/K

Bases : liq. NH_3 (or) $R-NH_2$



* proton donors : 1) Alcohols (CH_3OH, CH_3CH_2OH, iproH, t_{BuOH})

2) aq. NH_4Cl

3) Amines / Ammonia

If alcohols & aq. NH_4Cl not used, Amines / Ammonia acts as proton donors.

* Solvents :— Dry Ethers

Et_2O, THF, dioxane

Applications :—

*) Reduction of conjugated olefins into isolated olefins.

*) Reduction of aromatic hydrocarbons ⟶ unconjugated olefins.

(or) 1,4-dihydro products

*) " " Simple carbonyl compds ⟶ alcohols.

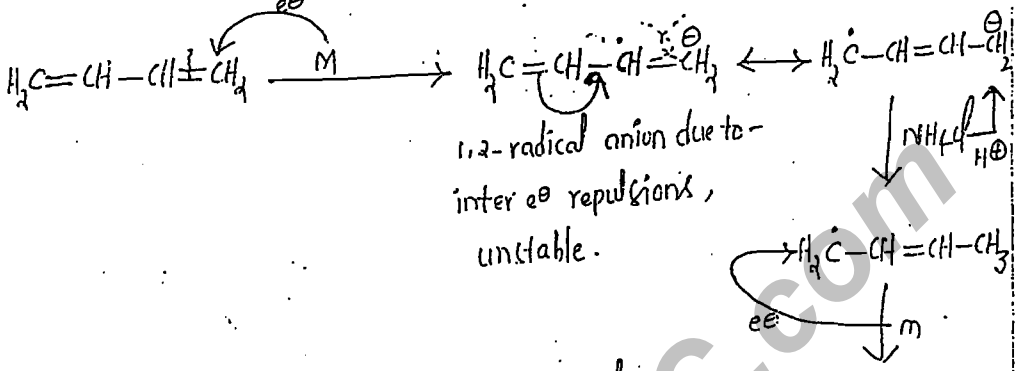
* Redn of α,β-unsaturated carbonyl compds ⟶ Sat. alcohols + Sat. carbonyl compounds + unsaturated alcohols.

5) Reduction of Alkynes into trans alkenes.

1) Reduction of conjugated alkenes → isolated alkenes.

$H_2C=CH-CH=CH_2 \xrightarrow[aq.\ NH_4Cl]{Metal/liq.NH_3} H_3C-CH=CH-CH_3$ (2-butene)

Mech:-



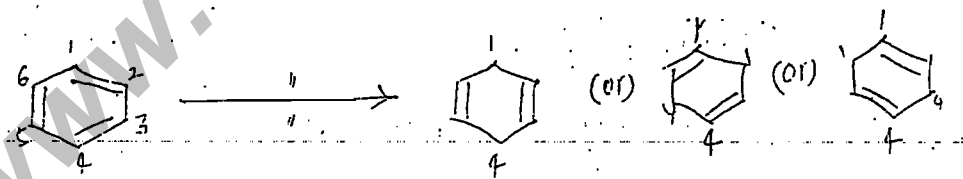
$H_3C-CH=CH-CH_3 \xleftarrow[H^{\oplus}]{NH_4Cl} H_2\overset{\ominus}{C}-CH=CH-CH_3$

$\rightarrow H_2C=\underset{CH_3}{\underset{|}{C}}-CH=CH_2 \xrightarrow[aq.\ NH_4Cl]{Li/liq.NH_3} H_3C-\underset{CH_3}{\underset{|}{C}}=CH-CH_3$

2) Reduction of Aromatic hydrocarbons : (Birch-Reductions) :

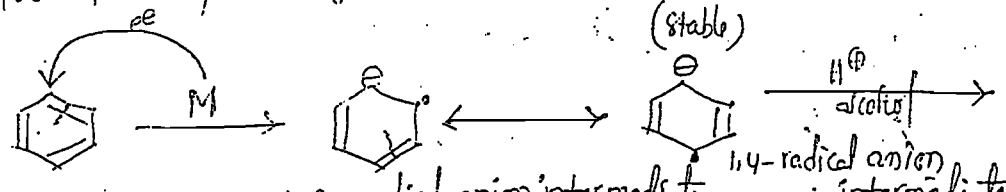
Aromatic Hydrocarbons $\xrightarrow[Alcohols]{M/liq.NH_3/R-NH_2}$ 1,4-dihydro products (partial reductions).

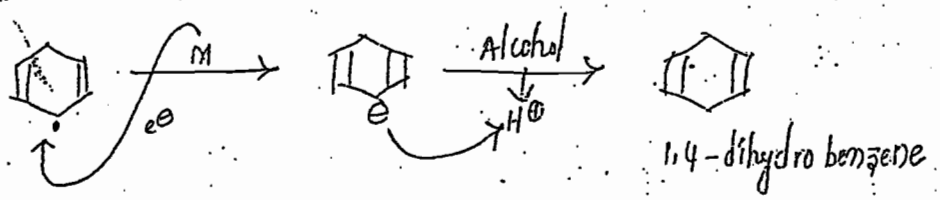
M = Li/Na/K



→ opposite positions (1,4) get reduced.

Mech:-

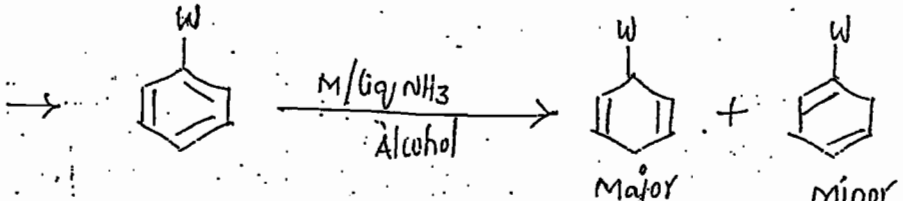


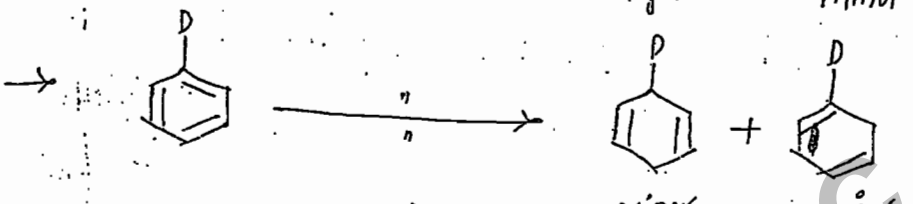


1,4-dihydro benzene

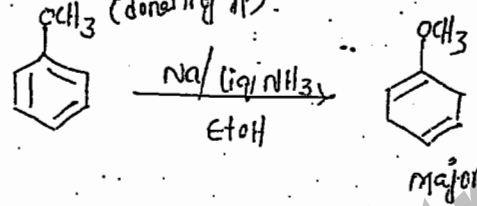
V. IMP:-

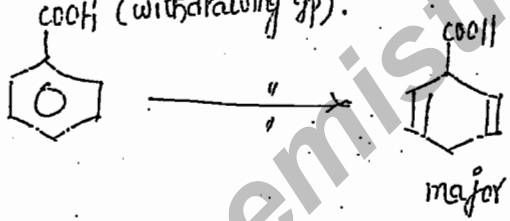
Regio Selectivity : Substituent Effects :





eg:-

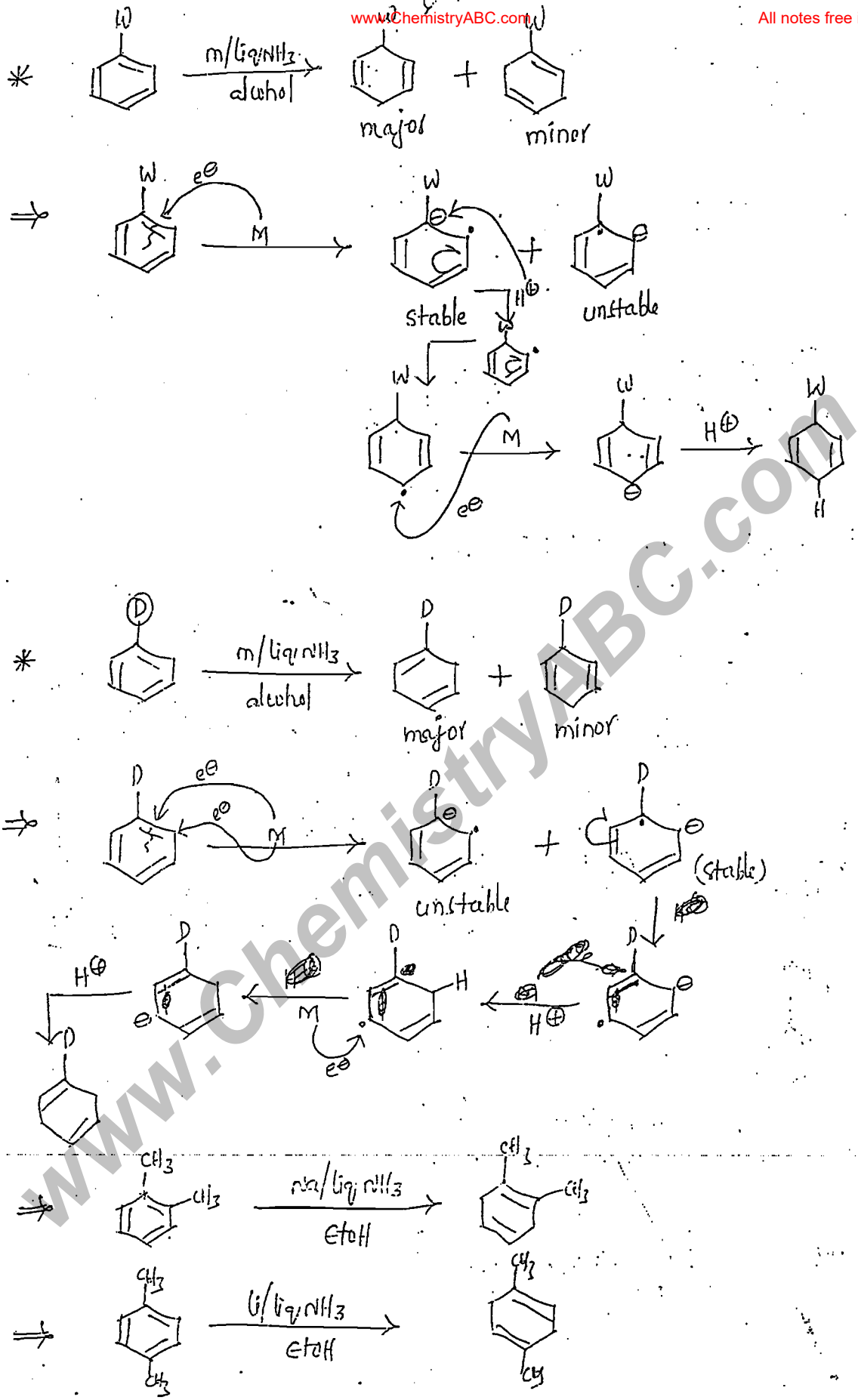


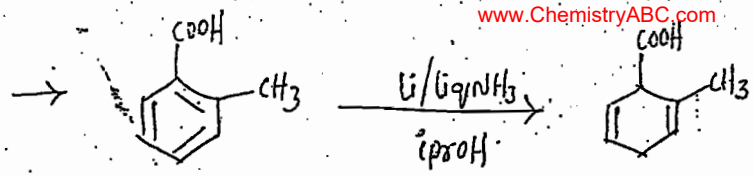


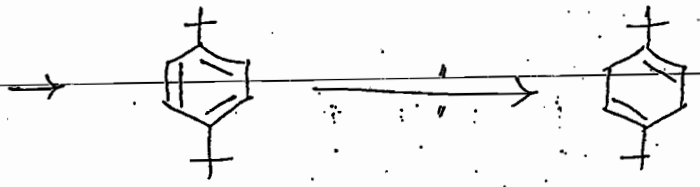
⇒ Aromatic skeleton attached substituent directs reduction in regio selectivity.

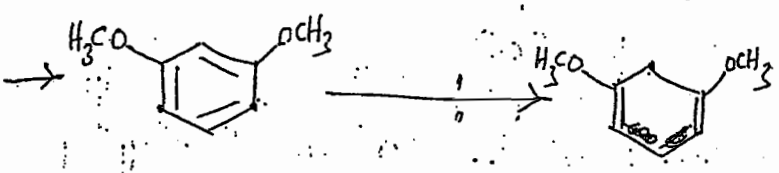
* on Aromatic skeleton, if withdrawing gp present, withdrawing gp attached position selectively get reduced ⇒ Ipso-Reduction, Resulting product predominate.

* If aromatic skeleton attached to ee donating gp, o-position of donating gp predominately reduced, resulting product major.









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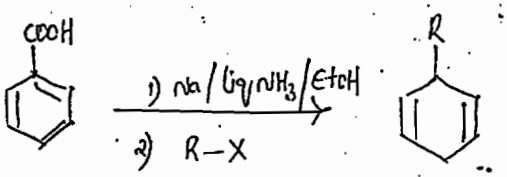
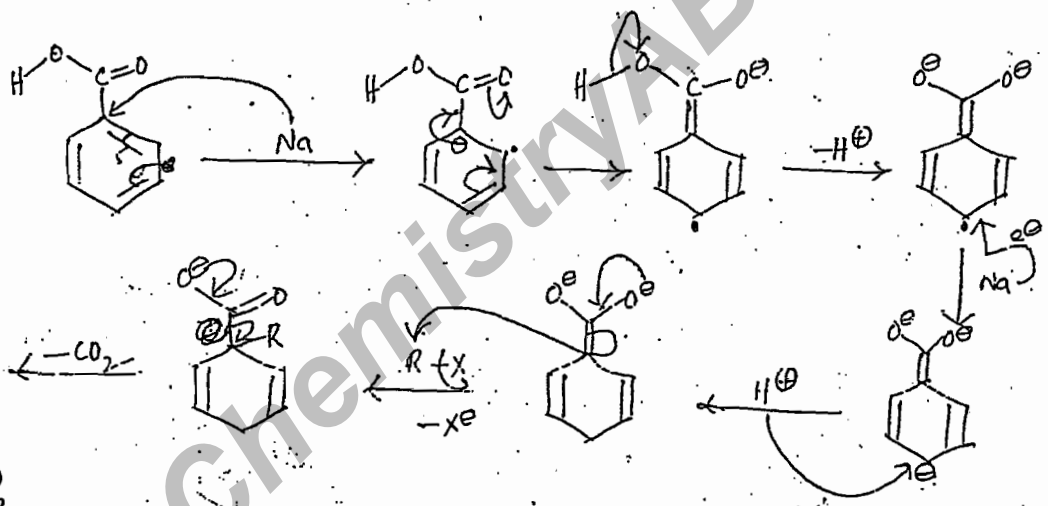
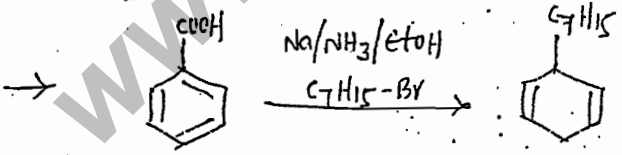
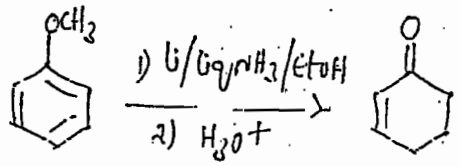
* 

Mech :- 



V. Imp :- 

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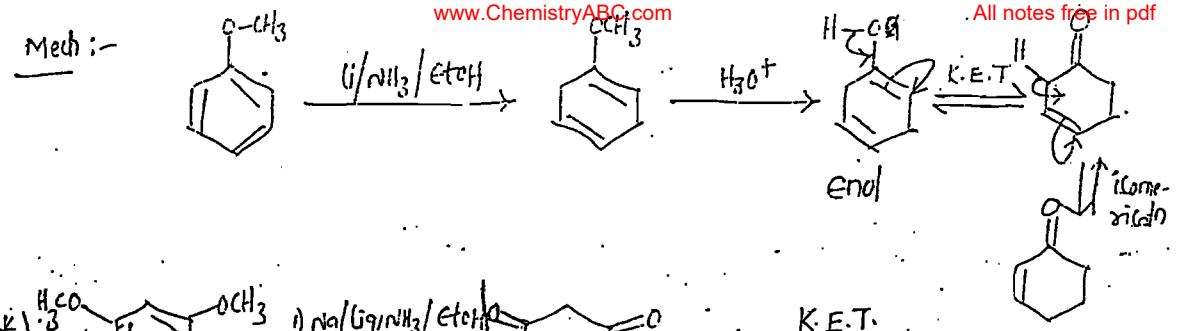

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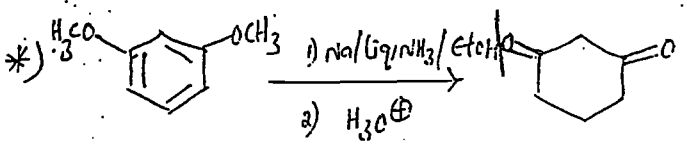
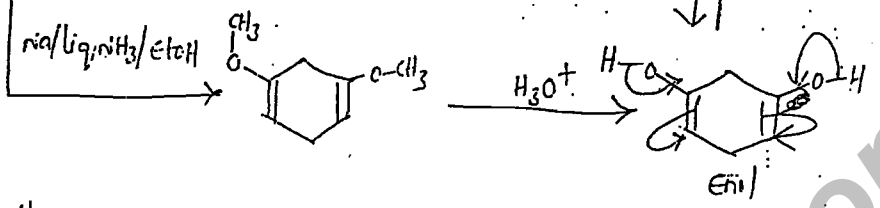


K.E.T.



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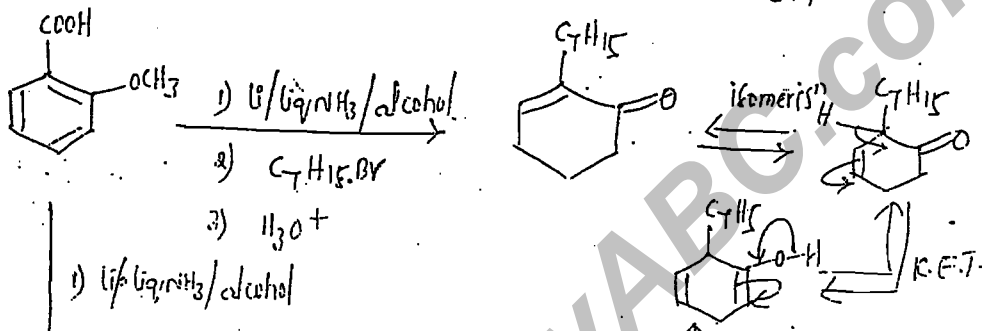

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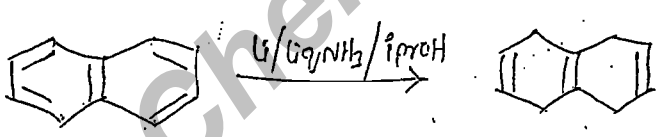

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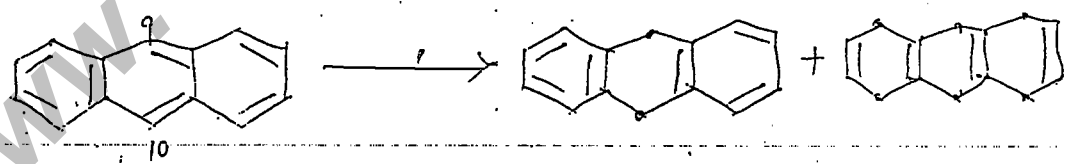

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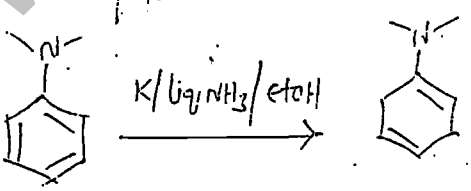
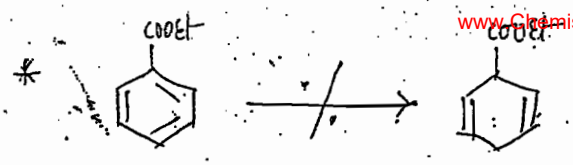
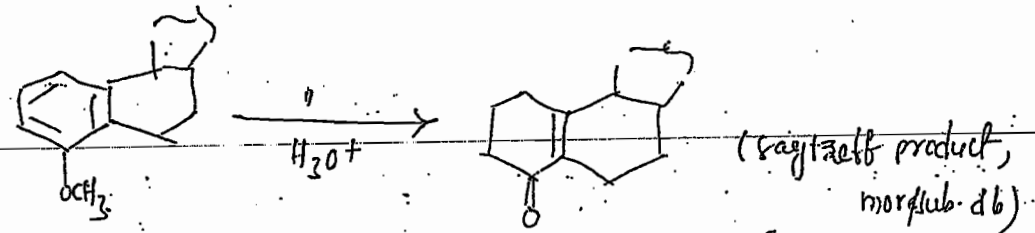
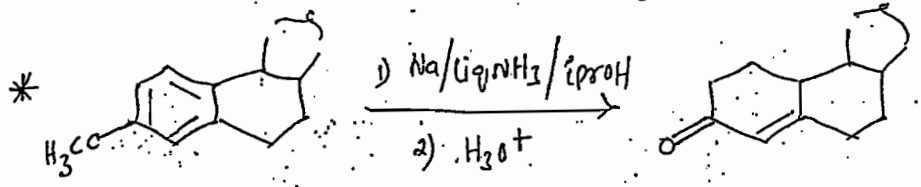
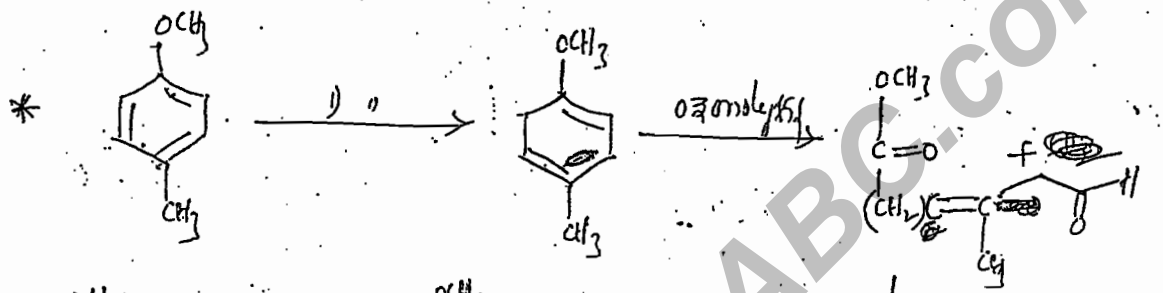
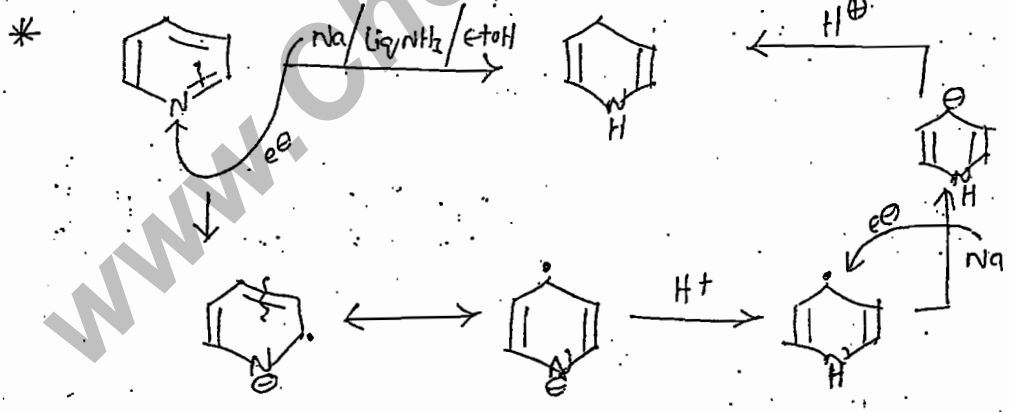


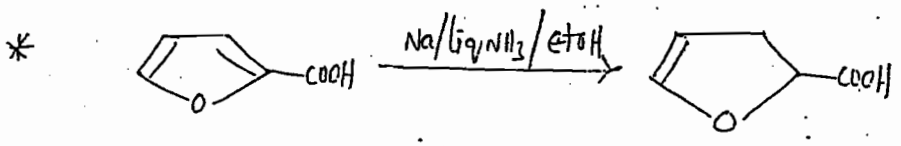


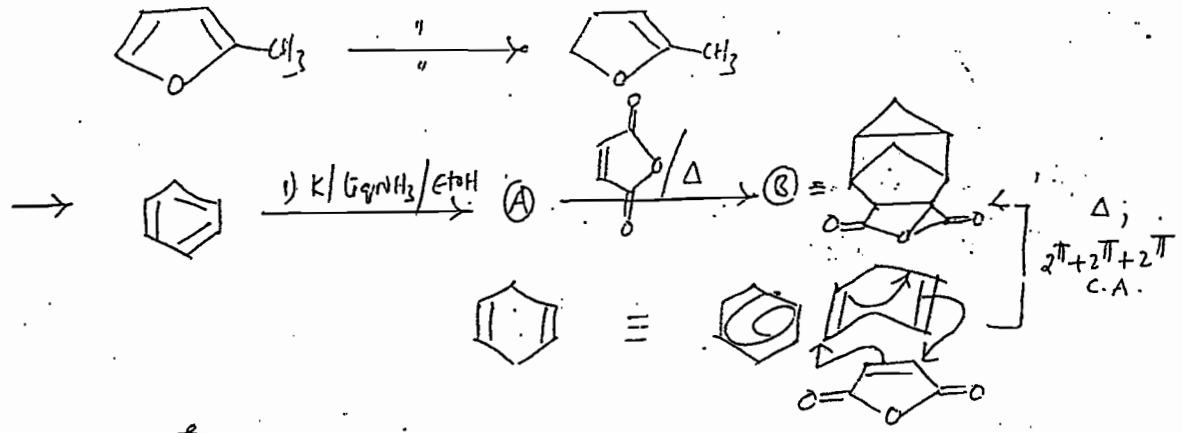


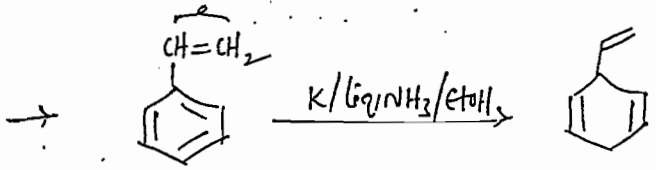


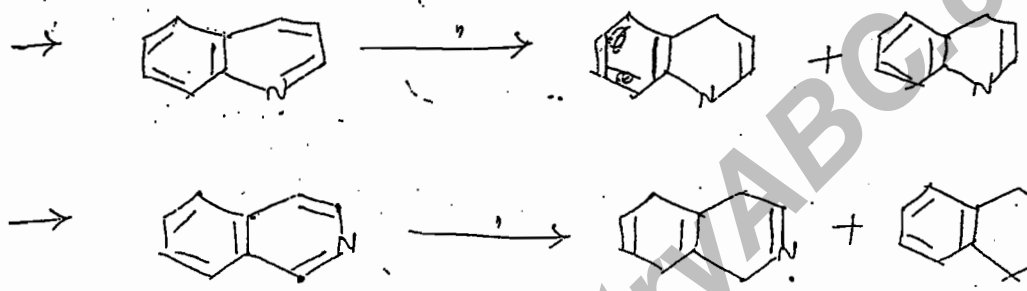




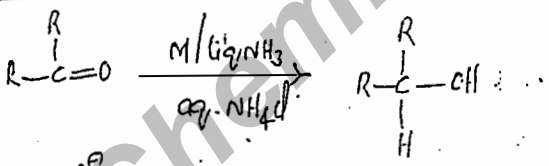


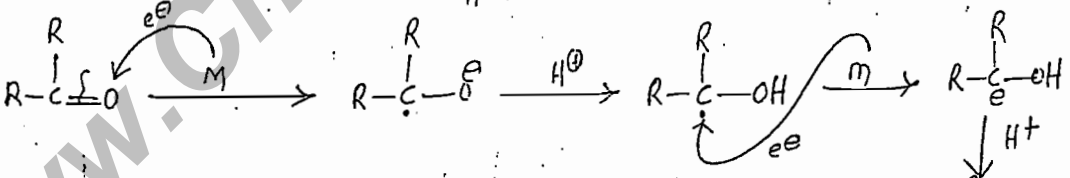


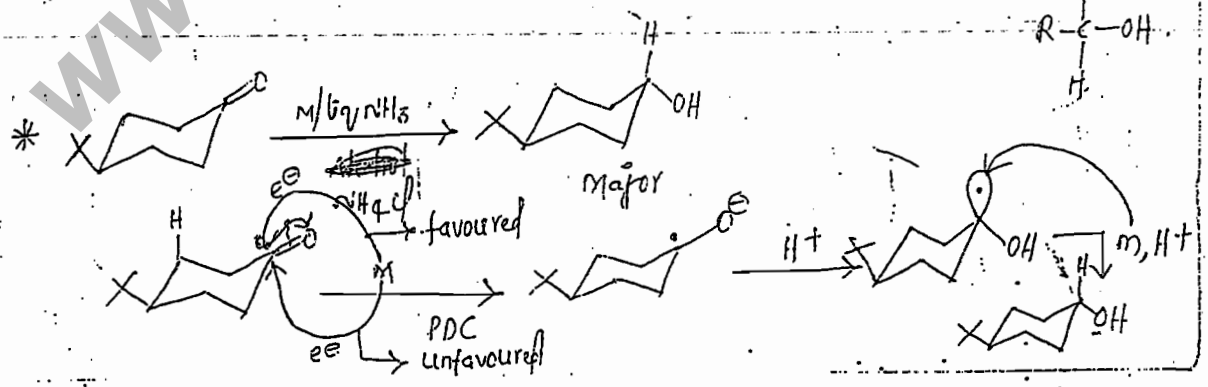


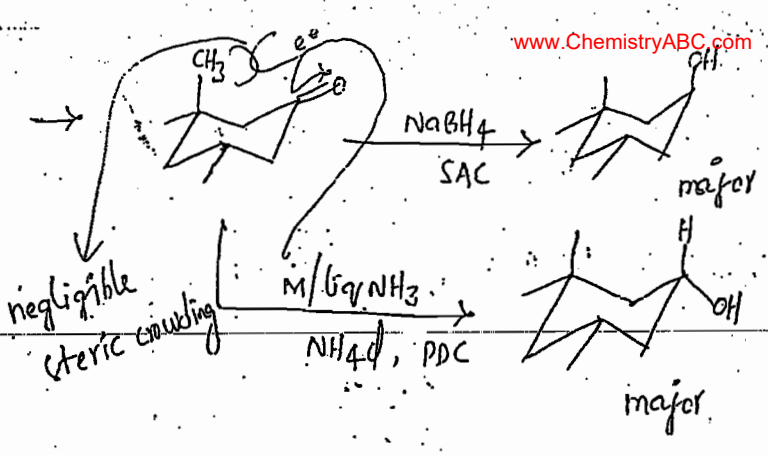


→ Reduction of simple carbonyl compds with M/liq.NH3 :

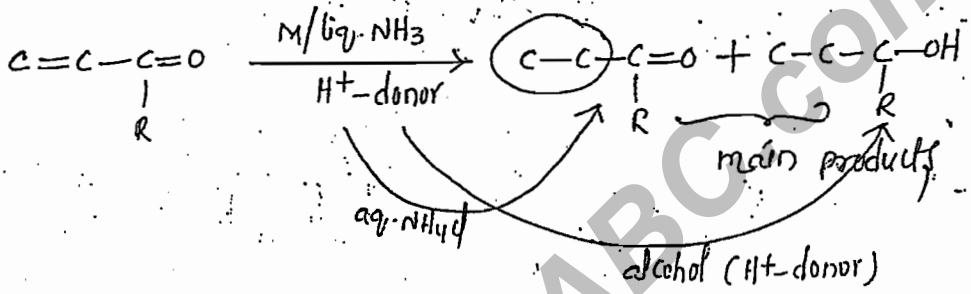
* 

* 

* 



→ Reduction of α,β-unsaturated carbonyl compounds.

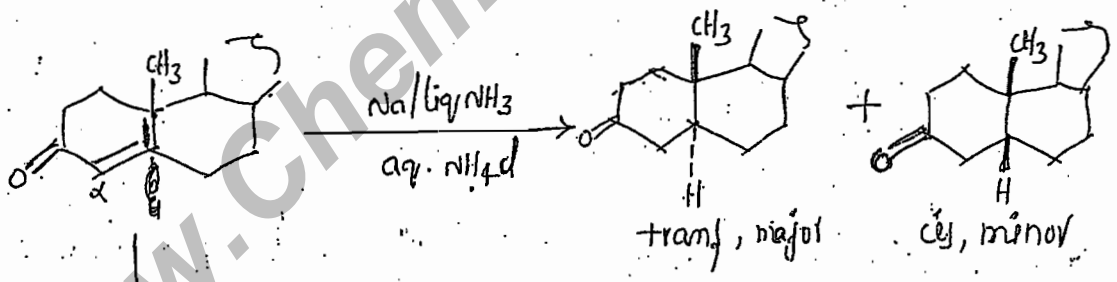


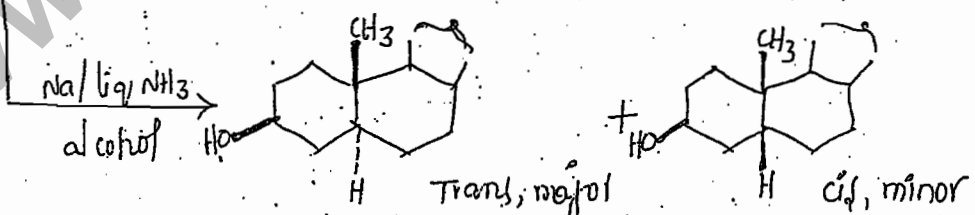
→ Selectivity in reductions depends on nature of proton donor.

In alcoholic medium, major product – sat. alcohol.

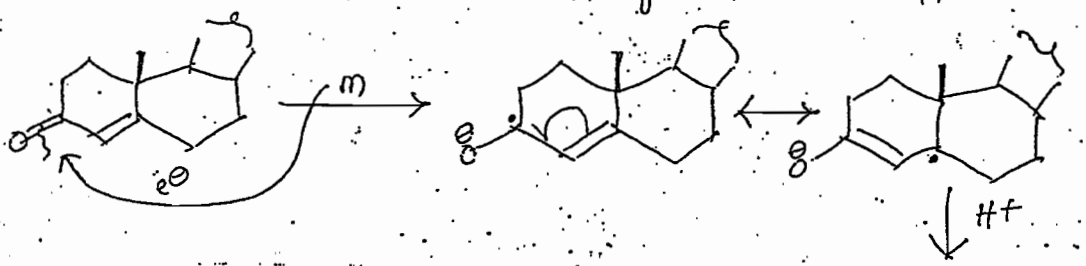
In NH_4Cl, " – sat. carbonyl compd.

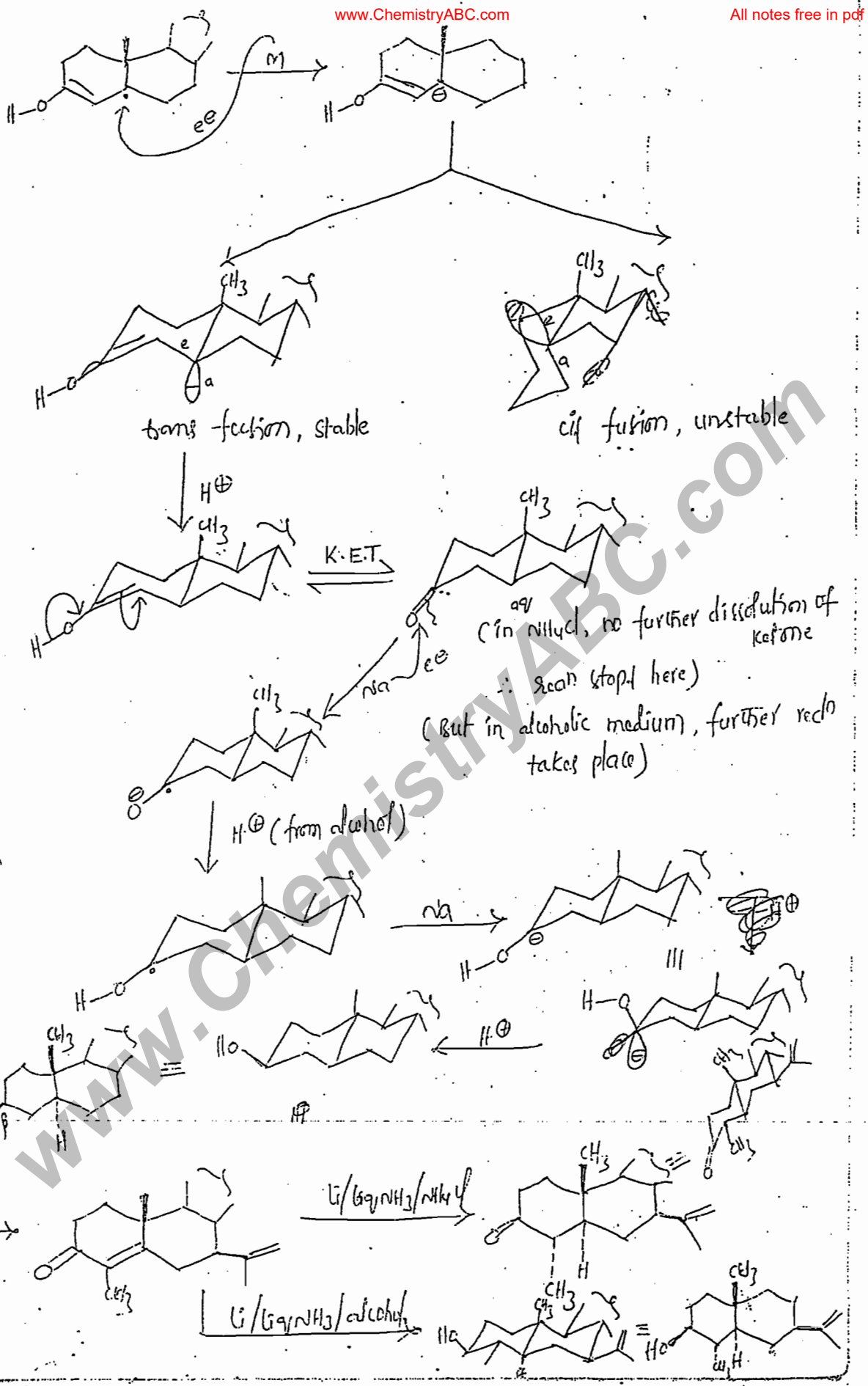
→

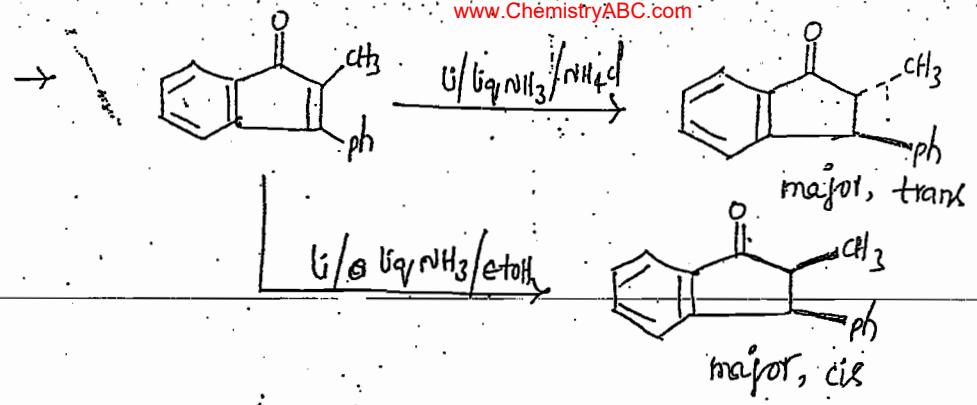


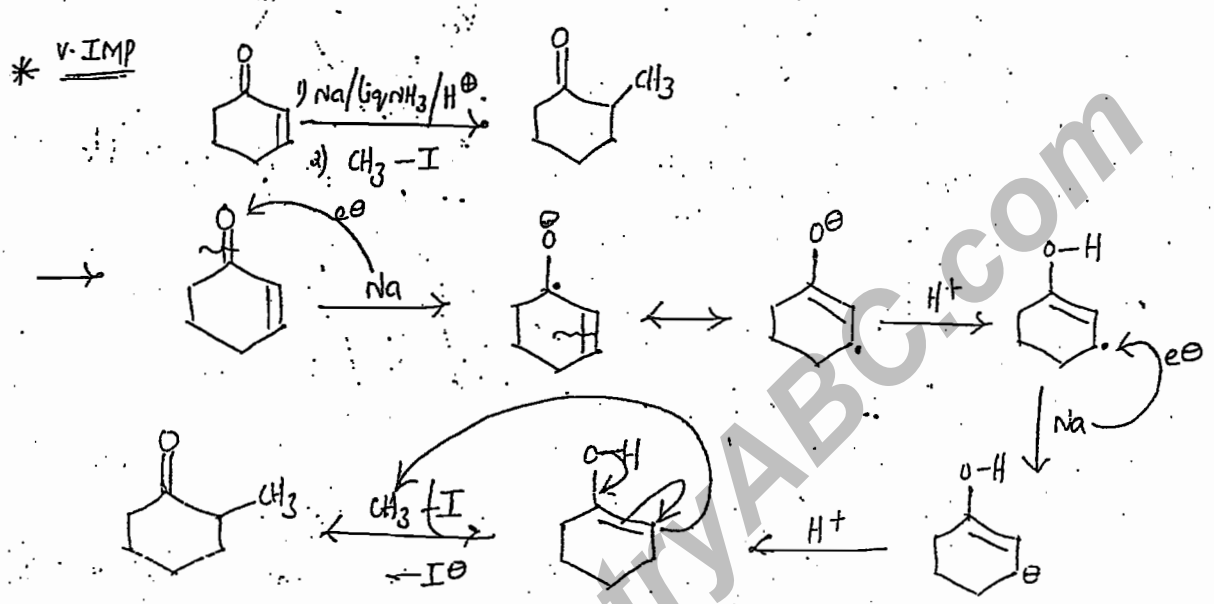


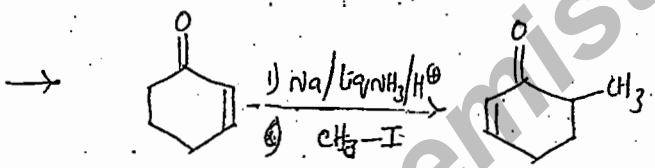
Mech:-

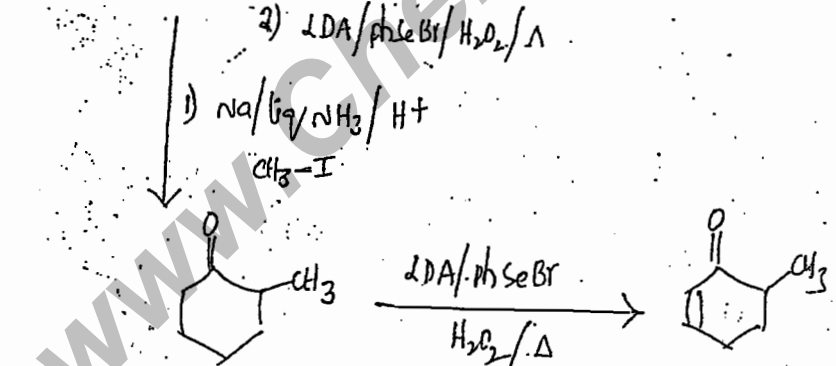


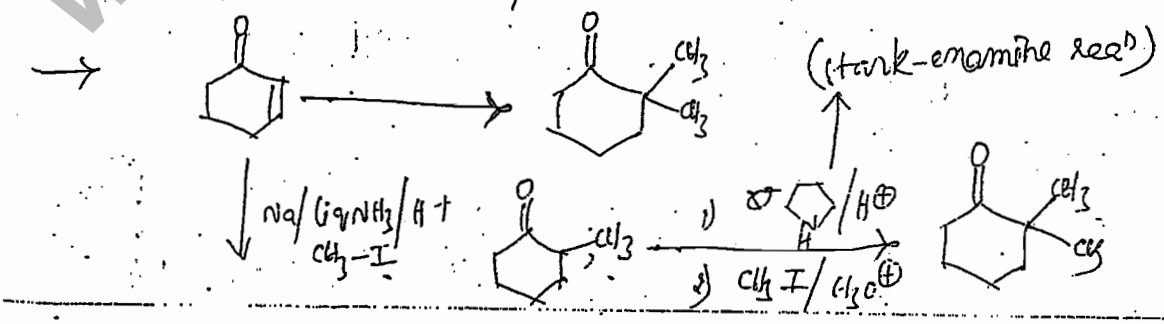


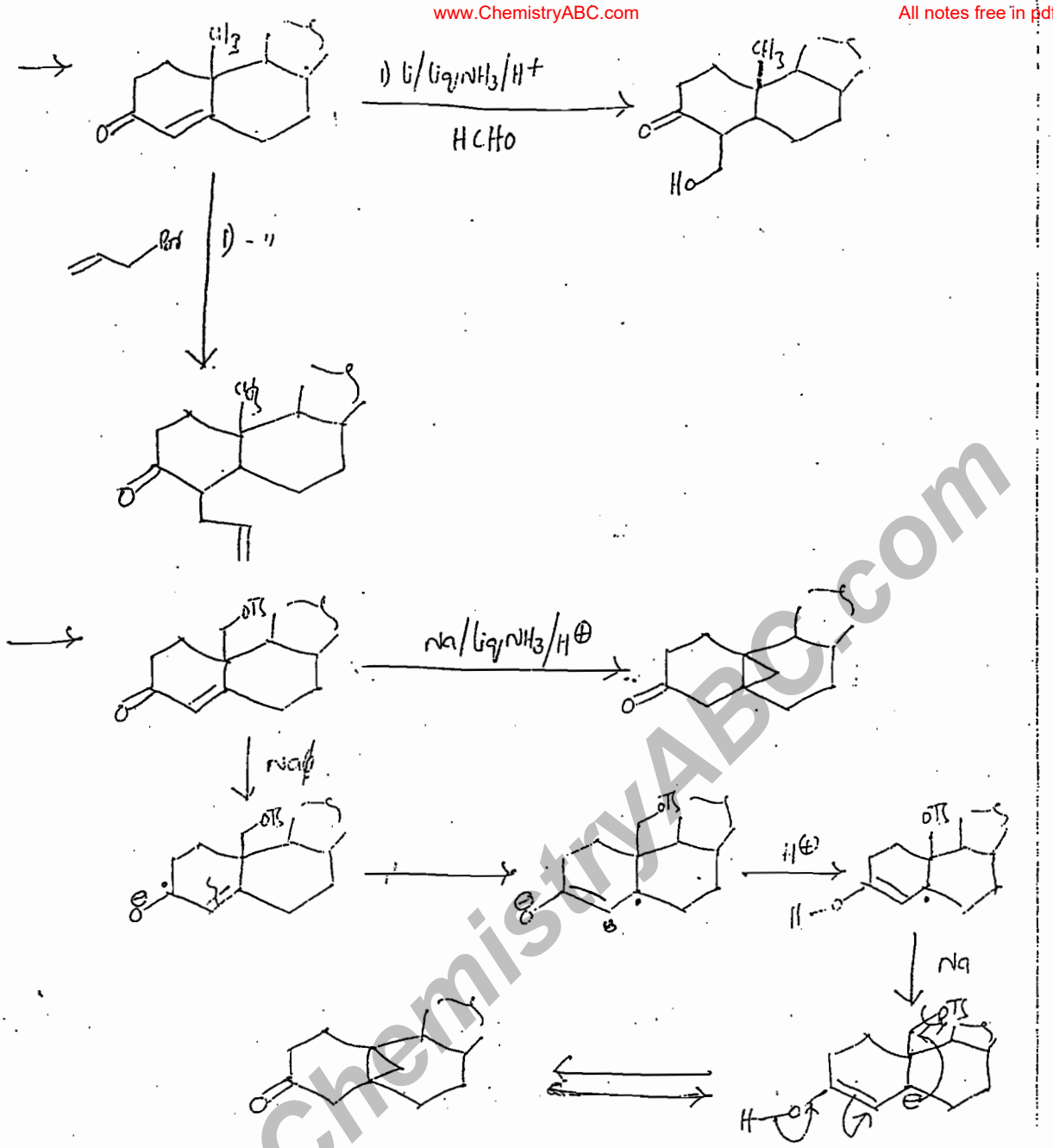










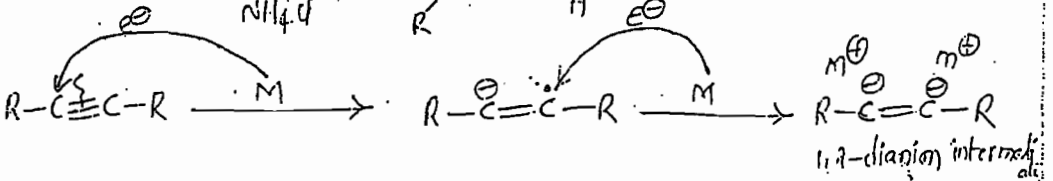


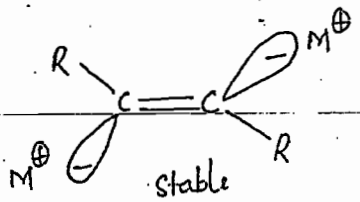
* Reduction of alkynes into trans olefins :—

M = sodium

$$R-C\equiv C-R \xrightarrow[NH_4Cl]{M\,(Na/liq.NH_3)} \underset{R}{\overset{H}{\diagdown\!\!\diagup}}\!\!=\!\!\underset{H}{\overset{R}{\diagdown\!\!\diagup}}$$

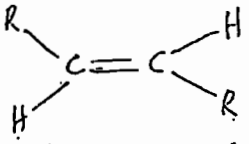
Mech :-



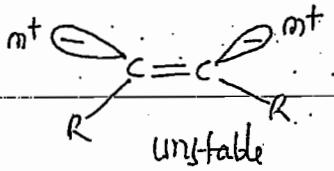


stable

H_3O^+

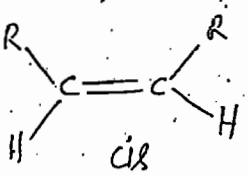


trans, major



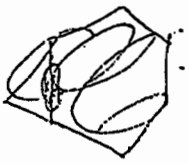
unstable

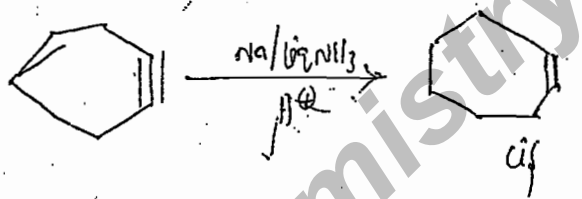
H_3O^+



cis

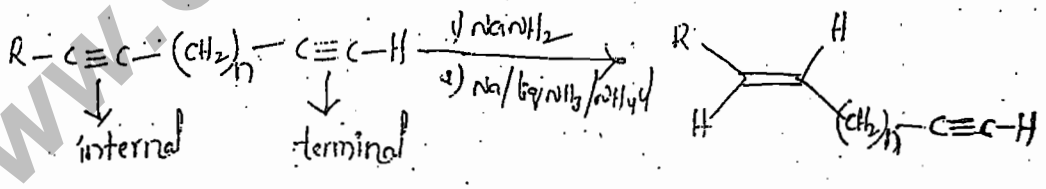
minor

→  In the case of reduction of cyclic alkynes, cis olefins are major. Trans olefins are minor.

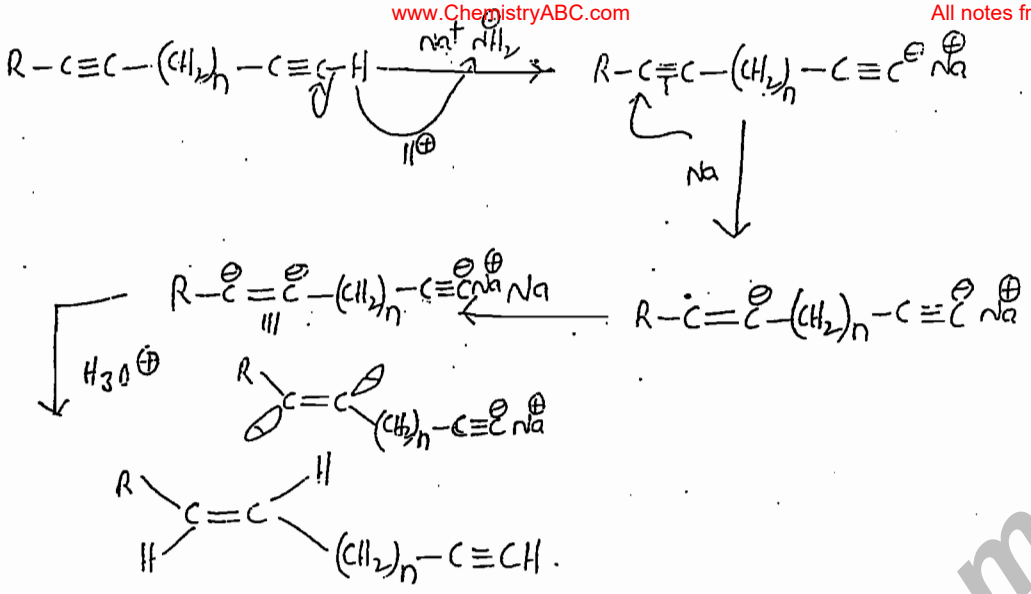


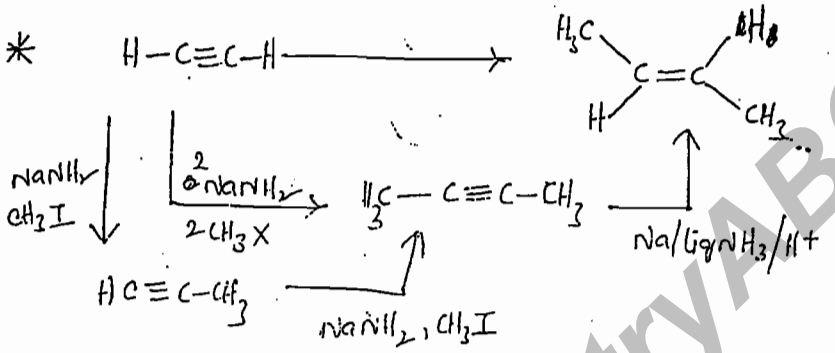
cis

→ In reduction of terminal alkynes, $(NH_4)_2SO_4$ additives are preferred to enhance the rate of scan (reduction).

→ 

If alkyne having internal, terminal triple bonds, selective reduction of internal triple bond possible by making terminal to sodium salt.





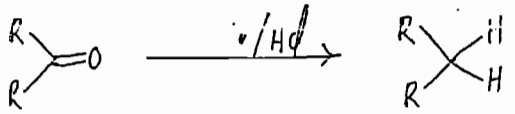
18/05/08

* Electron transfer acid medium Reduction :- Metal/acid.

CLEMMENSON'S REDUCTION:

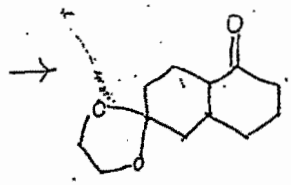
→ conversion of carbonyl compounds into correlponding hydrocarbons

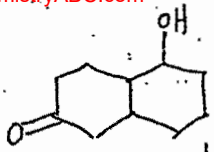
* Carbonyl compd $\xrightarrow{Zn\text{-}Hg/HCl}$ Hydrocarbon.



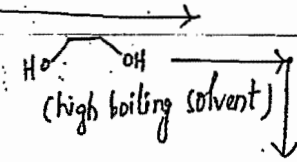
* LIMITATIONS:

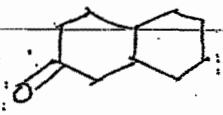
1) Acid-labile groups get effected





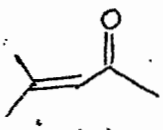
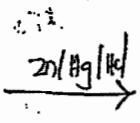
(partial reduction)

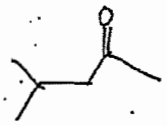




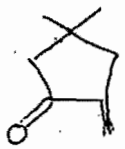
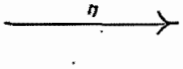
vigorous conditions

2) In α,β unsaturated carbonyl compds, may ⓐ reduce selectively only unsaturation.

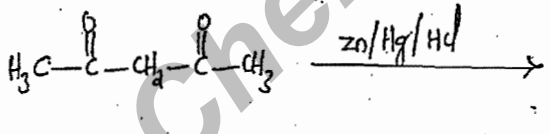



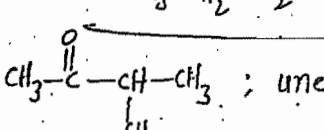


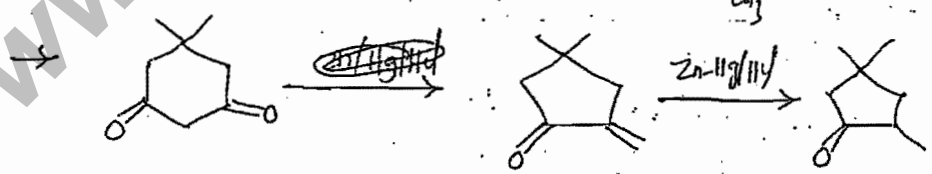
mesityl oxide

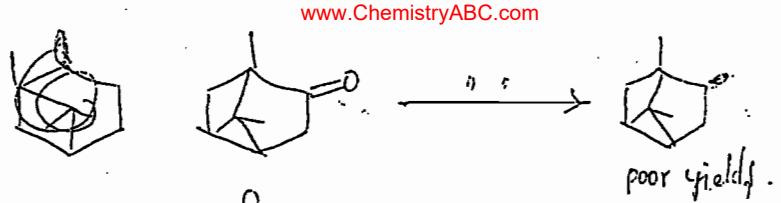
3) 1,3/1,4 – dicarbonyl compds may undergo R.A.



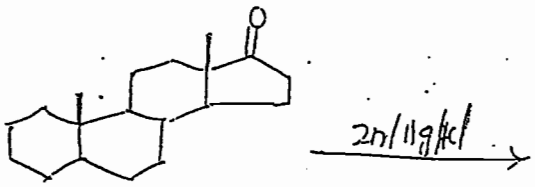




4) ⓐ demmenson's reduction inefficient in redn of high mol. wt. carbonyl compounds.

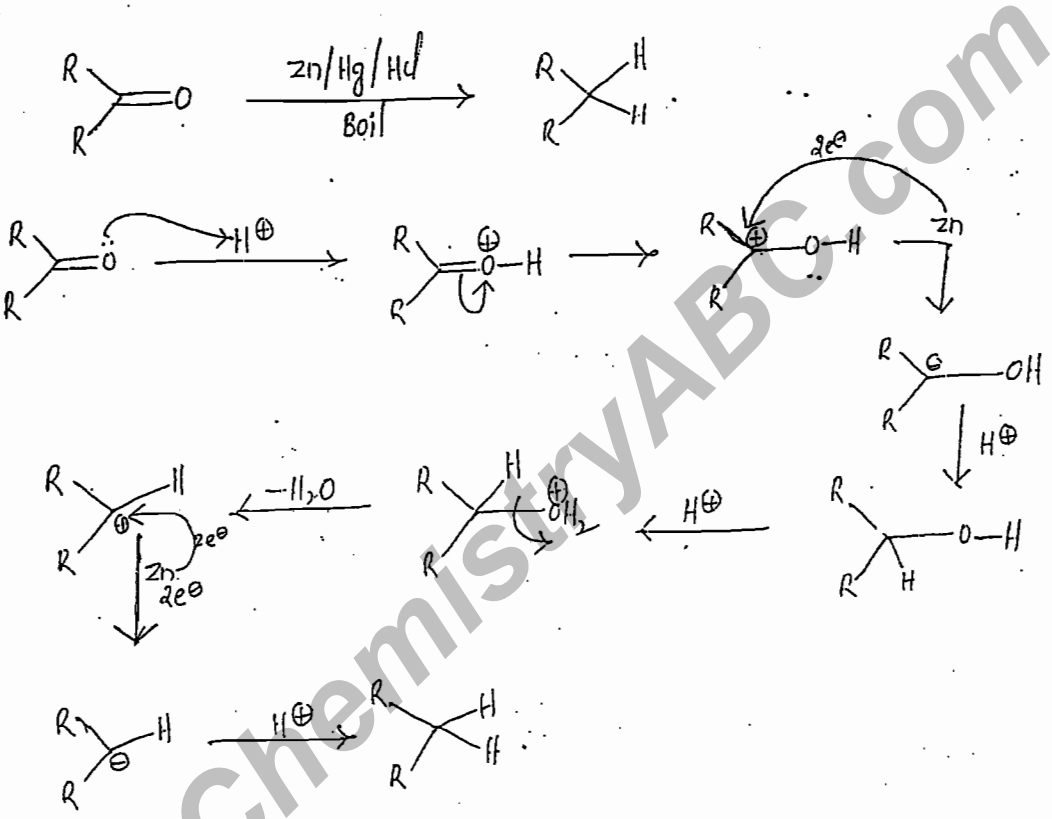


poor yields.



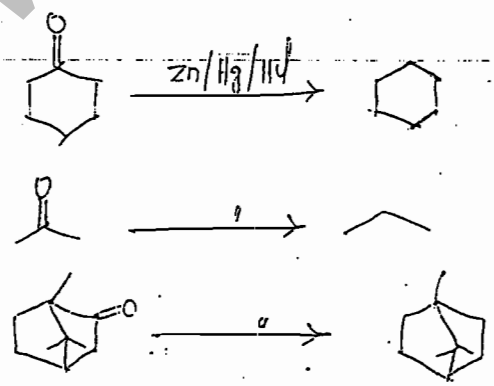
very low % yield.

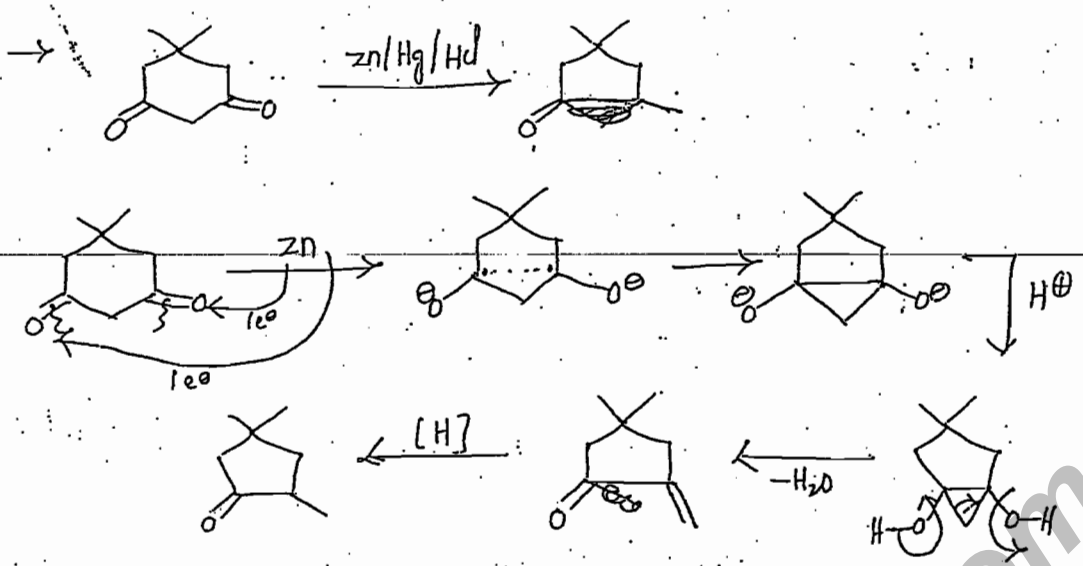
Mechanism :- "uncertain mech" (experimental evidences fully not established)



Redn taking place by producing carbocation & carbanion intermediate.

* eg:-





* Role of mercury : It is the medium in which Zn^{+2} ions get dissolved.

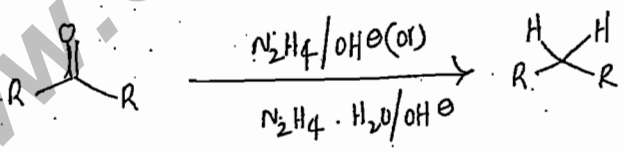
Non-metallic Reducing agents :—

1) $N_2H_4/OH^{\ominus}$ 2) Di Imide : N_2H_2

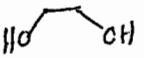
I. wolf-Kishner Reductions :

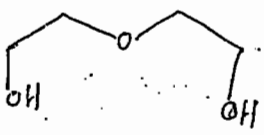
→ Alternative to clemmenson's reduction, converts carbonyl compds into hydrocarbons.

→ Reducing agents : $N_2H_4/OH^{\ominus}$ (or) $N_2H_4 \cdot H_2O/OH^{\ominus}$



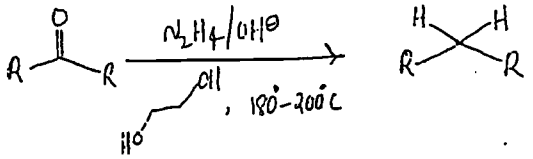
* Solvents :— High boiling solvents : high temp. reductions.

1) Ethylene glycol : 

2) diethylene glycol. 

* W.K. Reductions are high (180-200°C) temp. reductions.

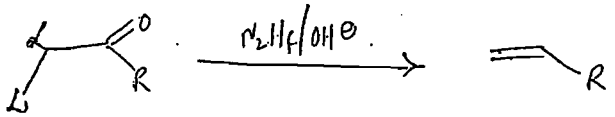
∴ High boiling solvents are required.



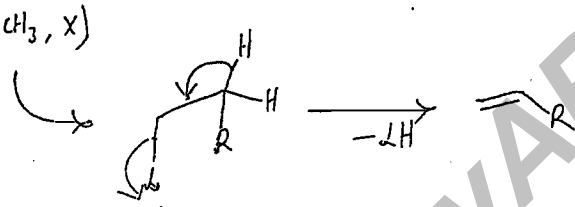
LIMITATIONS :-

1) High temp. reductions

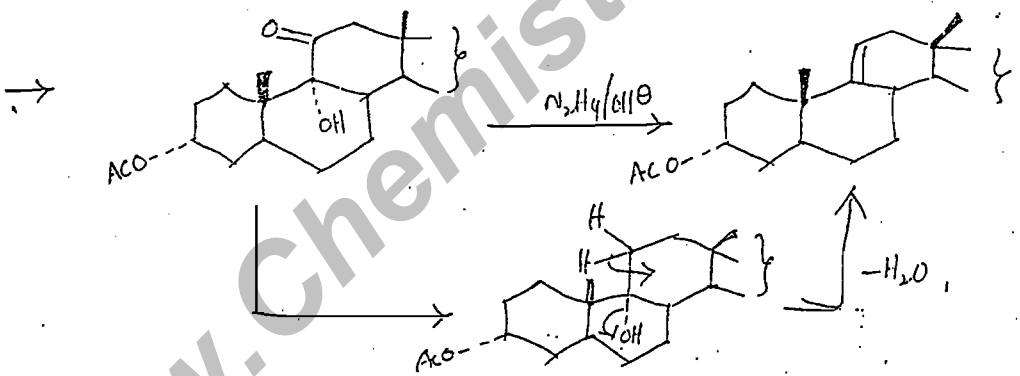
2)



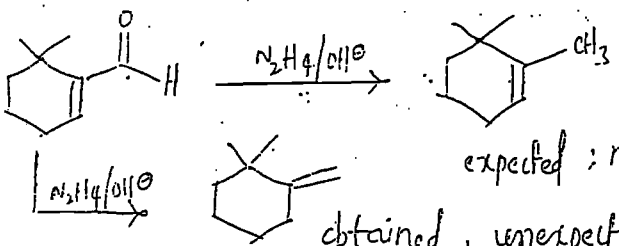
(L = OH, OCH_3, X)



Leads to presence of LG, elimination followed by reduction.



3) Isomerisation of double bond



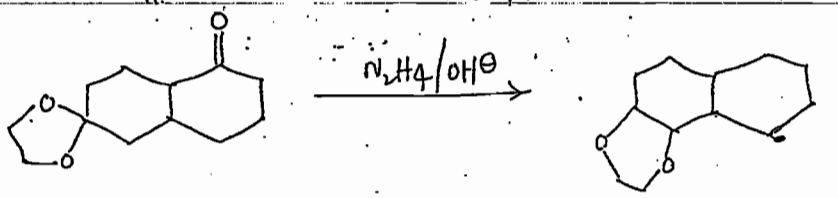
expected ; not obtained

obtained, unexpected

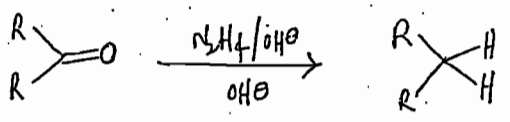
Advantages :-

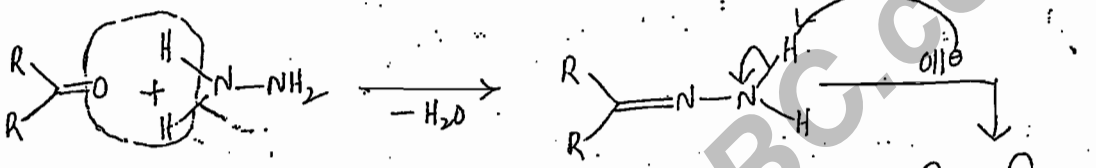
1) High mol. wt. carbonyl compounds readily get reduced.

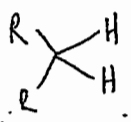
2) acid-labile groups unaffected.



Mech :-

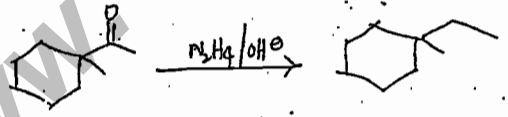


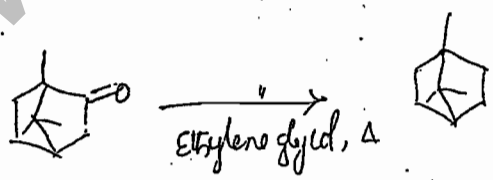


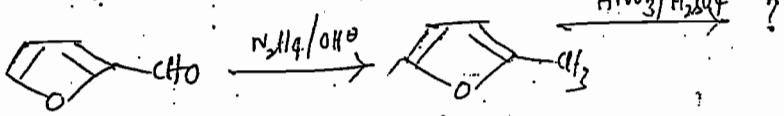


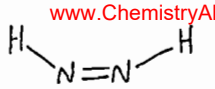
→ carbanion intermediate, → non-metallic

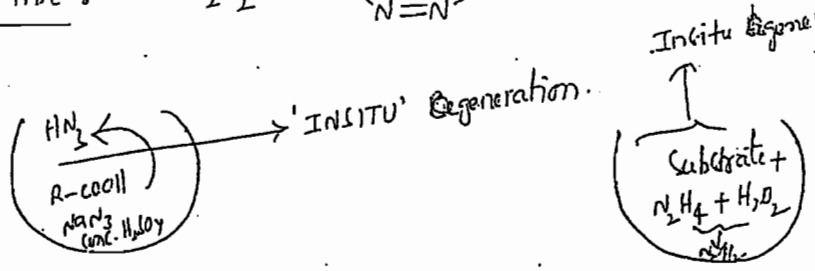
eg :-







DIIMIDE :— N_2H_2 : 

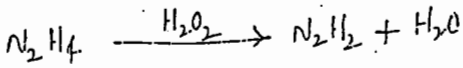


→ Diimide is highly unstable, not possible to preserve. ∴ commercially not available, its generation — 'INSITU' generation.

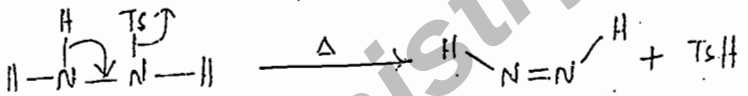
→ Reagent which is generated in the course of reaction 'Incitu' generation.

→ following are the methods for Incitu generation of diimide.

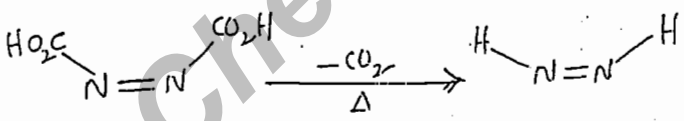
1) By oxidn of N_2H_4 with H_2O_2



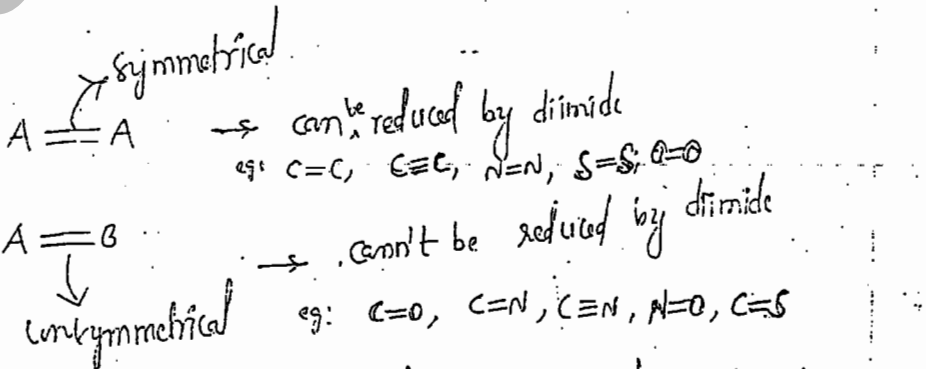
2) By thermal decomposition of tosyl hydrazide



3) Thermal decomposition of Azo-dicarboxylic acid.



Applications :—



1) unsaturation attached atoms, identical — symmetrical unsaturations

eg: A=A , C=C, O=O, N=N, S=S

A≡A , C≡C, N≡N etc.

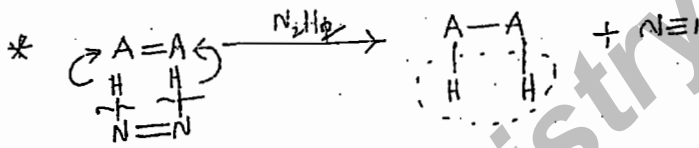
→ If unsaturation attached atoms are different, unsaturation unsymmetrical.

→ eg: A=B , A≡B, C=O, C=N, C=S, N=O, C≡N

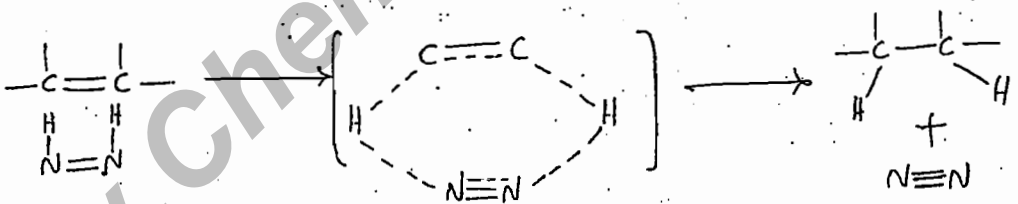
use of diimide :-

→ Diimide reduces only symmetrical unsaturations, unsym. unsaturation unaffected. That means C=O, C≡N, C=S, C=N ⊙ functions not reduced.

→ Reductions of diimide - "syn ~~catalytic~~ hydrogenations". Similar to simple catalytic hydrogenations.

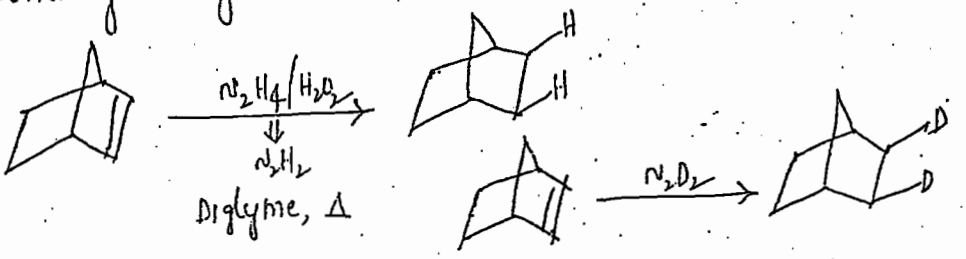


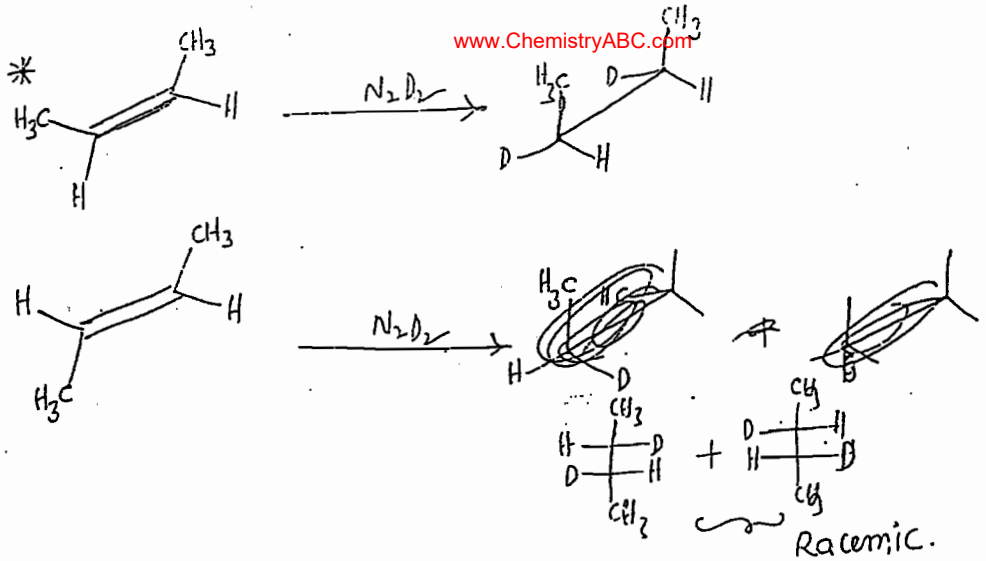
Mech:- concerted group transfer hydrogenation.

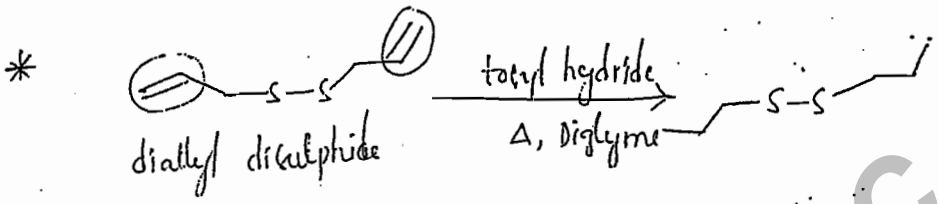


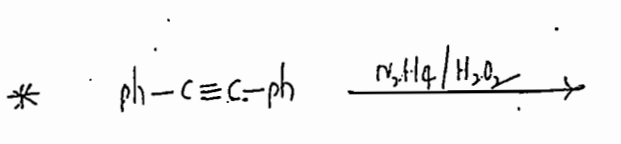
six membered cyclic T.S

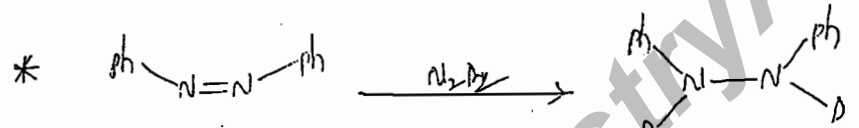
* preferentially do hydrogenation at sterically less crowded face/side.

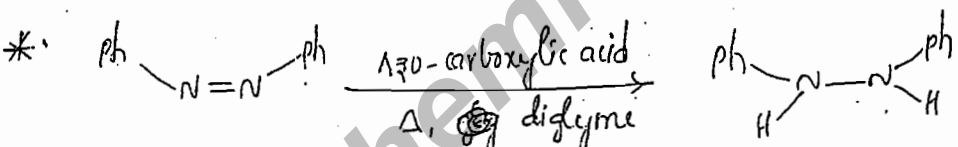










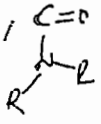


Catalytic Hydrogenations :—

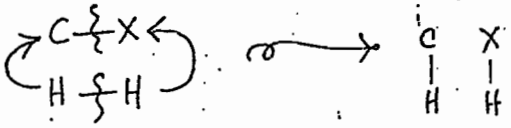
* Hydrogenation of any unsaturation with H_2 gas in the presence of catalyst called "catalytic hydrogenation".

* Unsaturation $\xrightarrow[\text{solvent/catalyst}]{H_2 \text{ gas}}$ hydrogenated product.

↓

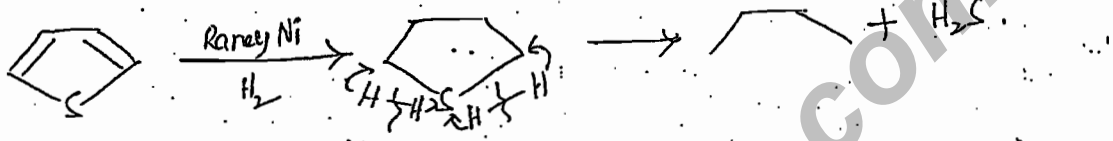
C=C, C≡C,  , N=O, C≡N, C=N, C=O (or ), C=S, S=S, N=N, C=N–OH

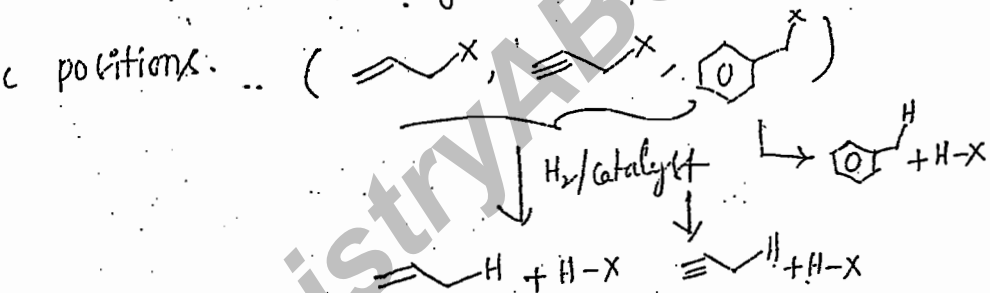
* Hydrogenolysis :-



breaking of σ-bond by adding H_2 gas - 'hydrogenolysis'.

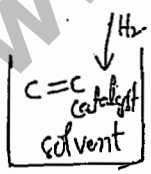
→ Hetero atom σ-bonding readily participates in hydrogenolysis with H_2 gas.

→ 

→ highly reactive positions for hydrogenolysis - allylic, benzylic, propargylic positions. .. 

⇒ catalytic hydrogenations classified into following groups / types.

- Heterolytic hydrogenation
- Homolytic hydrogenation.



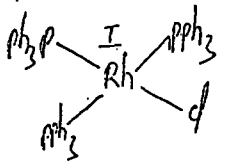
→ if catalyst insoluble in solvent - heterogeneous (heterolytic hydrogenation)

→ " soluble " - homogeneous (homolytic hydrogenation).

→ catalysts are simple metals, metal oxides, metal sulphides

eg:- Ni, Pt, Pd, PbS, PtO_2

→ catalyst must be with organic ligand.

eg:- Wilkinson's catalyst. $(PPh_3)_3 \overset{I}{Rh}Cl$ 

* ~~Heterogen~~ Hydrogenolysis is possible only in Heterolytic hydrogenation
* " " not " in homolytic hydrogenation.

* All types of org. frs can be hydrogenated — heterogeneous
* only db & triple bonds (olefins, alkyl) get hydrogenated — homogeneous
* very difficult to predict stereochem. of hydrogenation product in heterogeneous systems. (usually 'syn').
* Every homogeneous hydrogenation is 'syn hydrogenation.'
* very easily to carry out — heterogeneous
  very difficult to " — homogeneous.
* poor in selectivity, ~~hydro~~ — heterogeneous
* Excellent in selectivity — homogeneous.

⇒ Types of heterogeneous catalysts: PtO_2, $CuCr_2O_4$, PdS, PbS

metals, metal-oxides, metal sulphides

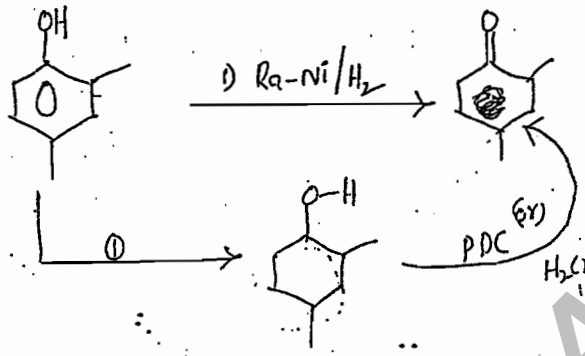
d-block: Ni, Pt, Pd, Fe, Rh, Ru, Ir

* Lindlar's catalyst : $Pd, CaCO_3 \cdot PbO$, cis hydrogenation of alkynes.

* Adam's catalyst : $PtO_2/AcOH$ — redn of esters, amides, olefins

* Raney-Ni : Dissolution of Ni-Al alloy in NaOH precipitates raney-Ni.

* used for hydrogenation of aromatic hydrocarbons, hydrogenolysis etc.

⇒ 

* $CuCrO_4$: mainly for redn of amide, esters, nitriles, azo frs etc.

* Rate of heterogeneous hydrogenations depends on

1) Temp, pressure
2) Amount of catalyst
3) Nature of catalyst
4) " " substrate
5) Nature of solvent. → polar solvents preferred (eg: alcohols, acetic acid). MeOH/iPrOH

⇒ 1) ↑se in temp ↓es rate of hydrogenation.

⇒ ↑se in pressure, ↑es " . ($\approx$ 200–300 atm).

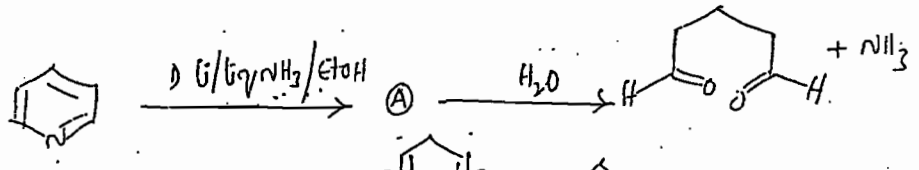
2) ↑se in amount of catalyst, slightly ↑es rate of hydrogenation,

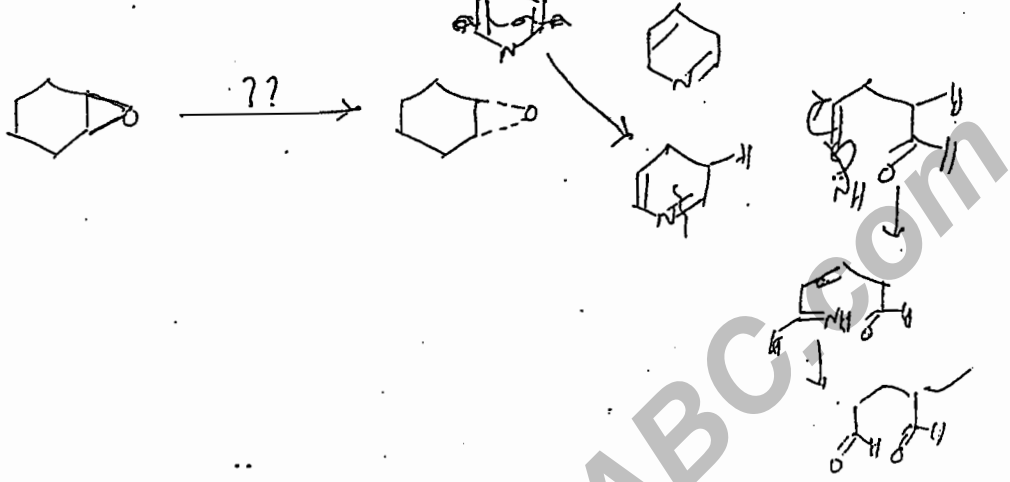
3) If surface area of catalyst more, hydrogenations faster.

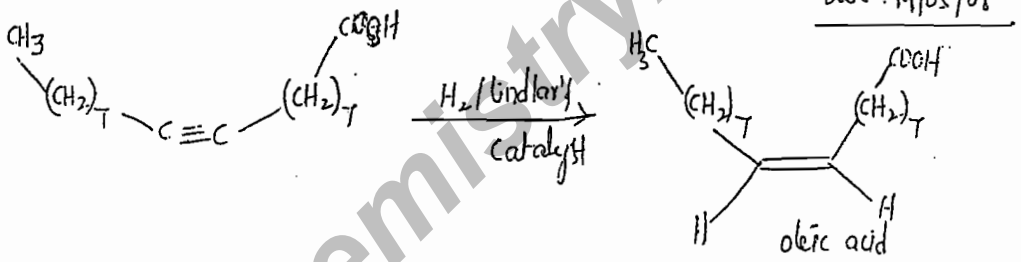
4) Polar substrates (carbonyl, ester etc) are faster in hydrogenation in heterogeneous medium.

Exercise:-

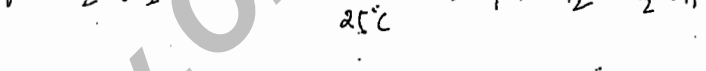
*

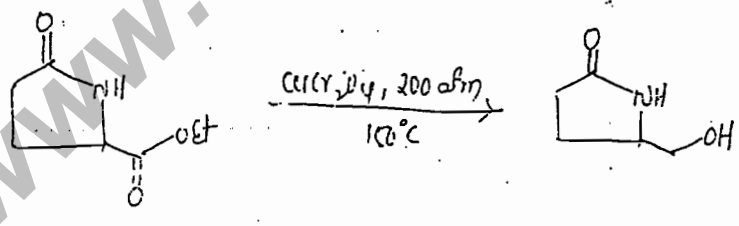
1) 

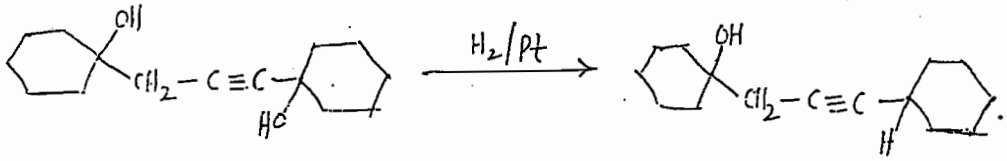
2) 

* 

Date : 19/05/08

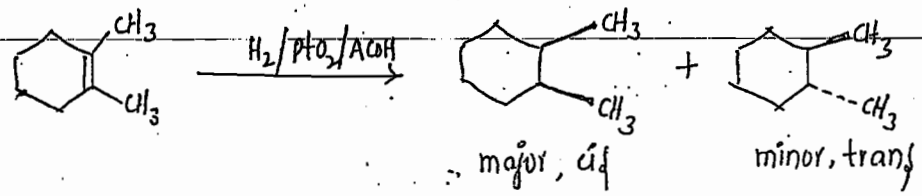
* 

* 

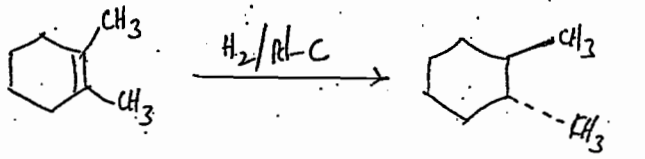
* 

* Stereochemical aspect :—

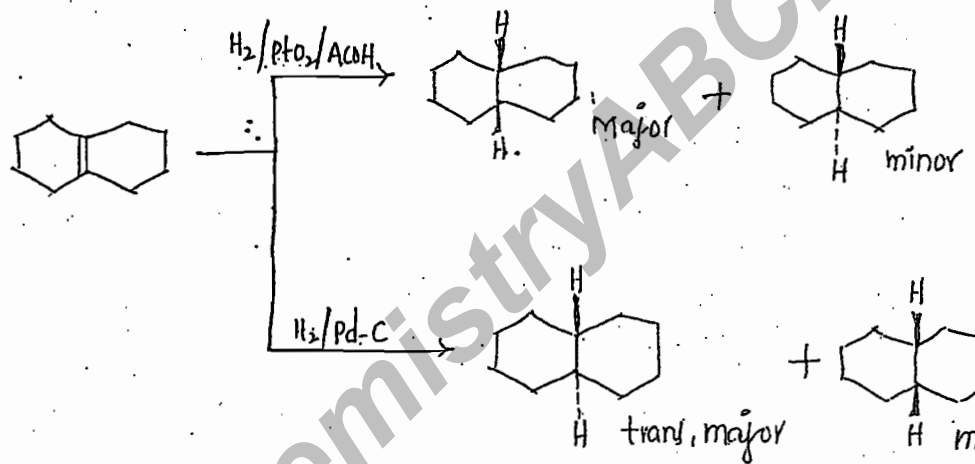
→ Usually syn-hydrogenation.

→ 

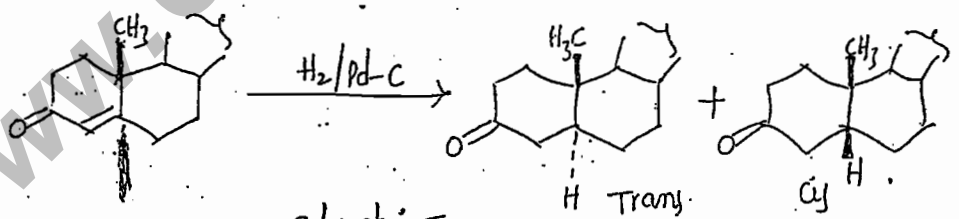
∴ major, cis minor, trans

→ 

major minor

→ 

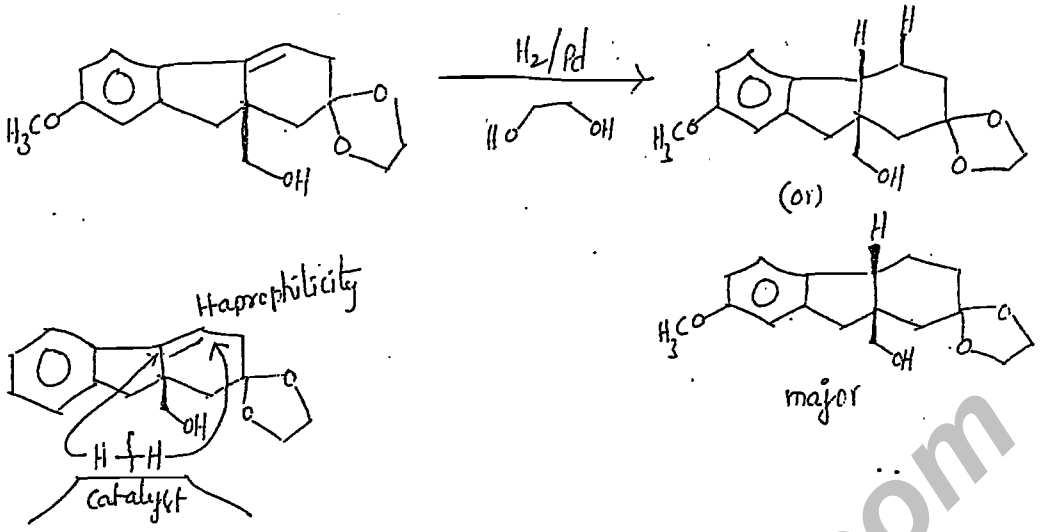
→ Solvent Effect :—

* 

Solvent :—

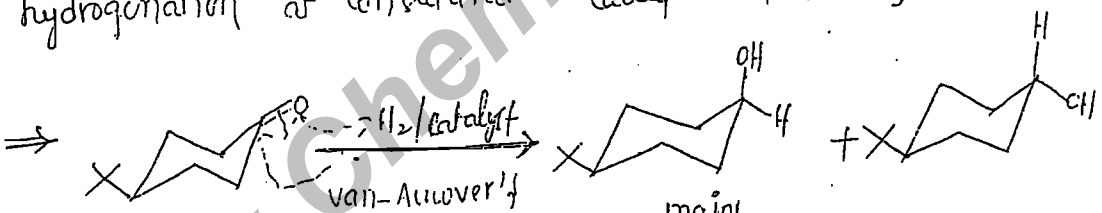
EtOH	41%	55%
EtOH + 10% HCl	7%	93%

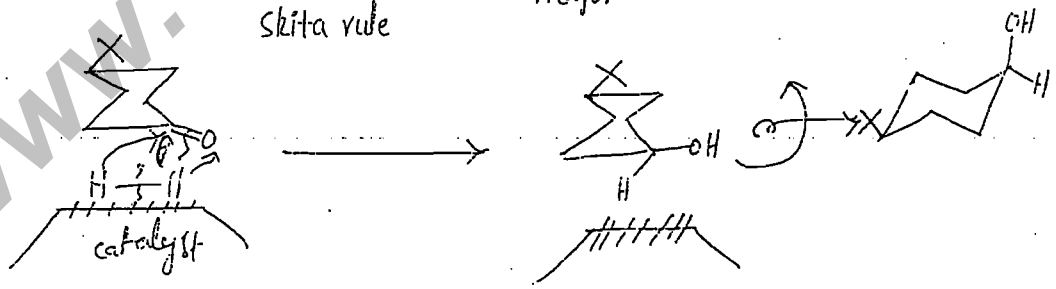
* Haprophilicity :-



→ polar group of substrate co-ordinate with surface of the catalyst. unsaturation which is near to co-ordinating group, facial selectivity in hydrogenation controlled by direction in which co-ordinating group attached to surface of catalyst.

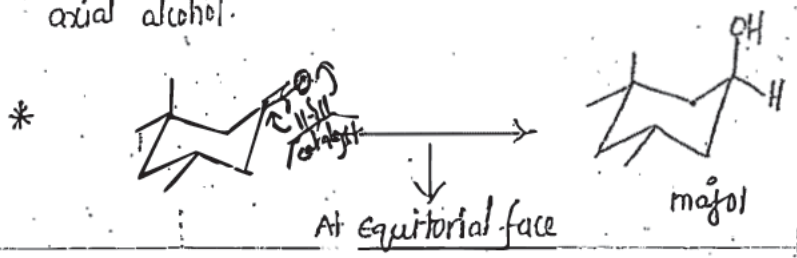
whenever the polar or co-ordinating group controls selectivity in hydrogenation of unsaturation called "Haprophilicity."

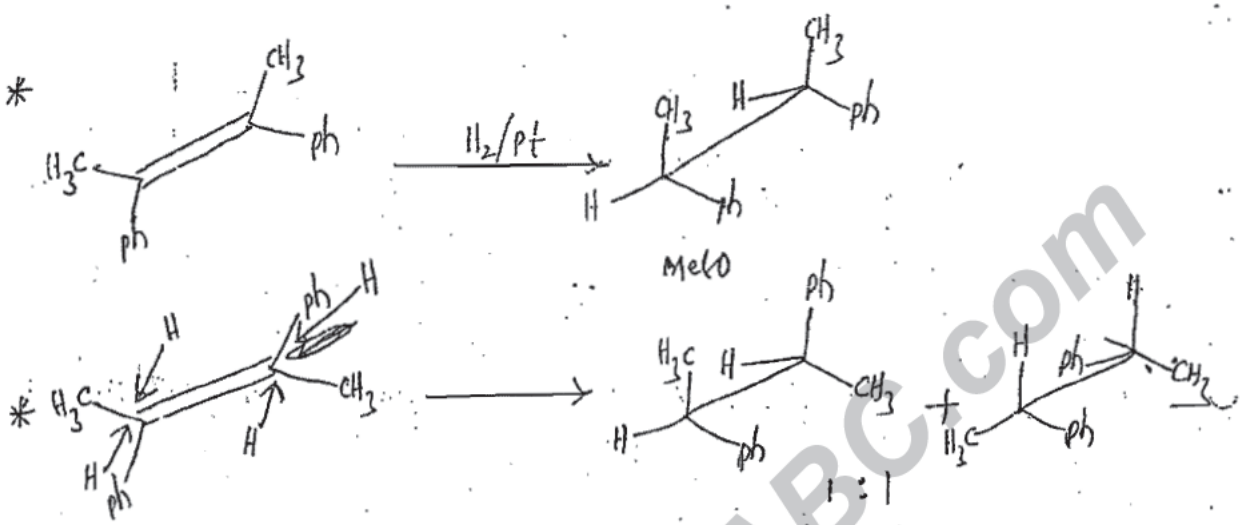




→ equitorial face of carbonyl exposed to surface of catalyst, preferential hydrogenation at equitorial face, the resulting major product

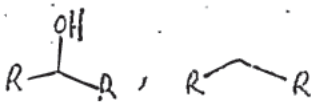
'axial alcohol'





* Reactivity order of functional groups in heterogeneous catalytical Hydrogenation :—

→ Function $\xrightarrow{H_2/catalyst}$ product

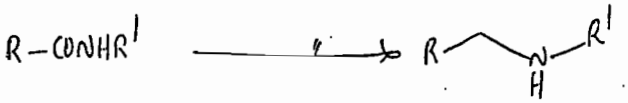
$R-\overset{O}{\overset{\|}{C}}-Cl$	,	$R-CHO$, RCH_2OH
$R-NO_2$	,	$R-NH_2$
$R-C\equiv C-R$	,	 , $R-CH_2-CH_2-R$
$R-CHO$	,	$R-CH_2OH$
$R-CH=CH-R$	,	$R-CH_2-CH_2-R$
$R-\overset{O}{\overset{\|}{C}}-R$	,	

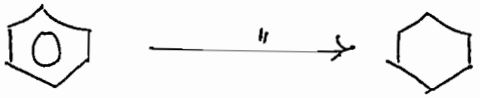
→ $Ph-CH_2-O-R \xrightarrow{"} Ph-CH_3 + R-OH$

→ $R-C\equiv N \xrightarrow{"} R-CH_2-NH_2$

Polycyclic Aromatics : ——"——→ partially reduced product

$R-COOR' \xrightarrow{"} R-CH_2-OH$

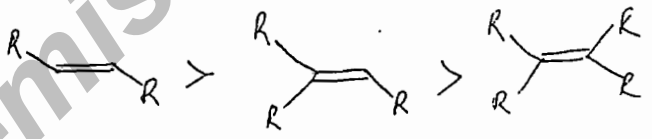
$R-CONHR' \xrightarrow{"}$ 

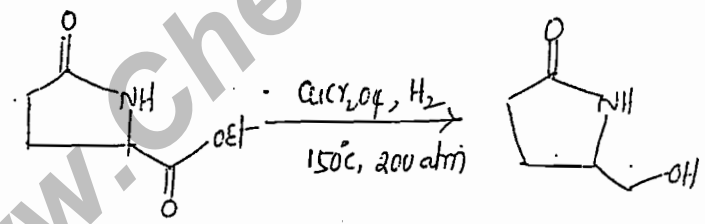


$R-CO_2^- Na^+ \xrightarrow{\times}$ Inert

→ Top to bottom, reactivity order ↓ (eg)

Reactivity order in Olefines :—

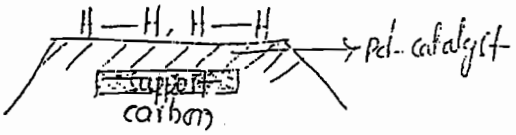
$R-CH=CH_2 >$ 

→ 

* Support :— support is the inert material at which the catalyst is attached or adsorbed.

eg: Pd—C → Support

↓ Catalyst



V.IMP

HOMOGENEOUS – CATALYTIC HYDROGENATION :—

→ catalyst soluble in org. solvents – homogeneous

→ compound with org. ligands.

eg:- WILKINSON'S CATALYTIC HYDROGENATIONS.

* Wilkinson's catalyst : Rh^{I} – complex

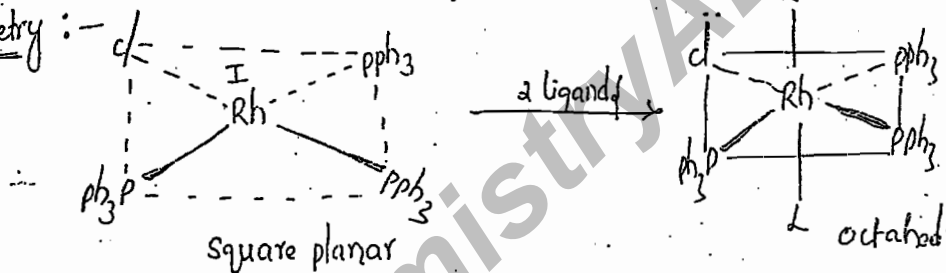
$(PPh_3)_3 Rh^{I} Cl$ tri(triphenyl phosphorous) chloro Rhodium (I).

⇓

red coloured substance with high m.pt.

$$Rh^{III}Cl_3 \cdot 3H_2O \xrightarrow[Boil/C_6H_6]{PPh_3 \text{ excess}} (PPh_3)_3 Rh^{I} Cl$$

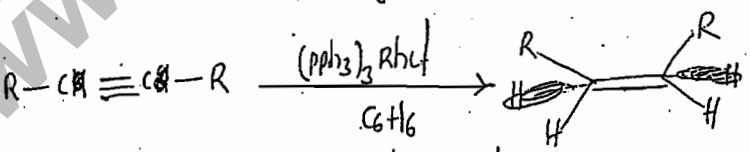
Geometry :-



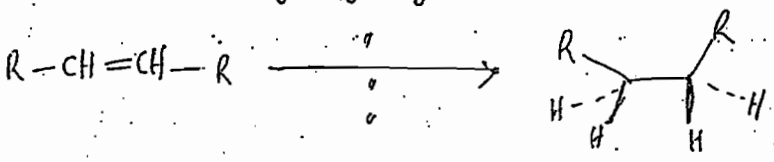
→ wilkinson's catalyst will not follow 18 e⊖ rule. ∴ co-ordinatively unsaturated complex.

∴ solvent : C_6H_6

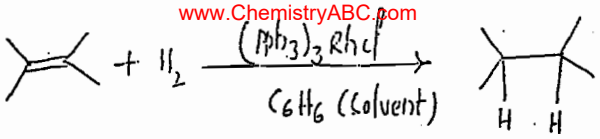
* Hydrogenation of alkenes/alkynes with wilkinson's catalyst :

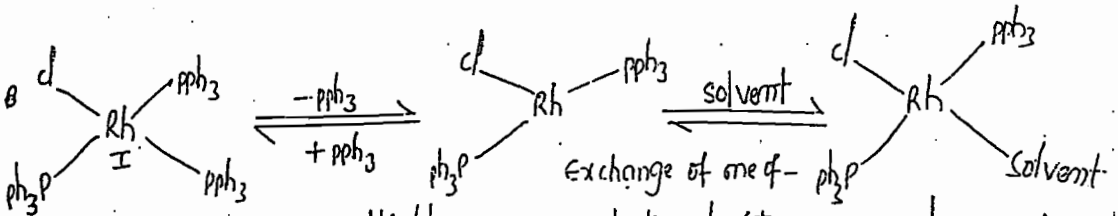


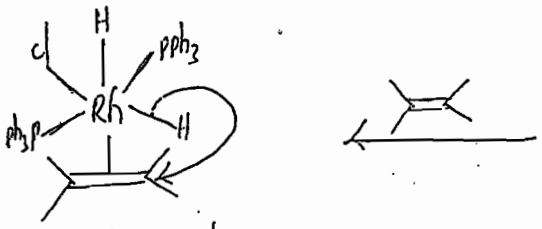
syn-hydrogenation



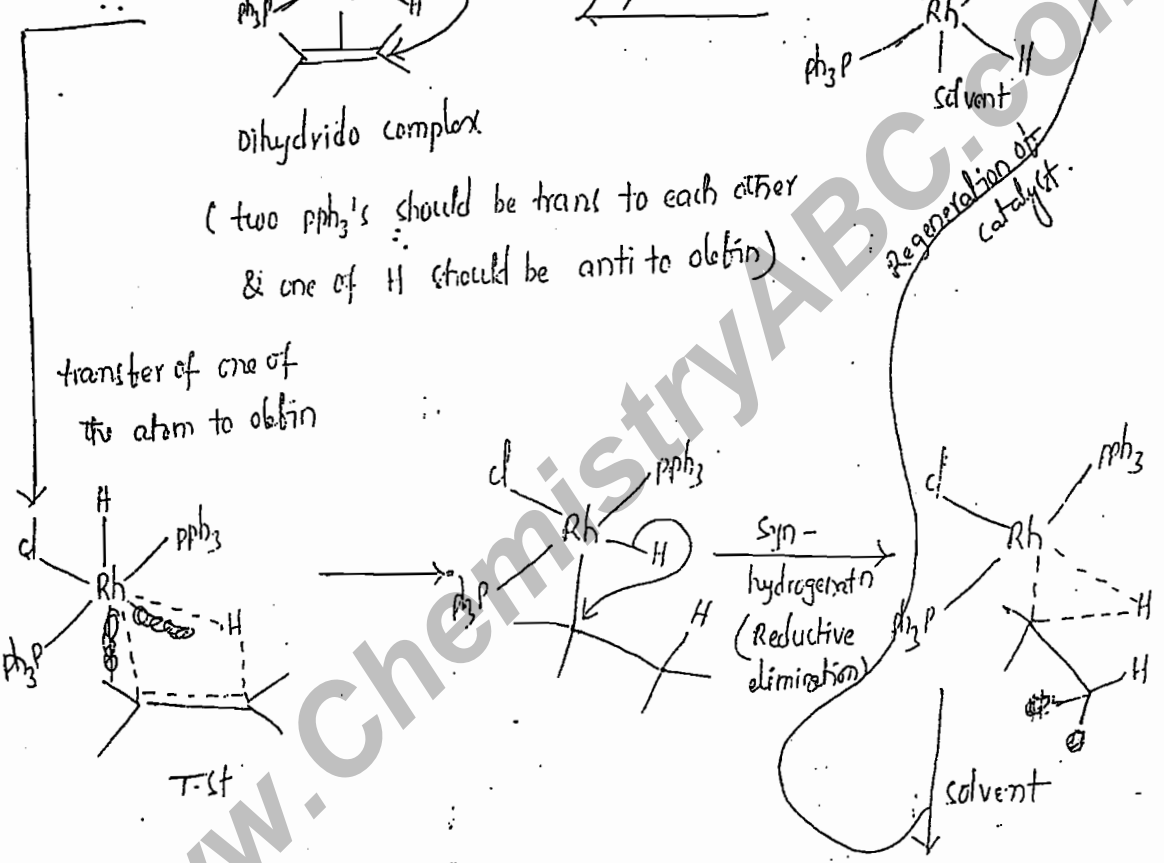
Mech.:- V.IMP.

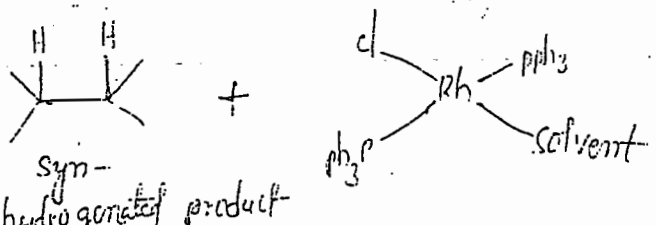






(two PPh_3's should be trans to each other & one of H should be anti to olefin)





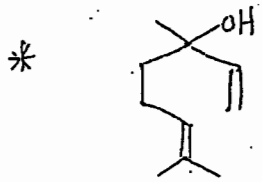
→ Regeneration of catalyst followed by Recycling of hydrogenation at olefin.

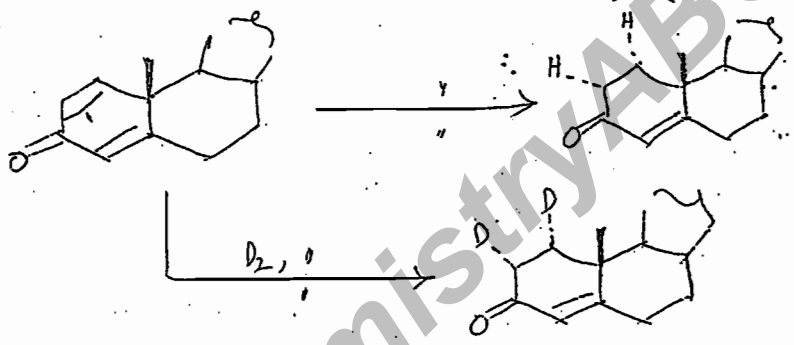
Stereo chemical Aspects :-

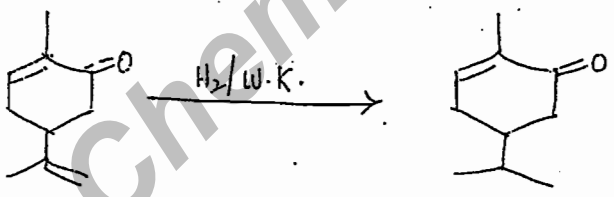
→ Syn-hydrogenation / Regio Selective / face-Selectivity / Stereo Selectivity.

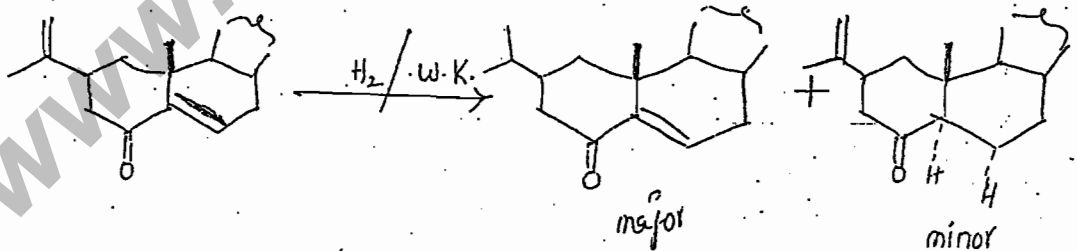
* In olefins, if several double bonds are present, wilkinson's hydrogenation preferentially takes place at less substituted olefine - Regioselectivity.

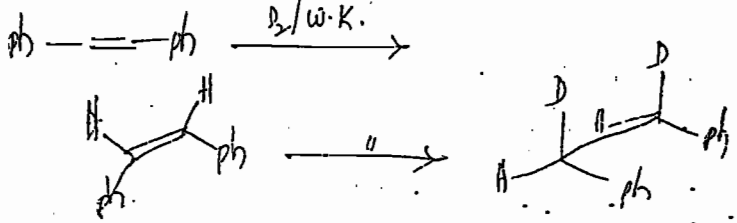
* At unsaturation if there is a crowding, hydrogenation preferentially at sterically less crowded face/side.

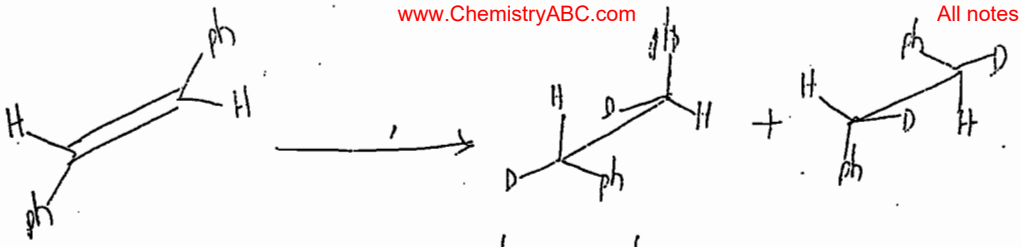


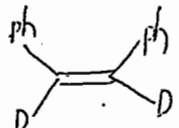










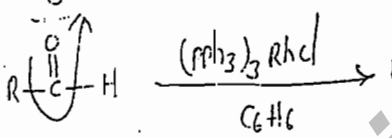
* ph–C≡C–ph $\xrightarrow[C_6H_6]{D_2/\text{W.K.}}$ 

N_2D_2

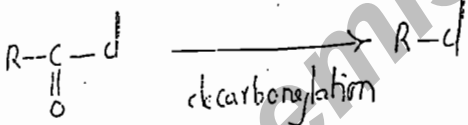
* OTHER APPLICATIONS OF W.K :–

V.IMP
1) Decarbonylation of aldehydes & acid-halides.
2) Desulphonylations
3) Loss of Formyl chlorides from long carbon chain acid chlorides.

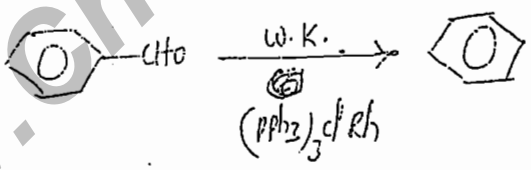
1) Decarbonylation :

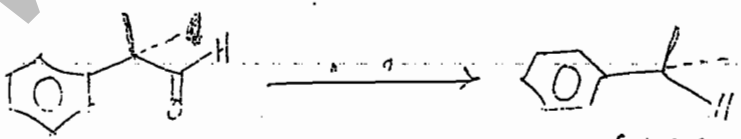


$\xrightarrow[C_6H_6]{(PPh_3)_3RhCl}$ R–H

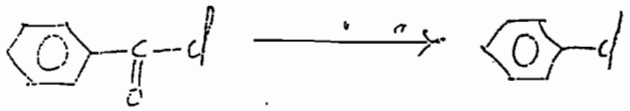


*V.imp :–

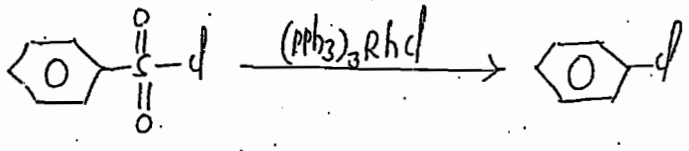




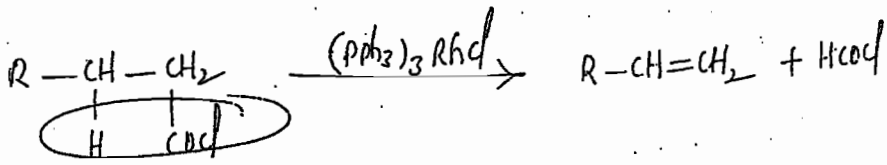
Cumene

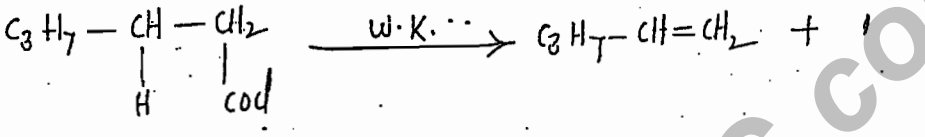


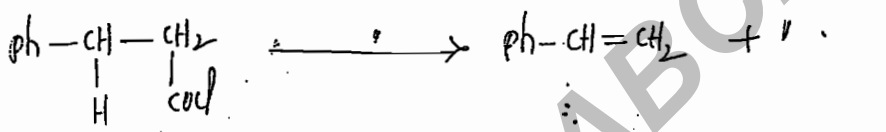
a) Desulphonylations :-



3) ~~Loss of formyl chloride~~ :







20/05/08

ORGANO METALLIC REAGENTS

→ compounds having carbon and metal bonding - organo metallic reagents.

→ IMPORTANCE :-

→ organo metallic Reagents used for functional group interconversions and C-C bond formations.

∴ In organic synthesis, OMR very much helpful in carbon chain lengthening.

→ In metal & carbon bonding, carbon more e.n. than metal, ∴ metal-carbon bonding highly polar, carbon carries -ve charge and metal carries +ve charge.

→ organo metallic Reagents are good source for carbanion nucleophile.
∴ develops new C-C bonding by attacking at electrophilic 'C' centre

$M^{\delta+}-C^{\delta-} \xrightarrow{\text{solvent}} M^{\oplus} + C^{\ominus}$

M : metal carbanion

M : d-block elements ; Cu, Pd, Hg, Zn

I/IIA : Li / Mg

* organo magnesium Reagents

* organo Lithium "

* " zinc "

* " copper "

* " palladium "

* " Tin "

* " Silicon "

* " lead "

* " mercury "

* Li–C, Mg–C : Cu–C, Pd–C } moderately polar ; Pb–C, Hg–C } less polar

Li–C, Mg–C : more polar ⇓ fast in releasing $C^{\ominus}$; highly reactive

Cu–C, Pd–C ⇓ neither slow nor fast in releasing $C^{\ominus}$. moderately reactive.

Pb–C, Hg–C ⇓ slow in releasing $C^{\ominus}$ less-reactive

* ORGANO MAGNESIUM Reagents : "Grignard" reagents.

→ In C.Mg : C (e.n : 2.5) — Mg (e.n : 1.3) $\Rightarrow C^{\delta-}-Mg^{\delta+} \longrightarrow [C^{\ominus}] + Mg^{\oplus}$

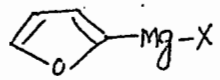
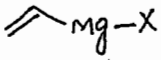
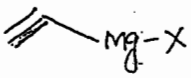
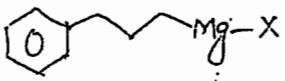
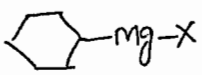
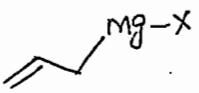
→ very good source for carbanions, widely used in org. synthesis compared to any other OMR.

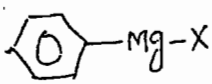
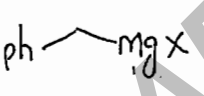
Formulae :- $R-Mg-X$

R = org. groups. R = alkyl, alkenyl, alkynyl
X = halo groups. alicyclic, aromatic,
hetero aromatic, aralkyl,
allyl, benzyl, propargyl

X = F, Cl, Br, I ; but Fluoro combination is less common.

eg: $H_3C-Mg-X$

$R-Mg-F$; $R-Mg-Cl$; $R-Mg-Br$; $R-Mg-I$.

Preparation :-

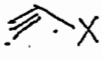
→ organo halo compounds $\xrightarrow[\text{Dry Ethers}]{Mg}$ organo Magnesium halide (Grignard).

→ $R-X \xrightarrow[\text{Dry ether}]{Mg} R-Mg-X$ (R = org. group)

Reactivity w.r.t. organic group :

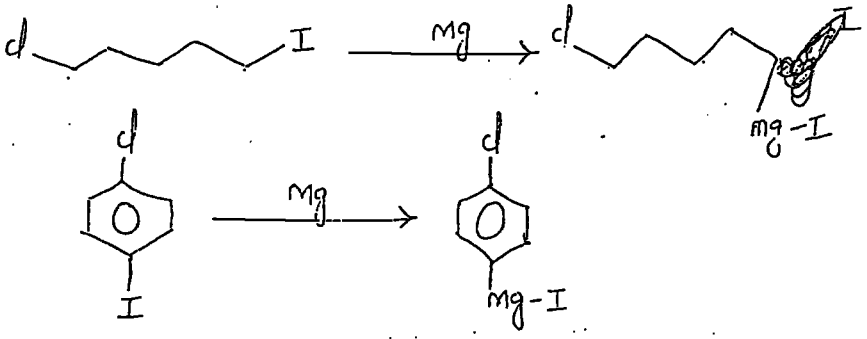
⇒ Allyl, benzyl halides > 3°-alkyl halides > 2°-alkyl halides > 1°-alkyl halides >

alkenyl halides > aryl halides > alkynyl halides

Reactivity order w.r.t. Halo group :

$$R-I > R-Br > R-Cl > R-F$$

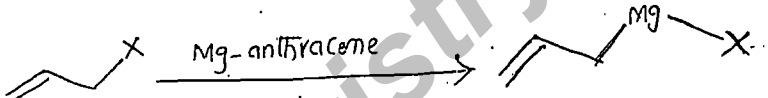


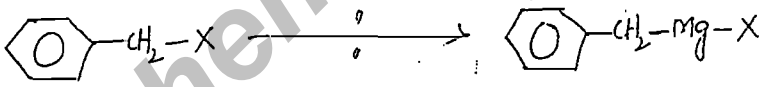
* Limitations :-

→ Allyl/ Benzyl halides are highly reactive with pure 'Mg', rean may be explosive.

∴ In prepn of Grignard of allyl, benzyl halides, instead of pure Mg, Mg-anthracene complexes are used. which lessens reactivity of Mg in Grignard formally.

eg:-





* V. Imp :-

→ Fluoro compds (R-F) are inert or highly unreactive in formation of Grignard.

∴ I_2 or ether is taken as catalytic medium.

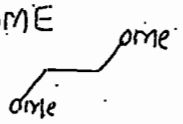
$$R-F \xrightarrow[\text{Ether}]{Mg} R-Mg-F \quad \text{poor yields}$$

I_2 ($R-F \xrightarrow{Mg/I_2 \text{ or Ether}} R-Mg-F$; high yields

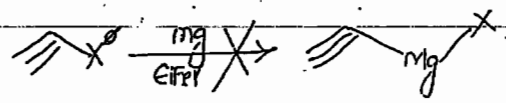
$R-I \xrightarrow{Mg} R-Mg-I$)

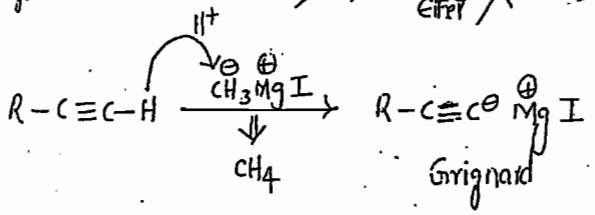
* vinyl & aryl halides less reactive in formation of Grignard.

∴ High boiling solvents must be used eg:- THF, DME

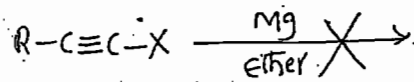


* Alkynyl halide :





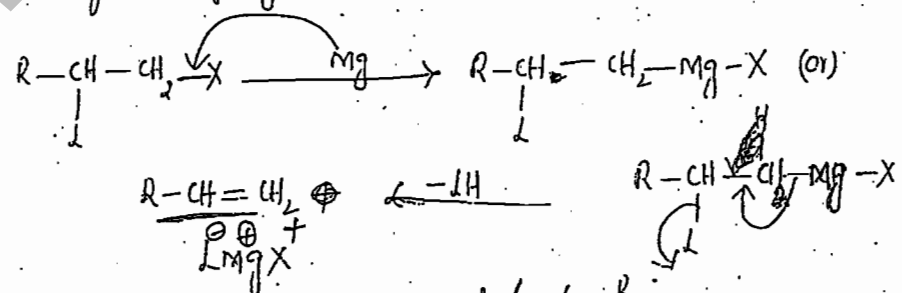
Alkynyl grignards not possible to prepare with general methods. Alternate indirect method by reacting terminal alkyne with readily available 'Grignards'.

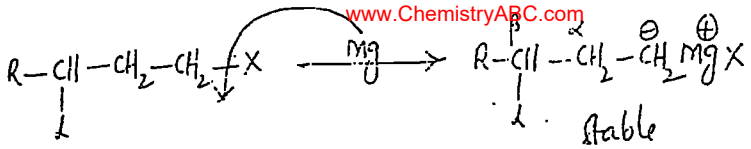


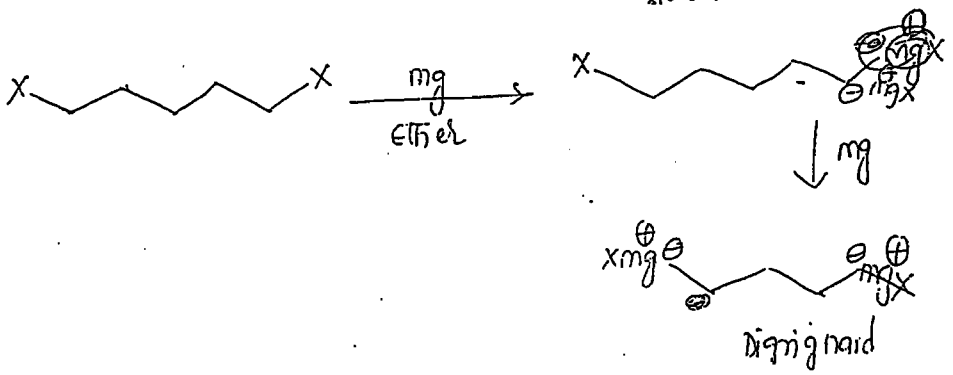
Alternative method :

→ Grignard acting as base, substracting H+ from terminal alkyne, then converting alkyne into Grignard.

* At α-position of Grignard, if there is a leaving group, Grignard get destabilised by undergoing elimination.







Digrignard

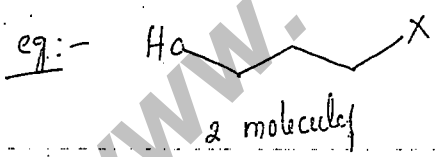
2) whenever halo compd is having fn capable in reacting with grignard, difficult to prepare grignard, because molecules themselves reacting with grignard.

Acidic groups : $-OH$, $-COOH$, $-C\equiv C-H$, $-SO_3H$, $-NH_2$, $-SH$, $-\overset{\overset{O}{\|}}{C}-\overset{H}{\overset{|}{N}}-H$

polar unsaturated fn : $-\overset{\overset{O}{\|}}{C}-H$, $-\overset{\overset{O}{\|}}{C}-$, $-\overset{\overset{O}{\|}}{C}-OR$, $-\overset{\overset{O}{\|}}{C}-N<$, $-\overset{\overset{O}{\|}}{C}-X$,

$-\overset{\overset{O}{\|}}{C}-O-\overset{\overset{O}{\|}}{C}-$, $-C\equiv N-$, $C=N$, $N=C=O$, 

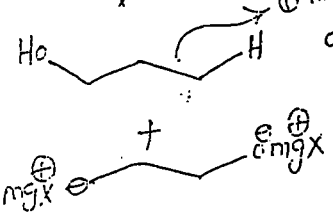
all these groups shouldn't be present in halo compd in prepn of grignard.

eg:- 

2 molecules 2 molecules

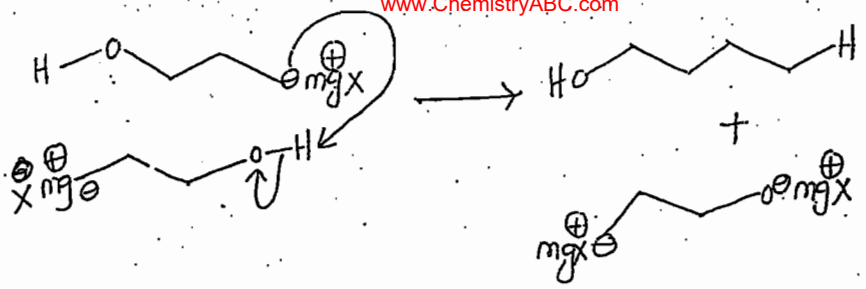
cannot be preserved for long time.

After 1 hr



① molecule lost its grignard character

out of two, only one is left over.



* Grignard prepn should be done in inert & dry conditions.

$$R^{\ominus}\,{}^{\oplus}MgX \xrightarrow{H-O-H} R-H + Mg(OH)X$$

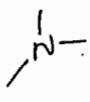
Grignard reacts with H_2O & decomposed to hydrocarbon.

$\therefore$ H_2O shouldn't be taken.

* $RMgX \xrightarrow{O_2} R-O-O-Mg-X$

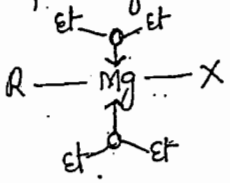
O_2 reacts with Grignard, produces peroxide. $\therefore$ Inert conditions should be employed.

Solvents :— * Dry Ethers, Et_2O, THF, DME.

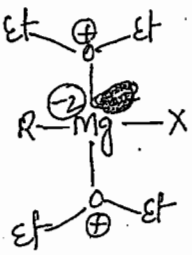
* C_6H_6, toulene (supporting agent : 3° amine) ; If dry ethers not available, C_6H_6 or toulene in combination with 3° amines can be used. eg:  ,  , etc.

Role of Solvent :— (Ethers).

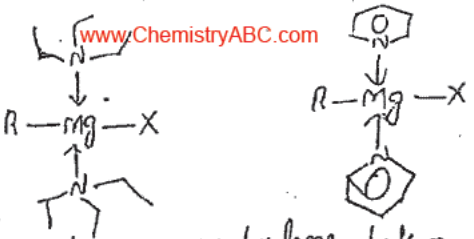
→ Ether solvents gives additional stability for Grignard by co-ordinating with Mg of Grignard.



(or)



→ In benzene,



In the place of ether, benzene or toulene taken, 3°-amines are additionally used, because, benzene, toulene cannot stabilise grignard.

→ 3°-amines can stabilised as by co-ordination with mg of grignard

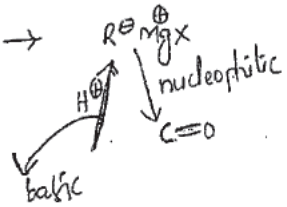
Date : 23/05/08

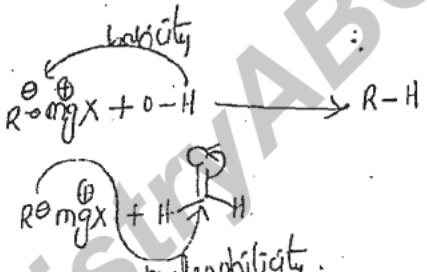
→ In soln state, Grignard exist with following equilibria.

$$2\ RMgX \rightleftharpoons R_2Mg + MgX_2$$

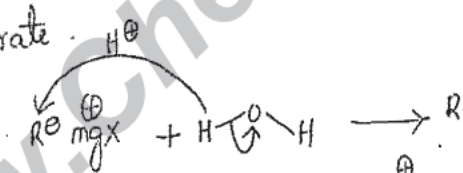
Chemical properties :-

→

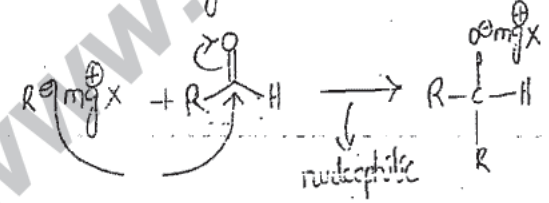




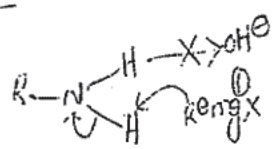
→ Grignard reagent acts as base & nucleophile based on nature of other substrate.



→

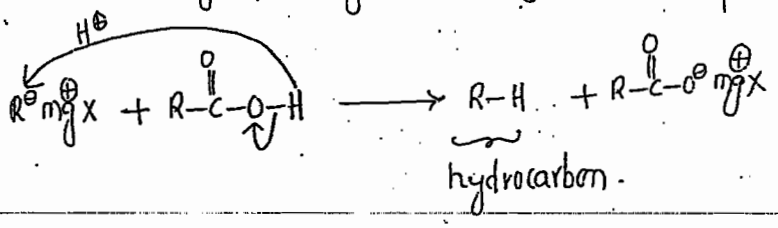


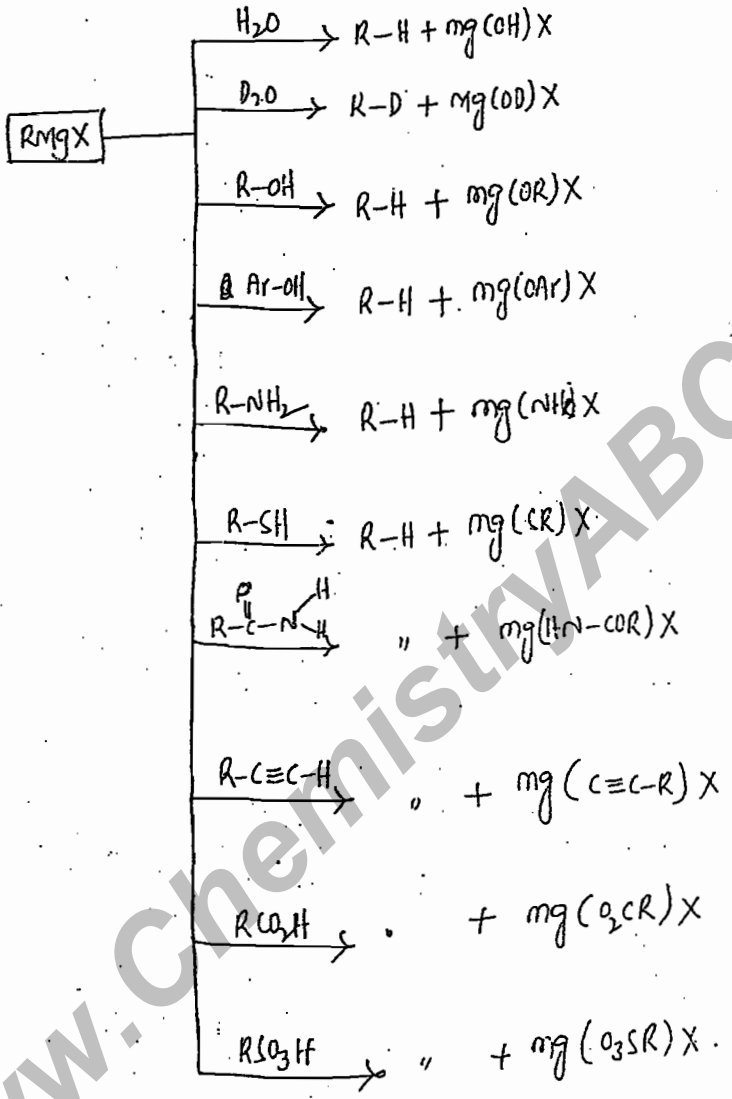
Grignard as Base :-



Grignard reasonably powerful base, can abstract H+ ion from all org. acidic groups.

→ on reaction with acidic group, Grignard converts into corresponding hydrocarbon.





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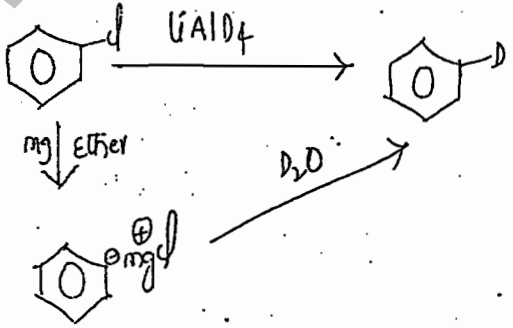
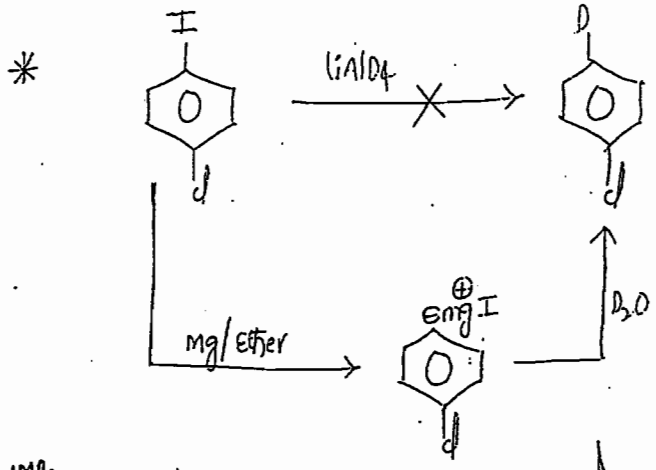
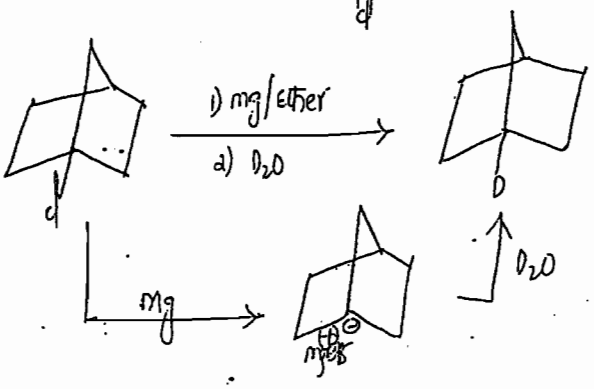
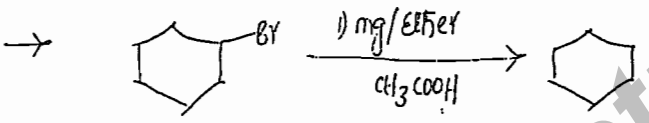




V. IMP.

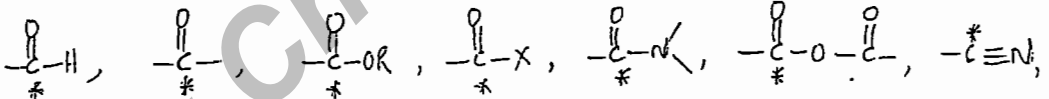




Date: 24/05/08

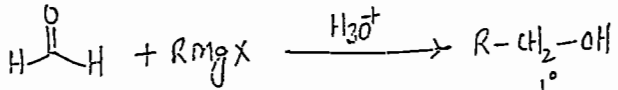
* Grignard as Nucleophile :-

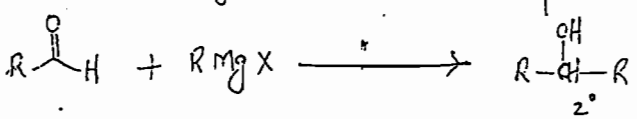
→ Grignard attacks at different electrophilic carbon, then develop new C-C bonding.

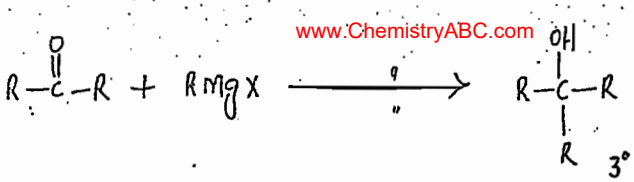


→ Nucleophilic additions at carbonyl carbon :

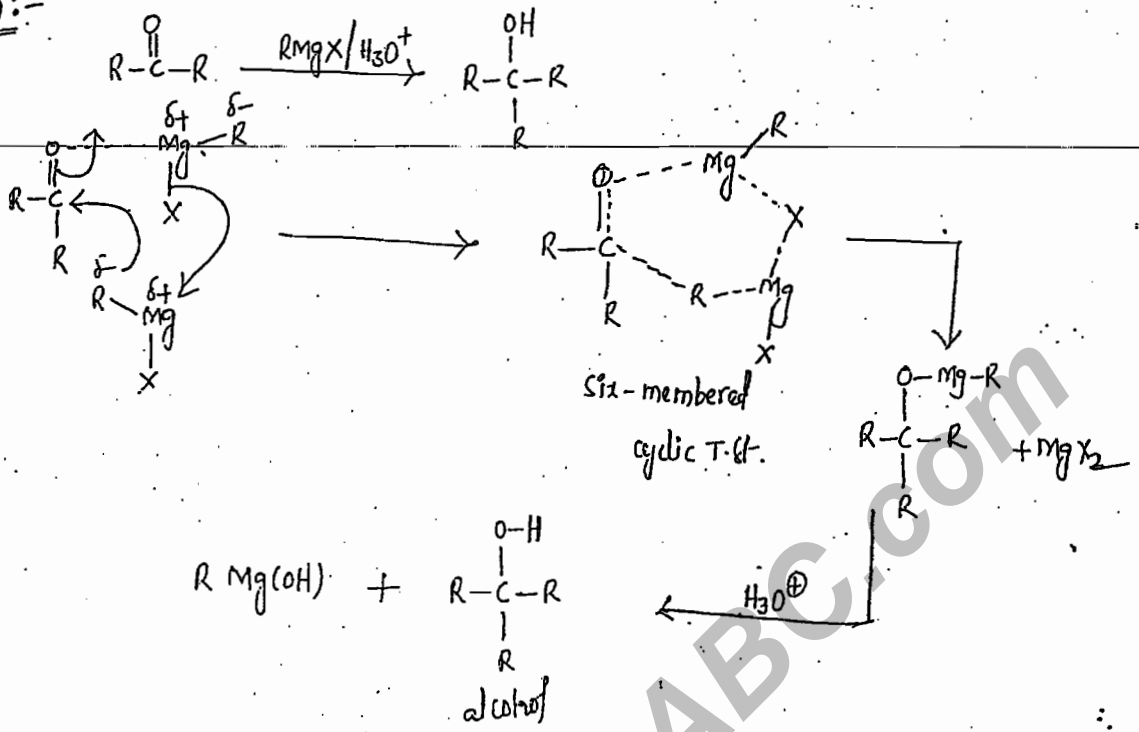
Carbonyl comp'ds $\xrightarrow[H_3O^+]{\text{Grignard}}$ Alcohols





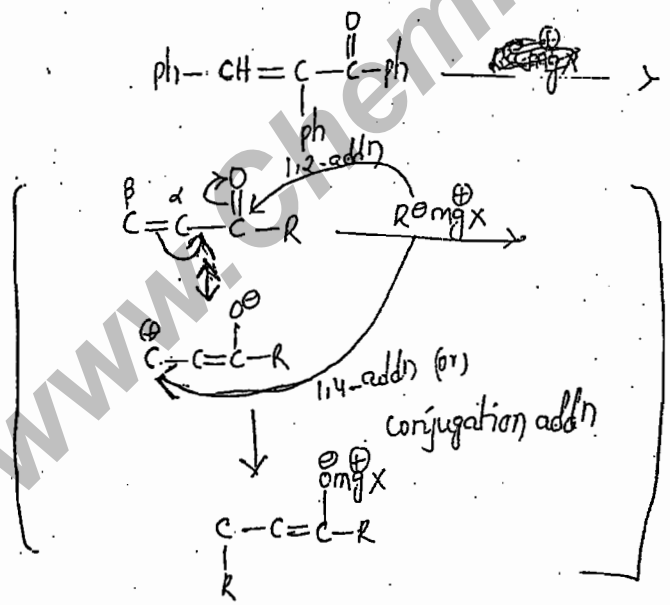


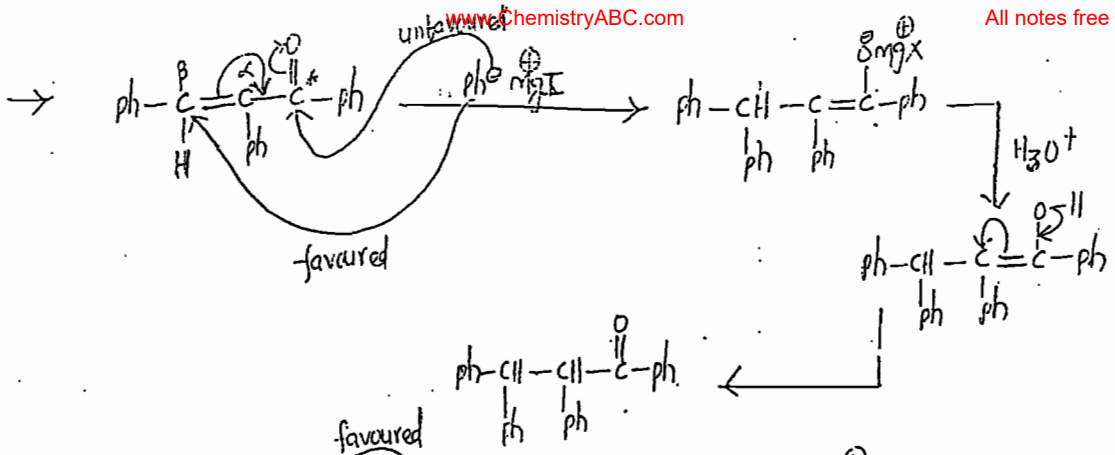
Mech:-

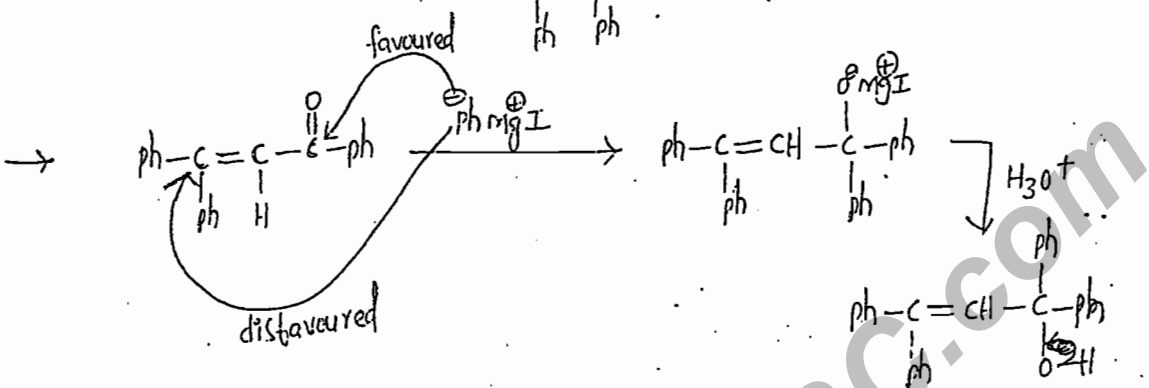


* Steric crowding : Grignard additions :

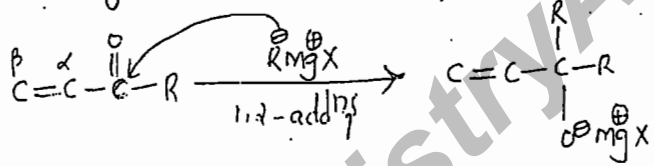
eg: α,β-unsaturated carbonyl compounds.

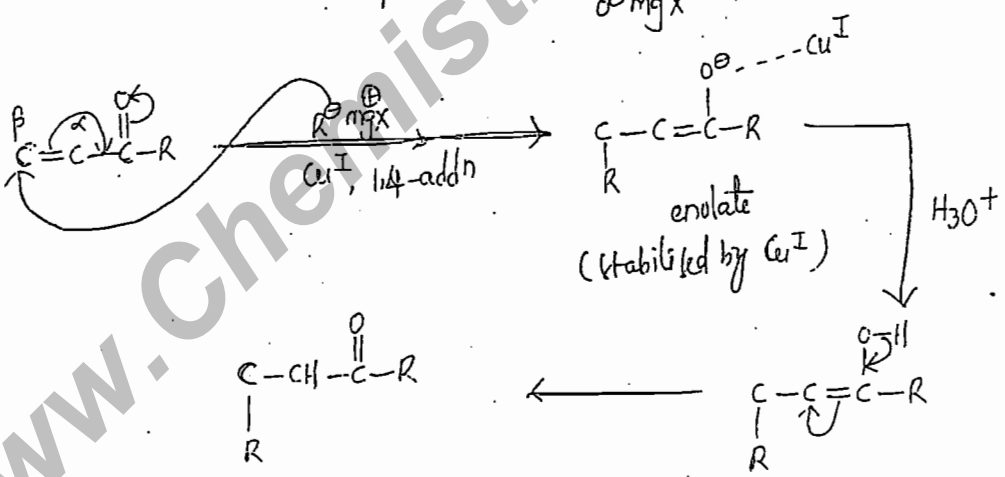






→ Regio Selectivity in grignard additions at α, β-unsaturated carbonyl compds.

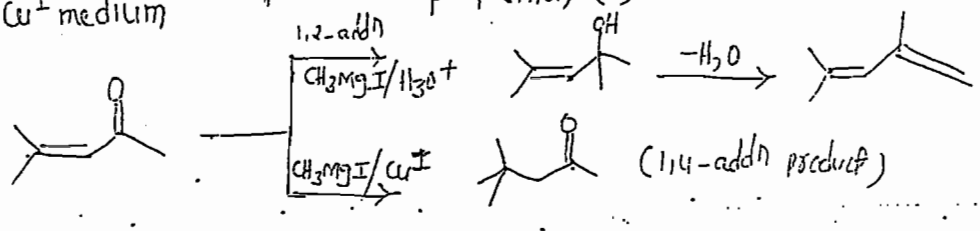


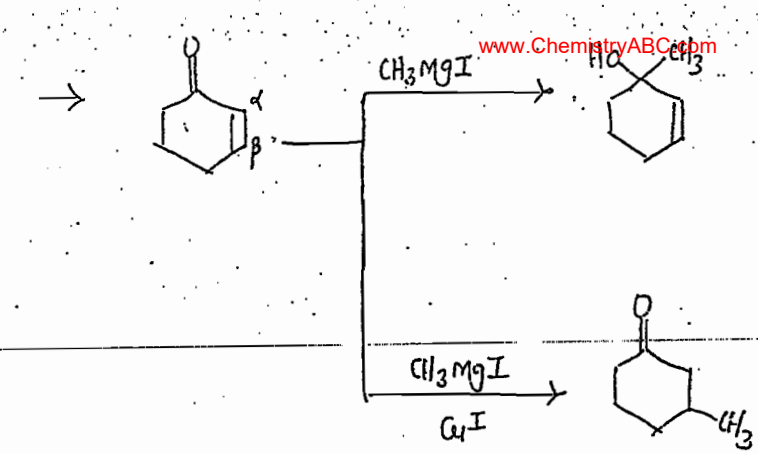


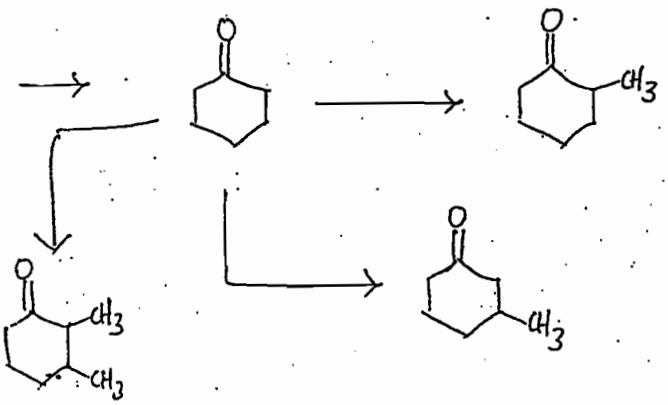
→ with simple Grignard adding at carbonyl carbon

→ , Cu^I medium " β- position (or) 1,4-addn

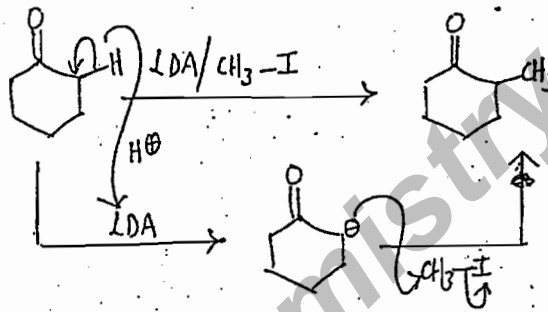
VIMP eq:-

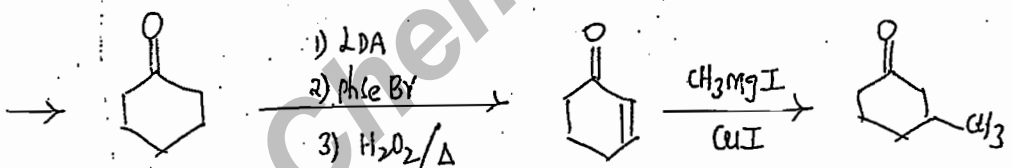


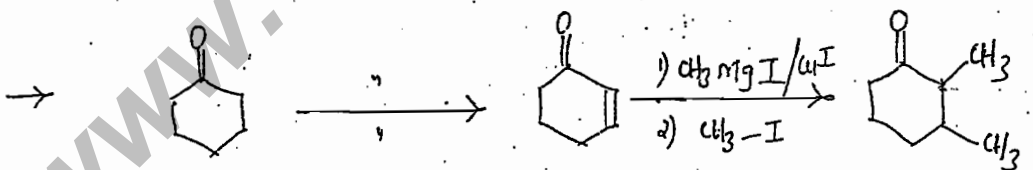


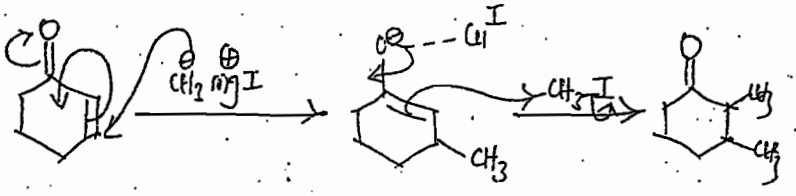


AN:-









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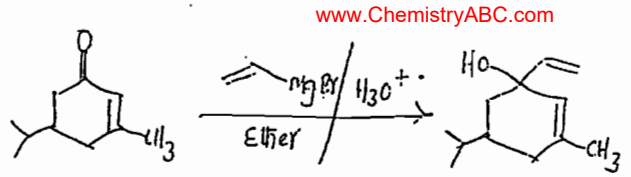
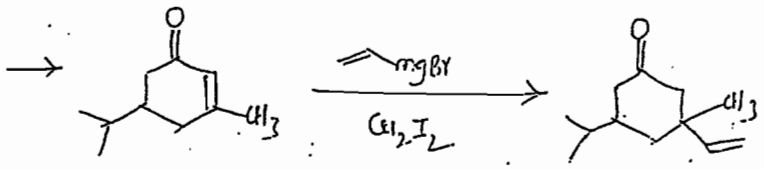
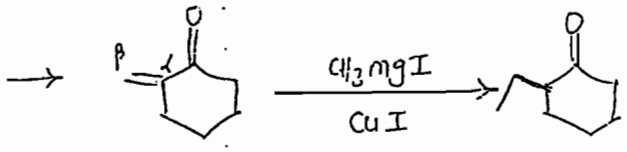
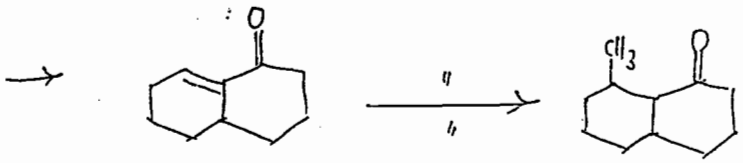




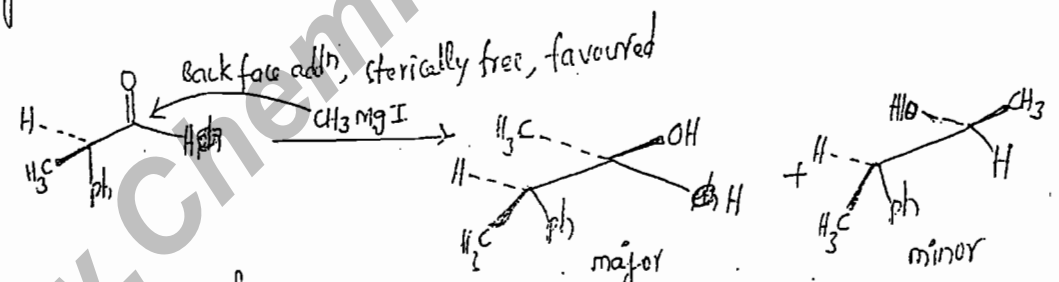


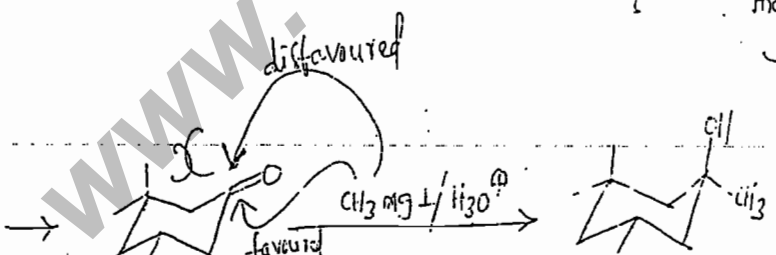


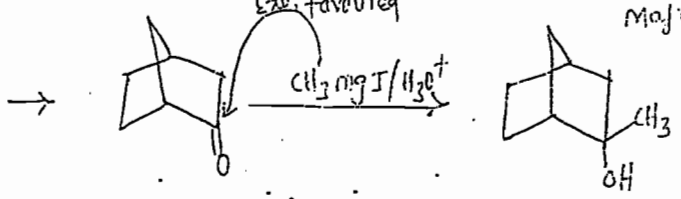
→ Stereo Selectivity : In RmgX additions.

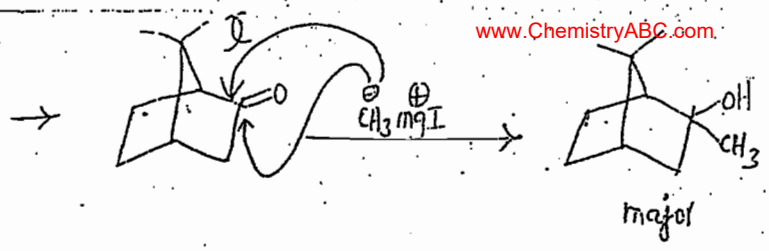
→ At a carbonyl cn, if there is a steric crowding, preferential addn at sterically less crowded side or face of carbonyl.

*

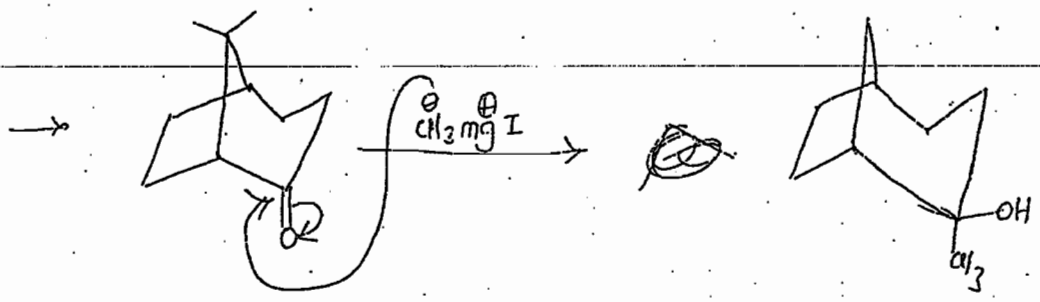


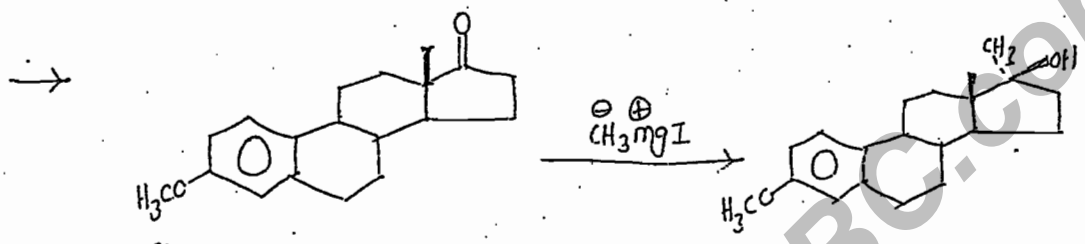






major



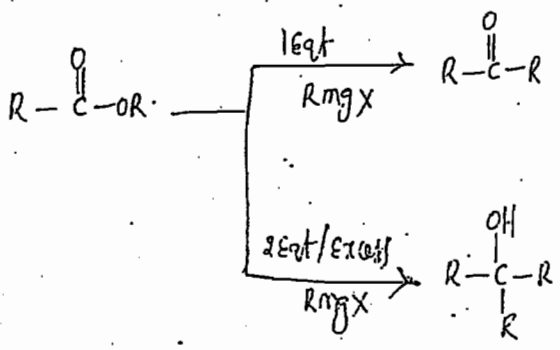


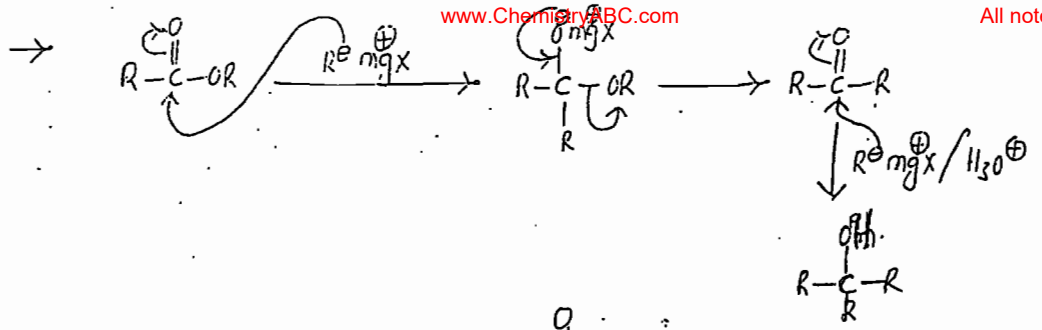
* Grignard addn at acid-derivatives :—

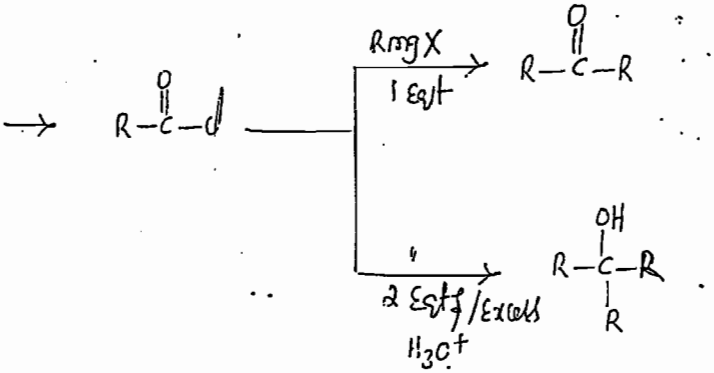
Ester
Acid-halide
Amide
Anhydride

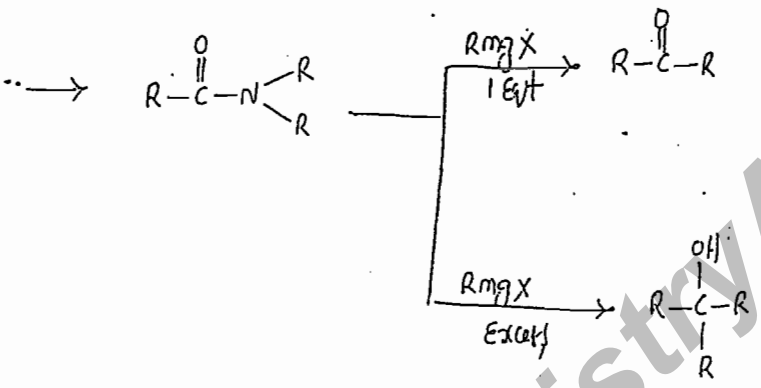
1eqt RMgX → carbonyl compounds

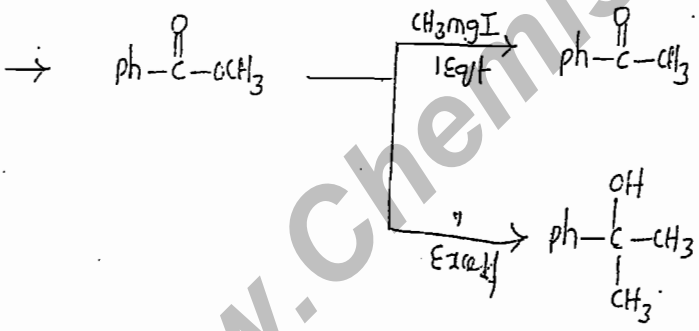
Excess RMgX (or) 2Eqt RMgX → Alcohol

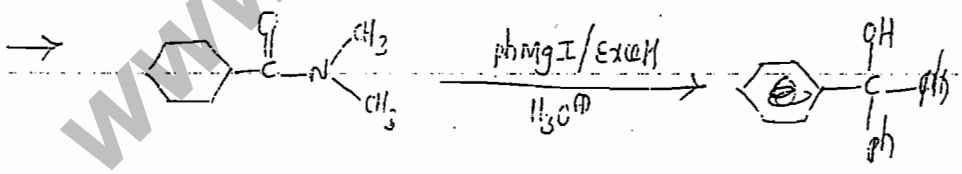


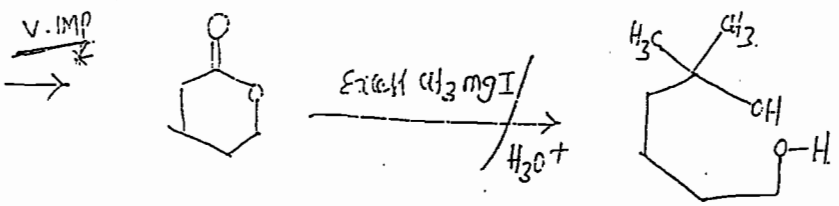


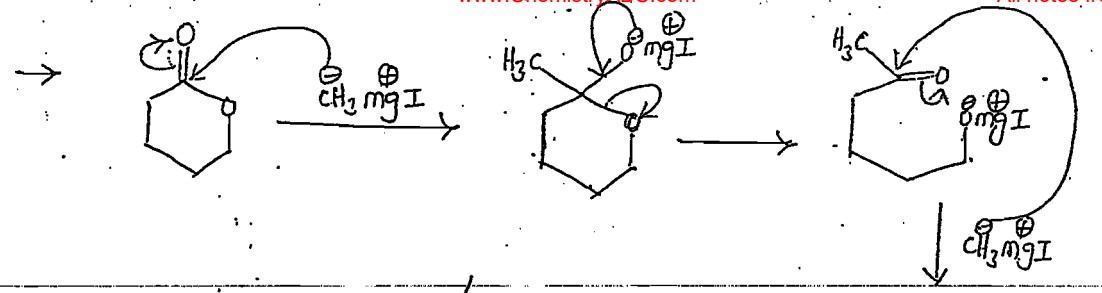


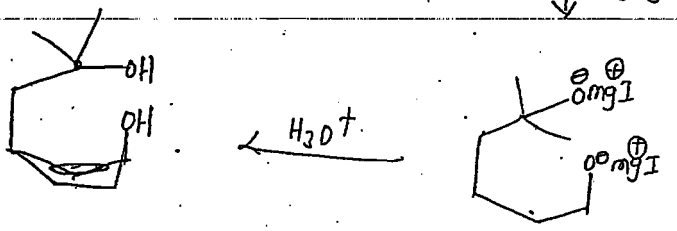


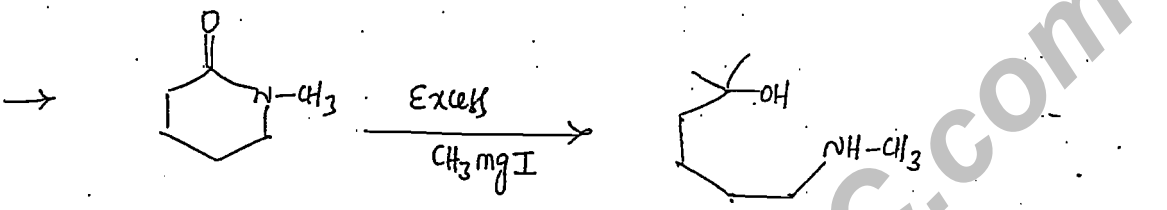




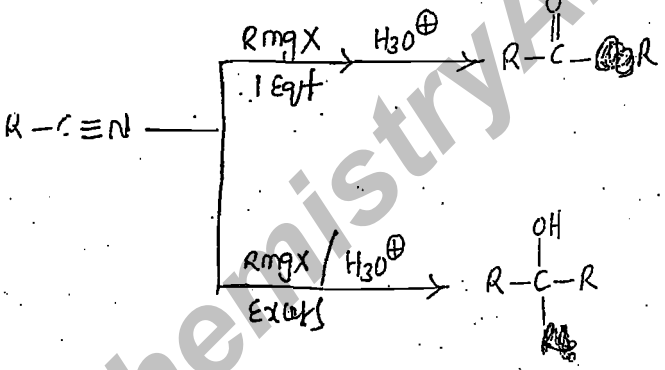


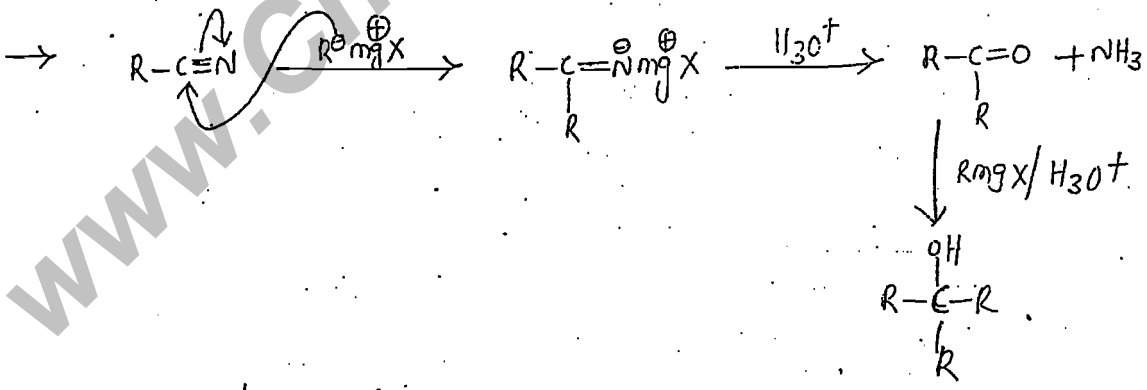


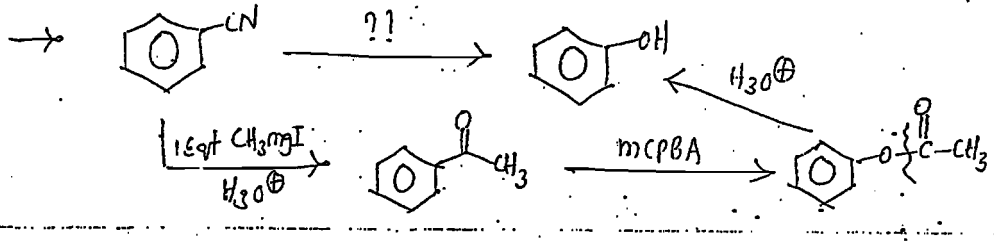




* With Nitrile :-

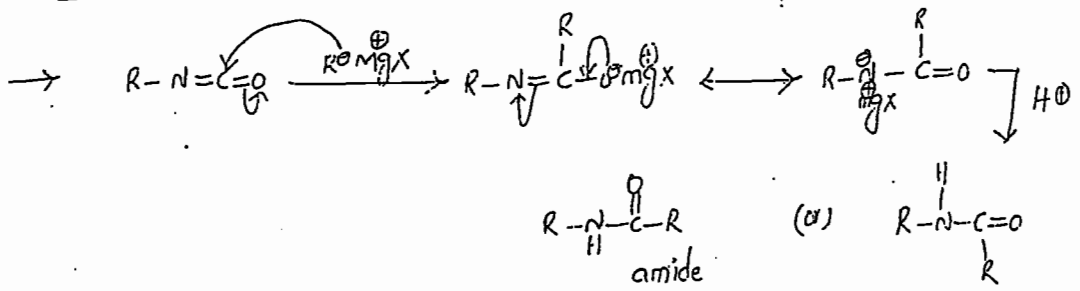




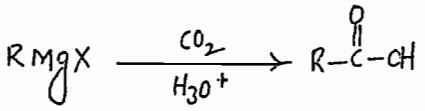


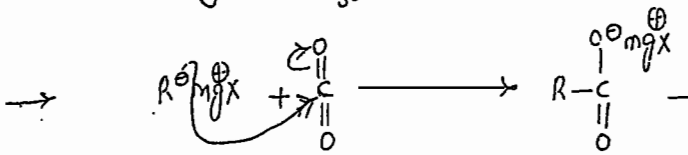
25/05/08

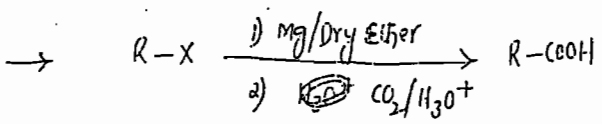
* with isocyanate :

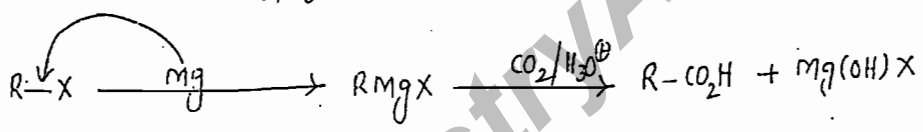


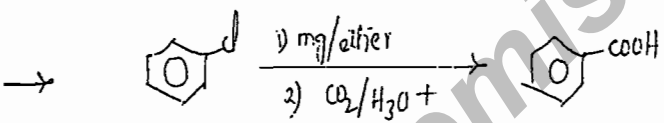
* with CO_2/CS_2 :

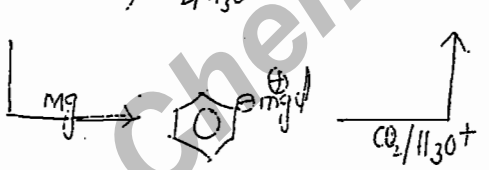




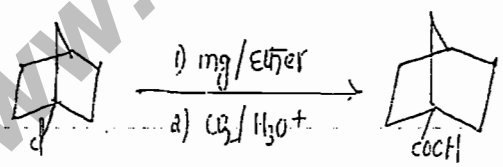




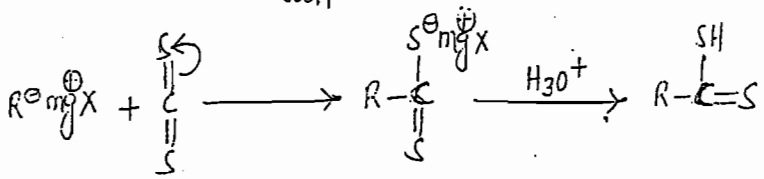




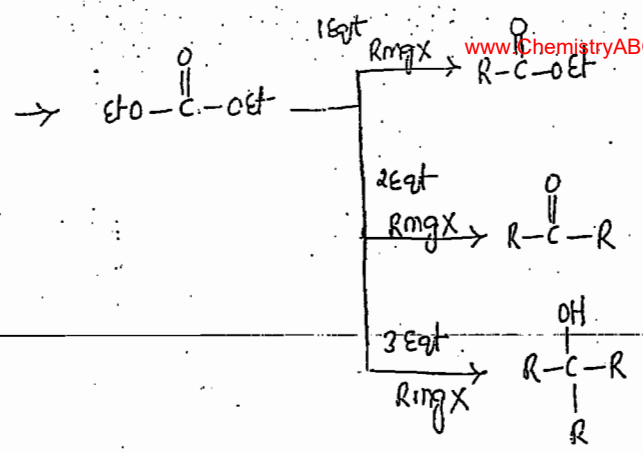
* v.imp.

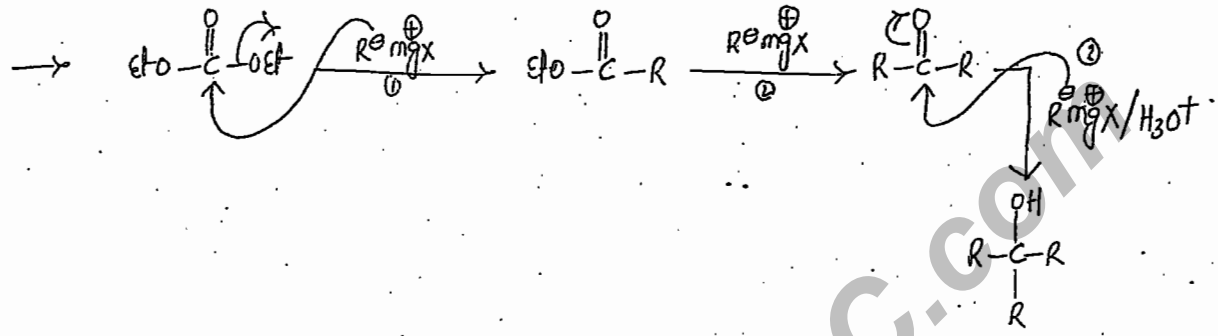


* with CS_2 :

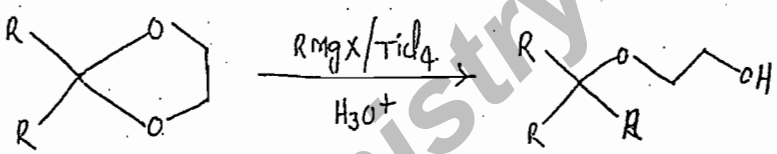


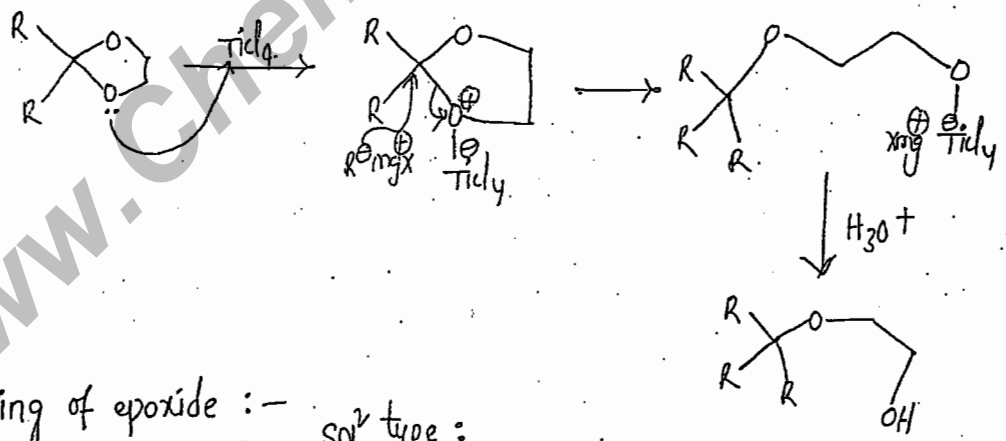
STUDENT XEROX 9030000126





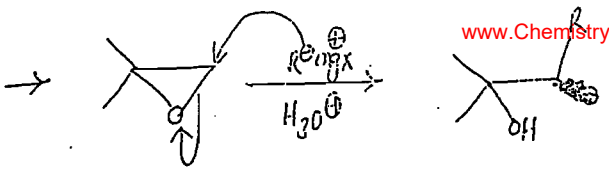
→ In lewis acid medium, acetals, ketals gets opened by RMgX.

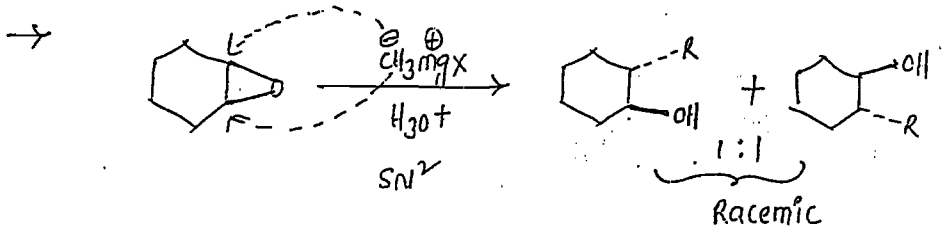


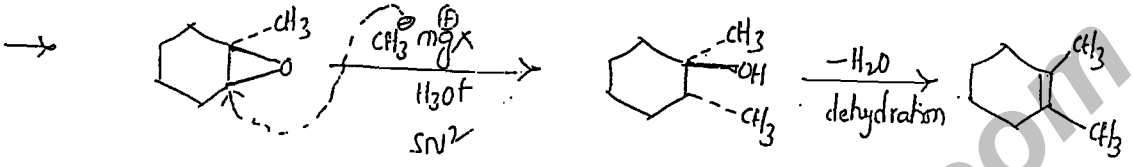


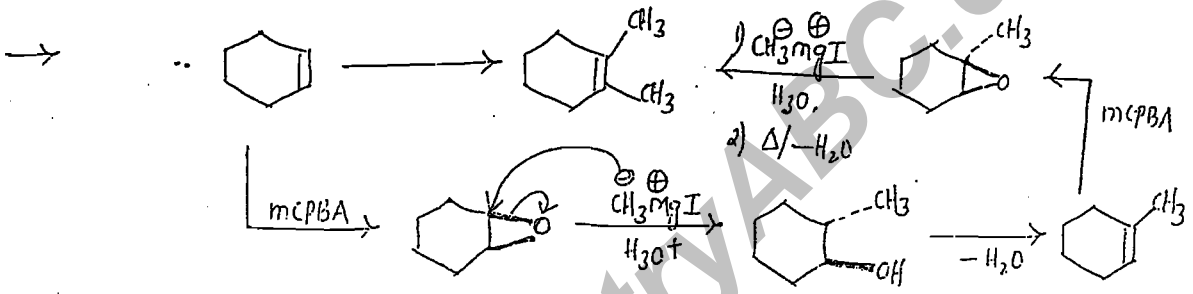
* opening of epoxide :- S_N2 type :

→ Grignard opens epoxide by attacking at sterically less crowded position.

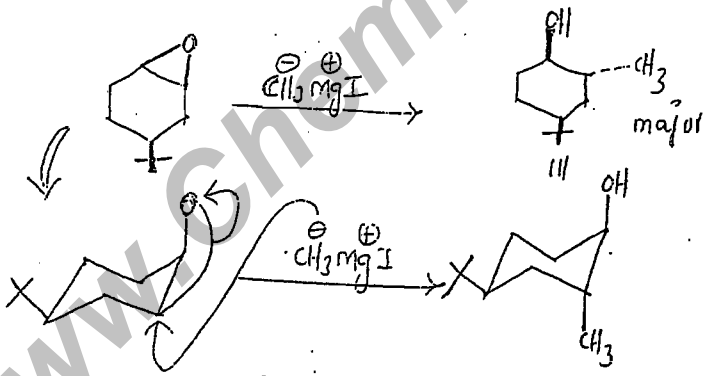


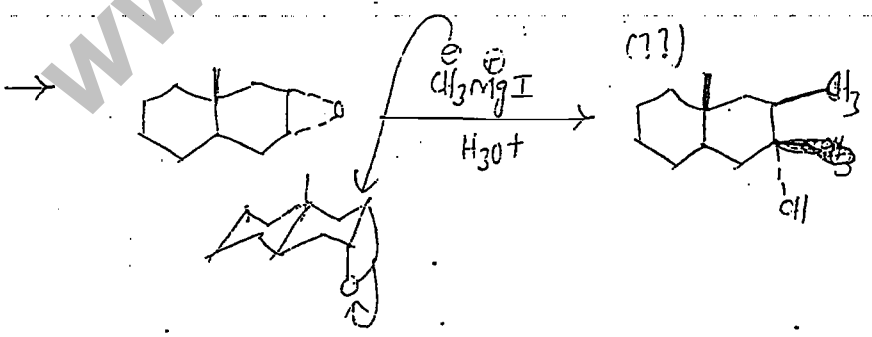


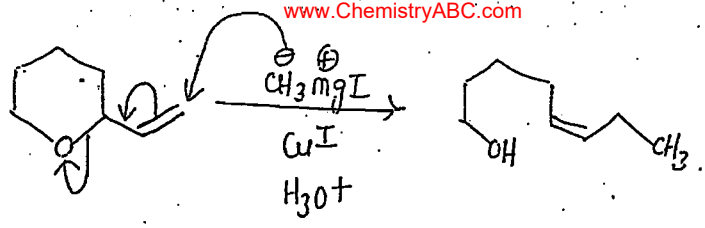


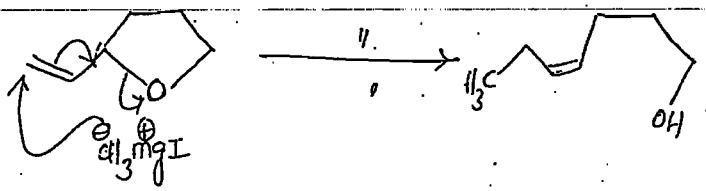


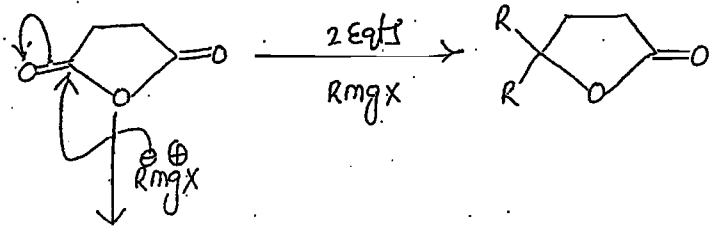
→ In conformational rigid epoxide, opening from axial direction.

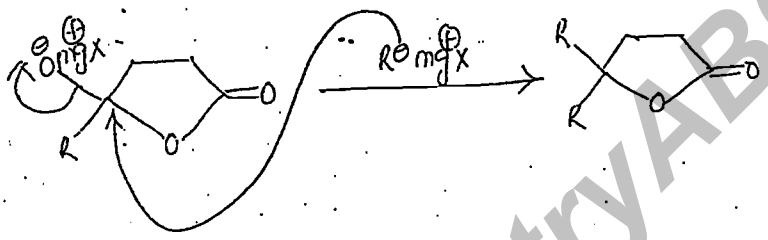


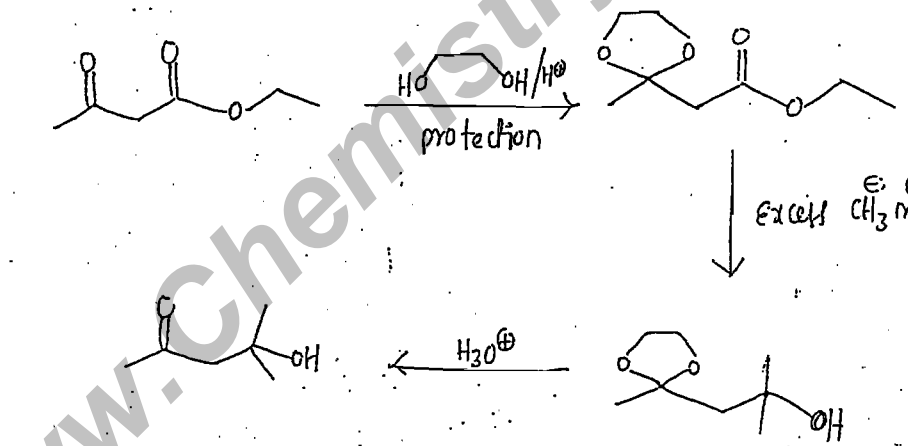


→ 

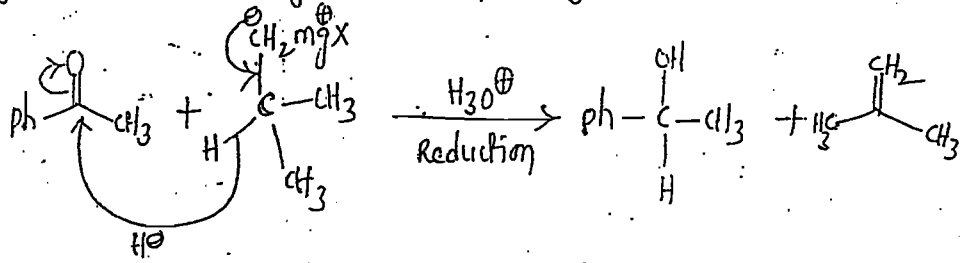
→ 

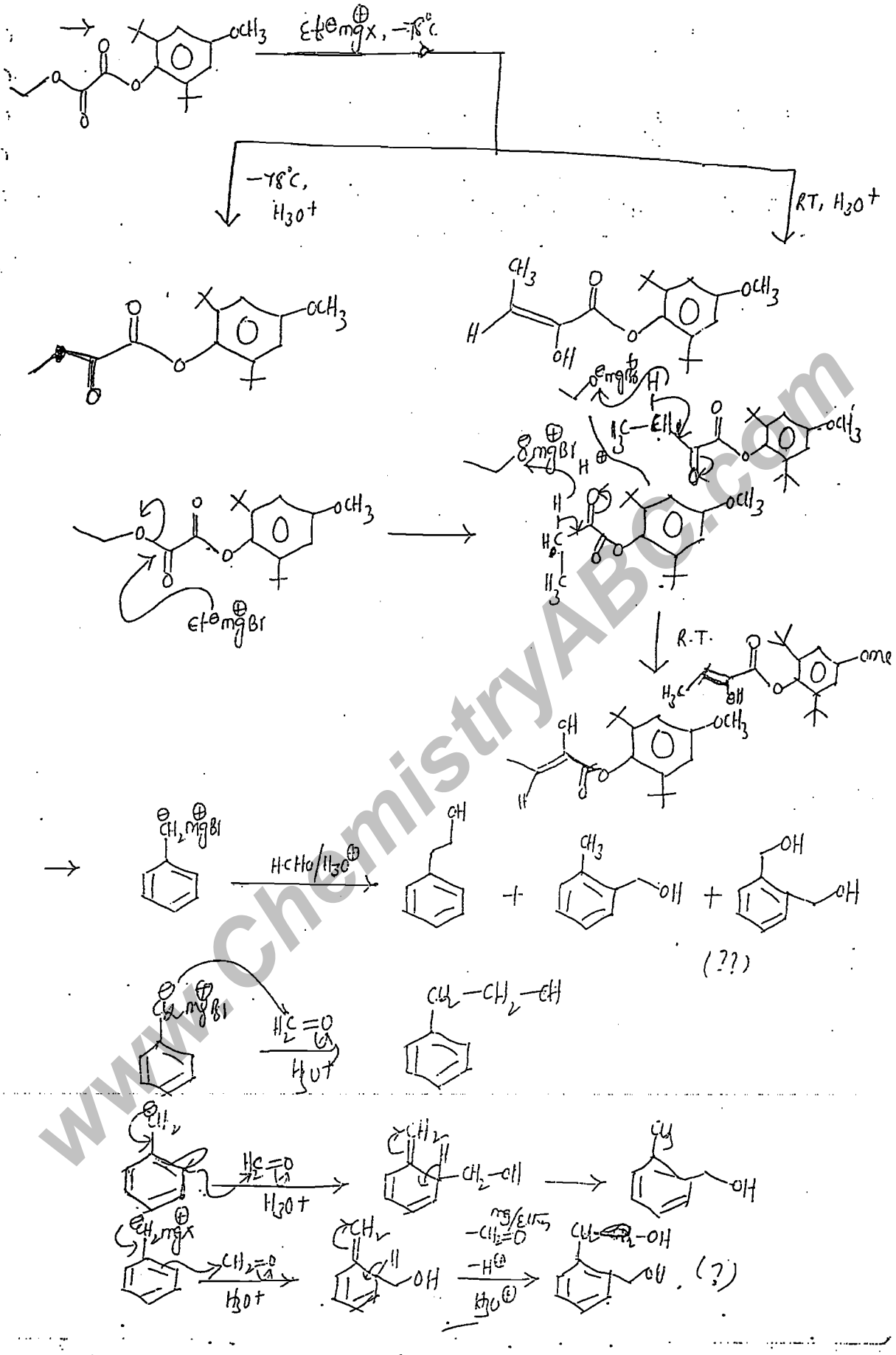
→ 

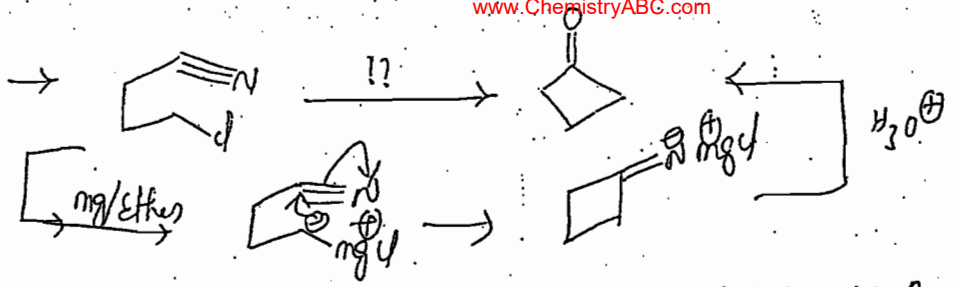


→ 

→ Grignard reagent may act as reducing agent like LAH.







→ ORGANO – COPPER REAGENTS :– (Gilman's Reagents)

→ R_2CuLi

R = any organic group, alkyl, alkenyl, alkynyl, aryl, allyl, benzyl, hateryl..

→ widely used GILLMAN'S REAGENT, lithium dimethyl cuprate.

$(CH_3)_2CuLi$ (or) Me_2CuLi

* Exists in dimeric form. (in soln)

$[(CH_3)_2CuLi]_2$

Preph :–

→ $CuX + CH_3Li \xrightarrow[\text{Ether}]{\text{Dry}} CH_3Cu + LiX$

$CH_3Cu + CH_3Li \rightarrow (CH_3)_2CuLi$

→ compared to Grignard reagents, less reactive due to low polarization of C–M bonding

→ Gilmann's reagent source for carbanion nucleophile.

solvents :– Dry ethers, Et_2O, THF, DME etc.

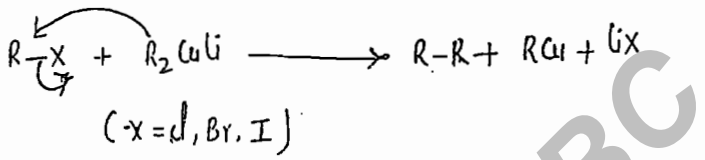
→ low-temp. reacts, less than 0°C.

Applications :—

1) Displacement of halo group.
2) " " tosyloxy group.
3) opening of Epoxide
4) conjugative addns at α,β-unsaturated carbonyl compounds.
5) convert acid halides into ketones.

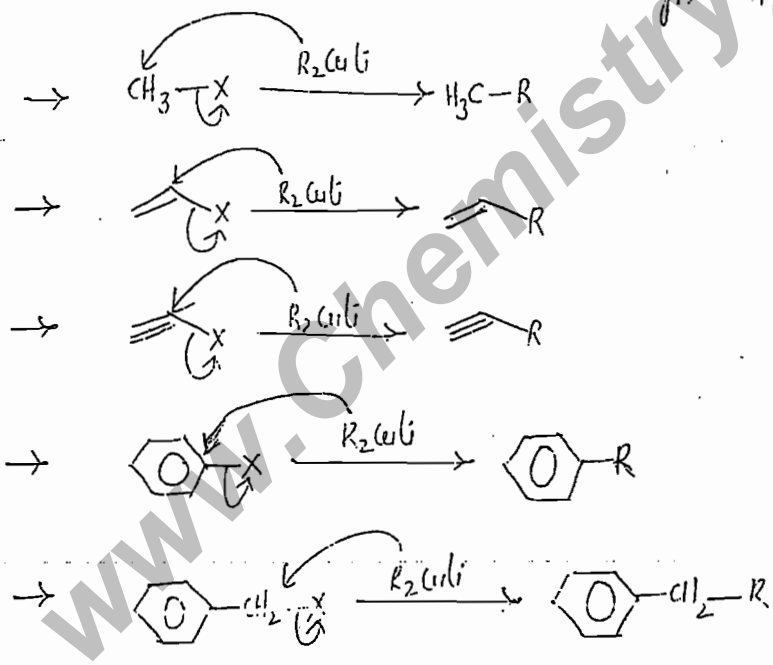
26/05/08

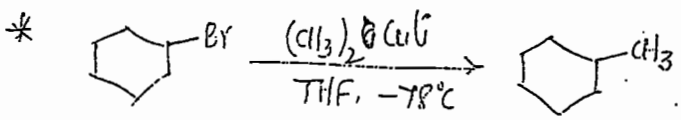
I. Displacement of Halo group :—

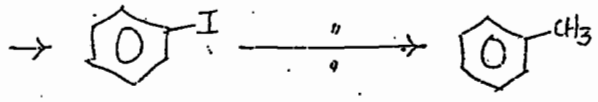


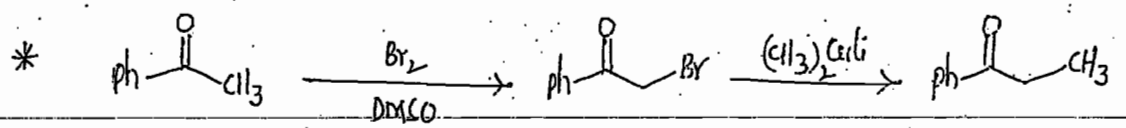
(-X = Cl, Br, I)

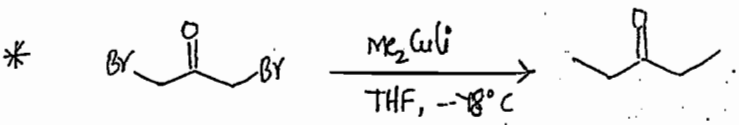
R = any organic group; alkyl, alkenyl, alkynyl, aryl, aralkyl, allyl, benzyl etc

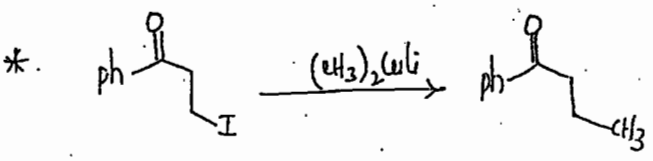




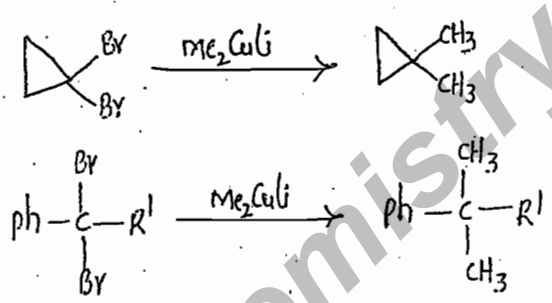




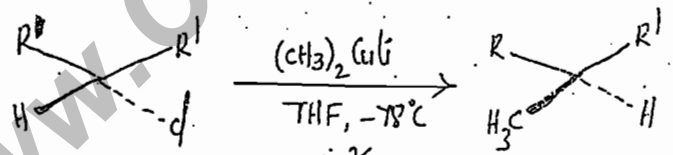


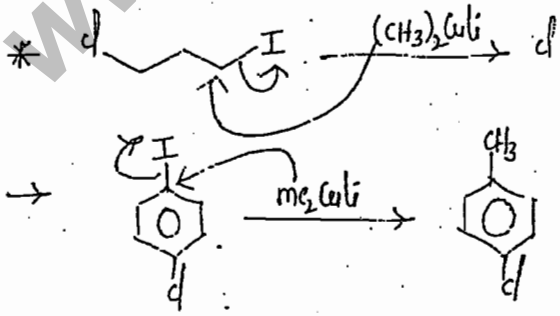


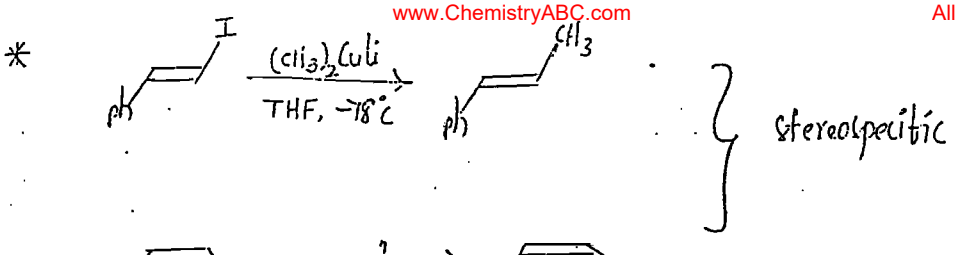
* gemineal halo part of cyclopropyl or benzylic position displaced with Gilhman's reagent.

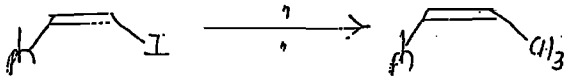


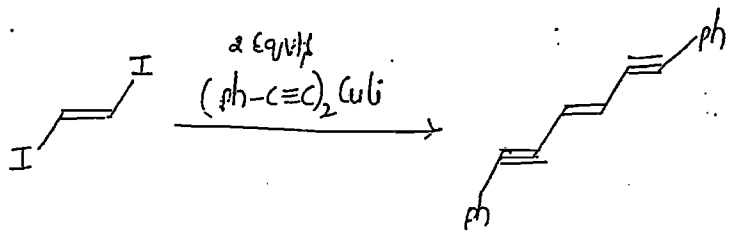
* If chiral centres present, displacement is SN^2 type.

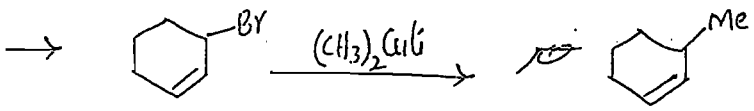






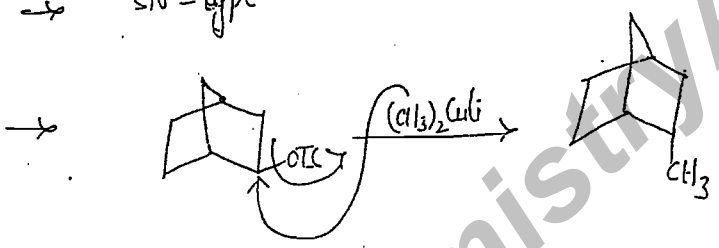


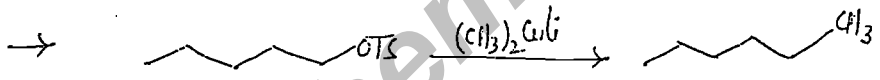




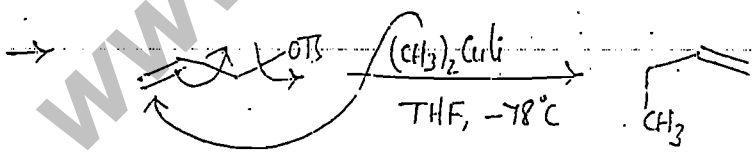
II. Displacement of Tosyloxy groups :—

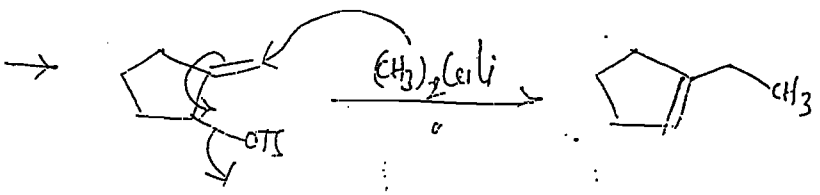
→ S_N2-type

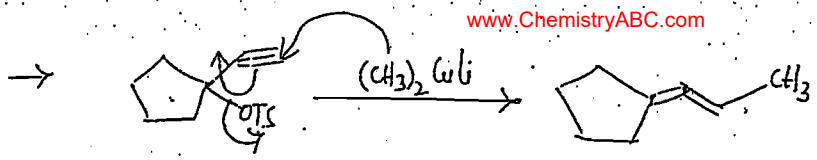




Near to -OTs group, if there is an unsaturation, the Gilman's reagent attacks at unsaturation, followed by loss of -OTs group.

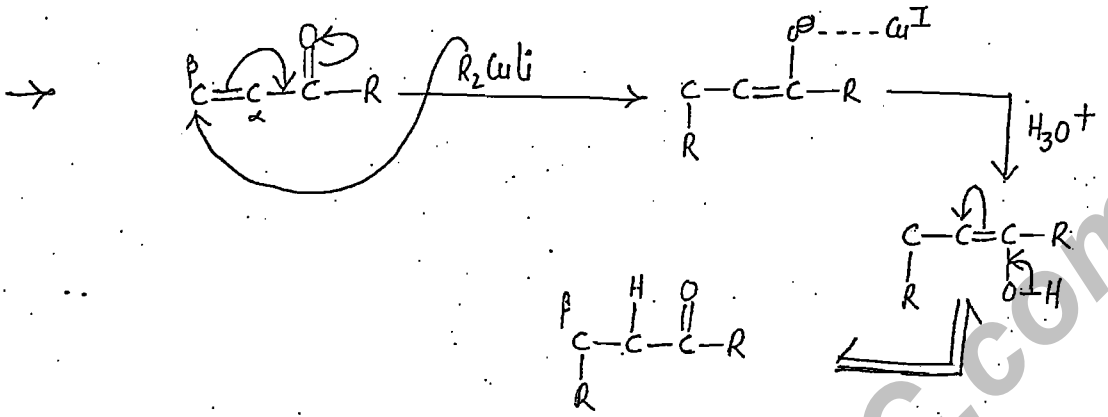


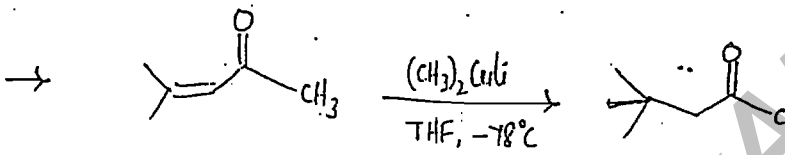


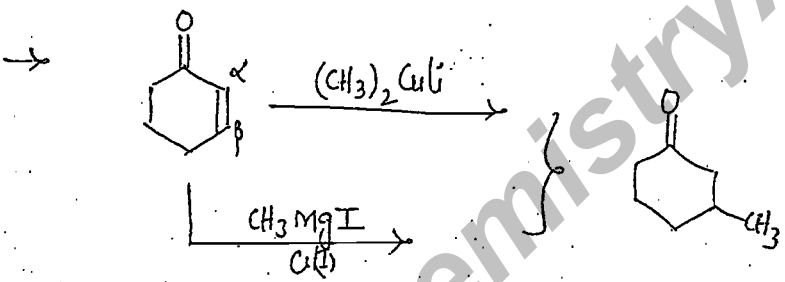


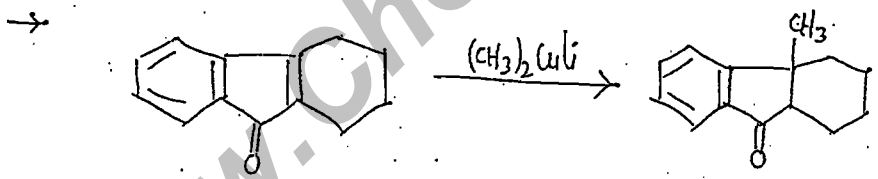
III. conjugative addn at α,β – unsaturated C.C.

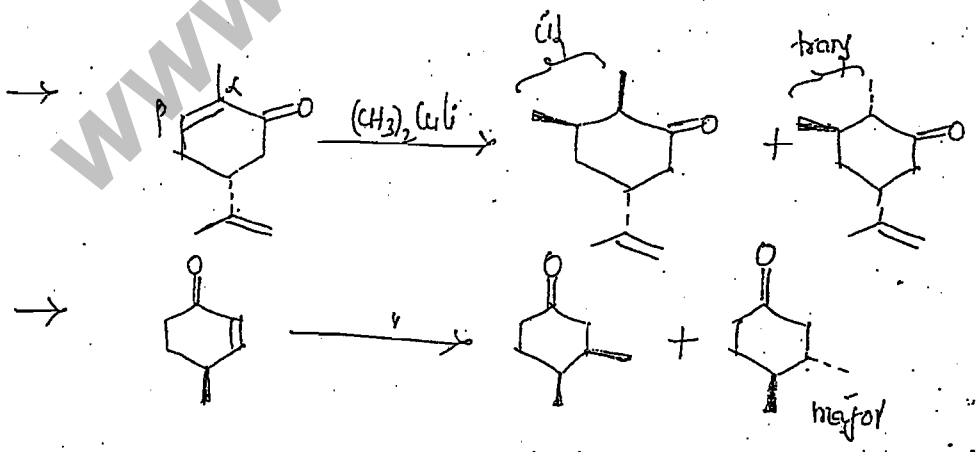
→ 1,4 – additions

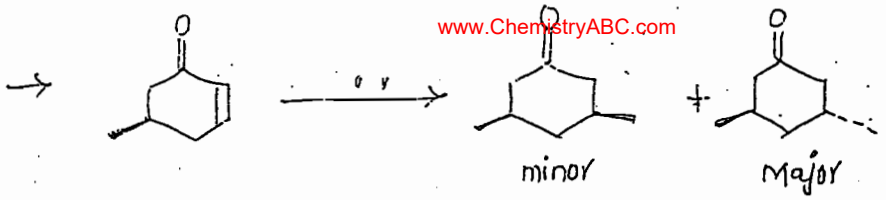


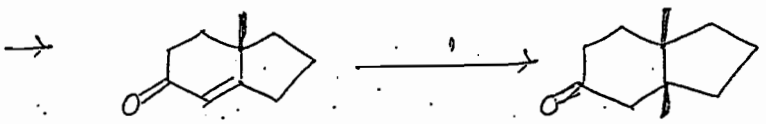




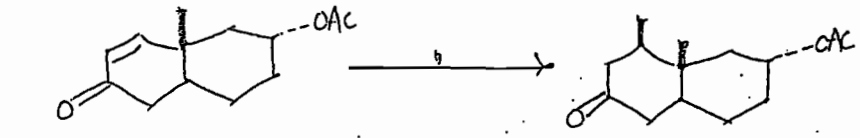


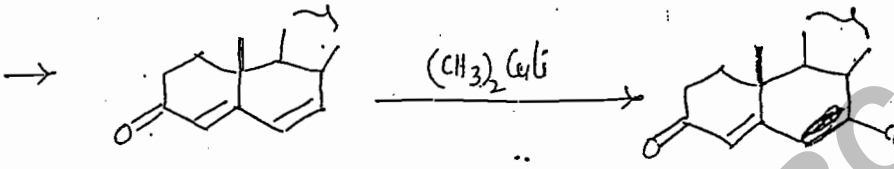




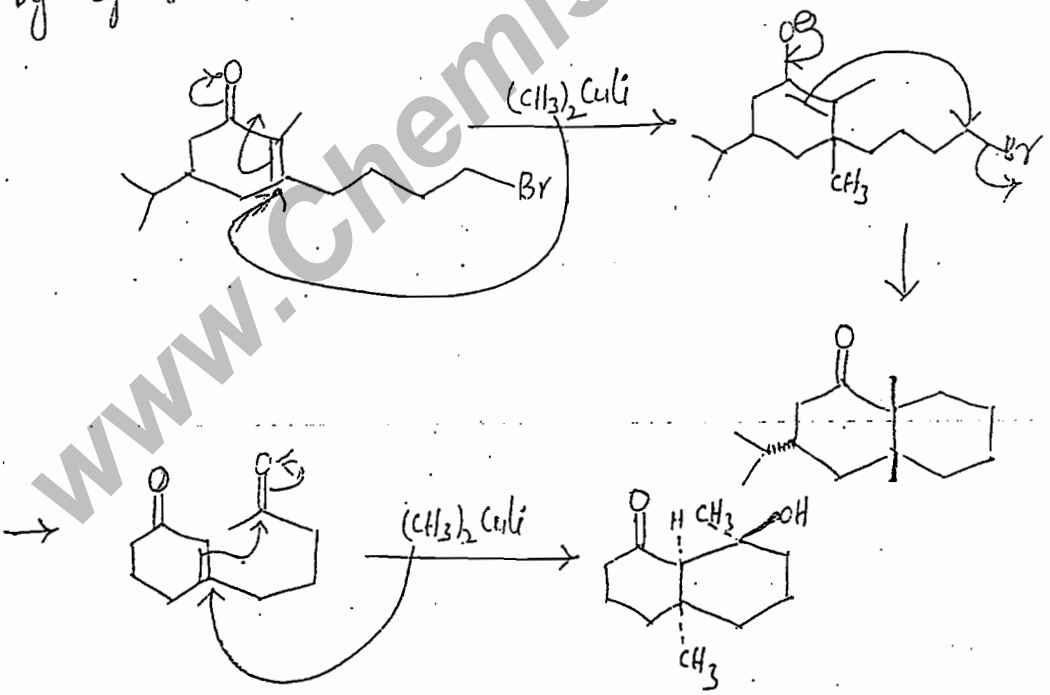


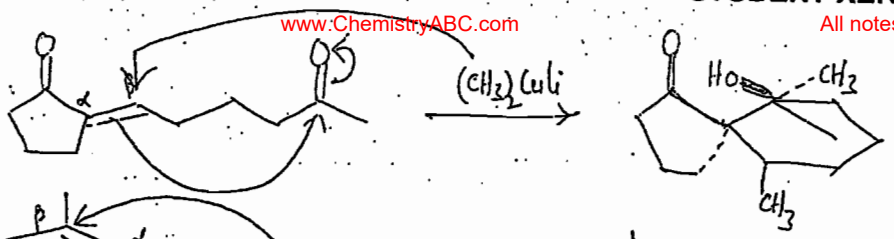
Cis; more stable.

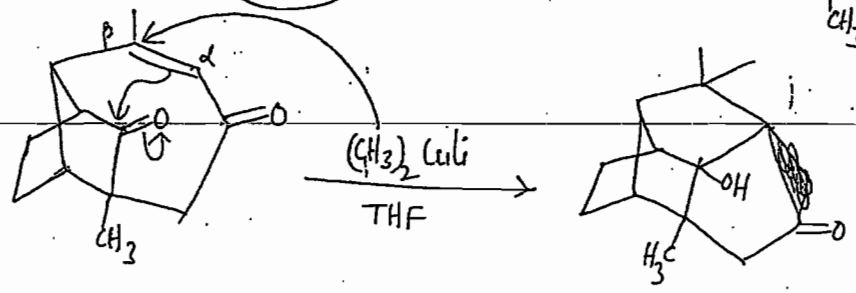


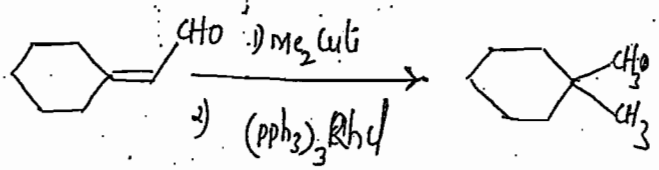


** In conjugated carbonyl compd, if there is a leaving group or electrophilic centre, with gilman's reagent conjugative addn followed by cyclisation.



→ 

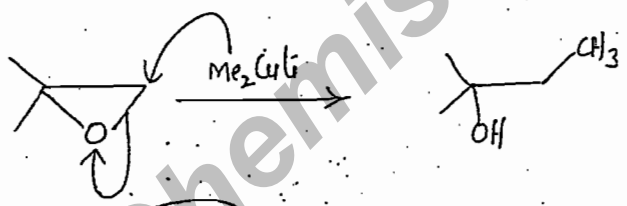
* 

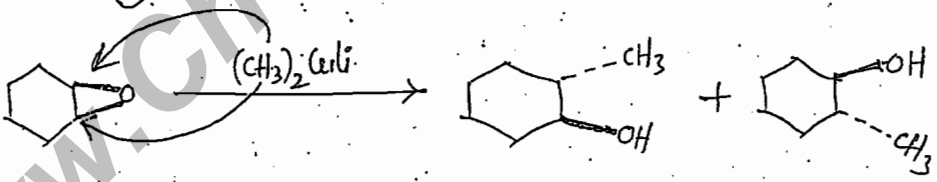
* 

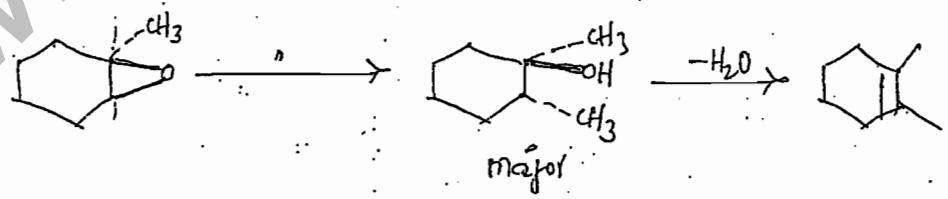
* IV. OPENING OF EPOXIDE :

Regioselectivity : opens at sterically less crowded position.

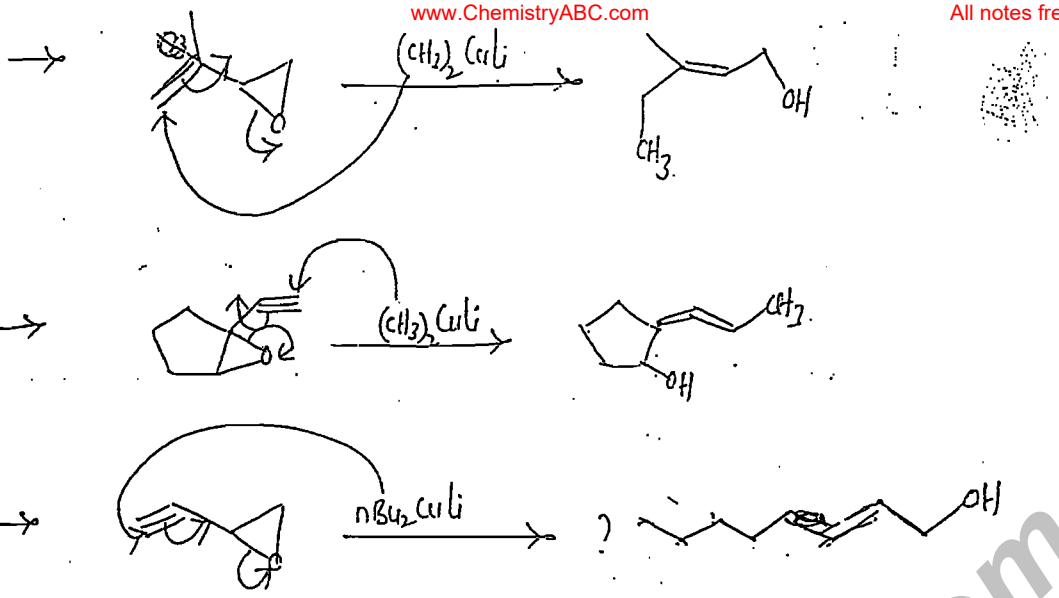
Stereoselectivity : S_N2 type.

→ 

→ 

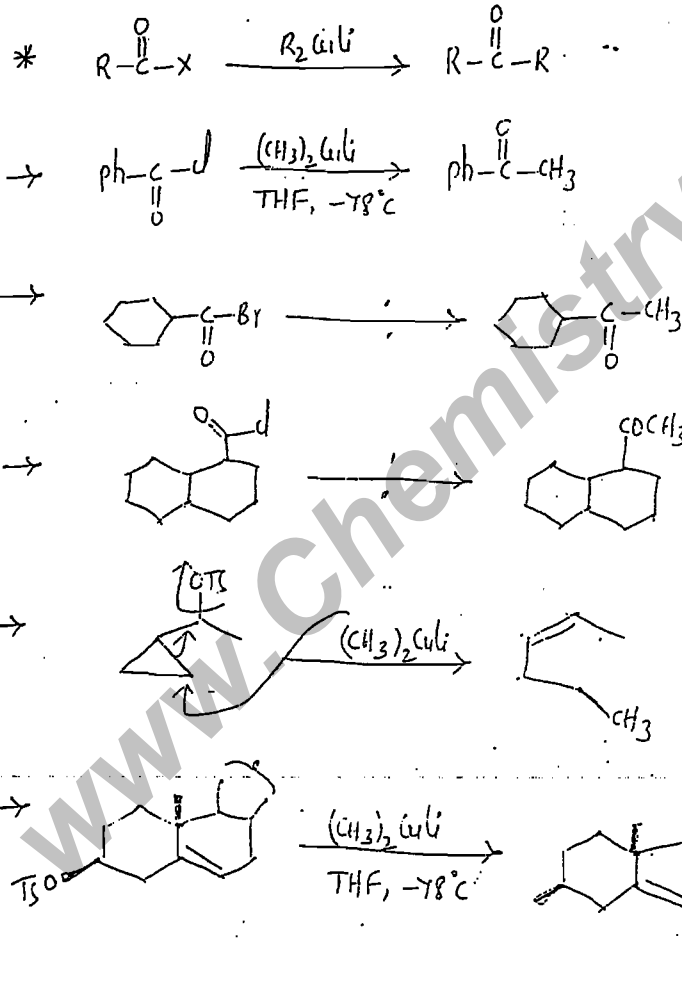
→ 

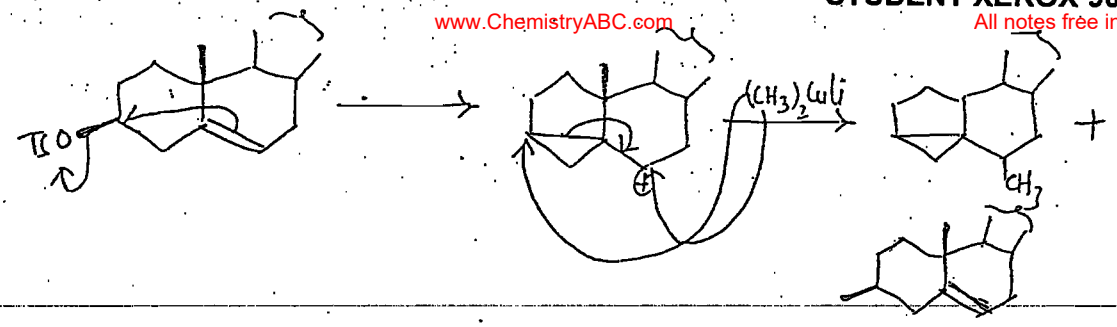
→ near to unsatn, if there is a epoxide, Gilman's reagent attacks at unsatn.

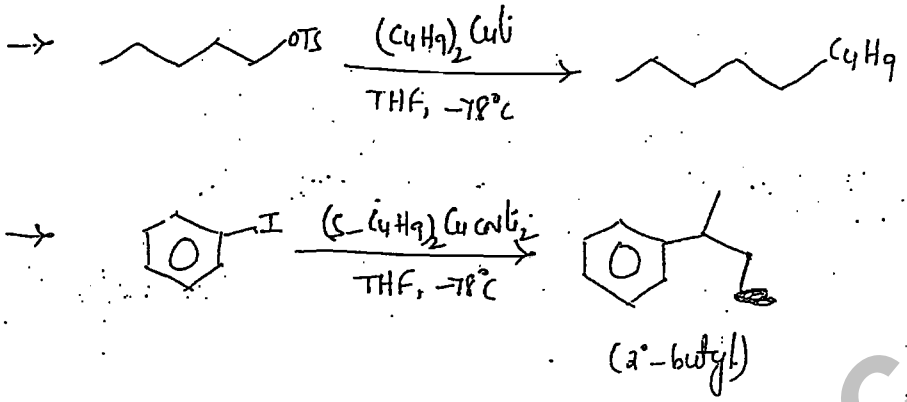


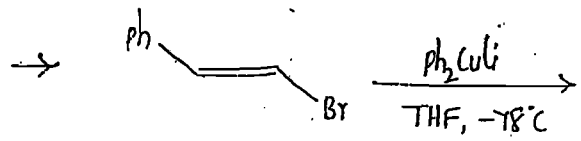
Date : 27/05/08

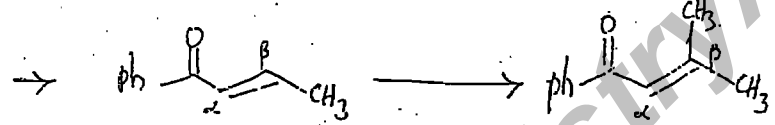
V. Acid Halides convert into Ketones :-

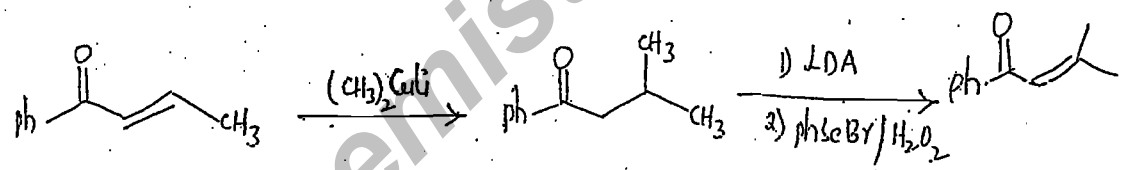


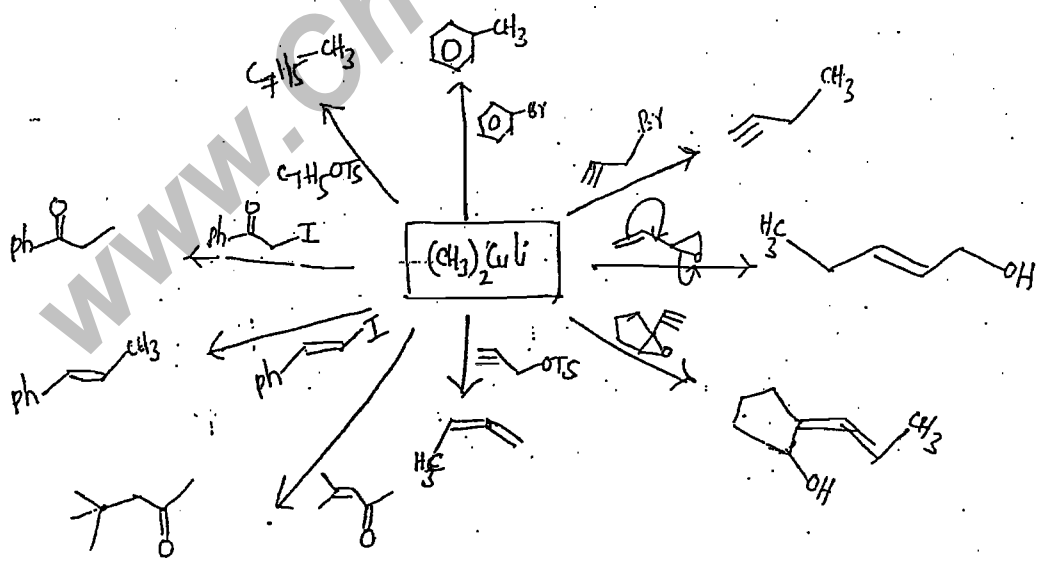












* ORGANO-ZINC REAGENTS :—

Reformatsky Reaction :—

$\overset{\delta-}{C}-\overset{\delta+}{Mg}$

$\overset{\delta-}{C}-\overset{\delta+}{Zn}$

↓

less polar

∴ organo zinc Reagents are less reactive and more selective than Grignard reagent.

→ organo zinc Reagent selectively attacks only reactive carbonyl fn of carbonyl compounds

→ All other carbonyl fn. inert ; esters, acid halides, anhydrides, amides etc.

→ cann't open epoxides.

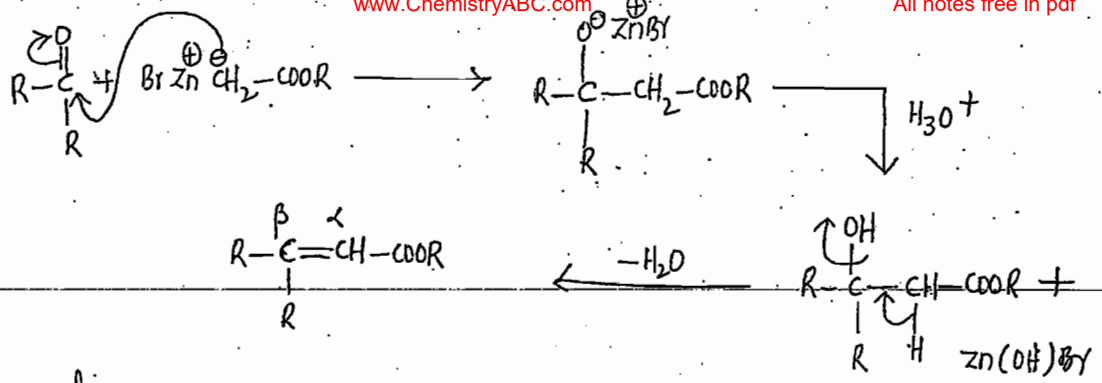
Reformatsky Rean :—

→ conversion of carbonyl compounds into α,β-unsaturated esters with Zn-metals/ α-bromo ester.

Carbonyl compound $\xrightarrow[\text{Solvent}]{Zn/\alpha\text{-Bromo ester}}$ β-hydroxy esters $\xrightarrow{-H_2O}$ α,β-unsat. esters.

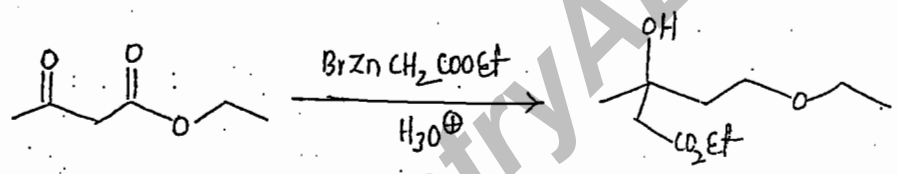
$R-\underset{\underset{R}{|}}{\overset{O}{\overset{\|}{C}}}-H \xrightarrow[\text{Ether/dry}]{ZnBr-CH_2-COOR} R-\underset{\underset{R}{|}}{\overset{OH}{\overset{|}{C}}}-CH_2-COOR \xrightarrow{-H_2O} R-\underset{\underset{R}{|}}{C}=CH-COOR$

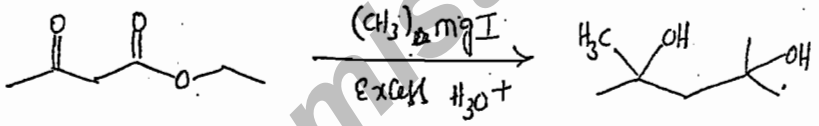
$Br-CH_2-COOR \xrightarrow{Zn} Br\overset{\oplus}{Zn}\overset{\ominus}{C}H_2-COOR$



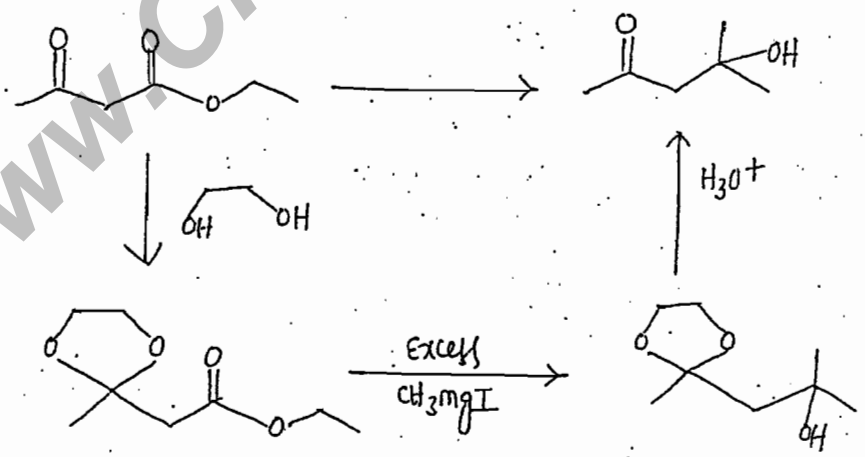
* Metal - zinc
* carbanion intermediate rean.
* C–C bond formation rean
* α-position of ester develops new bonding at carbonyl carbon.
* Selective addn only at carbonyl of aldehydes & ketones.

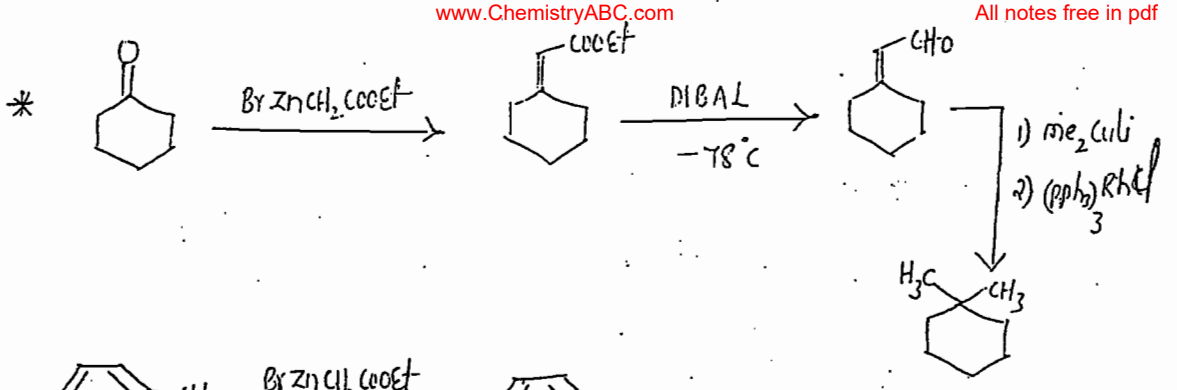
eg:-

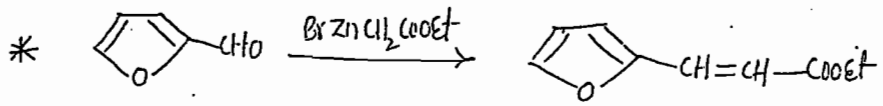


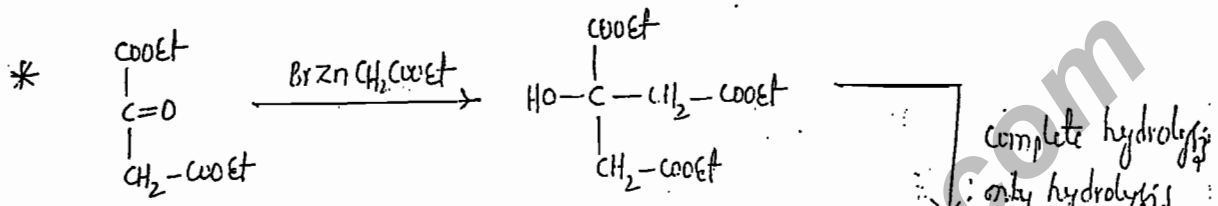


Reactivity: Ketone > Ester









citric acid

ORGANO-LITHIUM REAGENTS :—

$\overset{\delta-}{C}-\overset{\delta+}{Li}$ } Highly polarised

$\overset{\delta-}{C}-\overset{\delta+}{Mg}$

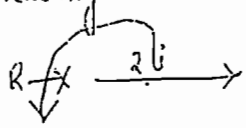
∴ C–Li bonding is more polarised than C–Mg bonding, compared to Grignard reagent, highly reactive.

organo lithium reagents exist in aggregation.

General presentation $[RLi]_n$ $(n \geq 2)$

Solvent :— Dry Ethers, Et_2O, THF, DME.

Prep :— 1) By reacting 'Li' with organo halo compound. Industrially viable method.



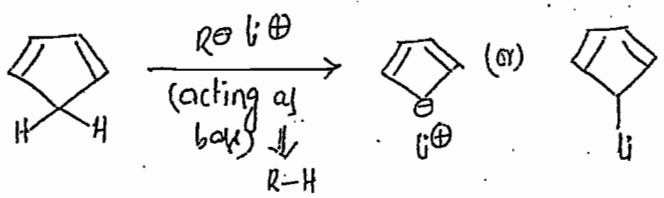
$R-X \xrightarrow{2\,Li} R-Li + Li-X$

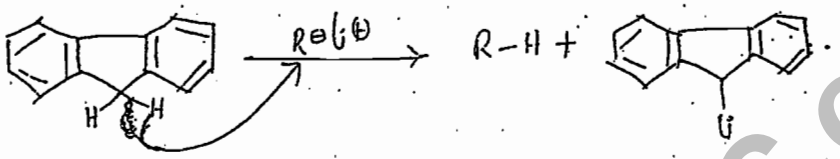
$$R-X \xrightarrow{2Na} R-R + NaX$$

wurtz

Wurtz reany are competetive reanf.

2) By Metallation at acidic carbon





3) By meta/ halo exchange :

$$R-X + {}^{1}R\ominus Li\oplus \longrightarrow R\ominus Li\oplus + {}^{1}R-X$$

$$n_{Bu}-Cl + CH_3-Li \longrightarrow n_{Bu}-Li + CH_3-Cl$$

Applications :--

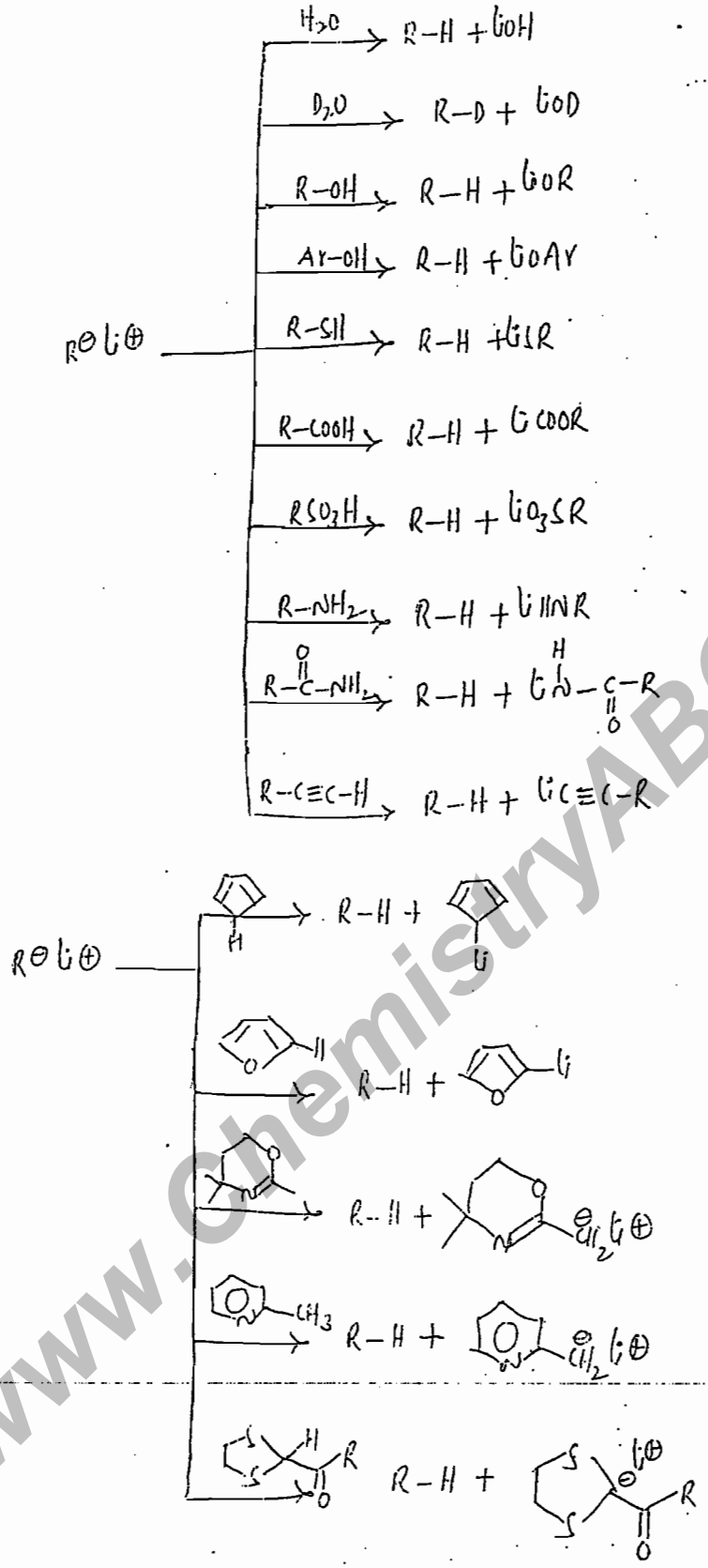
* organo lithium reagents are powerful bases as well as nucleophiles than grignard reagents.

O.L.R. as Base :—

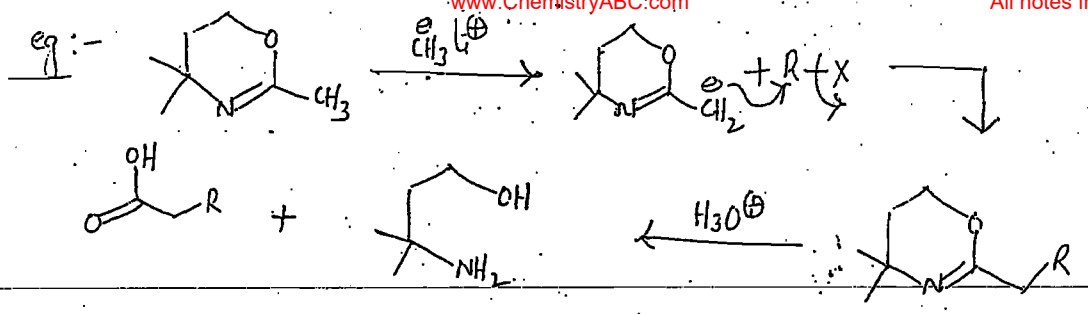
→ O.L.R. compds strong bases, abstract proton even from weakly acidic groups.

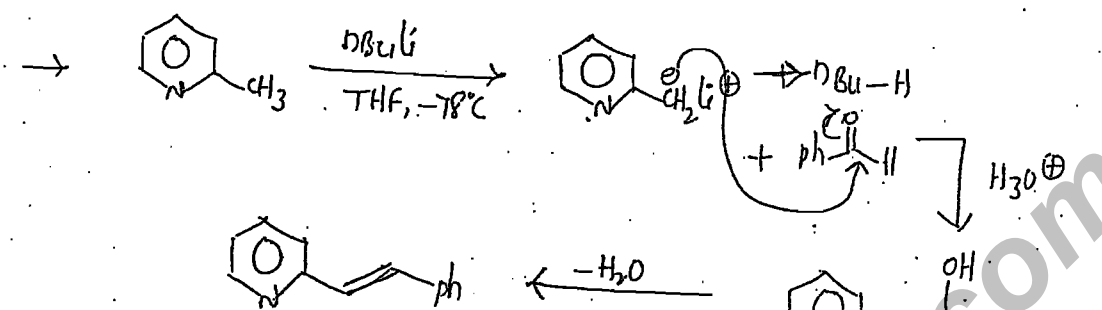
$$R\ominus Li\oplus \xrightarrow{R-COOH} R-H + R-COO\ominus Li\oplus$$

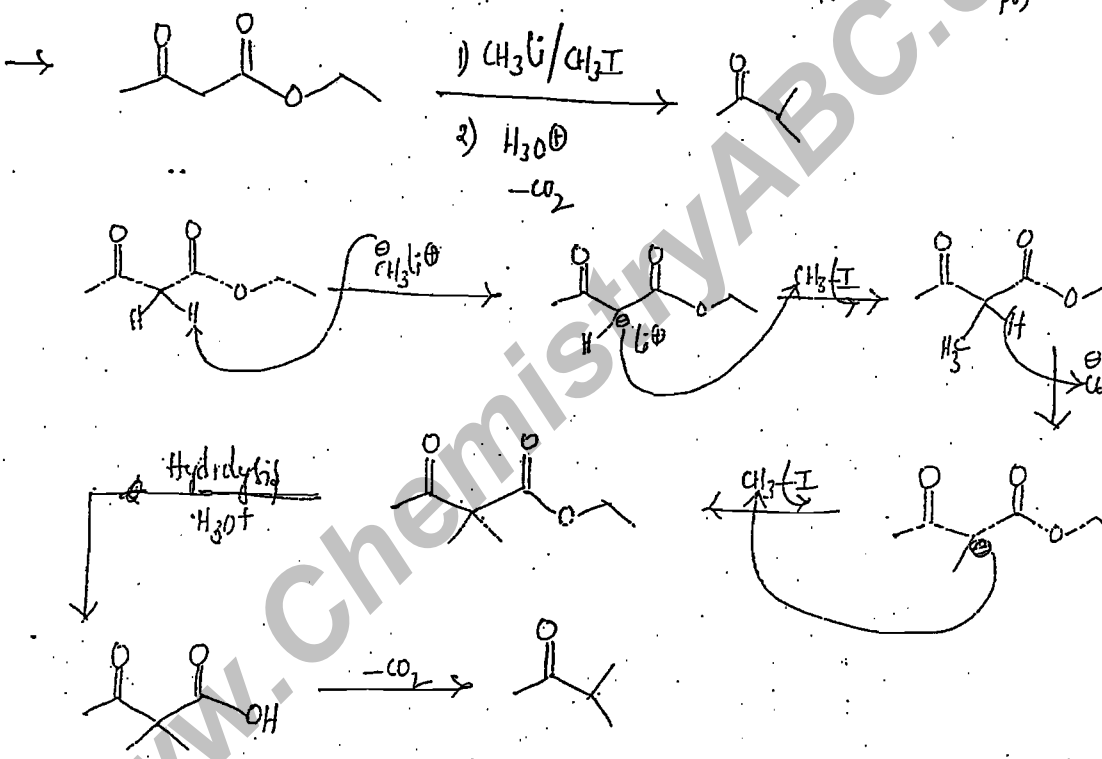
After abstraction of proton, converts into corresponding hydrocarbons.



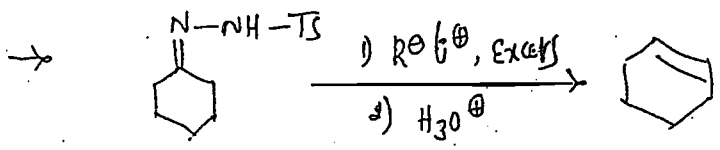
eg :-

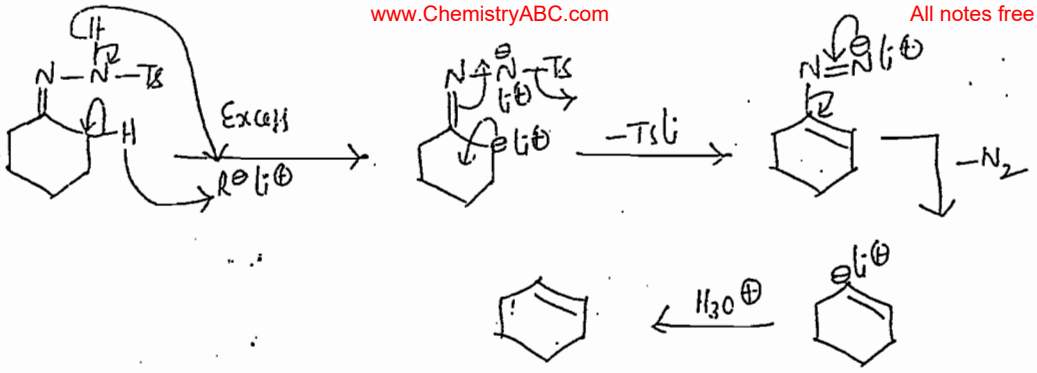


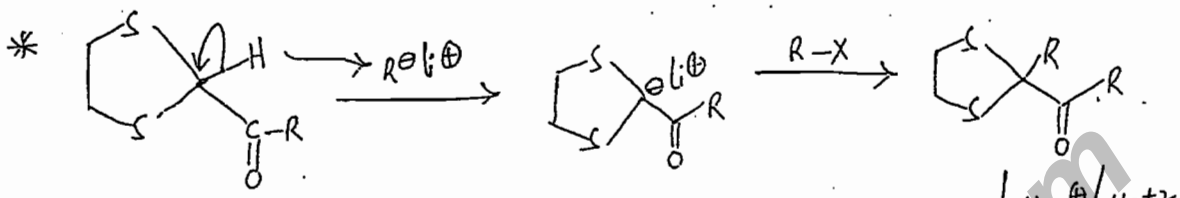


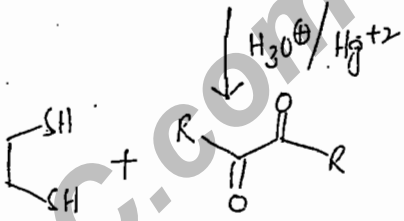


* SHAPIRO – REACTION :–



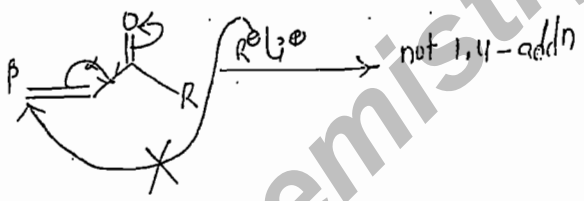






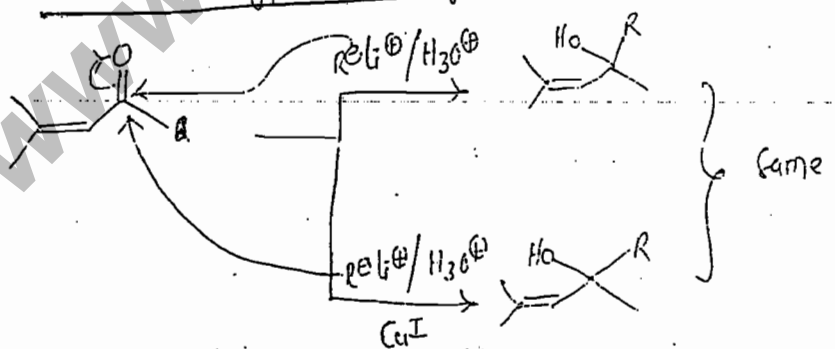
As Nucleophiles :-

→ O.L.R. are powerful nucleophiles, compared to grignards, attacks even at higher sterically crowded carbonyl.



addn

O.L.R. always at Carbonyl -ing whether Cu^I ions present or absent.

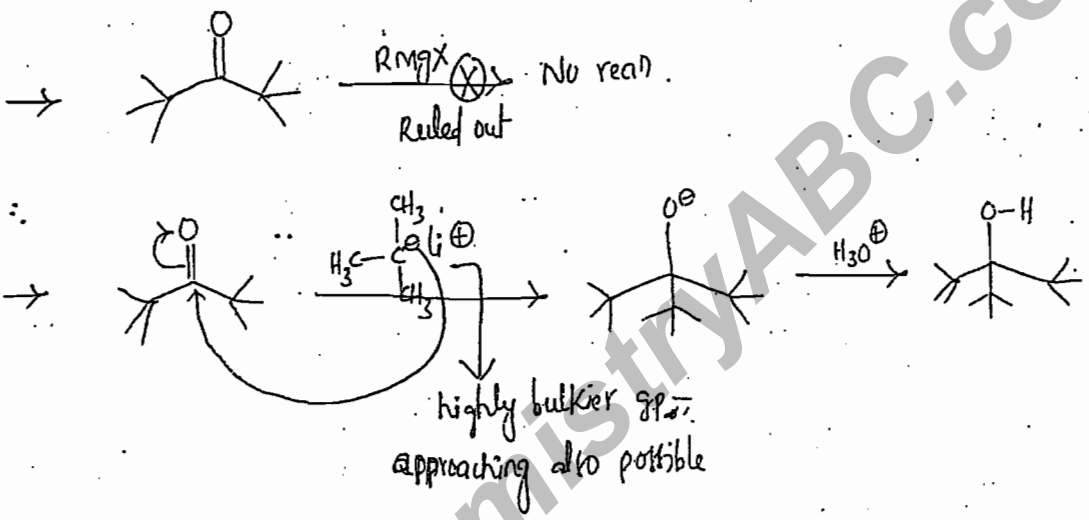


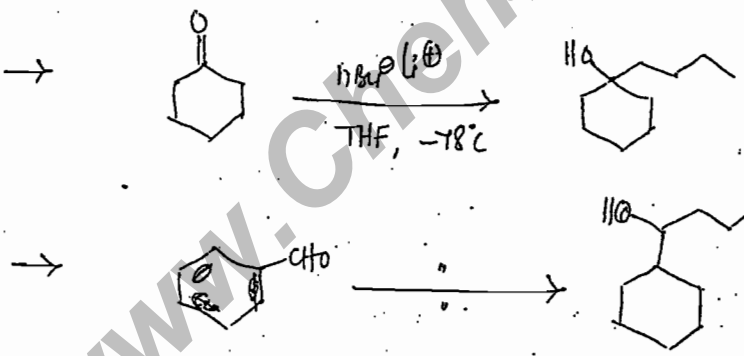
No conjugative or 1,4-addn.

Applications :-

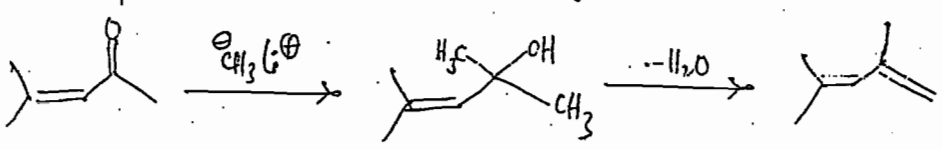
1) Additions at carbonyl function.
2) " " carboxylic acid.
3) " " nitriles/CO_2
4) Displacement of Halo group
5) Opens epoxide

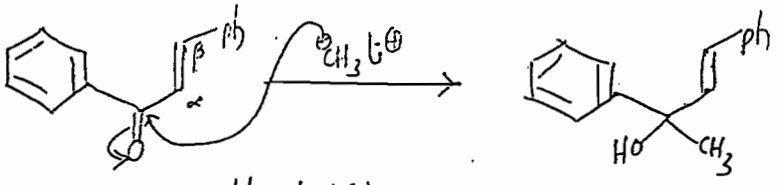
1) capable in attacking at sterically crowded carbonyl function.





* 1,2- additions in α,β unsaturated carbonyl compd.



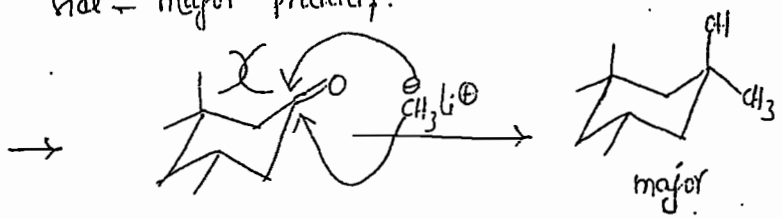


No addn at 'β'

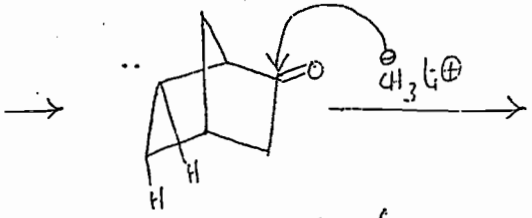
'Chalcones'

* Stereo chemical Aspects :—

Similar R-Li reagent attacks carbonyl at sterically less crowded side → major products.

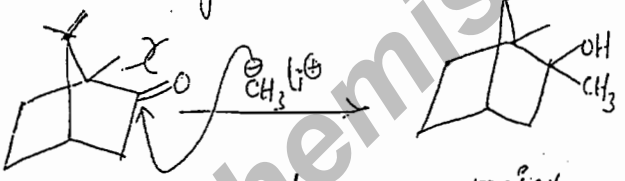


major



major

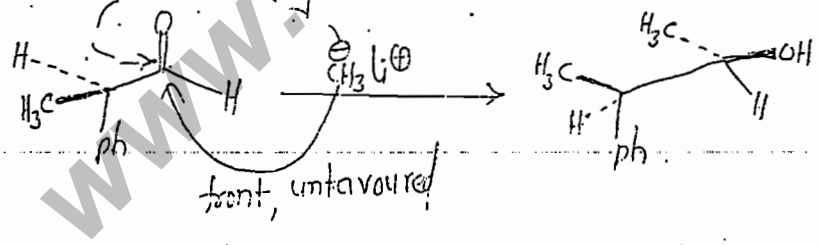
Exo if sterically free



Endo if favoured

major

back favoured

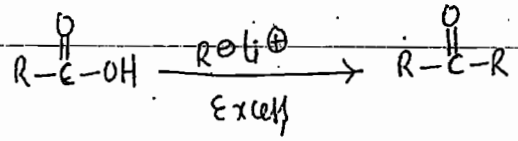


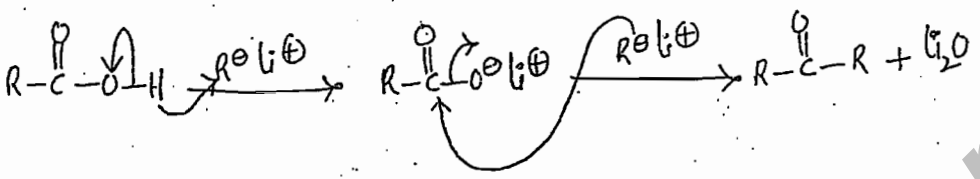
front, unfavoured

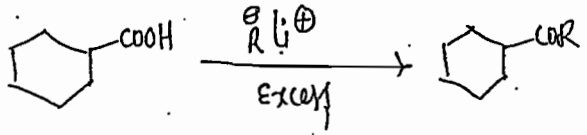
at chiral centre Small 'H' back side (favoured).

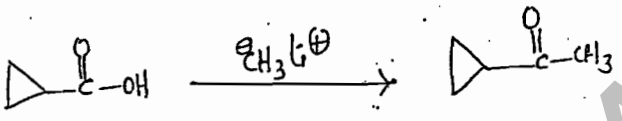
** 2) Addn at carboxylic acids :-

→ convert carboxylic acid to ketone.

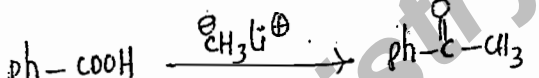




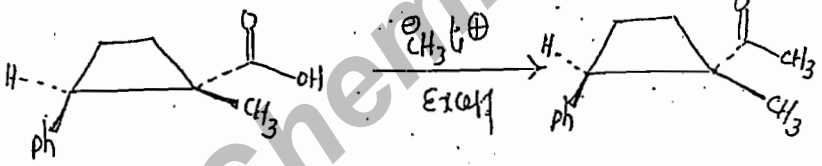




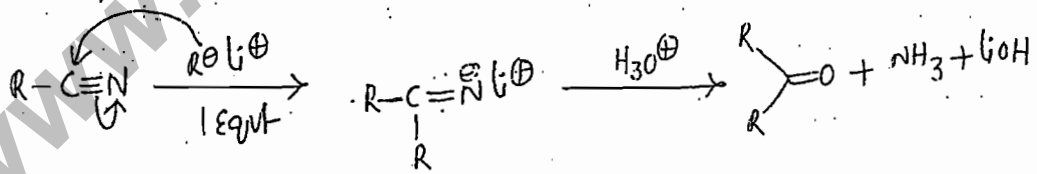
convert benzoic acid into acetophenone

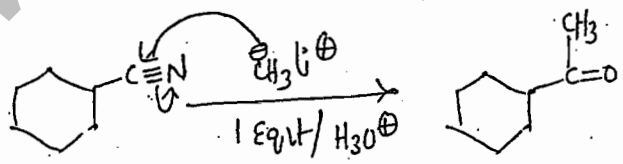


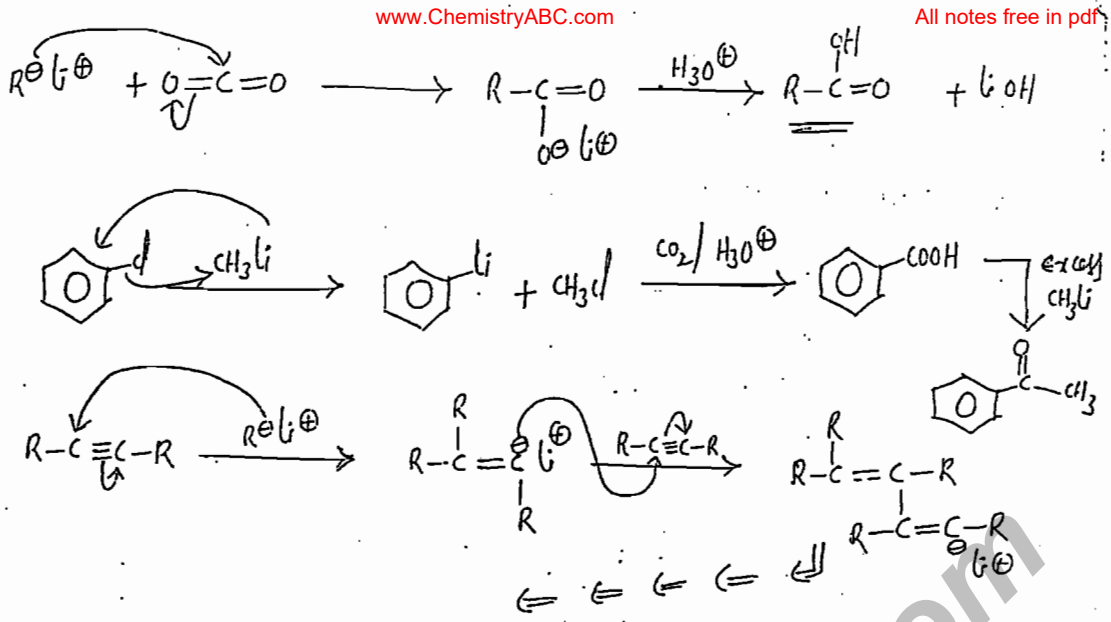
*



3) Additionj at nitriles, CO_2, even @ or, alkenej, alkynej etc.

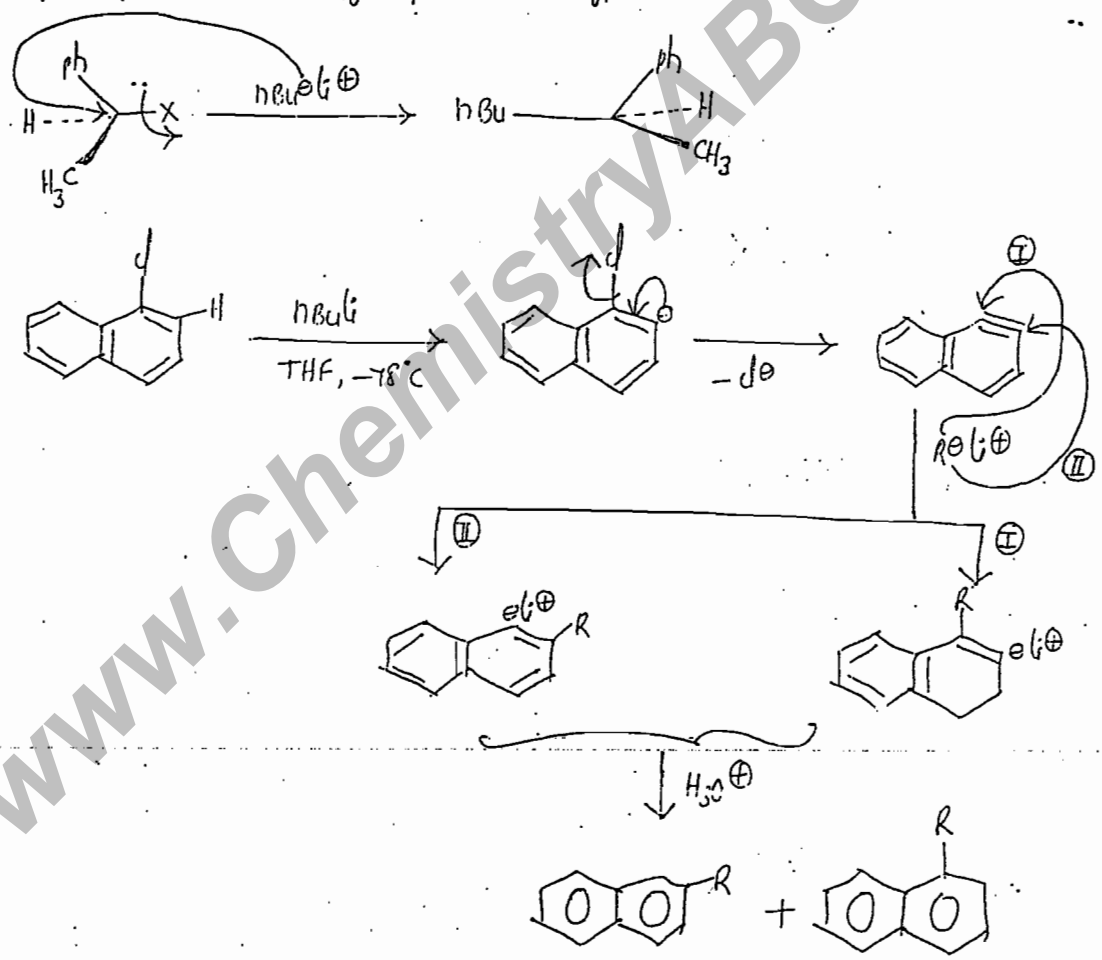






whenever we want to stop the rean, add $H^{\oplus}$

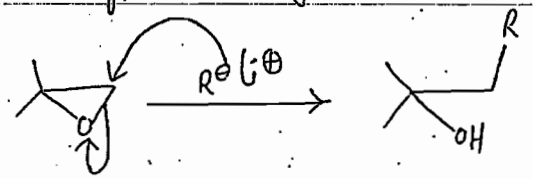
4) Displacement of Halo group : S_N^i-type

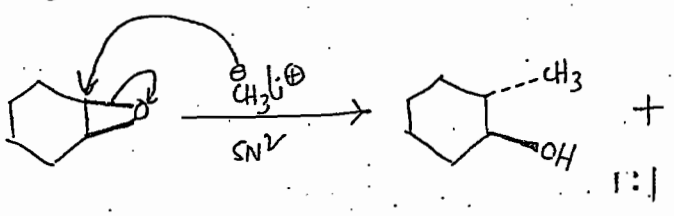


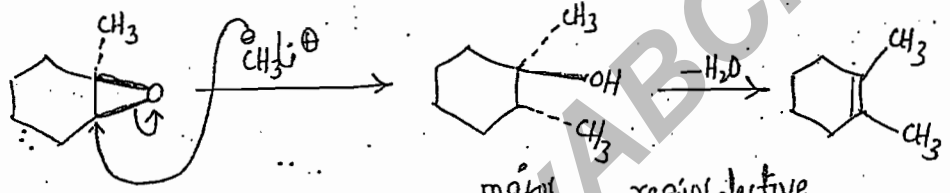
* opens Epoxides :-

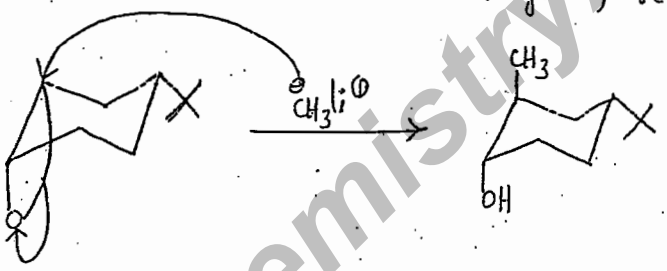
→ sterically less crowded

→ S_N2 type - opening.

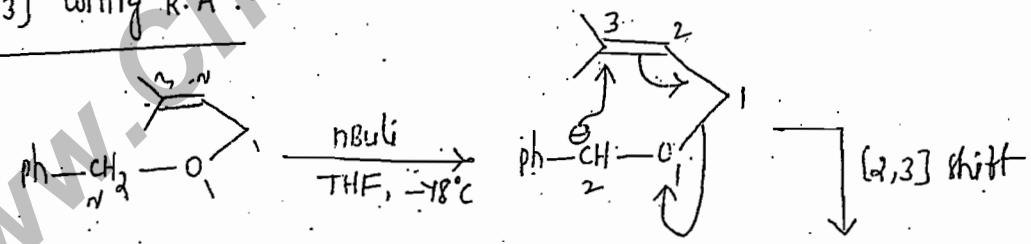
→ 

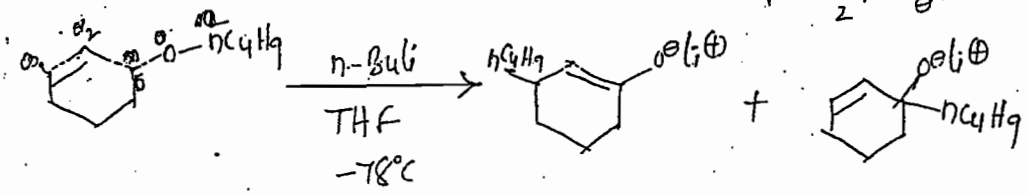
→ 

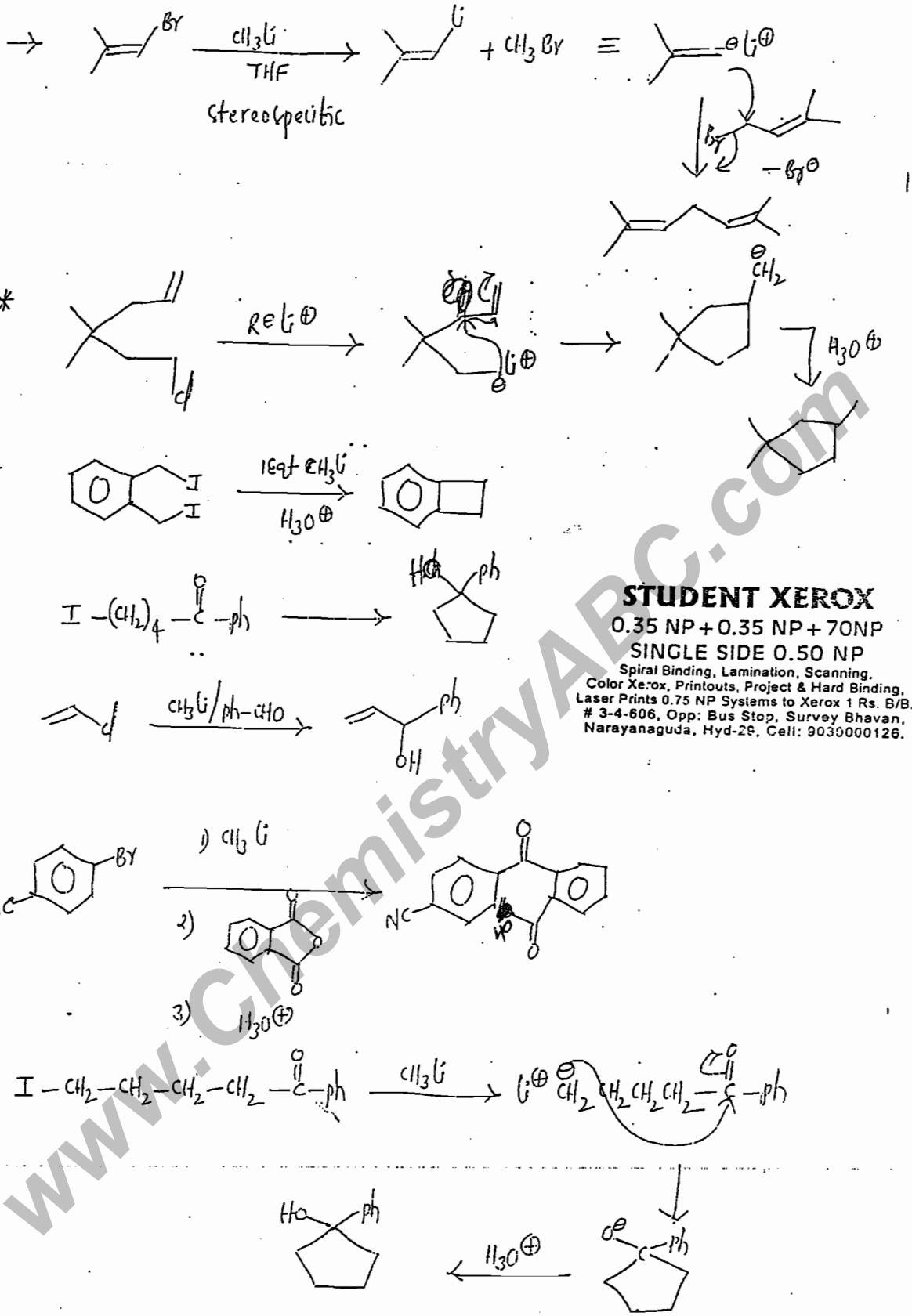
→ 
major, regioselective.

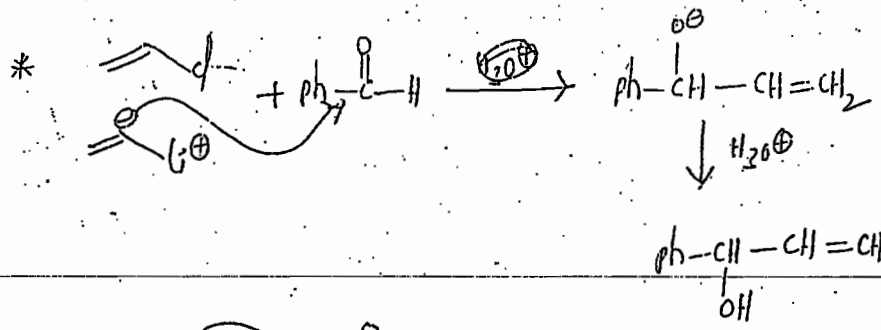
→ 

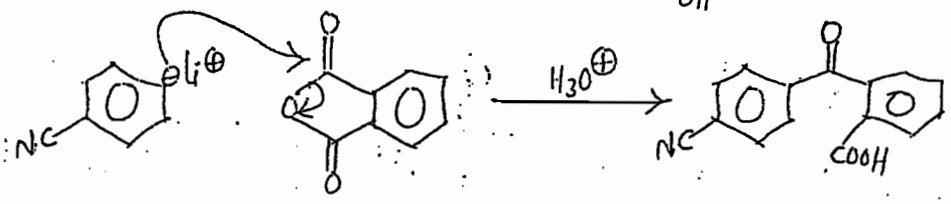
* [2,3] wittig R.A :-

→ 

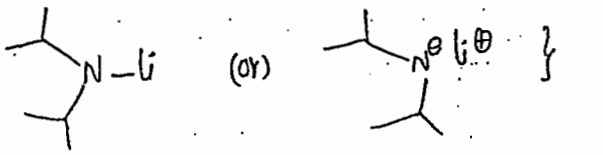
→ 



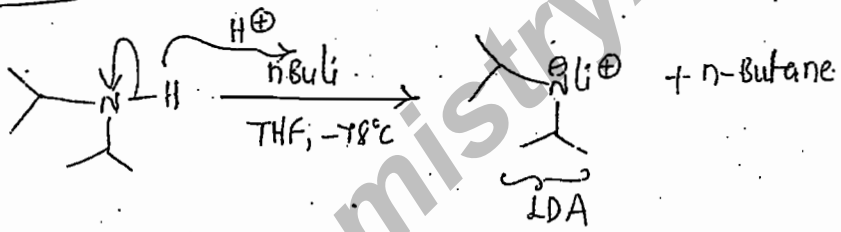




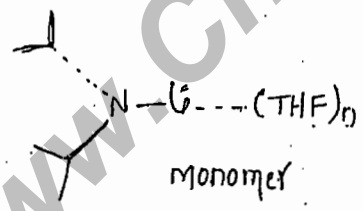
Lithium Diisopropyl Amide : LDA

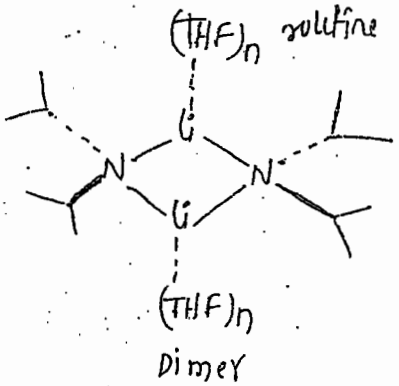


Preparation :-



In soln state, LDA exists in monomeric as well as dimeric form





(THF)n solvent in preparing LDA.

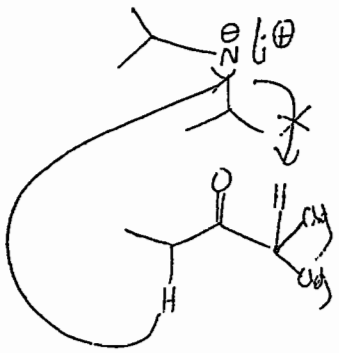
Solvent :- Dry Ethers,

Et_2O, THF, DMF

lower temperature : 0°C to -78°C.

Application :—

1) LDA is non-nucleophilic strong base.



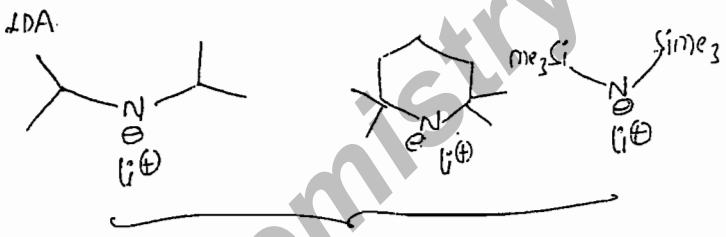
Harpoon base.

→ Abstracts proton even from weakly acidic position.

→ Due to bulkiness preferentially abstract proton from sterically less crowded side (Regioselectivity)

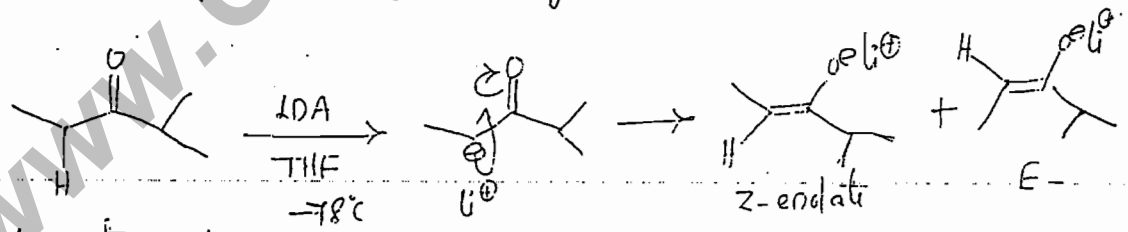
→ Non-nucleophilic bases are called Harpoon Bases.

eg:—



Harpoon Base

1) Enolate formation : Regioselectivity :



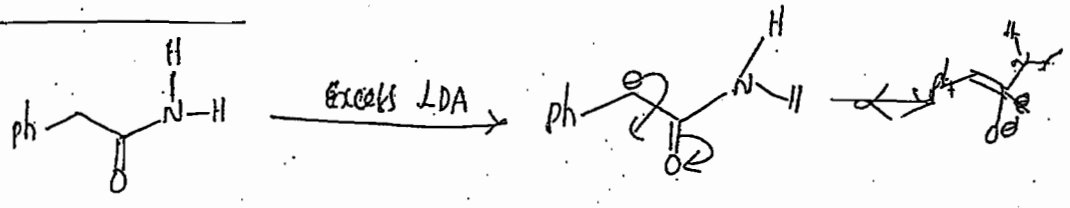
abstracts proton from sterically less crowded

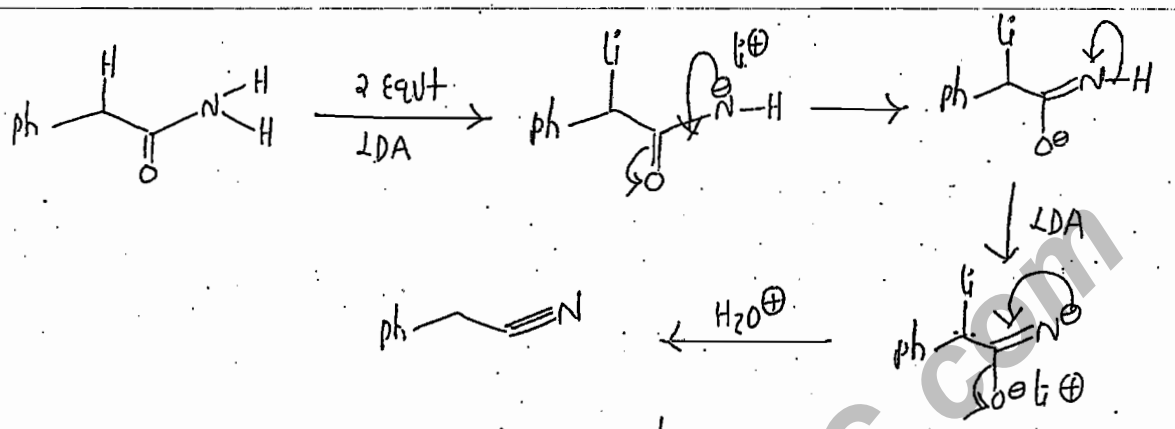
Z-enolate more (major)

E-

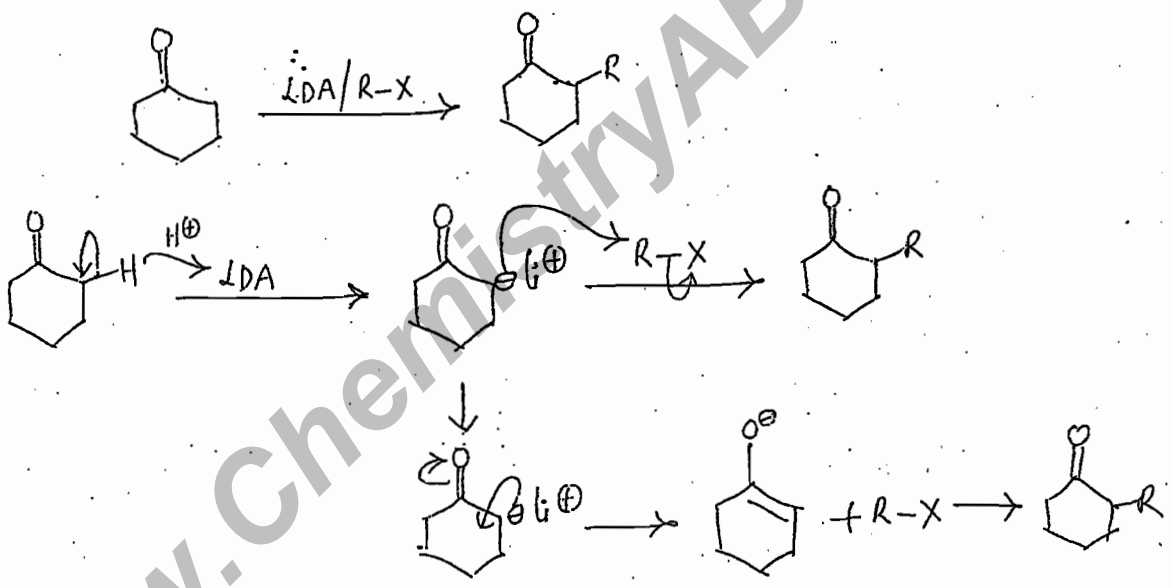
Z-enolate is major, because, sterically free

2) Amide to Nitrile :-



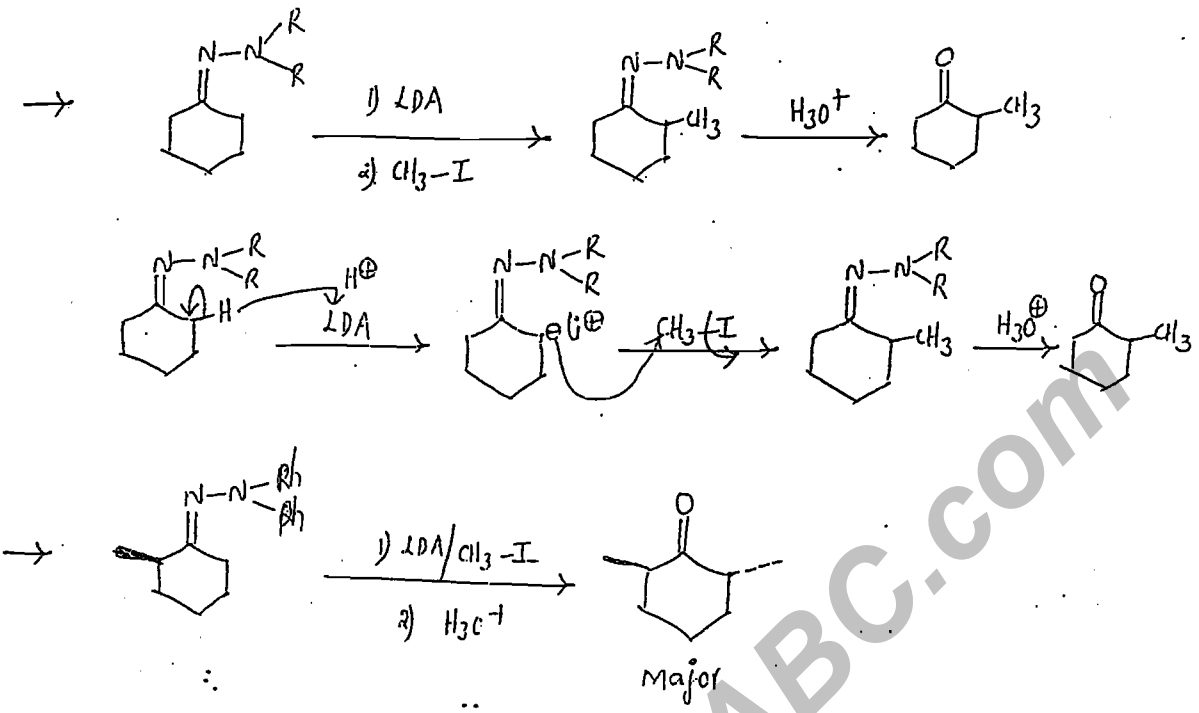


3) α- alkylation of carbonyl compounds.



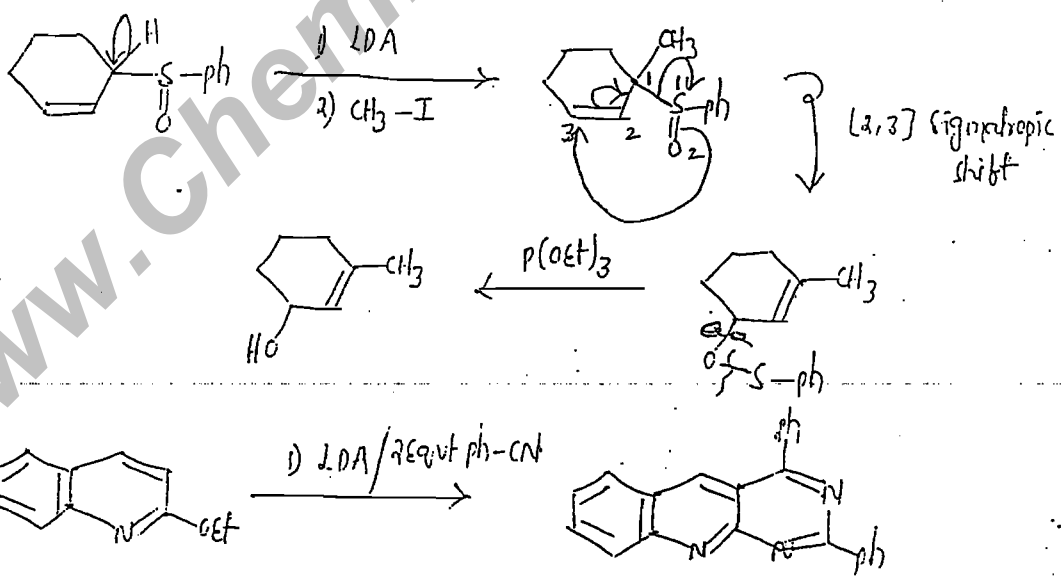
Date : 28/05/08

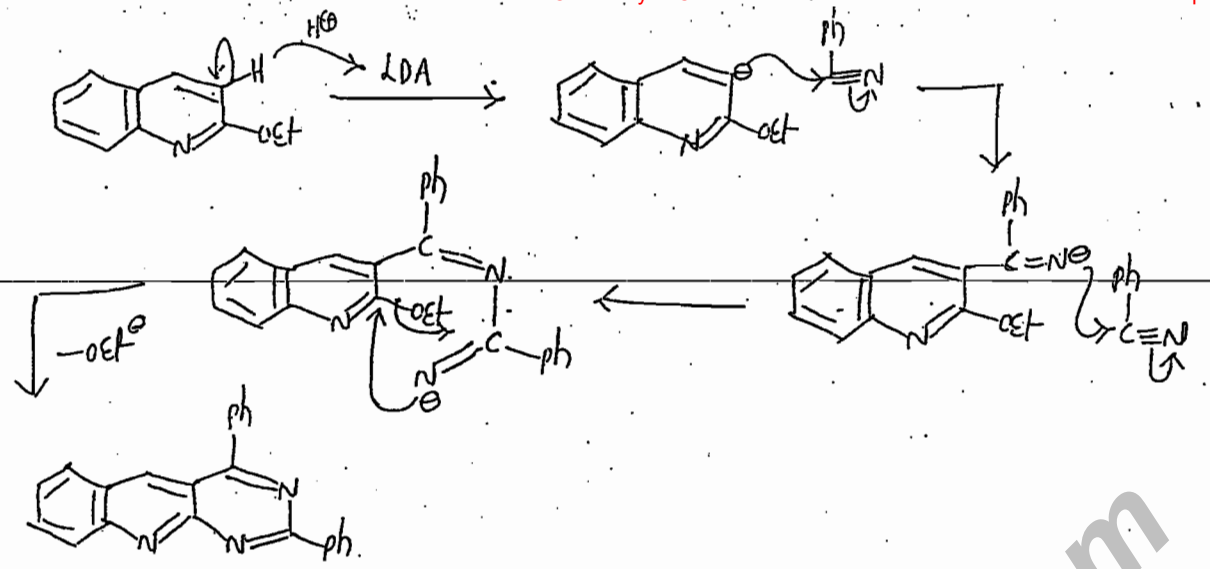
* α- Alkylation of Hydrazones :



→ Mislow – Evan's Rearrangement :–

→ [2,3] Sigmatropic shift of Sulphoxides.





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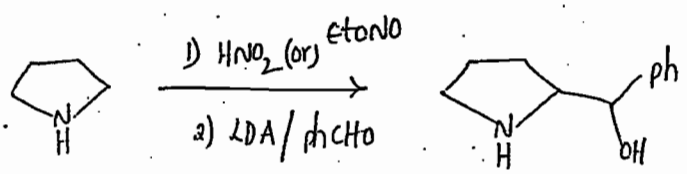
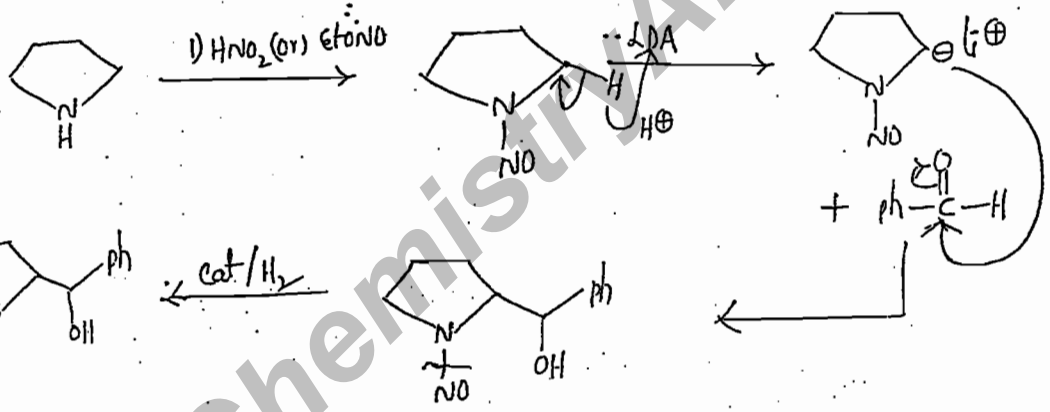
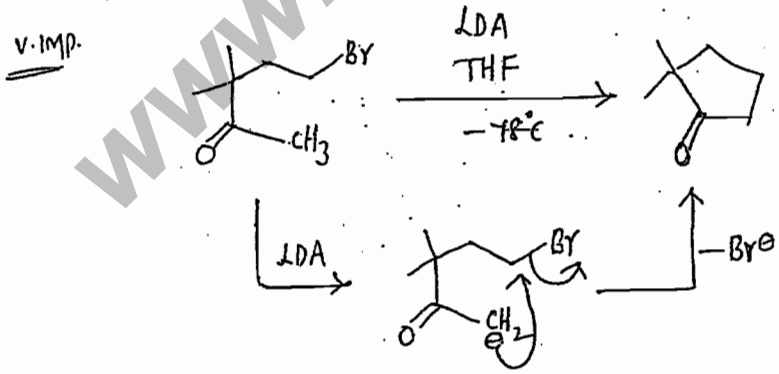
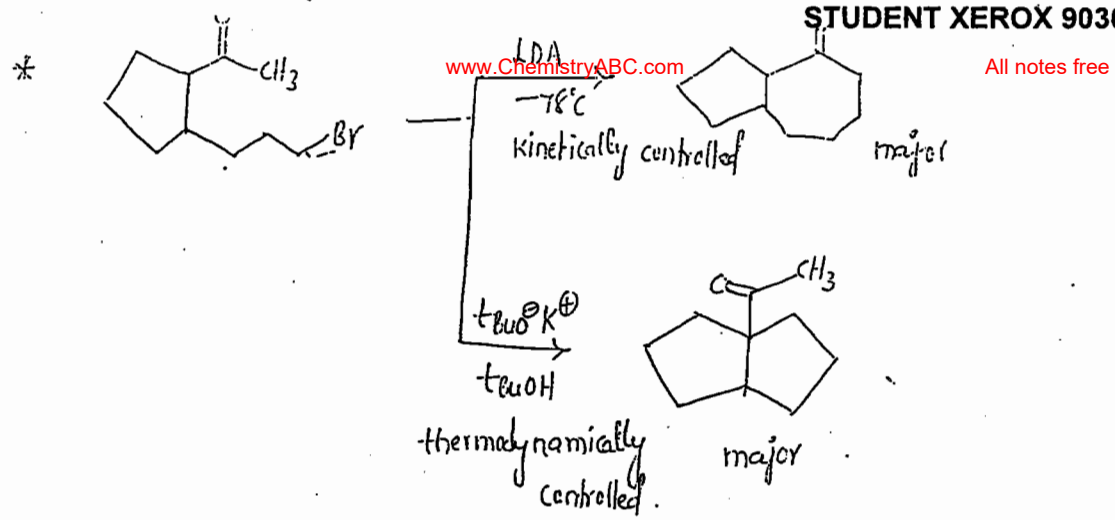


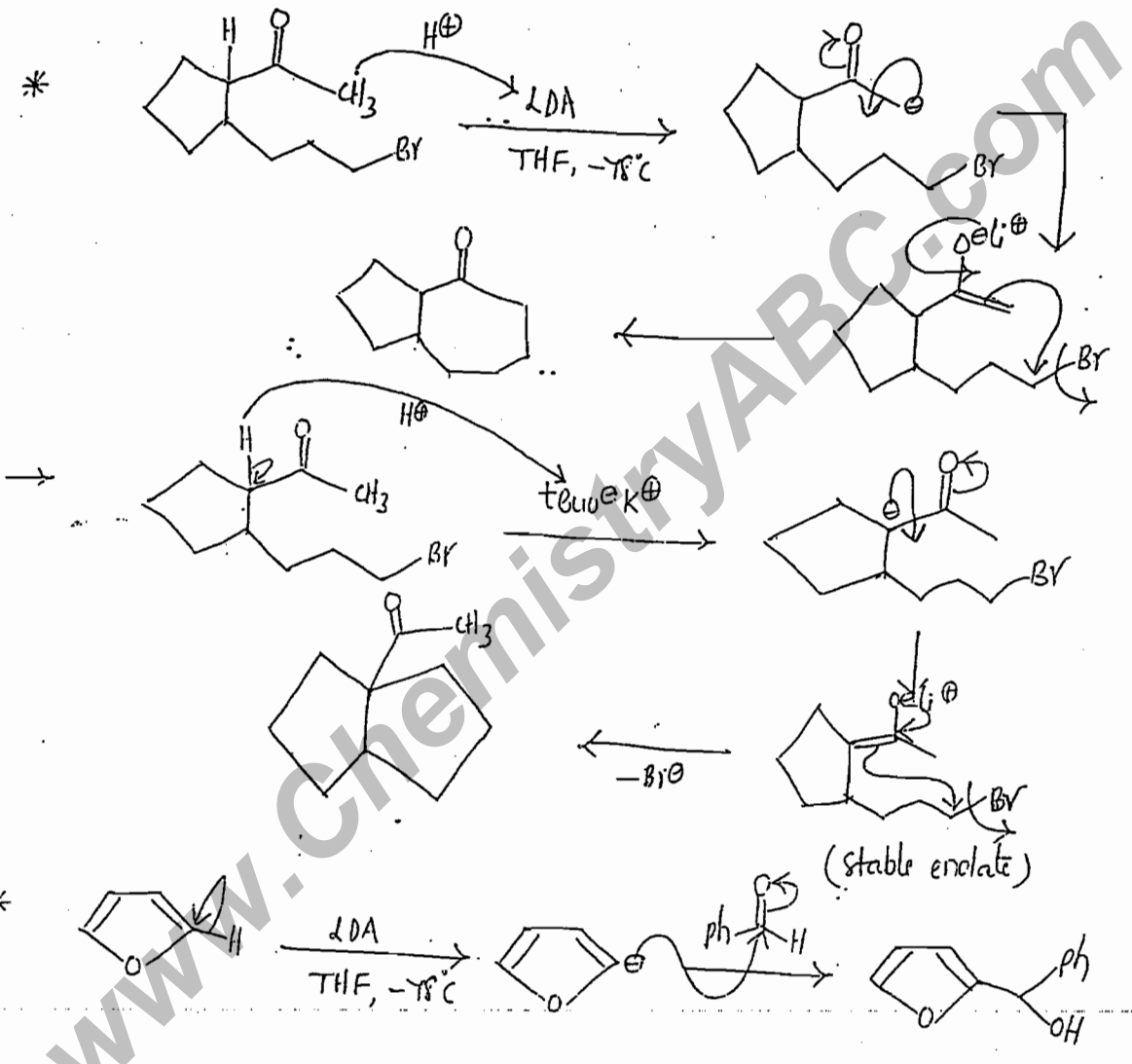


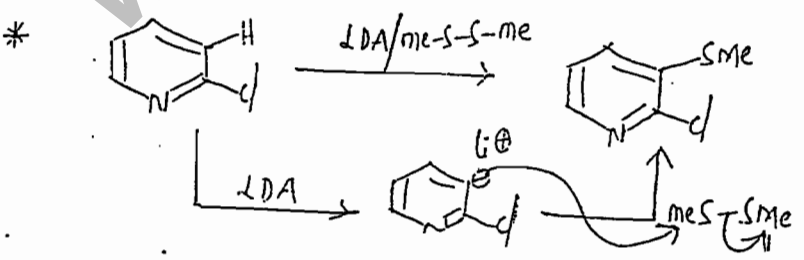
* cyclisations :—

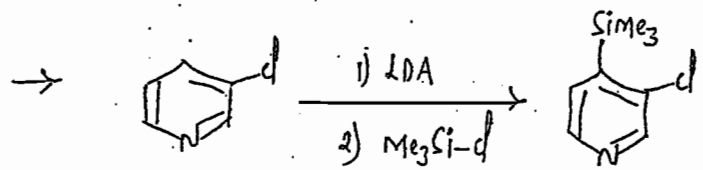
V.IMP.



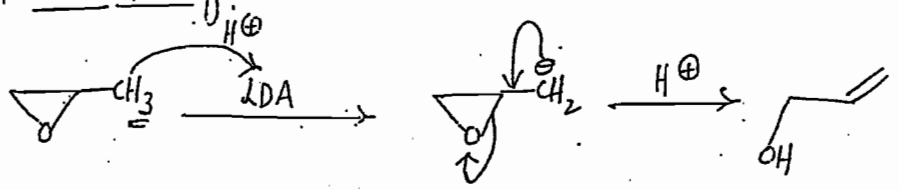


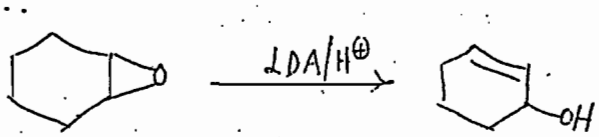


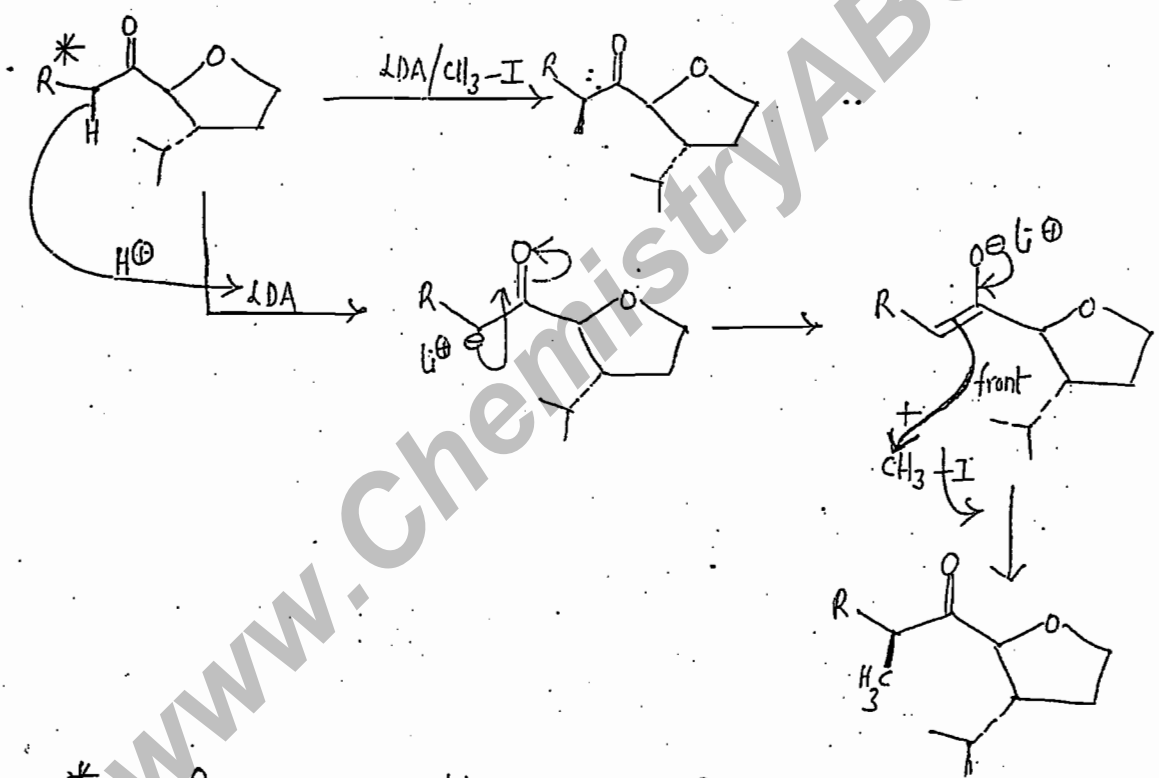


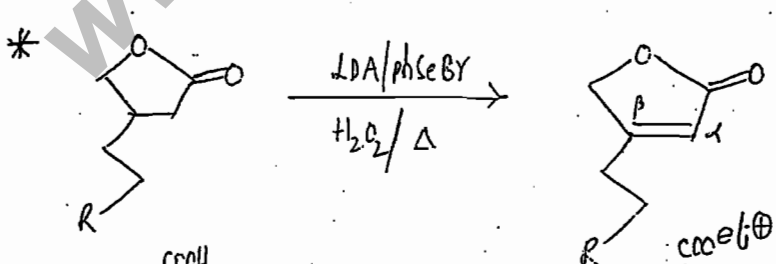


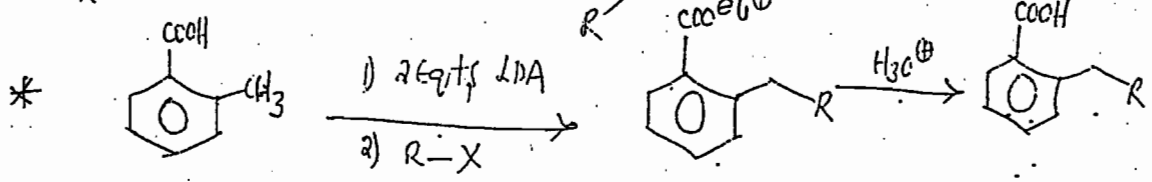
→ Epoxide opening :

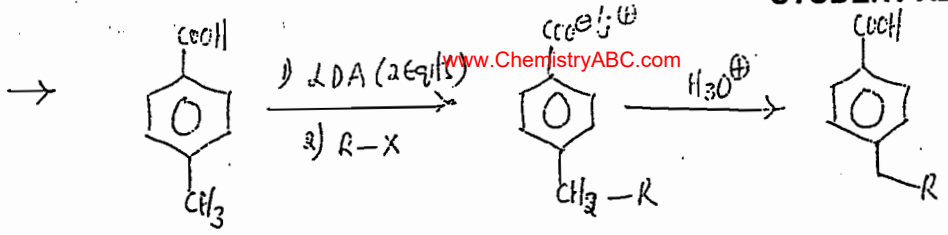




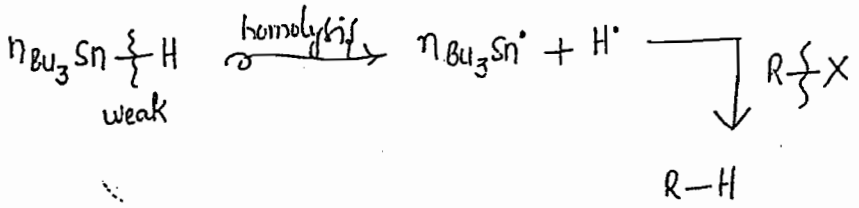






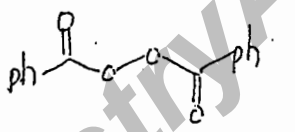


* Tri-n-butyl-Tin Hydride :— (nBu_3Sn-H).



→ Tri-n-butyl-Tin Hydride is a good source for Hydrogen radical. used for reductions in org. synthesis.

→ Reacy of Tri-n-butyl Tin hydride similar to Halogenation of alkanes in light.

→ (Free radical initiators –  (Benzoyl peroxide)

AIBN)

→ $nBu_3Sn-H \xrightarrow[AIBN]{h\nu/\Delta}$

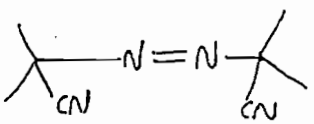
(or) $nBu_3Sn-Sn\,nBu_3$

→ The radical initiators for tri-n-butyl tin hydride are

light/thermal/AIBN/$nBu_3Sn-Sn\,nBu_3$

⇓

widely used radical initiator for nBu_3SnH.

(Azo Bis Isobutyro Nitrile) 

Solvents :-

→ Aromatic Hydrocarbons

C_6H_6, Toulene, xylene etc.

Applications :-

1) Displacement of Halogroup (Best compared to LAH)

conversion of halo compd into hydrocarbons.

$$R-X \xrightarrow[\text{Initiator}]{n Bu_3SnH} R-H$$

2) Displacement of Nitro group.

conversion of nitro compds into hydrocarbons.

$$R-NO_2 \xrightarrow[\text{"In"}]{n Bu_3SnH} R-H$$

3) conversion of sulphides into thiols.

$$R-S-R \longrightarrow R-S-H$$

4) opens epoxides/ cleaves xanthates

1. Displacement of Halo group :

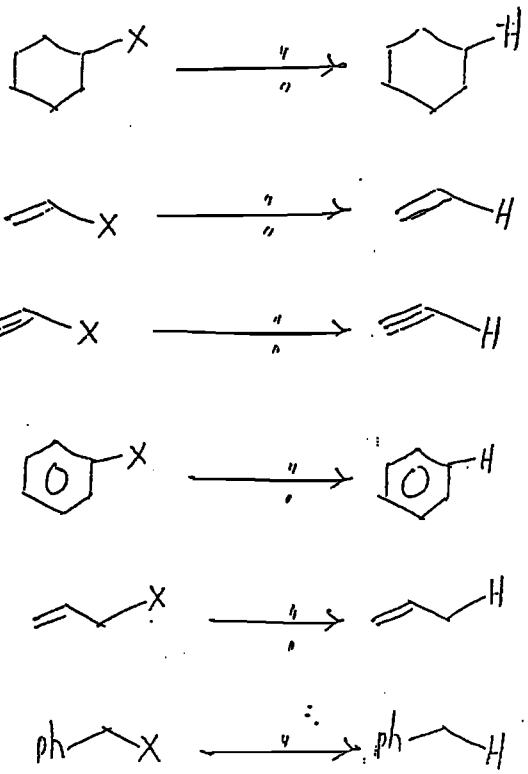
$$R-X \xrightarrow[AIBN,\ h\nu]{n Bu_3SnH} R-H$$
$$C_6H_6$$

R = any organic group

Alkyl, alkenyl, alkynyl, aryl, allyl, benzyl etc.

X = F, Cl, Br, I (any halogen)

$CH_3-X \xrightarrow[AIBN]{nBu_3SnH} CH_3-H$



Date : 29/05/08

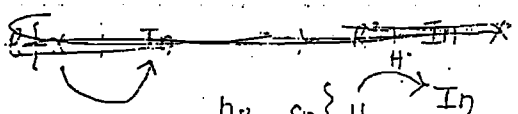
* Reactivity order :-

Allyl / Benzyl halides > 3°-alkyl > 2°-alkyl > 1°-alkyl > vinyl > aryl > alkynyl > alkenyl

$\Rightarrow$ R-F > R-Cl > R-Br > R-I

Mech :- $R-X \xrightarrow[h\nu,\ AIBN]{nBu_3SnH} R-H + nBu_3Sn-X$

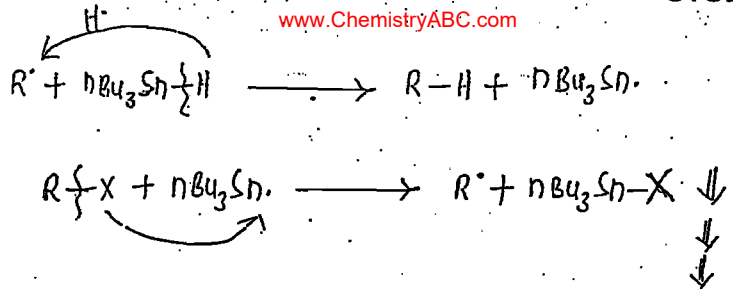
Initiation :



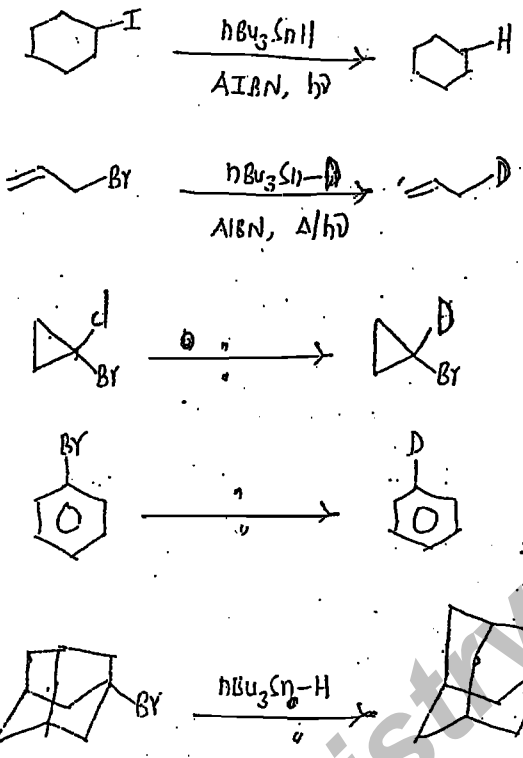
propagation :

$nBu_3Sn-H \xrightarrow{In} nBu_3Sn^{\bullet} + In-H$

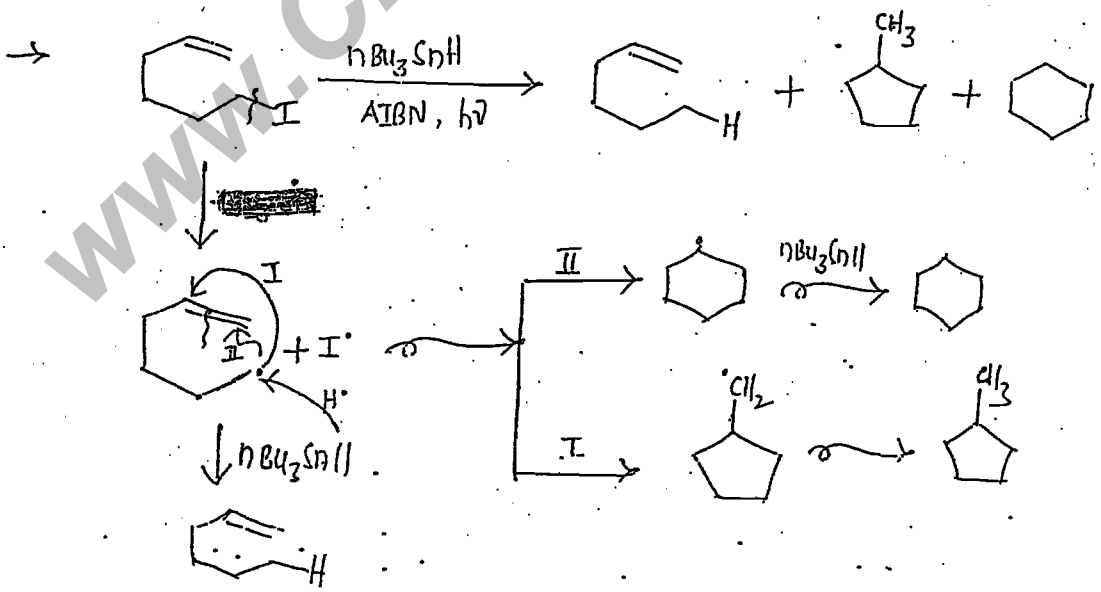
propagation :- $R-X + nBu_3Sn^{\bullet} \longrightarrow R^{\bullet} + nBu_3SnX$

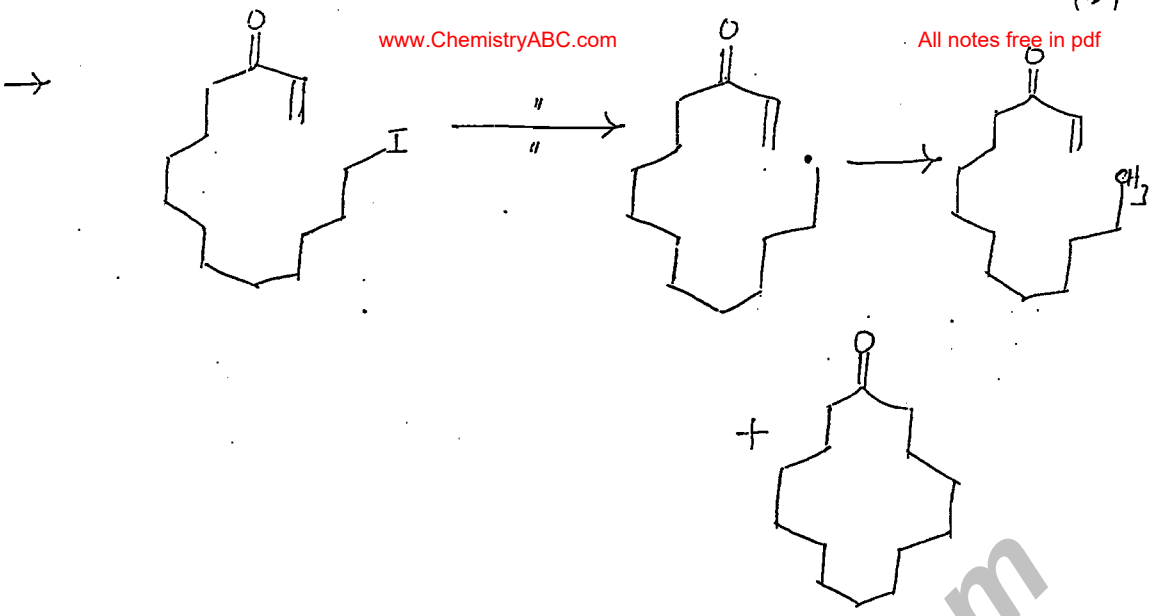


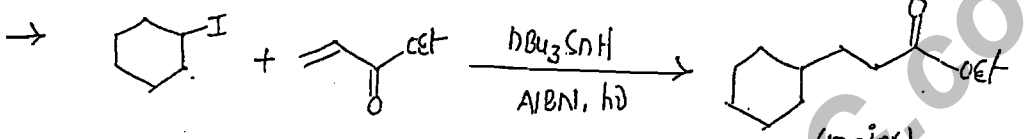
* eg:-

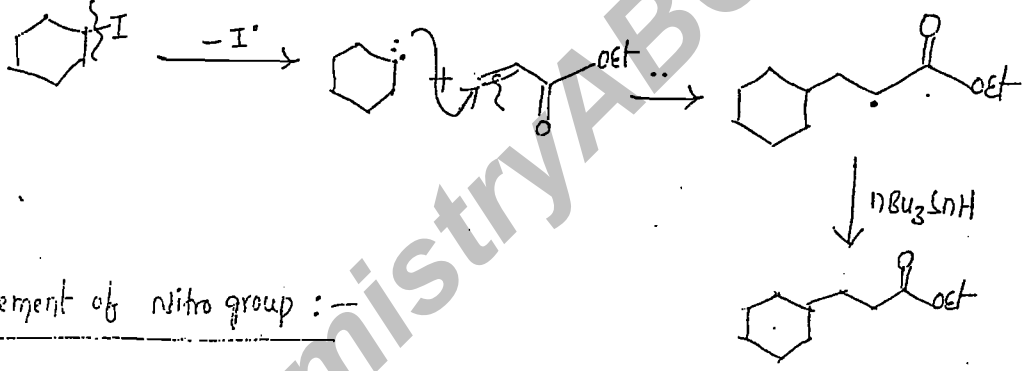


→ If halo compd having unsaturatn in trin-butyl tin hydride reagt, even unsatn also might participate.

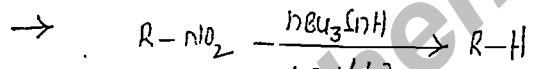


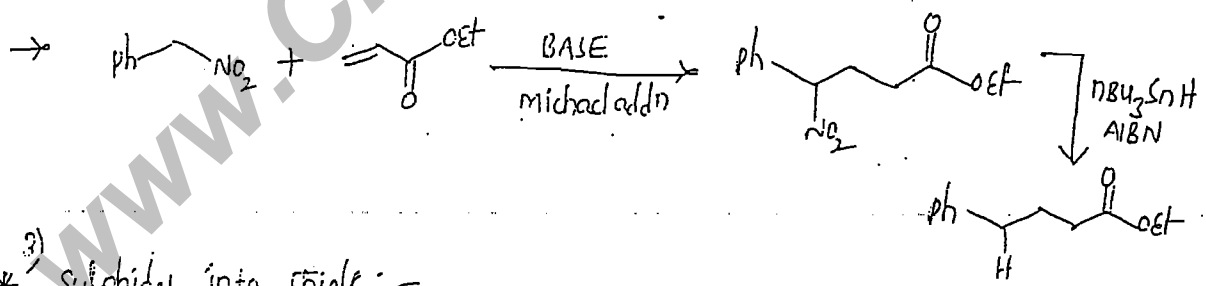




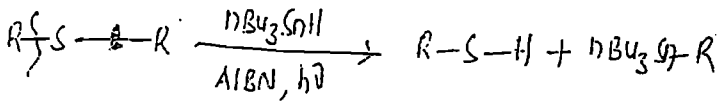


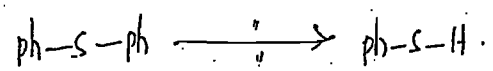
2) Displacement of nitro group :—



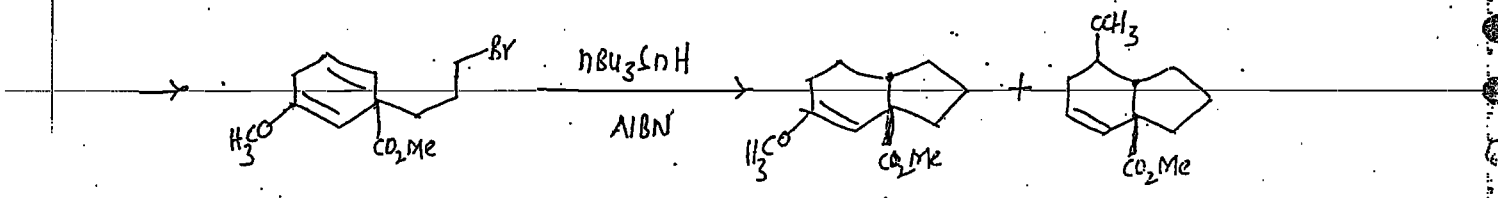


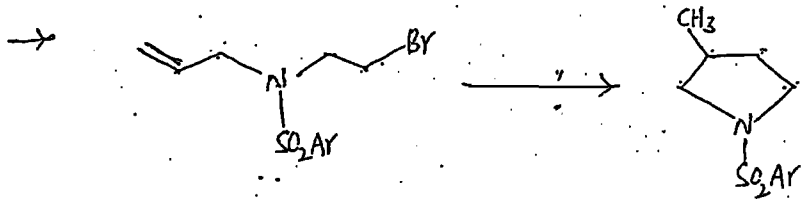
* 3) Sulphides into thiols :—

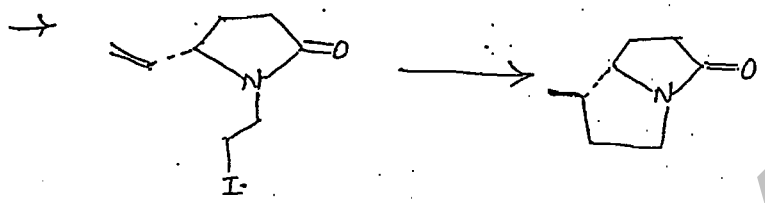


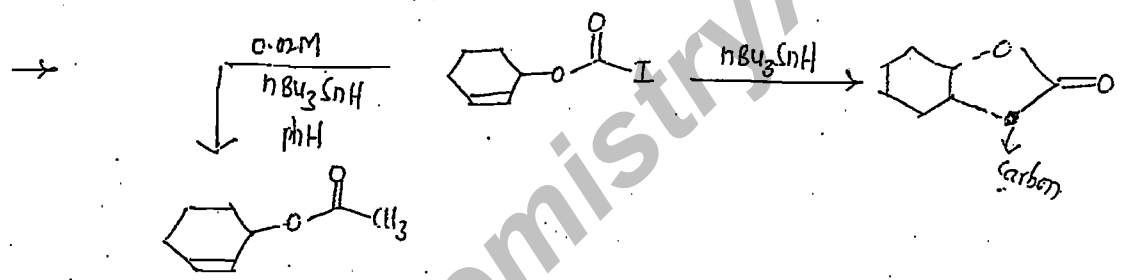


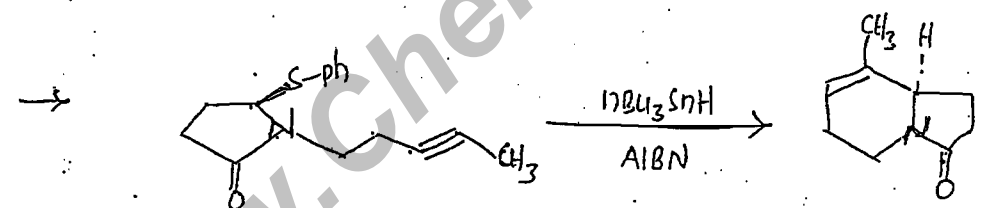
SOME MORE EXAMPLES :—

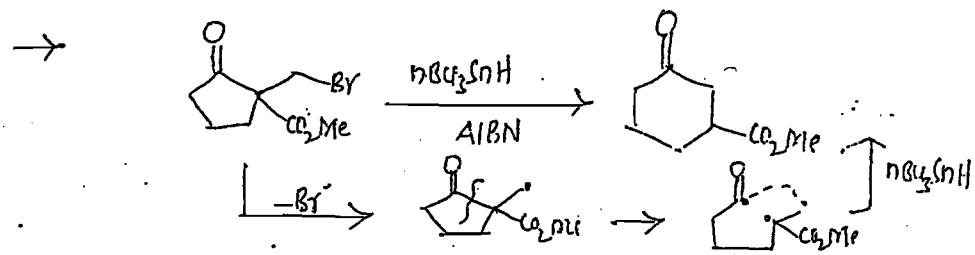


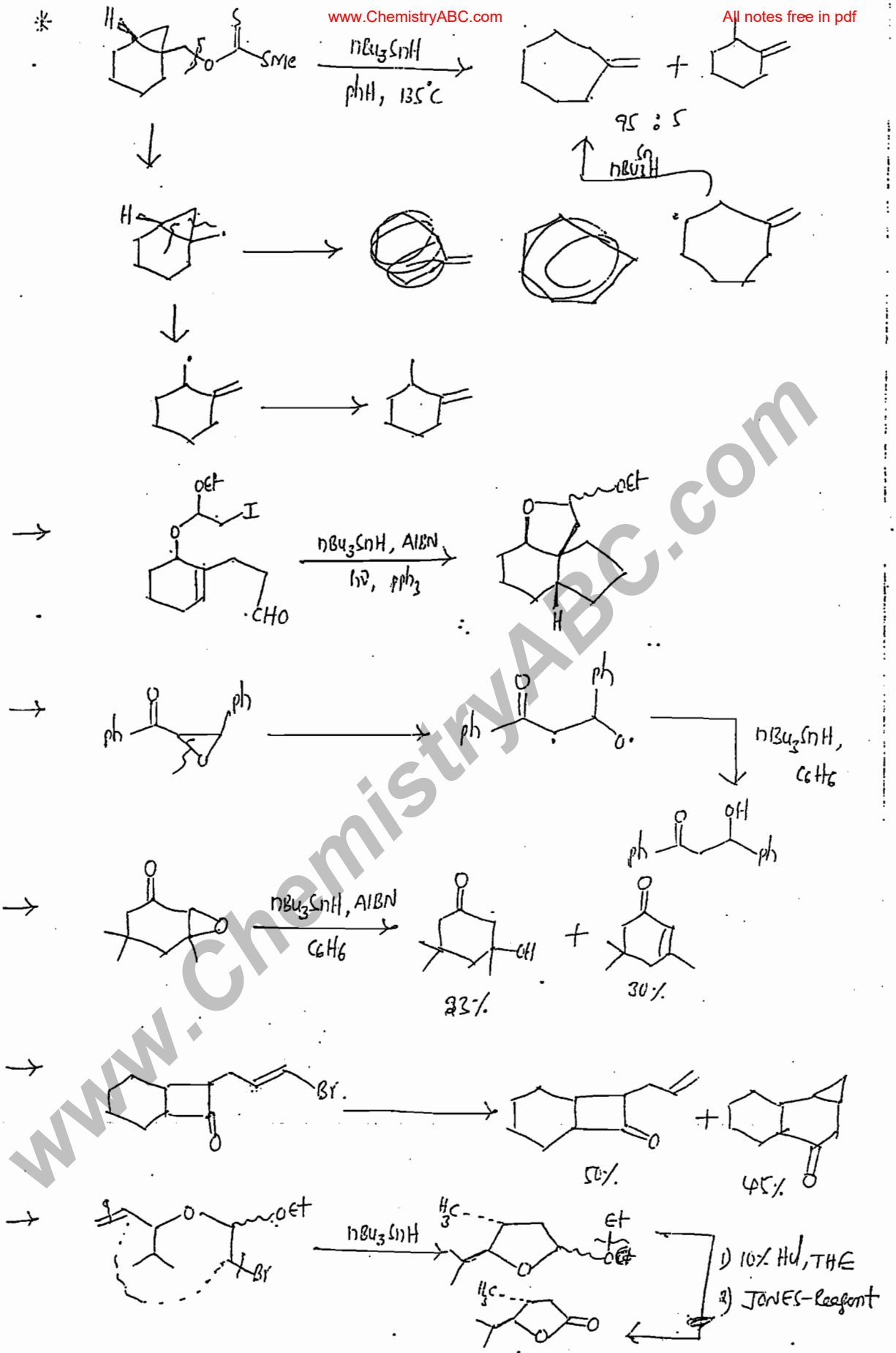


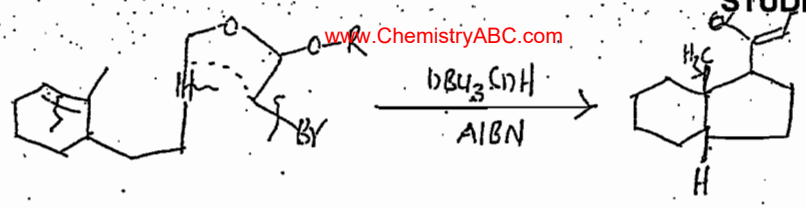




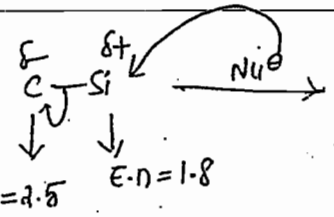






→ 

* ORGANO-SILICON REAGENTS :-

⇒ 

→ C–Si bond is polar, can be cleaved @ ⊕ by attacking $Nu^{\ominus}$ at Si.

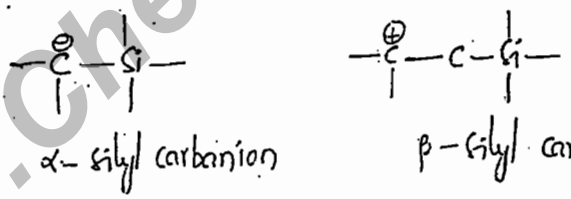
→ '⊕' 'Si' will have more affinity towards high e.n. atoms & nucleophiles, because resulting bond is stronger.

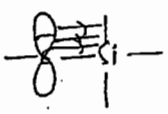
eg:- F^-, OH^-, Cl^- etc.

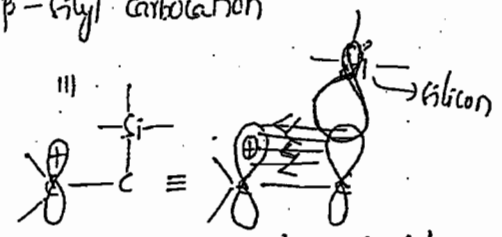
→ Source for $F^{\ominus}$: $nBu_4\overset{\oplus}{N}F^{\ominus}$

" " $OH^{\ominus}$: NaOH, KOH etc

" " $Cl^{\ominus}$: HCl

→ 





Stabilisn of c⊕ by C–Si sigma bonding.

→ Si can stabilise α-carbanion, β-carbocation.

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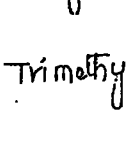
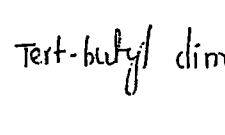
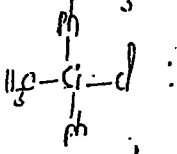
→ Stabilisn of α-silyl carbanion probably due to overlapping of empty d-orbitals of silicon with atomic orbital of carbanion.

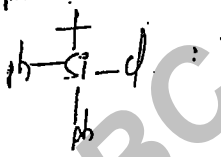
* Stabilization of β-silyl carbocation due to overlapping of empty p-atomic orbital of carbocation and Si–C, σ-bonding orbitals.

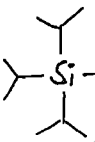
→ widely used 'Si' compounds in org. Synthesis.

1) Trimethyl silyl chloride,  : TMSCl → Most common silyl reagent used in org. reacns.

2) Tert-butyl dimethyl silyl chloride :  : TBDMSCl

3) Diphenyl methyl silyl chloride :  : DPMSCl

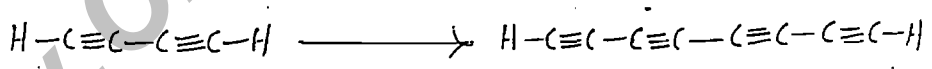
4) Tert-butyl diphenyl silyl chloride :  : TBDPSCl

5) Tri isopropyl silyl chloride :  : TIPSCl

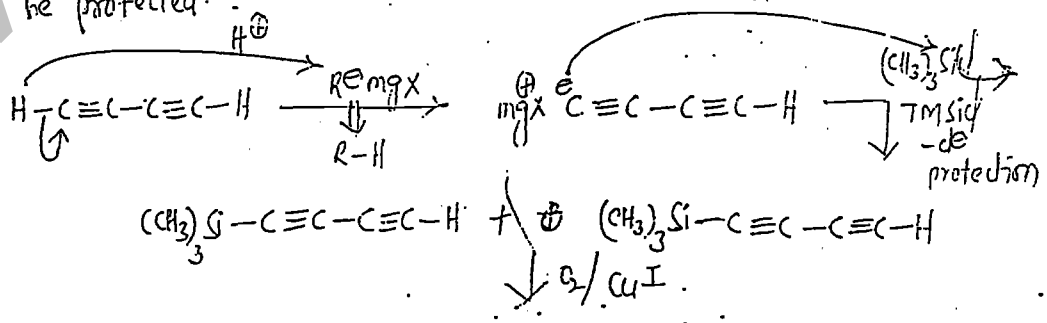
Applications :–

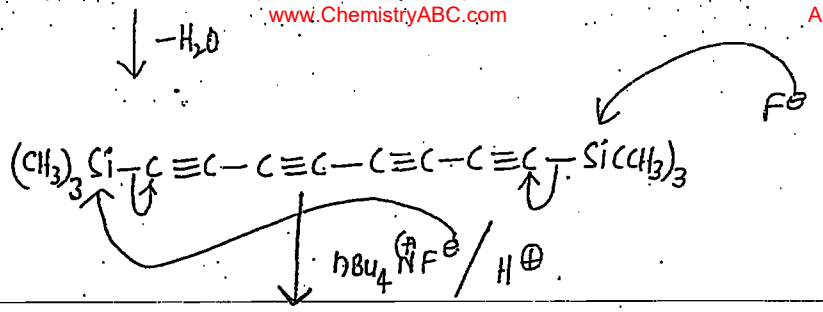
I) As protecting groups :

Silyl compds are good reagents for protection of acidic fng gps for terminal alkynes & alcohols.

2 Equiv: 

To prepare 8C' alkyne product, one of the termini of reactant should be protected.

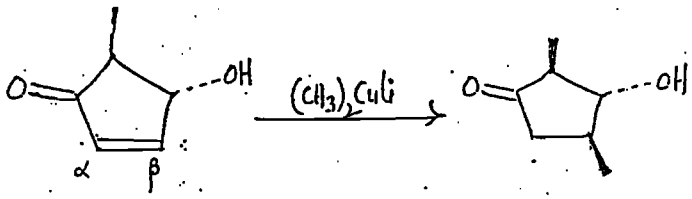




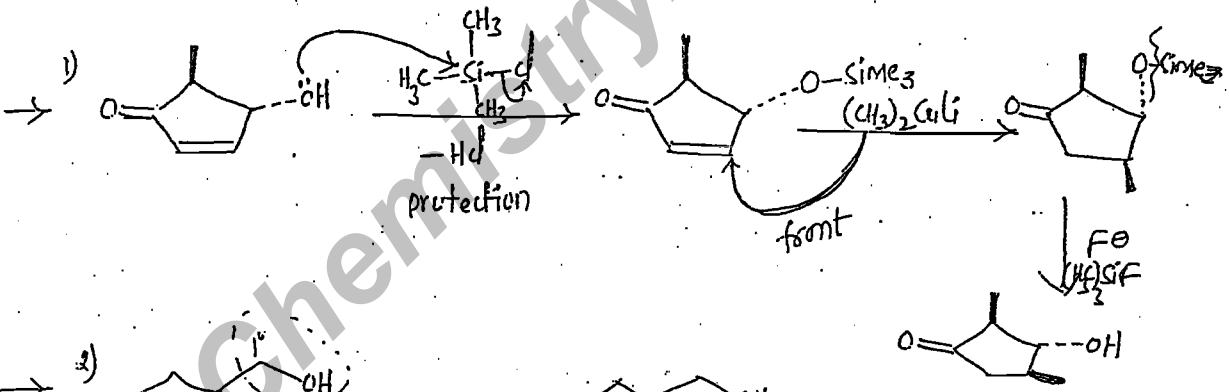
$H-C\equiv C-C\equiv C-C\equiv C-C\equiv C-H$.

* V.IMP

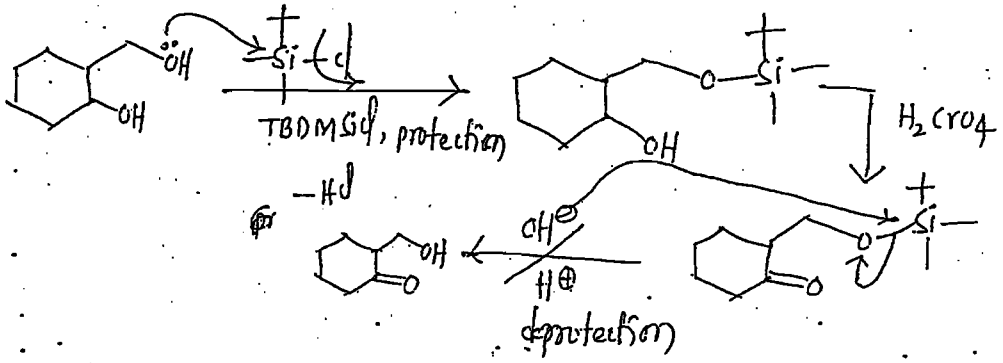
2) protection of alcohols :—



(free -OH may involve in rean with Gilman's reagent, ∴ it should be protected before addn of Gilman's reagent) ∴



for Selective oxidn of 2° alcohol, 1° alcohol must be protected.



* Stabilization of β-silyl carbocation due to overlapping of empty p-atomic orbital of carbocation and Si–C, σ-bonding orbitals.

→ widely used 'Si' compounds in org. Synthesis.

1) Trimethyl silyl chloride, $H_3C-\overset{CH_3}{\underset{CH_3}{Si}}-Cl$: TMSCl → Most common silyl reagent used in org. reacns.

2) Tert-butyl dimethyl silyl chloride : $H_3C-\overset{+}{Si}-Cl$: TBDMSCl

3) Diphenyl methyl silyl chloride : $H_3C-\overset{Ph}{\underset{Ph}{Si}}-Cl$: DPMSCl

4) Tert-butyl diphenyl silyl chloride : $Ph-\overset{+}{Si}-Cl$: TBDPSCl

5) Tri isopropyl silyl chloride : $\left(\right)-Si-Cl$; TIPSCl

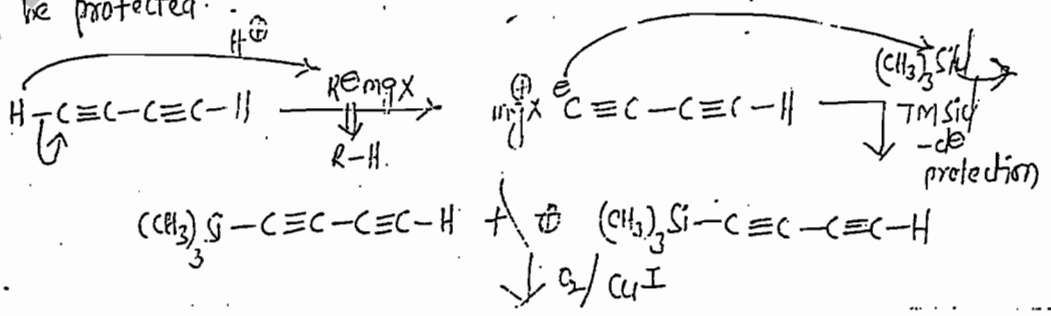
Applications :-

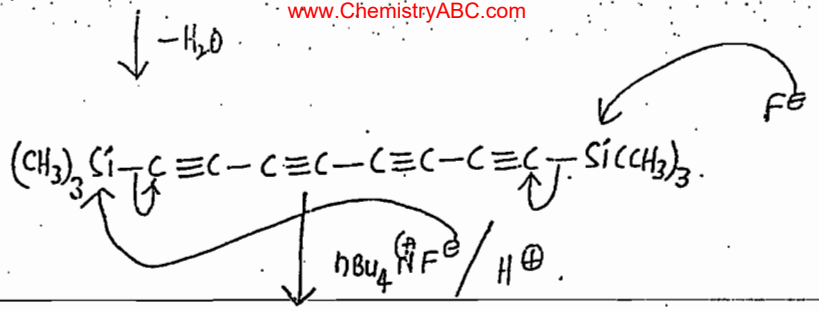
I) As protecting groups :

Silyl compds are good reagents for protection of acidic fng gps for terminal alkynes & alcohols.

2 equiv $H-C\equiv C-C\equiv C-H \longrightarrow H-C\equiv C-C\equiv C-C\equiv C-C\equiv C-H$

To prepare 8 C' alkyne product, one of the termini of reactant should be protected.

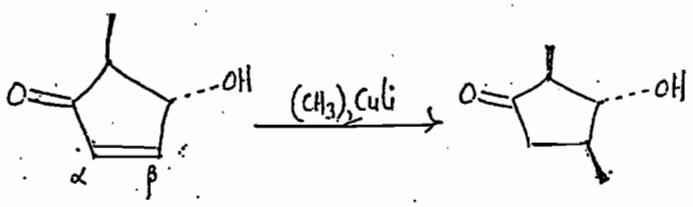




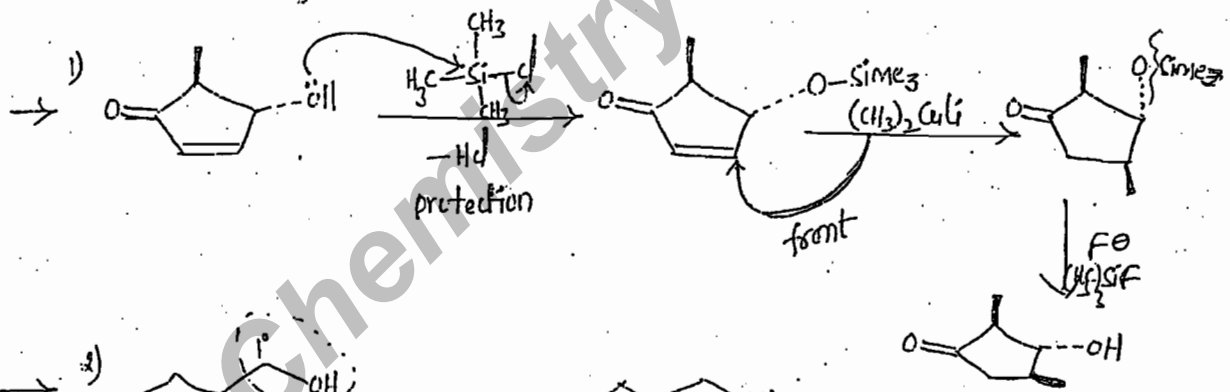
$$H-C\equiv C-C\equiv C-C\equiv C-C\equiv C-H$$

* V.IMP

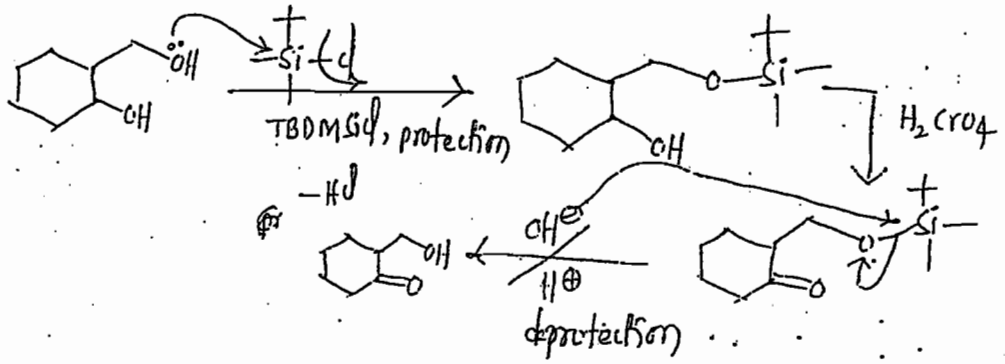
2) protection of alcohols :-



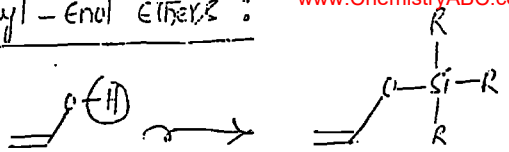
(free -OH may involve in rean with Gilman's reagent, ∴ it should be protected before addn of Gilman's reagent) .



For Selective oxidn of 2° alcohol, 1° alcohol must be protected.

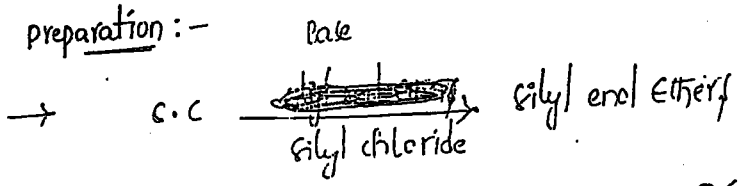


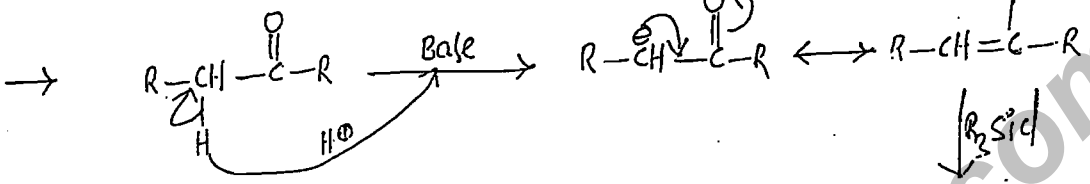
II. Silyl – Enol Ethers :

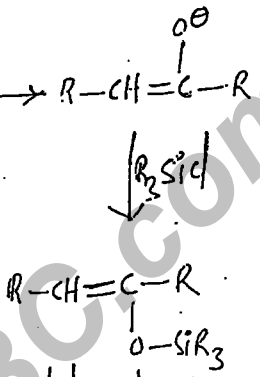


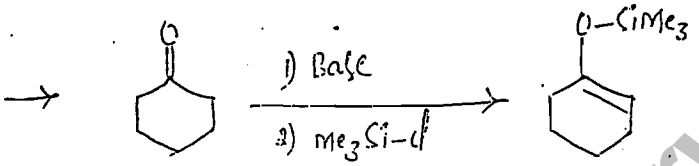
enol — Silyl enol ether

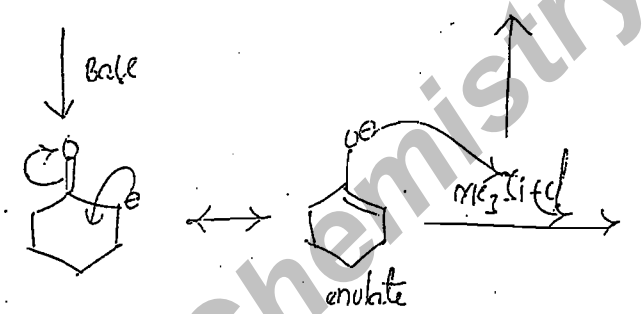
preparation :-

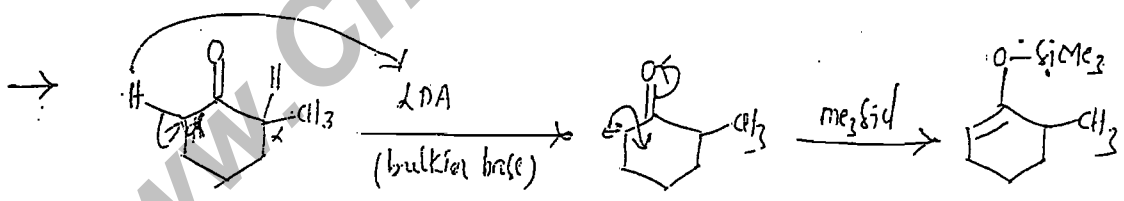


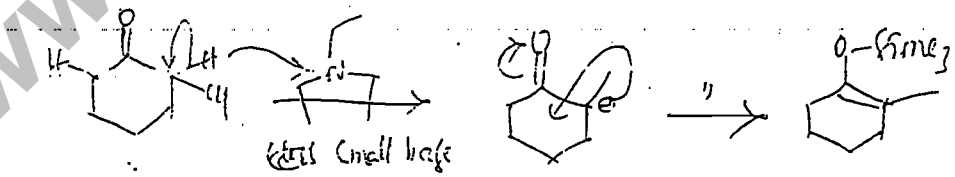












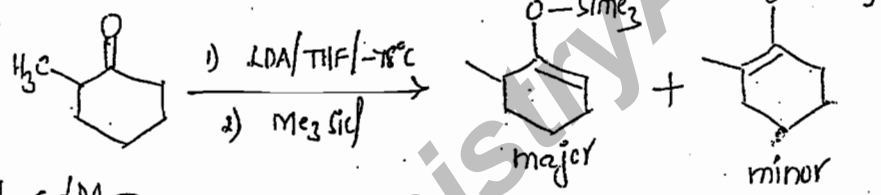
⇒ Regioselectivity in silyl enol ethers formn :—

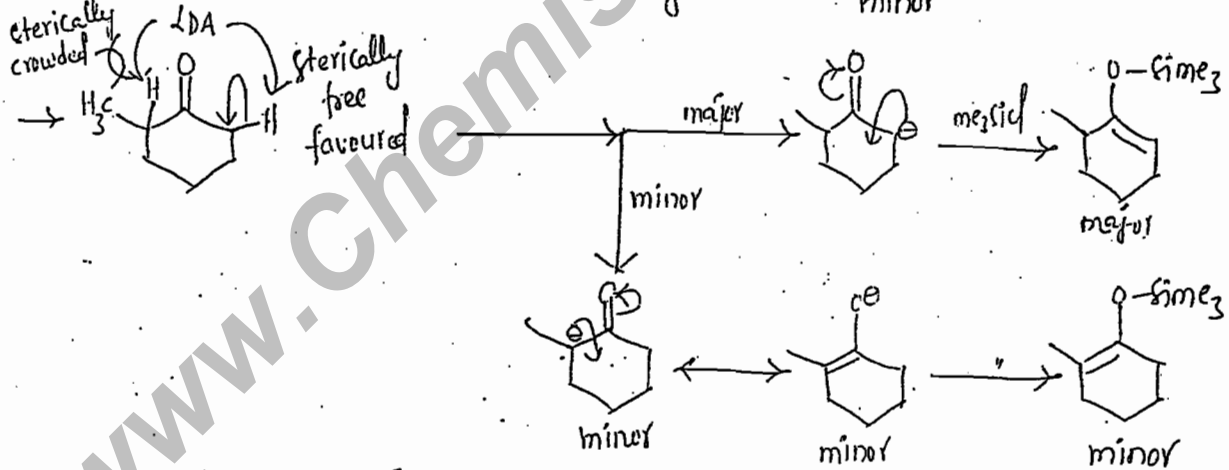
⇒ Regioselectivity depends on size or bulkiness of the base.

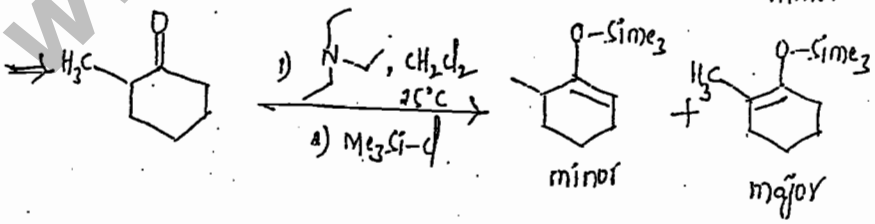
→ If large size base used, eg: LDA, less substituted silyl enol ether major, kinetically controlled. Due to steric crowding, LDA or bulkier base preferentially abstracts proton from less substituted α-position, resulting product is major.

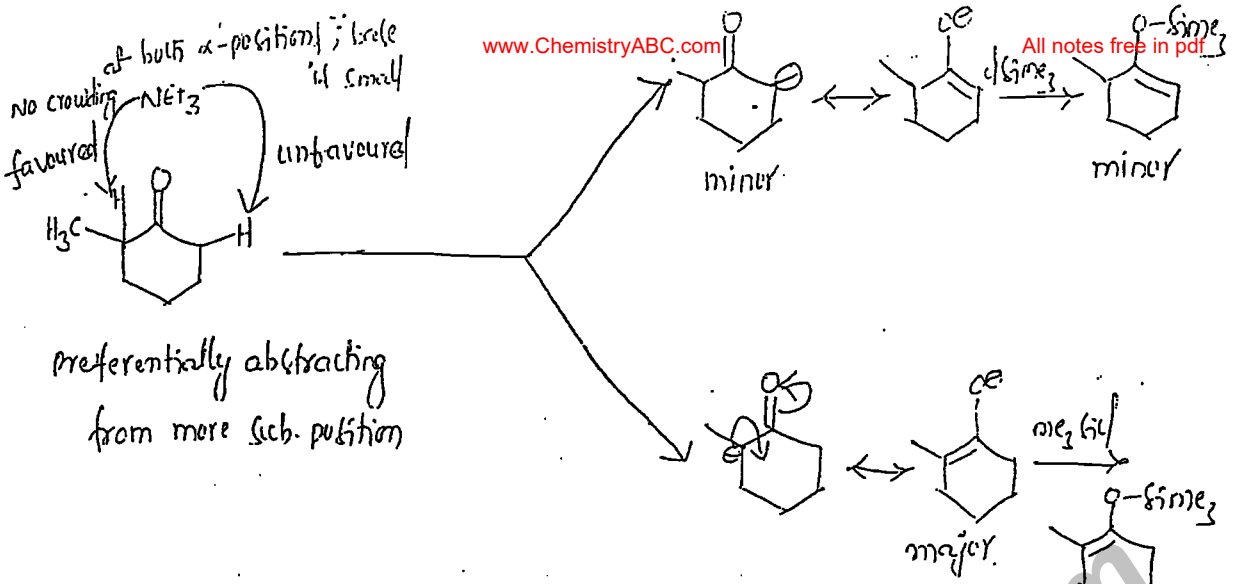
→ If small size base used, eg: Et_3N, more substituted silyl enol ether is major. Thermodynamically controlled, small size base preferentially abstracts proton from more sub. α-position. (steric crowding absent). Produces stable silyl enol ethers as major product.

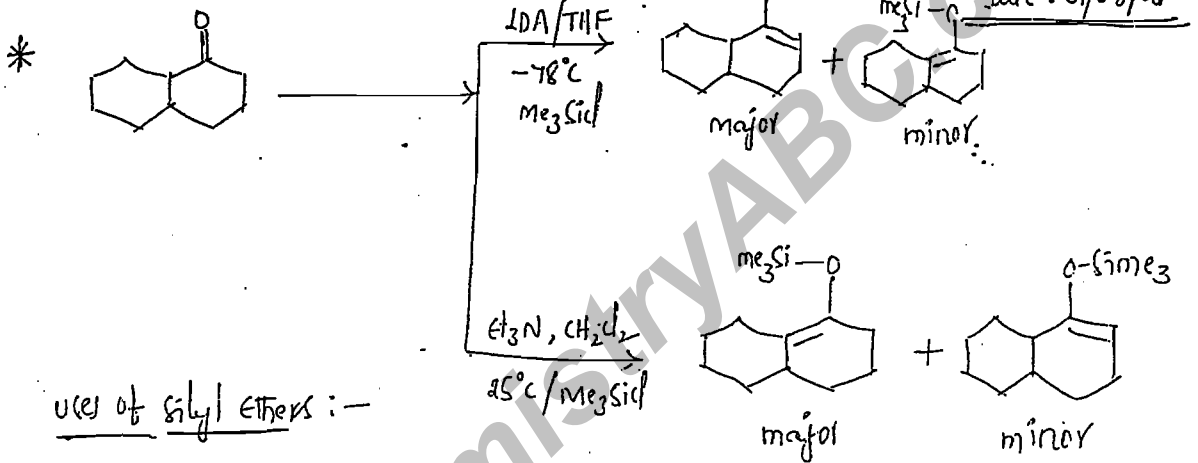
*V. IMP

→ 

→ 

→ 

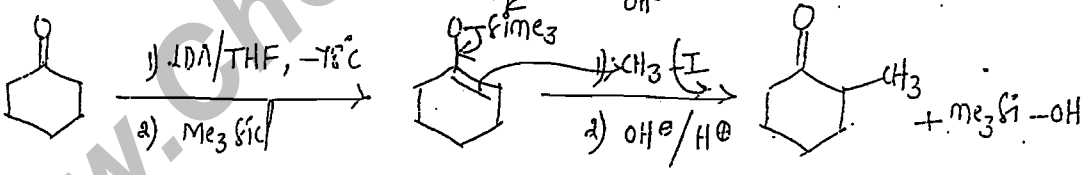


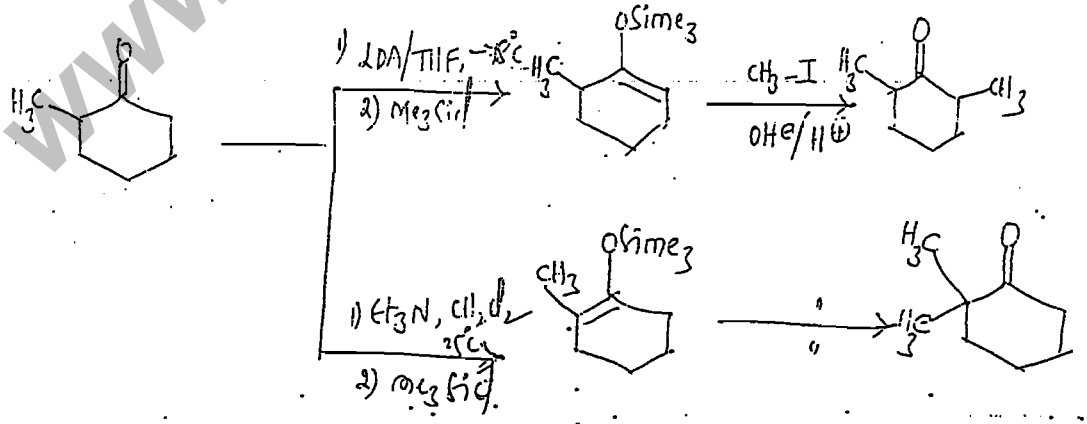


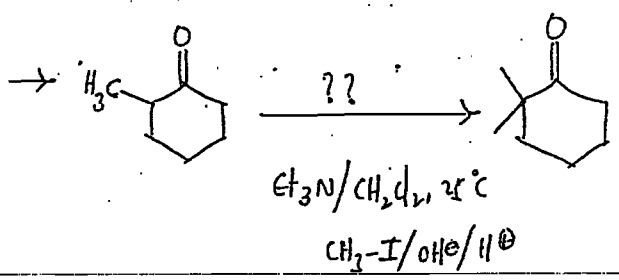
Date : 31/05/08

Uses of silyl ethers :-

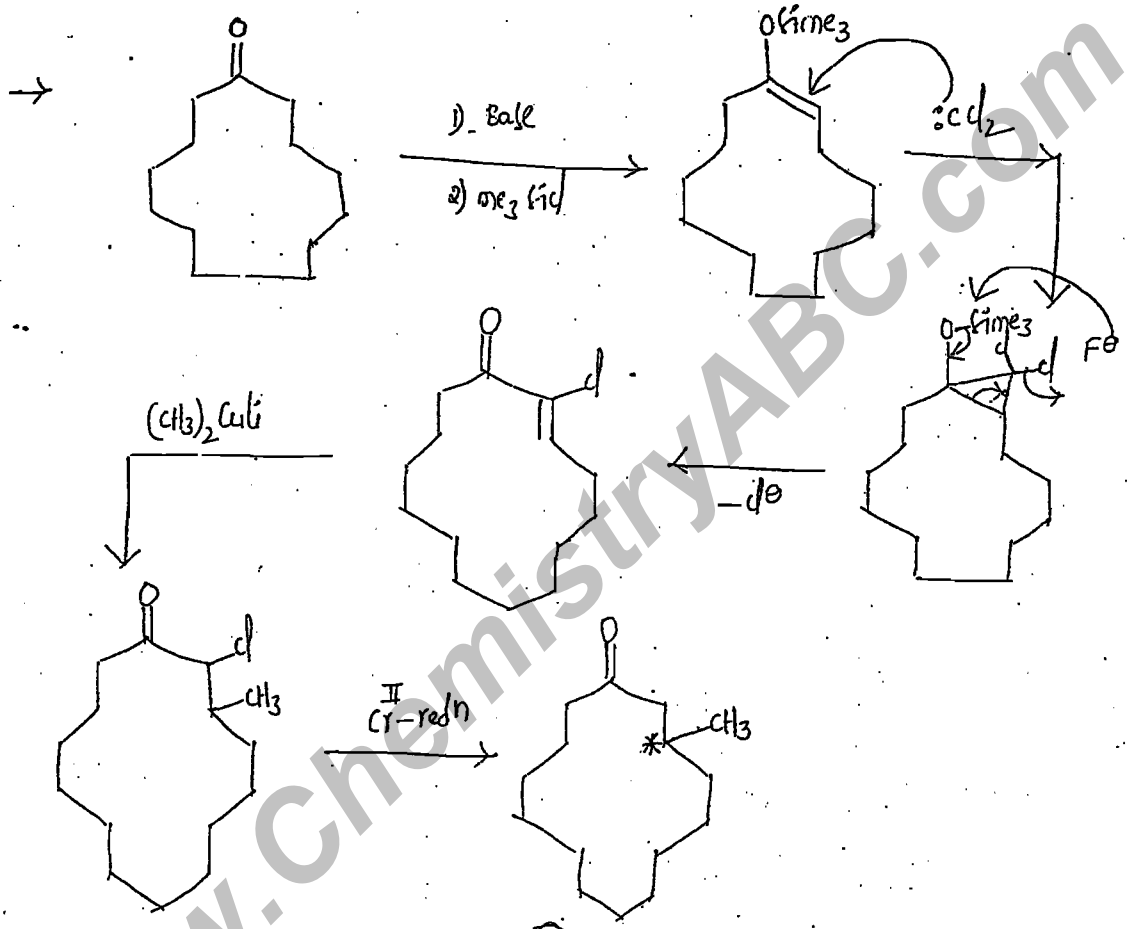
* a) α-alkylation of carbonyl compounds







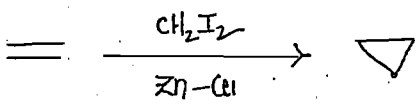
→ *b) Ring Expantions :—



⊕ Racemic

⊕ Mulcone

c) SIMMON'S-SMITH REACTION :—

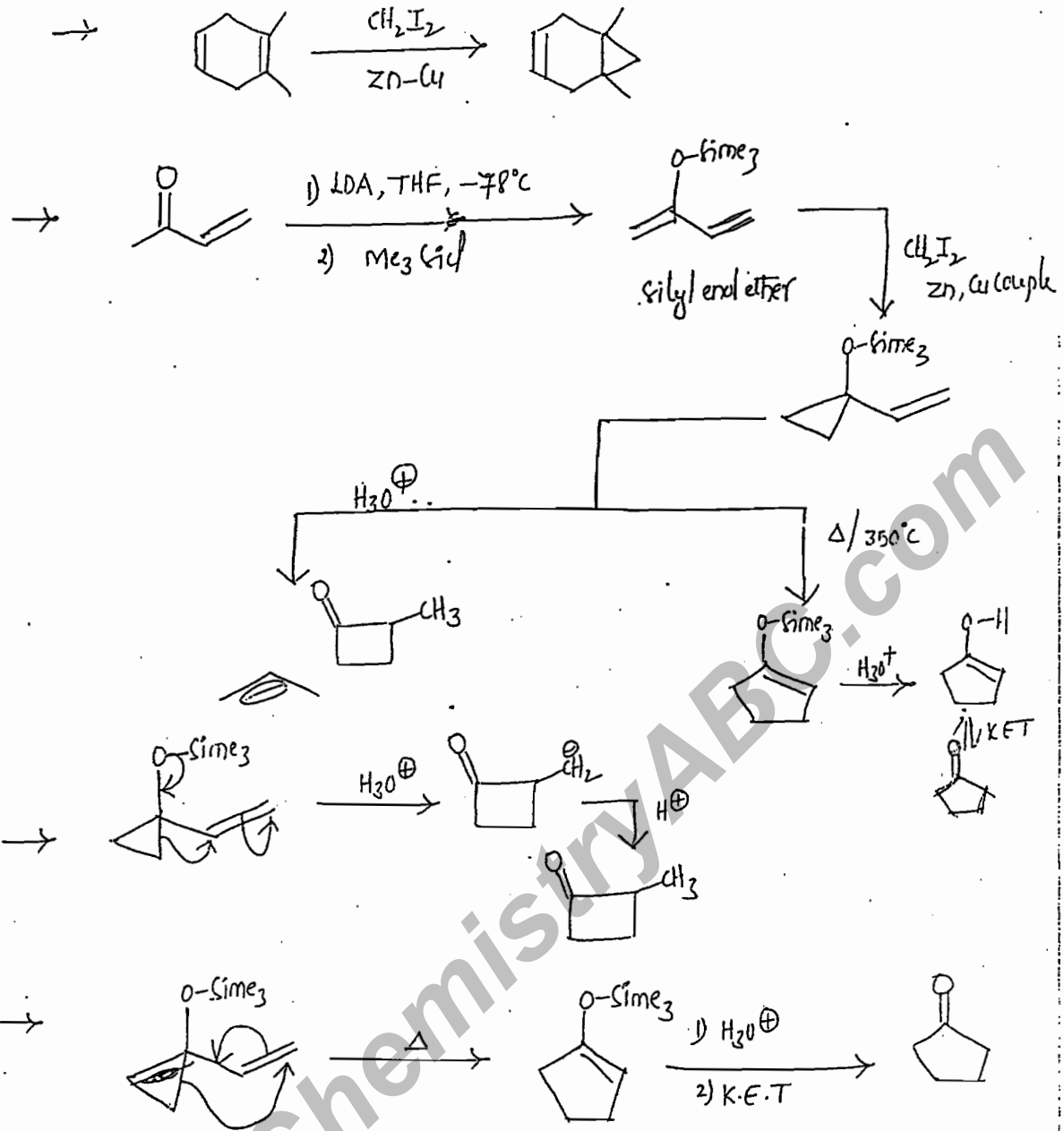


} Simmon Smith reaction.

cyclopropanation of olefine with CH_2I_2/Zn-Cu couple

⇩

Simmon-Smith reaction



3) α-silyl carbanions : "Peterson's olefination"

→ Alternative to "Wittig reaction"

→ conversion of carbonyl compds into olefins with lithio or magnesio derivatives of silyl reagents called "peterson's olefination".

→ Reaction intermediate - β-hydroxy silanes which undergo

Spontanious or acid/base catalyced decomposition produces olefines.

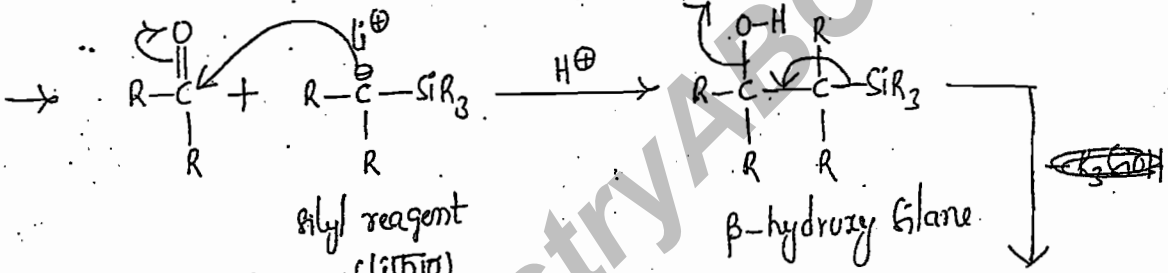
→ By products are trialkyl silanols (or) hexa alkyl disiloxanes which are highly volatile, easy to remove from rean mixture. &

→ carbonyl compounds + lithio (or) magnesio silyl reagent → β-hydroxy silane

Spontaneous (or) acid/base

hexa alkyl disiloxanes ←$-H_2O$— Trialkyl silanols + olefine

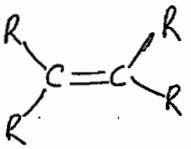
biproducts.

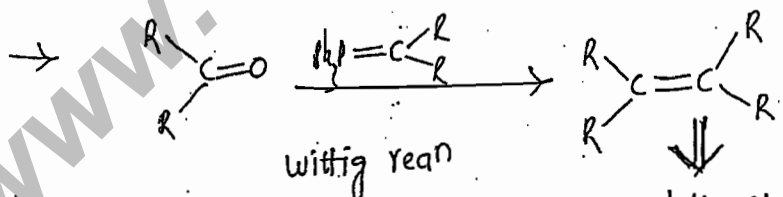
→ 

silyl reagent (lithio) — β-hydroxy silane

$R_3Si-O-SiR_3$ ←$-H_2O$— $2R_3SiOH$ +

highly volatile, easy to remove from rean mixture



→ 

wittig rean — not volatile

difficult to get in-pure form

→ Removal of biproduct triphenyl phosphorous oxide in wittig rean not simple.

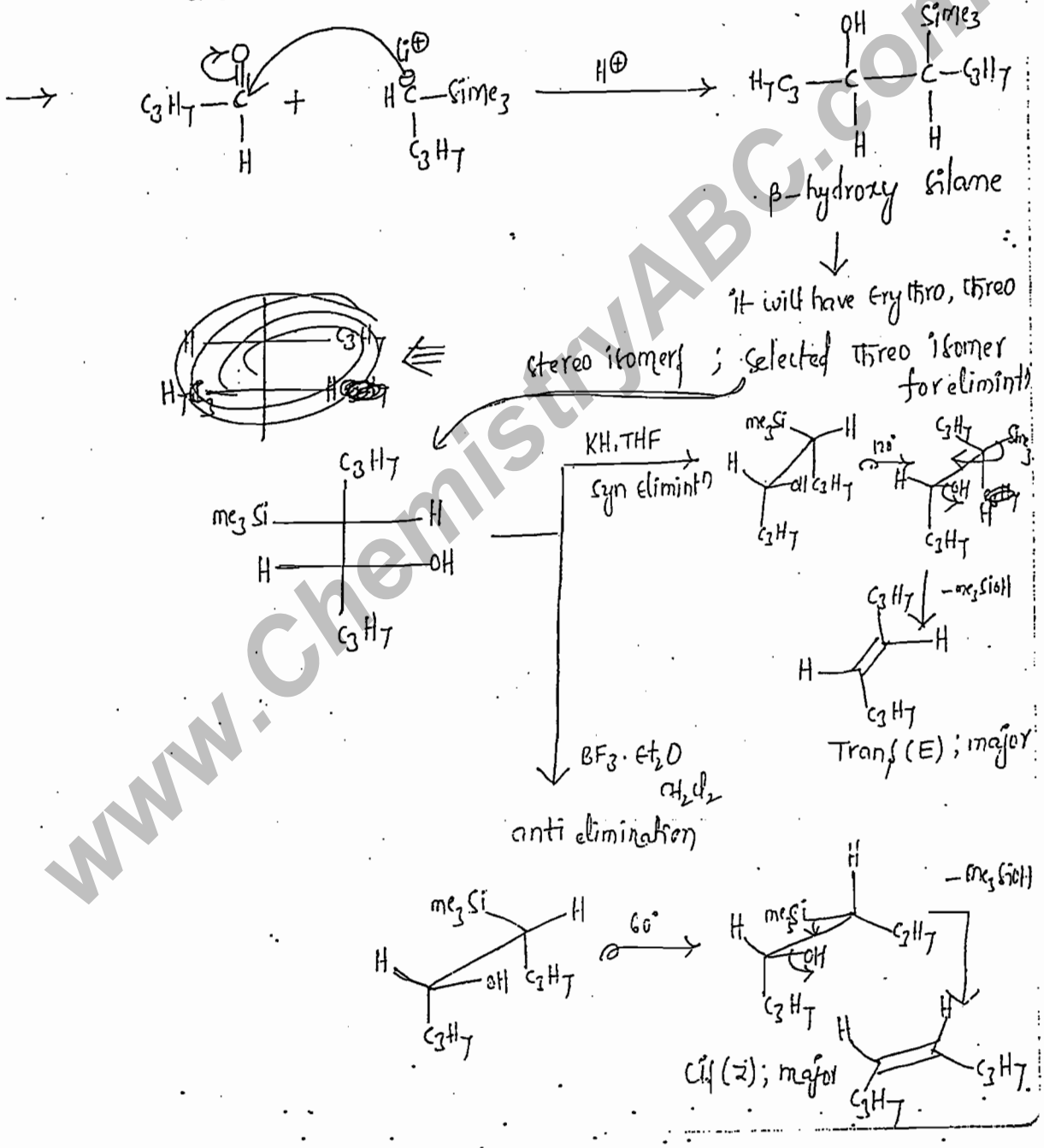
→ There is a practical advantage for 'peterson's olefination' over wittig reaction.

Because in peterson's olefination, byproduct removal easier, but not in "wittig reany"

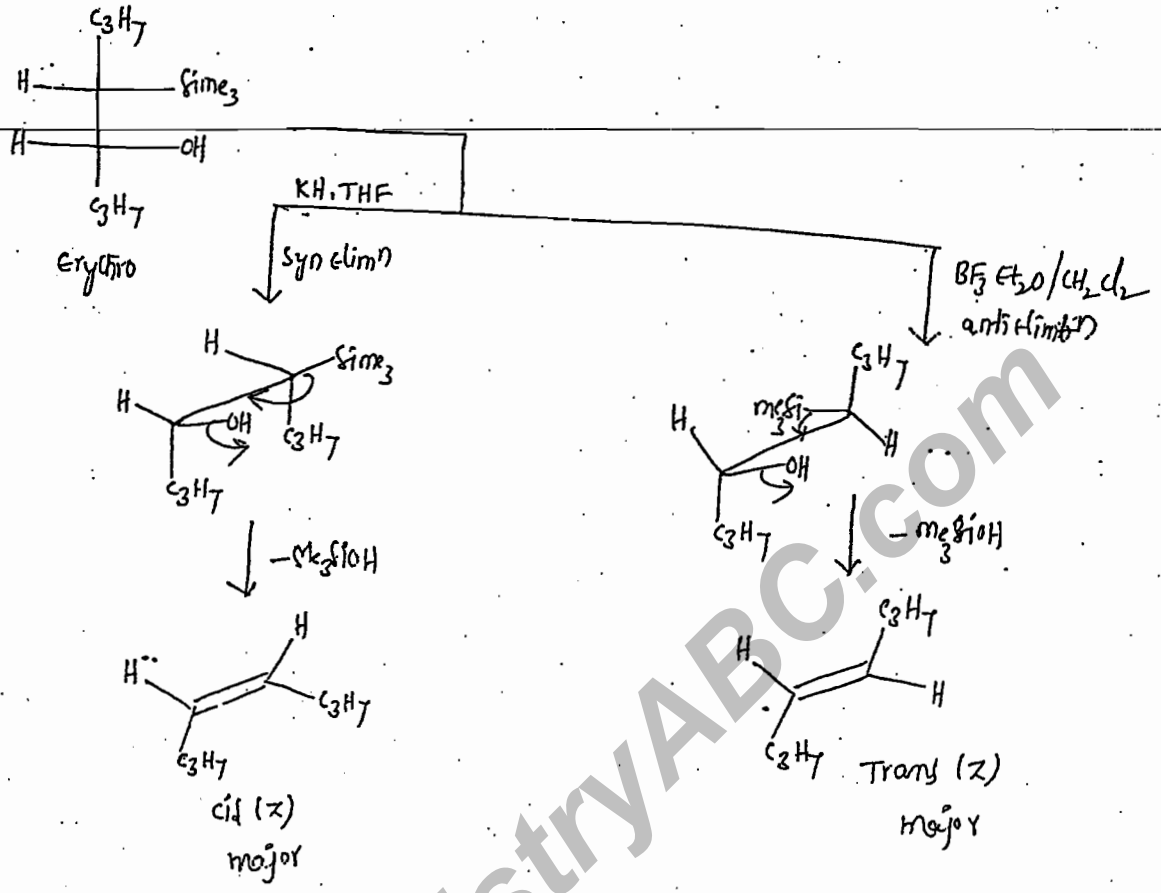
→ The stereochem. of olefine depends on reaction conditions & nature of stereo isomer of β-hydroxy silane intermediate.

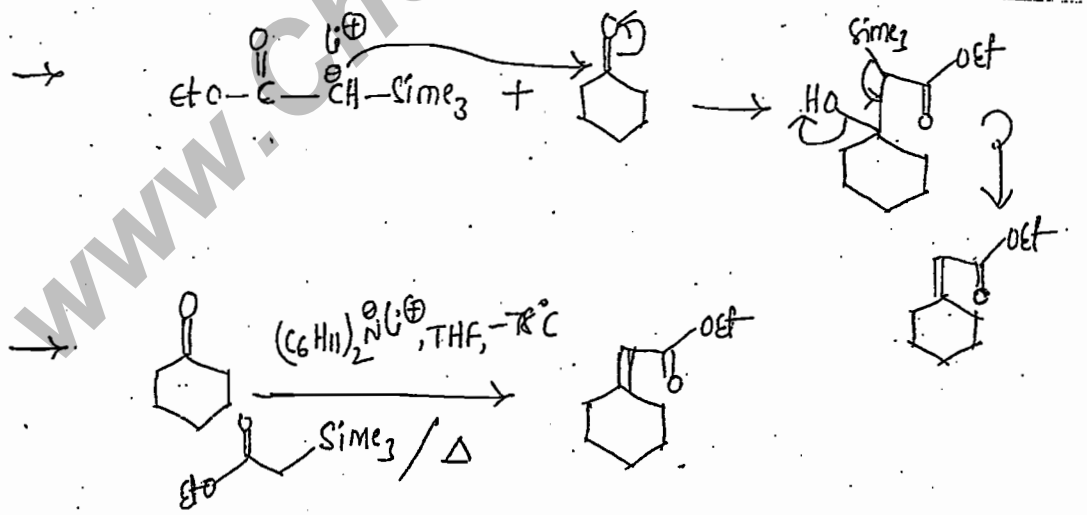
→ In Basic medium – syn elimination

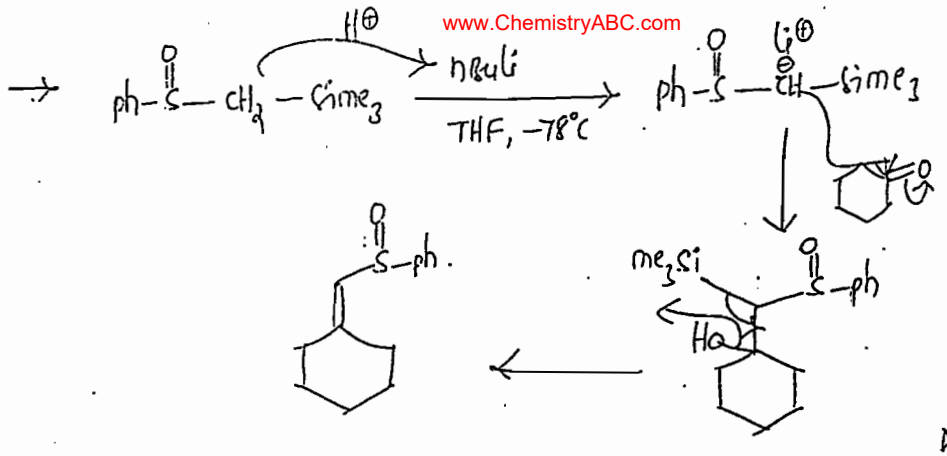
, acidic " – anti " predominent.



→ Show products from erythro stereoisomer in acidic/basic medium.



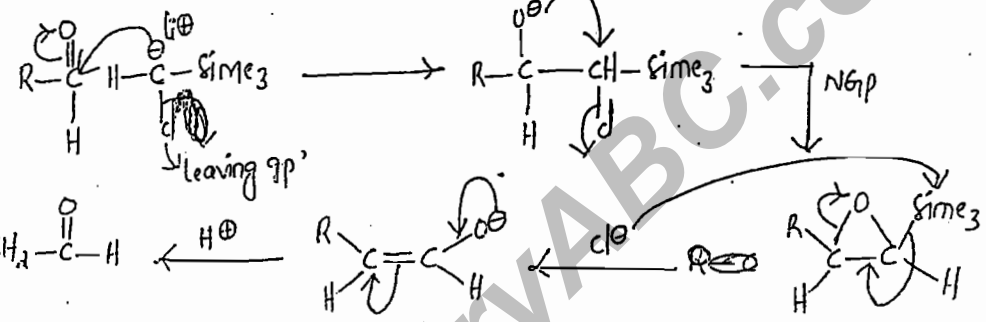




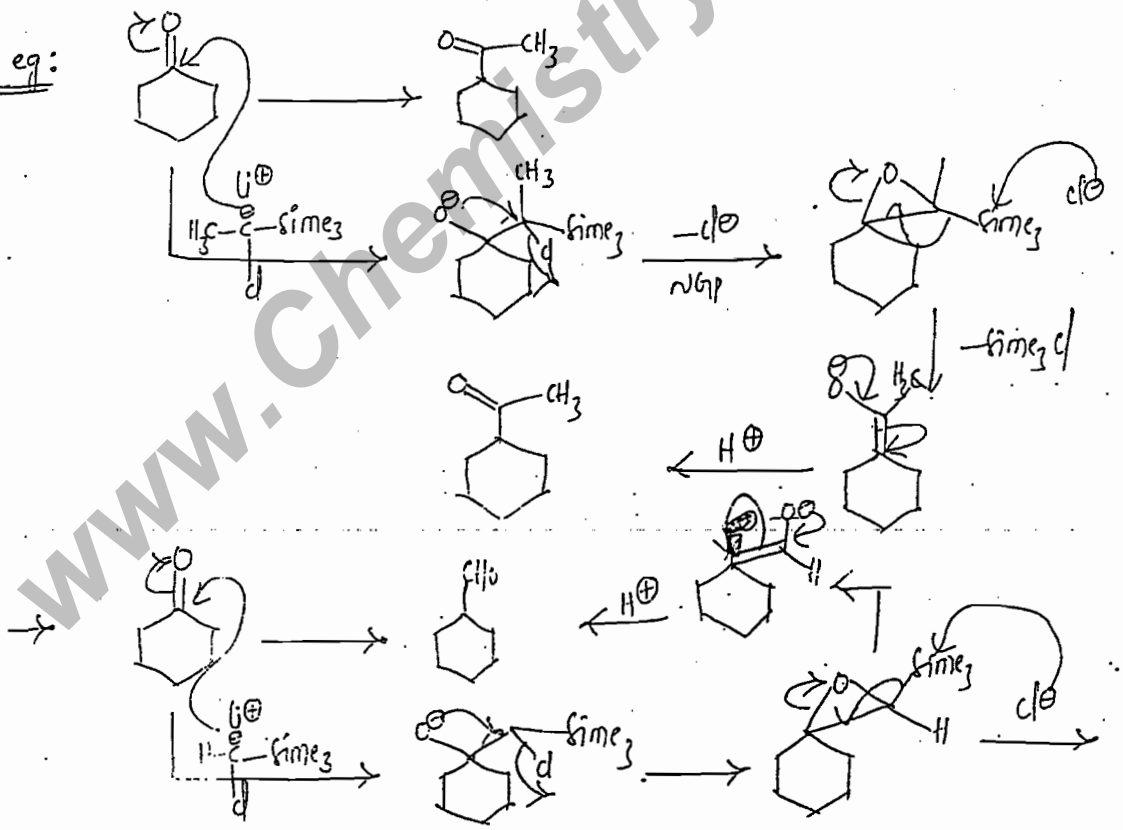
Date : 01/06/08

→ If there is a leaving gp at α-silyl carbanion, the products are carbonyl-compds. ⇒ "Homologation of carbonyl compounds".

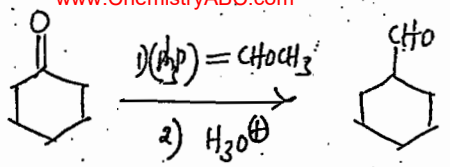
V.IMP :-

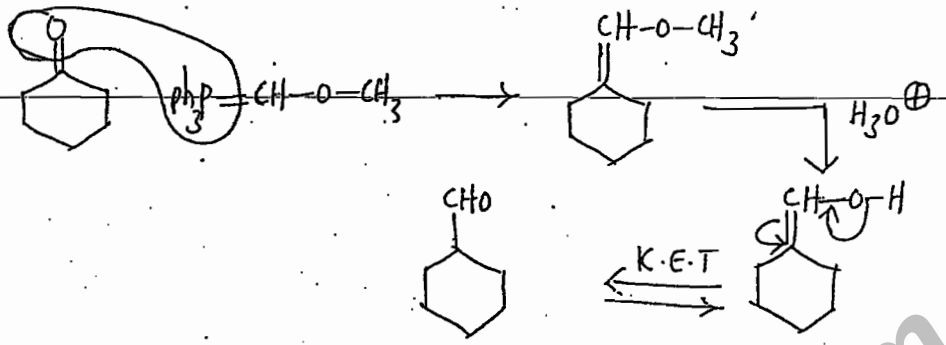


eg:

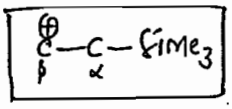


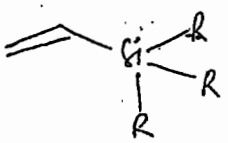
→ Wittig reaction :





*. Alkenyl Silanes :





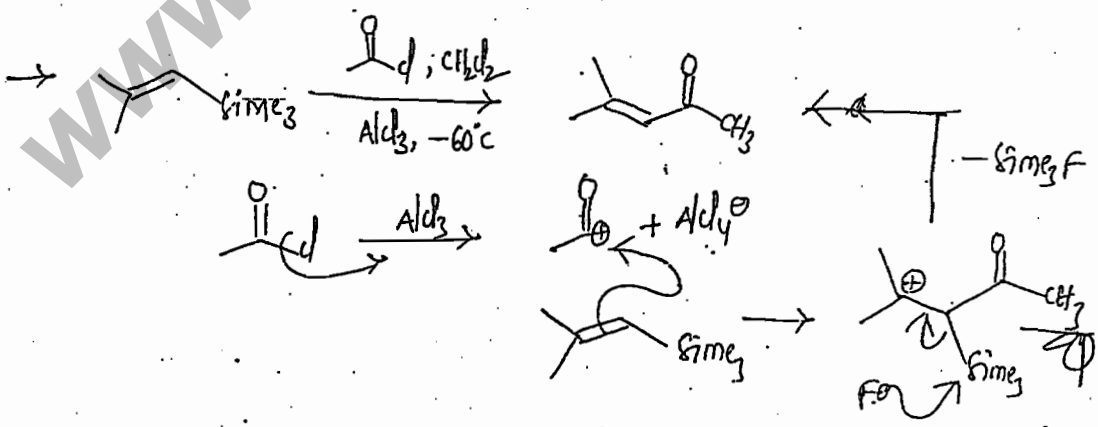
Alkenyl silanes participate in electrophilic subn catalysed by lewis acids $AlCl_3$, $SnCl_4$, $BeCl_4$, etc

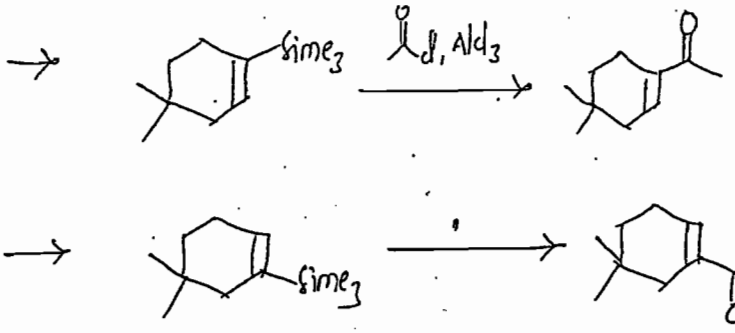
→

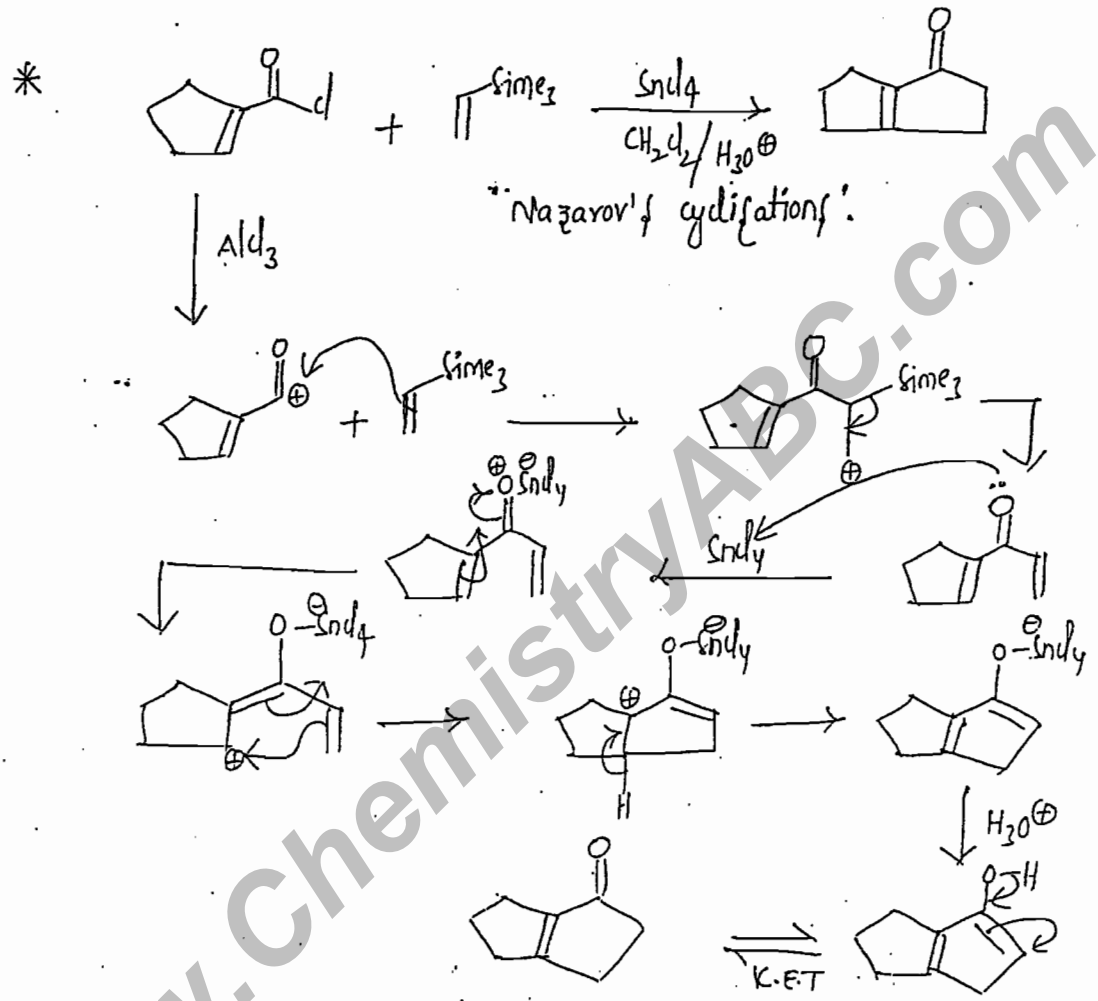
β-Silyl carbocation
(stable)

* the attacking $E^{\oplus}$ takes silyl group position.

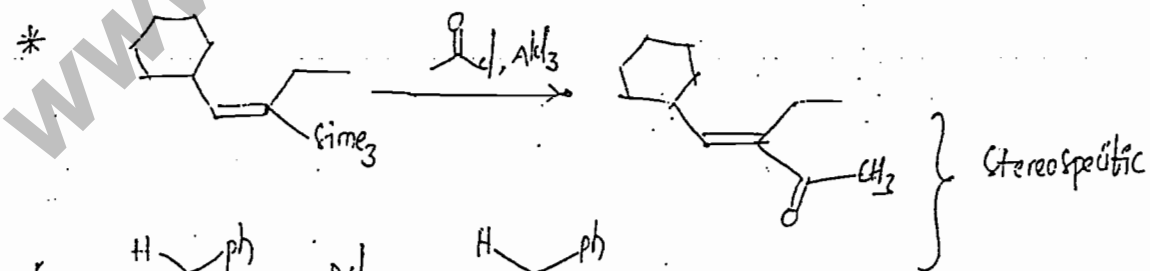
→



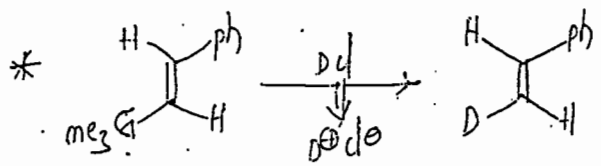




"Nazarov's cyclisations".



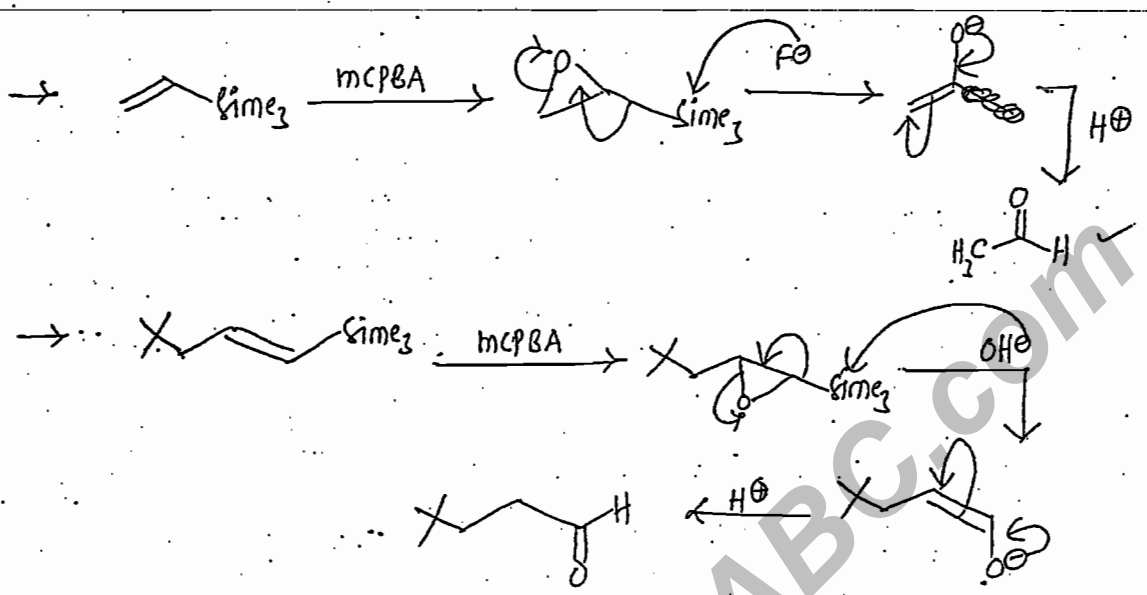
Stereospecific



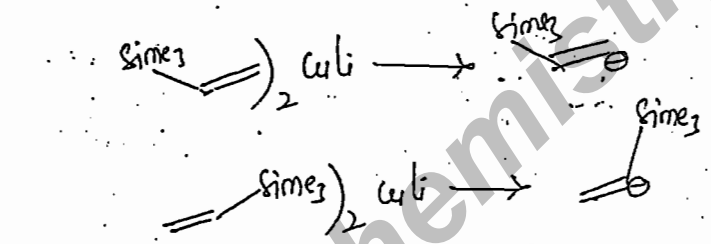
" leaving silyl gp positions taken by attacking electrophiles, ∴ stereospecific"

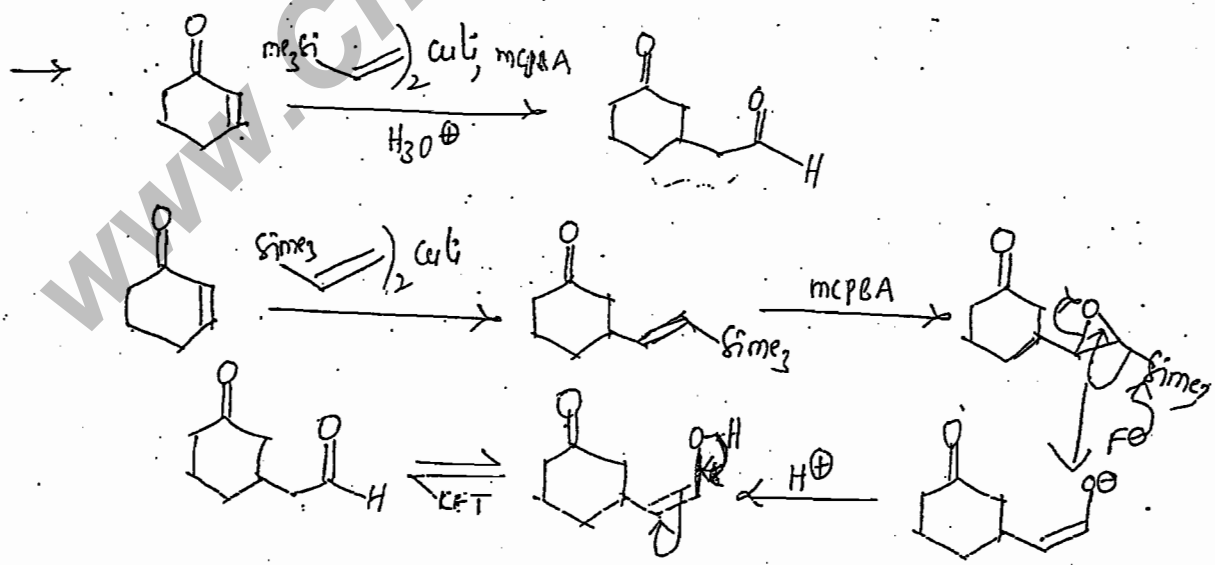
* preparation of carbonyl compd from alkenyl silanes :—

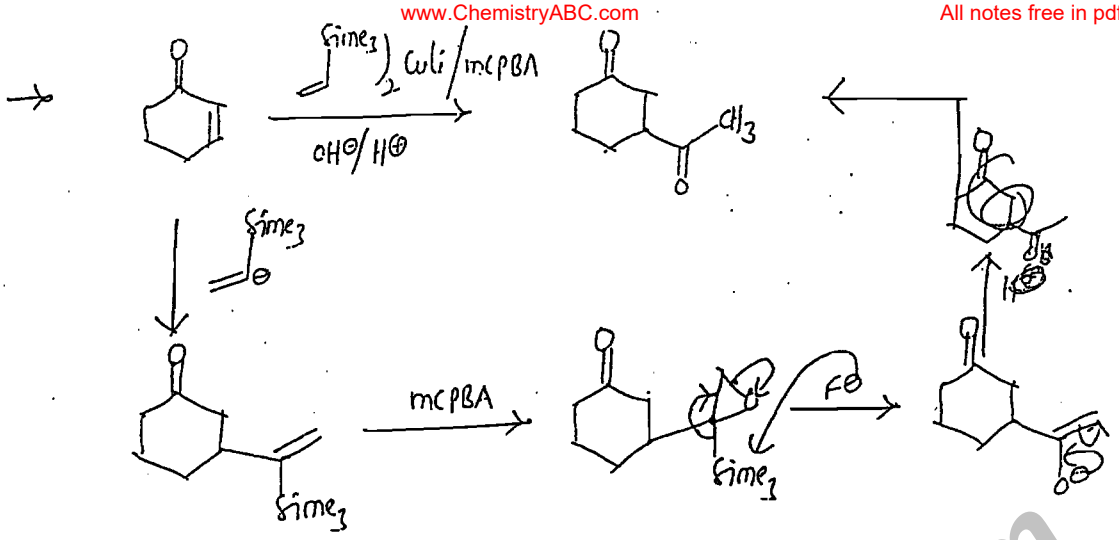
. Alkenyl silane $\xrightarrow{mCPBA}$ Epoxide intermediate $\xrightarrow{F^\ominus/Cl^\ominus/OH^\ominus}$ carbonyl compd.



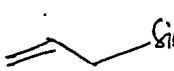
* $(CH_3)_2CuLi \longrightarrow \overset{\ominus}{C}H_3 + H_3C\,Cu + Li$

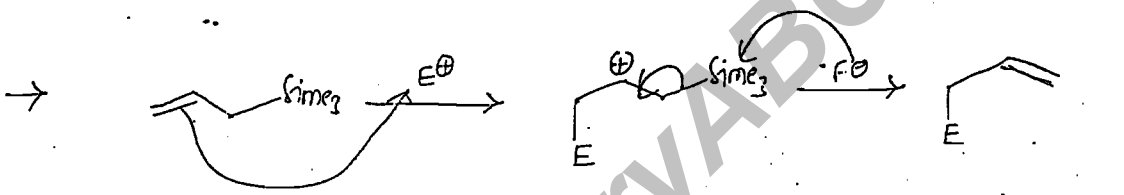




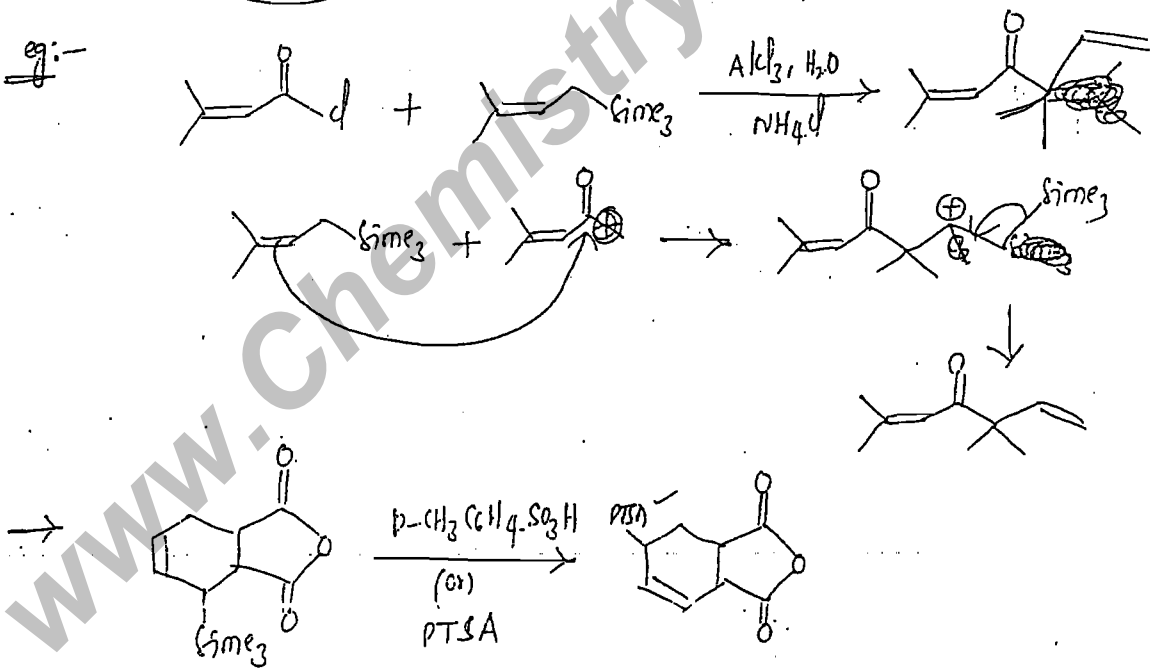


* Allyl Silanes :-

→  undergo electrophilic substn catalysed by lewis acids

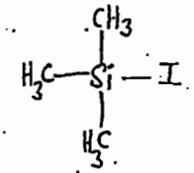


eg:-



* 1) Trimethyl silyl Iodide :— TMSI (or) TMSiI

→ $(CH_3)_3SiI$ (or)

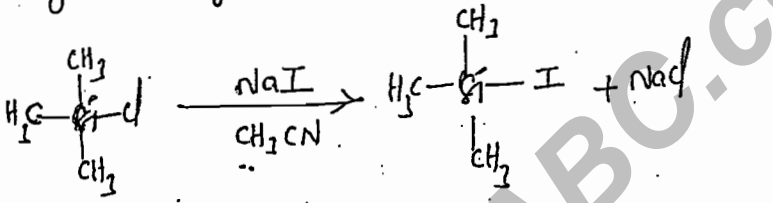


→ TMSI is unstable compound, sensitive to light & moisture.

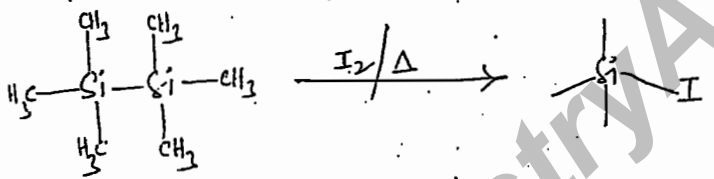
∴ It's prepn is "insitu preparation".

Methods for Insitu preparations :—

1) By reacting trimethyl silyl chloride with NaI/CH_3-CN.



2)

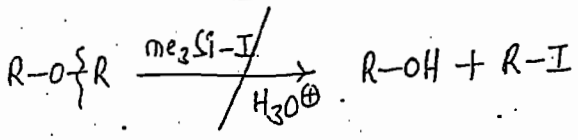


Applications :—

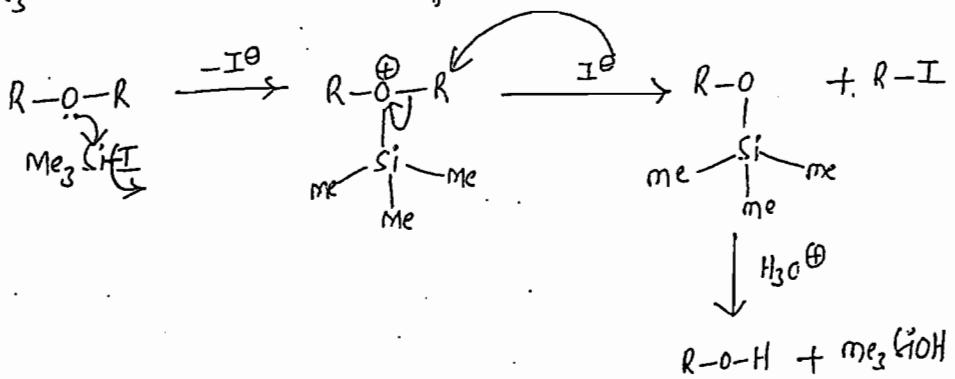
1) Excellent reagent for cleavage of ethers.
2) cleavage of Ethers
3) " " Acetals / ketals
4) convert alcohols into Iodides.
5) " Sulphoxides . Sulphides.

1) cleavage of ethers :—

Into alcohols, Iodides.



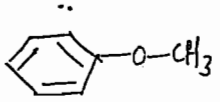
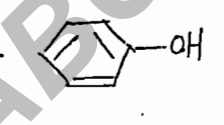
Me_3SiI is the electrophilic agent.

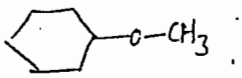
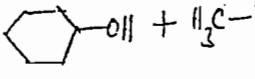


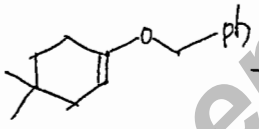
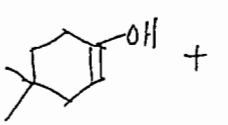
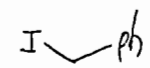
→ In unsymmetrical ethers, weaker ether bonding get cleaved.

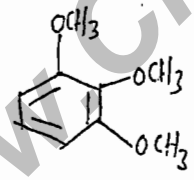
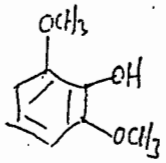
→ $R-O-R^1 \xrightarrow[H_3O^\oplus]{Me_3Si-I} R-OH + R^1-I$

strong weak

eg:- →  $\xrightarrow[H_3O^\oplus]{Me_3Si-I}$  + H_3C-I

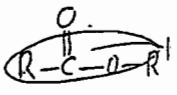
→  →  + H_3C-I.

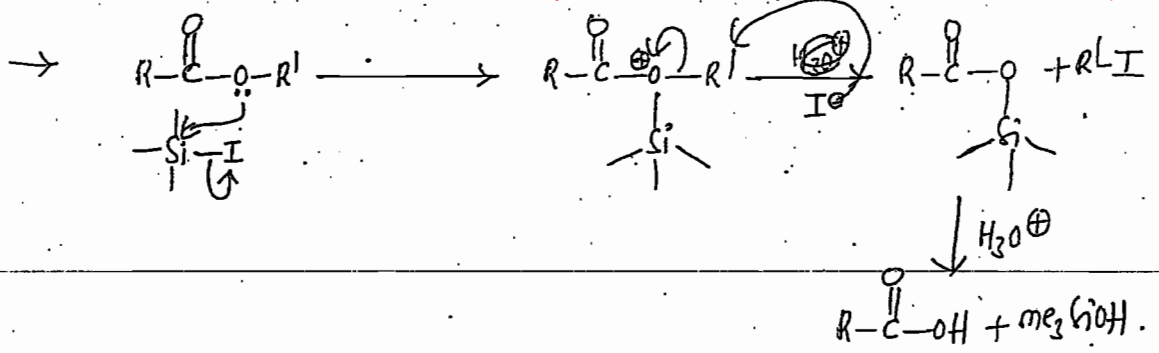
→  $\xrightarrow[(or)\ me_3SiCl/NaI\ H_3O^\oplus]{me_3Si-I}$  + 

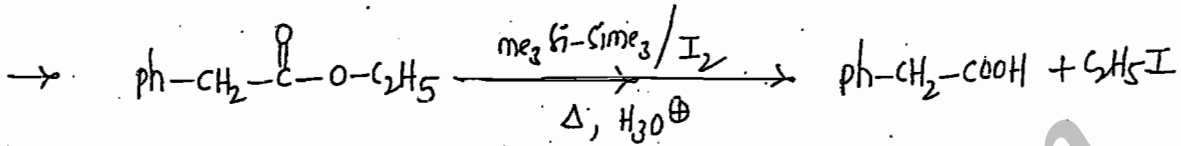
→  $\xrightarrow[H_3O^\oplus]{TMeSiI}$  + CH_3-I

→ **4) cleavage of Esters into acids & Iodides :--**

→ $R-\overset{O}{\overset{\|}{C}}-O-R^1 \xrightarrow[H_3O^\oplus]{me_3SiI} R-\overset{O}{\overset{\|}{C}}-OH + R^1-I$

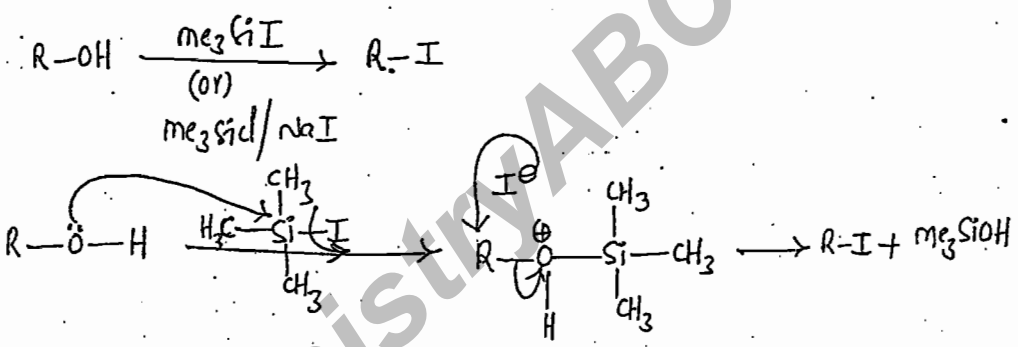
→ 

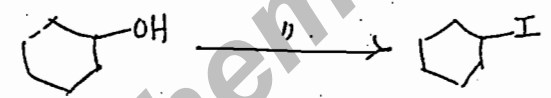


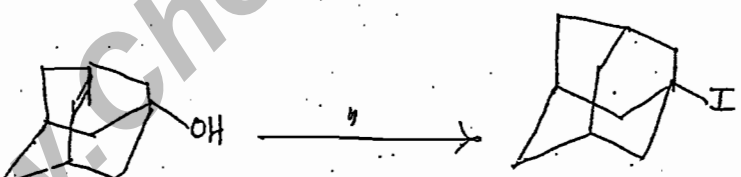


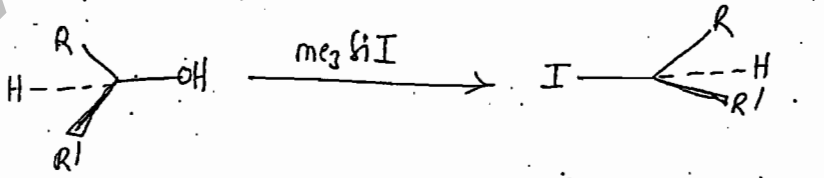
* 4) conversion of alcohols into Iodides :

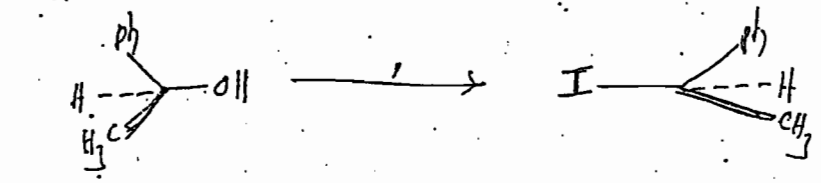
→ S_N^i type



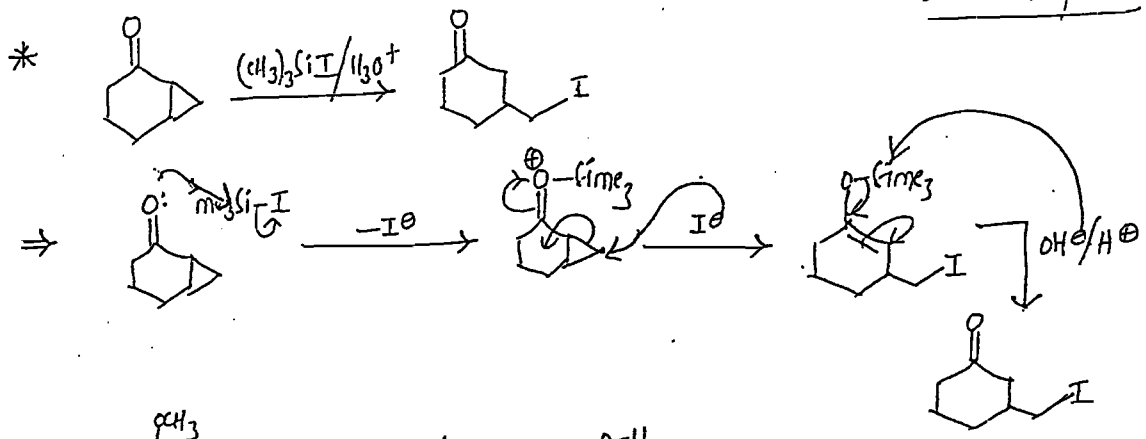


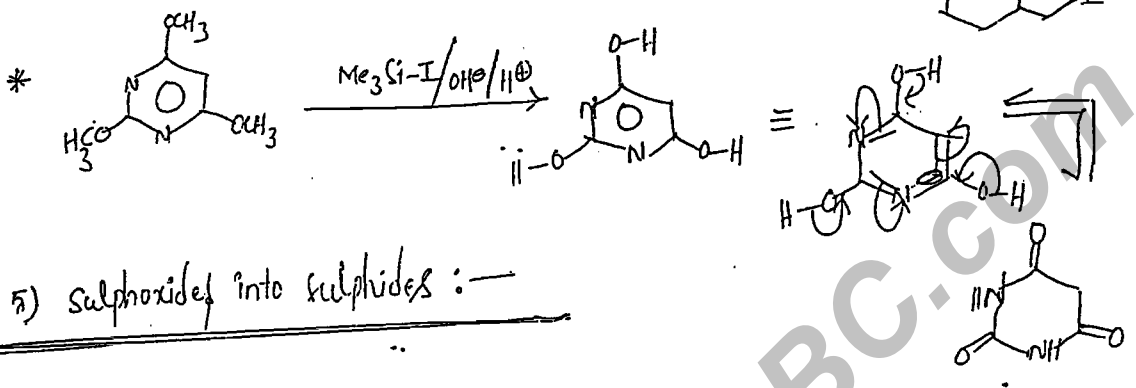




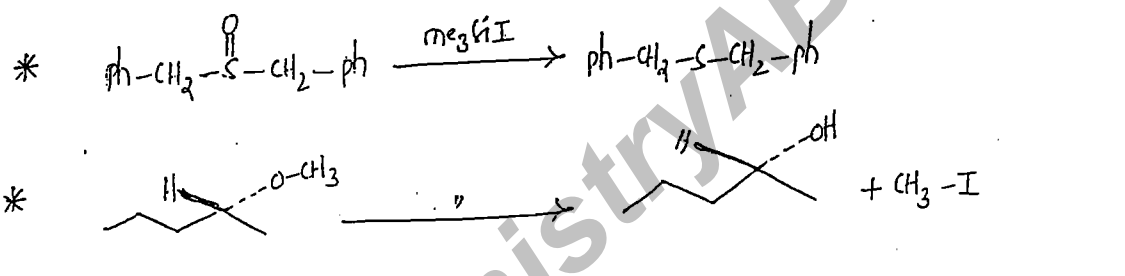


Date : 02/04/08

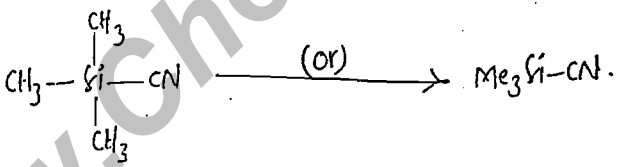


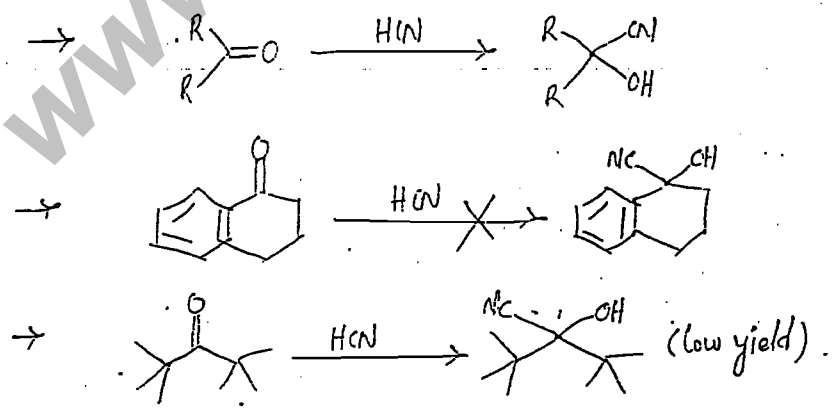


5) Sulphoxides into sulphides :—



d) Trimethyl silyl cyanide :—





* Me_3SiCN useful reagent, attacks at carbonyl of aldehydes or ketones.

→ In a catalytic medium, lewis acids / cyanide ion (CN^-) produces silyl ethers of cyanohydrins of corresponding carbonyl compounds.

---

* carbonyl fns which are inert or unreactive with HCN / also readily reacts with Me_3SiCN. gives silyl ethers of cyanohydrins.

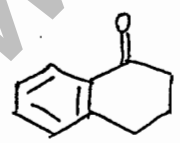
* silyl ethers of cyanohydrins on hydrolysis produces simple cyanohydrins which, may further converted into amino alcohols or hydroxy acids with good % of yields.

→ C=C $\xrightarrow{Me_3SiCN}$ silyl ethers of cyanohydrines $\xrightarrow{\text{mild hydrolysis}}$ cyano hydrines

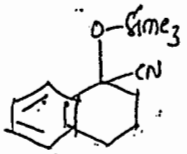
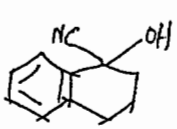
cyano hydrines → (hydrolysis) Hydroxy acids; (LiAlH4) Amino alcohols

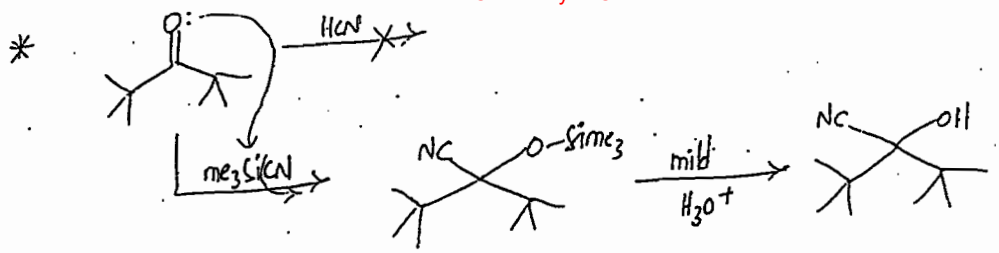
→ $R-\underset{\underset{R}{|}}{\overset{\overset{O}{\|}}{C}}$ $\xrightarrow[CN^{\ominus}]{Me_3SiCN}$ $R-\underset{\underset{R}{|}}{\overset{\overset{O-SiMe_3}{|}}{C}}-CN$ $\xrightarrow{\text{mild hydrolysis}}$ $R-\underset{\underset{R}{|}}{\overset{\overset{OH}{|}}{C}}-CN$

$R-\underset{\underset{R}{|}}{\overset{\overset{OH}{|}}{C}}-CN$ → ($H_3O^{\oplus}$, boil) $R-\underset{\underset{R}{|}}{\overset{\overset{OH}{|}}{C}}-CO_2H$; (LAH) $R-\underset{\underset{R}{|}}{\overset{\overset{OH}{|}}{C}}-CH_2-NH_2$

→  $\xrightarrow{HCN}$ ✗

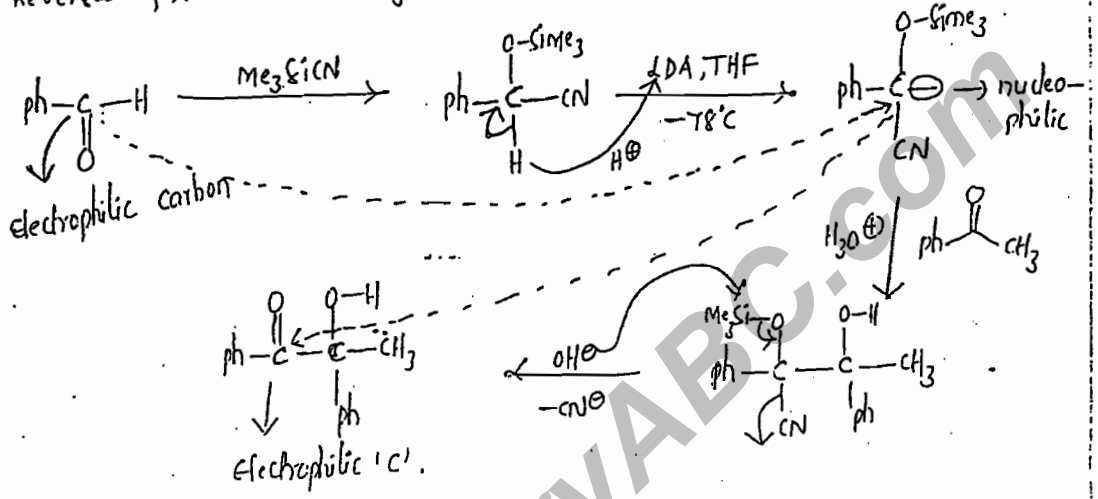
α-tetralone

α-tetralone → (Me_3SiCN)  $\xrightarrow[\text{hydrolysis}]{\text{mild, } H_3O^+}$ 

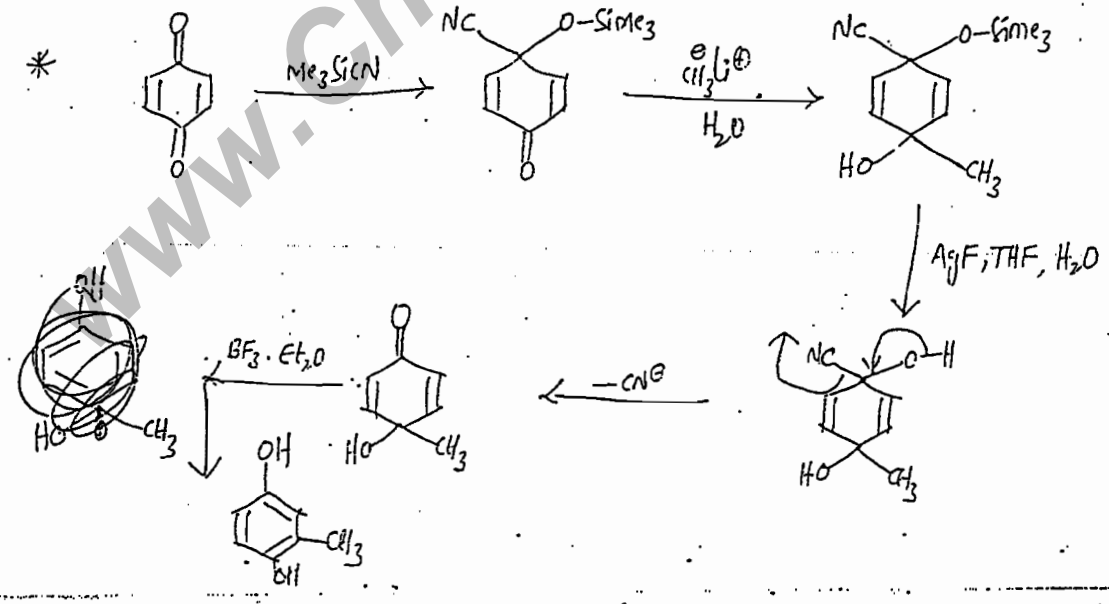


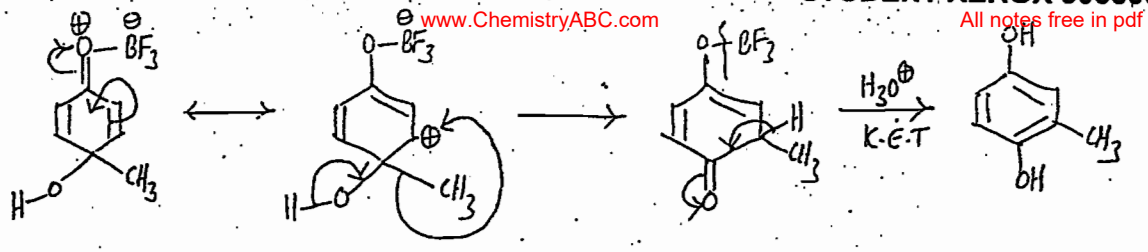
* $C^{\ominus} \longrightarrow C^{\oplus} \longrightarrow C^{\ominus} \longrightarrow C^{\oplus}$

* Reversal of polarity at 'C' atom in synthetic steps called "umpolung" character.



* In the case of conjugated carbonyl compds with HCN, predominent product 1,4-addn product, but Trimethyl silyl cyanide gives 1,2-addn product, not 1,4-addn product (conjugative addn product).

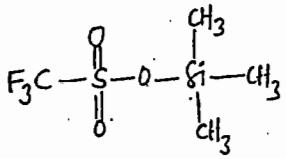




3) Trimethyl Silyl TRIFLATE :-

$F_3C-SO_3^{\ominus}$ — trifluoromethyl Sulphonic acid anion
↳ Triflate.

⇒ $F_3C-SO_3SiMe_3$ (or) $Me_3SiSO_3CF_3$

⇒ 

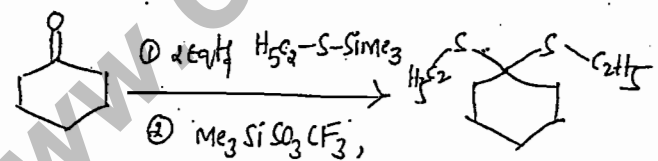
→ powerful silylating agent for acidic groups (carboxylic acidic, phenolic, alcoholic etc).

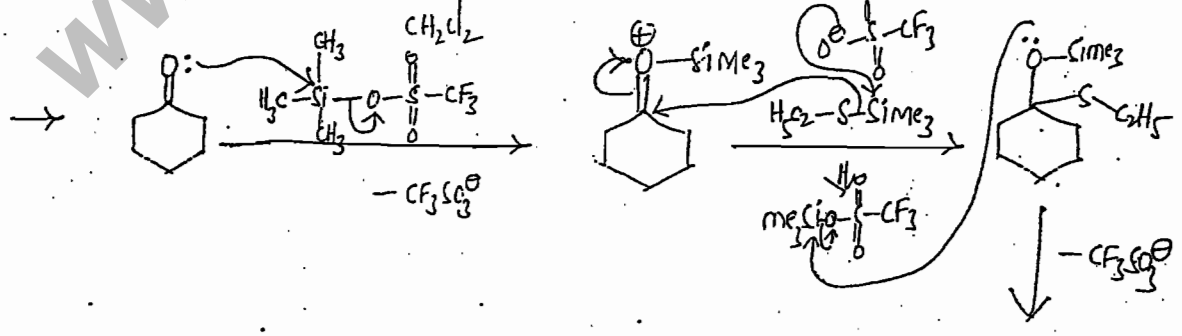
→ Used as catalyst for nucleophilic reacn. (adding or substitutions).

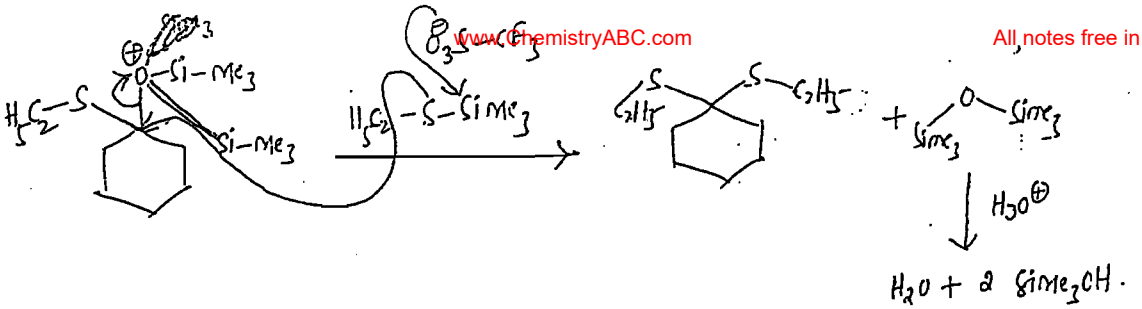
→ If supporting catalysts are lewis acids/cyanide ions used, reacns are fast.

Eg :-

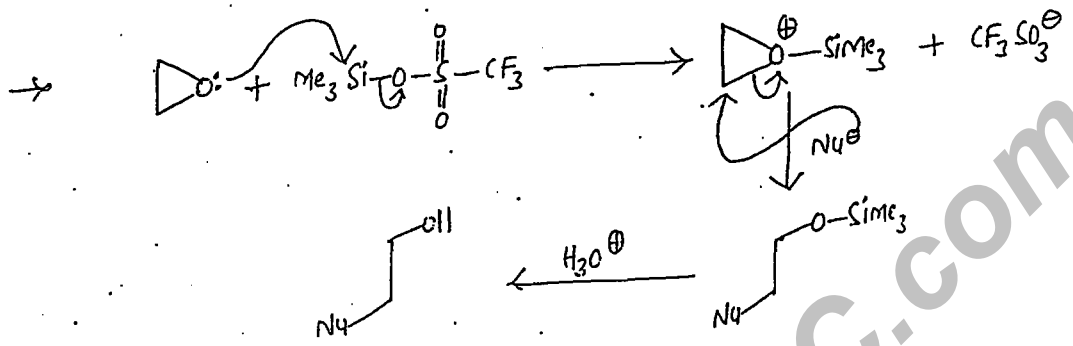
→ 1) Thioketals/ thioketal formation :-

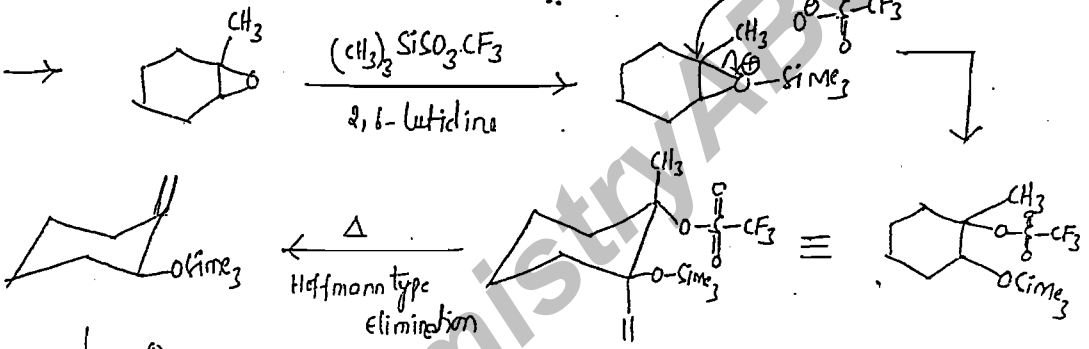


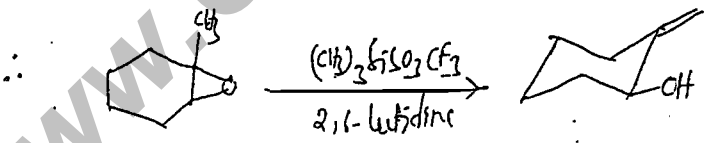




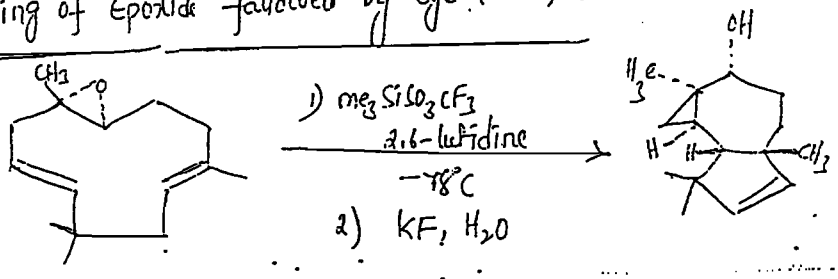
2) opening of Epoxide :—

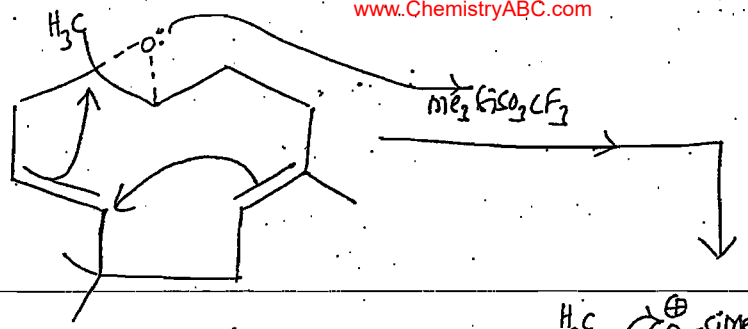


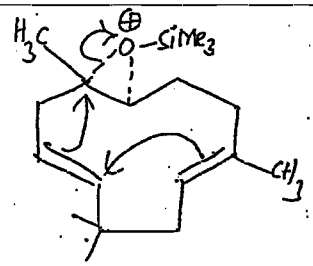


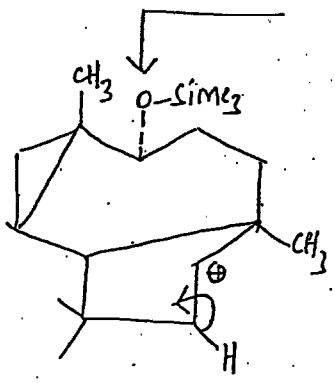


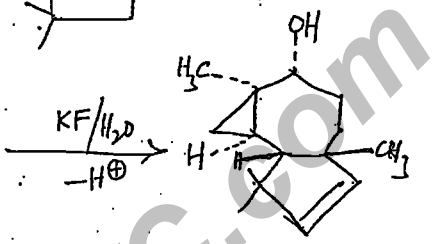
3) opening of Epoxide followed by cyclization :—





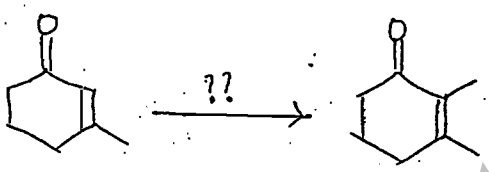






(H)

*
H.W.



* HYDROBORANTIONS :

Reagents : BH_3 (or) B_2H_6 / $R-BH_2$ / R_2BH

alkyl borane

→ $C=C \xrightarrow[(or)\ BH_3]{B_2H_6}$ $C(H)-C(H)(BH_2)$ + $C=C \xrightarrow{II}$ $C(H)-C(H)(BH-C=C)$

dialkyl borane

β alkyl borane

$C(H)-C(H)(B(C=C)-C(H)=C(H))$ trialkyl borane

→ Addn of BH_3 group to alkene or alkyne with BH_3 or B_2H_6 or alkyl boranes called "hydroboration". resulting products are alkyl boranes.

→ olefine $\xrightarrow[BH_3]{B_2H_6\ (or)}$ Alkyl boranes

→ "Degree of "Hydroboration" depends on nature of olefine (subn on olefine) and no. of H's at 'B' in boranes.

→ ① $H_3C-CH=CH_2 \xrightarrow[①]{B_2H_6\ (or)\ BH_3}$ $H_3C-CH_2-CH_2-BH_2$ $\xrightarrow[②]{CH_3-CH=CH_2}$ $(CH_3CH_2CH_2)_2BH$

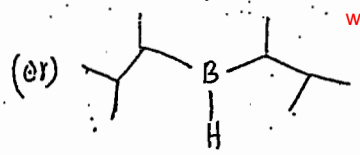
$\xrightarrow[③]{CH_3-CH=CH_2}$ $(CH_3CH_2CH_2)_3B$

② $(CH_3)_2C=CH-CH_3$ $\xrightarrow[①]{BH_3}$ $(CH_3)_2CH-CH(CH_3)-BH_2$ $\xrightarrow[②]{}$ $(CH_3)_2C=CH-CH_3$

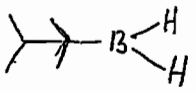
$\not\rightarrow$ $[(CH_3)_2CH-CH(CH_3)]_2BH$

DISIAMYL BORANE

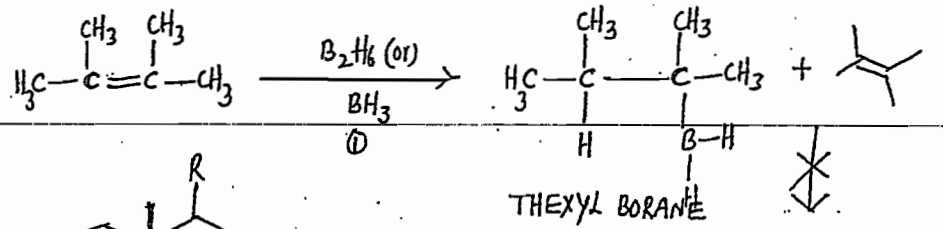
∴ due to steric crowding, rean stopped at second step only

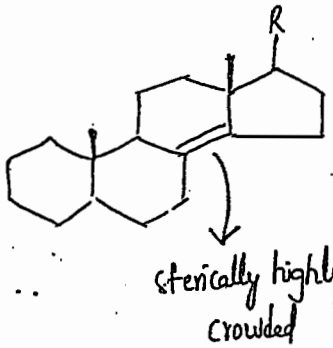


(or)



(or)

→ 3) 

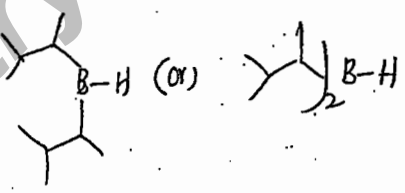
4) 

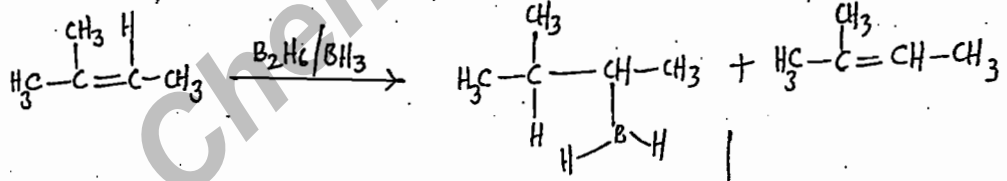
B_2H_6 or BH_3 → no hydroboration

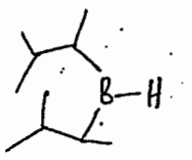
⇒ From top to bottom (① to 4) eqn), crowding at olefine ↑ed, degree of hydroboration ↓ed.

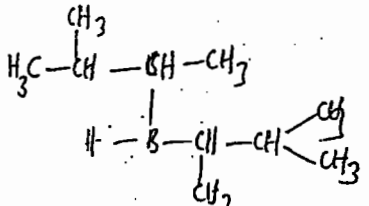
Date : 23/06/08

* Types of Alkyl Boranes :—

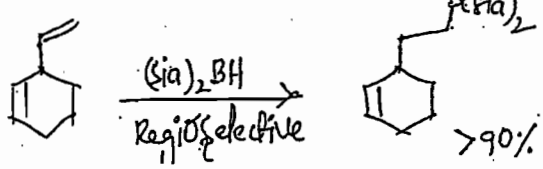
1) DISIAMYL BORANE :— $(Sia)_2BH$ 

→ 

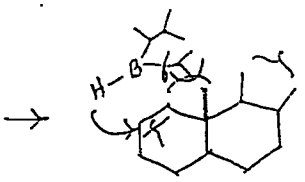


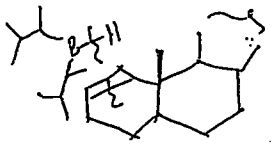
≡ 

→ Disiahyl boranes used for selective hydroboration on olefines.

→ 

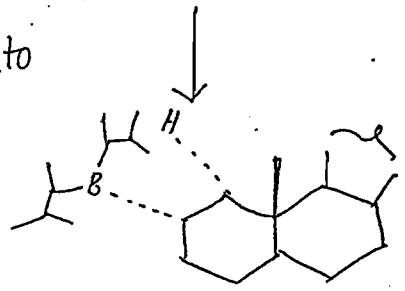
(selectively do hydroborations at less sub. defines)





"sterically crowded approach"
(∵ angular methyl very close to substituted 'B')

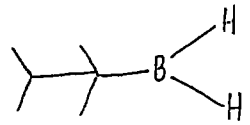
sterically free approach → favoured



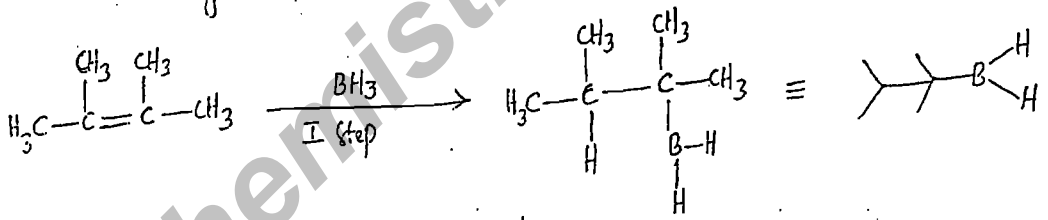
> 90%.

2

*) THEXYL BORANES :-

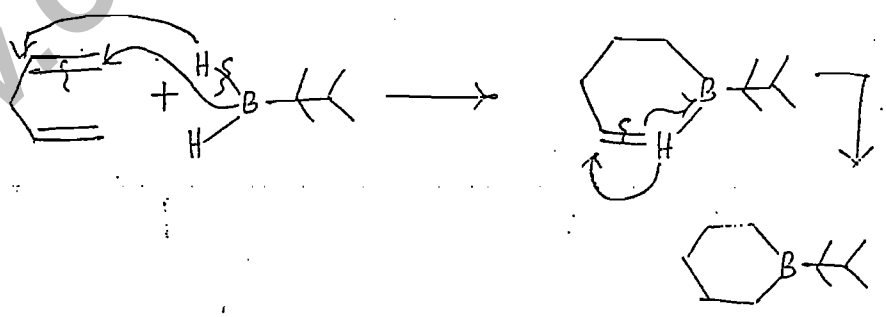


"monoalkylated Borane".

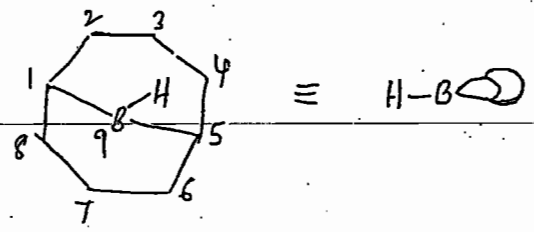


→ used mainly for 'Hydroboration' of dienes.

eg:-



3) 9-BBN : 9-BORA BICYCLO [3 3 1] NONANE :—



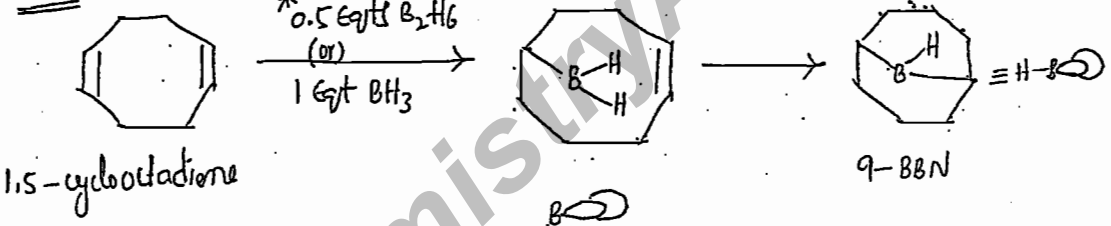
→ dialkylated 'Borane'.

→ Thermally stable, can be used even at high temps for hydroborations.

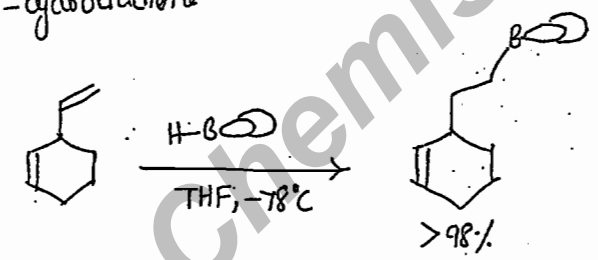
→ Due to steric crowding, its hydroborations are highly selective.

→ If compound having more than one type double bonds, approximately 100% selective hydroborations at less sub. olefinic double bonds.

→ prepn :—



→



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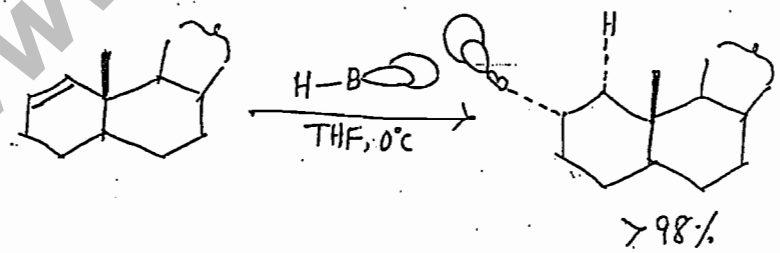


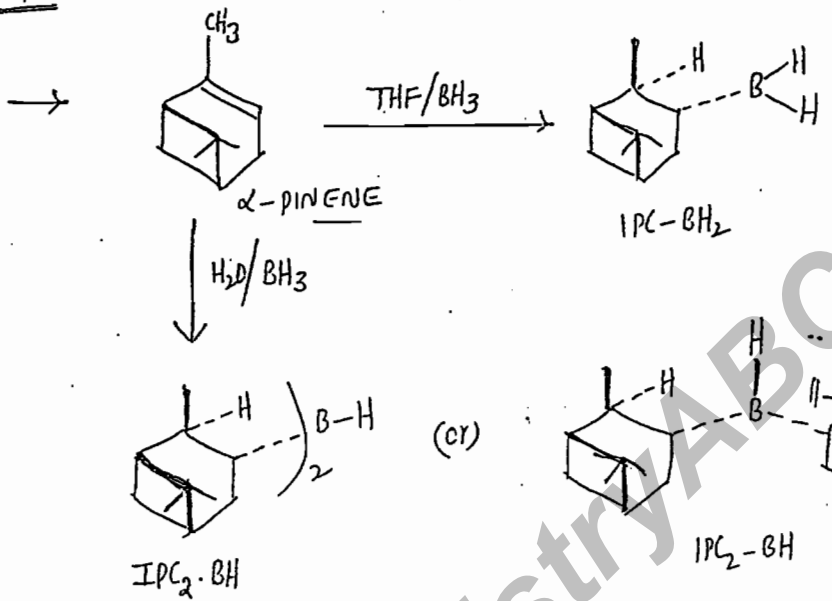
4) CHIRAL BORANES :—

→ $IPC-BH_2$, IPC_2-BH

$IPC-BH_2$:— Isopino campheny/ Borane

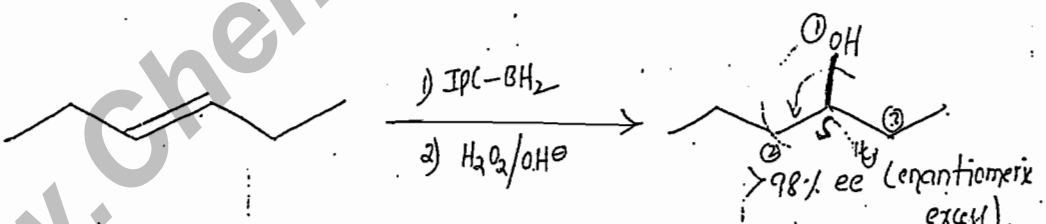
IPC_2-BH ; Di-ISOPINO "

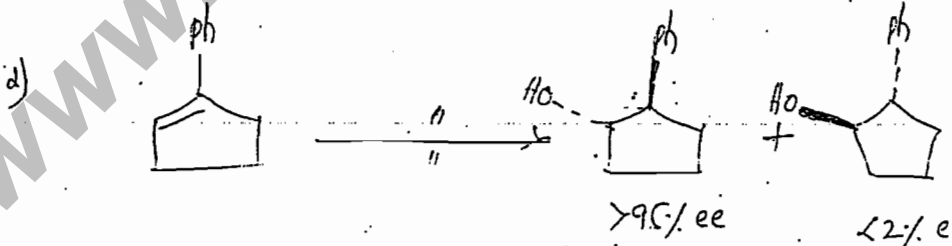
prepn :—

→ 

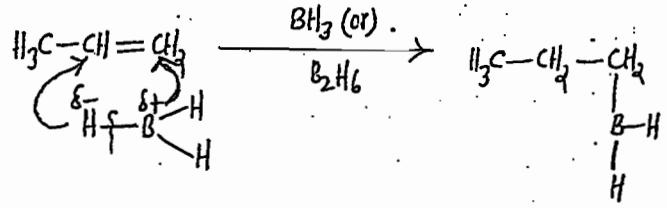
→ These boranes used for stereoselective hydroborations.

Eg :—

1) 

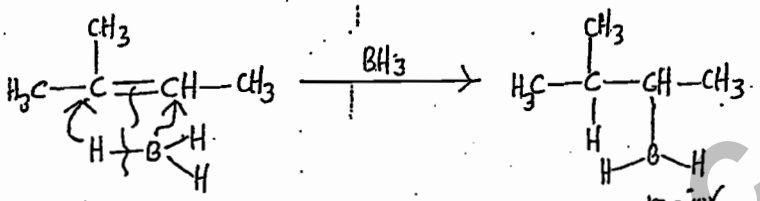
2) 

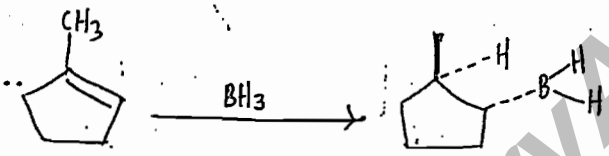
* In the case of unsymmetrical olefines, hydroborations according to markonikov's rule

⇒ 

In unsym. olefins hydroborations, H's should be attached to more alkylated 'C', B to less sub. olefinic carbon.

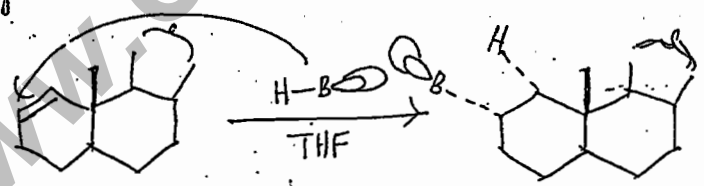
– Regioselectivity.

→ 

→ 

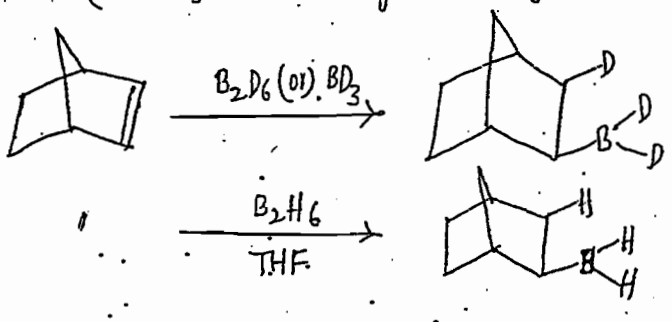
* Stereo selectivity (stereo specificity) :–

→ Near to unsaturatn, if there is a steric crowding, hydroboratn preferentially takes place at sterically less crowded face or side of db.

→ 

(Regio as well as stereoselectivity).

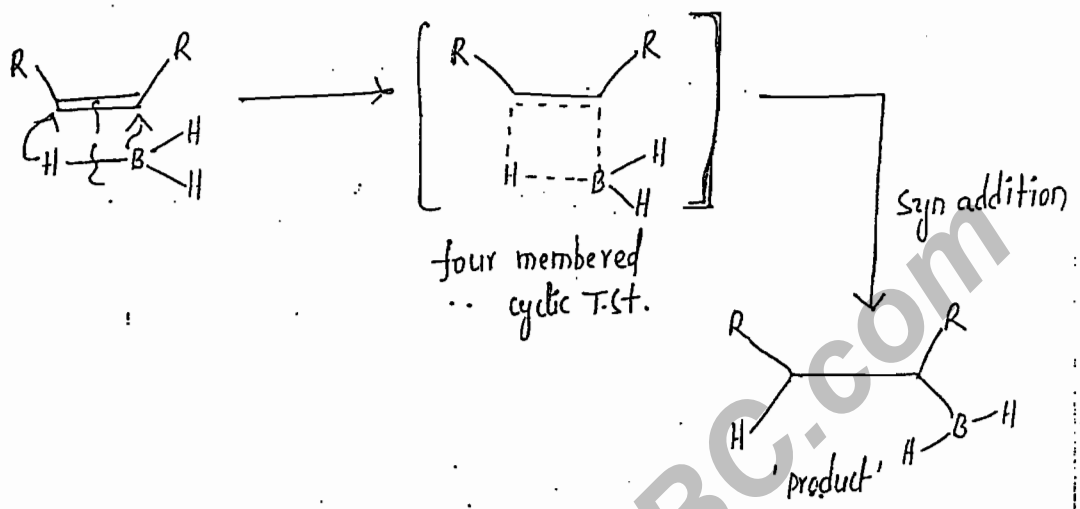
(Back face sterically free, hydroboratn at back face)

→ 

Mech :- Syn - Hydroboration. (addition).

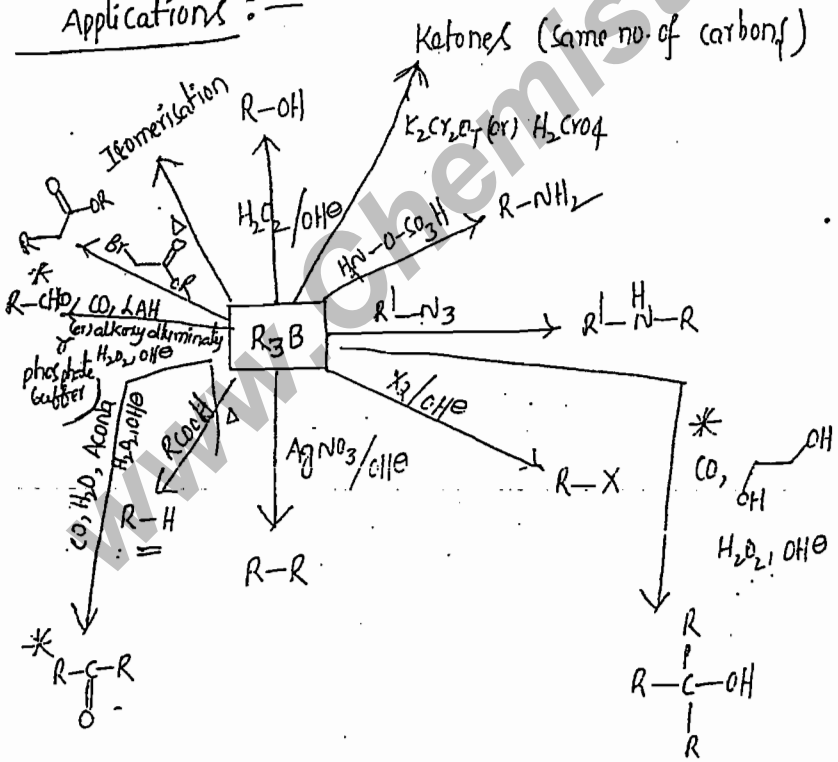
→ Hydroborations are concerted additions.

→ Simultaneous cleavage & formation of bonds.

→ 

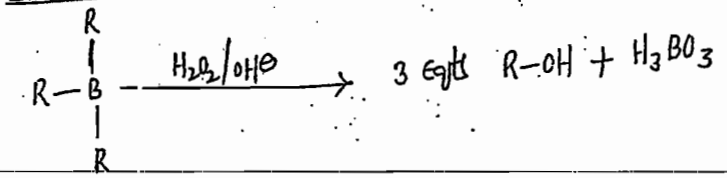
** Alkyl Boranes are versatile intermediate to generate variety of new fng in org. synthesis.

Applications :-



Mech:-

1) $H_2O_2/OH^\ominus$



⇒ $H_2C=CH_2$: 1) B_2H_6 2) $H_2O_2/OH^\ominus$ → H_3C-CH_2-OH

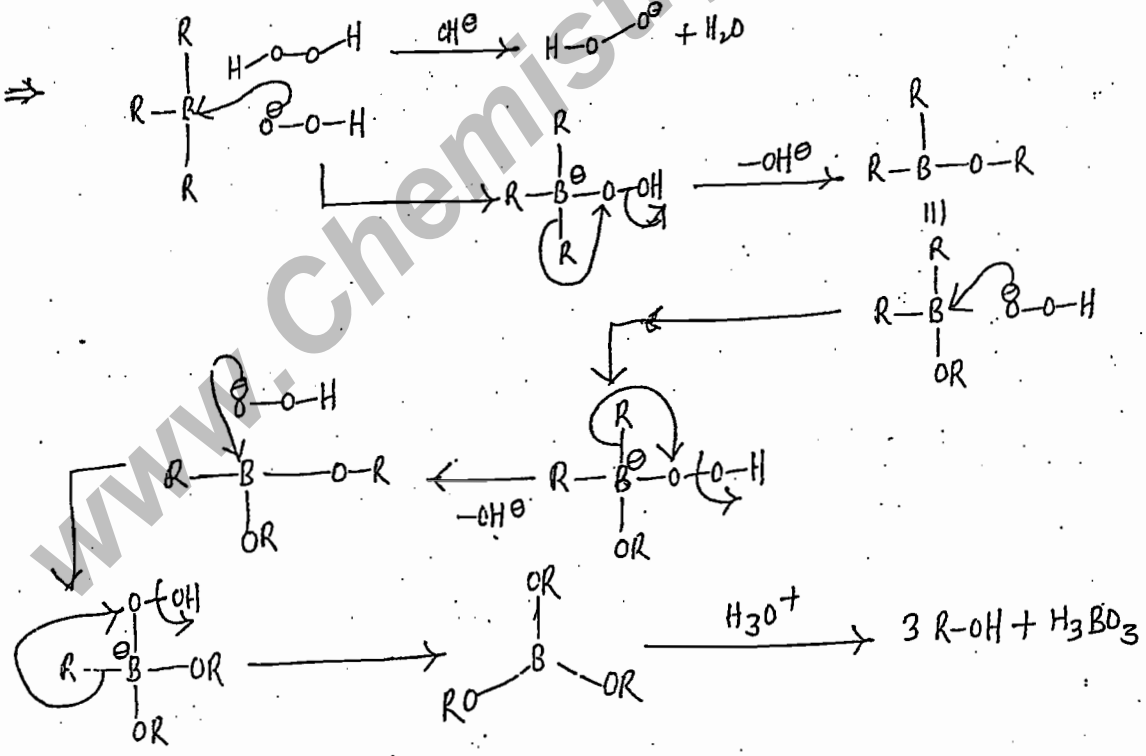
⇒ $H_3C-CH=CH_2$ $\xrightarrow{B_2H_6}$ $H_3C-CH_2-CH_2-BH_2$ $\xrightarrow{H_2O_2/OH^\ominus}$

anti markonikov's product → $H_3C-CH_2-CH_2-OH$

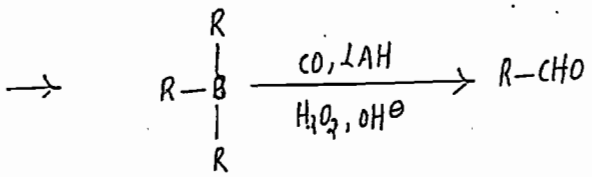
⇒ $H_3C-CH=CH_2$ $\xrightarrow[H_2SO_4]{H_2O/Hg^{+2}}$ $CH_3-CH(OH)-CH_3$

Markonikov's addn

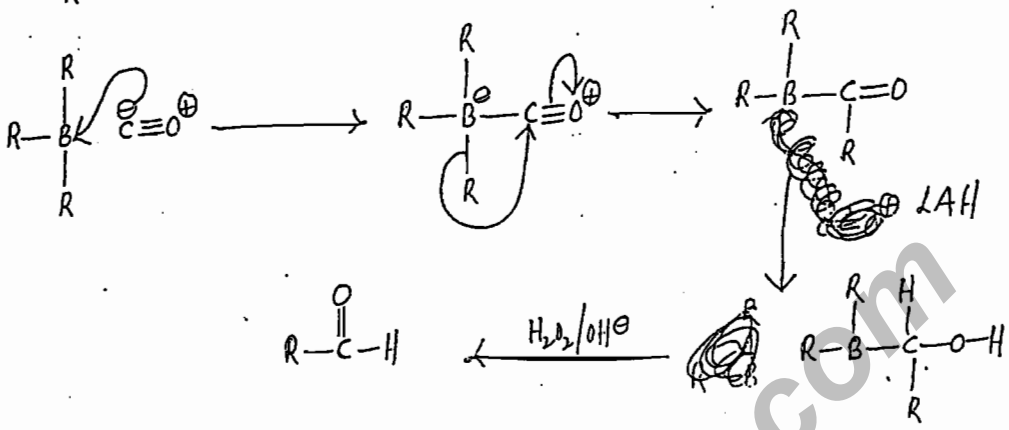
⇒



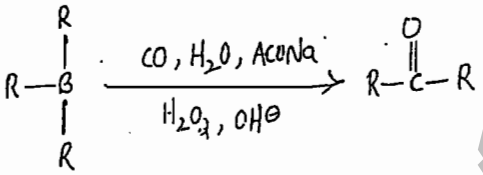
* 2) Aldehyde formations :



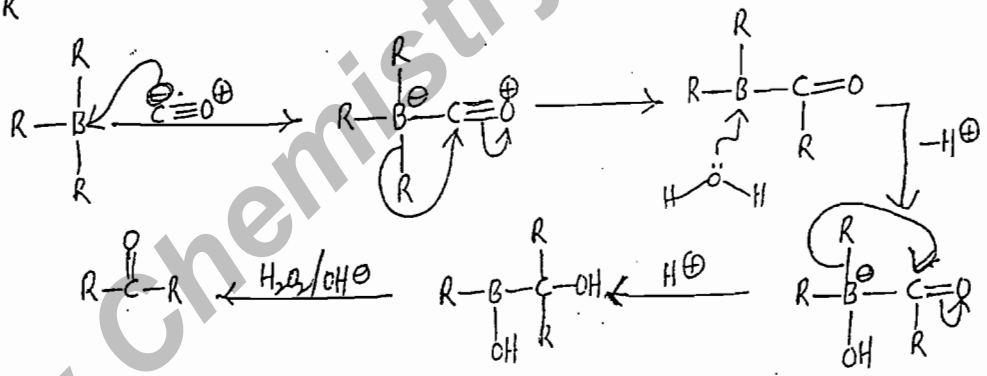
mech :–



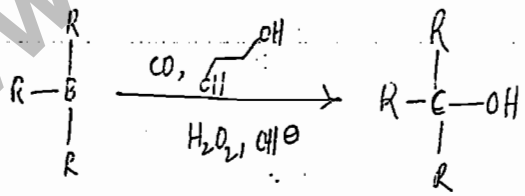
3) Ketone formation :–



Mech :–



→ 4) 3°-alcohol formation :



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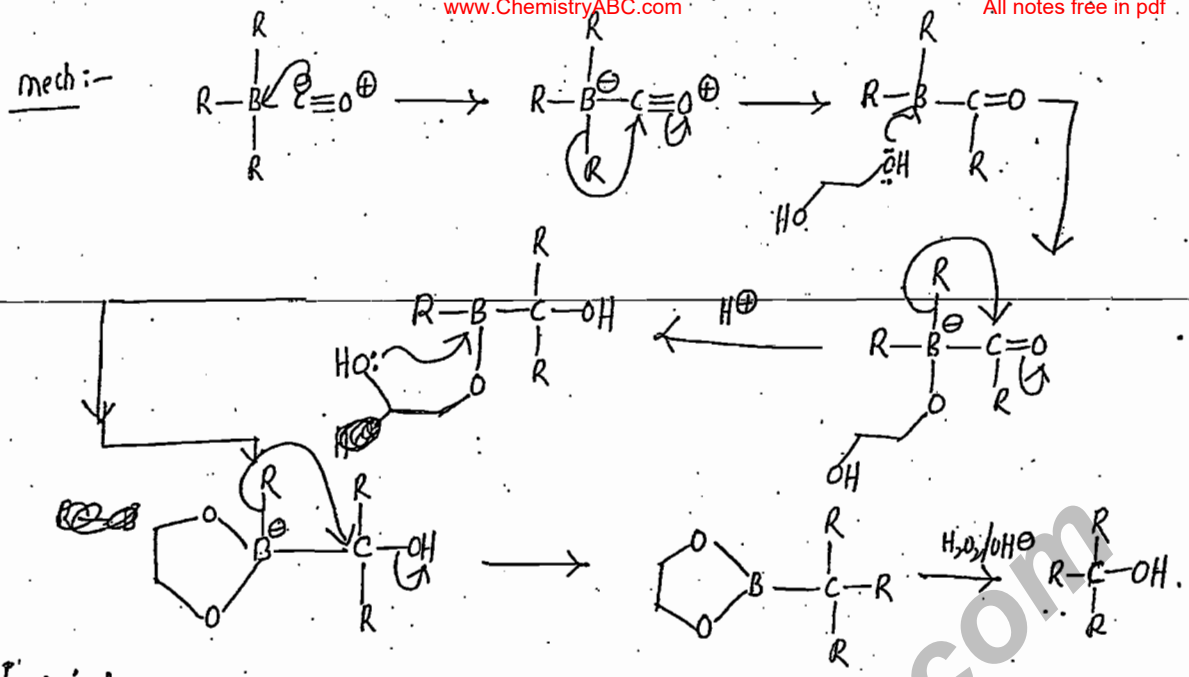
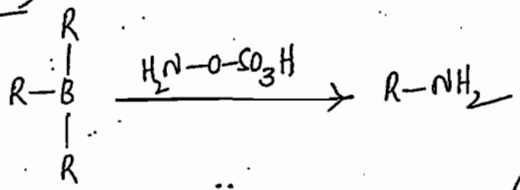
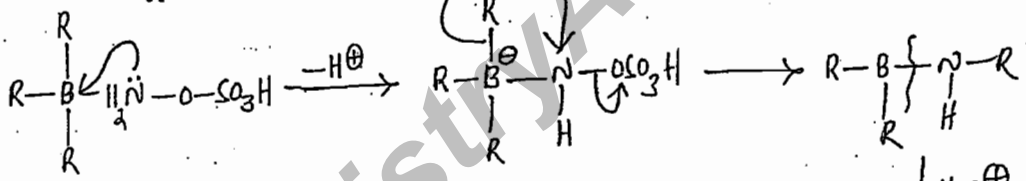
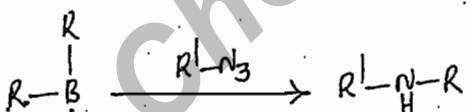


5) 1° Amine

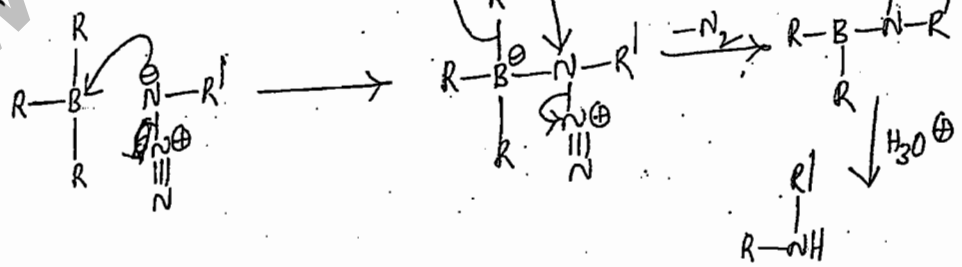




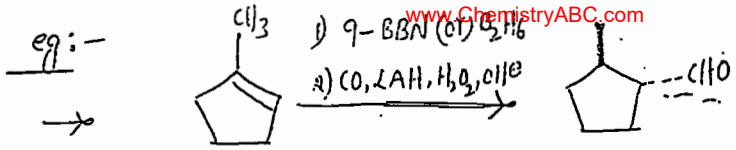
6) Sec-amines:

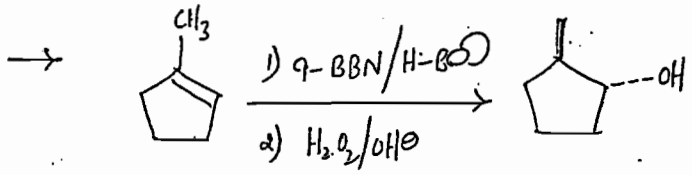


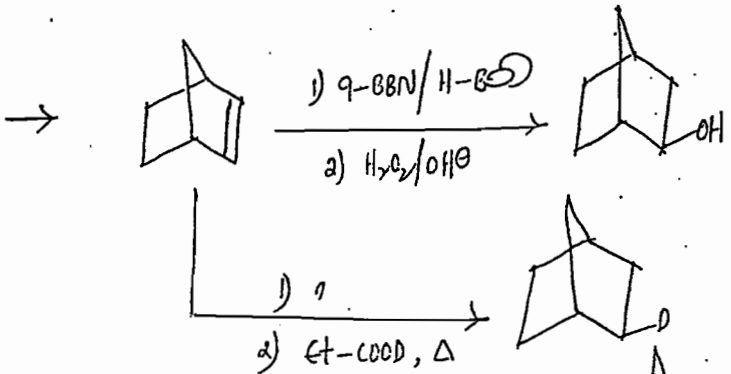
mech:-

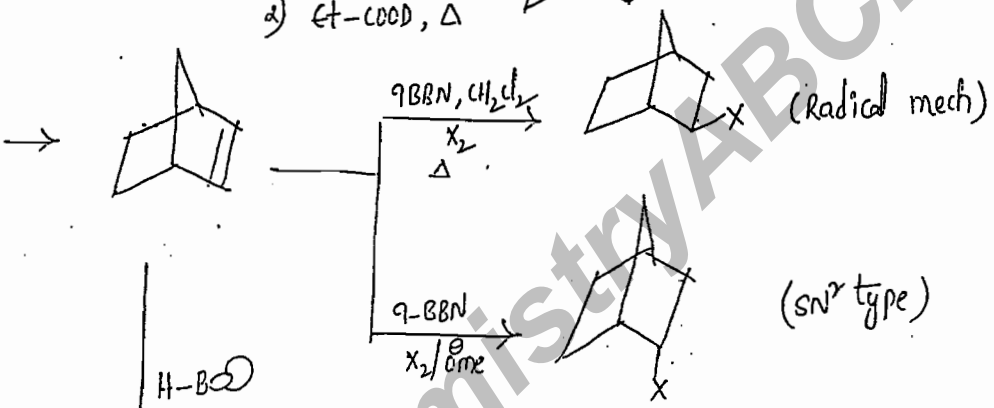


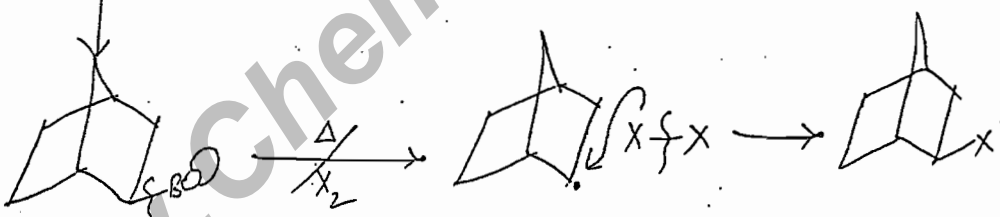
eg:-

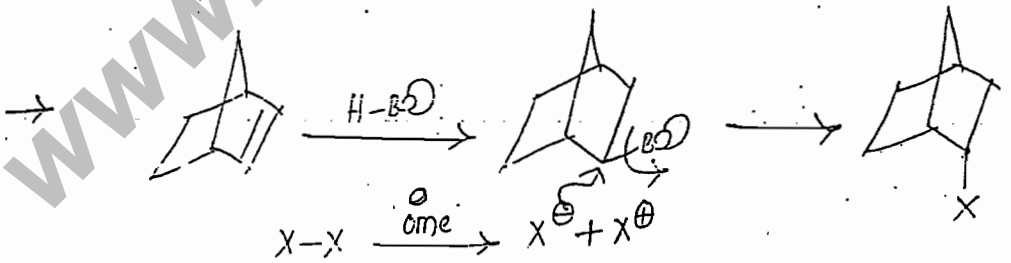


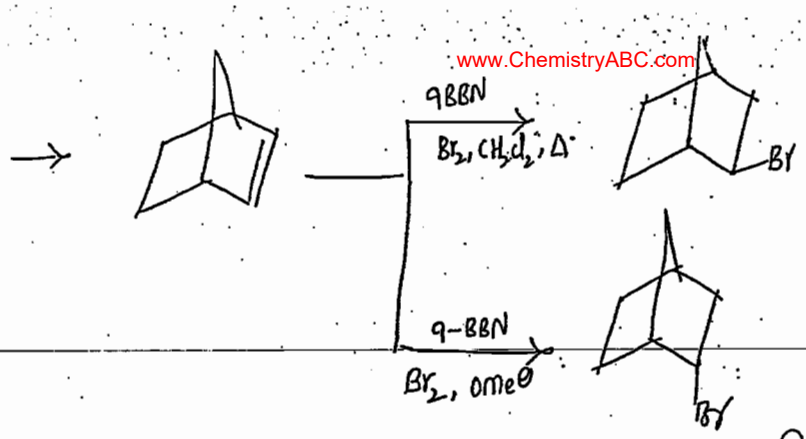


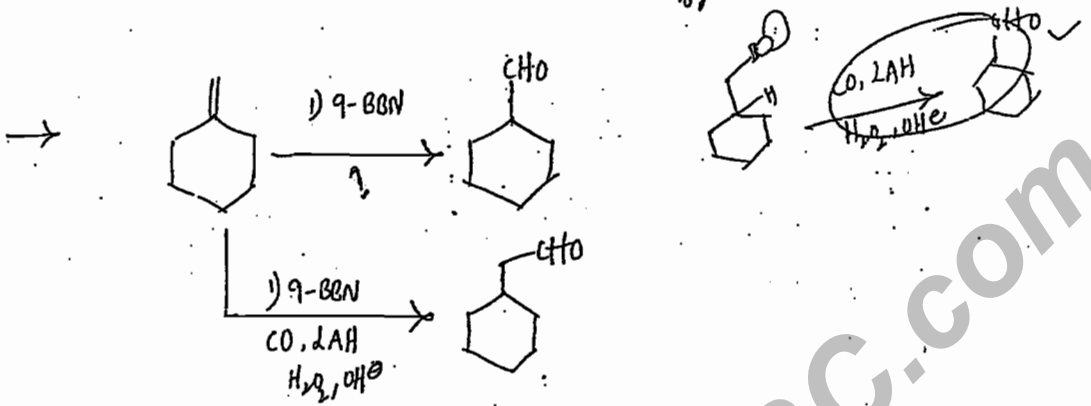


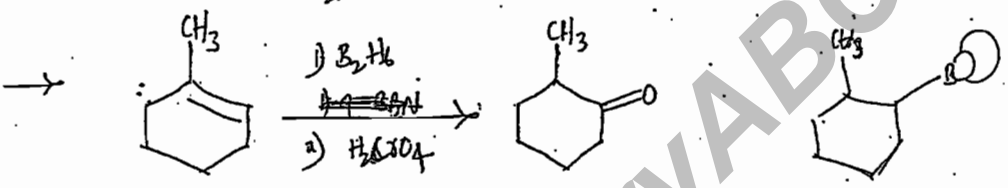






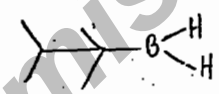


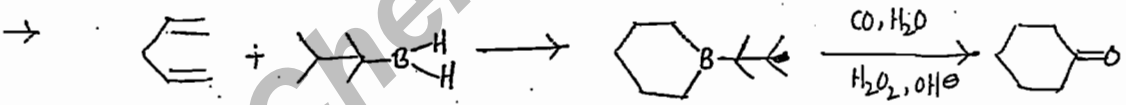


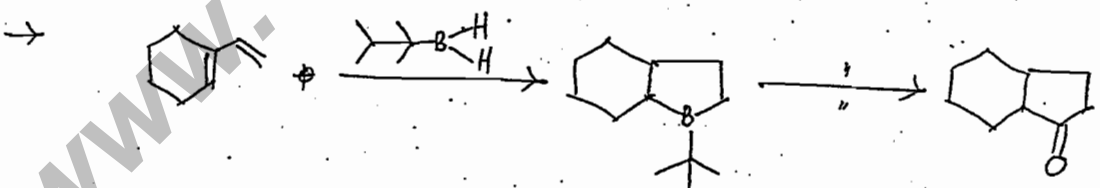


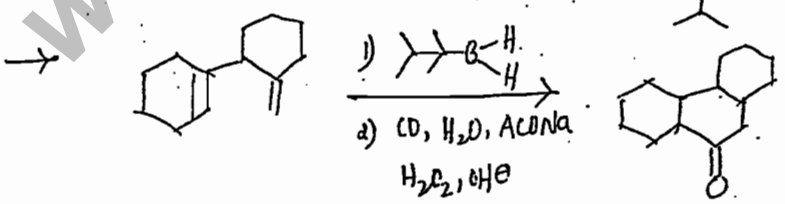
Date : 06/06/08

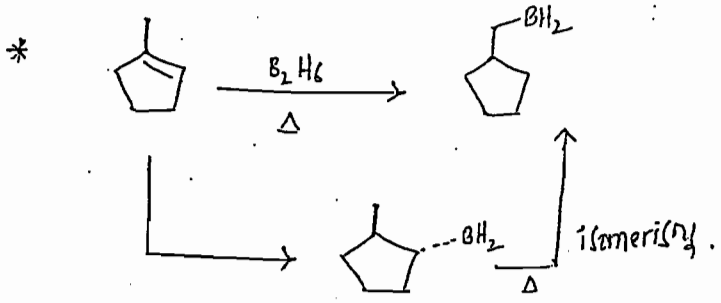
* THEXYL BORANE :—

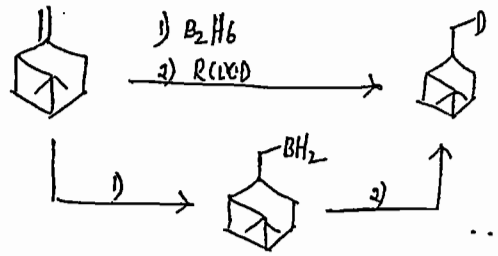


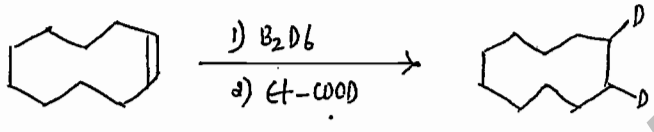


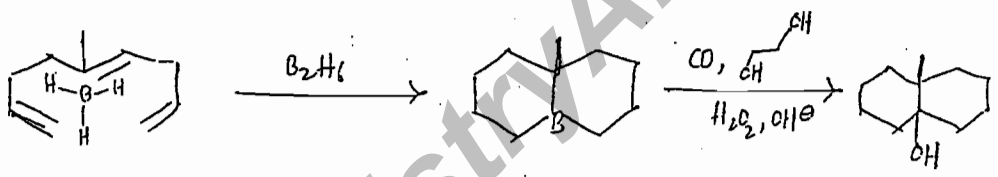


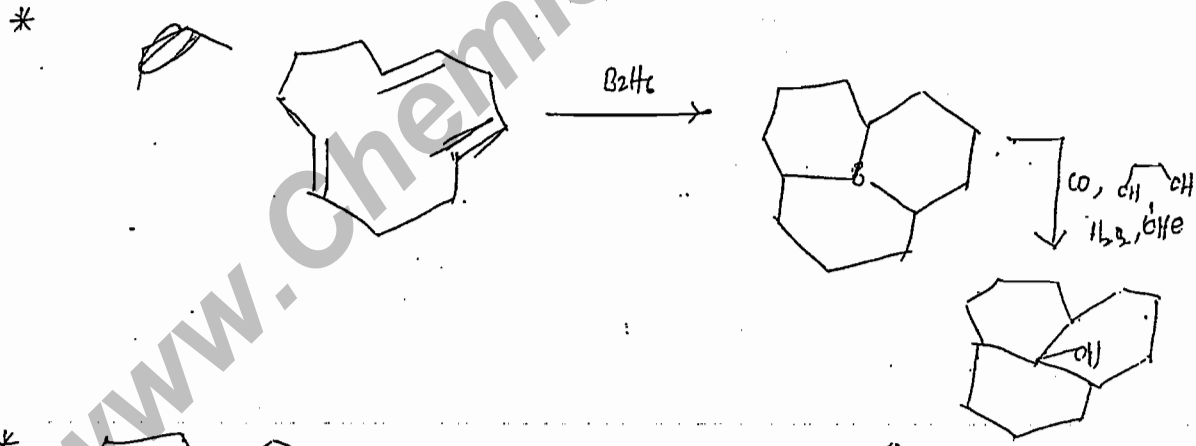


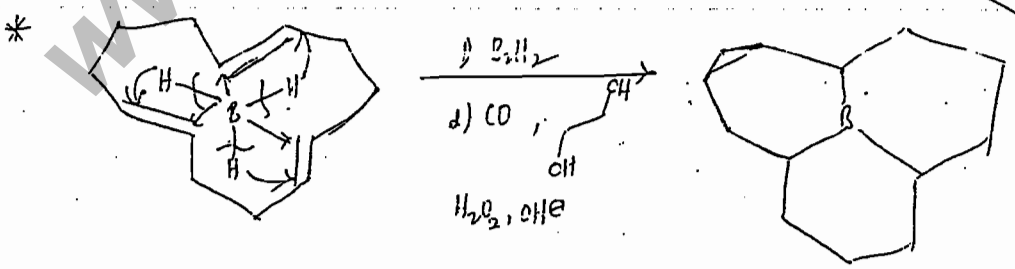




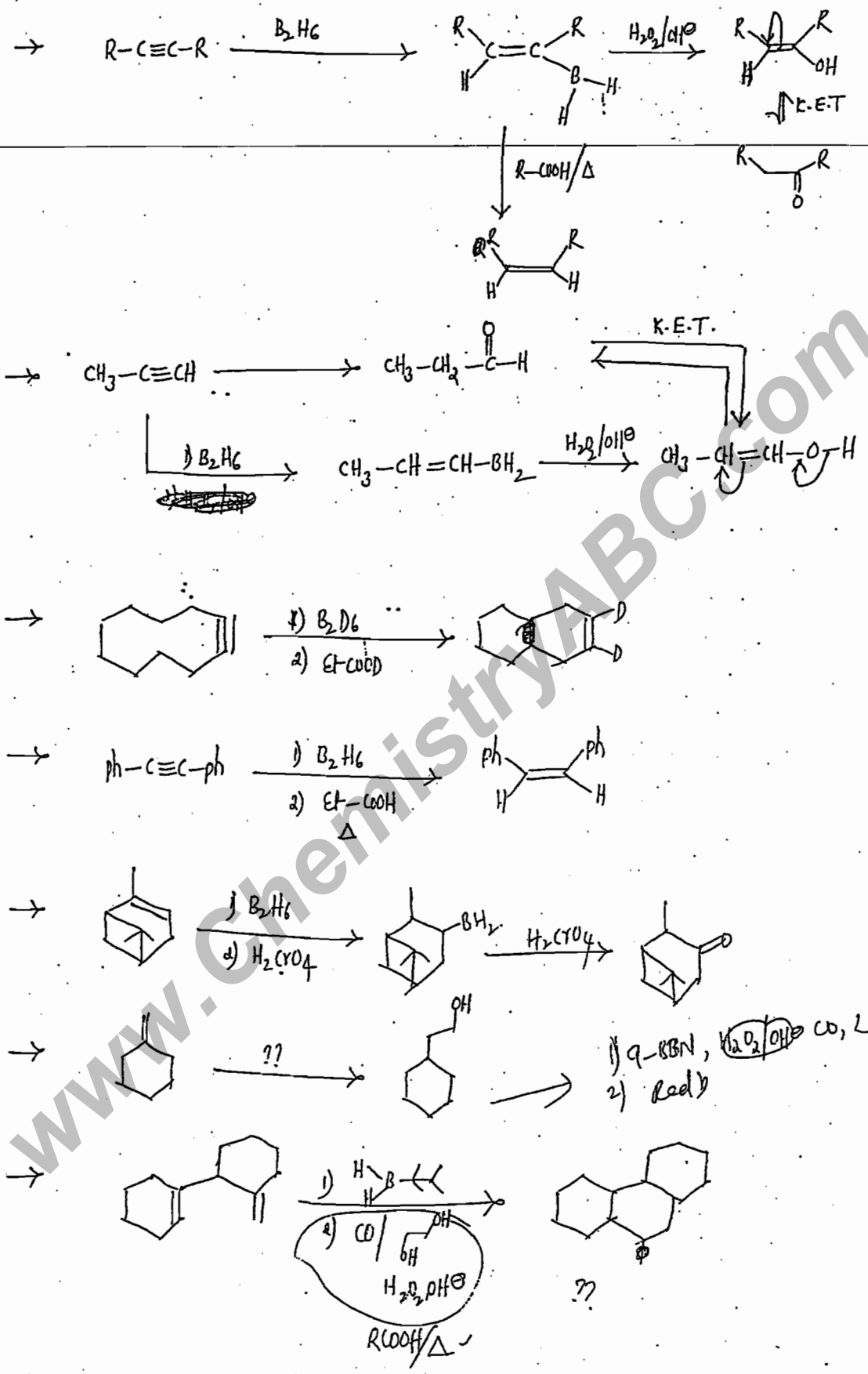








HYDROBORATIONS AT ALKYNES :—

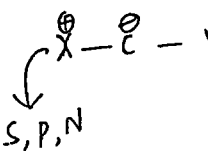


* ORGANO-PHOSPHOROUS REAGENTS :— Wittig-Reans :

→ Conversion of carbonyl compounds into olefins with "phosphorous ylides" or "phosphoranes" called "wittig rean".

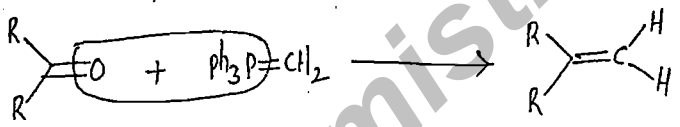
→ C.C. $\xrightarrow[\text{(or) phosphoranes}]{\text{phosphorous ylide}}$ olefines.

→ compound having hetero atom–carbon bonding with opposite charges.



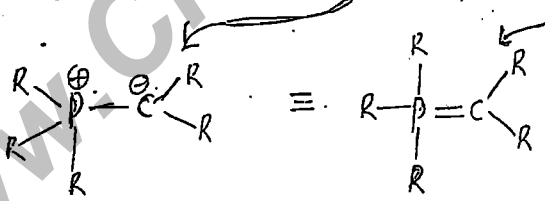
→ Any carbonyl compd can involve in 'wittig rean'. Aromatic, aliphatic – aldehyds, ketones ...

→ C.C's having acidic H also involve in a "wittig rean".

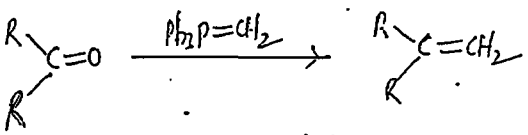
* 

∴ Removal of this by product

YLIDE: wittig Reagent: phosphorous ylide/phosphoranes. / - difficult.

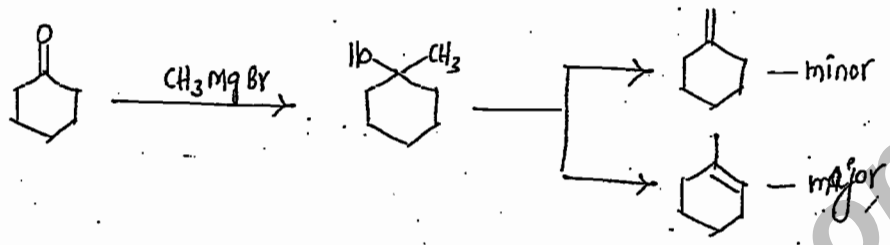
→ 

→ phosphorous Y-lides are source for carbanion, attacks at electrophilic 'C' develop new C–C bonding in Synthesis.

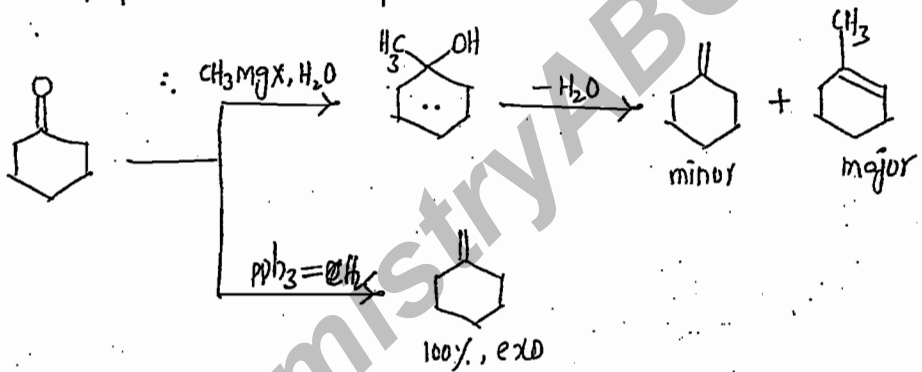
* 

1) In wittig rean, potition of db in olefines certain, always db develops at a carbonyl carbon.

2) wittig rean with high yields easily produces mono, di, tri Substituted olefines, but not tetra sub. olefines.

3) 

'wittig rean' will produce single structural isomer of olefine, it is the only best method to prepare exo-olefines.

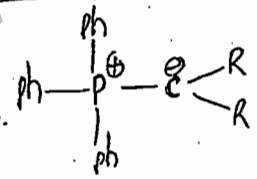


4) Easy to carryout

5) Ambient conditions enough for it.

6) Dry & inert conditions maintained.

Stability of wittig-Reagent :-



→ presence of e⊖ withdrawing groups ↑↑ stability, presence of e⊖ donating gps ↓↓ stability of wittig reagent.

* withdrawing > > Donating

Stability ↑ed.

→ Stable YLIDE > Semi-stable YLIDE > unstable YLIDE

→ slow, fast

→ Stable wittig reagents are less reactive in C-C bonding.

→ presence of donating gp. makes wittig reagent more reactive.

→ 1) $Ph_3\overset{\oplus}{P}-\overset{\ominus}{C}H-COOEt$

2) $Ph_3P^{\oplus}-\overset{\ominus}{C}H-H$

3) $Ph_3P^{\oplus}-\overset{\ominus}{C}(CH_3)-H$

4) $Ph_3P^{\oplus}$ (aromatic)

Stability order : ④ > ① > ② > ③

Reactivity order : ③ > ② > ① > ④

(cyclopenta dienyl anion aromatic, ∴ ④ phosphorous YLIDE is highly stable, almost inert in wittig reacn).

→ No reacn.

* preparation :—

→ wittig reagents prepared from halo compounds.

Halo-compound $\xrightarrow[\text{base}]{Ph_3P}$ phosphorous YLIDE / W.R.

→ $R-CH_2-X \xrightarrow{"} R-\overset{\ominus}{C}H-\overset{\oplus}{P}Ph_3 \equiv R-CH=PPh_3$

(X = Br, I) phosphorane

→ $R-CH_2-X \xrightarrow[SN^2,\ -X^\ominus]{:PPh_3} R-CH_2-\overset{\oplus}{P}Ph_3$ ($X^\ominus$, $H^\oplus$)

phosphonium halide intermediate

↓ base

$R-\overset{\ominus}{C}H-\overset{\oplus}{P}Ph_3$

YLIDE

Base : LDA, $R^\ominus Li^\oplus$, $Li^\oplus\overset{\ominus}{N}(SiMe_3)_2$, $NaNH_2$, NaH, KNH_2, $RO^\ominus$, 3°-amines.

Lithium hexamethyl disilazide

→ In wittig rean to generate phosphorous YLIDE if li bases are used called 'lithium salt wittig reany'.

→ without 'li' called "salt free W.R"

If other bases are used. called "salt free wittig reactions".

→ $R-\underset{R}{C}=O \xrightarrow[PPh_3/\overset{\ominus}{C}H_3\overset{\oplus}{Li}]{R-CH_2-Br} R-\underset{R}{C}=C\begin{matrix}H\\R\end{matrix}$ } Lithium salt W.R.

'olefins'

↓

$R-\overset{\ominus}{C}H-\overset{\oplus}{P}Ph_3$

→ $\xrightarrow[PPh_3/NaNH_2]{R-CH_2-Br}$ $\begin{matrix}R\\R\end{matrix}\!\!>\!C=C\begin{matrix}H\\R\end{matrix}$ } salt-free W.R.

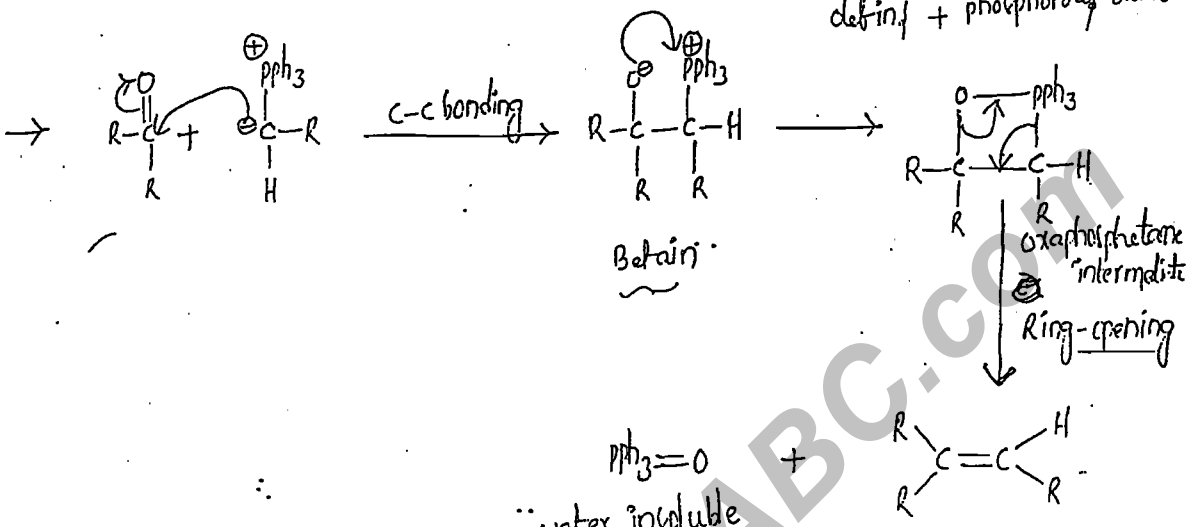
Date : 06/06/08

Mechanism :—

C.C + phosphorous ylide → Betain intermediate —cyclisation→ oxaphosphetane intermediate

↓

defined + phosphorous oxide

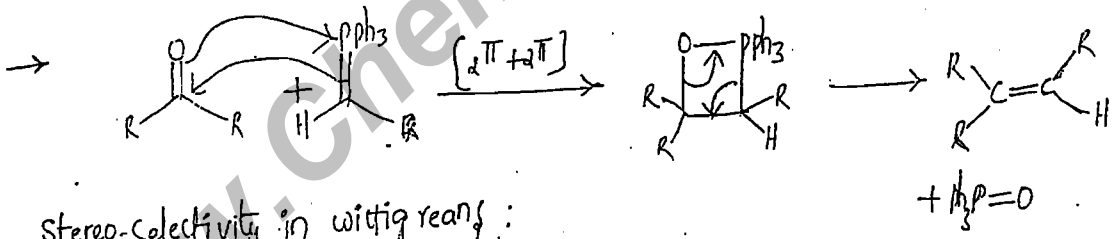


$Ph_3P=O$ + alkene

∵ water insoluble

difficult to remove

→ In few wittig reans, Betain formation not observed, ∴ proposed alternate mech i.e, $_2\pi + _2\pi$ cyclo addition b/w carbonyl fn & phosphorane.



$+ Ph_3P=O$

Stereo-selectivity in wittig reans :

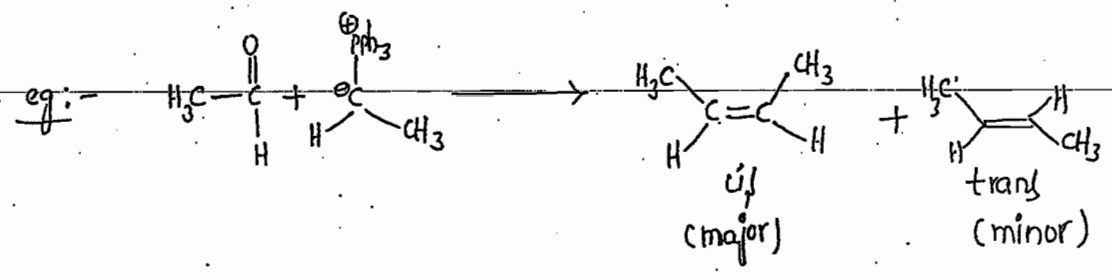
→ Difficult to predict stereoselectivity in wittig reans, but, following - generalised rules, approximately predict stereochem. of resulting olefines. (cis/Z or Trans/E).

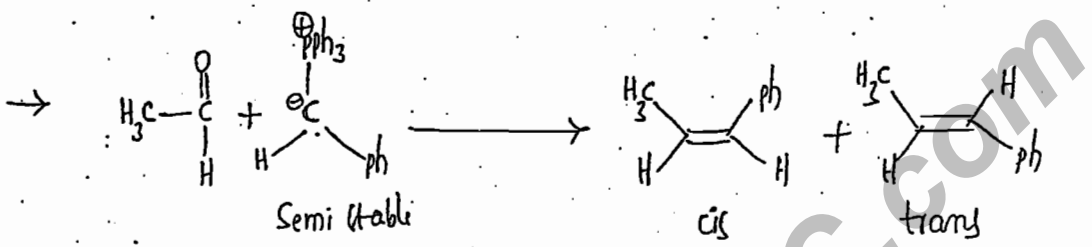
1) In wittig reans, if phosphorous ylide unstable, major cis-olefine or Z-olefine.

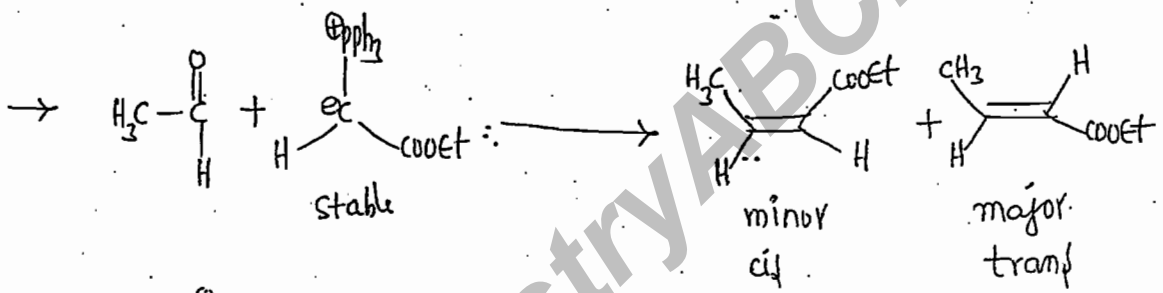
2) If phosphorous Y-LIDE stable, major trans-olefines or E-olefines.

3) If Y-LIDES are semi stable, mixture of cis-trans olefines.

eg:-







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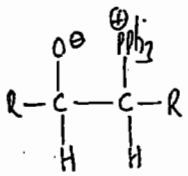
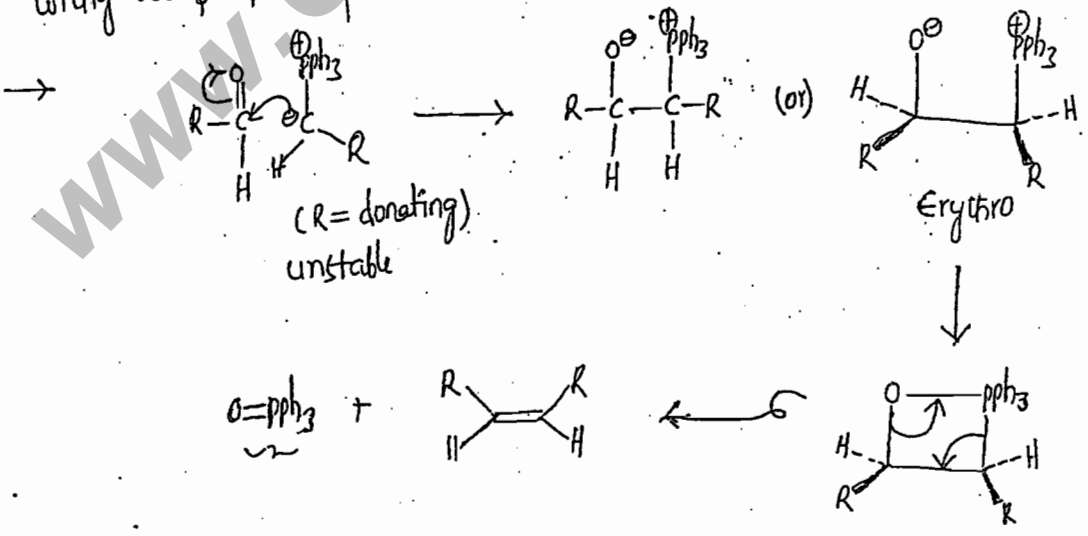
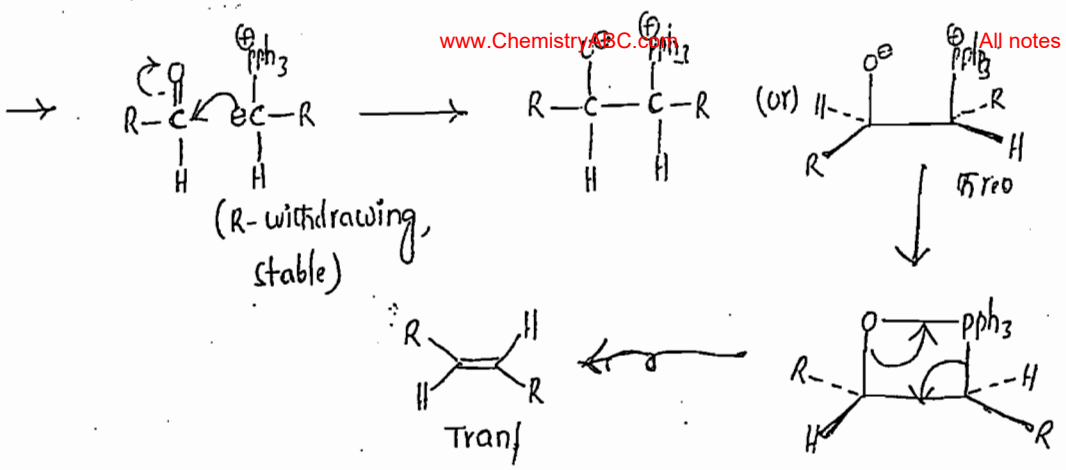
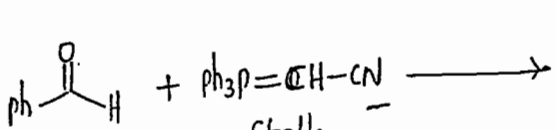


→ unstable Y-LIDES with reaction proceeds via 'erythro Betains'. stable Y-LIDES with reactions proceeds via 'threo Betains'.





→ Salt free 'wittig rean' with unstable YLIDES approximately 100% cis or z-olefines as products.

→  Stable

∴

E (major) ≈100%

→ Limitations :—

1) Byproduct $ph_3P{=}O$ is insoluble in water, difficult to remove from rean mixture.

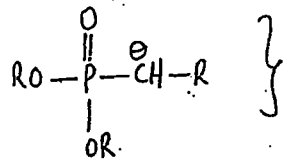
2) Not easy to prepare tetrasubstituted olefines.

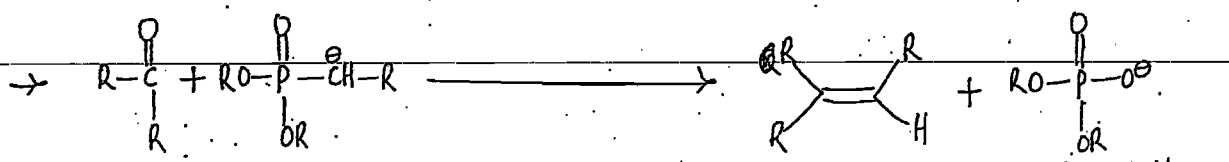
3) Difficult to predict stereo selectivity.

→ To correct some of these defects of wittig reans, wittig reagent is modified, instead of simple phosphorous YLIDES, phosphoric acid diesters, phosphonates taken (modified @ W.R.)

Modified wittig Reaction :— (Horner-wadsworth-Emmon's rean / wittig-Horner Rean).

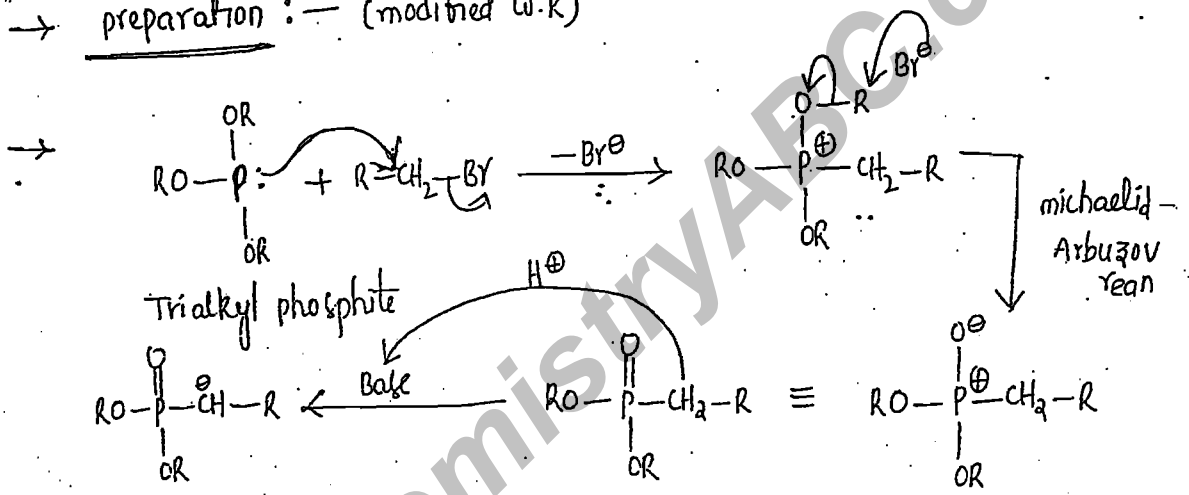
Modified wittig reagent : phosphonates



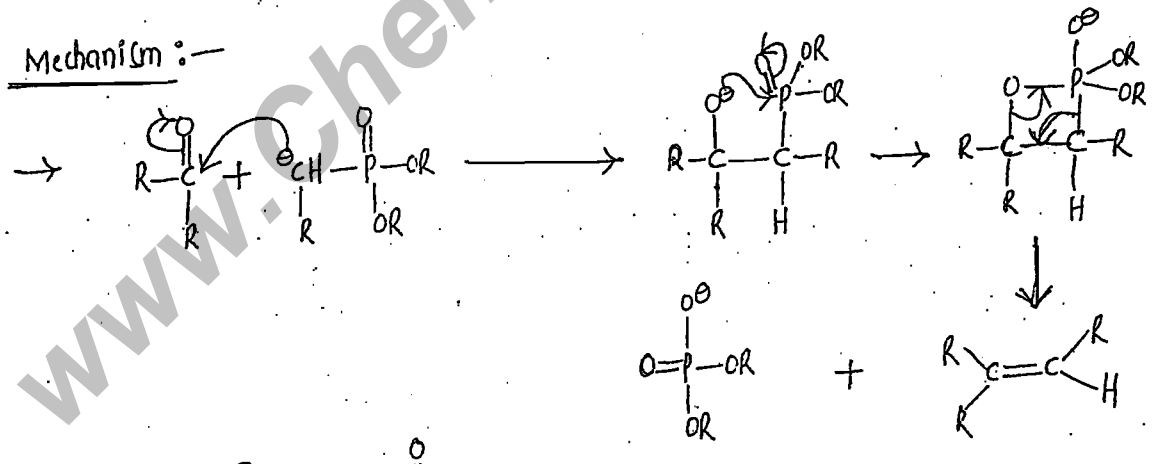


→ Modified W.R. is (E) selective reaction i.e, E (or) Trans olefine is the major olefine.

→ preparation :— (modified W.R)



Mechanism :—



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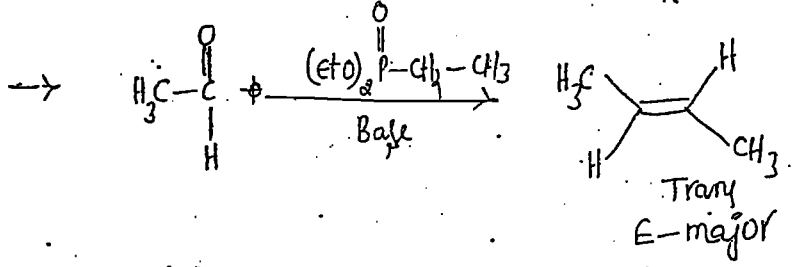
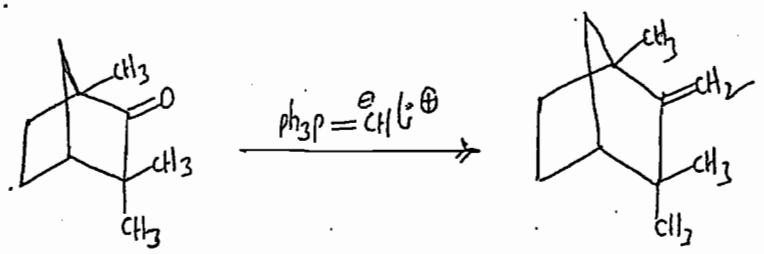


Examples for W.R :-

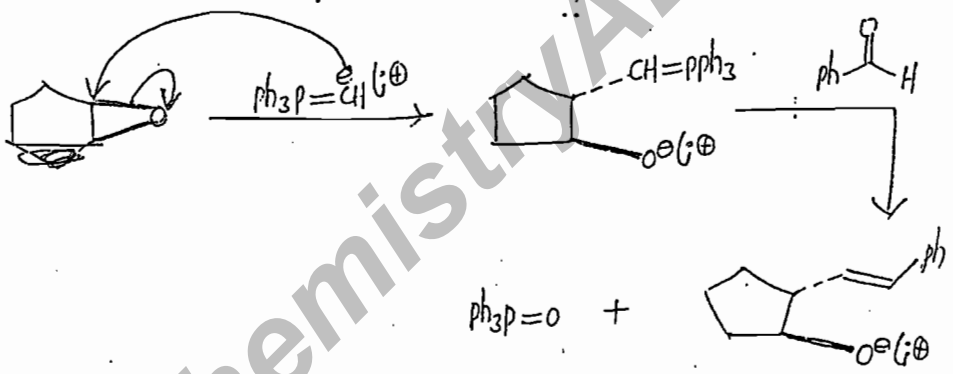
→ Sterically crowded carbonyl frys cannot be attacked by simple W.R.

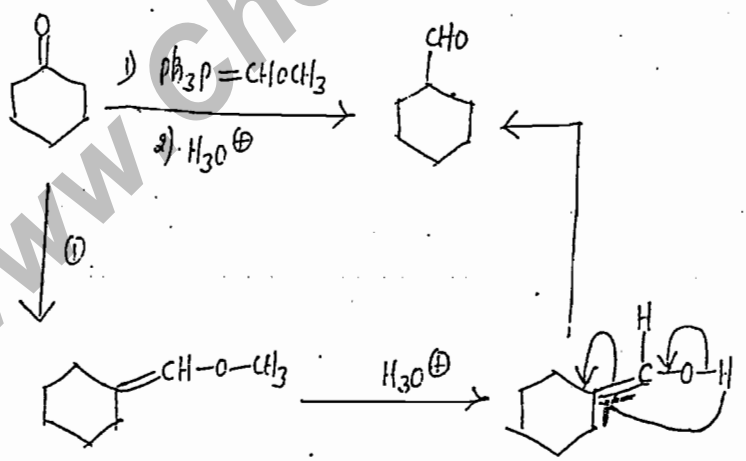
∴ In these carbonyl compds, wittig reary, anion of wittig reagents are used.

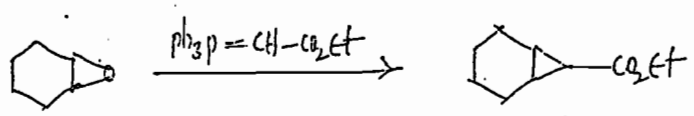
→ 

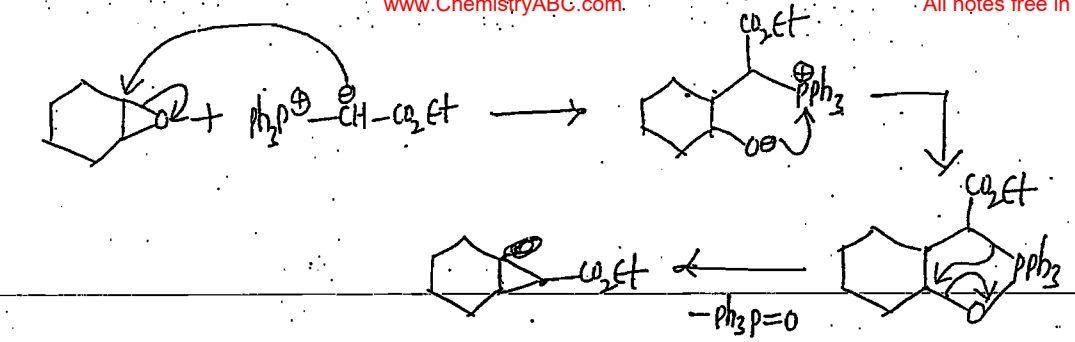
$$Ph_3P=CH_3 \xrightarrow[THF,\ -78^\circ C]{n\text{-}BuLi} Ph_3P=\overset{\ominus}{C}H\,Li^{\oplus}$$

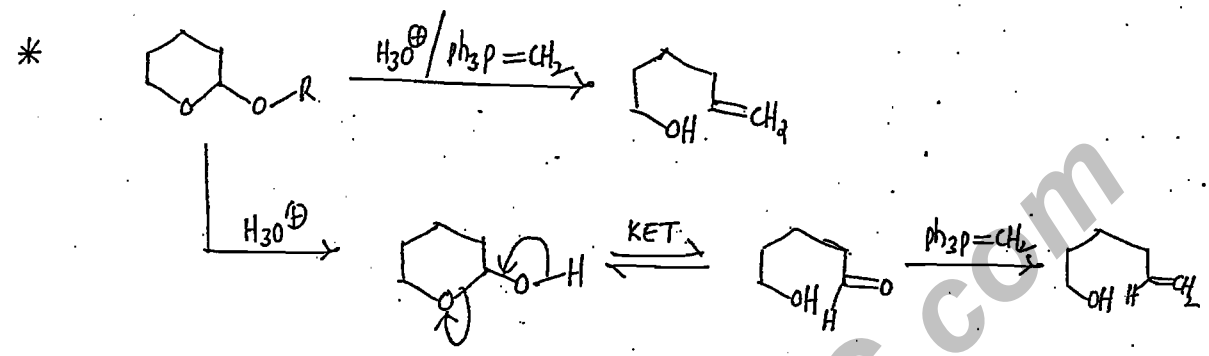
→ Also used for opening of epoxides.

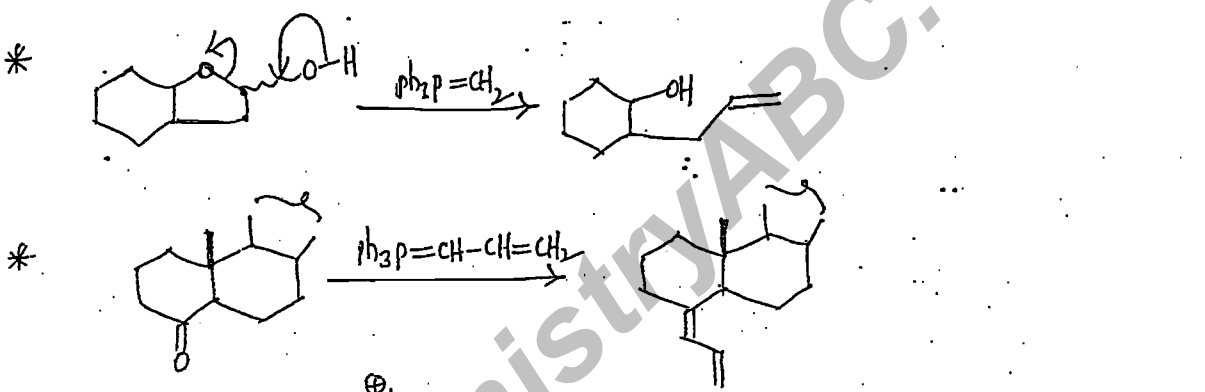
→ 

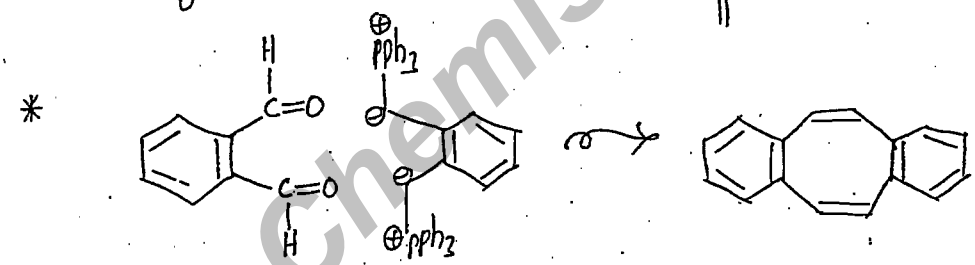
→ 

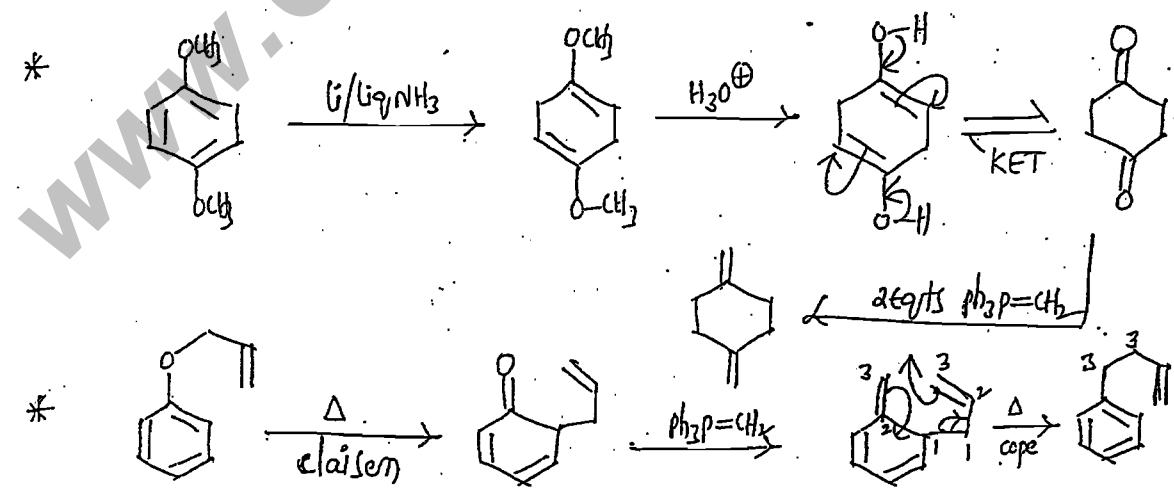
→ 

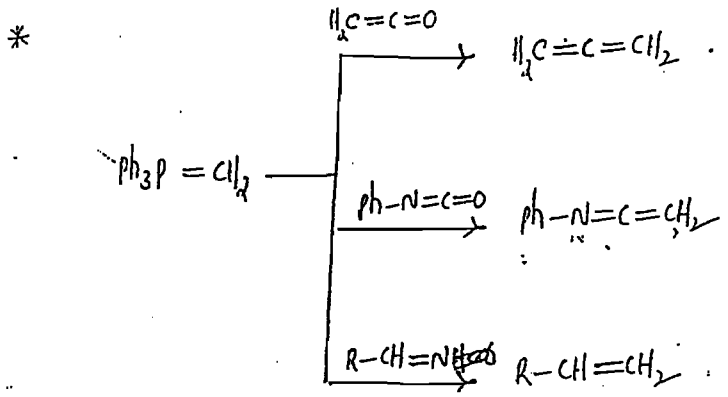


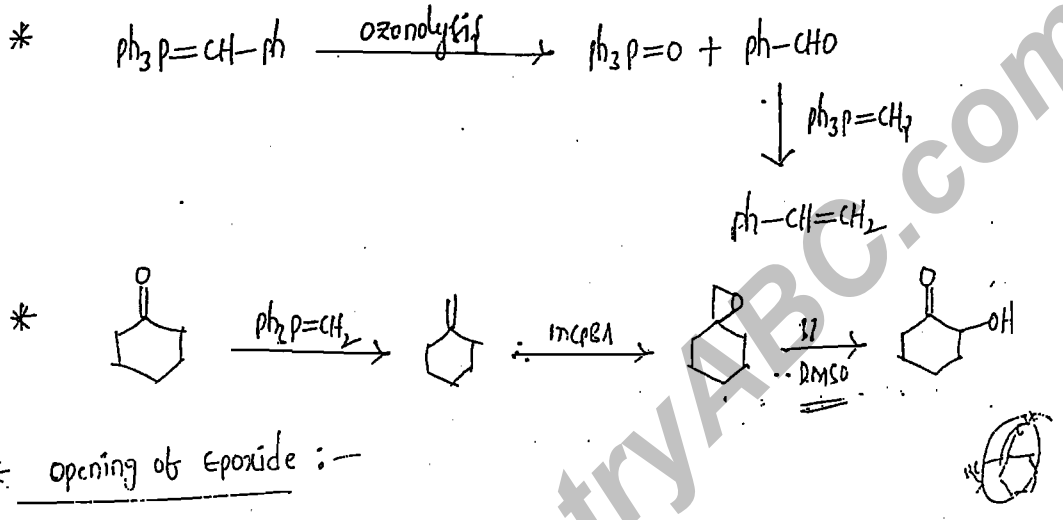


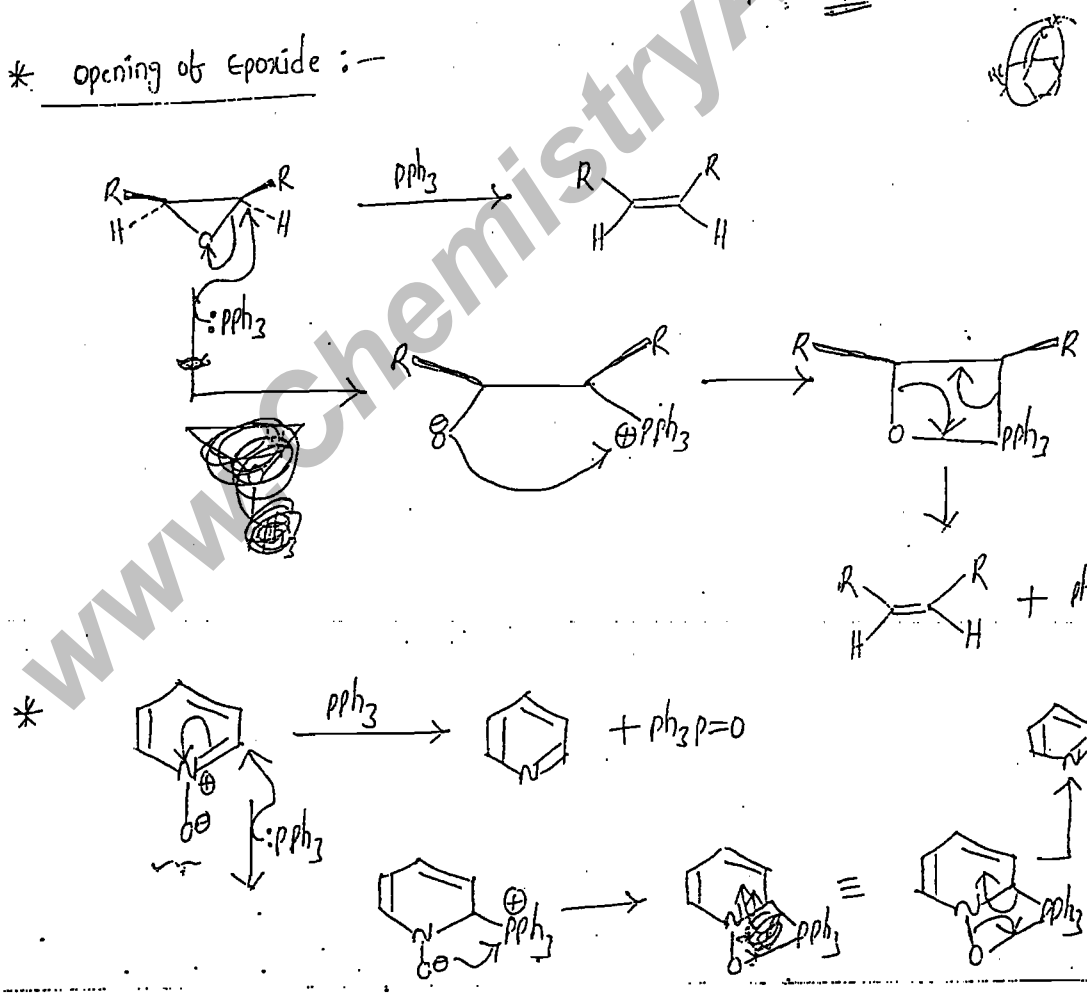


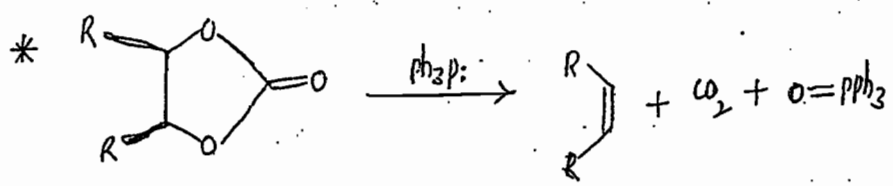




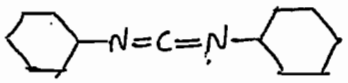


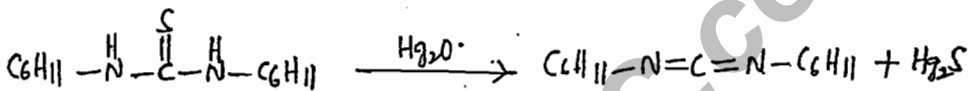






* DCC or DCCD (Dicyclohexyl Carbodi Imide) :—

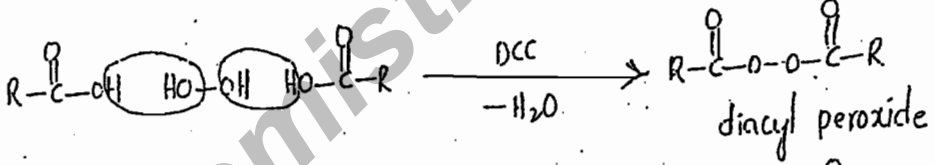
→  (or) $C_6H_{11}-N=C=N-C_6H_{11}$

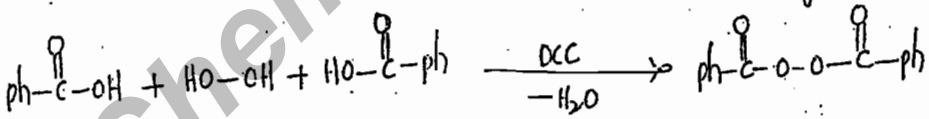
Preph:— 

Applications:

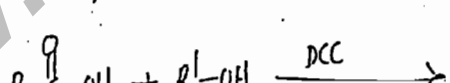
→ Dehydrating agent used for removal of H_2O in Synthetic.

1) Diacyl peroxide :

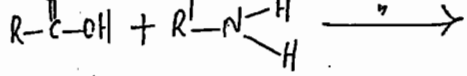


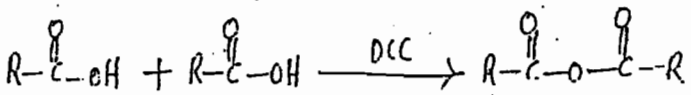


2) Ester-formation

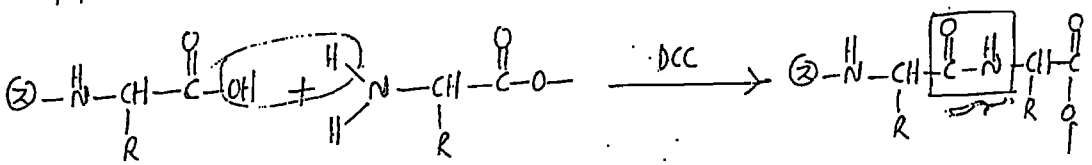


3) Ether — " : $R-OH + R'-OH \xrightarrow{"} R-O-R'$

4) Amide — " : 

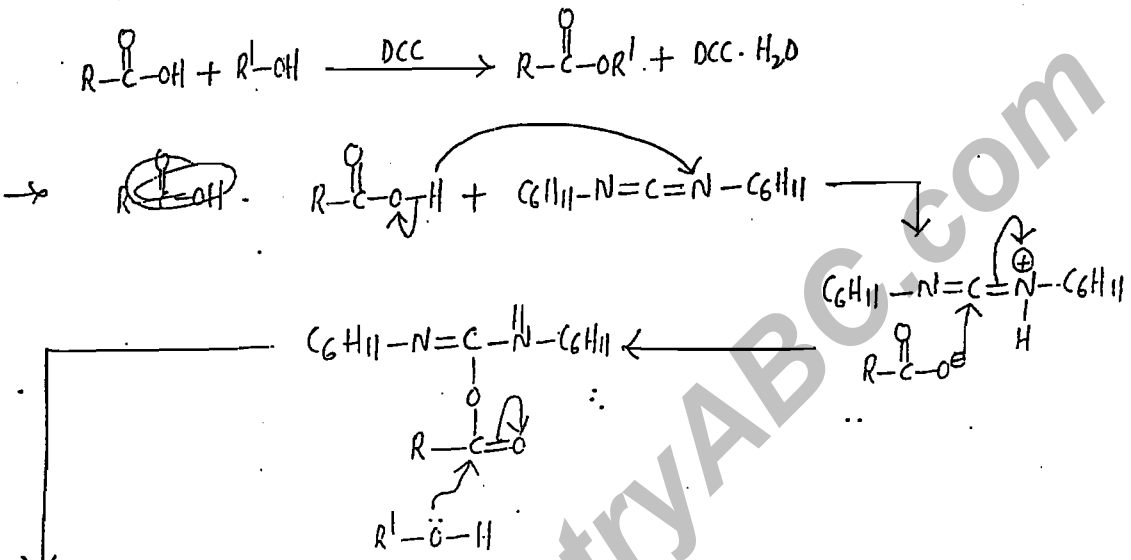
5) Anhydride " : 

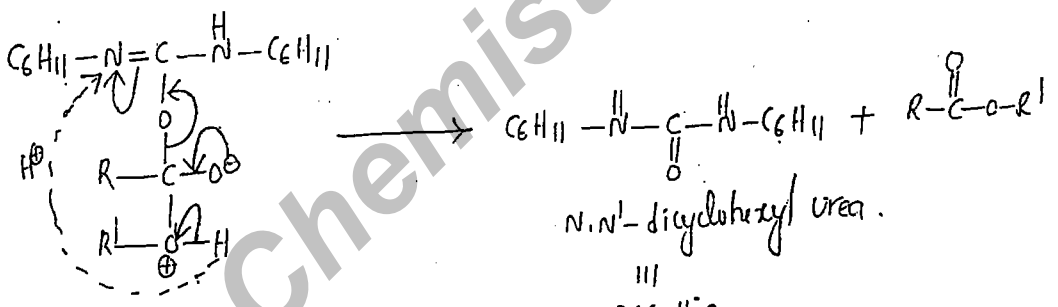
* In peptide formation :

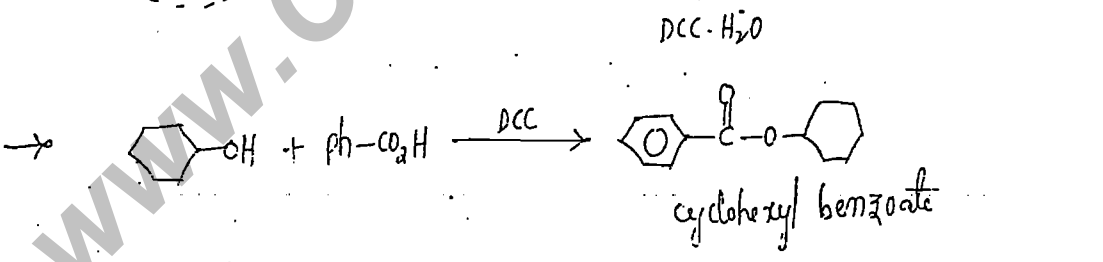


* v. imp :- (CSIR)

*① Mech. for ester formation :

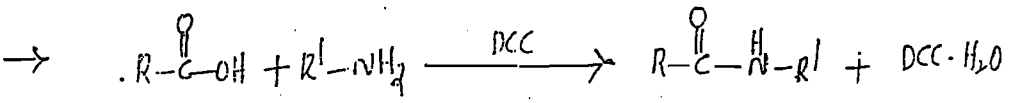


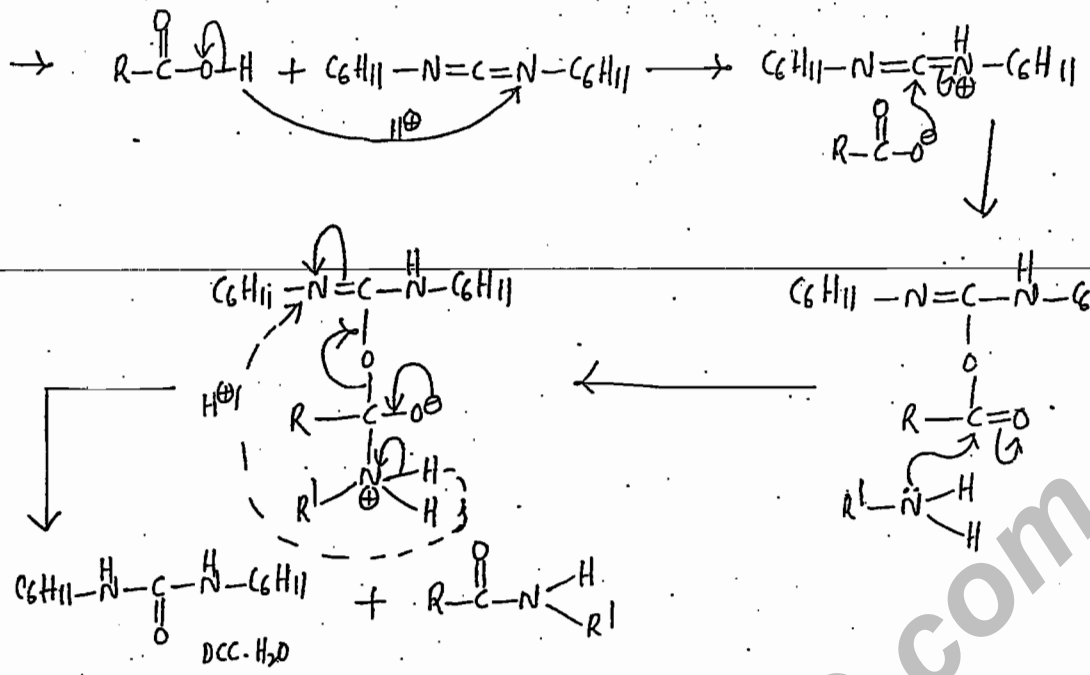




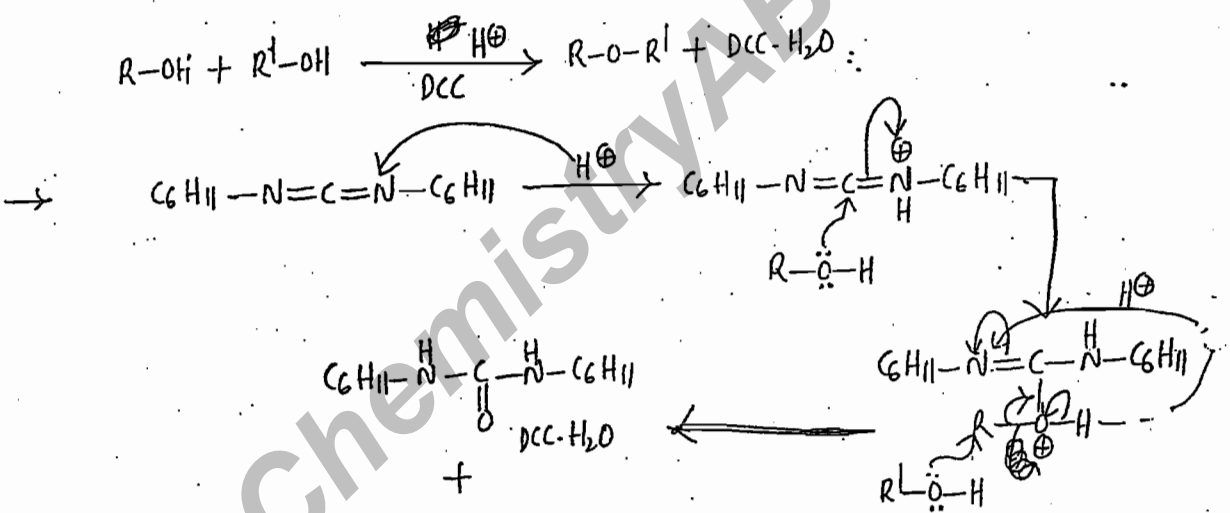
cyclohexyl benzoate

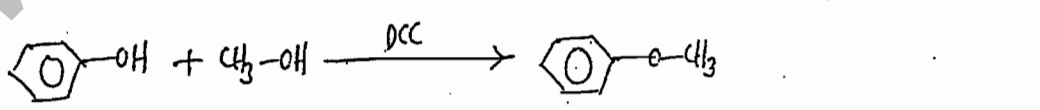
② Amide - formations :-



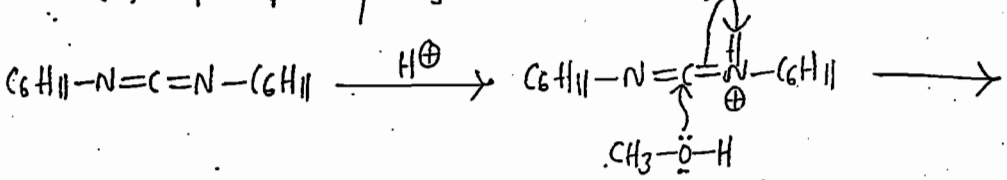


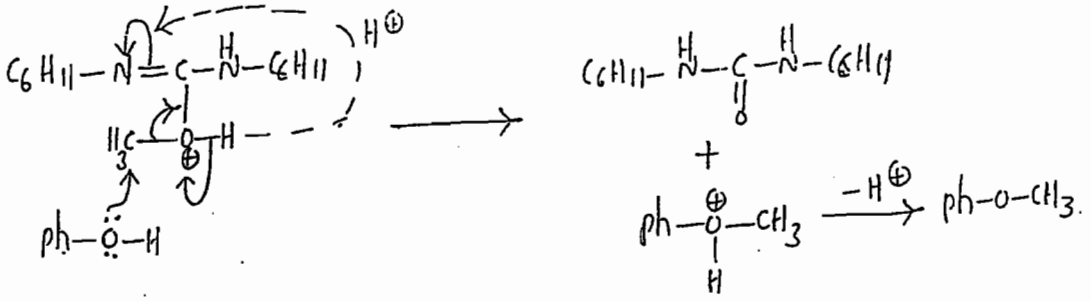
3) Ether formation :—





(first participant is CH_3OH & then ph-OH).



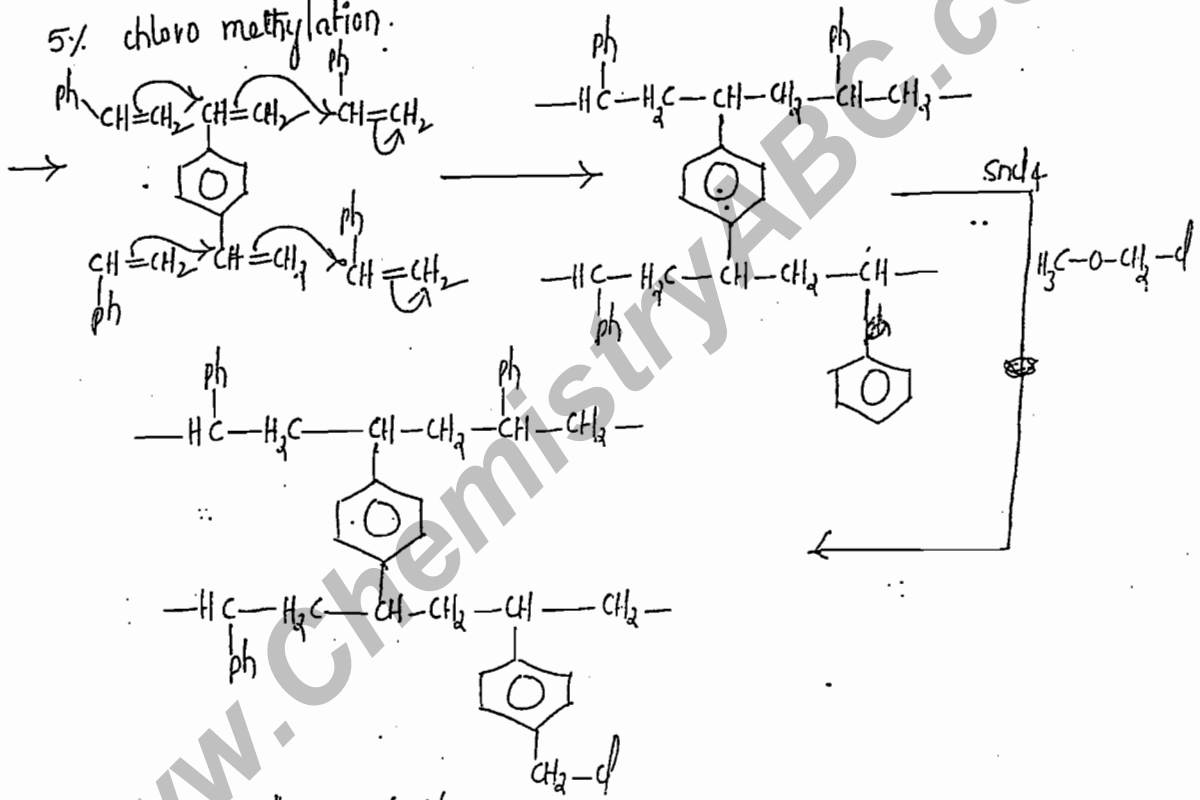


* Merrifield – Resin :— (Solid-phase peptide Synthesis).

(or)

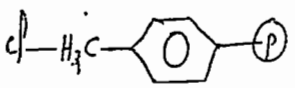
Automated peptide synthesis.

→ 'Merrifield-Resin' is co-polymer of 1,4-Divinyl benzene & styrene with 5% chloro methylation.



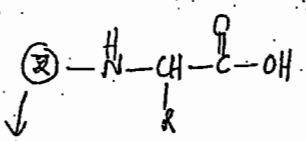
'Merrifield Resin'

(or)



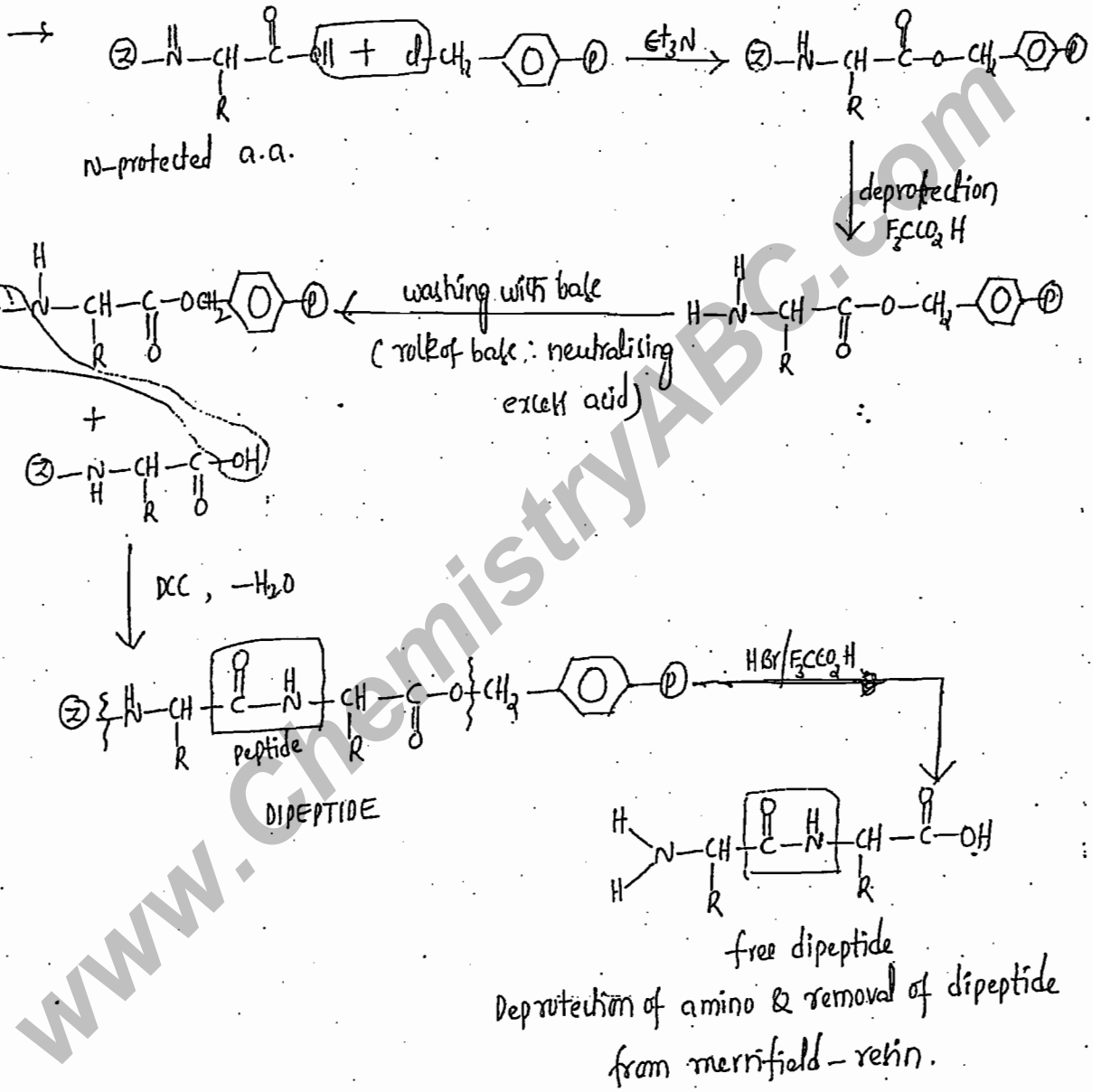
'simplest presentation of merrifield resin'.

peptide-synthesis :



Z : ph-CH_2-O-C(=O)-NH-CH(R)-C(=O)-OH

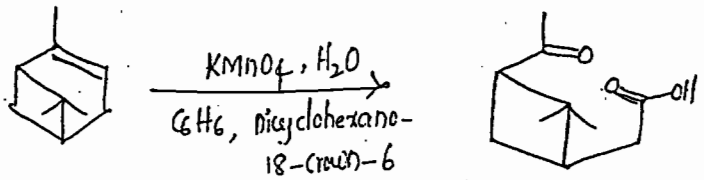
benzoyloxy carbonyl

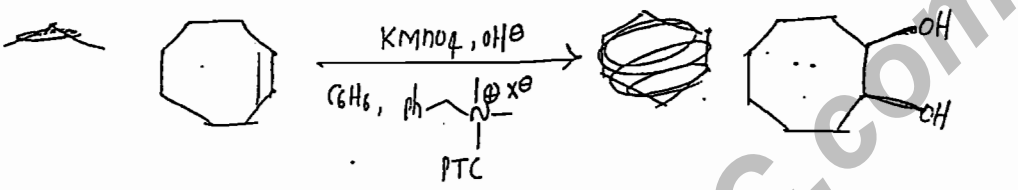


Deprotection of amino & removal of dipeptide from merrifield-resin.

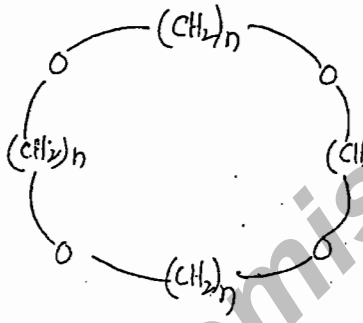
5) Industrially viable reactions.

Eg:- → PTC common for all types of organic reacn. i.e, substn, additions, eliminations, Rearrangements, C-C bond formations, oxidations, redns etc.

→ 



→ Crown-ethers :-

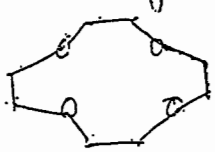


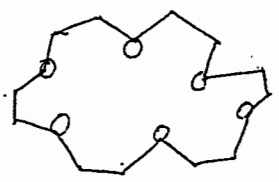
→ Macrocyclic polyethers with regular arrangement of oxygens called "crown-ethers".

→ Generally crown-ethers having $+O-CH_2-CH_2-O+_n$ repetetive unit.

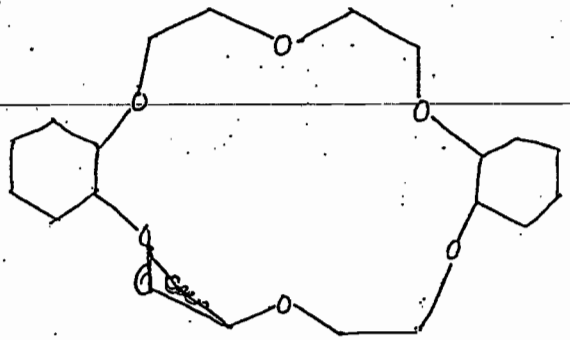
Naming :-

→ Total no. of atoms involved in ring formation → crown — total no. of oxygens involved in ring formation.

→  12-crown-4

 18-crown-6.

→ Dicyclohexano-18-crown-6



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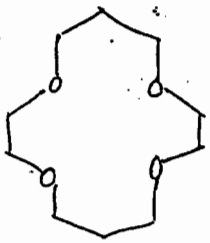
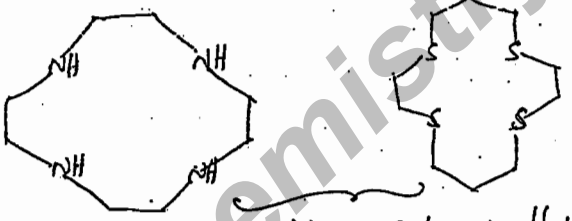


14-crown-4

→



Hetero crowns resemble simple crown ethers

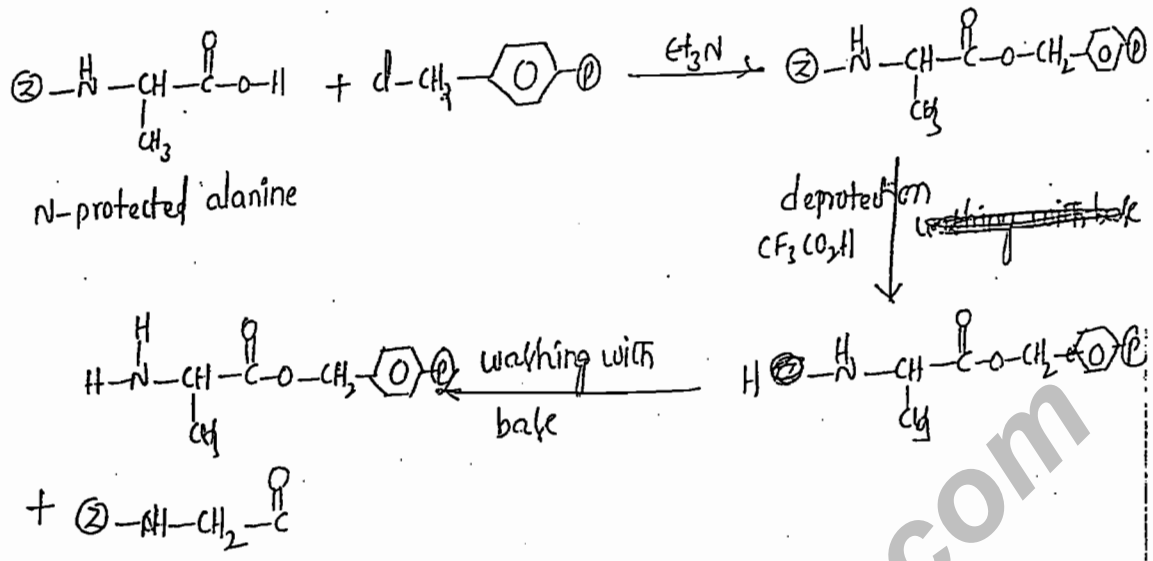
→

cryptands

→ Bicyclic, Tricyclic higher order crowns (mixed heteroatoms) called "cryptands".

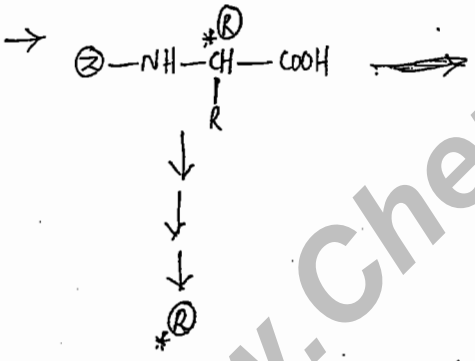
The behaviour is similar to simple crowns.

⇒ Gly-Ala : prepn :--



Advantages :-

07/06/08



1) In merrifield-resin peptide synthesis, optically pure amino acids retains configuration in the product. No racemisations (or) inversions etc.

2) High % of yield, short time synthesis.

3) No competetive reacns.

4) Any desired peptide can be synthesised.

*) phase-Transfer Catalysis : PTC :-

org phase
$x^{\ominus}$ aq. phase → interphase

→ Majority of org. reacn takes place in org. solvent medium. But, there are reasonable no. of reacn in which the starting materials are org, Inorg, components.

→ There reacn inefficient in org. solvent medium, to enhance rate & % of yield of these reacn, alternate experimental technique - PTC.

→ In PTC experiments, the soln is completely immiscible with organic & aqueous medium.

organic substrate soluble in org. solvent, Inorg. substrate soluble in aq. or water (aq. solvents).

→ with the help of phase transfer catalyst, org., Inorg. components are brought into single phase i.e, either org. or aq. phase.

→ once, both starting materials placed in single phase, involve in collisions, enhances rate of reacn and % yields of the products.

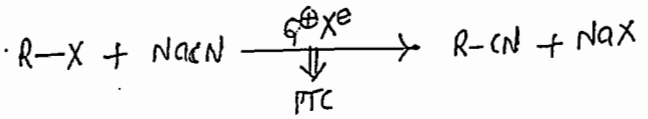
PTC :- Any substance transfering group/ion from one phase to other phase. i.e, aq. phase to org. phase (or) vice-versa in chemical change called 'PTC'.

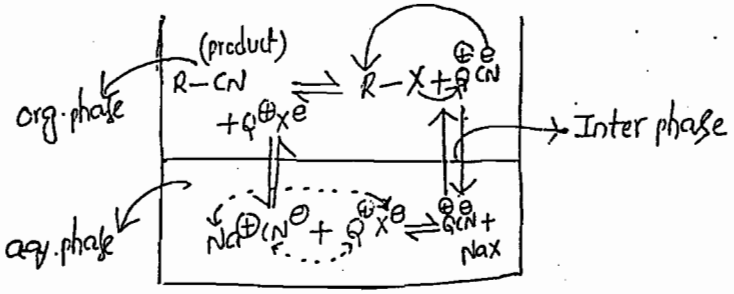
eg :- $\underbrace{R-X}_{\text{organic}} + \underbrace{NaCN}_{\text{Inorg.}} \longrightarrow R-CN + NaX$

To do this above reacn, selection only org. solvent not sufficient, becoz, one of the starting material Inorg, insoluble in org. solvents.

→ PTC method or technique helpful

Mech:— PTC $Q^{\oplus}X^{\ominus}$ ≡ PTC





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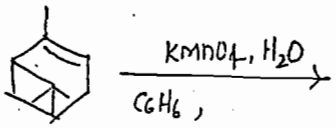

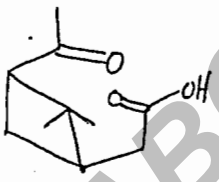

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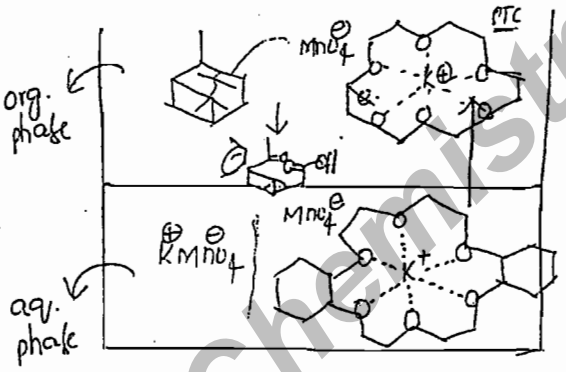
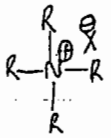
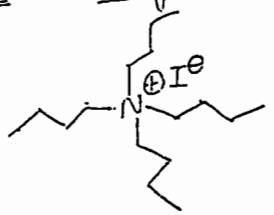


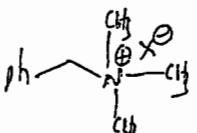
eg:— 1) Quarternary Ammonium Salts :—

$Q^{\oplus}X^{\ominus}$  ($X^{\ominus}$ = Cl, HSO_4^-, $CN^{\ominus}$, halide)

eg: Tetra n-butyl Ammonium Iodide (TBAI)

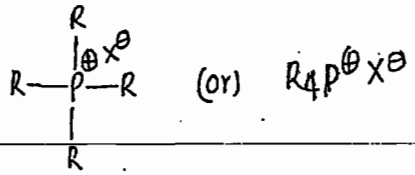


;



benzyl, trimethyl amm. halide

2) Tetraalkyl phosphonium salts



(or) $R_4P^{\oplus}X^{\ominus}$

3) Crown - Ethers

4) Chiral - Alkaloids; "CINCHONA DERIVATIVES".

Limitations :—

1) It should be soluble in org. as well as aq. phases

2) It should easily able to transfer groups / ions from one phase to other phase (aq. to org. phase or vice-versa).

3) Readily available

4) Should not chemically react with any one starting material.

5) After completion of rean, PTC should be easily removable.

6) Should able to ↑ rate of rean, followed by enhancement of % of yield of the product.

7) PTC should not be with toxic properties.

Date : 08/01/08

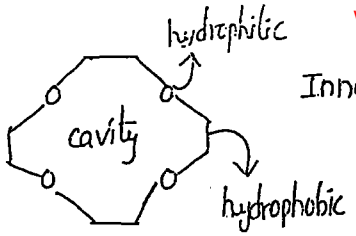
Advantages of PTC :—

1) PTC makes rean efficient by ↑ing rate & % of yields of products.

2) Easy to carryout the Expt.

3) Reduces quantity of organic solvent, rean becomes cheaper.

4) Environment friendly reany / pollution free reany.

→ 

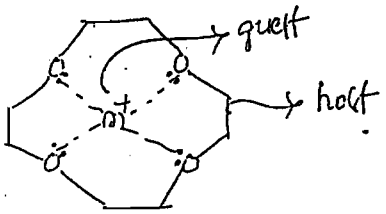
Inner gap of crown ethers called "cavity".

→ oxygens orientation towards cavity

→ crown-ethers with hydrophilic & hydrophobic groups, ∴ soluble in org. as well as aq. solvents.

→ cavity size depends on nature of crown-ether.

→ with ↑se in no. of atoms in ring formations, cavity size ↑es.

→ 

→ crown ethers can hold ions/groups etc. provided there is a size matching of cavity of crown ethers and ions/groups.

→ crown ether - host, entering ion/group - guest

∴ Host-Guest relation (lock & key model).

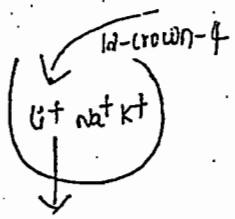
→ Li^+ Na^+ K^+

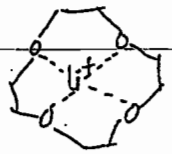
Li^+ ion size matches with cavity size of 12-crown-4. K^+ ion size matches with cavity size of 18-crown-6.

Applications :—

1) used for separation of metal ions

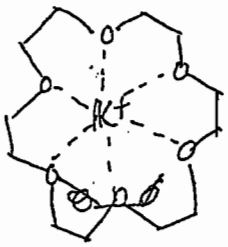
eg: IA group metal ion sep : $Li^+/Na^+/K^+$

→ 



12-crown-4 for sepn of $Li^{\oplus}$ from Na^+/K^+ mixture.

18- " -6- " " $K^{\oplus}$ " Li^+/Na^+ "



2) Crown ethers used as PTC

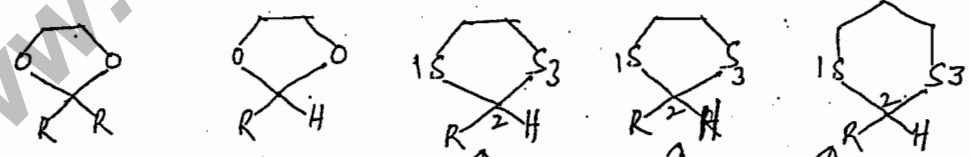
3) chiral crown-ethers used for sepn of Racemic modification.

4) Some of the org. compds' mixture also possible to separate with crown-ethers.

eg: 1) phenol + acetophenone

2) aniline + anthracene

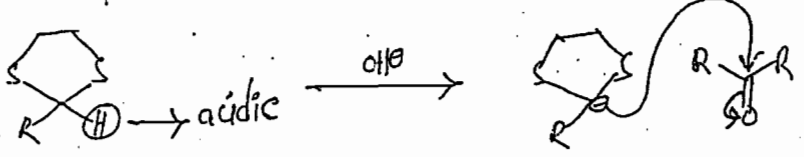
⇒ 1,3-DITHIANES:—

→ 

1,3-dithio acetals (or) ketals

1,3-dithianes

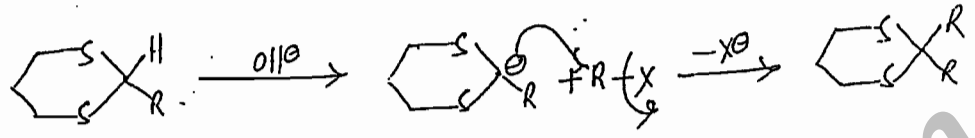
→ Resembles acetals or ketals

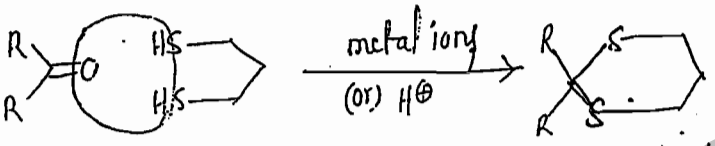
→ 

Importance of 1,3-DITHIANES :-

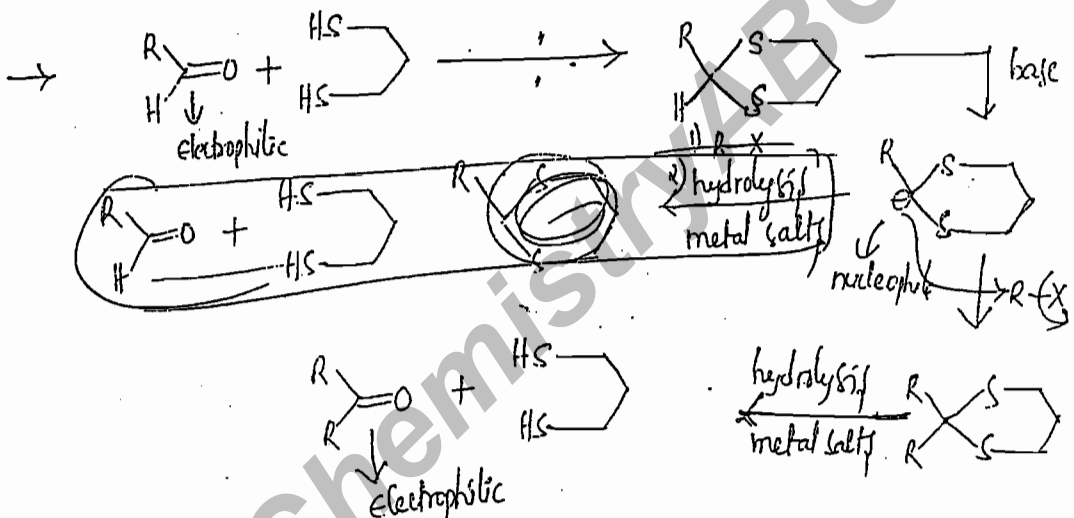
→ 'carbon' group attached to two S's, due to -I.E. of 'S' atoms, acidic.

In the preference of strong base, by loosing protons produces carbanion intermediate used for new C-C bond formations by attacking at electrophilic C' centres.

→ 

→ 

not useful

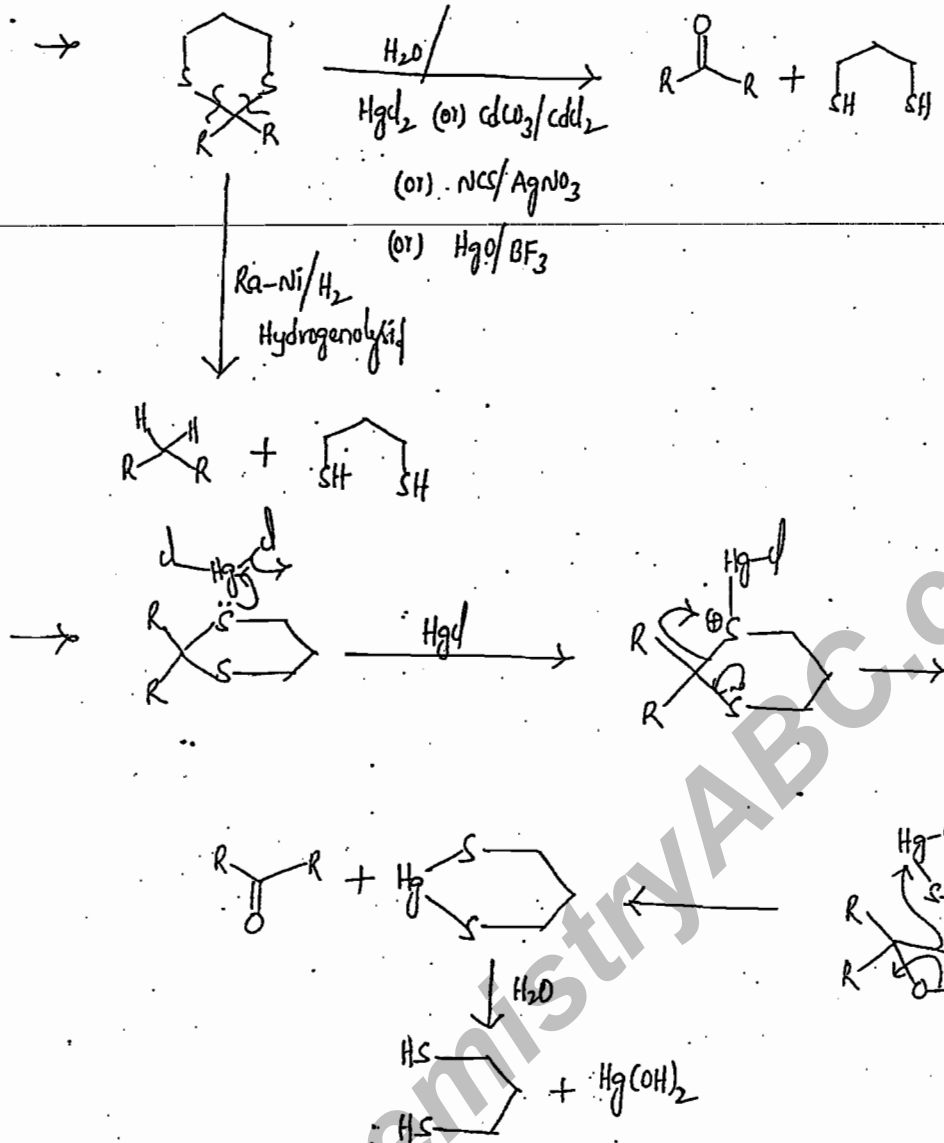
→ 

→ 1,3-DITHIANES are with 'umpolung' of character

→ Transformation of electrophilic 'C' into nucleophilic 'C', then its reversal called "umpolung". (or) Reversal of polarity at same 'C' atom in synthesis called "umpolung".

→ for reversal of polarity, 1,3-dithianes are best mediators.

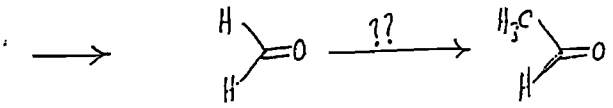
Date : 09/06/08

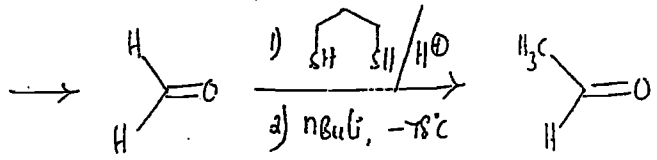


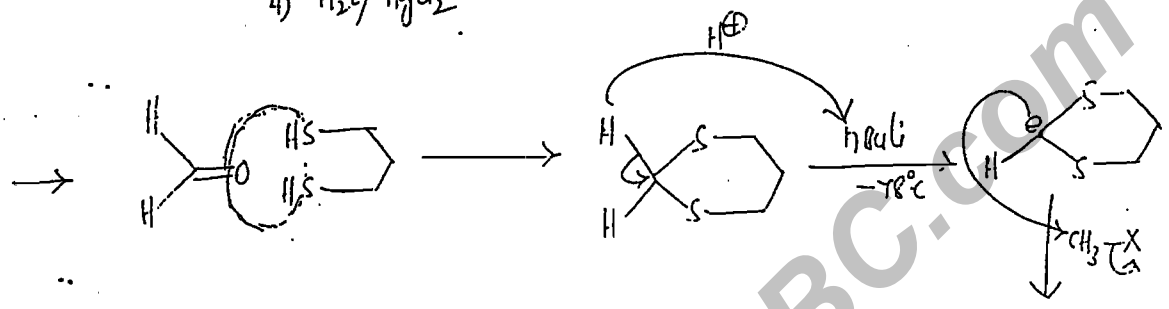
Applications :—

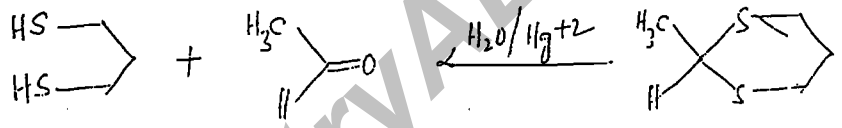
1) converts aldehydes into aldehydes with 1st in carbons.
2) " " " ketones
3) " " " 1,2-dicarbonyl compounds
4) " " " 1,3— "
5) " " " Hydroxy carbonyl compounds
6) " " " Hydrocarbons

I) Aldehyde ——→ Aldehyde

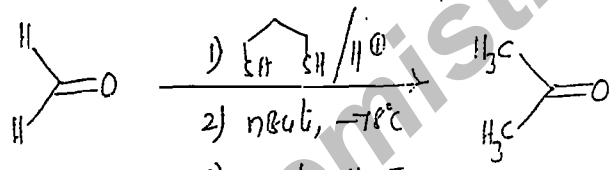


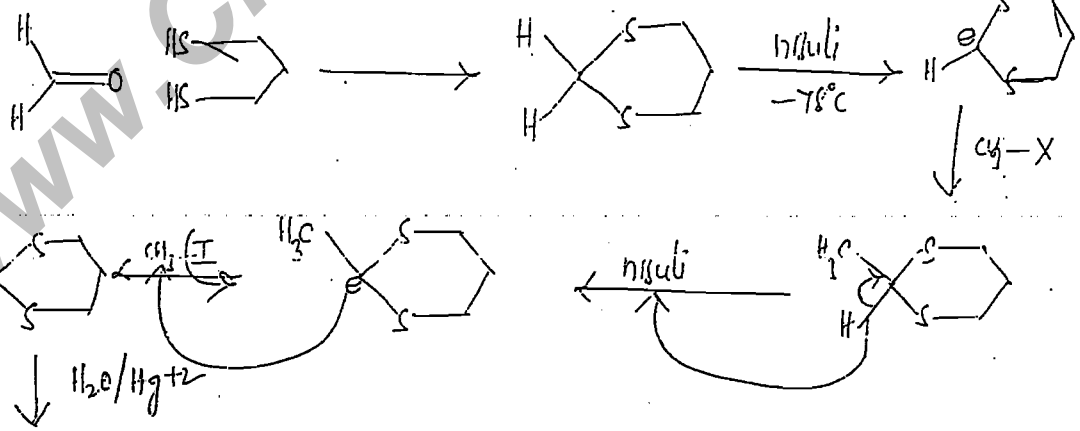


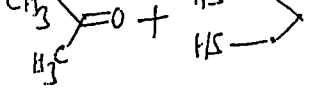


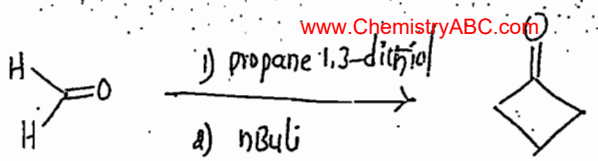


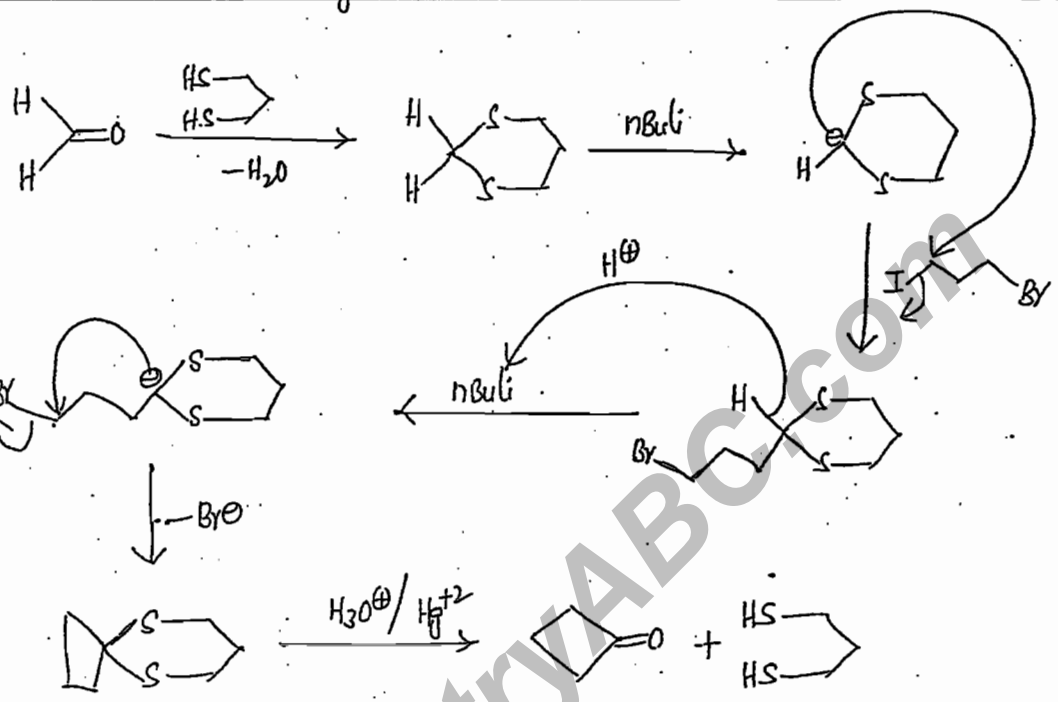
2)



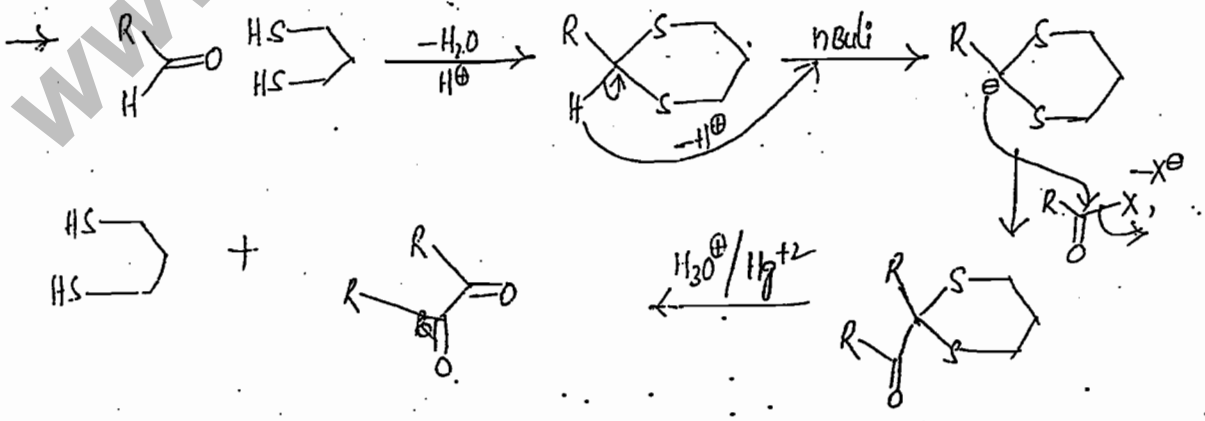


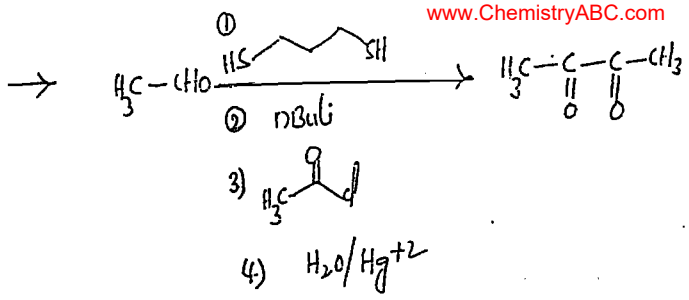


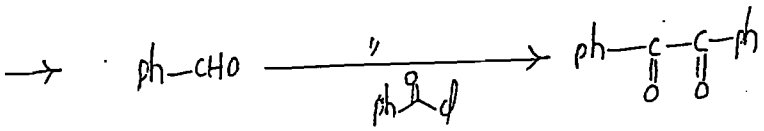
3) 



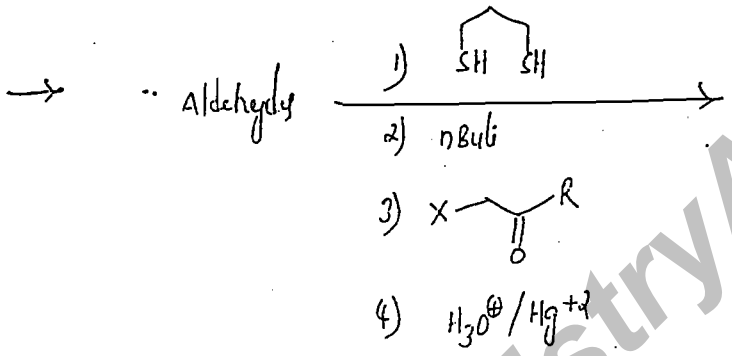
4) Aldehydes  1,2-dicarbonyl compds

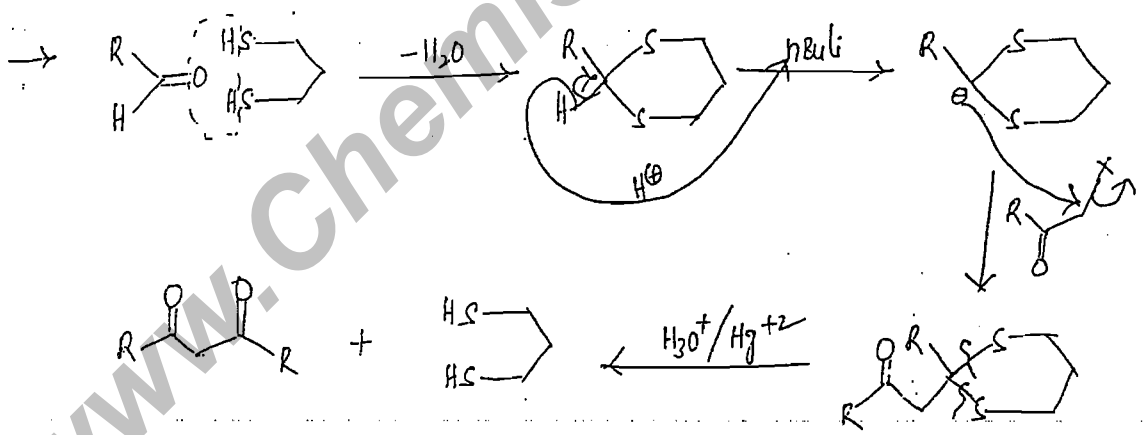


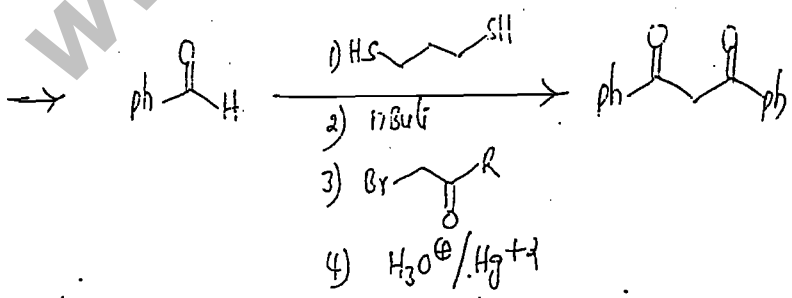




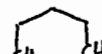
→ Aldehydes ⟶ 1,3-dicarbonyl compounds :-

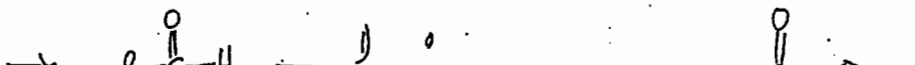


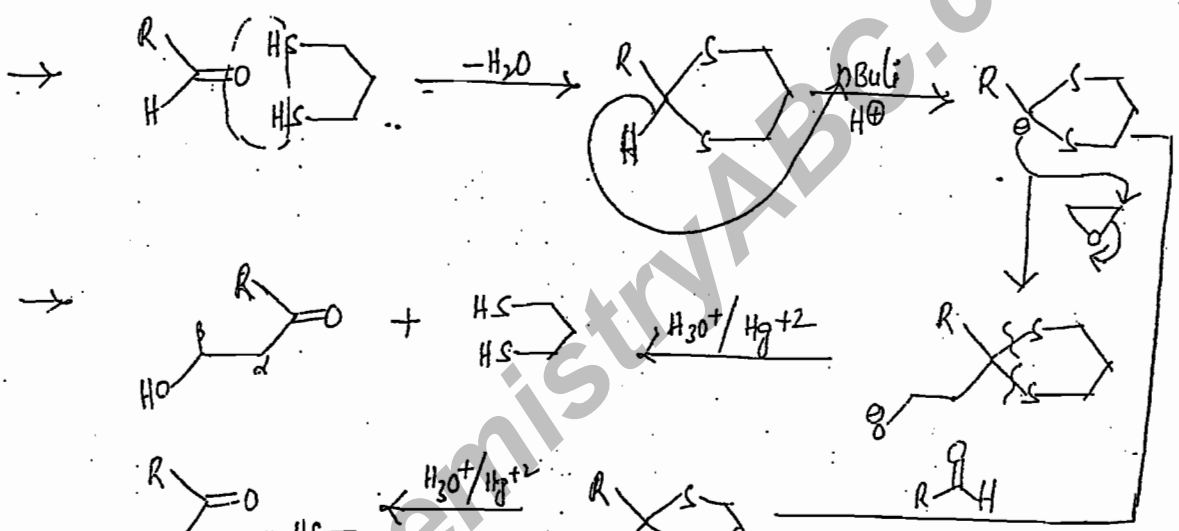




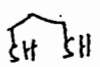
⇒ Aldehydes ⟶ Hydroxy ketones :

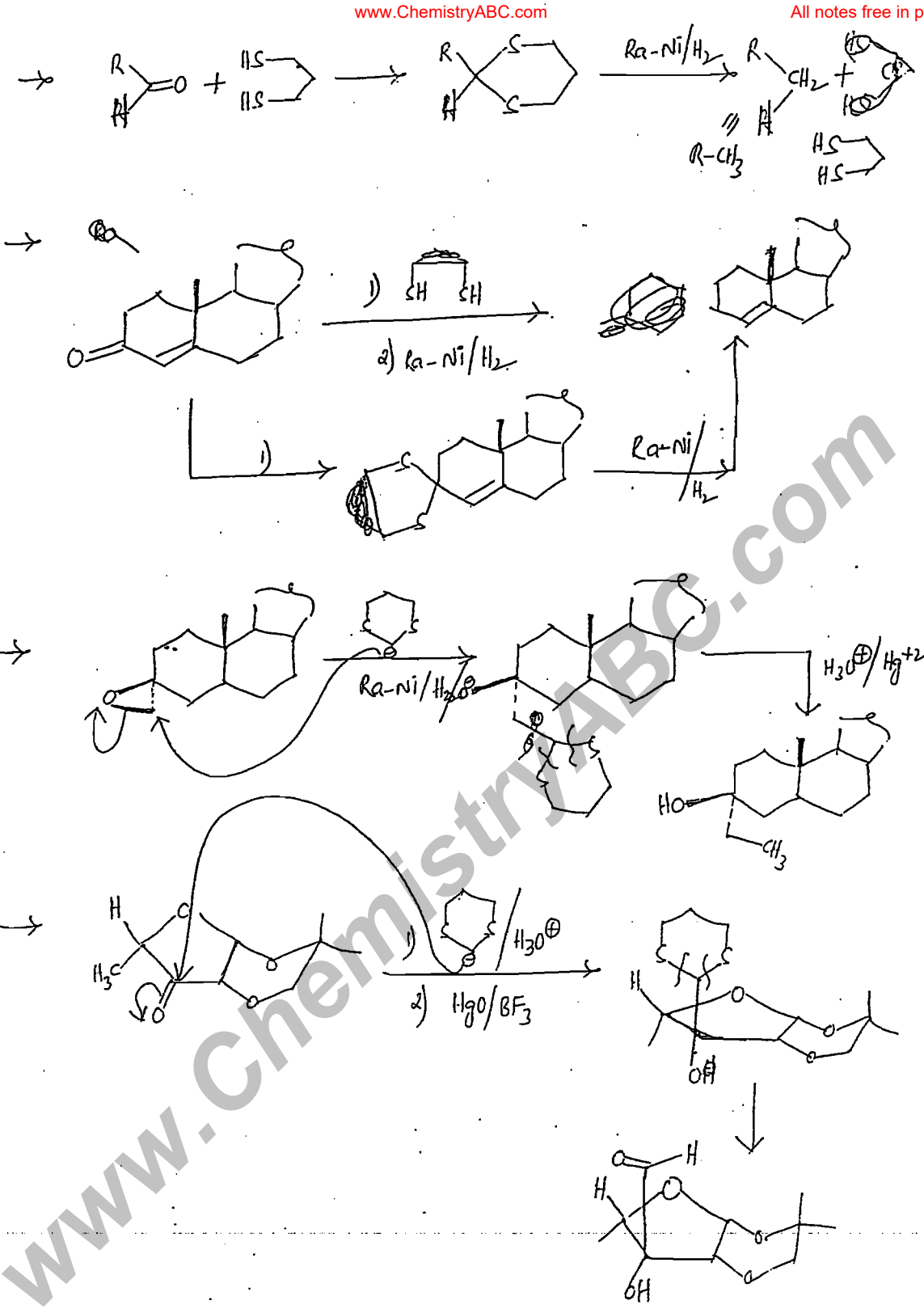
→ Aldehydes —(1)  /H⊕ (2) nBuLi, −78°C (3)  (4) H_2O/Hg^{+2} → hydroxy ketones

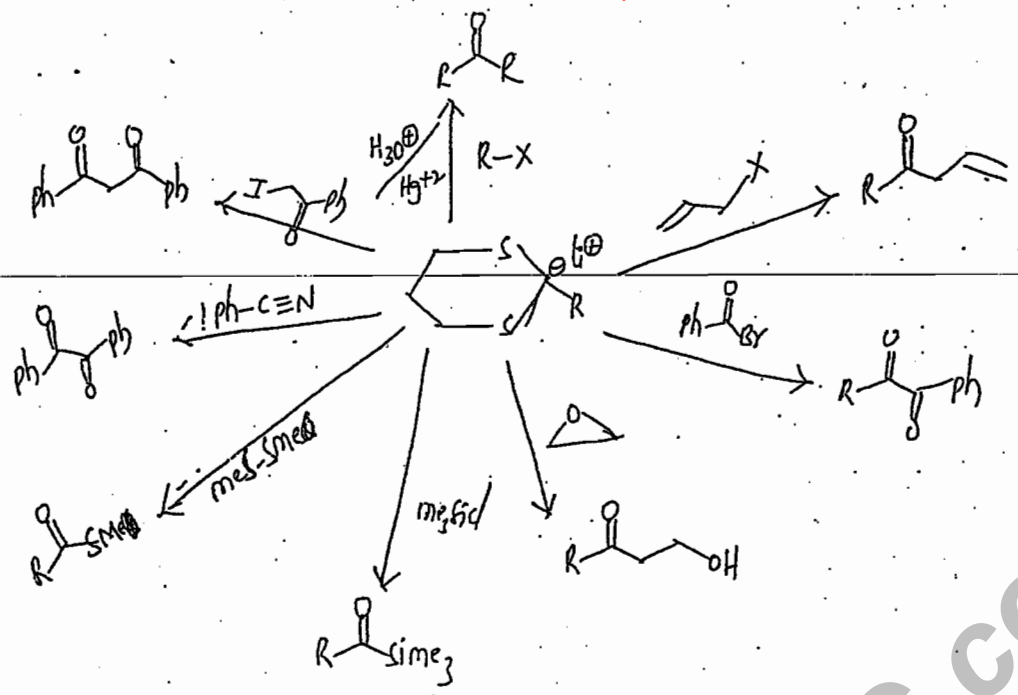
→ 



⇒ Aldehydes (ketones) to Hydrocarbons :—

→ C=C —(1)  (2) Ra-Ni/H_2 → Hydrocarbon





Date: 19/04/08
Saturday.

Named Reactions
(Paper I and paper II)

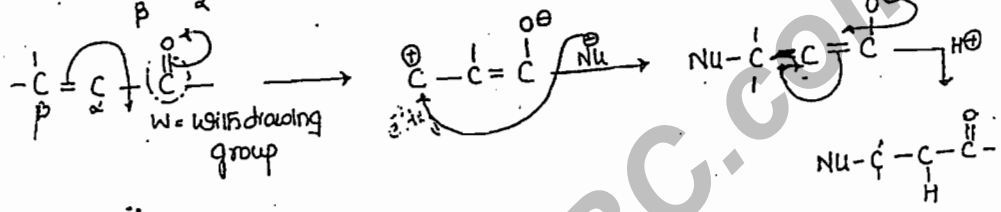
I paper-II Named reactions.

i) Michael additions (or) Michael reactions.

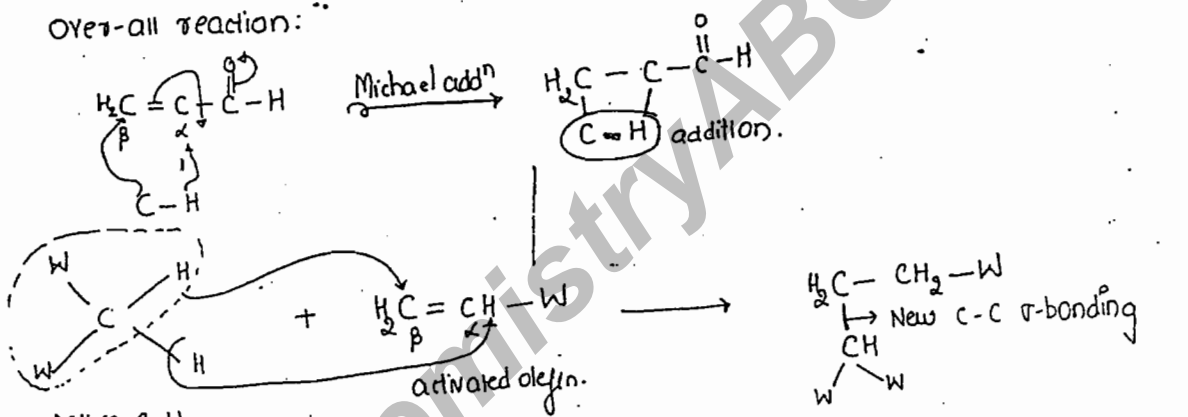
→ Addition of active C-H function at α-β-unsaturated olefin or activated olefin in basic medium called michael reaction/addition

→ New carbon-carbon bond developed at β-position of activated olefin.

Suppose $C_\alpha = C_\beta - W$. β(C_2)-carbon becomes more electron deficient such carbon called activated carbon.

i/e 

Over-all reaction:



Active C-H function (or) Acidic C-H function michael donor

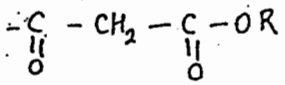
Michael acceptor

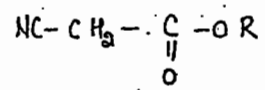
Michael donors: They should readily ionise into carbanion and proton.

O_2N-CH_2 , RO_2C-, CH_3- , $-\overset{O}{\overset{\|}{C}}-CH_2$,

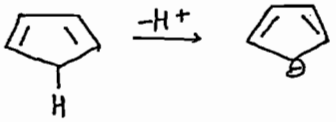
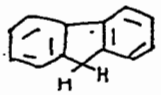
$HC(=O)-CH_2-$, β-diketo $-\overset{O}{\overset{\|}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-$

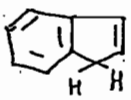
β-Nitro carbonyl compound : $-O_2N-CH_2-\overset{O}{\overset{\|}{C}}-$

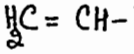
β- Keto ester 

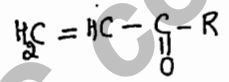
β- cyano esters 

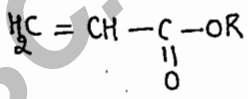
→ With increase in number of withdrawing group, acidic strength increases.

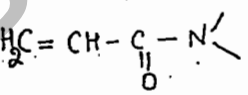
Cyclopentadiene  Flourene 

Indene 

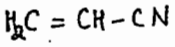
Michael acceptors : 

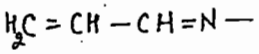
→ α, β- unsaturated carbonyl compounds 

→ α, β unsaturated esters 

→ 

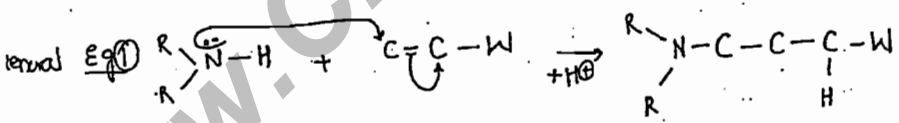
→ α, β unsaturated Nitro compounds ($CH_2=CH-NO_2$)

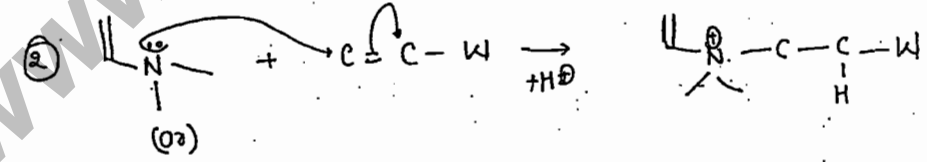
→ α, β-unsaturated cyano compounds 

→ α, β- unsaturated amines 

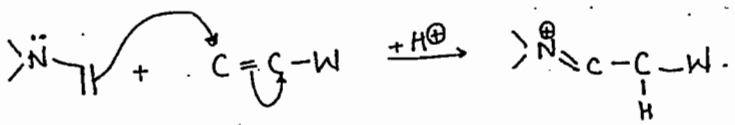
Here all the β- positions are electron deficient.

→ Amines and Enamines also can be used as michael donor

General Eq① 

② 

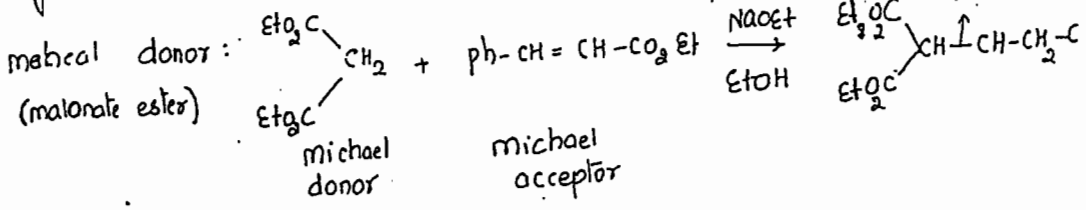
(or)



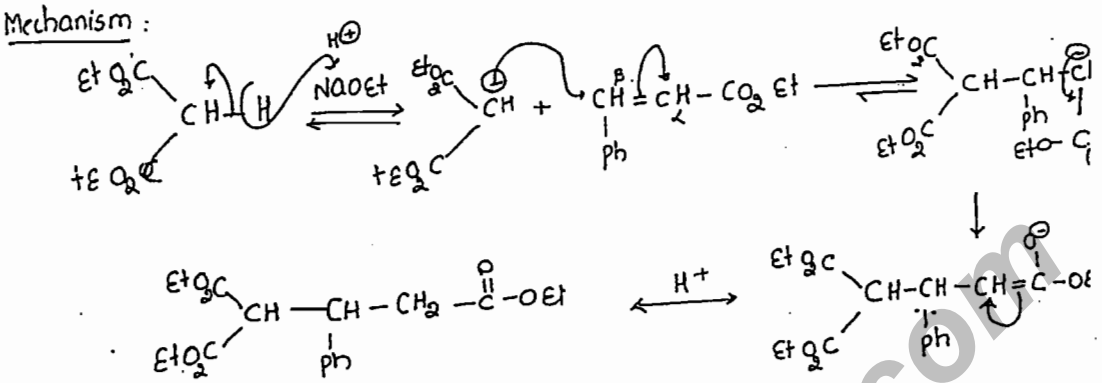
21/04/08
Monday

Mechanism for Michael addition:

Michael donor: (malonate ester)

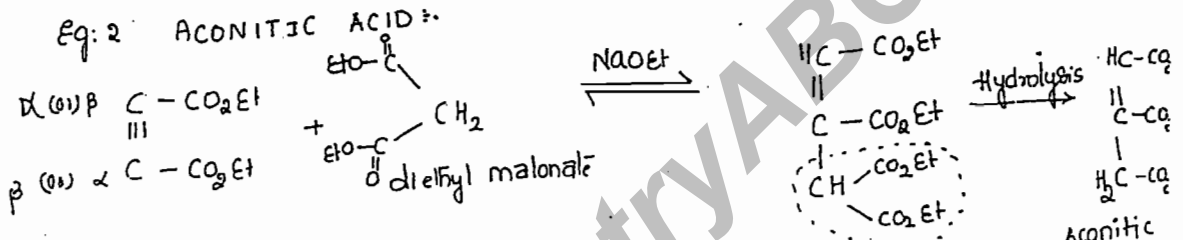


Mechanism:

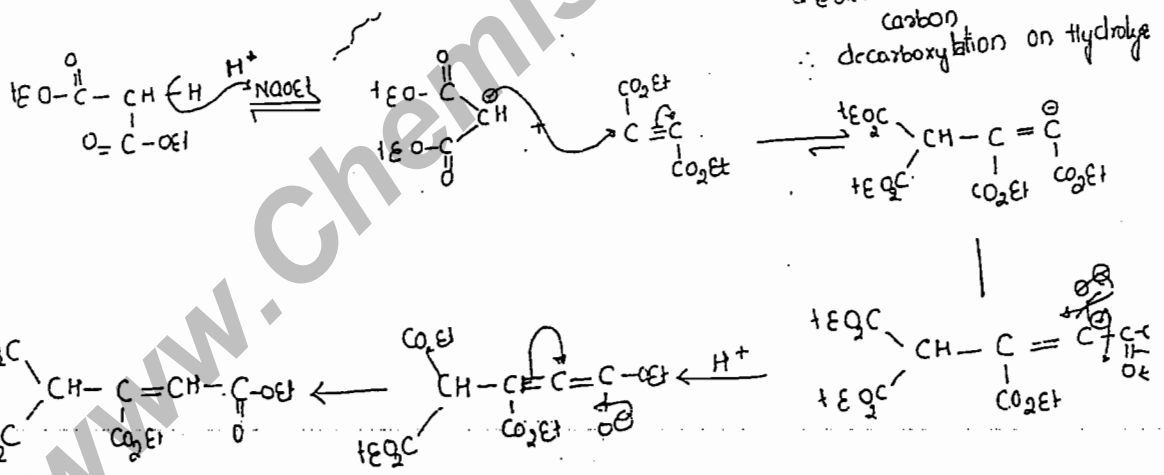


M. adduct.

Eg: 2 ACONITIC ACID:

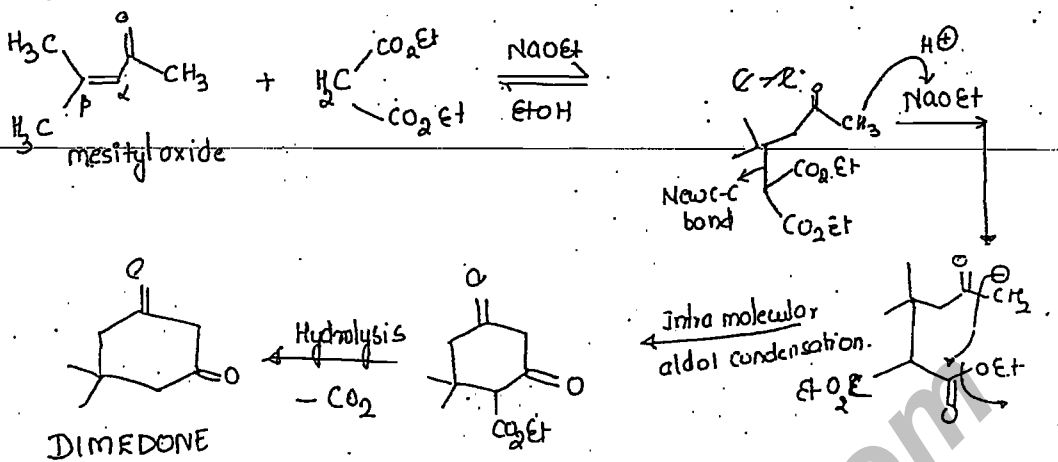


Mechanism:

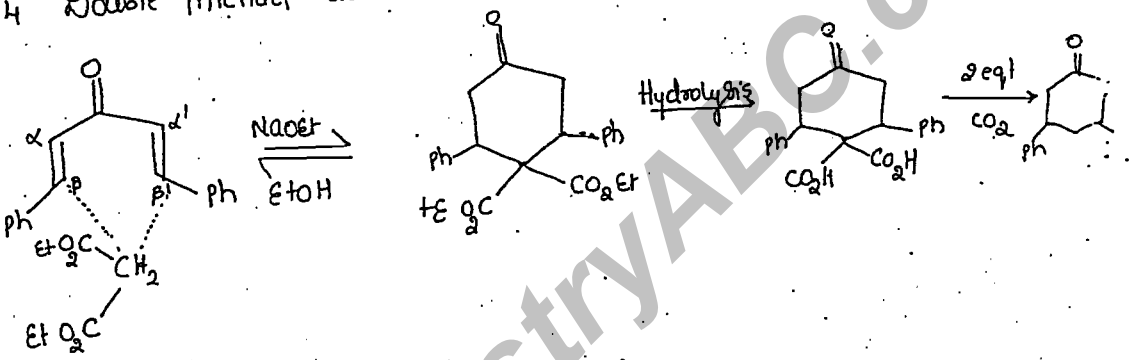


2 ester's on one carbon decarboxylation on hydrolysis

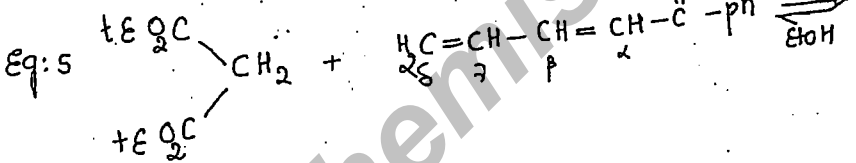
Eq: 3 DIMEDONE FORMATION:

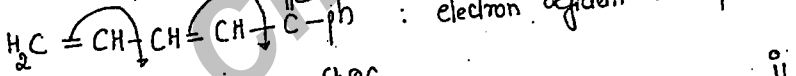


Eq: 4 Double michael additions with in a same molecule.

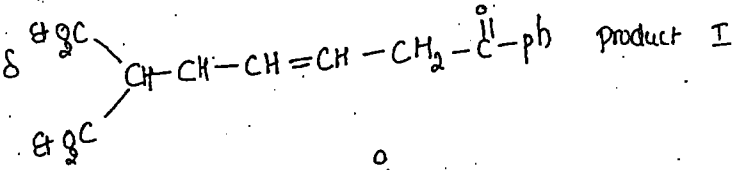


Eq: 5

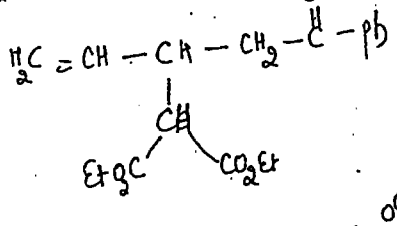




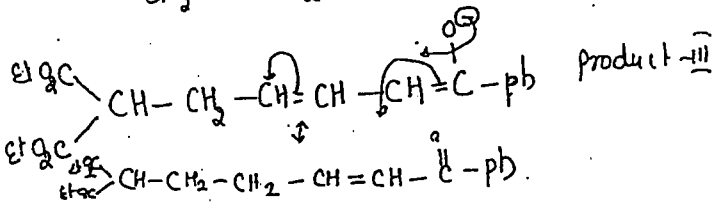
(1) New C-C bond at δ



(2) New C-C bond at β

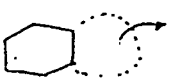


3) New C-C bond at δ

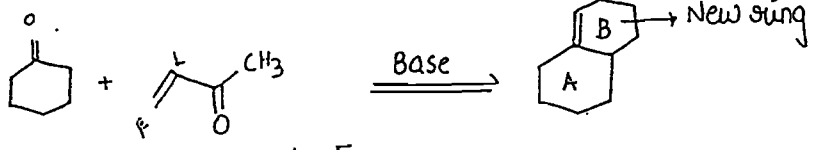


Robinson ANNULATION's is a combination of 2-reactions i,e Michael reaction and aldol condensation or aldol reaction.

ANNULATION: Developing New ring on existing rings called annulations.

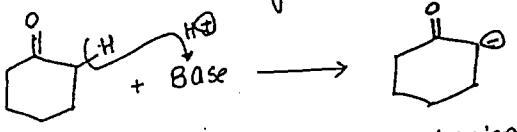


Eg: 1.

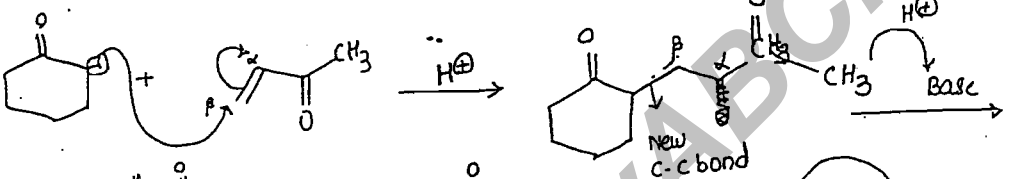


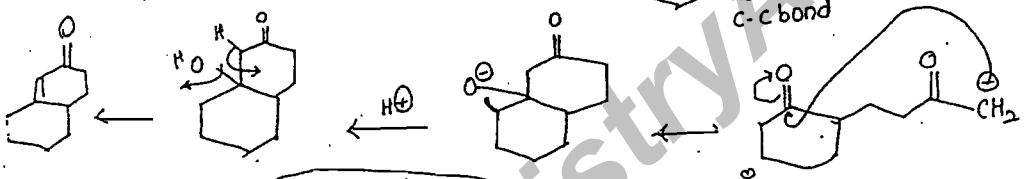
methyl vinyl ketone (M.V.K)

Mechanism: firstly Michael addition.

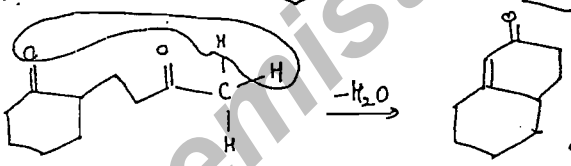


carbanion.

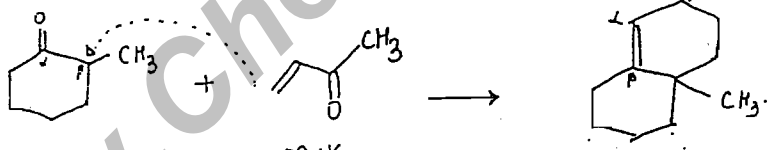




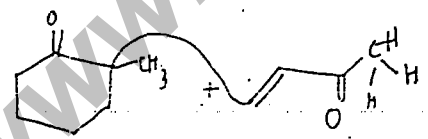
Simply

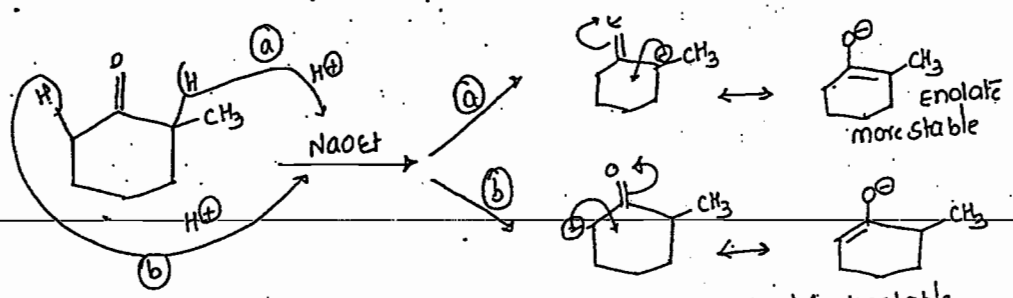


Eg: 2



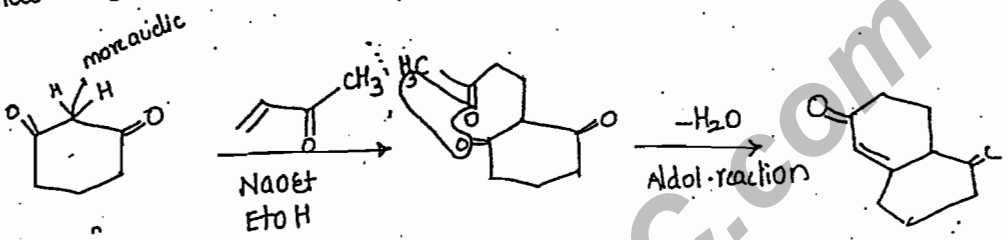
MVK



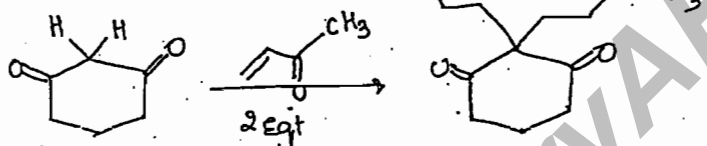


∴ b path is not taken into consideration because of producing unstable enolate.

Eg: 3

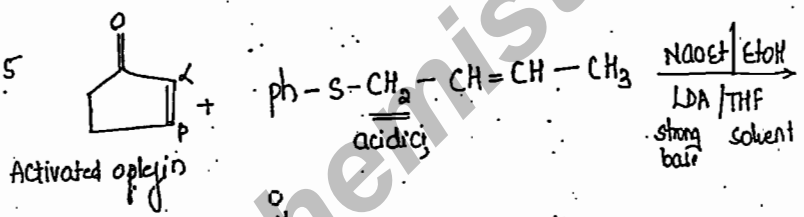


Eg: 4

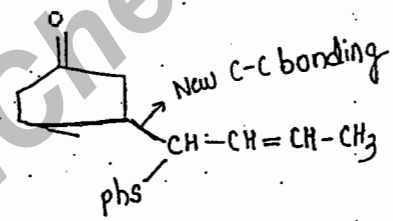


→ No intra-molecular aldol cyclisations. because it gives a strained cyclic system

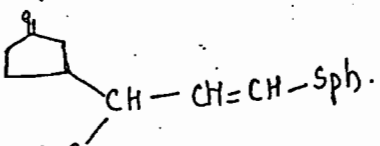
Eg: 5

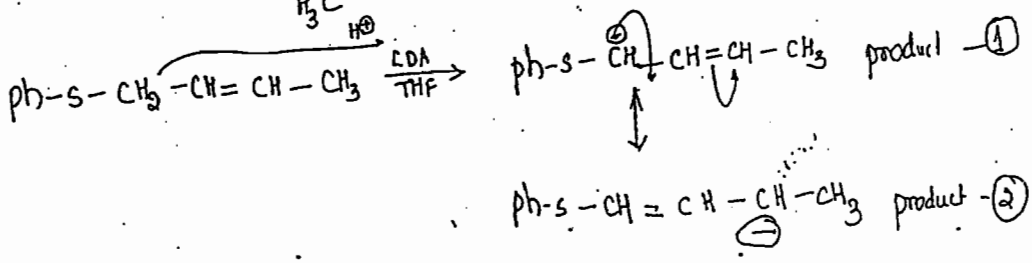


Products : 1

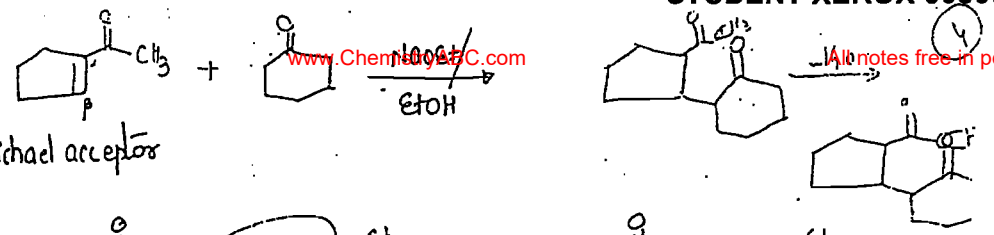


product : 2

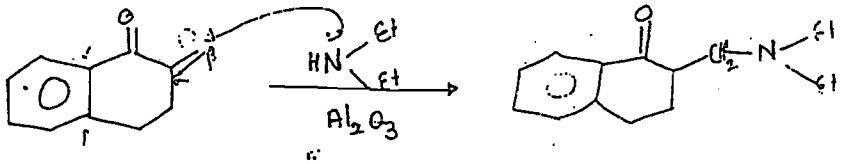




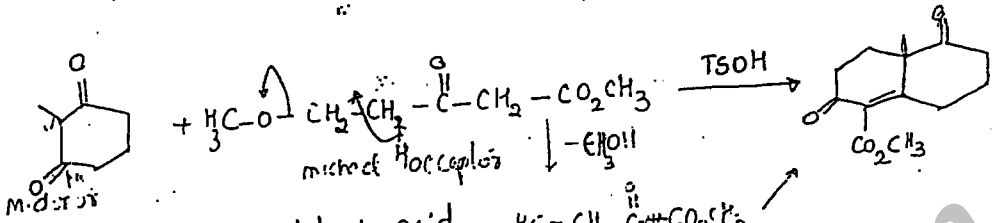
Eq: 6



Eq: 7

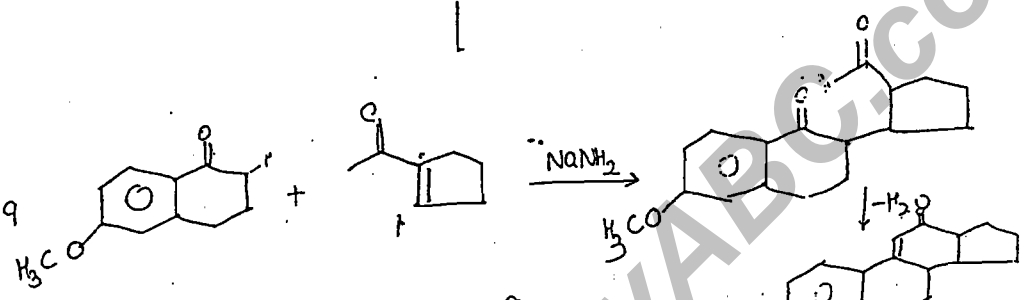


Eq: 8

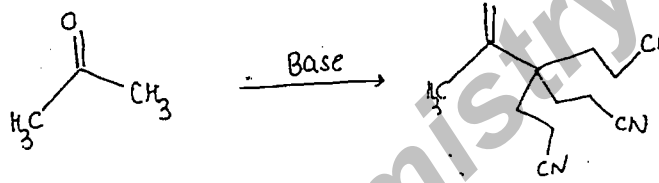


TSOH = p-Toluay sulphonic acid.

Eq: 9



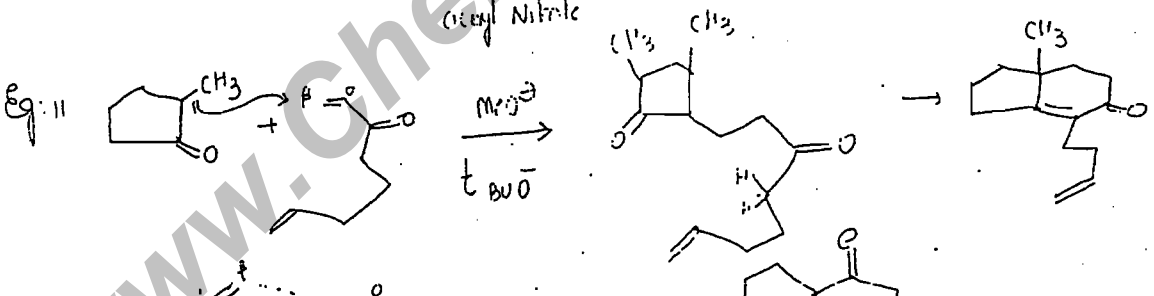
Eq: 10



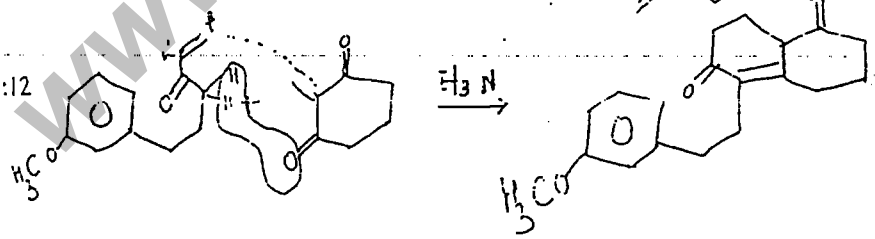
Eq of

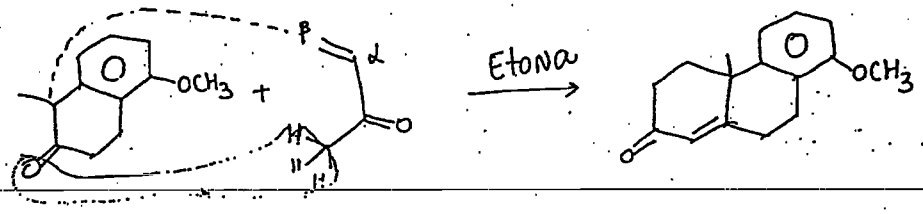
Cetyl Nitrile

Eq: 11



Eq: 12



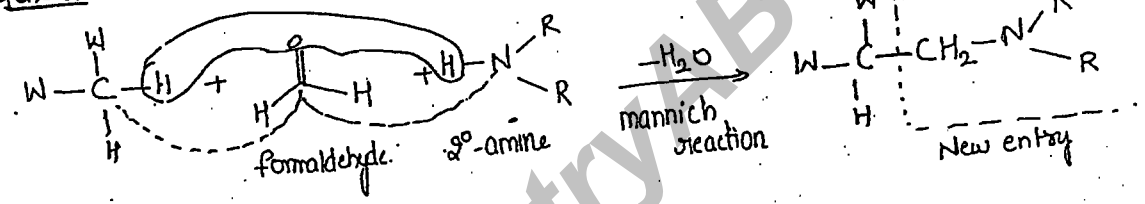


II) MANNICH-- Reaction :

Amino-methylations at active positions involving formaldehyde (HCHO) and 2°-Amine called mannich reactions.

Resulting products are mannich bases / mannich salts.

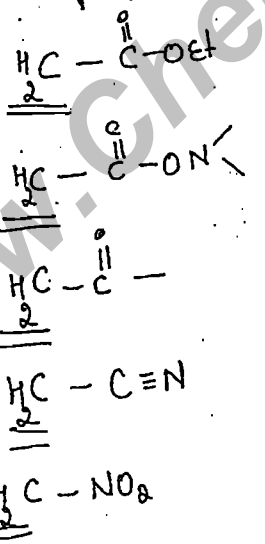
General: Active function → Carbanion + H+

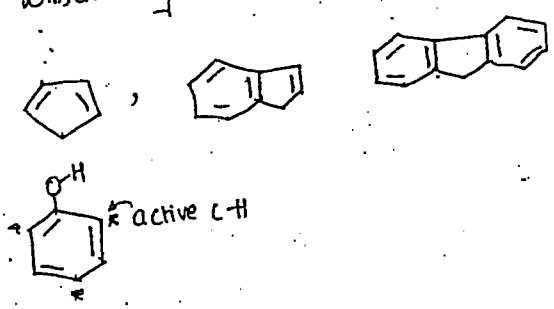


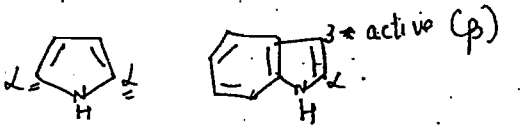
Eg: for active C-H function:

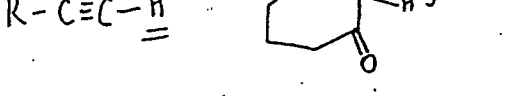
→ C-H group attached to withdrawing fundion is active C-H

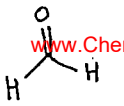
Eg's :

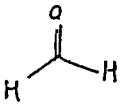




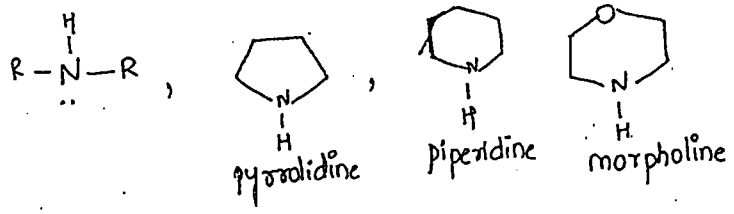


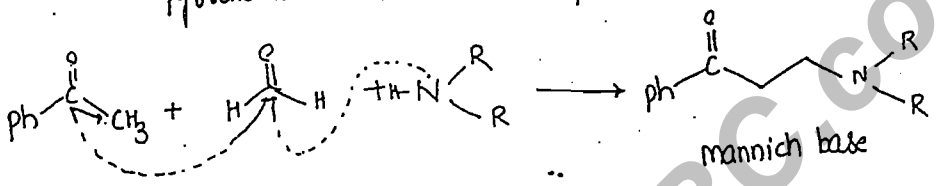


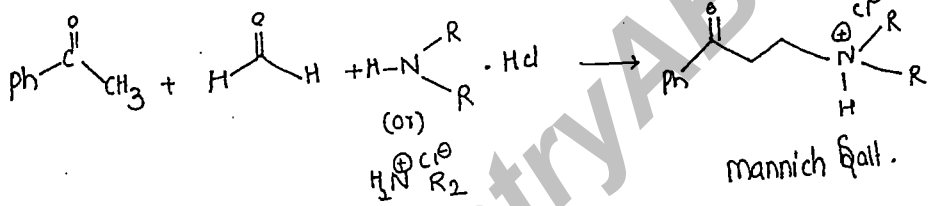
Active C-H function +  + 2°-Amine → mannich base (or) Amino-methylations at active positions. (5)

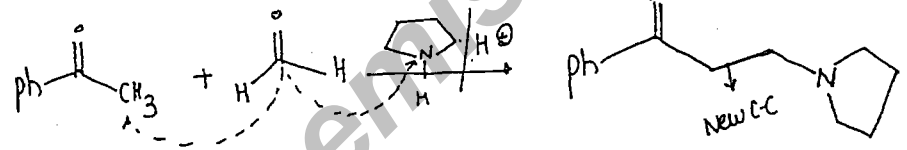
Active C-H function +  + salt of 2°-Amine → mannich salt.

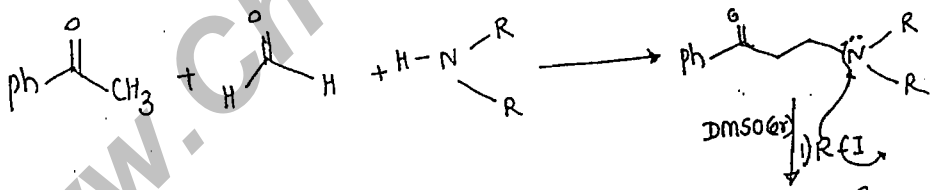
2°-amines may be cyclic or accyclic.

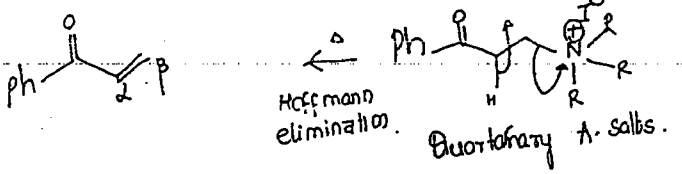


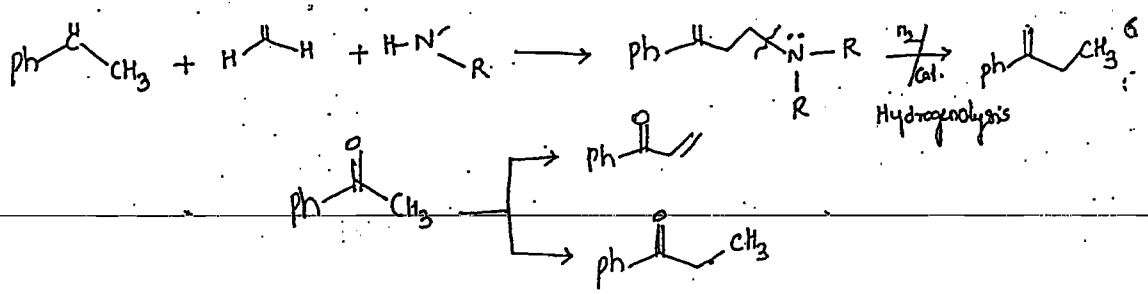
Eq.1 



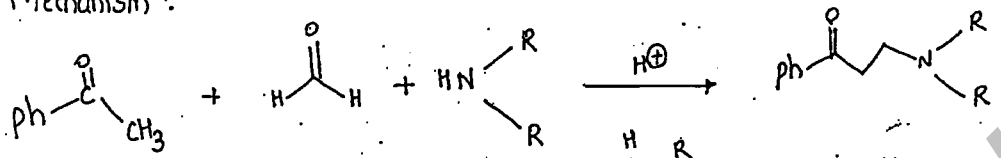
Eq:2 

Eq:3 

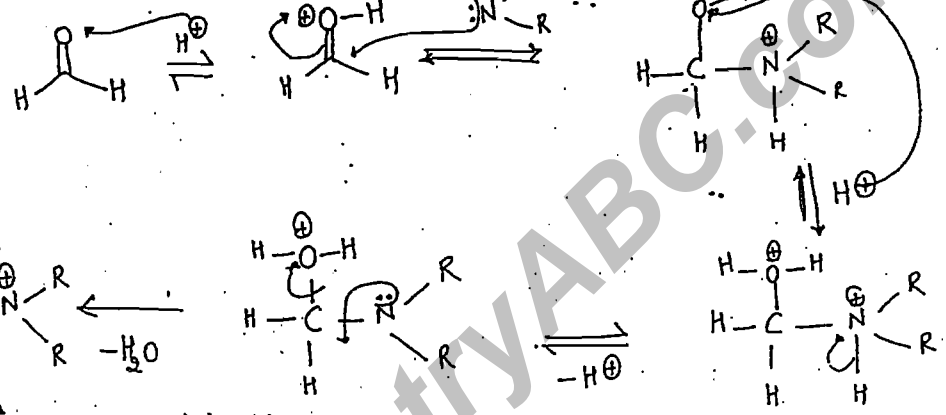




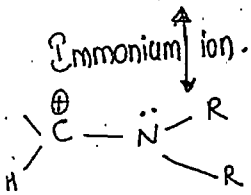
Mechanism :

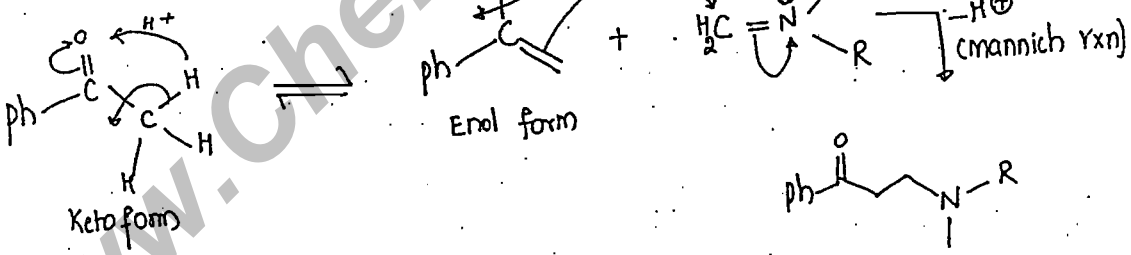


Step: 1 :



Immonium ion (or) Iminium ion.

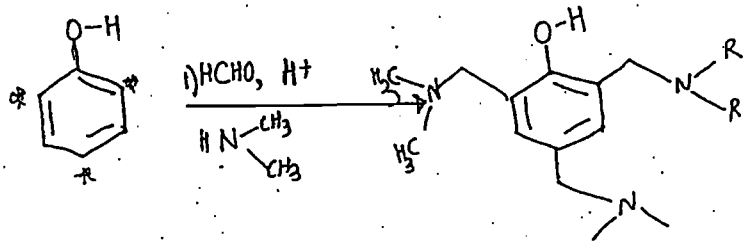




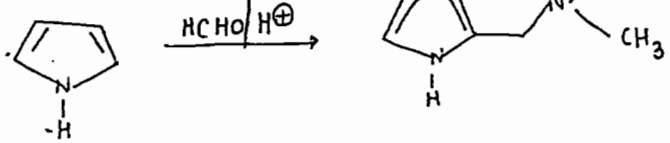
Keto form

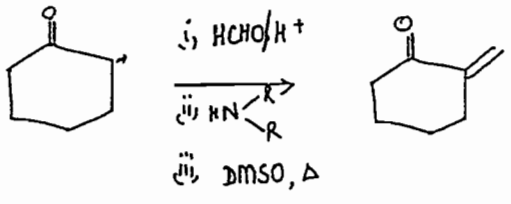
Mannich base.

Eg :-



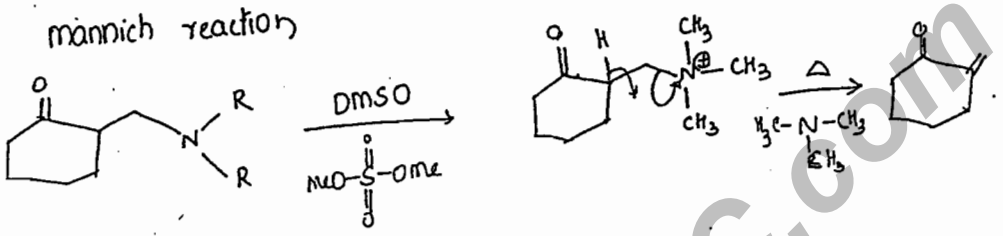
Eg: 5 $H_3C-C\equiv C-H$ $\xrightarrow{HCHO/H^+}$ $H_3C-C\equiv C-CH_2-N(CH_3)_2$ (6)

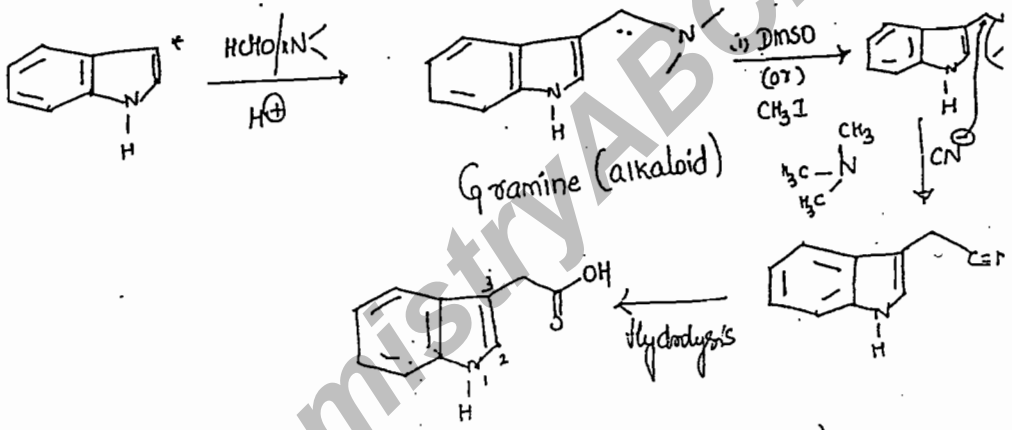
Eg: 6  (HCHO/H⊕)

Eg: 7  Explain

i) HCHO/H+
ii) HN(R)R
iii) DMSO, Δ

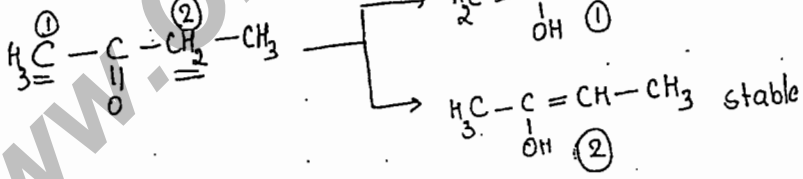
i) Mannich reaction

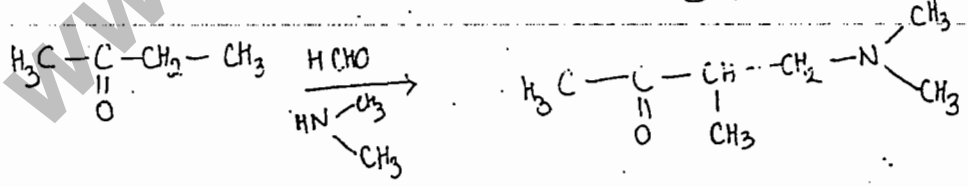


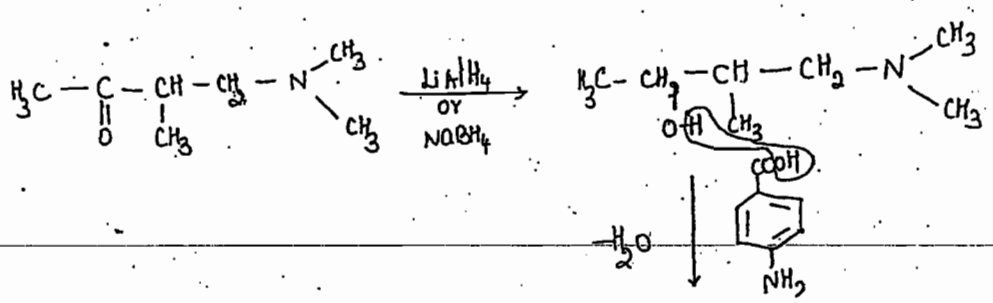
Eg: 8 

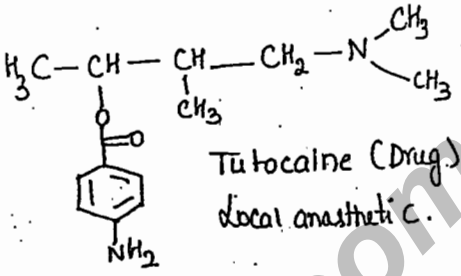
Gramine (alkaloid)

Heteroauxin (Indole-3-acetic acid)
(drug)

Eg: 9 

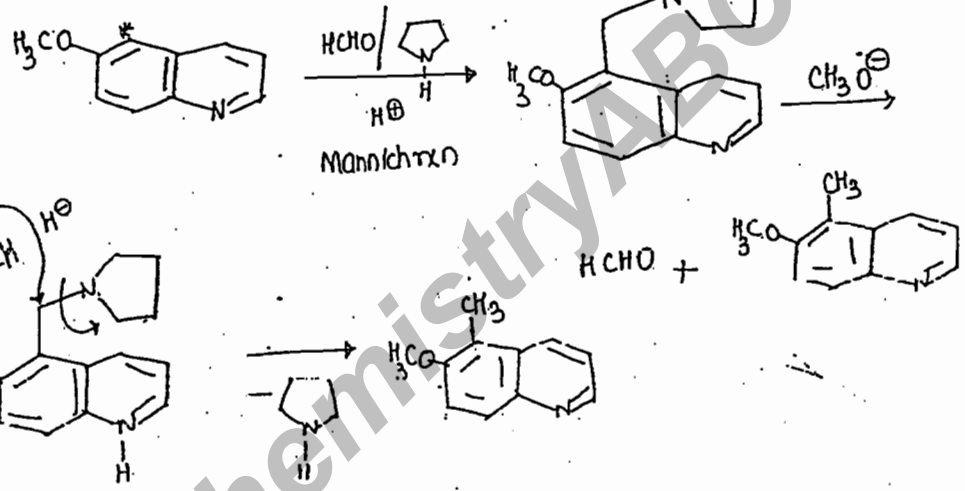






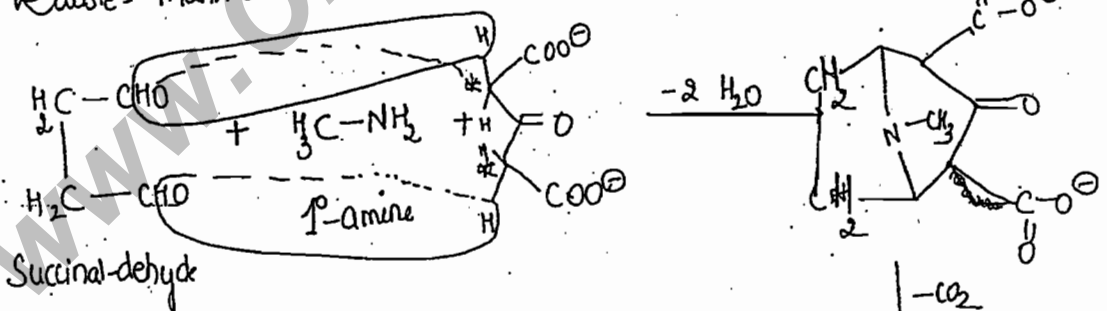
Tutocaine (Drug)
Local anasthetic.

Eg: 10.



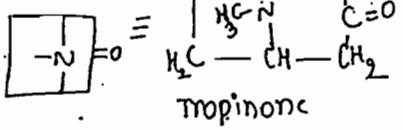
Mannichrxn

Double - Mannich - reaction :



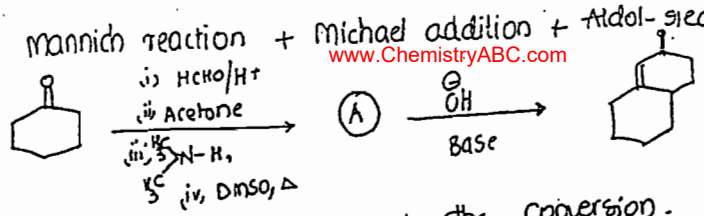
Succinal-dehyde

Tropinone one of the intermediate in the preparation of atropine alkaloid

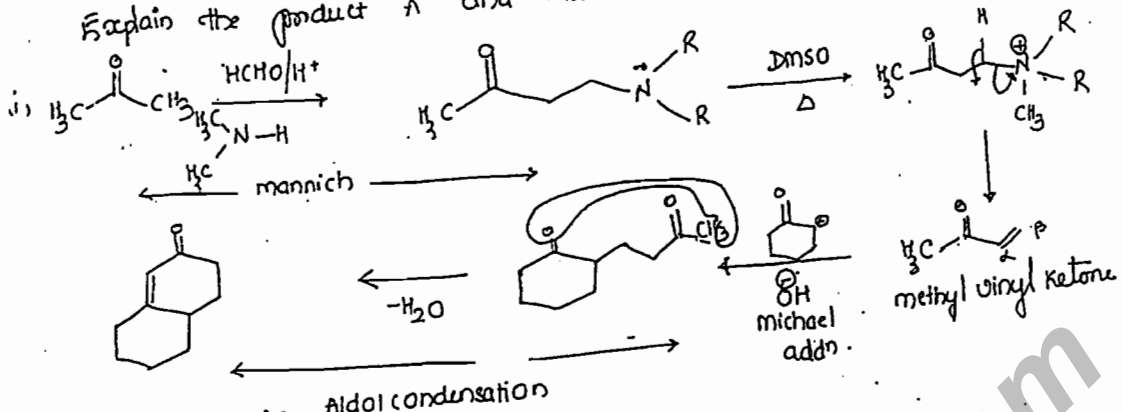


Tropinone

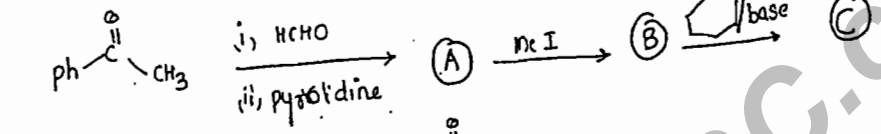
Eg: Mannich reaction + Michael addition + Aldol-reaction.



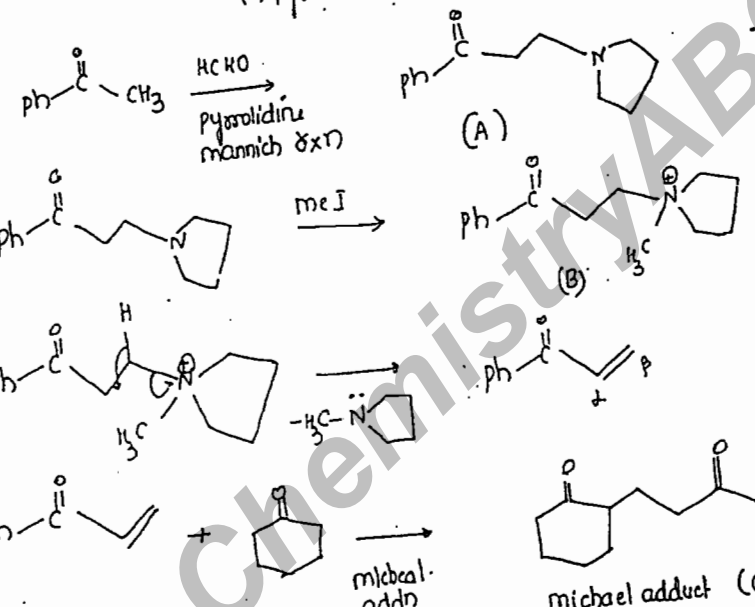
Explain the product A and the conversion.

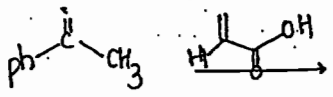


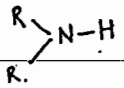
Eg:

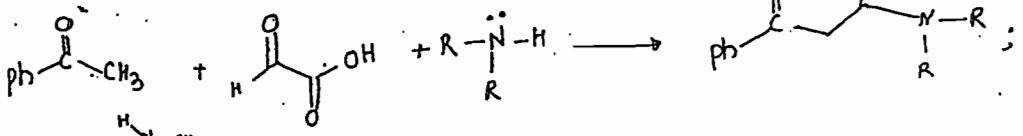


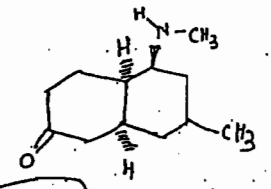
Ans

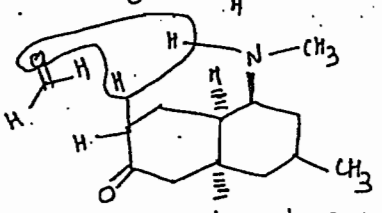


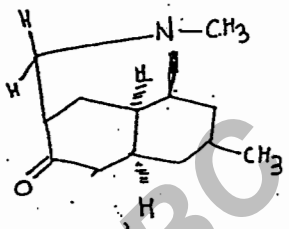
Eg:  Product



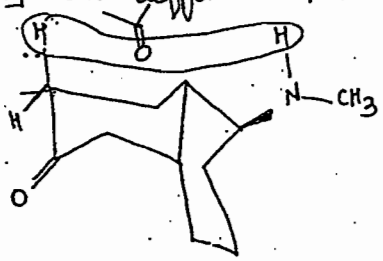


Eg: 



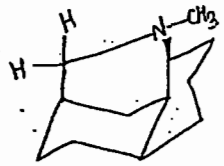


Same eg with different representations.



2-decalone

cis-decalin

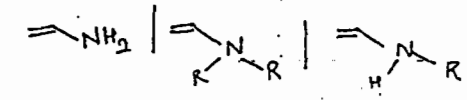


28/04/08
TUESDAY

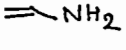
STORK – ENAMINE REACTION

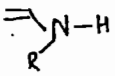
Enol = vinylalcohol  ENE + OL = ENOL

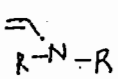
Enamine

Enamine = ENE + Amine 

amino olefin's

1° Enamine : 

2° Enamine : 

3° Enamine : 

Preparation of Enamine :

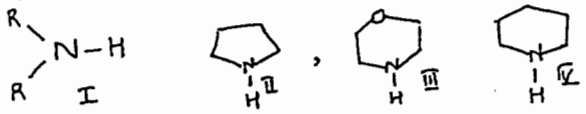
Carbonyl compound + Amine $\overset{H^{\oplus}}{\rightleftharpoons}$ Enamine

→ Enamine formation is reversible.

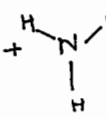
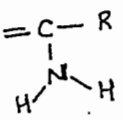
Carbonyl compound should be atleast with one α-Hydrogen.

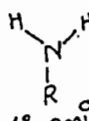
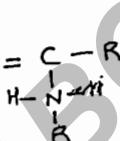
→ $R-\underset{\alpha\text{-position}}{CH_2}-\overset{O}{\overset{\|}{C}}-R$ + Amine (acyclic or cyclic) $\rightleftharpoons$ Enamines.

→ Enamines from 2° amines are stable

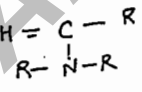
Amines : 

Reactivity order : I > II > III > IV

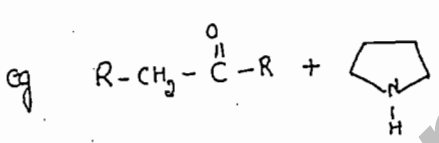
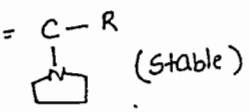
eg: $R-CH_2-\overset{O}{\overset{\|}{C}}-R$ +  $\overset{H^{\oplus}}{\rightleftharpoons}$  1° enamine (unstable)

eg: $R-CH_2-\overset{O}{\overset{\|}{C}}-R$ +  $\overset{H^{\oplus}}{\rightleftharpoons}$  unstable.

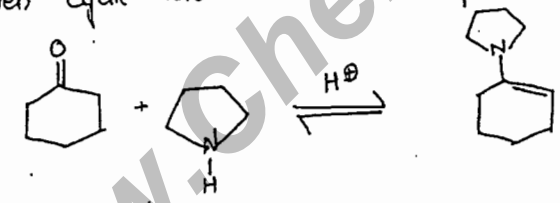
1° amine

eg: $R-CH_2-\overset{O}{\overset{\|}{C}}-R$ +  $\overset{H^{\oplus}}{\rightleftharpoons}$  (stable)

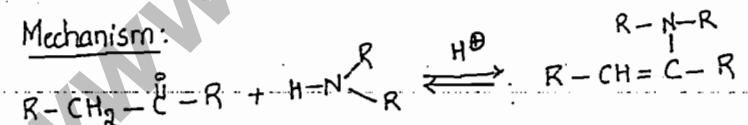
2° amine.

eg  $\overset{H^{\oplus}}{\rightleftharpoons}$  (stable)

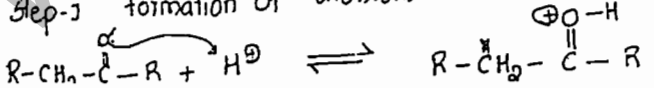
Even cyclic ketones also readily forms enamines.

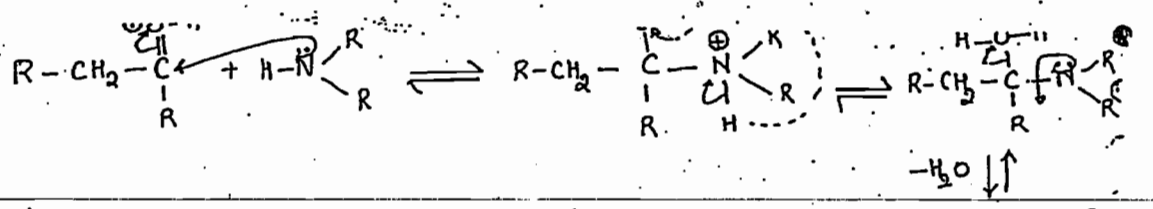


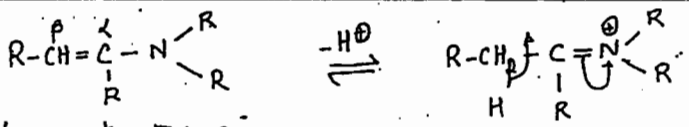
Mechanism :



Step-1 formation of oxonium ion.





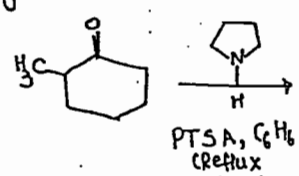


α,β-unsaturated amines (Enamine)

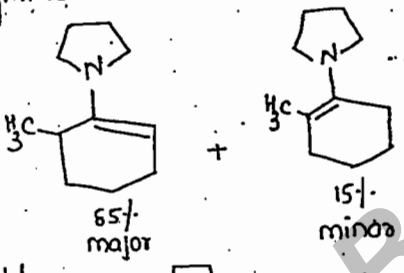
Regioselectivity :

In the case of unsymmetrical Ketones; Enamine formation is regioselective

v.imp **

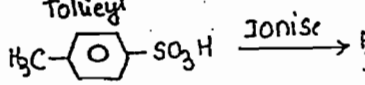


PTSA, C_6H_6 (Reflux)

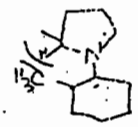


65% major + 15% minor

para Toluene Sulphonic acid (or) para-Toluyl Sulphonic acid



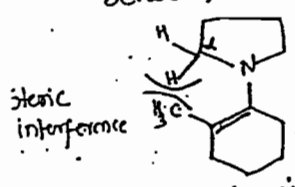
→ Unsymmetrical Ketones forms mixture of Enamines in unequal ratio. Enamine which is less substituted major or predominat product i,e orientation of double bond preferentially at less substituted α-position of carbonyl compound.



→ Reason :

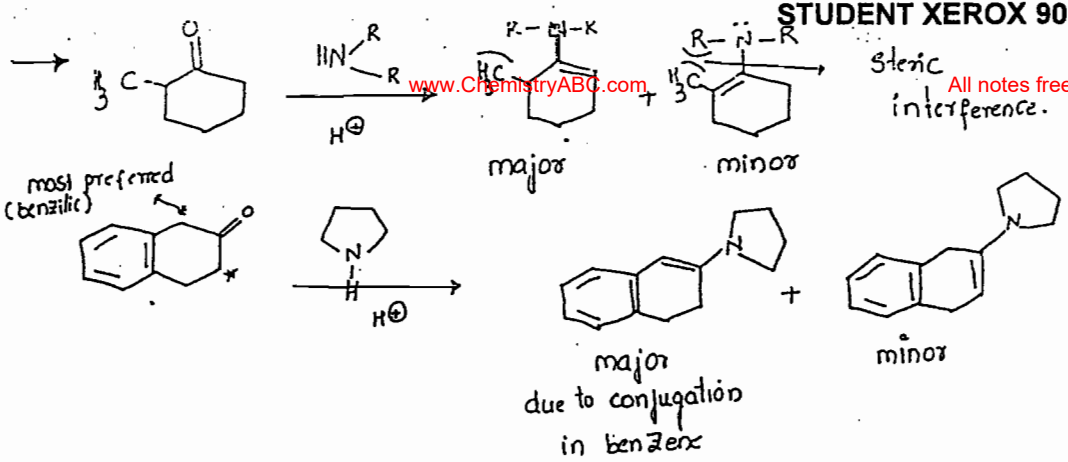
→ Major enamine free from steric interference, because unsaturation (double bond) with small size H

→ In minor enamine there is a steric interference between Bulkier methyl substituent of olefin and α-methylene group of Ammine Nitrogen, decreased Resonance or conjugation between lone pair of Nitrogen and π-unsaturation.



Steric interference

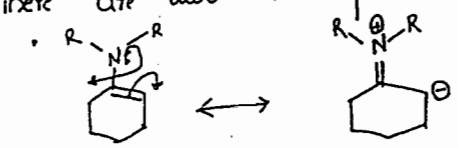
unstable ∴ MINOR



STORK - ENAMINE REACTION :

→ Electrophilic attacking at enamine is Stork enamine reaction

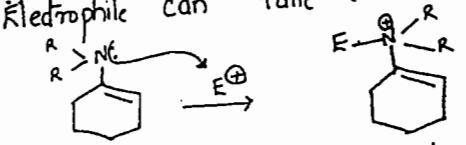
→ There are two Nucleophilic centres in enamine.



Nitrogen is Nucleophilic Centre.

Carbon Nucleophilic centre

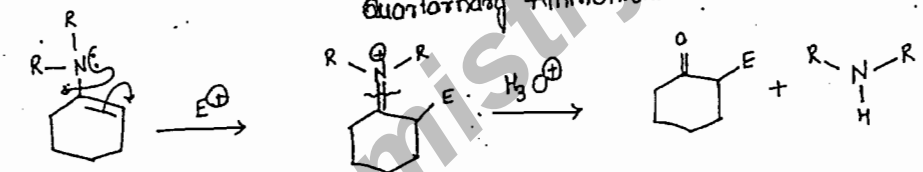
→ Electrophile can take (attack) at these two positions.

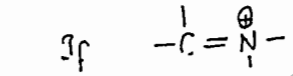


Quartornary ammonium.

→ dissolves in H_2O

→ not useful for organic synthesis.



If  → Emonium ion and

Emine on Hydrolysis in acidic water decomposes into carbonyl and amine functic

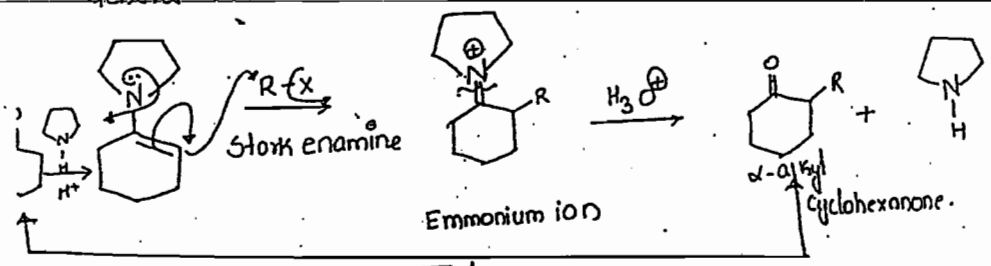
This rxn is useful for organic synthesis

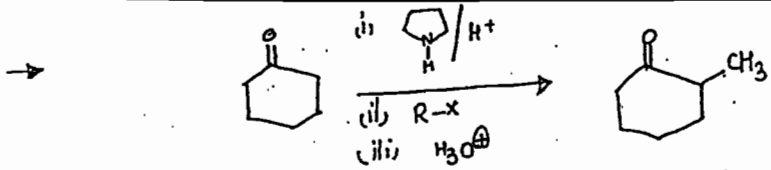
→ In Stork enamine the reaction's taking place at carbon Nucleophile useful for organic synthesis because develops new C–C bonding

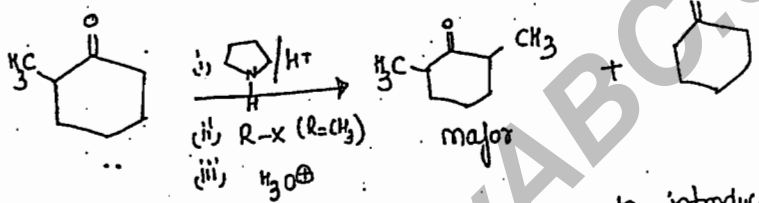
Best Electrophiles:

Eg: Carbon electrophiles: $\overset{\oplus}{C}H_3$, $\overset{\oplus}{C}(=O)-R$, $\overset{\oplus}{C}H_2-Ph$, $\overset{\oplus}{C}H_2$

General rxn:

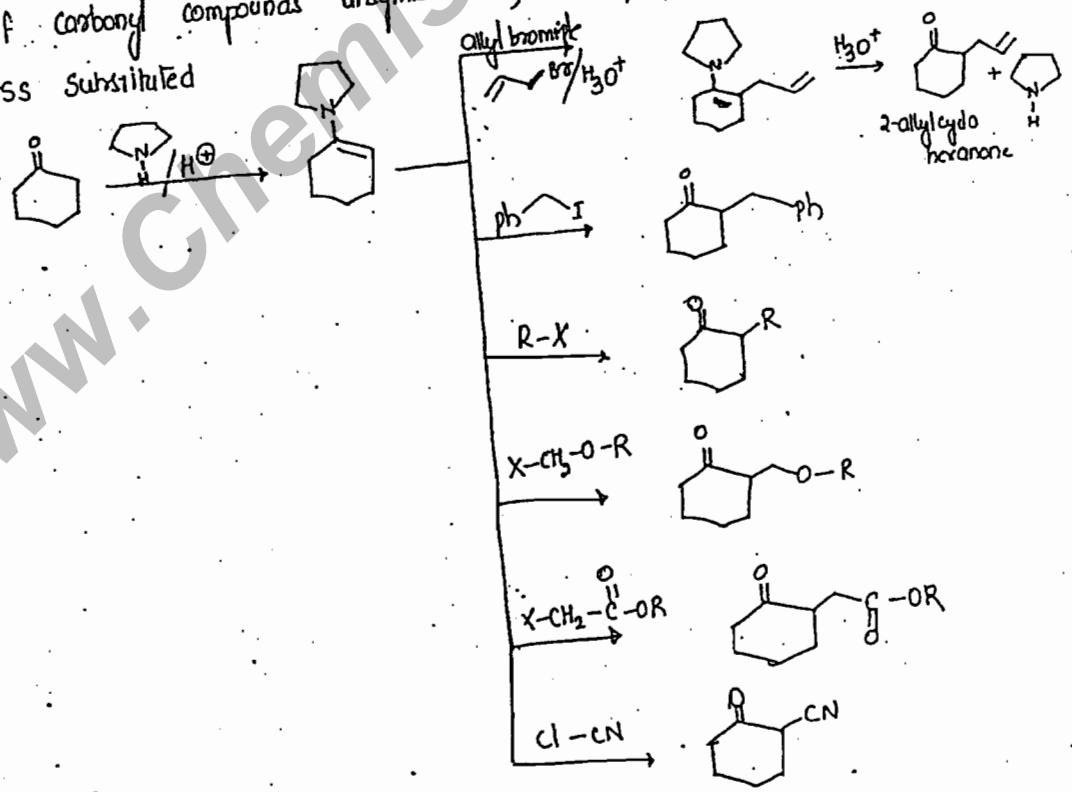


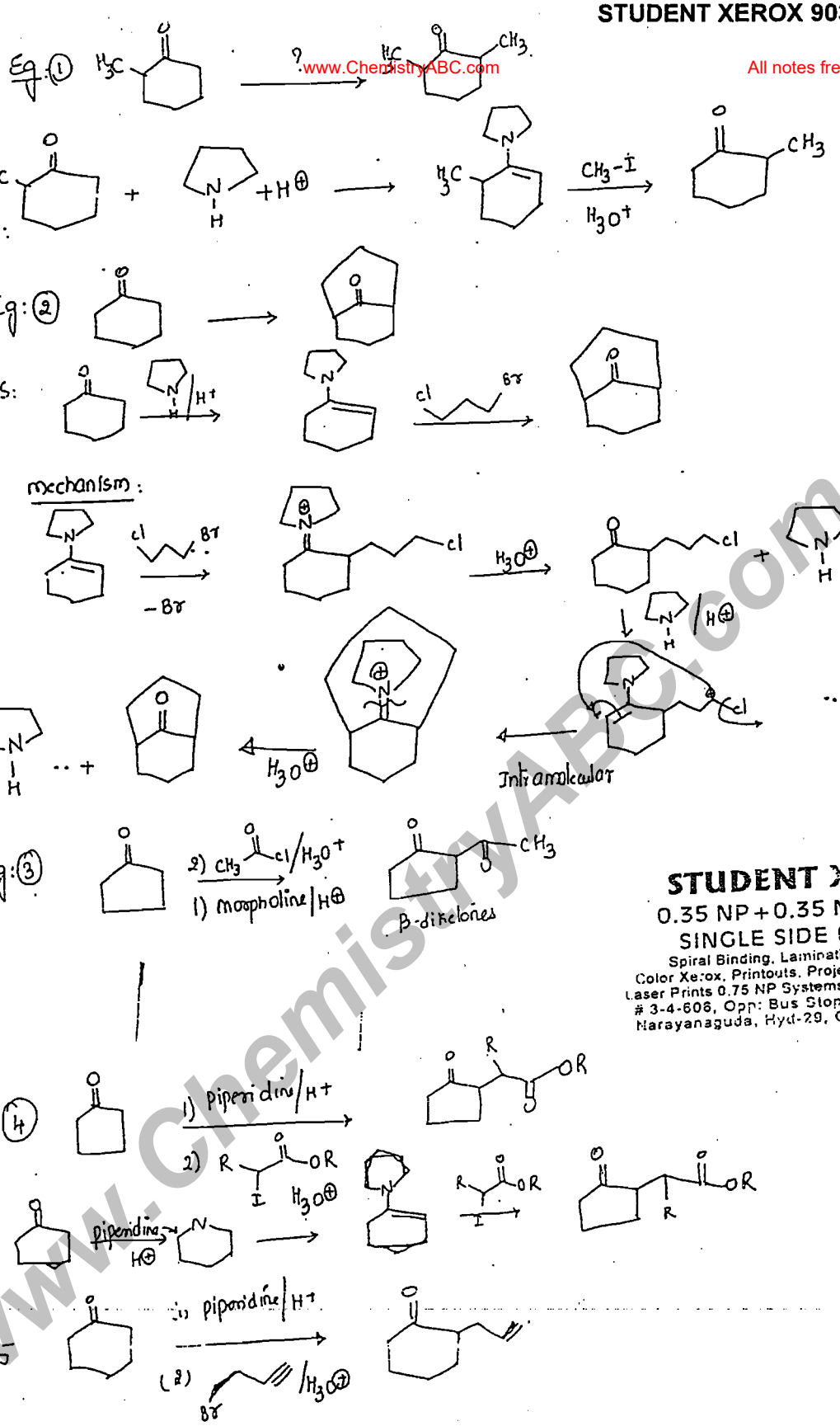




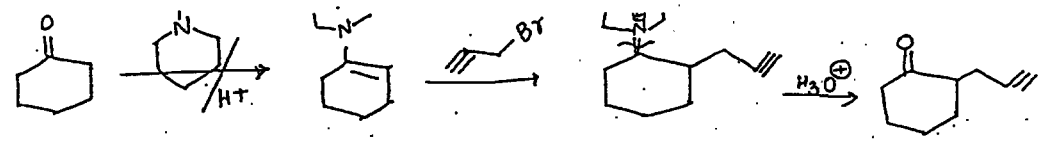
→ Stork enamine rxn's are indirect methods to introduce electrophilic carbon groups at α-position of carbonyl compounds.

→ If carbonyl compounds unsymmetrical, Electrophilic attacking preferentially at less substituted

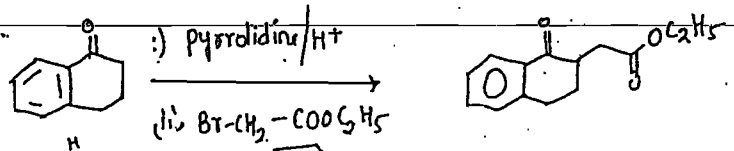




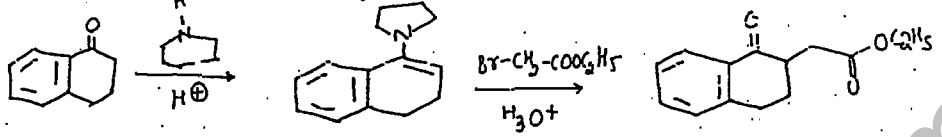
Ans.



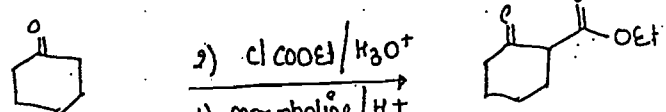
Eg: (6)



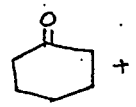
Ans:



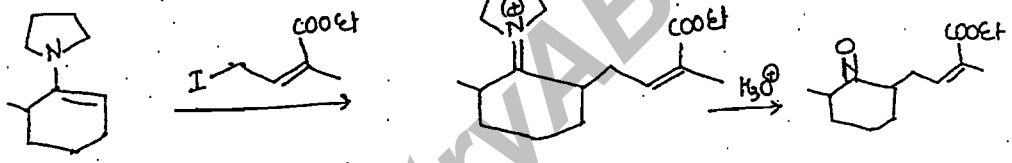
Eg: (7)



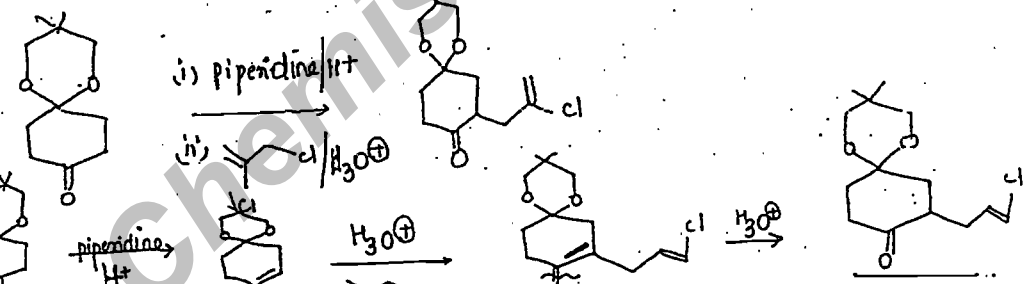
Ans:



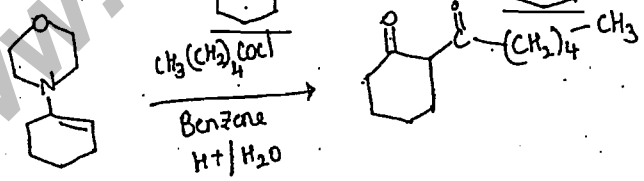
Eg: (8)



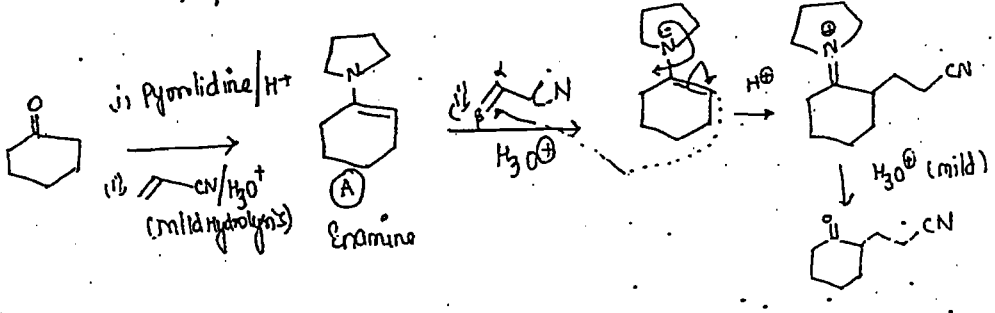
Eg: (9)

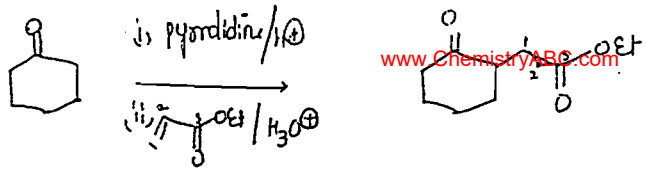


Eg: (10)

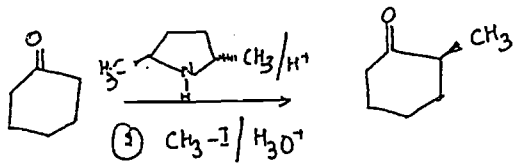


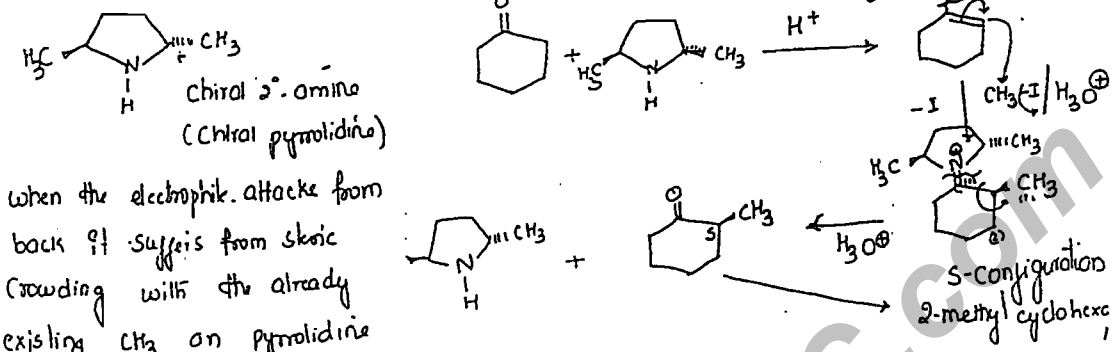
Eg: 11





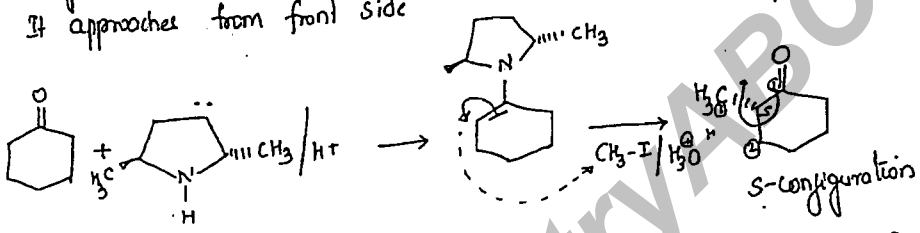
v. Unsymmetric stork enamine rxn:





→ When the electrophile attacks from back it suffers from steric crowding with the already existing CH_3 on pyrrolidine

∴ It approaches from front side



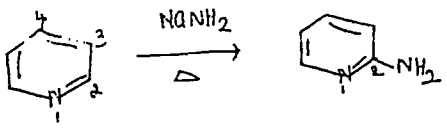
→ Whether double bond orientation at right / left side of Enamine resulting product is same.

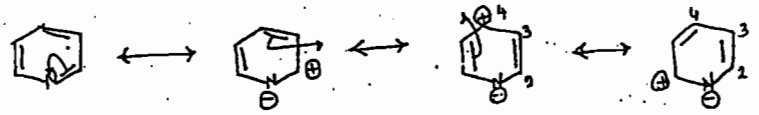
CHICHIBABIN – REACTION:

→ Amino methylation at Nitrogen Heterocyclic by using sodium or potassium amides at high temperature is called chichibabin reaction.

→ It is aromatic Nucleophilic substitution.

Very good Nitrogen Heterocyclic for chichibabin rxn is pyridine.

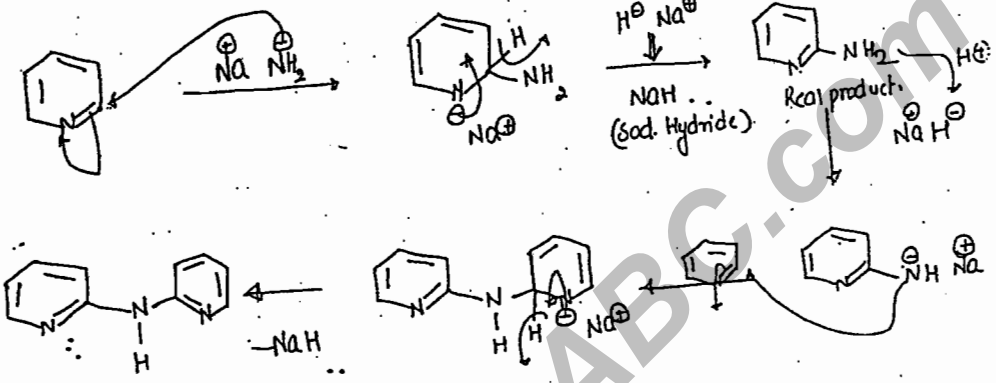




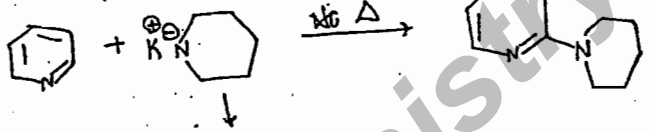
→ most predominantly Nucleophilic substitution takes place at C_2 than C_4 because of nearest −I effect. C_3 position is not at all Electrophilic.

Mechanism:

Eg:1

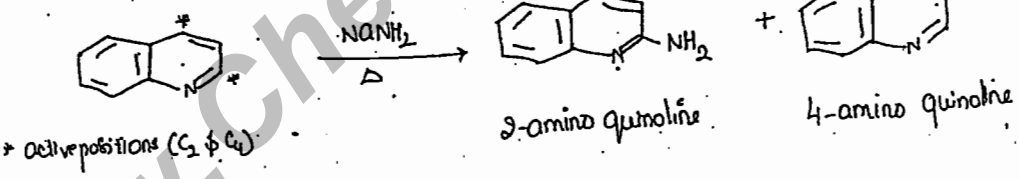


Eg:2



potassium piperidine

Eg:3

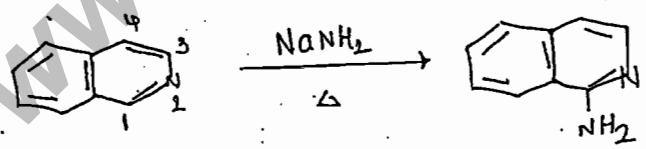


* active positions (C_2 & C_4)

2-amino quinoline

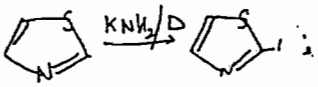
4-amino quinoline

Eg:4

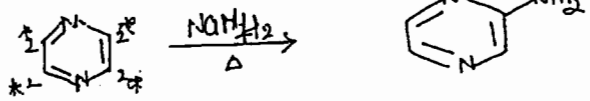


Iso-quinoline

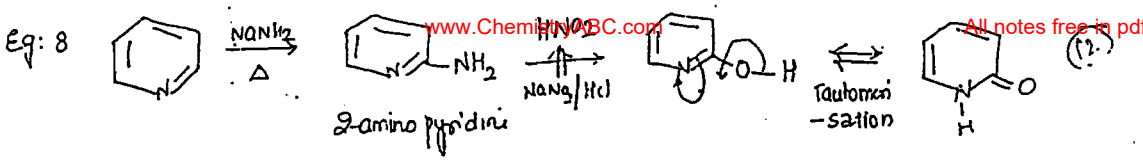
Eg:6

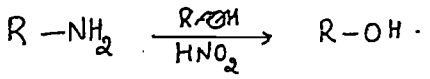


Eg:5



Eg: 8





imp. * SHAPIRO – REACTION :

→ Indirect conversion of carbonyl compound into olefin.

Carbonyl compound $\xrightarrow{TS\text{-}NHNH_2}$ Tosyl hydrazone $\xrightarrow[\text{2 eqts of strong base}]{\Delta,\ H_3O^{\oplus}\ (or)\ \text{Excess}}$ olefin.

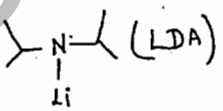
Intermediate

SHAPIRO REACTION

→ Conversion of Tosyl hydrazone of carbonyl compound into olefin with excess or 2 equivalents of strong base called shapiro reaction.

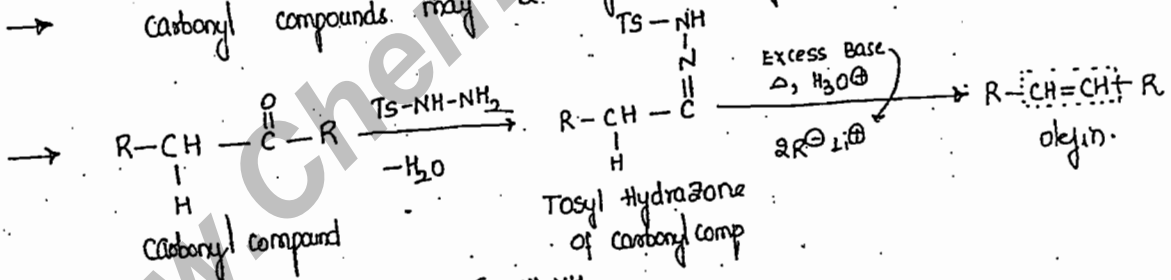
→ Strong bases : Organo dithium Compounds $R^{\ominus}Li^{\oplus}$ $CH_3^{\ominus}Li^{\oplus}$ $nBu^{\ominus}Li^{\oplus}$

R = CH_3 or n-butyl

Soda mide, ($NaNH_2$) dithium di-iso propyl amide  (LDA)

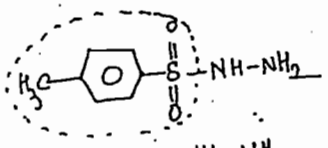
Limitation : Carbonyl compounds should be with al.least with one hydrogen atom at α- position.

→ carbonyl compounds may be cyclic or acyclic

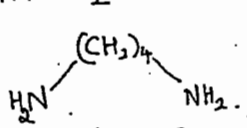
→ 

→ $R-CH_2-\overset{O}{\overset{\|}{C}}-R \xrightarrow[\text{ii) 2eq of } R^{\ominus}Li^{\oplus}]{\text{i) } TS\text{-}NH\text{-}NH_2}{\text{iii) } \Delta,\ H_3O^{\oplus}} R-CH_2-CH-R$

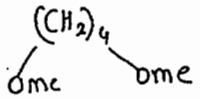
Mechanism :

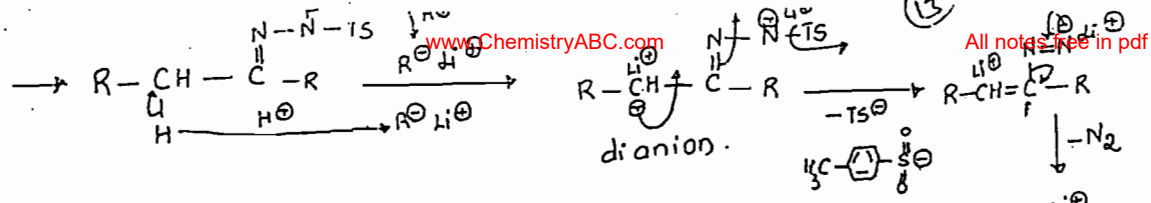
TS-NH-NH$_2$ = 

TS – NH – NH$_2$.

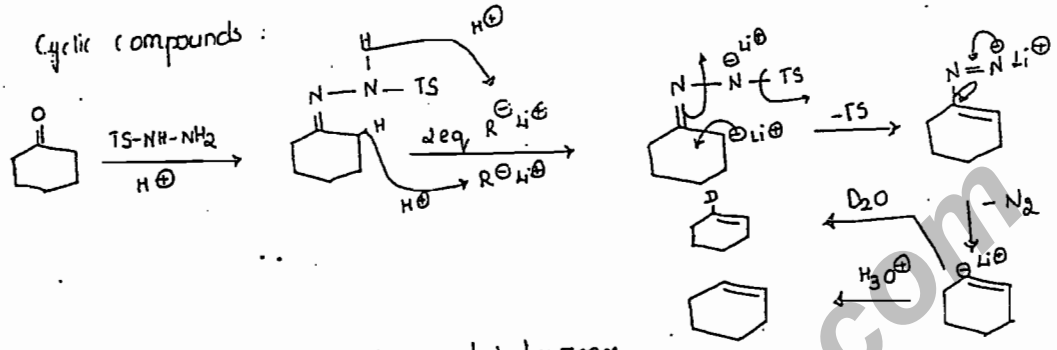
Solvents : Highly polar solvents : 

Tetra methylene diamine



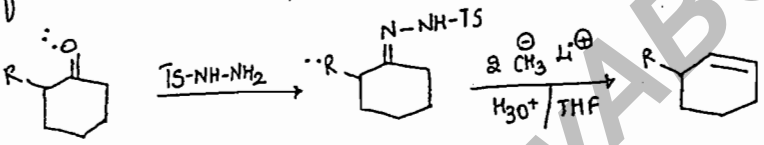


→ Cyclic compounds :

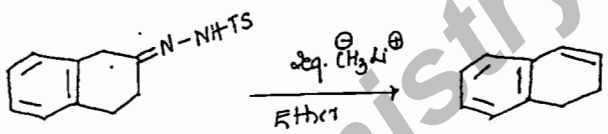


→ In case of unsymmetrical tosyl hydrazones, preferential orientation of double bond at less substituted α-position.

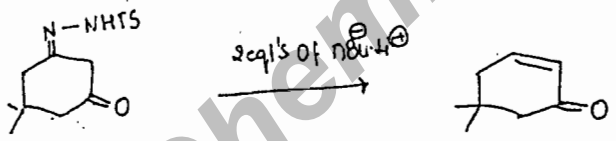
Eg: 1



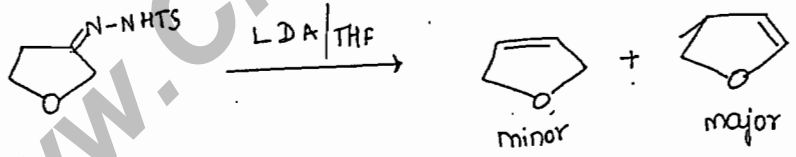
Eg: 2



Eg: 3

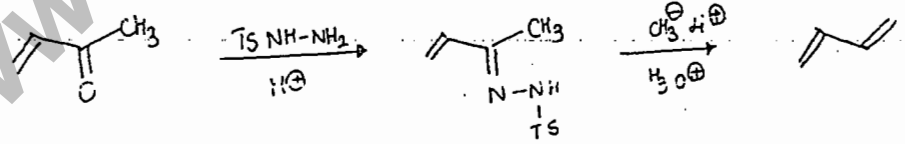


Eg: 4



→ major due to conjugation.

Eg: 5



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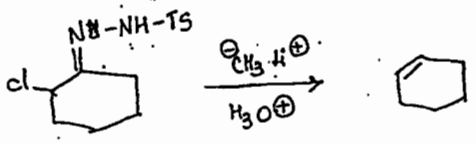

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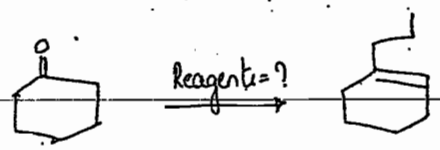

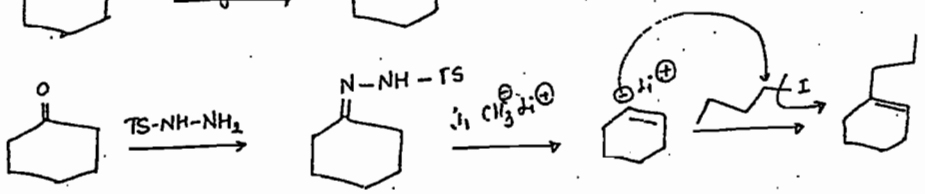

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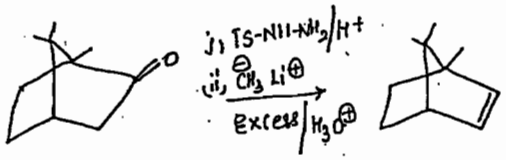
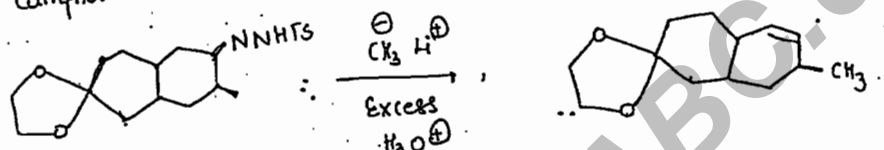


Camphor

Eg:



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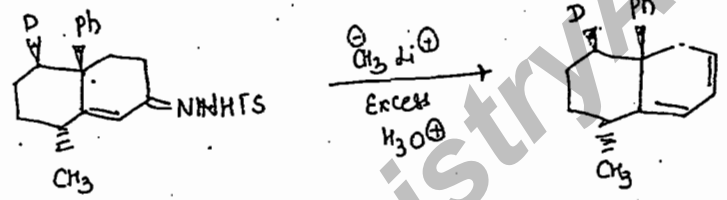
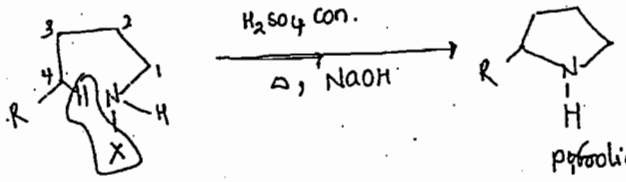


HOFMANN – LOEFFLER – FREYTAG REACTION: HLF – REACTION

→ Conversion of N-Halo amines having at least one hydrogen atom at C_4 or C_5 positions into 5, or 6-membered Nitrogen heterocyclic in acidic medium under Thermal or photochemical rxn's called HLF reactions

N-Halo amine having C_4-H/C_5-H —(conc. 1) H_2SO_4/F_3CO_2H 2) Δ/hν 3) NaOH)→ Saturated 5/6-membered heterocyclic Nitrogen.

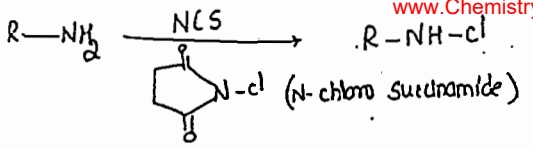
Eg:

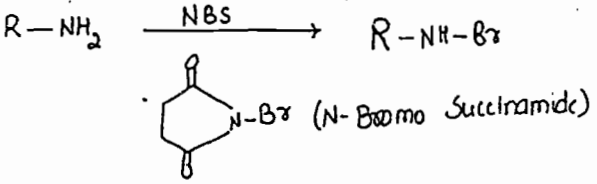


X = mostly Cl, Br

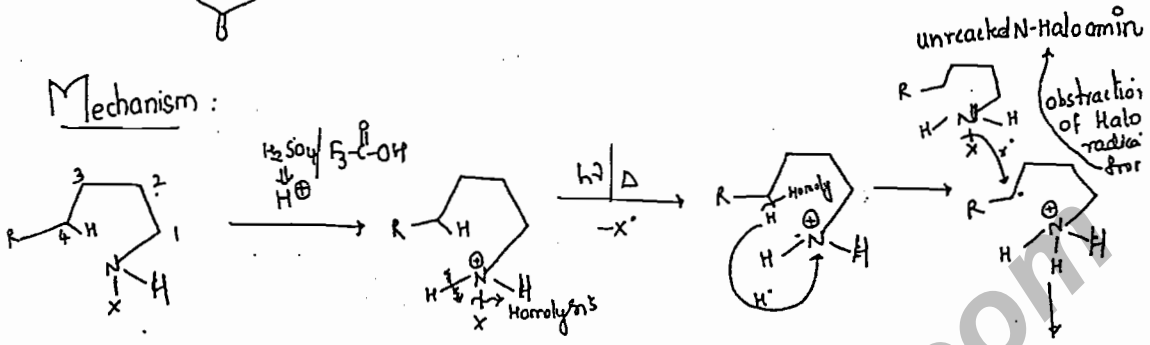
pyrrolidine

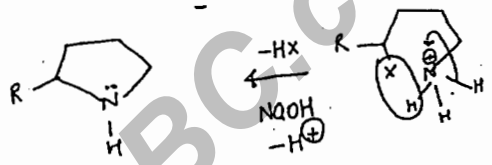
Preparation of N-halo amine





Mechanism :





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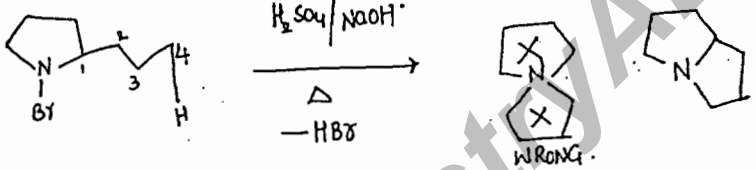
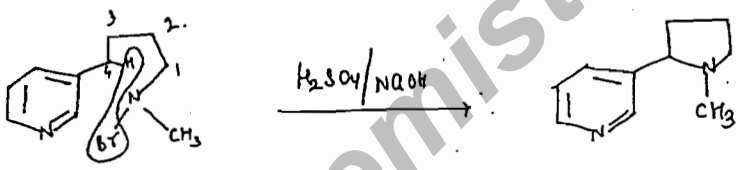
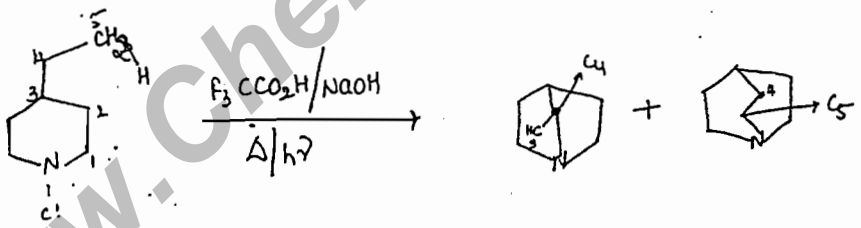


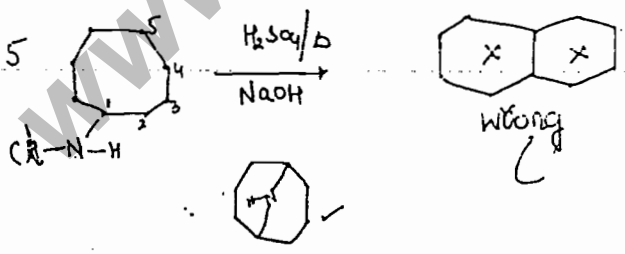
Eg: 2

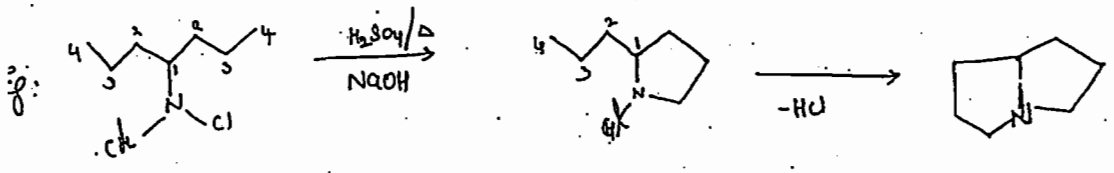


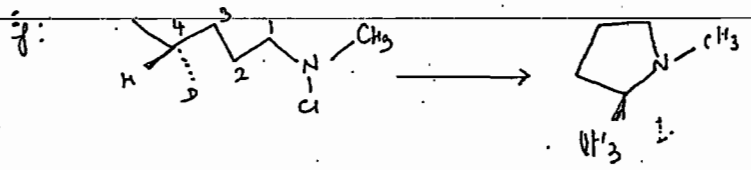
Eg: 3

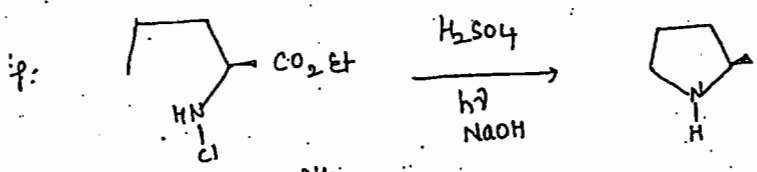


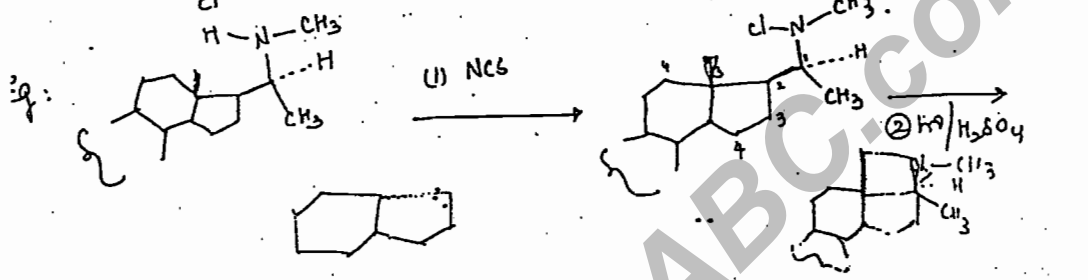
Eg: 5

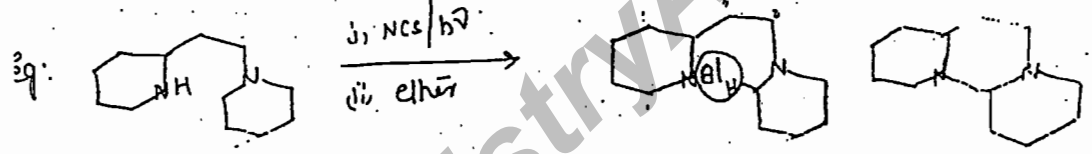


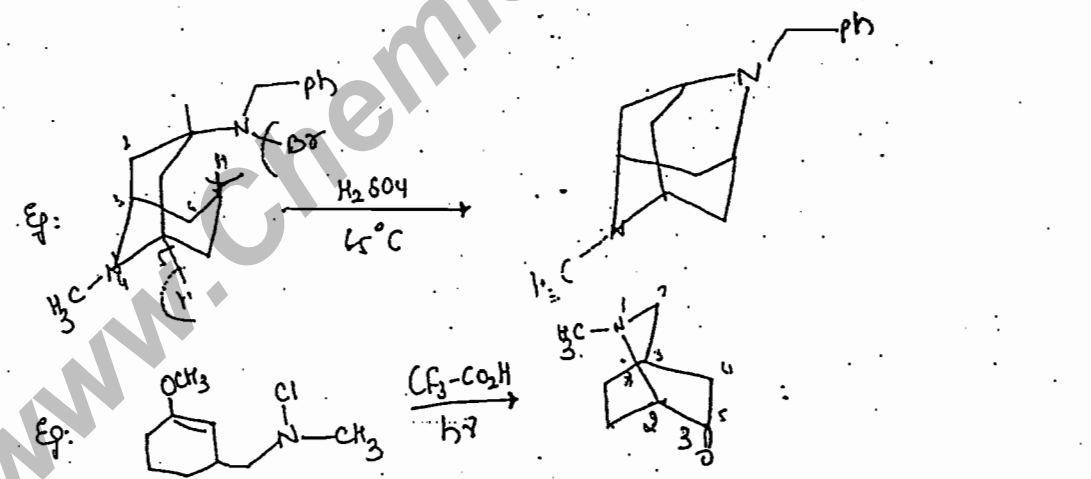










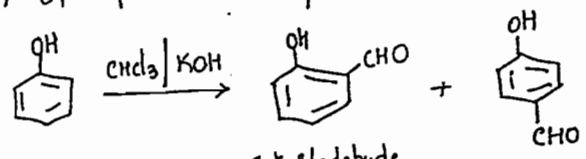


Paper - I Named reactions

Wed 23/04/08

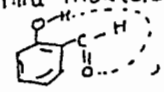
1) RIEMER – TEIMANN REACTION:

formylation of phenolic compounds with $CHCl_3$ / KOH, NaOH



Salicyladehyde ← structural isomers → These two products formed with unequal ratio's ∴ The rxn is Regioselective.

→ Intra molecular hydrogen bonding is developed by ortho product due to Intra M.H ortho have low B.p and can be separated by steam distillation.

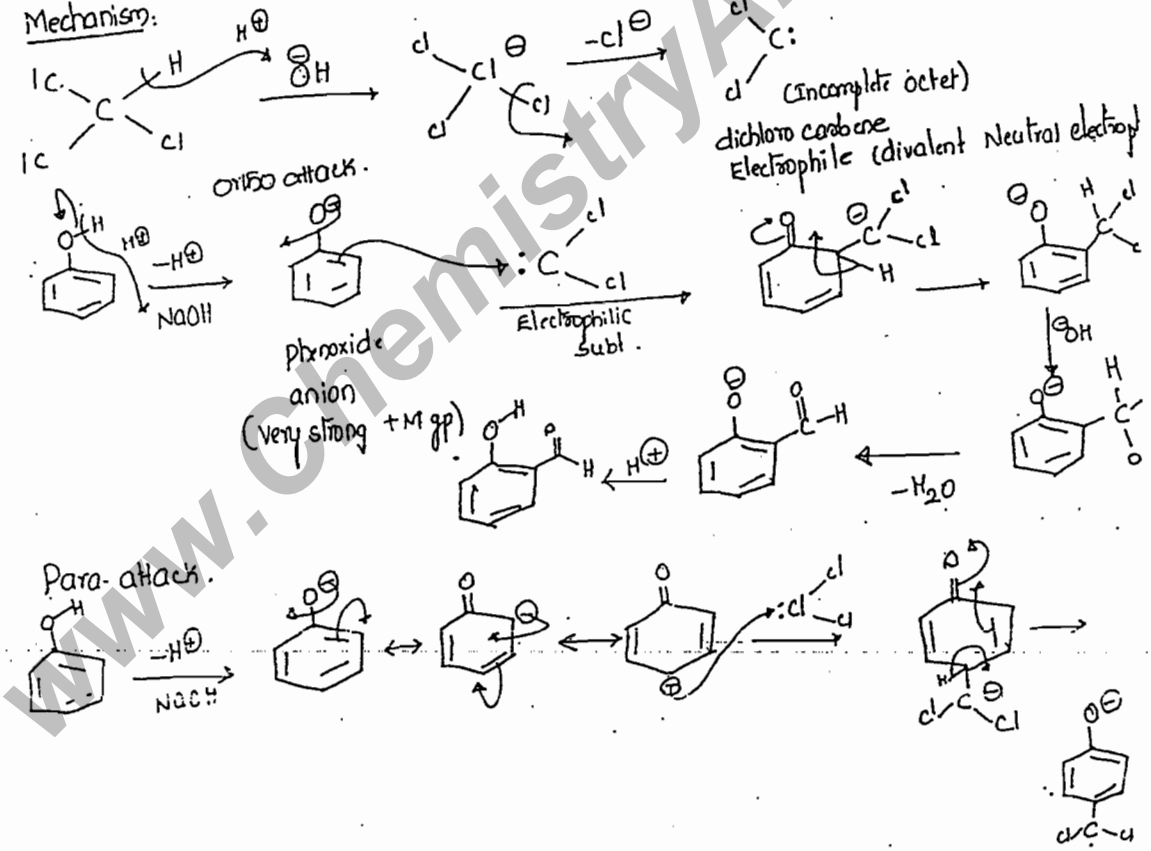


→ Where as para cannot. But para - develop Inter molecular Hydrogen bonding Due to Inter M.B, it has High boiling point.

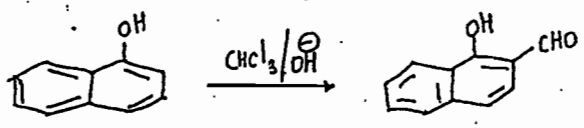
→ I.R can distinguish bolh Intra & Inter molecular Hydrogen bonding.

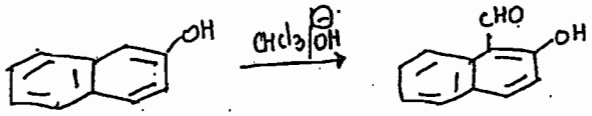
→ Product can be identified by 2,4 - DNP reagent. Reactant will not give +ve test for 2,4 DNP where as products show +ve Test.

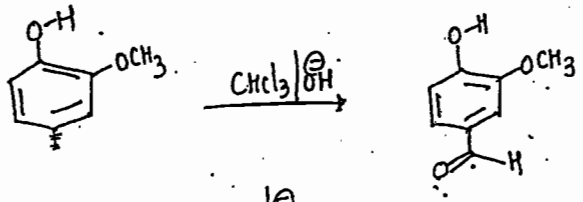
Mechanism:

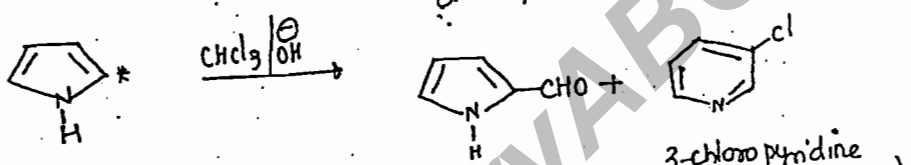


→ New C-C bond formation
→ Intermediate is dichloro carbene
→ It is an Electrophilic Substitution rxn.
→ Involvement of phenoxide anion.
→ It (Riemer-Tiemer rxn) is base catalysed rxn.

Eg: 2. 

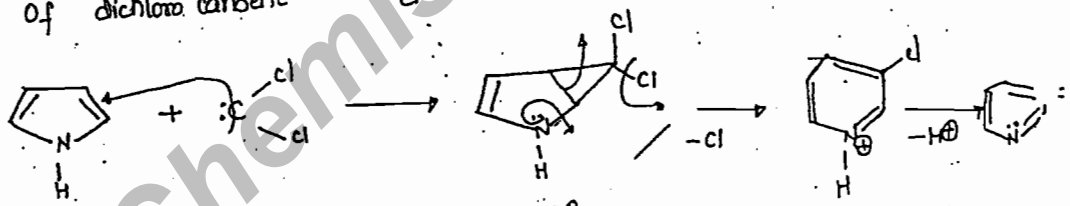
Eg: 3 

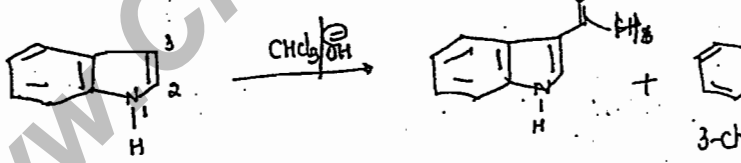
Eg: 4 

Eg: 5 

3-chloro pyridine (unexpected product)

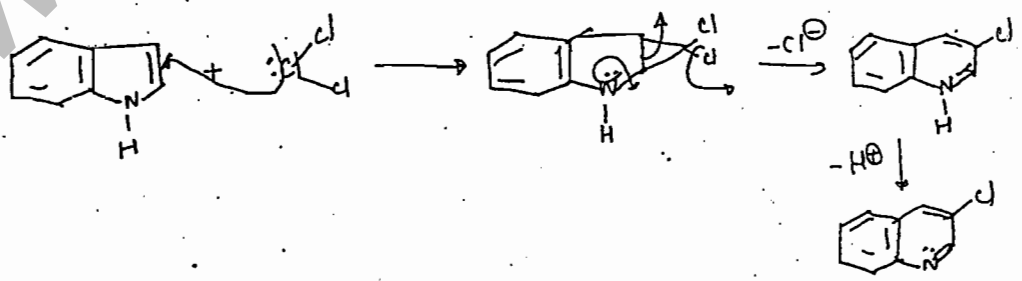
The unexpected product is due to the addition rxn of dichloro carbene on double bond of pyrrole



Eg: 6 

Indole

3-chloro Quinoline (unexpected product)

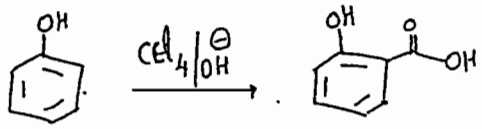


Q) Anisole and Aniline will not undergo R. T. Reaction, why.

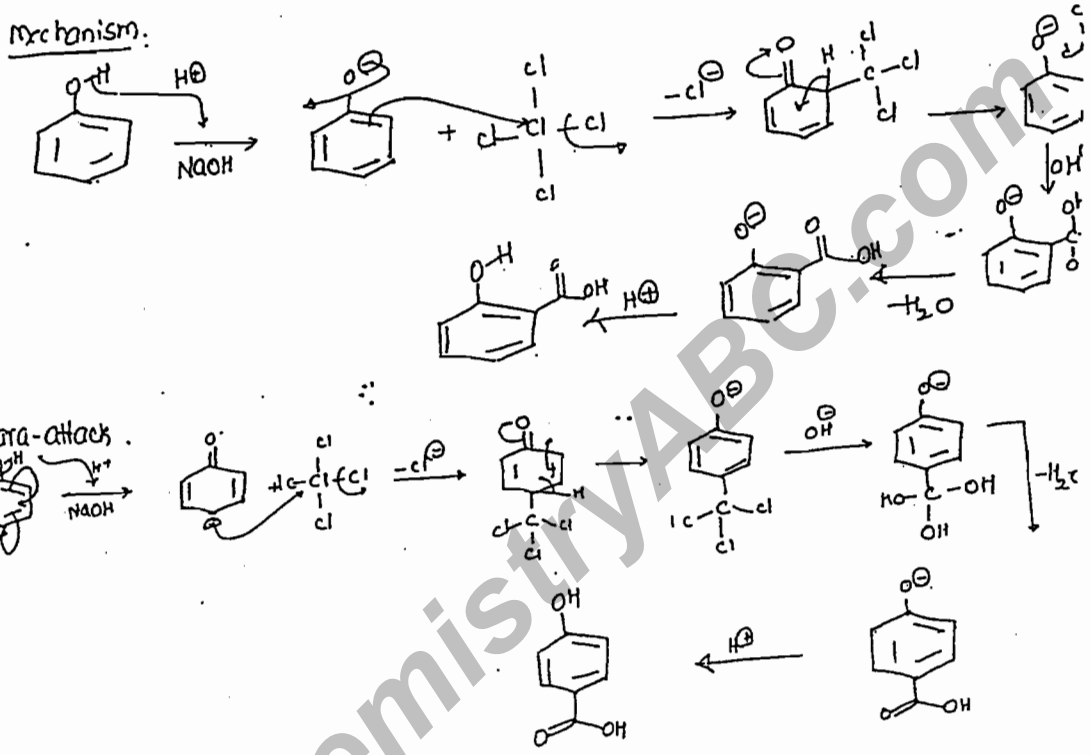
1) Anisole  It will not produce phenoxide ion ∴ (1b)

It cannot undergo R. T. Rxn.

Aniline  → It reacts with carbene and form Isocyanide

Eg: 

Mechanism:



Para-attack.

PERKIN'S REACTIONS:

→ Carbon-Carbon bond formation.

→ Nucleophilic addition at Carbonyl Compounds

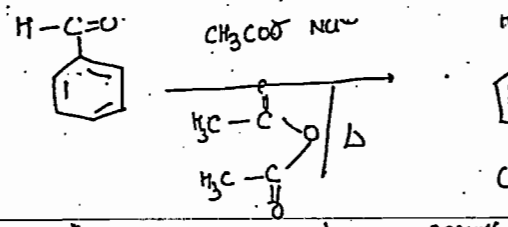
→ Carbanion intermediate

→ High temperature

→ Salt of Carboxylic acid / Anhydride

→ Conversion of aromatic Acid Hydrid. Aldehydes in to α,β-unsaturated Acid

Imp Salt of Acid / Anhydride

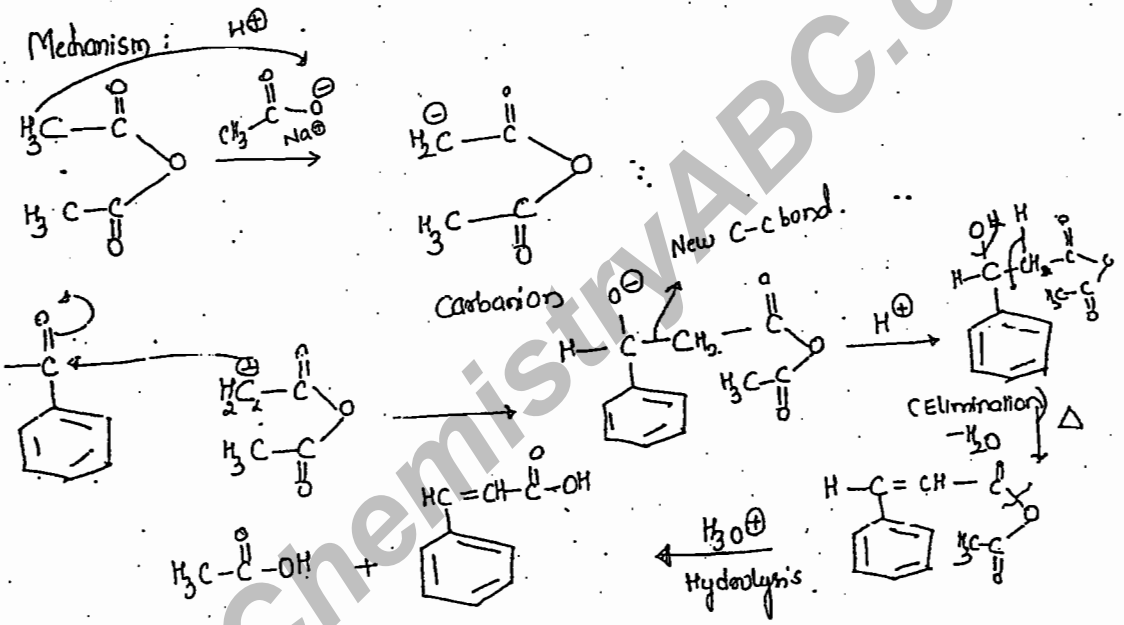
Eq:1 

CINNAMIC Acid

→ New C-C bonding formation occurs at carbonyl carbon and α-position of anhydride

→ Salt of carboxylic acid act as base abstracts a proton.

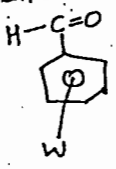
→ If anhydride not used salt of carboxylic acid acts as Nucleophilic centre

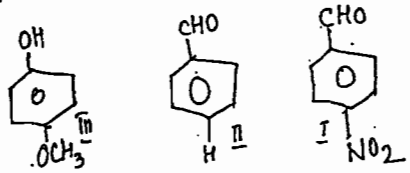
Mechanism : 

→ Cinnamic acid decolourises Br_2/H_2O and $KMnO_4$

→ Elimination followed by hydrolysis is perkin's rxn.

→ Base catalysed thermodynamically controlled product.

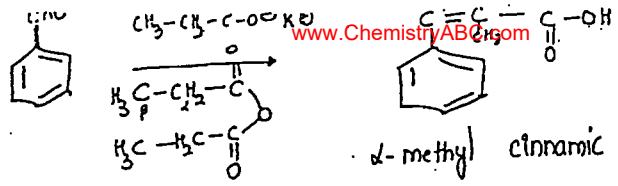
Presence of W.D.G's at aromatic skeleton of aldehyde increases the rate of perkin rxn's. 



Reactivity :

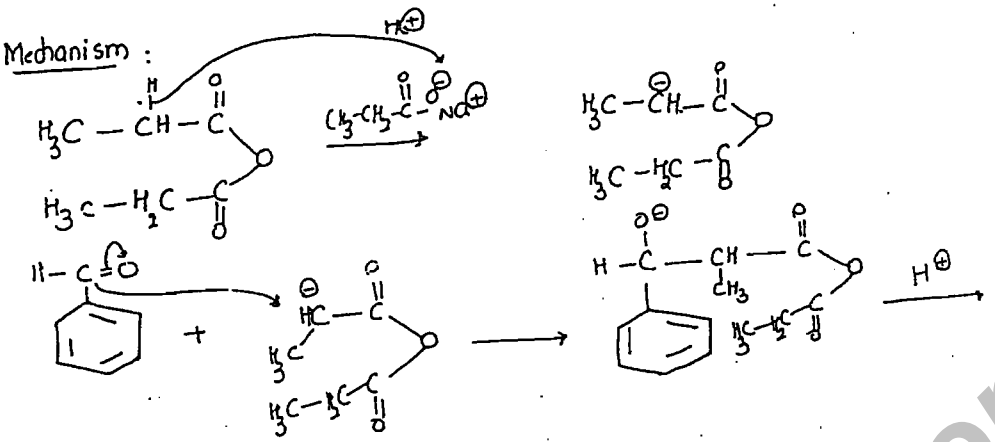
I > II > III

Eg: 2

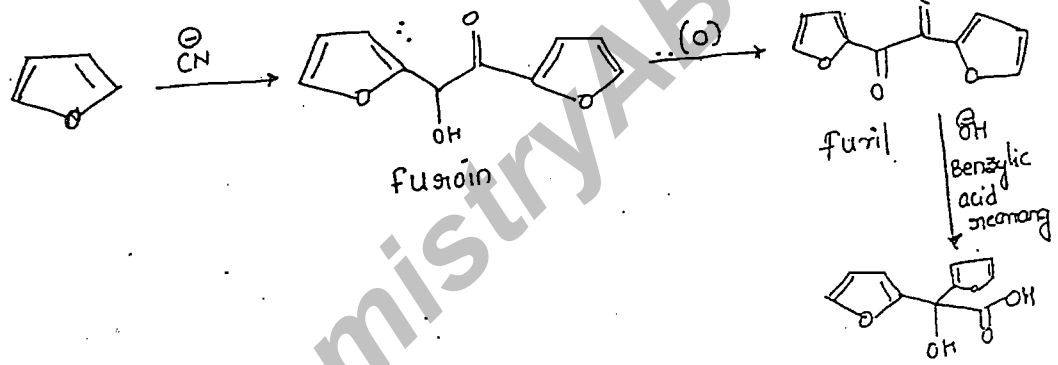


α-methyl cinnamic acid.

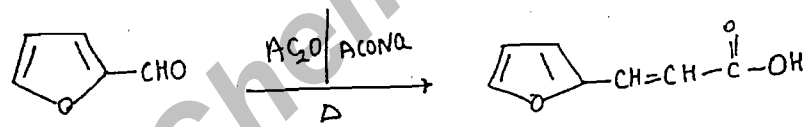
Mechanism :



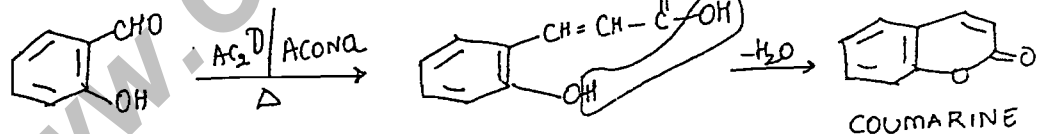
Eg:



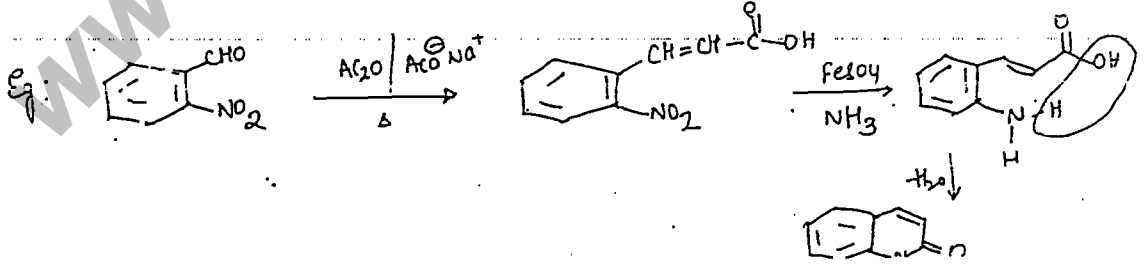
Eg:



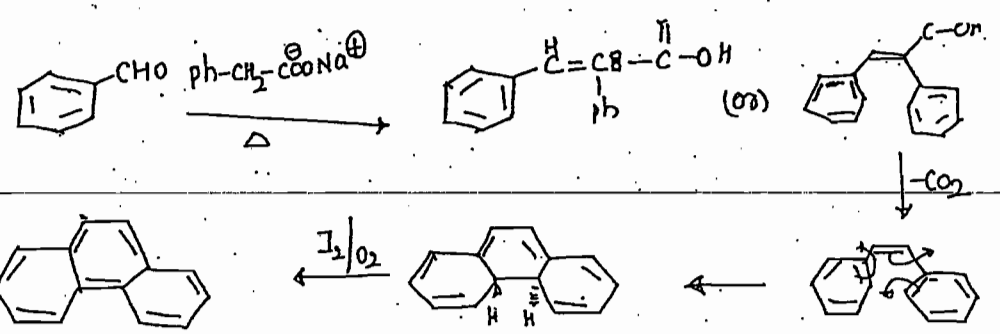
Eg:



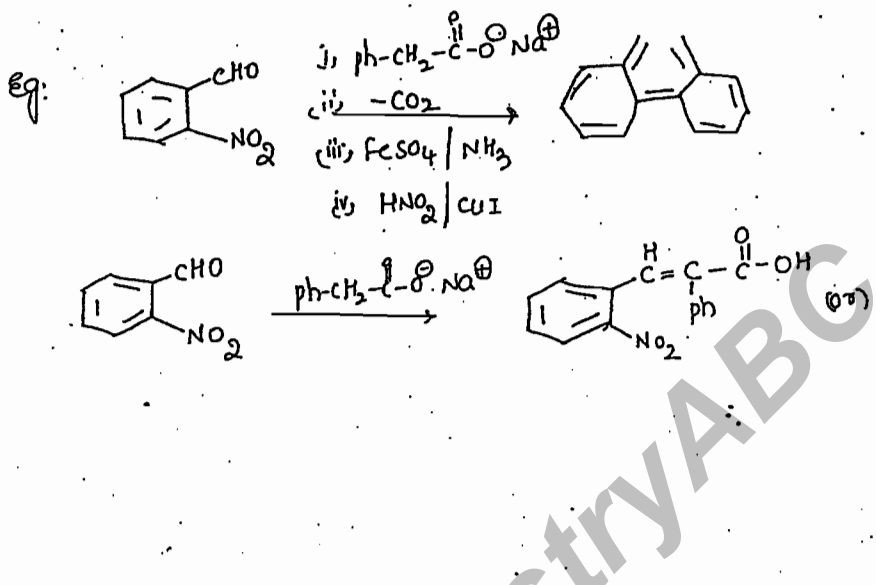
Eg:



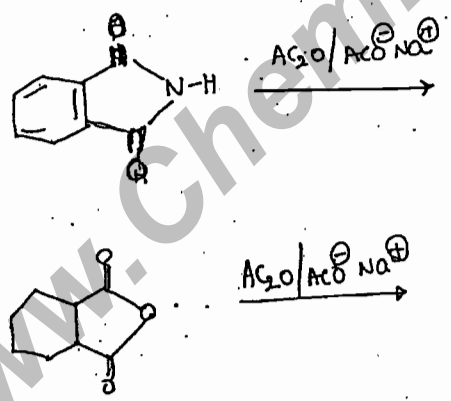
Eg:



Eg:



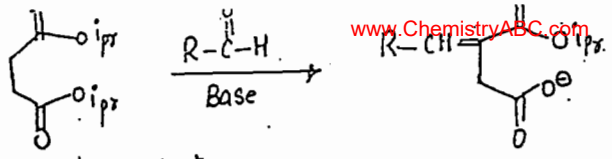
Eg:



STOBBE CONDENSATION:

→ Addition and elimination is called Condensation.

→ Condensation of aldehydes or ketones, at α-position of dialkyl Succinate in basic medium is called stobbe condensation.



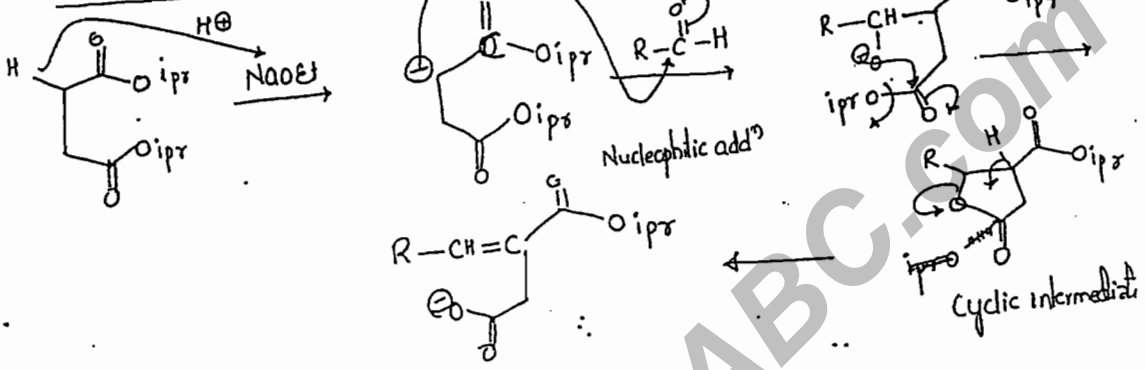
diisopropyl succinate

→ condensation at α-position of ester.

→ one of the ester group get Hydrolysed (ester not attached to double bond hydrolysed.

→ Bases used: NaOEt, NaH_2 $NaNH_2$:

Mechanism :

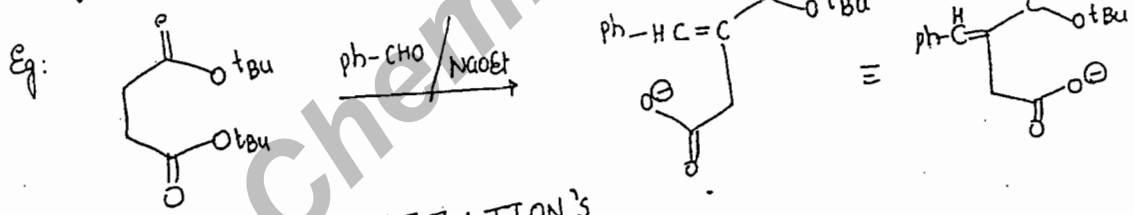


Carbanion intermediate

Nucleophilic addition at carbonyl function

Cyclic ester intermediate, C–C bond formation.

Eg:

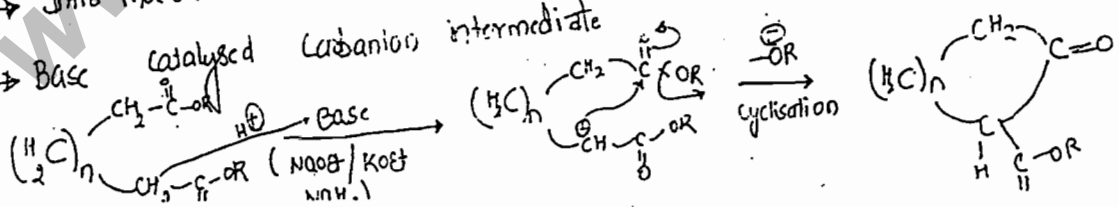


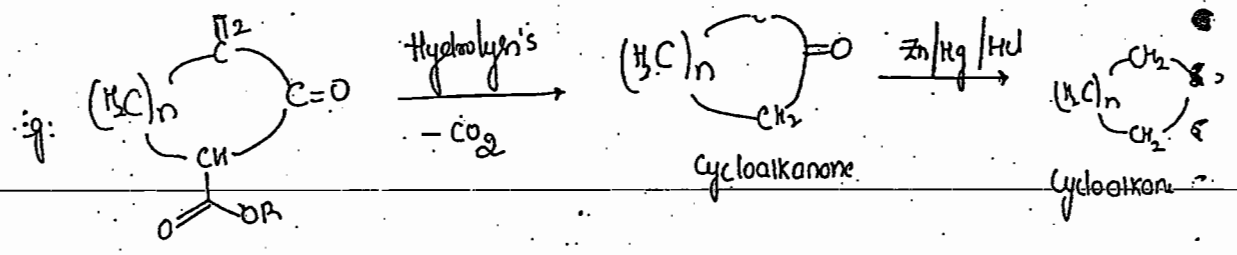
DIECKMAN'S CYCLIZATION'S

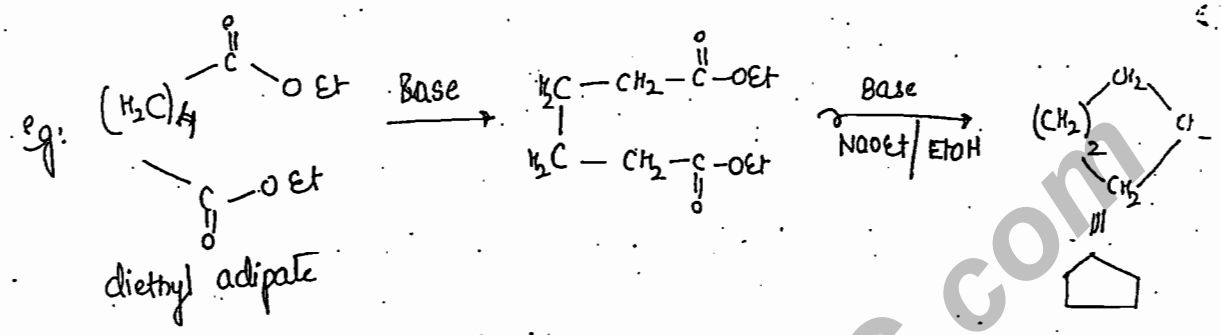
→ Method for Synthesis of Alicyclic compounds Bases: $NaNH_2$, 3° Amine

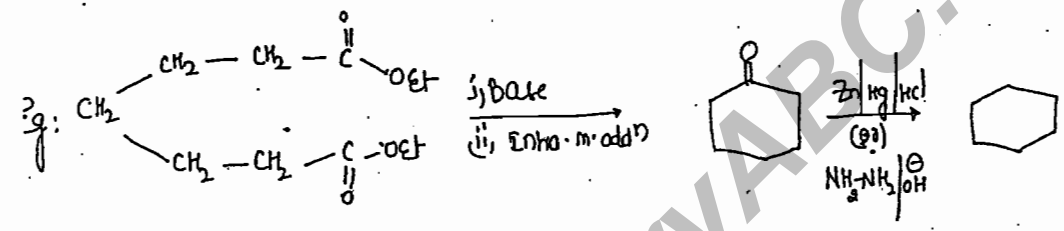
→ Intra molecular condensation reactions

→ Base catalysed Carbanion intermediate

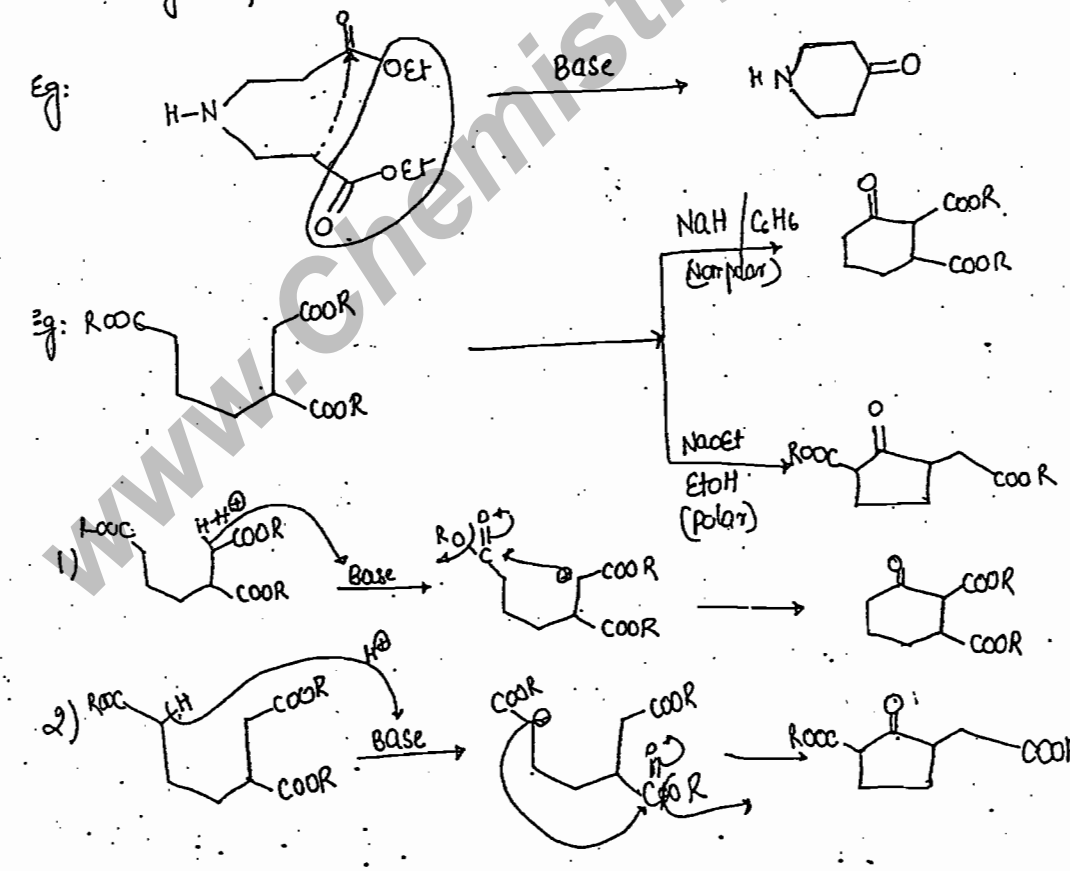








Pet-ether
Hexane
Benzene
Chloroform
Ethyl

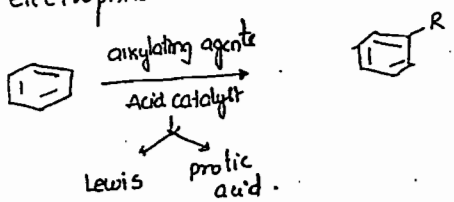


FRIEDEL-CRAFTS ALKYLATION:

→ Introducing of alkyl group at aromatic skeleton using alkylating agents in the presence of lewis acids or protic acids are friedel crafts alkylations.

→ C-C bond formation, Electrophilic substitutions.

→ Attacking electrophile carbocation.



→ Alkylating agents : (i) Halo alkanes → best, widely used and common.
(ii) Cycloalkane (Cyclopropane)
(iii) Alcohols
(iv) Epoxides
(v) alkenes, alkynes
(vi) Carboxylic acids.

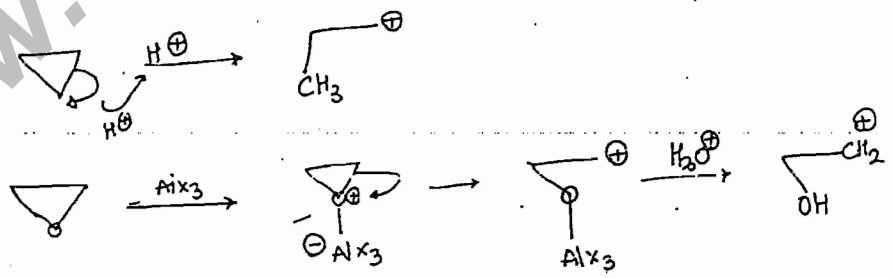
→ Lewis Acids : AlX_3, BX_3, $ZnCl_2$, $SnCl_4$, $SbCl_5$ etc.

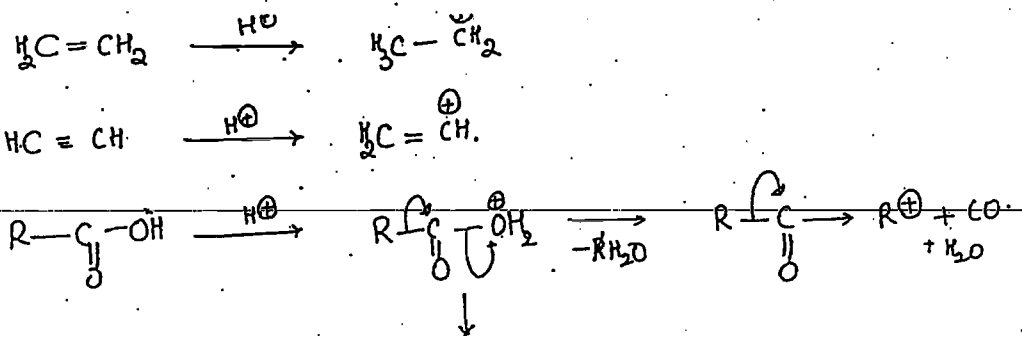
→ protic acids : H_3PO_4, polyphosphoric acid (PPA), HNO_3, H_2SO_4

→ Role of acid catalyst : Acid catalyst are helpful for ready / fast generation of carbocation intermediate from alkylating agent.

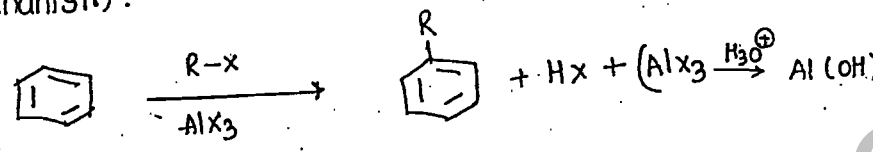
Eg: $R-X + AlX_3 \longrightarrow R-\overset{\oplus}{X}-\overset{\ominus}{Al}X_3 \longrightarrow AlX_4^{\ominus} + R^{\oplus}$

$R-OH + PPA \xrightarrow{H^{\oplus}} R-\overset{\oplus}{O}H_2 \xrightarrow{-H_2O} R^{\oplus} + H_2O$





Mechanism:

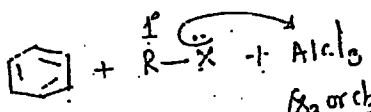


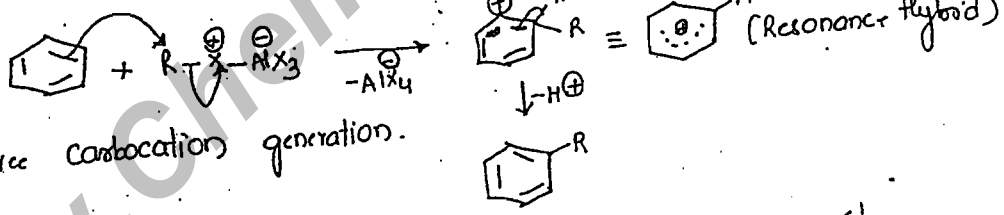
Reactivity w.r.t -Halide : R-F > R-Cl > R-Br > R-I

Reactivity w.r.t alkyl : 3°-alkyl halide > 2°-alkyl halide > 1°-alkyl halide

→ Mechanism depends on Nature of alkyl halide

→ 1°-alkyl halides friedel craft's alkylation, by generation of ion pair.



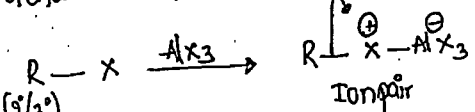


No free carbocation generation.

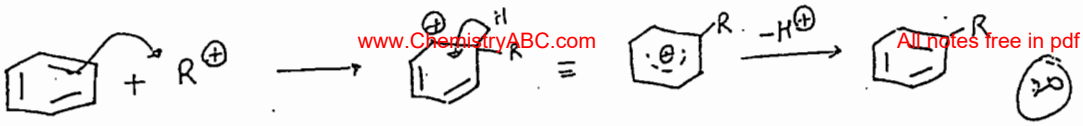
→ Attacking of Electrophile is the Rate determining step

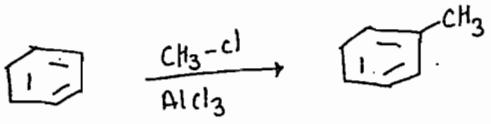
→ 3°/2° Alkyl halides.

Generates free Carbocation.



Free carbocation formation is due to stability of (2° or 3°) alkyl gp's

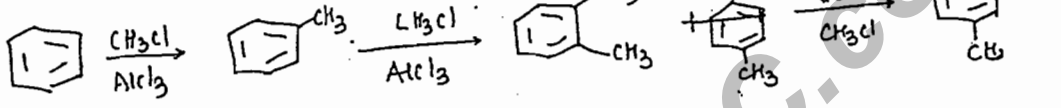


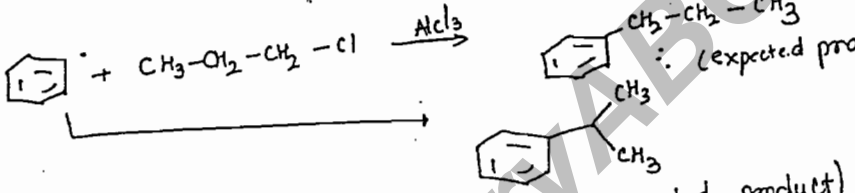
Eg: 

LIMITATIONS:

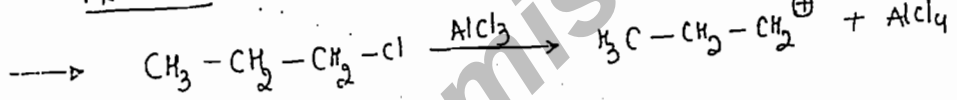
→ polyarkylation: In friedel craft alkylations, initially produced mono-alkylat product is more reactive than corraponding reactant. ∴ further alkylation takes place on mono-alkylated product, Resulting New products are poly alkylated product.

→ ∴ It is difficult to produce mono-alkylated products.

Eg: 

→ 

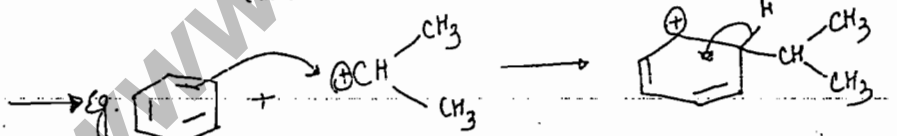
Explaination for unexpected product Mechanism:

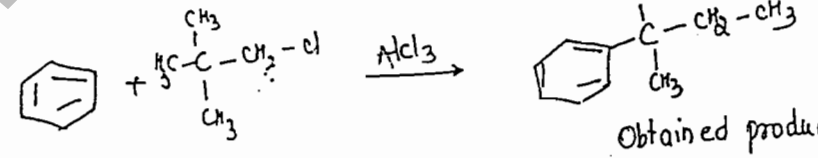
→ 

→ 

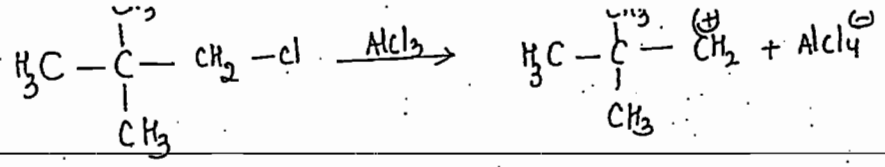
1°-Carbocation (unstable)

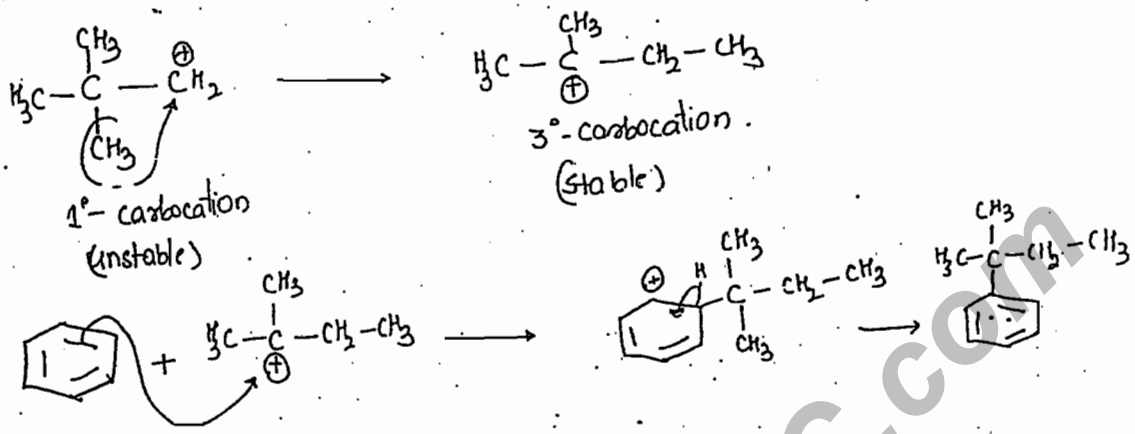
2°-carbocation (stable)

→ Eg: 

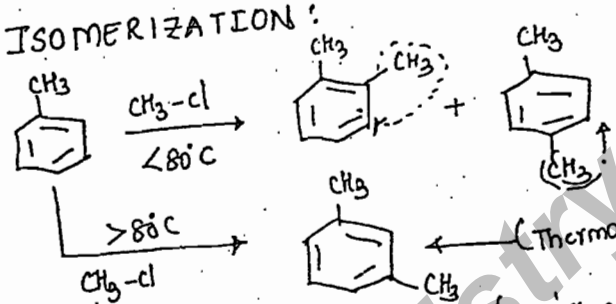
Eg: 

Obtained product.



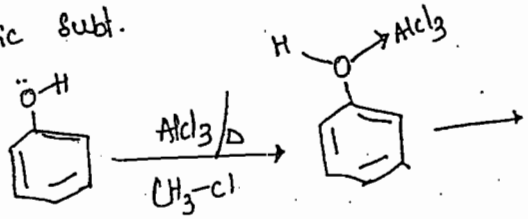


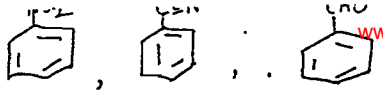
ISOMERIZATION :



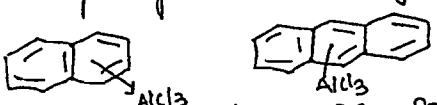
→ Probably at high temperature migration of group from ortho-para position to meta-position.

eg:  These compounds will does not undergo friedel crafts alkylation because lewis acids co-ordination with substituents make benzene less reactive towards Electrophilic subt.



→ 

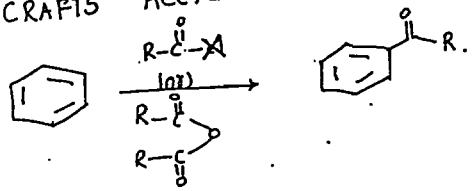
Because the substituents are electron withdrawing groups, ∴ make benzene very very electron deficient.



→ Friedel Crafts alkylation on polycyclic aromatic skeleton is difficult due to coordn of lewis acid with these aromatic polycyclic hydro-carbon.

Excess π-system makes co-ordn with lewis acid.

FRIEDEL CRAFTS ACCYLATIONS :



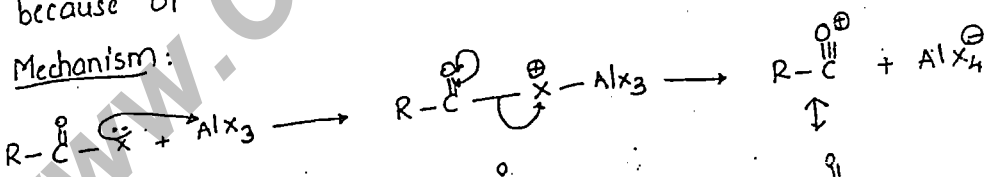
→ Best method to convert aromatic compound to ketones

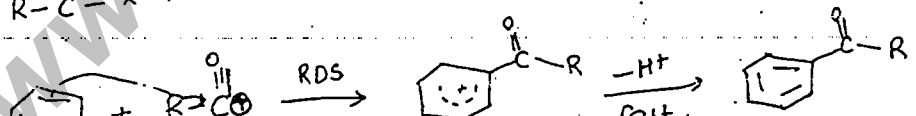
$R-\overset{O}{\overset{\|}{C}}-$ Acyl group, $H_3C-\overset{O}{\overset{\|}{C}}-$ Acetyl.

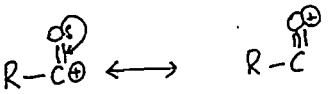
→ In friedel crafts alkylations aromatic hydrocarbon are converted into .. active compounds where as in friedel crafts acylation, the resulting product is less reactive than the reactant

→ acyl carbocation is attacking electrophile in friedel crafts acylation, these rxn's will not involve in any kind of rearrangement irrespective of R-group, because the carbocation formed is stabilised because of resonance. It doesn't involve in rearrangement.

Mechanism:





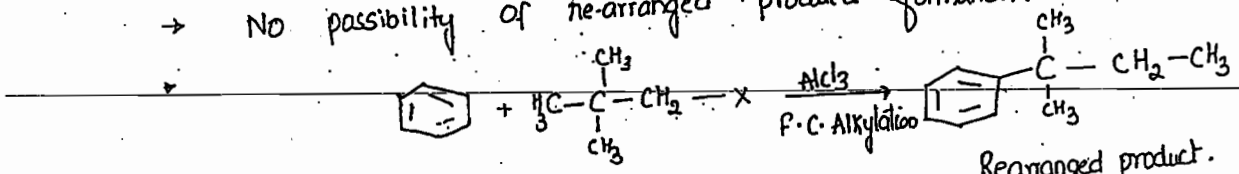


Stable due to Resonance

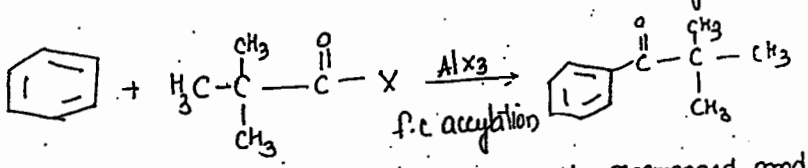
Advantages.

→ No poly acylations

→ No possibility of re-arranged products formation.



Rearranged product.



No- rearranged product

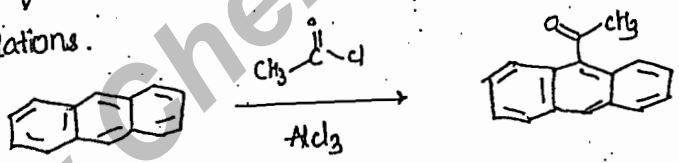
→ No isomerisations.

Limitations:

→ It is not possible to do F.C. acylation on  , because lewis acid co-ordinates with -OH, $-NH_2$ gp's and deactivates benzene.

→ Withdrawing groups attached Aromatic Skeletons also will not under f.c acylations  .

→ If specific conditions maintained polycyclic aromatic skeleton's undergo f.c acylations.



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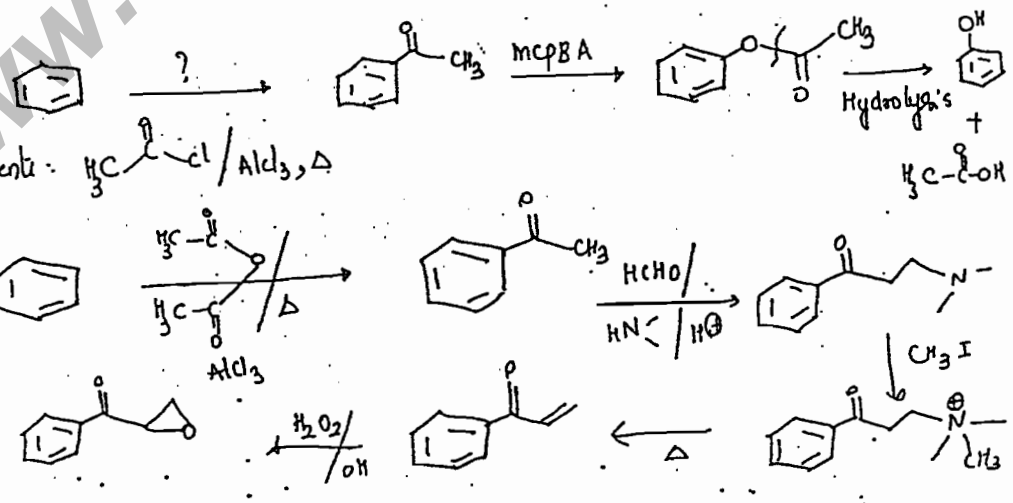
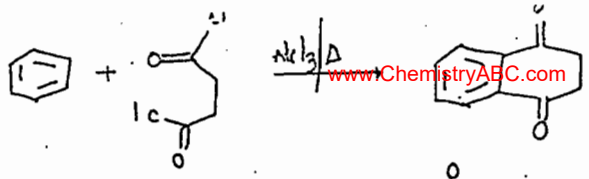
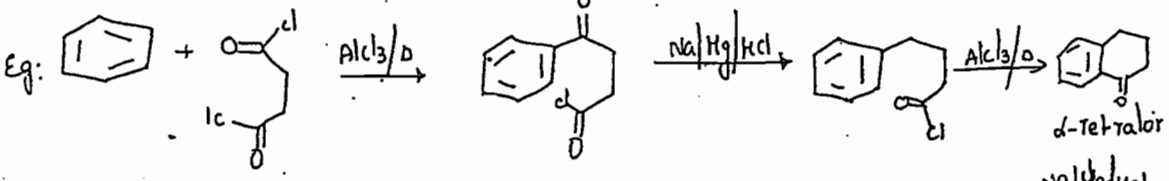
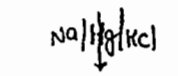
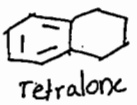
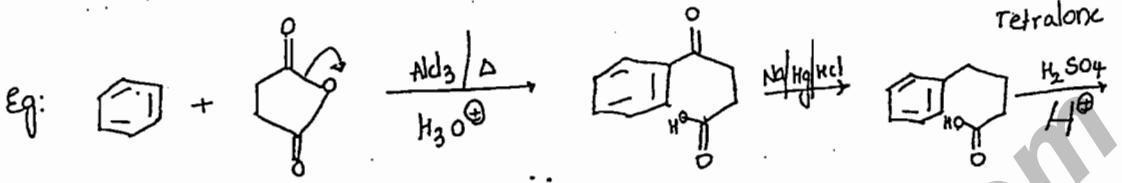


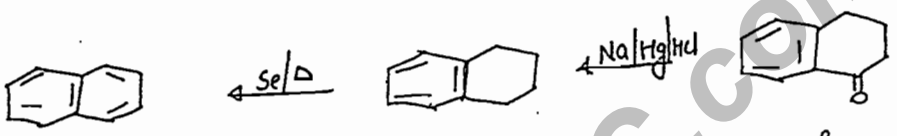
Eg: 

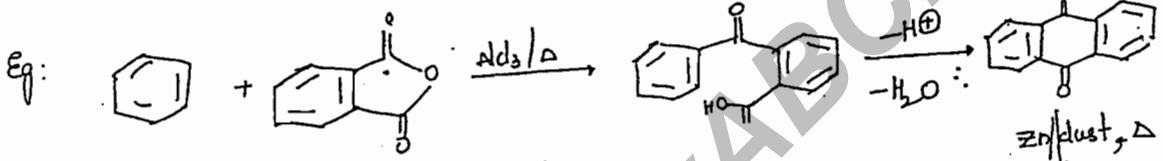
Eg: 

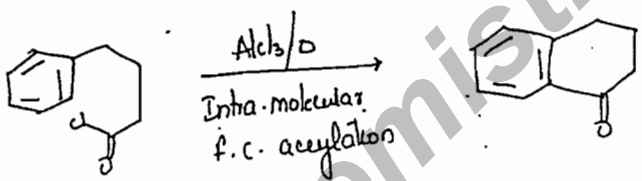


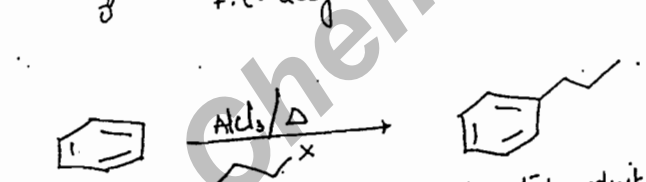


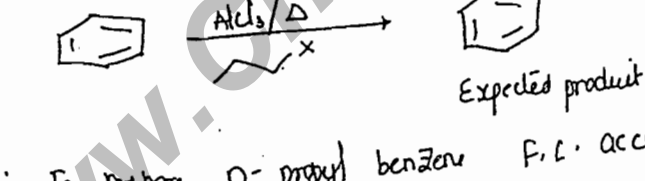
Eg: 



Eg: 

Eg: 

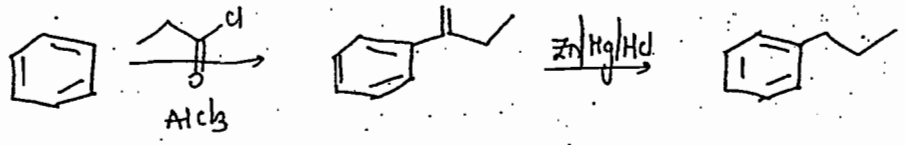
Eg: 

Eg: 

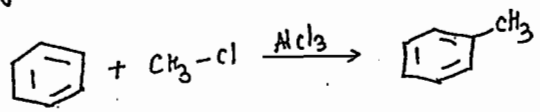
Expected product

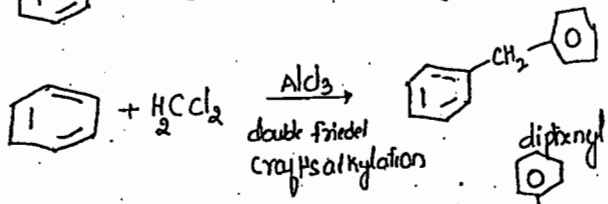
But obtained product.

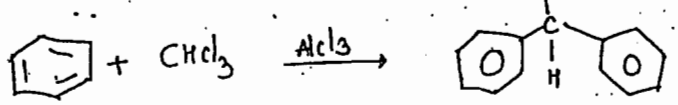
∴ To prepare n-propyl benzene F.C. acylation is proper method than F.C alkylation because in f.c alkylation instead of expected product, rearranged product is obtained.

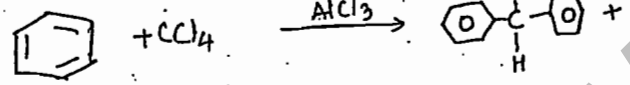


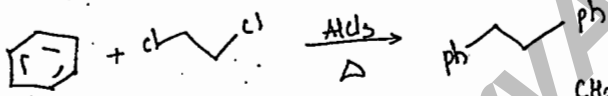
eg. for friedel Craft's alkylation.

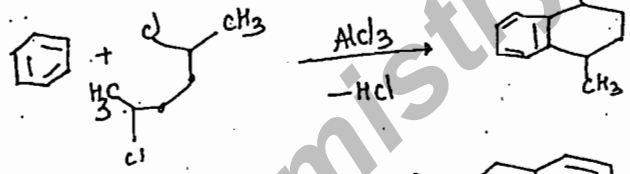
1) 

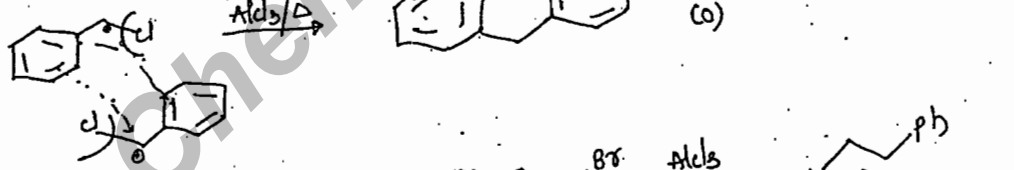
2) 

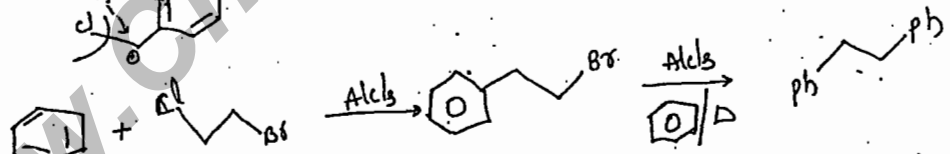
3) 

4) 

5) 

6) 

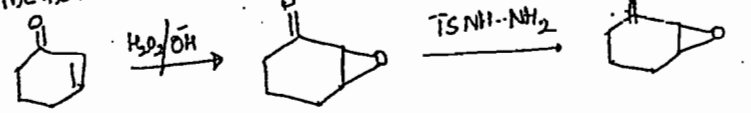
7) 

8) 

ESCHENMOSER: REARRANGEMENTS (FRAGMENTATION)

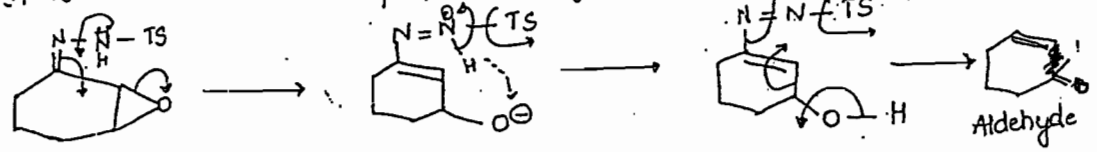
→ close to Shapiro reactions

→ Best method to prepare alkenyl ketones.



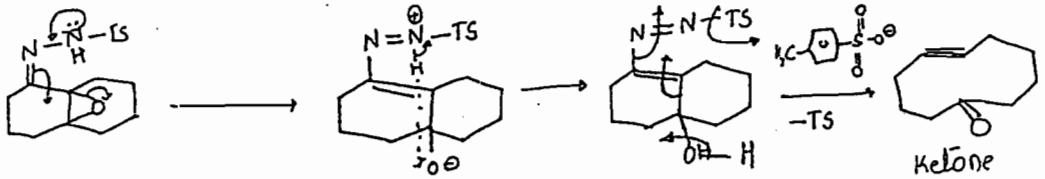
(23)

It is the method to prepare Alkenyl Ketones.



ESCHENMOSER R.A

Eg:



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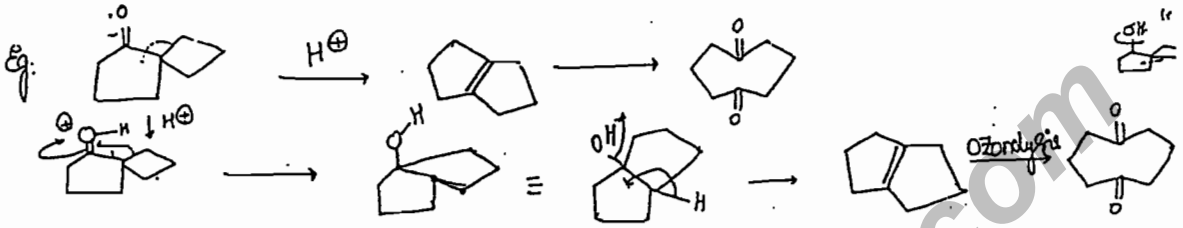

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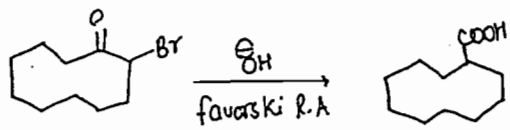
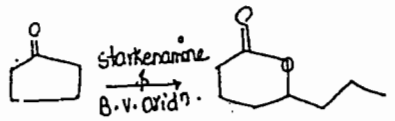
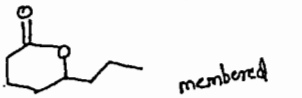


Ans.

Eg)





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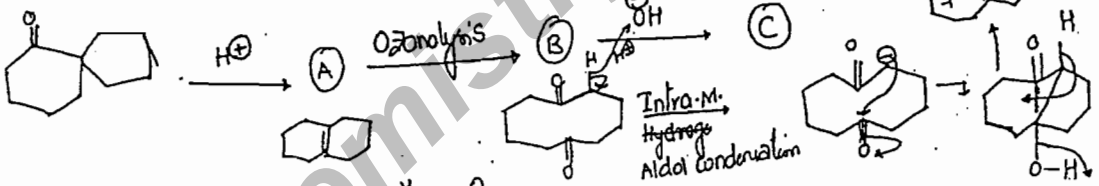

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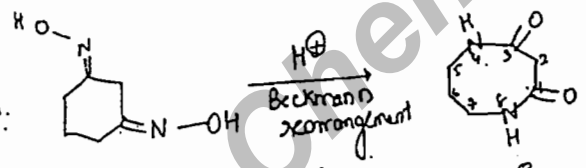

(2 times Beckmann Rearrangement)

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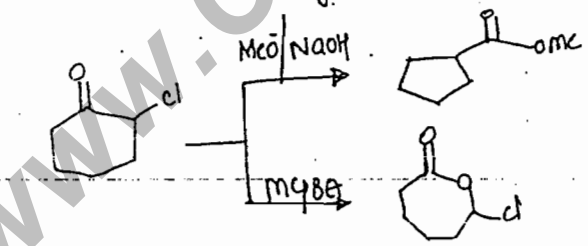

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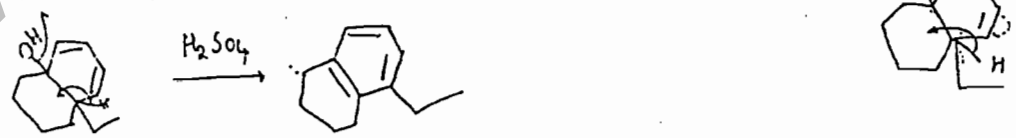

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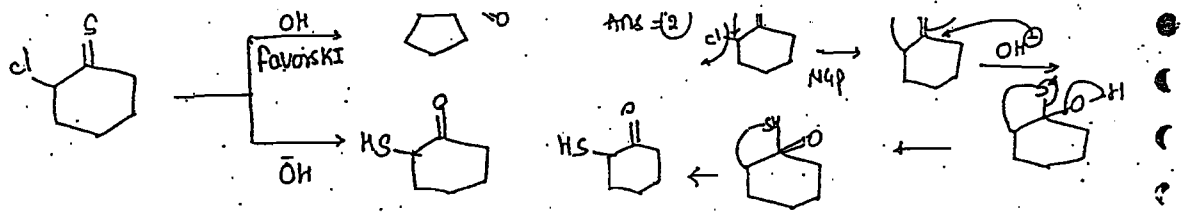

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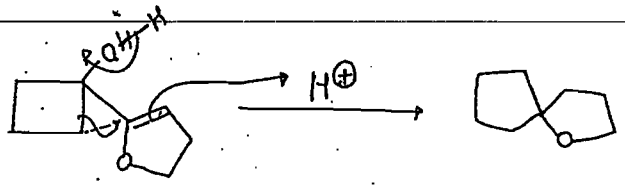

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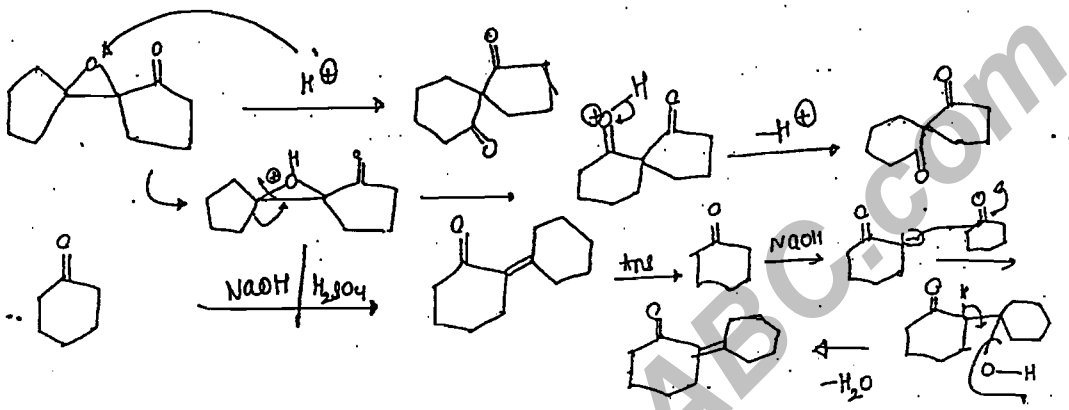
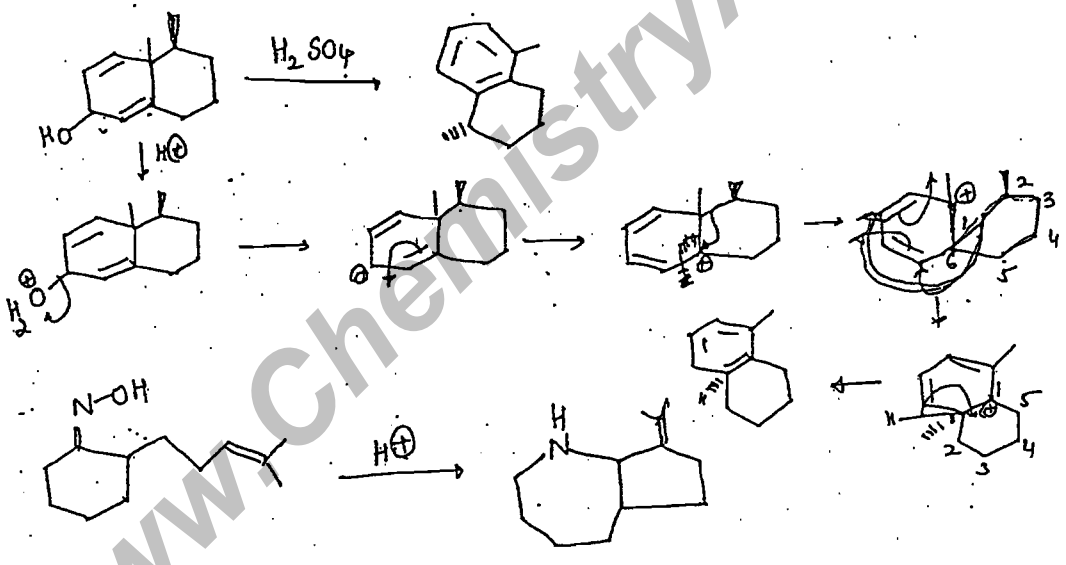


Eg:



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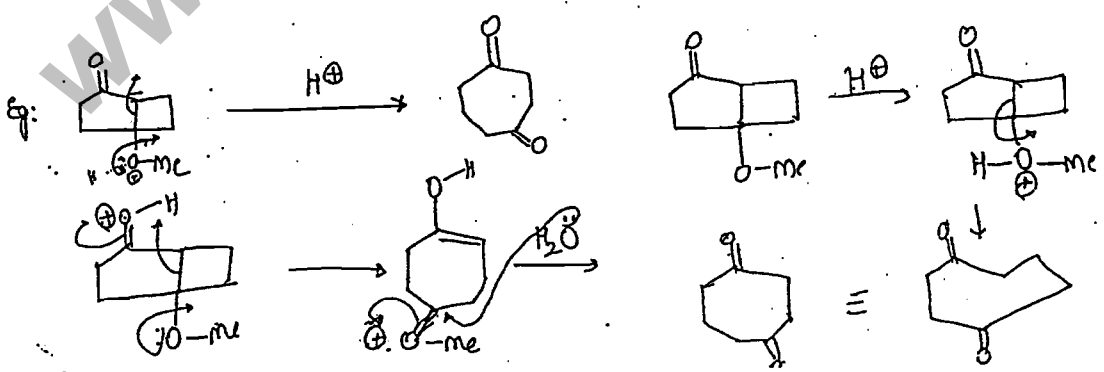

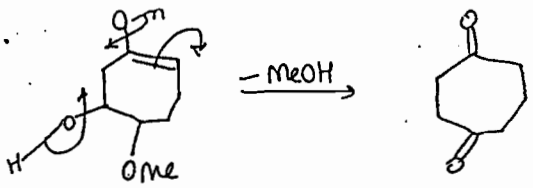

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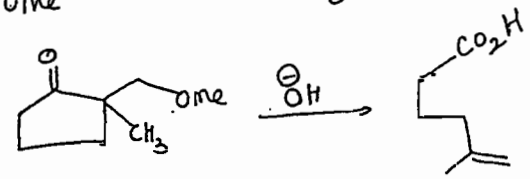
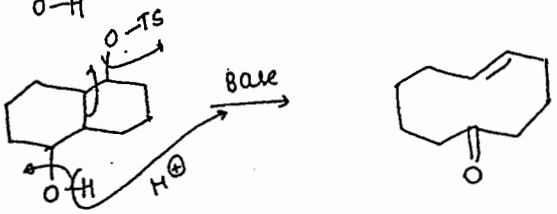
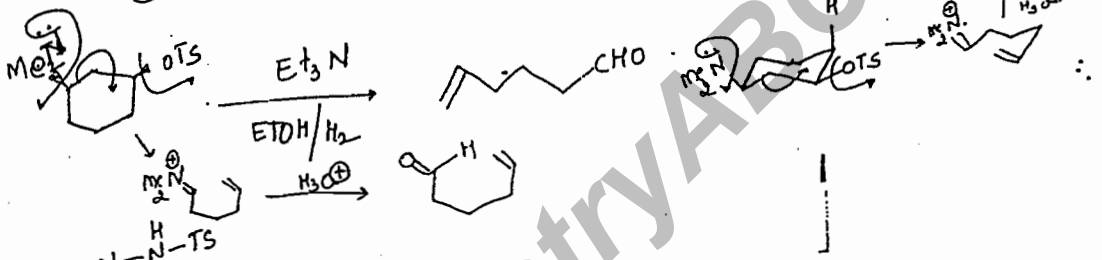


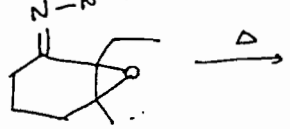
Eg:



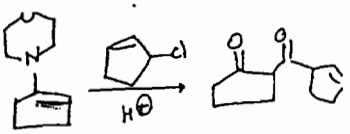
Eg:



Eq:



Ans:



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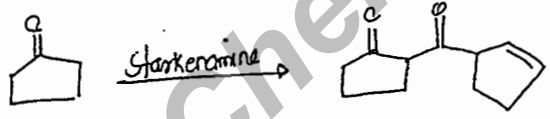
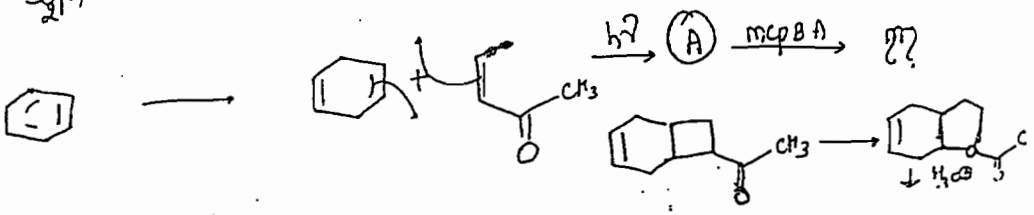
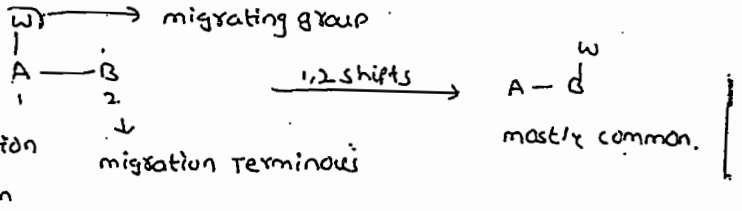


Eg:

Eg:

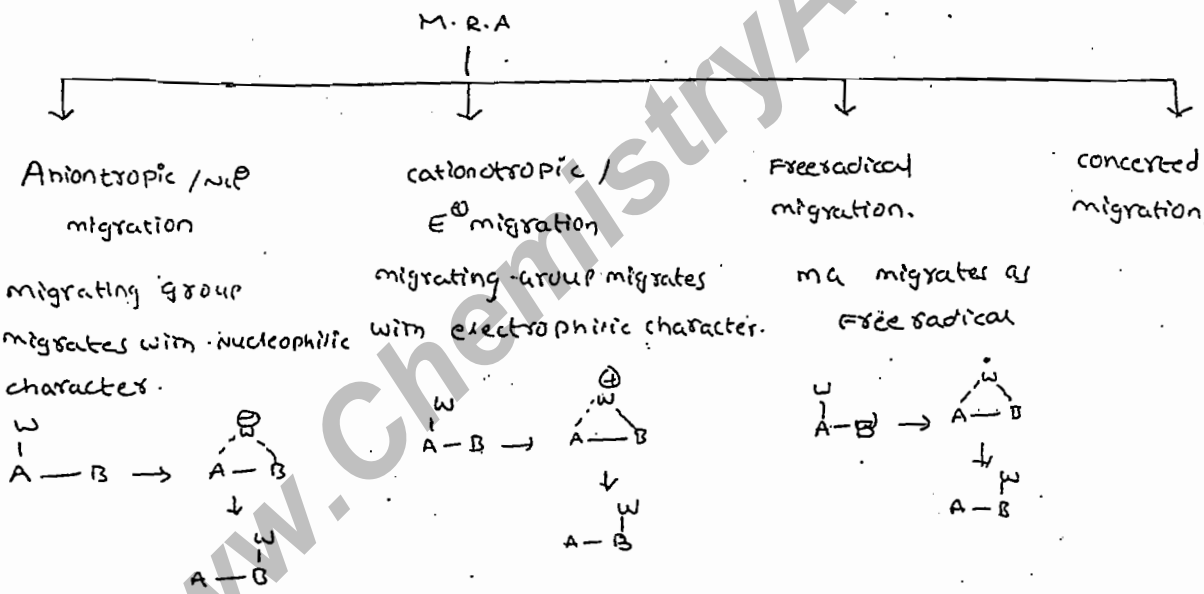


MOLECULAR REARRANGEMENTS :-

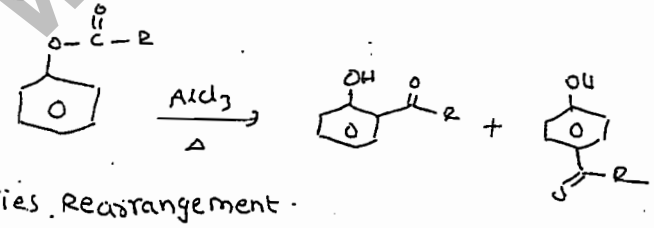


migration or shift of group/atom one position to another new position with in a molecule called molecular rearrangement.

* majority of molecular rearrangements are 1,2 shifts.
* Group which is migration group 'migrating group"
* Intial position of migration group " migration origin".
* Final position of migration group " migration Terminous".
* In some of the migration origin and migration terminous may be far off also called long range shifts/migrations.
* 1,2 - migrations also named as white more shifts.



migration to Aromatic ring :- migration terminous must be Aromatic group

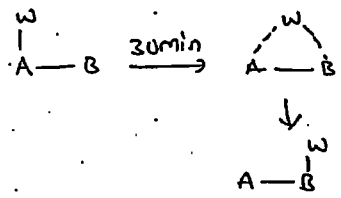


Fries Rearrangement.

MRA

Based on skeleton

Intra molecular R.A.



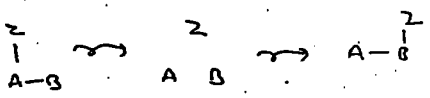
~~not~~ not ~~freely~~ independent

~~not detach each~~

In the course of M.R.A of migrating group in association with rest of the molecule, then Intra m.R.A. migrating group never becomes free, no detachment of m.gp. from the rest of the molecule.

Inter molecular R.A.

Rest of migrating group / in



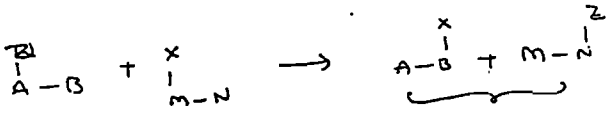
In the course of m.RA, m.gp ~~can~~ completely detaches & becomes free for some time (Independent) called Inter m.R.A.

(113)

EVIDENCES FOR INTRA & INTER MOLECULAR REARRANGEMENT :-

1) CROSS- OVER EXP (CHEMICAL Rea^n) :-

minimum '2' substituents.



cross over product.

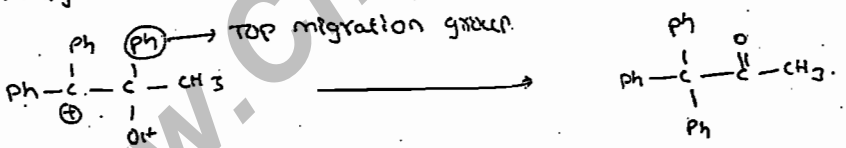
migration/shift of atoms (or) group from one molecule to another dif. product resulting products are called cross-over products.

* In cross over experiments, If cross- over products are obtained.

* Inter molecular R.A If cross over products not Obt

MIGRATORY APTITUDE:-

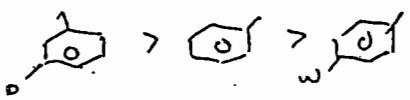
comparision of migration capacity of various groups. which are in completion for migrations.



$Ph > CH_3$.

In generally molecular RA Aryl groups migrations than Alkyl.

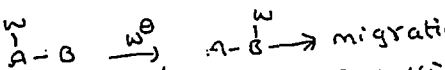
↓ Exch.

In aryl 

In alkyl 3^0-alkyl > 2^0 alkyl > 1^0- alkyl.

ANIONTROPIC / NUCLEOPHILIC MOLECULAR REARRANGEMENT

In this rearrangement terminous should be $e^{\ominus}$ deficient.



$e^{\ominus}$ deficient

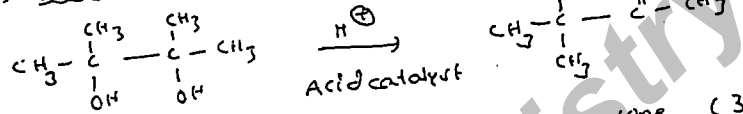
$(C^{+}, -\ddot{C}-)$ $(\ddot{N}:, -\overset{\oplus}{N})$, $(-O^{+})$

Based one receiving centre

- MRA to electron deficient carbon
  - * pinacol - pinacolone.
  - * wagner - meerwin
  - * wolf-rearn
- MRA to electron deficient 'N'.
  - * Hoffmann's
  - * curtius
  - * Lossen
  - * Schmidth
  - * Beckmann's
- MRA to electron deficient to oxygen.
  - * Baeyer-villiger.
  - * Dakin-reah / Dakin
  - * Alkyl Hydro peroxide.

MOLECULAR REARRANGEMENTS $e^{\ominus}$ DEFFICIENT CARBON:-

1) pinacol - pinacolone Rearrangement:-



pinacol (1,2-diol)

pinacalone (3°-butyl methyl ketone)

First Rearranyement observed on the 1,2 diol.

∴ given name "pinacol to pincalone"

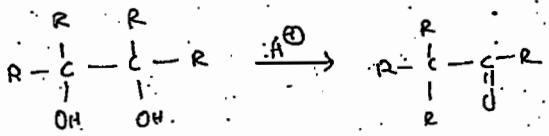
1) 1,2 diol → carbonyl

2) C-skeleton → change.

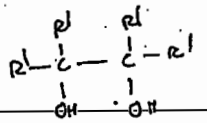
conversion of 1,2 diols into carbonyl compounds which change in carbon skeleton (1,2 migration) in acidic medium called pinacol - pinacolone. rearrangement.

* 3° alcohols (1,2 diols) ie pinacols molecular rearrangement very fast.

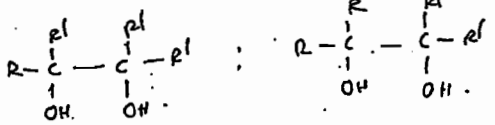
But even 1°/2° diols also involve in rearrangement.



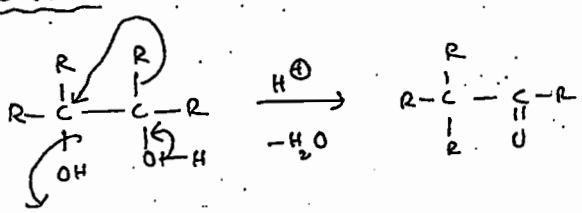
symmetrical 1,2 diols →



unsymmetrical 1,2 diols →

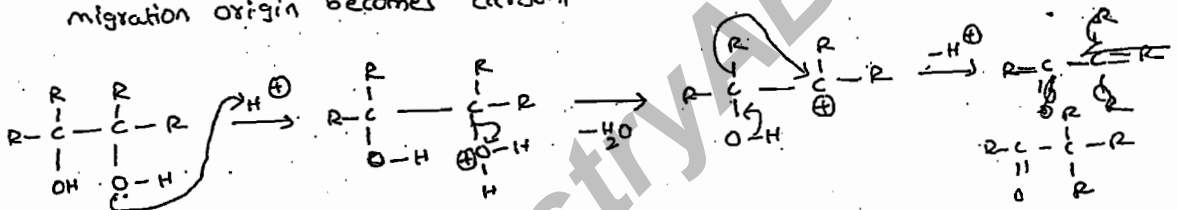


Mechanism:

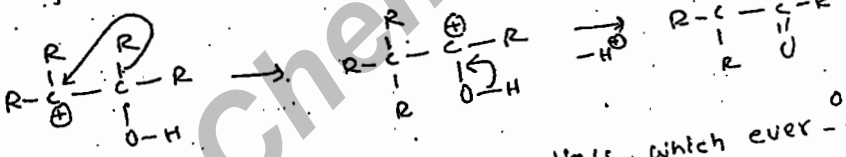


* white more 1,2 -shifts.

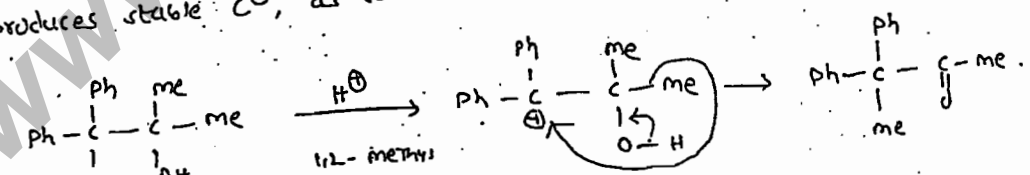
migration origin becomes carbonyl. Intermediates are $C^{\oplus}$.

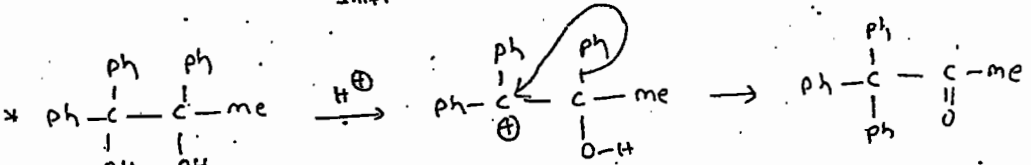


Symmetrical so any one of Hydroxy group $H^{\oplus}$ can be attacked.

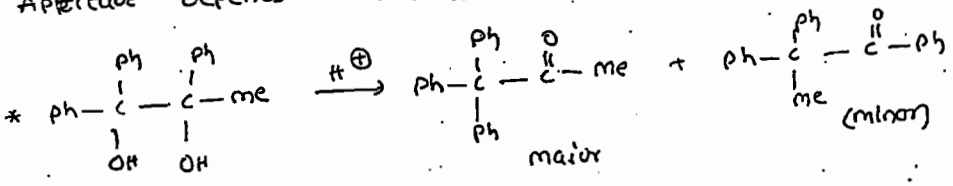


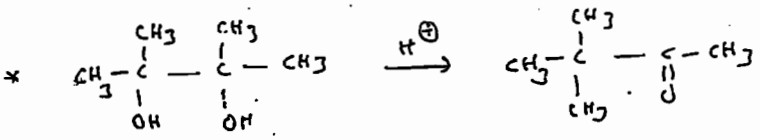
* In the case of unsymmetrical 1,2-diols which ever -OH groups removes produces stable $C^{\oplus}$, as to be prefered in attacking $H^{\oplus}$.

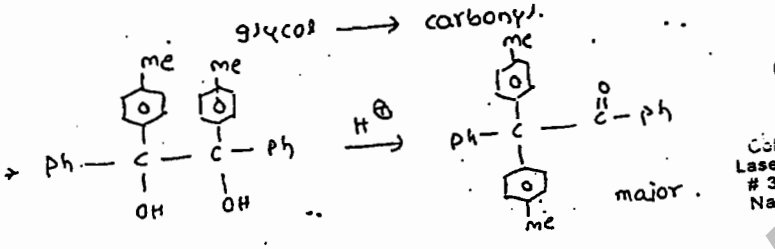


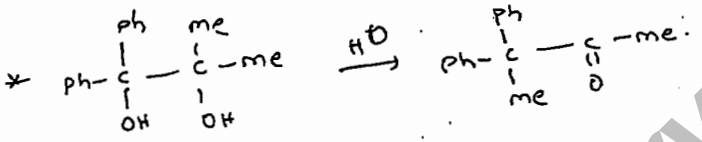


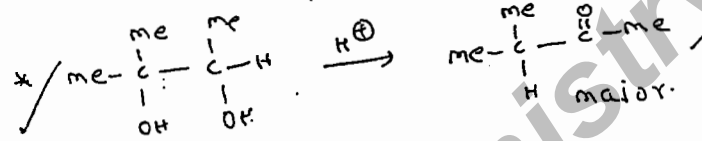
In migration of ---- If there is a migratory aptitude in pinacol-pinacalone Rearrangement mixture of products will be formed. But in general migratory Aptitude Aryl > H > Alkyl (But most of the times migratory Aptitude depends on rea^n conditions).

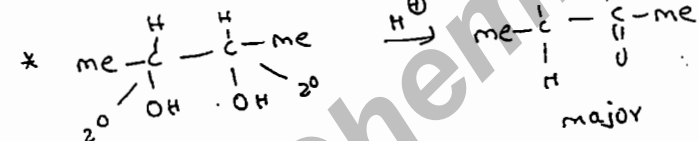


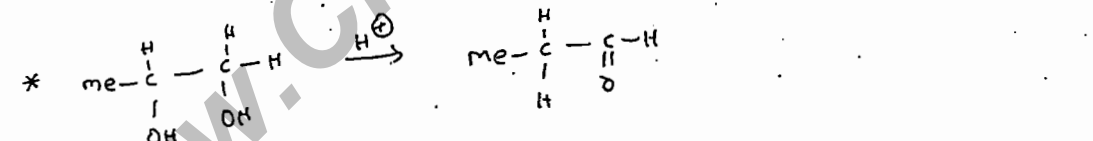


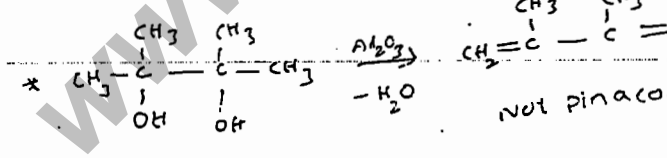


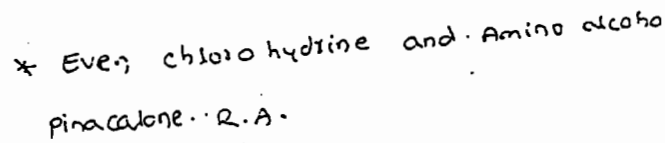






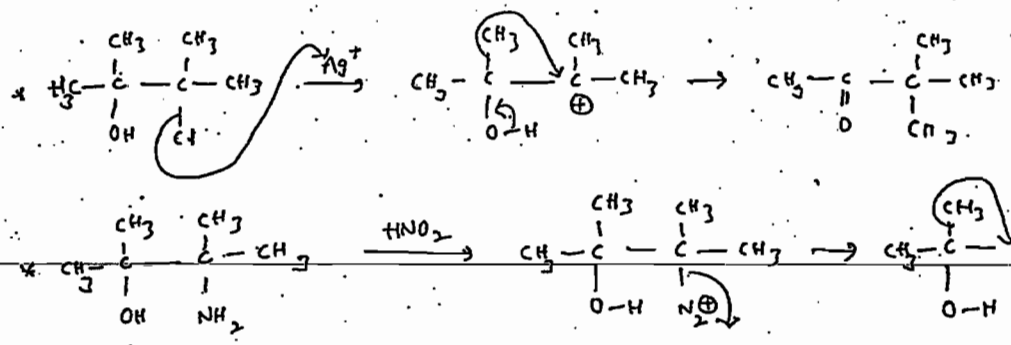




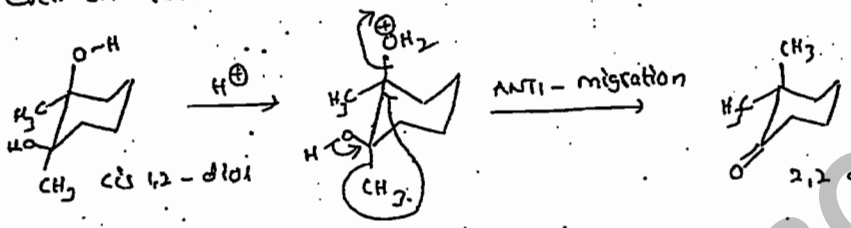


Not pinacol to pinacolone rearrangement).

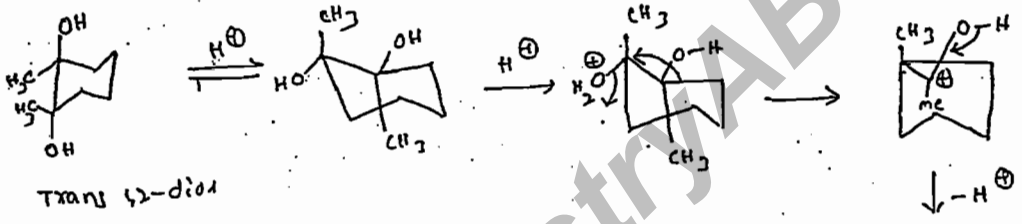
* Even chloro hydrine and Amino alcohol can also participate in pinacol-pinacalone R.A.



Even on cyclic system also pinacol, pinacalone rearrangement takes place.

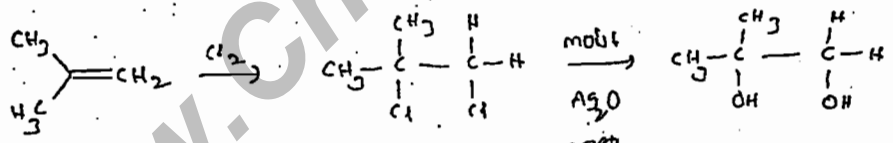


cis 1,2-diol — ANTI-migration — 2,2 dimethyl cyclo hexanone.

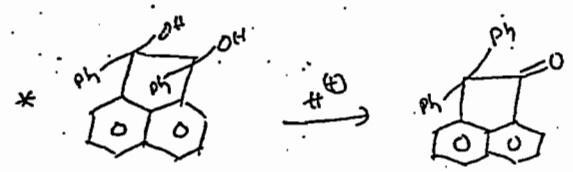


Trans 1,2-diol

1-methyl 1-Acetyl cyclo-pentane

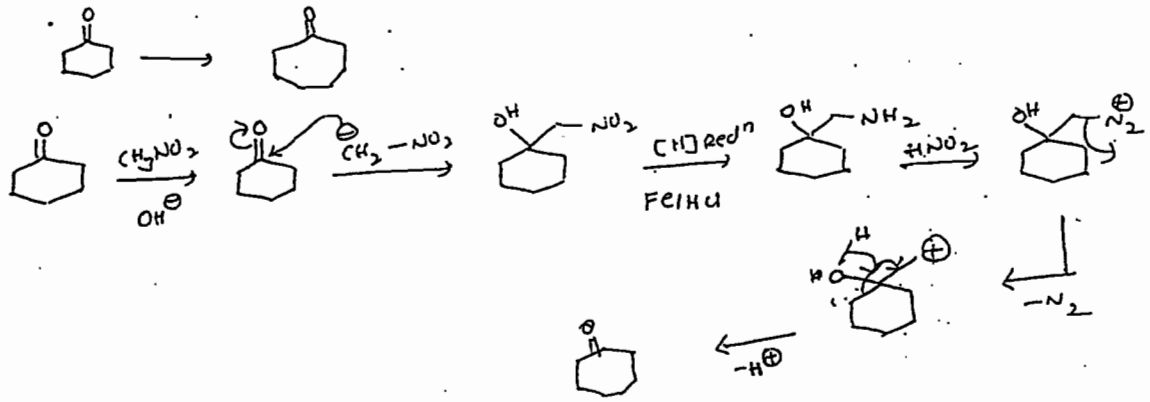


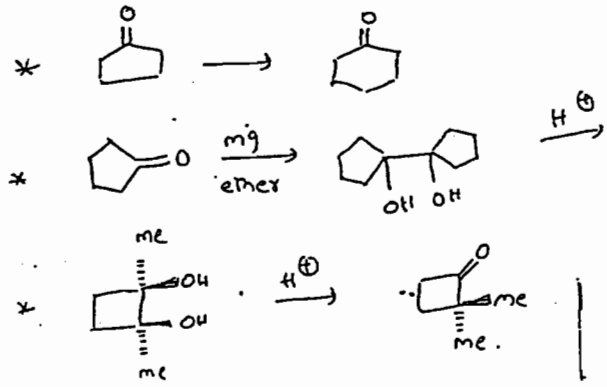
major

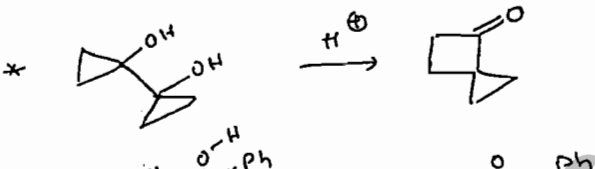


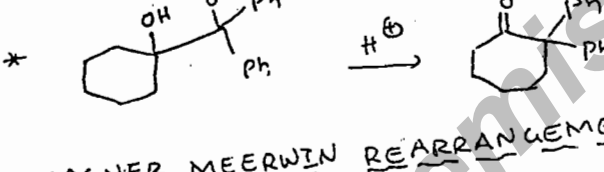
(Phenyl migration group) (Ring-Fan strain)

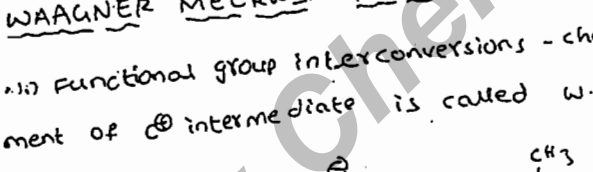
* Ring expansion with pinacol to pinacolone





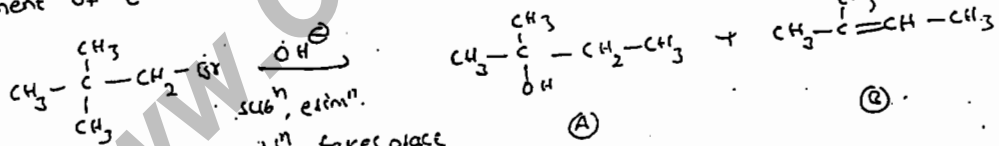


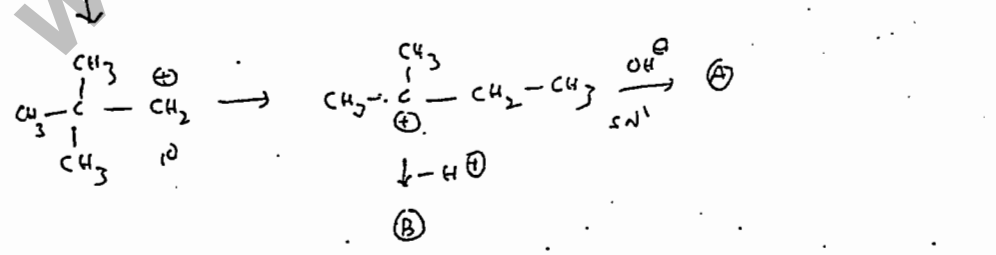


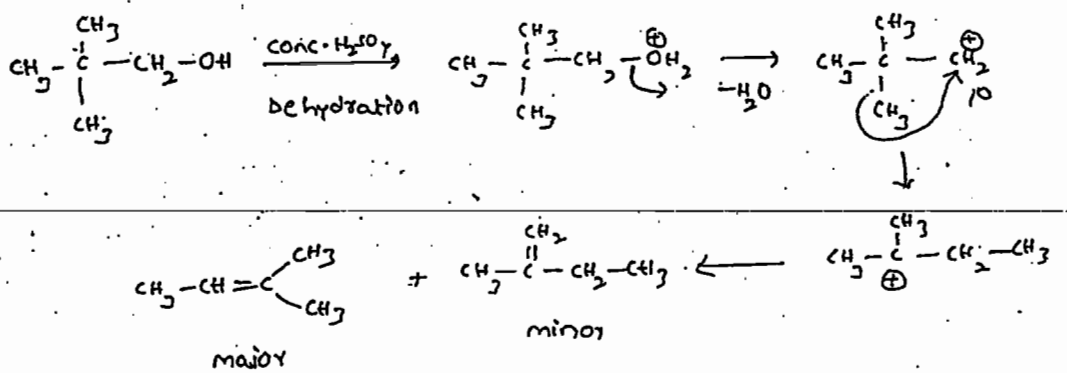


WAAGNER MEERWIN REARRANGEMENT :-

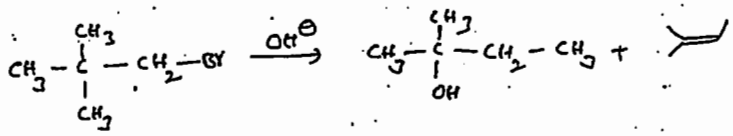
Functional group interconversions - change in carbon skeleton through rearrangement of $C^{\oplus}$ intermediate is called W.M.R.A.

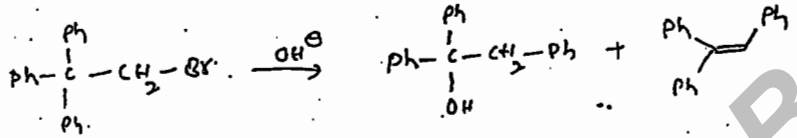


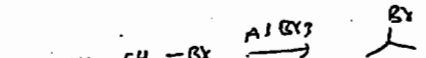




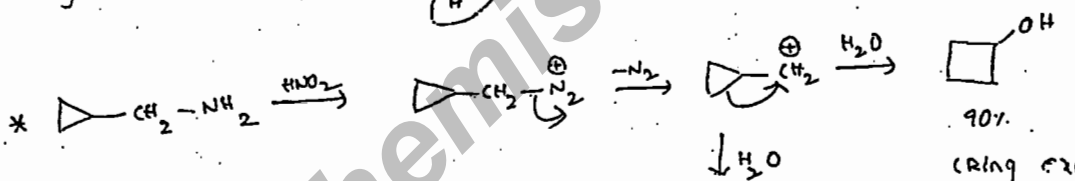
Neo-phile bromide Elimination:-

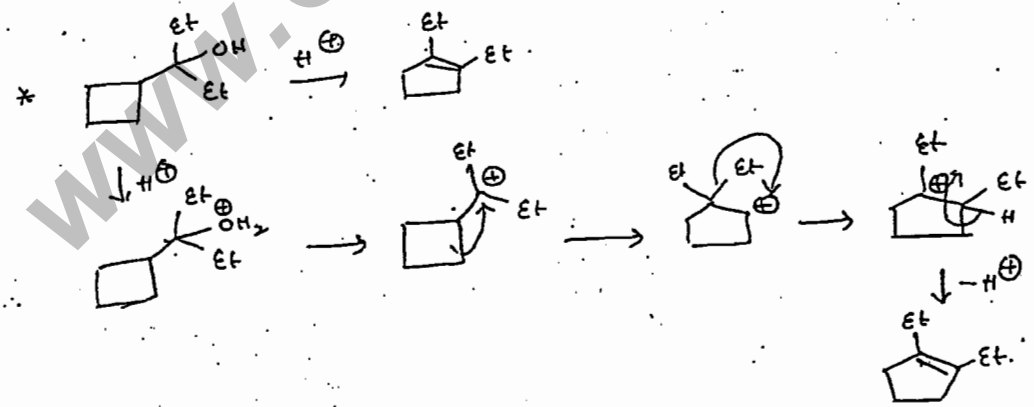


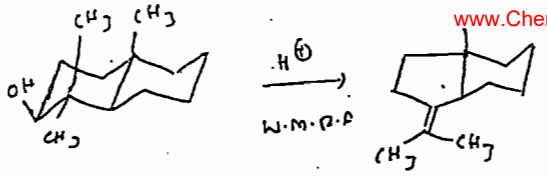




mech:-

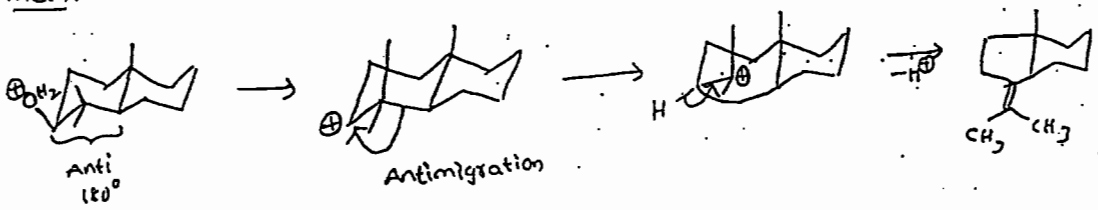






W.M.R.R

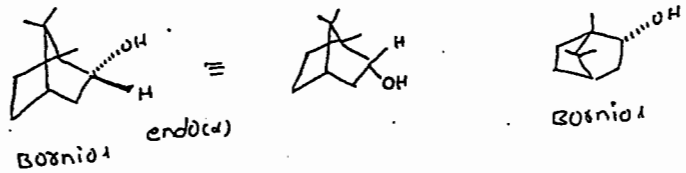
mech:-



Anti
180°

Antimigration

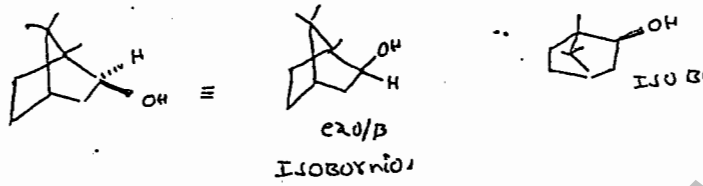
Terpenoid skeleton W.R.As:-



Borneol

endo(a)

Borneol



exo/β

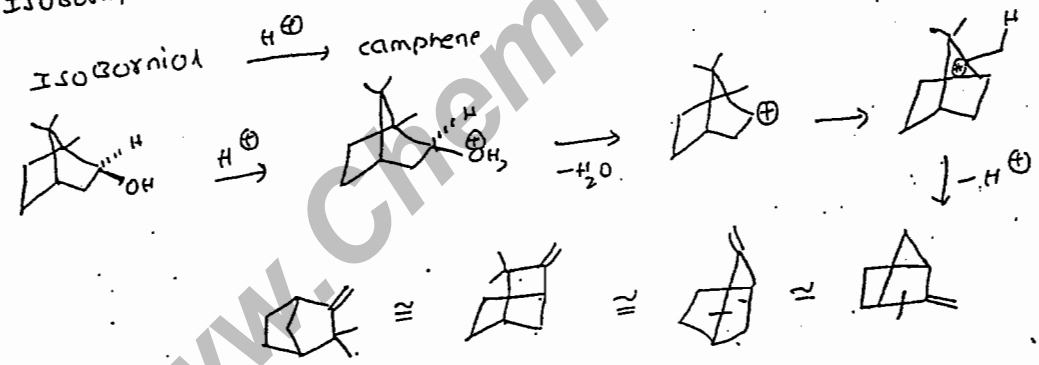
Isoborneol

Isoborneol.

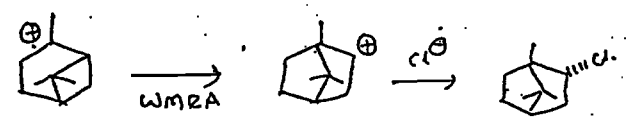
Isobornyl chloride

Bornyl chloride.

* Isoborneol $\xrightarrow{H^{\oplus}}$ camphene

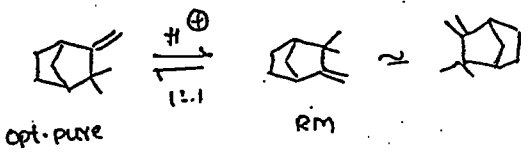


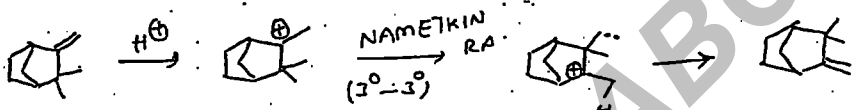
mech:-



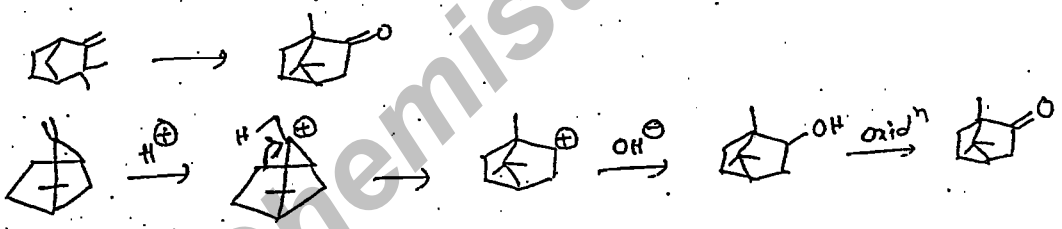
* CAMPHENE $\xrightarrow{HCl}$ ISOBORNYL CHLORIDE

RACEMIZATION OF CAMPHENE:-

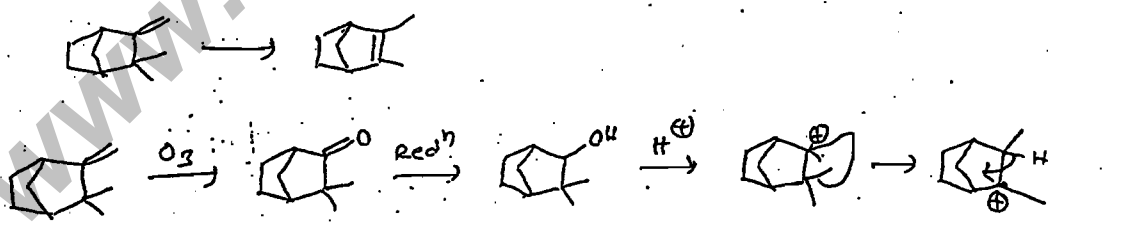


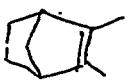


* camphene $\xrightarrow[2)\ OH^{\ominus}/oxi]{1)\ H^{\oplus}}$ camphor

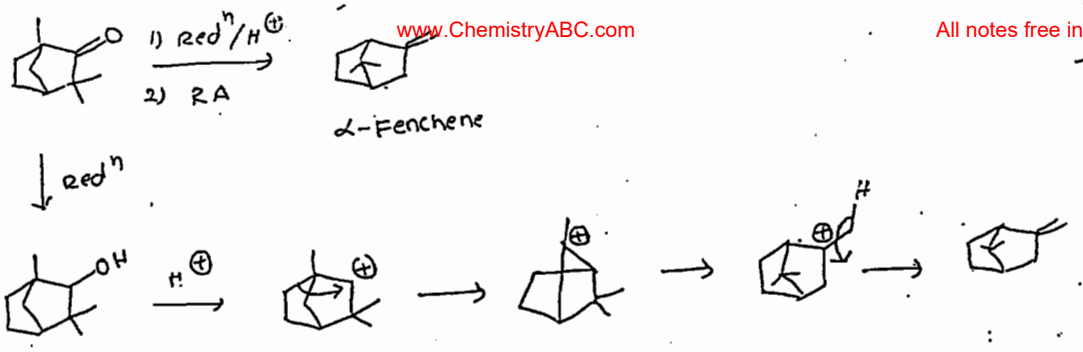


* camphene $\xrightarrow[3).\ H^{\oplus}]{1)\ O_3\ 2)\ Red^{n}}$ santonene

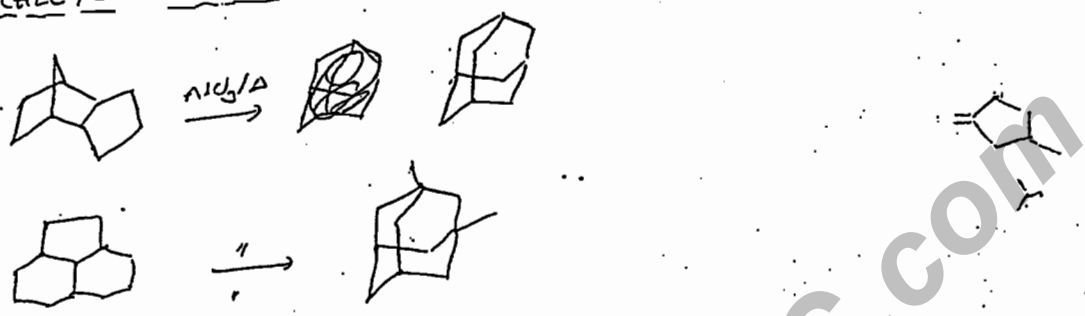




– santene



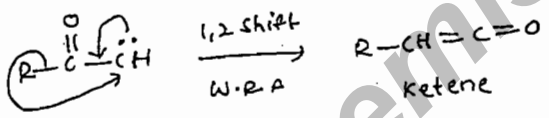
SCHLEYERS. ADAMANTATION :-



3) WOLF – REARRANGEMENT :-

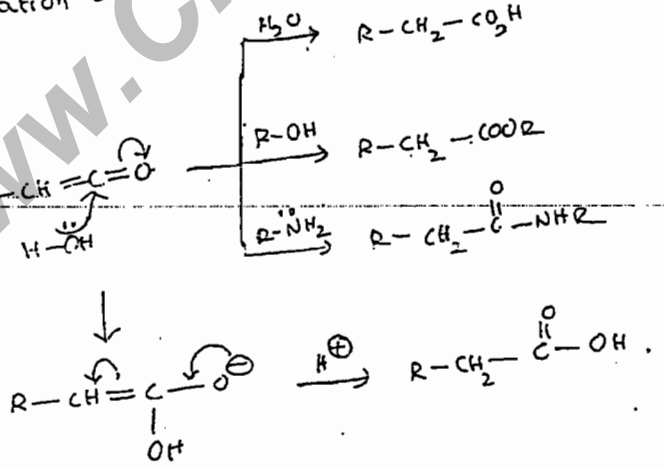
Acyl carbene ⟶ Ketene called wolf rearrangement.

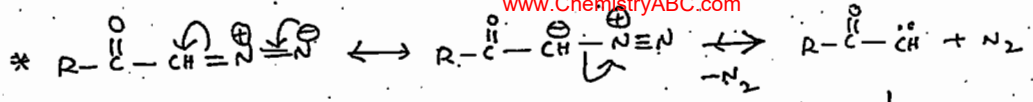
* These are catalysed by metalions / Higher Temp or light.
* W.R.A at high Temp thermal W.R.A.
* W.R.A at light called photochemical W.R.A.

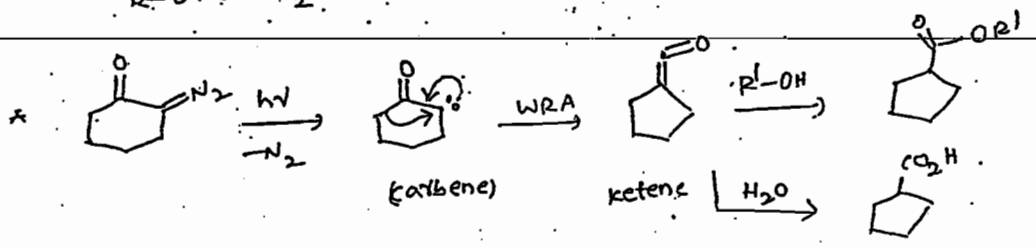


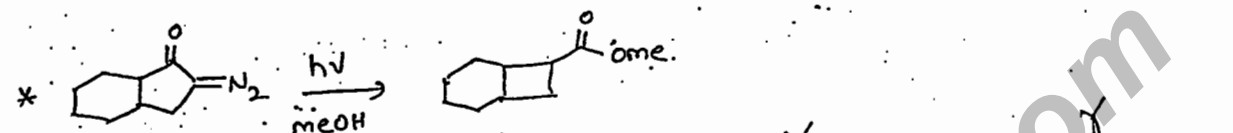
Acyl carbene.

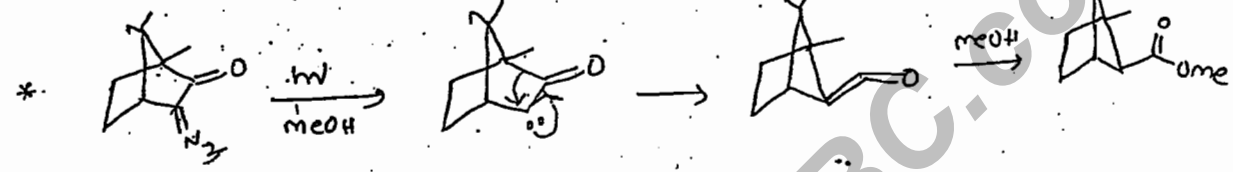
* migration of Acyl carbene is [1,2] shift.

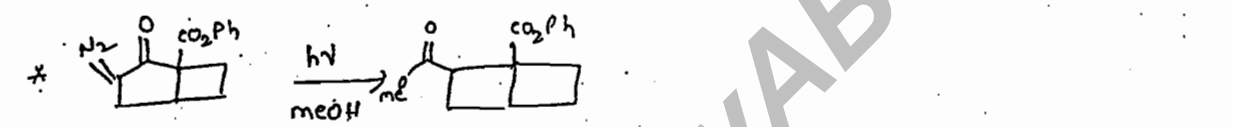






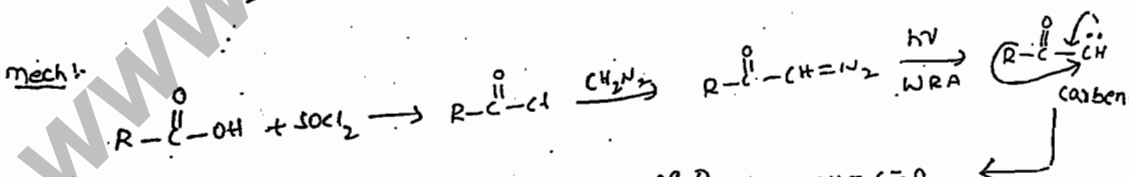


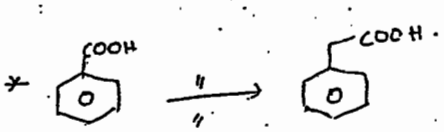


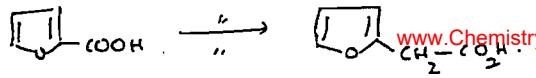


ARNDT - EISTERS SYNTHESIS :-

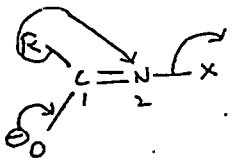
mech :-







REARRANGEMENT TO ELECTRON DEFFICIENT NITROGEN :-



1,2 Shifts $O=C=N-R$

ISOCYANATE (Intermediate)

Ex:- 1) Hoffmann's Rearrangement.
2) Curtius Rearrangement.
3) Schmidt Rearrangement.
4) Beckmann's "
5) Lossen " "

1) HOFMANN'S / HOFMANN'S HYPOBROMIDE R.A :-

1°-amide $\xrightarrow{X_2/OH^{\ominus}\text{ on}}$ 1°-amine.

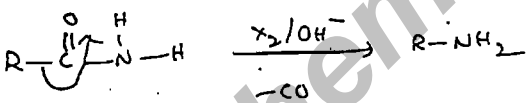
$OX^{\ominus}$ (Hypo halide)

(Basic medium)

* Reaction proceeds Through 'Nitrene' Intermediate.

* 1,2 shifts / White more shift.

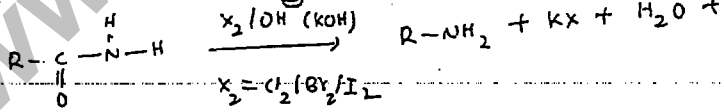
** $2^{\circ}/3^{\circ}$-Amide will not involved.



1°-amide

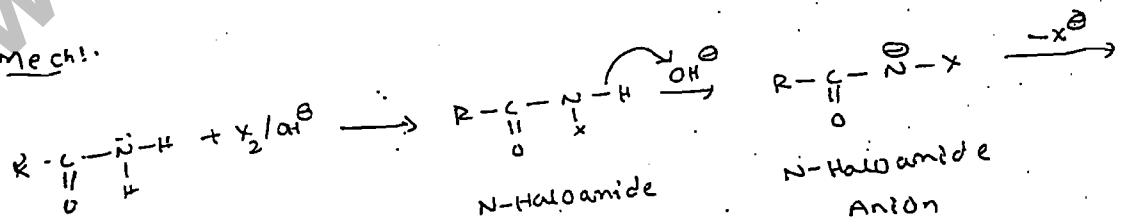
R = alkyl, Aryl, - - any (* decrease 1 carbon in formation of Amine)

mech:-



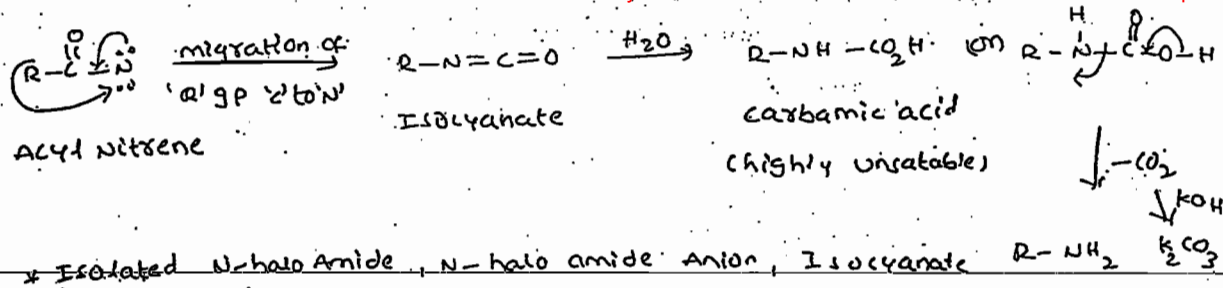
$X_2 = Cl_2/Br_2/I_2$

Mech:-

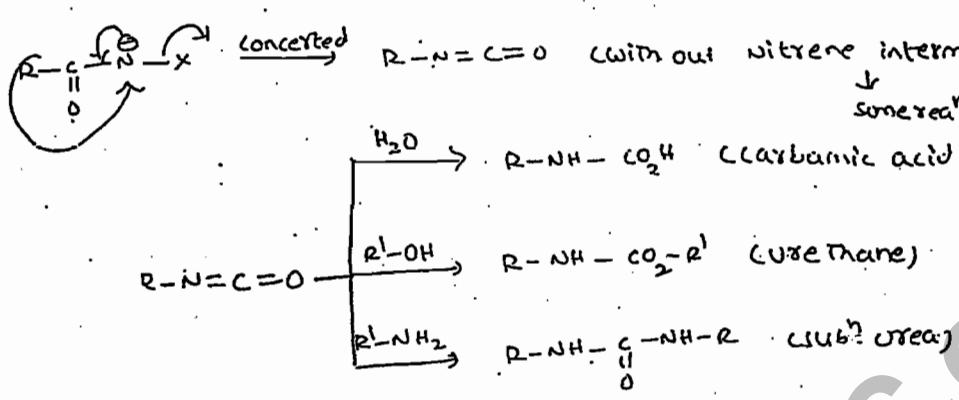


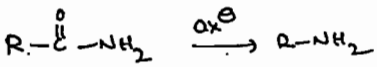
N-Haloamide

N-Haloamide Anion

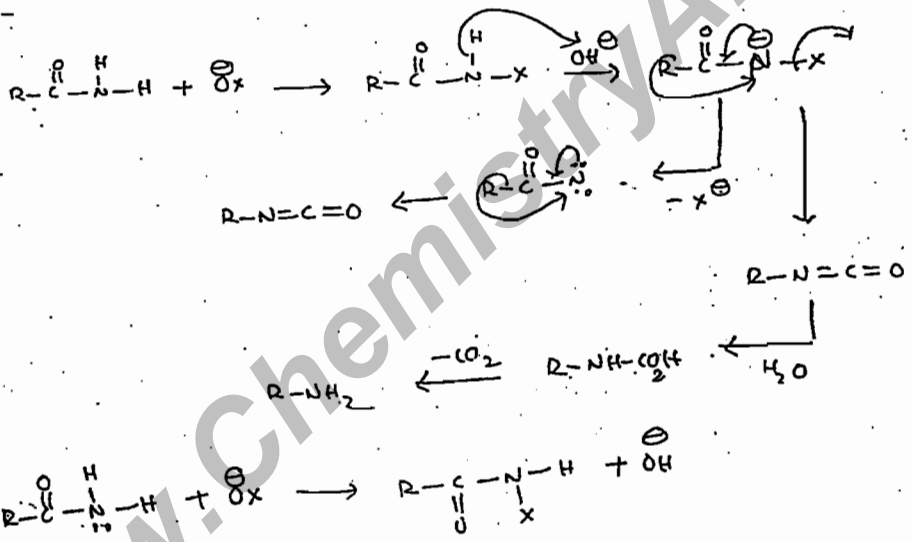


* Isolated N-halo Amide, N-halo amide Anion, Isocyanate





Mech:-



EVIDENCE:-

1) i) N-Halo Amide
   2) N-Halo Amide anion
   3) Iso cyanate intermediates are isolated.

2) Retention of configuration of migrating groups.
   (Intra molecular Rearrangement).

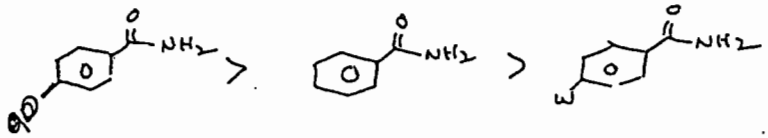
3) NO cross-over product identified.

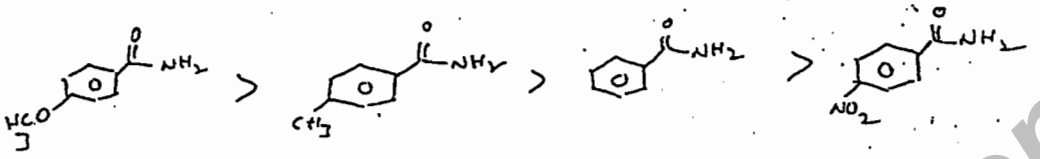
(Intra molecular R.A.

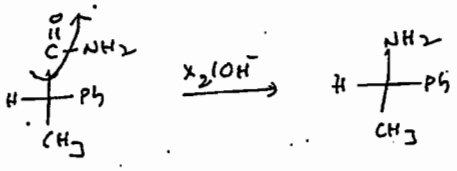
4) Electron donating groups presents. enhance rate of rea^n.

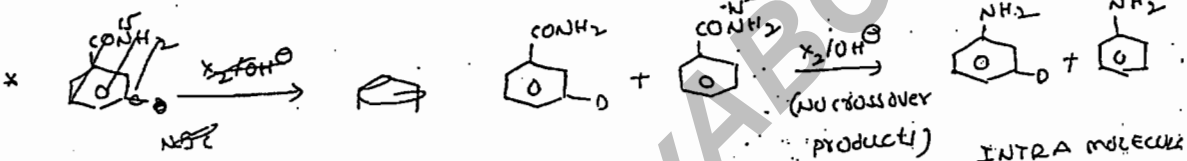
∴ migration of group is the "ROI"

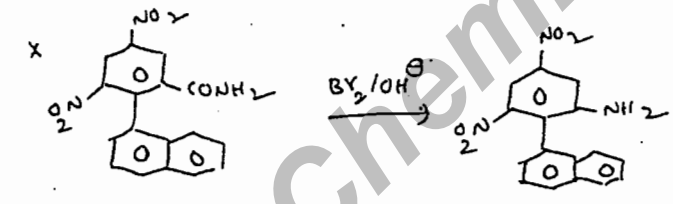
RATE OF REARRANGEMENT OF ~~Hoffmann's~~ HOFFMANN'S Rea^n:-

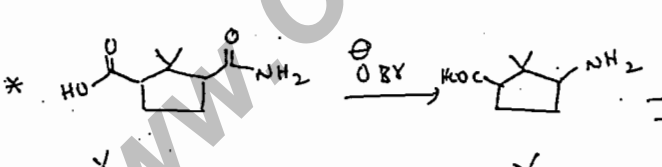


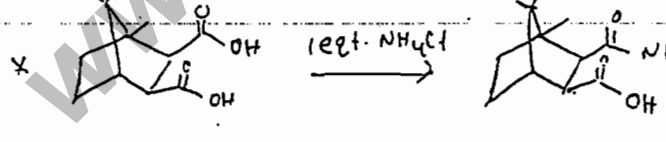


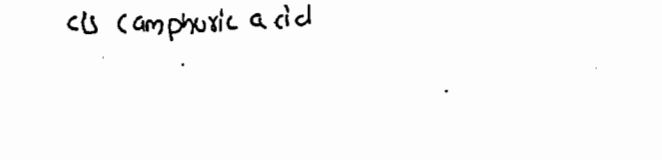




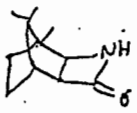


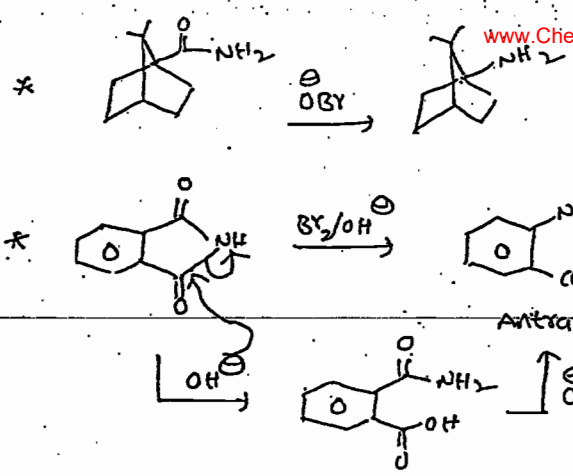


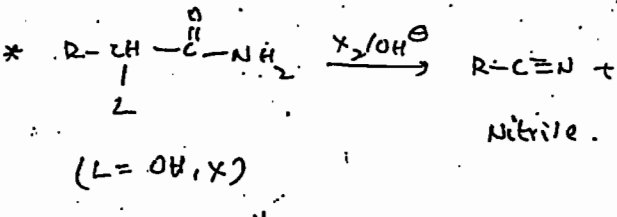


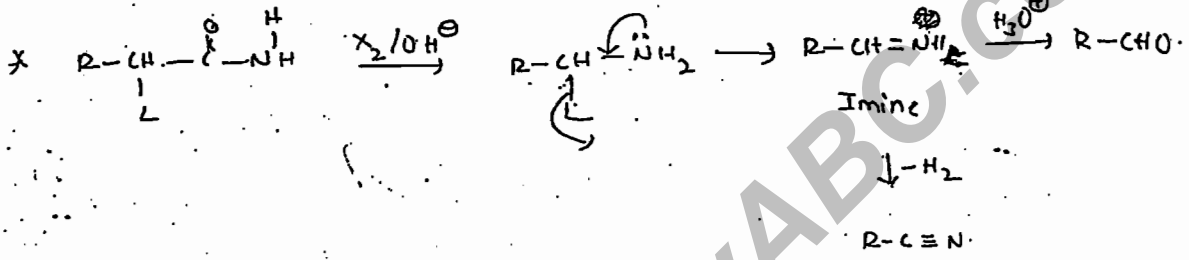


cis camphoric acid





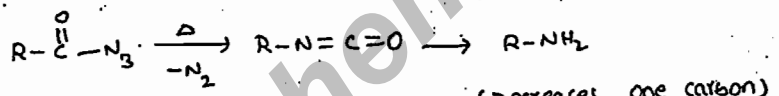




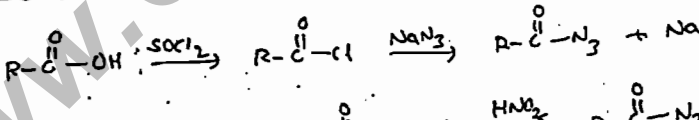
CURTIUS REARRANGEMENT:- Neutral medium

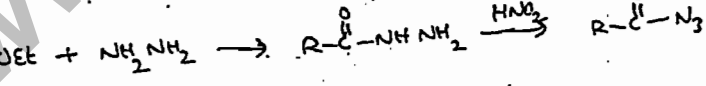
Acid Azide $\xrightarrow{\Delta}$ Isocyanate $\xrightarrow{H_3O^{\oplus}}$ $R-NH_2$

1,2 shift

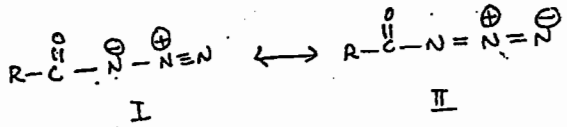


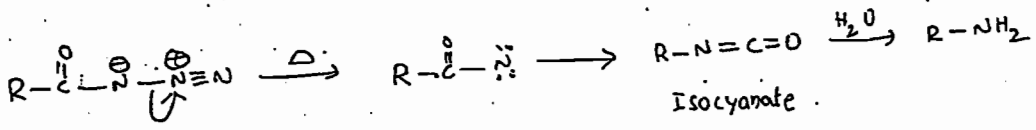
Prep^n of Acid Azides:-





mech:-

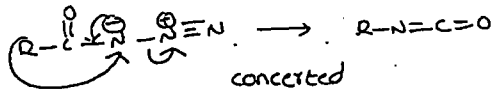




123

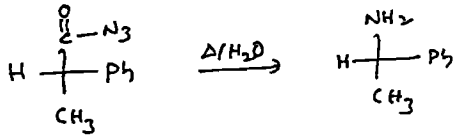
10.

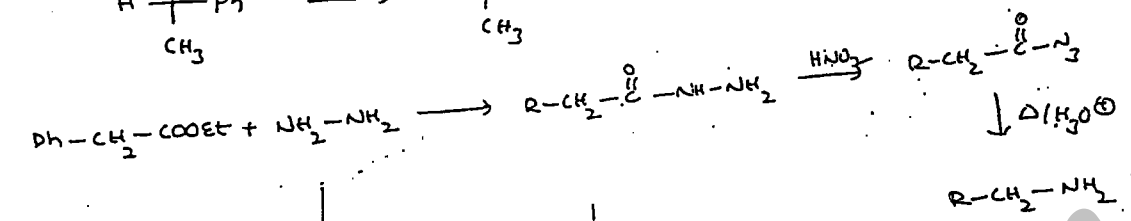
Some of the curtius Nitrene is not observed otherwise mech concerted.



concerted

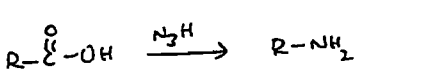
* Intra molecular RA (Retension of configuration of migration group).





SCHMIDT REACTION:

Carboxylic acid $\xrightarrow{HN_3}$ Hydrazoic acid $\rightarrow$ 1°-amine.



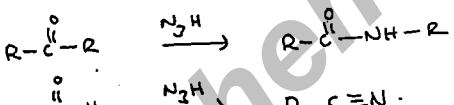
$NaN_3 + H_2SO_4 \rightarrow N_3H$.

* It is acid medium R.A.

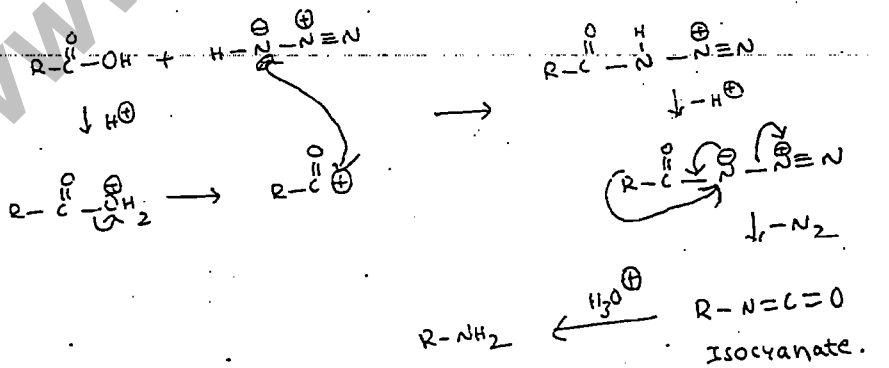
* Not only carboxylic acid even aldehydes and ketones also partici pates in a Schmidt Reaction.

Aldehydes $\xrightarrow{N_3H}$ Nitriles

Ketones $\rightarrow$ Amides

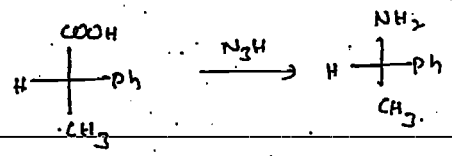


Mech:-

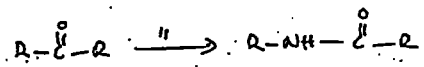


$R-NH_2$ $\xleftarrow{H_3O^{\oplus}}$ $R-N=C=O$ Isocyanate.

* Intra molecular Rearrangement Retention of configuration of migrating groups.



* Ketone $\xrightarrow{N_3H}$ Amides. [It is not Better. Best one is Beckmann].



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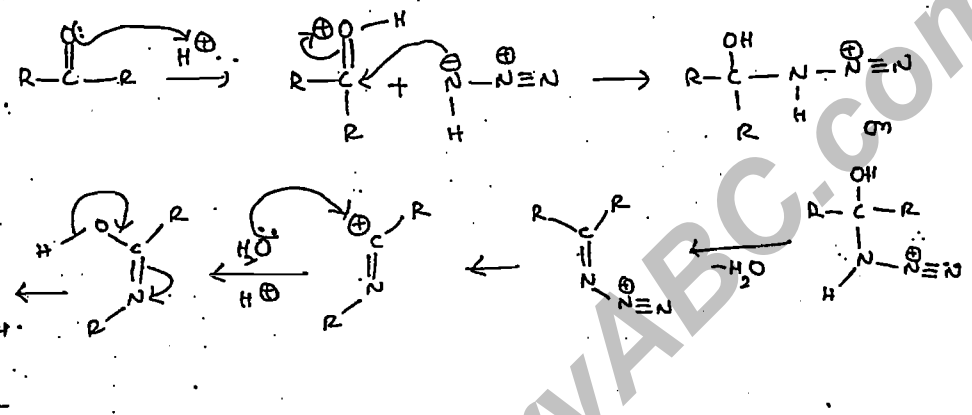
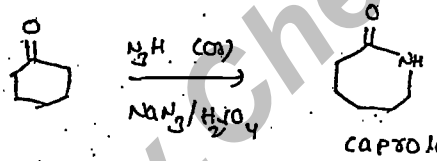


Amide

* $Ph-CH_2-CO_2H \xrightarrow[H_2SO_4]{NaN_3} Ph-CH_2-NH_2$

* $H_3C-C(=O)-CH_2-CO_2Et \xrightarrow{N_3H} H_3C-C(=O)-NH-CH_2-CO_2Et$.

* 

caprolactum

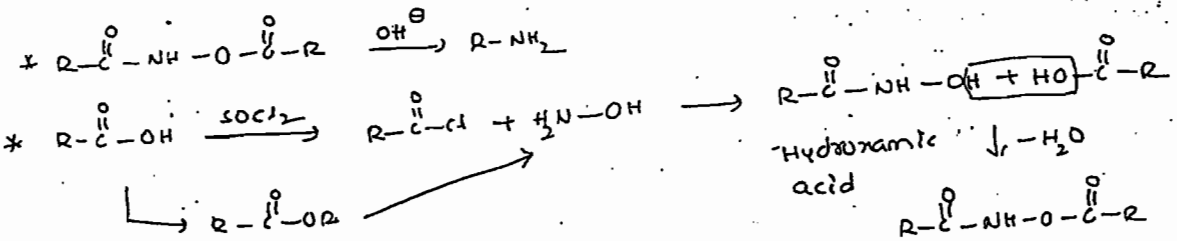
It is monomer of Nylon-66.

The best R.A for caprolactum preparation Beckmann R.A.

LOSSEN REARRANGEMENT:-

* Nitrene Intermediate. ! 1,2 shift.
* Basic medium.
* conversion of Hydroxymic Acid Ester into 1° amines in alkali.

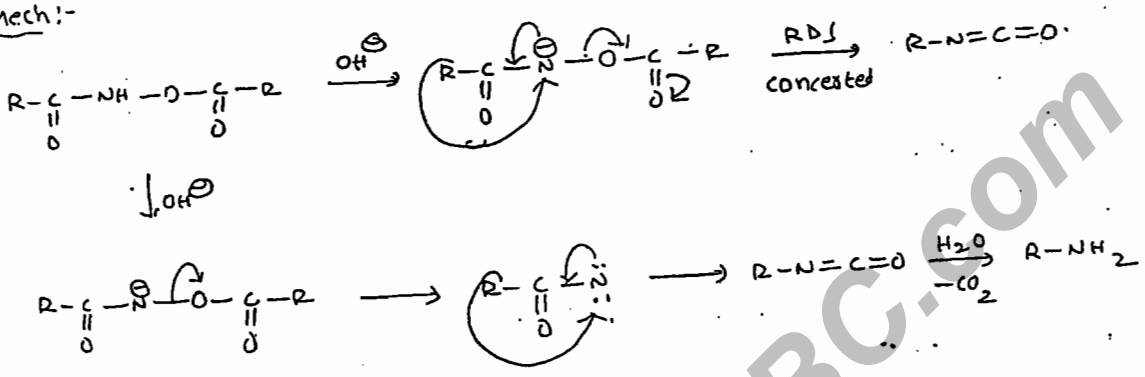
Hydroxamic Acid Ester $\xrightarrow{OH^\ominus}$ P-amines



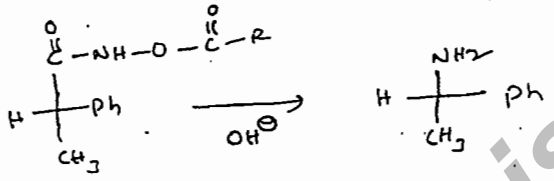
Hydroxamic acid

Hydroxamic acid ester.

Mech:-



Intra molecular:-



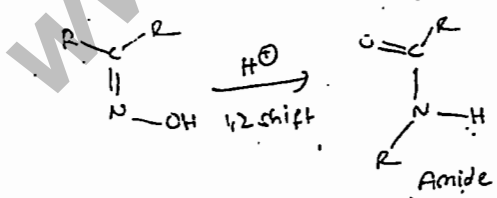
* Retention of configuration.

BECKMANNS - REARANGEMENT

OXIME $\xrightarrow[B.RA]{\text{Acid catalyst}}$ Amide $\xrightarrow{\text{Hydrolysis}}$ Amine + Acid.

conversion of oximes of Aldehydes / ketones into Amide in the presence of Acid catalyst.

* Inter conversion of functional group.



Amide

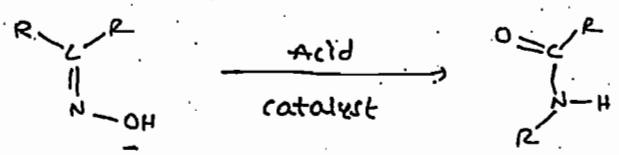
Acid – catalyst :-

protic acid :- HCl, H_2SO_4, [redacted], RCOOH, RSO_3H, $AcOH + HCl + Ac_2O$ (Beckmann)

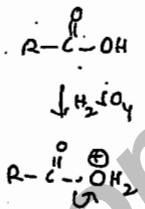
Non-protic Acid – Lewis acids :-

$SOCl_2$, PCl_3, PCl_5, $POCl_3$, SO_2, SO_3, $R-\overset{O}{\overset{\|}{C}}-Cl$, $R-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-R$, P_2O_5, BF_3

ROLE OF CATALYSIS :-

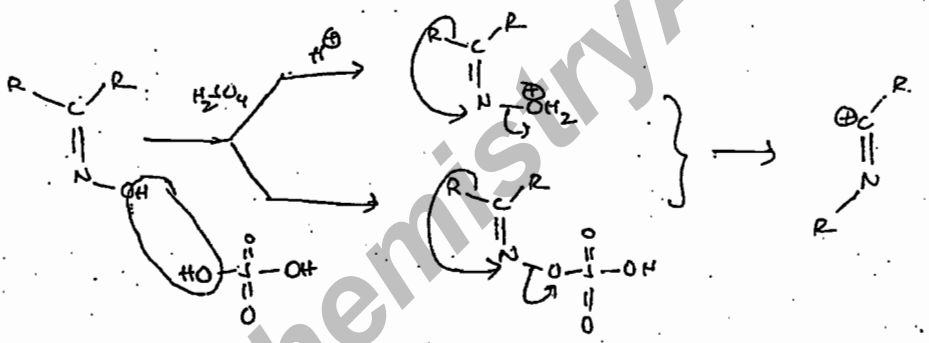


not Good leaving group



good leaving group.

* Acid catalyst makes 'OH' GROUPS as good leaving group in Beckmann Rearrangements.



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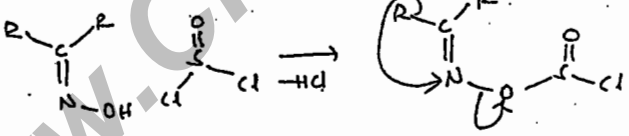

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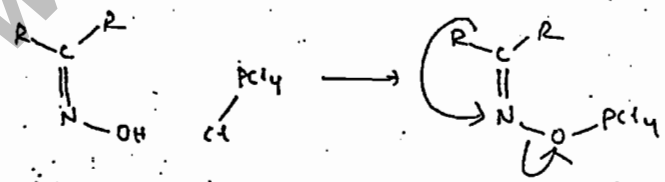

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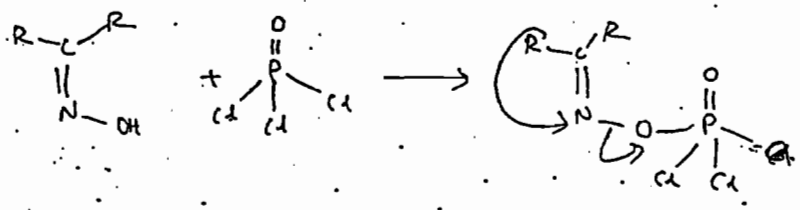
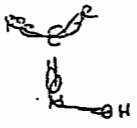


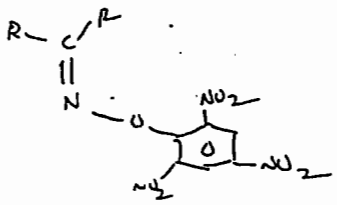
* With increase strength of acid catalyst rate of B.R.A

*  + ⊕ Increases.

$PhSO_3H > ClCH_2CO_2H > PhCO_2H > AcOH$.

* With Benzene sulphonic acid B.R.A fastes compare to other acids

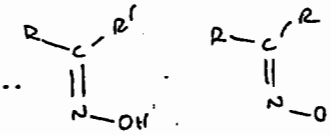
* Already in the reactant good leaving group no need to use acid catalyst

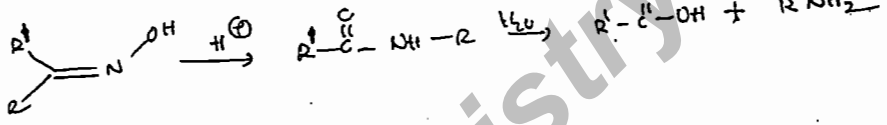


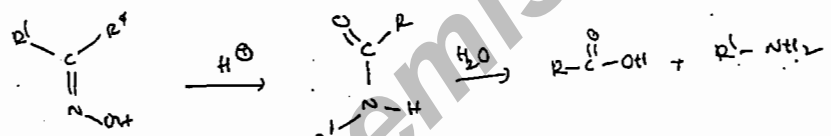
Picric acid derivative.

Good leaving group.

STEREO CHEMISTRY :-

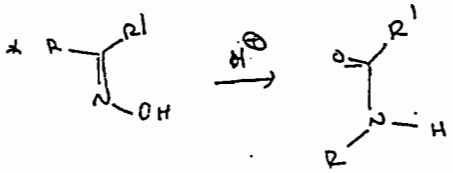
 Stereo Isomers (E/Z)



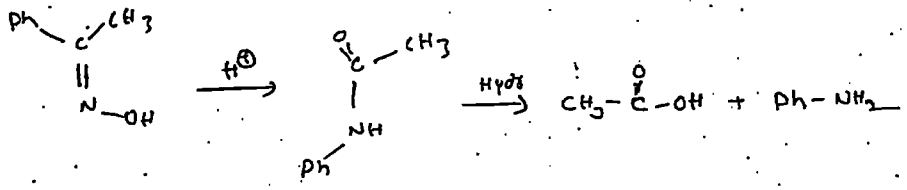


Anti migration

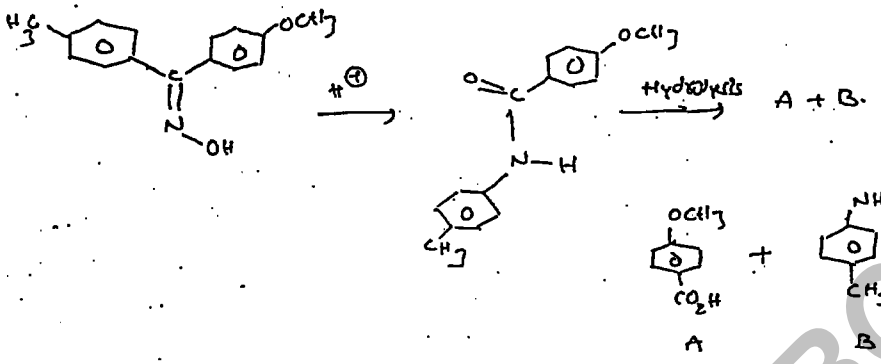
Unsymmetrical Ketoxime will have stereo Isomers always anti migrates from C → N on B.R.A. in the amine and Amide group attached to N always anti to OH in the oxime. From the products of BRA possible to determine configuration of keto oximes.

* 

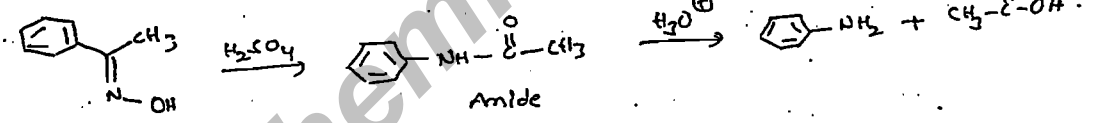
Keto oximes $\xrightarrow[BR]{H^{\oplus}}$ Amide $\xrightarrow{Hyd}$ Acid + Amine



Keto oximes $\xrightarrow{H^{\oplus}}$ Amide $\xrightarrow{\text{Hydrolysis}}$ p-anisoic acid & ~~p-toluic acid~~.

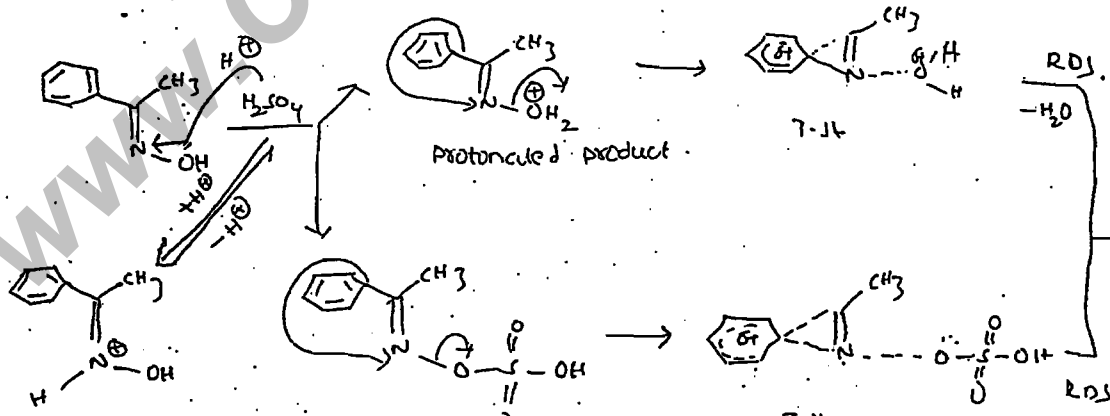


Mechanism:-



Amide

Beckman product



* major route. but No Beckman product. It is loss $H^{\oplus}$ and formed oxime again..

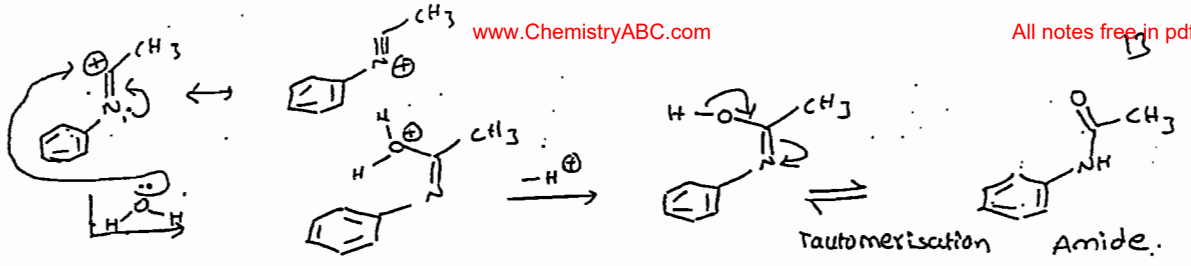
Protonated product

T.S.

* loss of leaving group and migration simultaneously.

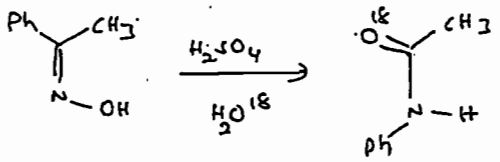
RDS

RDS



H_2O comes from solvent.

Tautomerisation Amide.

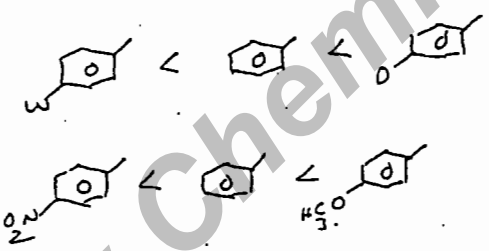
* 

The water molecule which is reattacking on $C^{\oplus}$ intermediate from the solvent. But not H_2O molecules loosed by Oxime

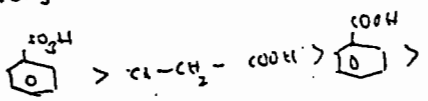
EVIDENCE:- Above reaction

Incorporation of labeled oxygen in amide indicating attacking of H_2O from solvent.

* migratory aptitude in Beckmann Rearrangement Aryl gp attached to wth drawing group migration is slow. compared with normal Aryl group and Aryl group attached to donating group.



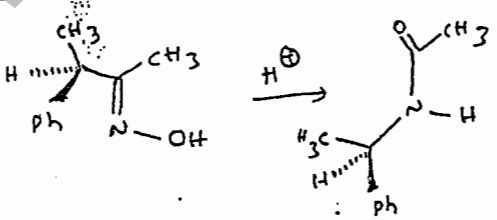
strength of acid catalyst:-



CH_3-COOH.

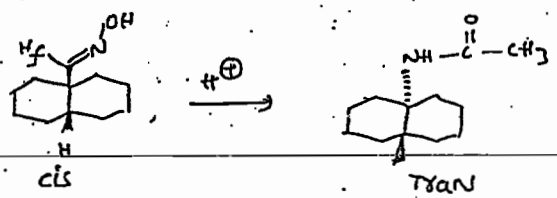
majority of B.R proved as Intra molecular R.A but few are inter molecular B.R.A.

STEREO CHEMICAL EVIDENCE:-



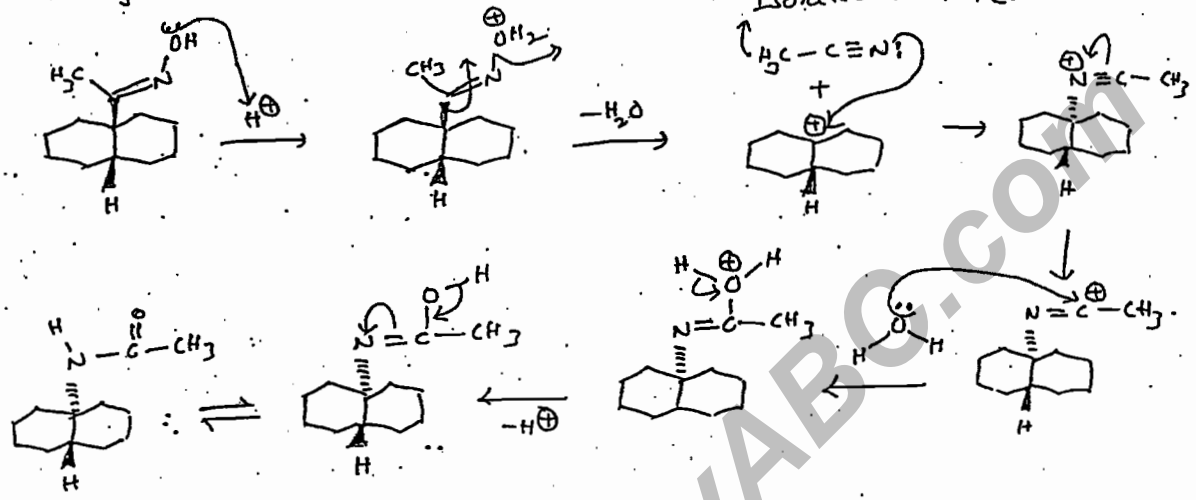
* No change in stereochemistry of migrating group.

migration takes place with retension of configuration or stereochemistry classified as Intramolecular Rearrangement. (majority of this compound).



change in stereochemistry or configuration of migrating group.

Isolated from Reaⁿ mixture.



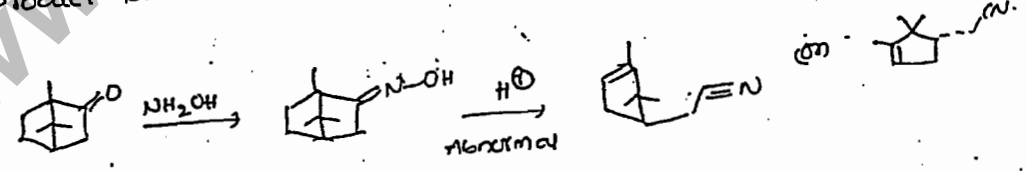
RATE OF B.R.A INFLUENCED BY

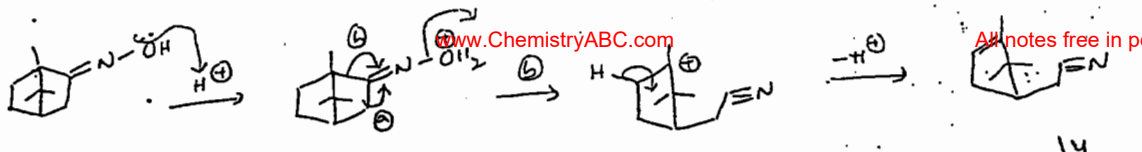
1) Increasing strength of Acid-catalyst.
2) polarity of solvent : more polar solvents enhance B.R.A.
3) presence of donating groups on migrating group or skeleton.

ABNORMAL BECKMANN REARRANGEMENT:-

OXIME $\xrightarrow{H^{\oplus}}$ NITRILE.

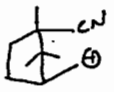
If product Nitrile R.A is called Beckmann A.A.



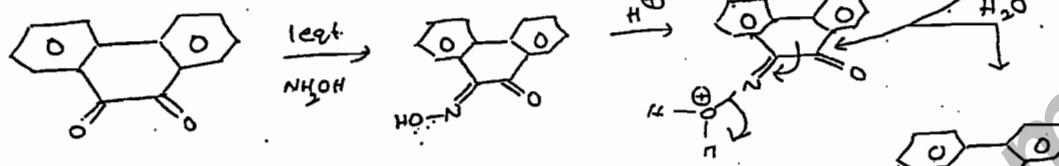


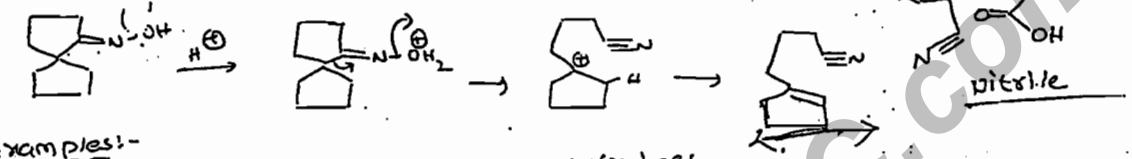
(a) ✱ Ruled out.

3° carbocation



3° carbocation (unstable)

✱ 

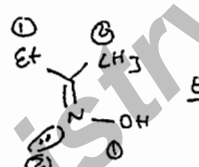
✱ 

Examples:-

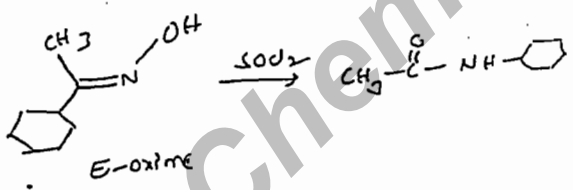
1) Determination of configuration of ketoximes.

Oxime $\xrightarrow[\text{B.R.A}]{H^{\oplus}}$ Amide $\xrightarrow{H_3O^{\oplus}}$ CH_3-CO_2H + $Et-NH_2$

Which group attached to NH_2 that is anti to 'OH' in Reactant.



E oxime.

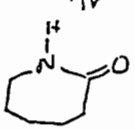


E-oxime

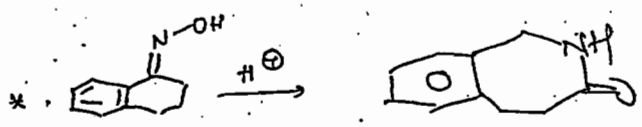
2) Prep^{n} of caprolactum (best method is B.R.A)

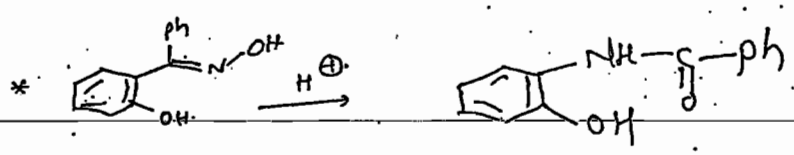
✱ $H^{\oplus}$ first attacks at –OH Not 'N'

✱ caprolactum is a monomer of Nylon-66



ε-caprolactum.





MOLECULAR REARRANGEMENT OF ELECTRON-DEFICIENT-OXYGEN:-

1) BAEYER-VILLIGER'S OXIDATION
2) ALKYL-HYDRO-PEROXIDE R.A
3) DAKIN-REACTION.

BAEYER-VILLIGER'S OXIDATION:-

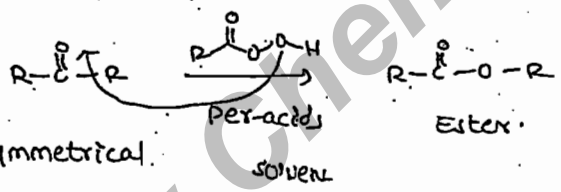
* Insertion of oxygen

* Aldehyde $\xrightarrow[\text{solvent}]{\text{per-acid}}$ carboxylic acids (or) esters

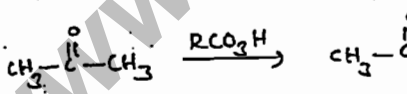
(Depends on nature of migrating group)

Ketone $\xrightarrow[\text{solvent}]{\text{per-acid}}$ Ester.

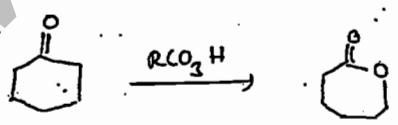
conversion of ketone to ester by using peracids called Baeyer-Villiger oxidn



Symmetrical Ketone — Ester.



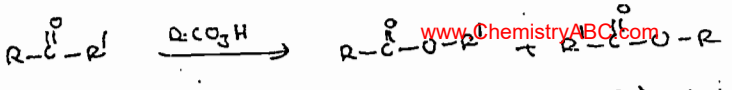
Methyl Acetate.



Lactones

* one of the Best method to prepare Lactones from ketones is -

Baeyer-villiger oxidn



major minor

"Regioselective"

Unsymmetrical Ketone :

* $R' > R$ migratory aptitude.

↳ * depends on migrating capacity of group.

* In the case of unsymmetrical ketone major & minor products depend on migratory Aptitude of groups

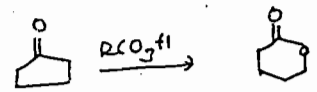
more migratory aptitude groups attachment to ester oxygen becomes major product. (or) preferentially insert oxygen b/w carbonyl carbon and more migratory aptitude group resulting product is major.

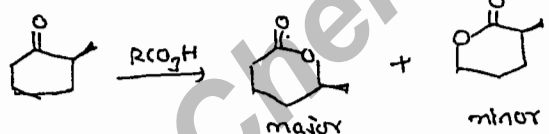
* unsymmetrical ketones Baeyer villiger oxidations are regio selective!!

MIGRATORY APTITUDE OF GROUPS :-

3^0-alkyl > cyclo Hexyl > 2^0-alkyl ≅ Benzyl ≅ phenyl > vinyl > 1^0-alkyl > cyclo propyl > methyl.

* Generally more Branched group more migratory Aptitude.

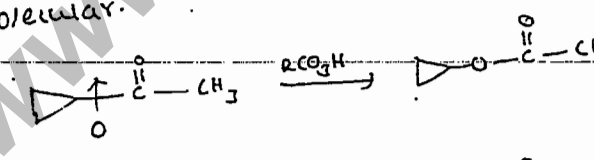


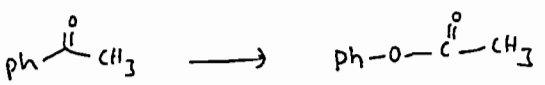


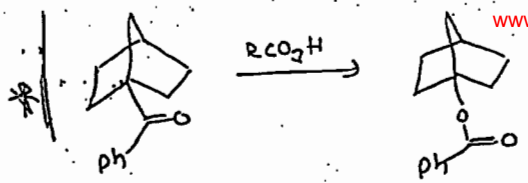
major minor

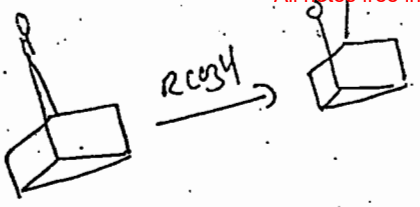
chiral group centre should not effected

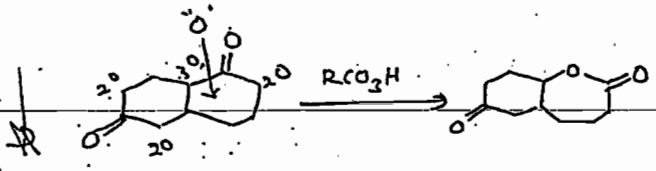
no change in stereo chemistry of chiral centres. stereo specific and Intra molecular.

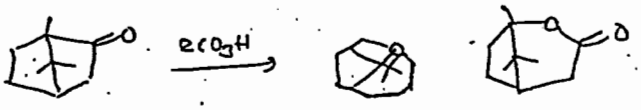












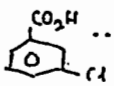
PER-ACIDS:-

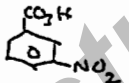
1) per-formic acid 'HCO$_3$H' . PFA.

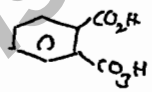
2) per-Acetic acid CH_3CO_3H . PAA.

3) Trifluoro peracetic acid F_3C-CO_3H 'TFPAA'

4) per Benzoic acid $Ph-CO_3H$ 'PBA'

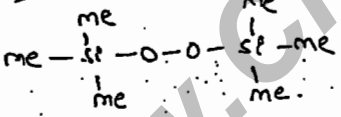
5) m-chloro per Benzoic acid  mCPBA.

6) m-Nitro per Benzoic acid  'MNPBA' (Good reagent)

7) per-mono phthalic acid 

Less common:-

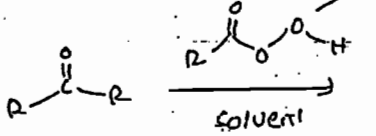
1) H_2O_2

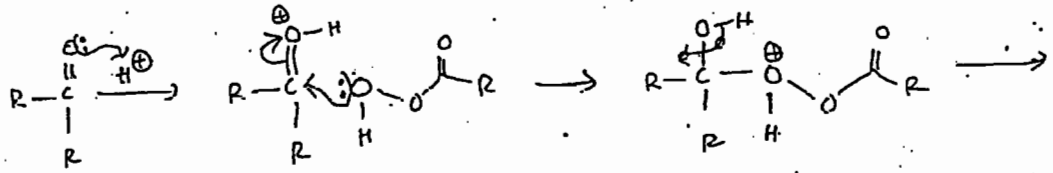
2) 

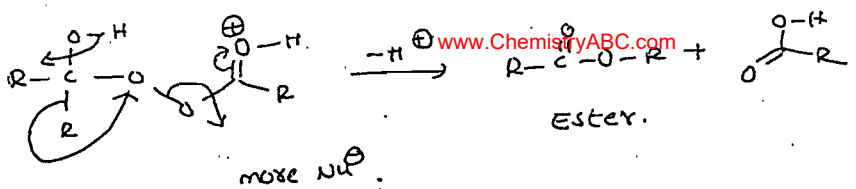
Bis (Trimethyl silyl) peroxide.

acidic as well as oxidising agent.

MECHANISM:-

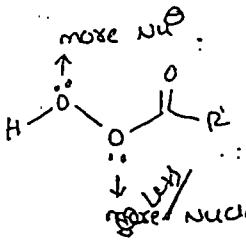
concerted : 





Ester.

16

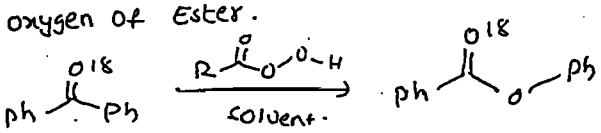


more Nucleophilic due to involved in Resonance.

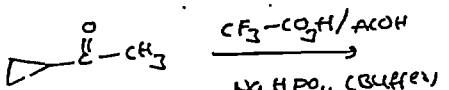
The biproduct acid is removed by washing with aq. $NaHCO_3$ soln.

* In B.V oxidn ketone carbonyl oxygen becomes carbonyl oxygen in esters. It never becomes ether oxygen of Ester.

Evidence:

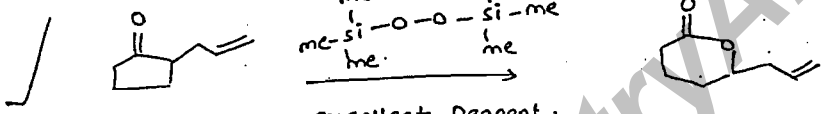


Example:-



$CF_3-CO_3H/AcOH$

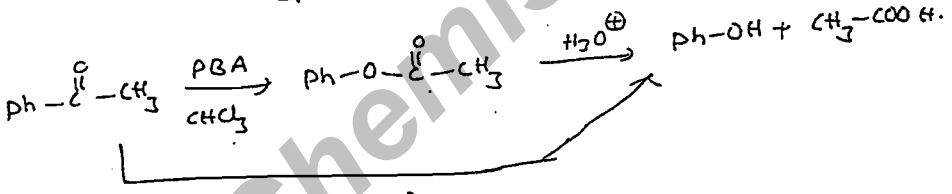
Na_2HPO_4 (Buffer)



excellent Reagent.

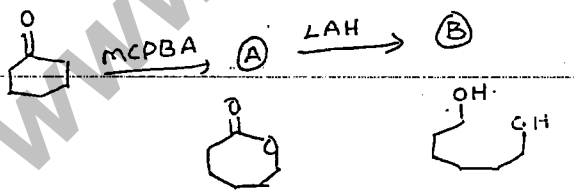
not effected on olefin.

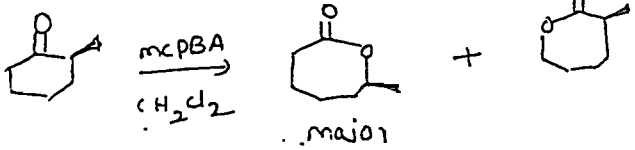
epoxidation restricted.



Good conversion.

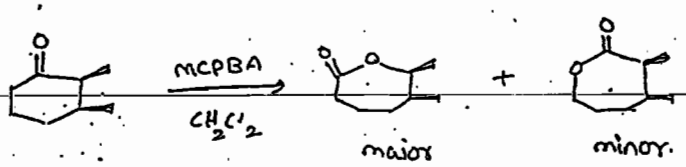
* 

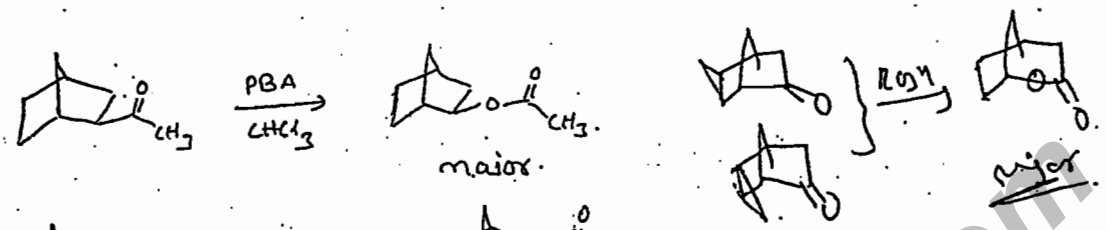


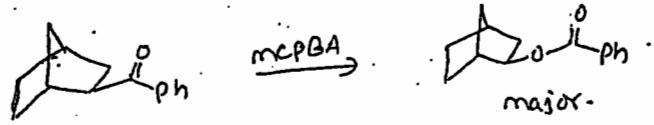


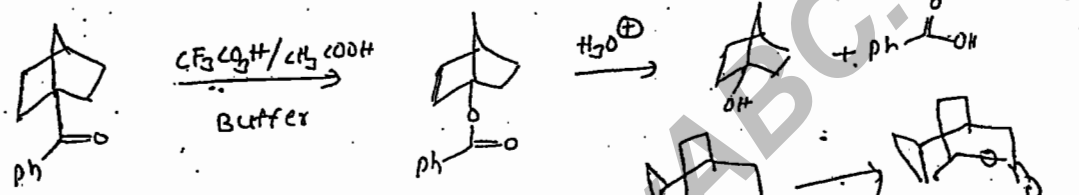
major

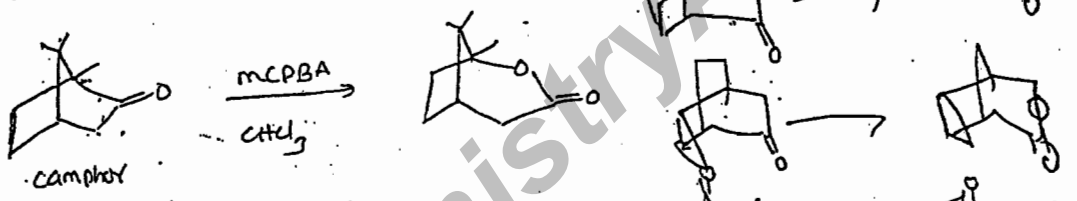
* 2-methyl cyclo Hexanone subjected to Baeyer villger oxid" - mixture of structural Isomers formed in unequal ratio. Highly distinguished with H^1-NMR.

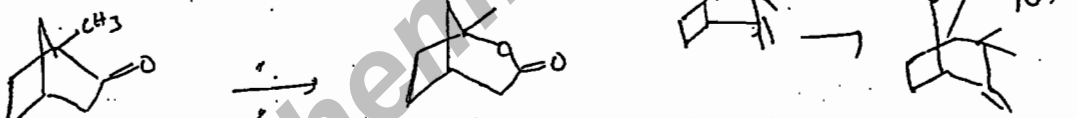


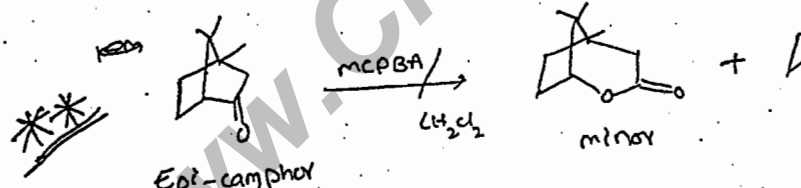






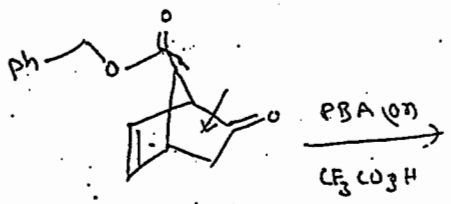






Abnormal B.V - products.

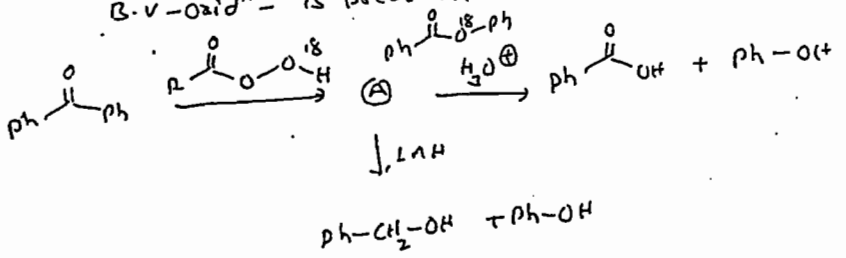
most probable due to sterically crowding in it molecule.

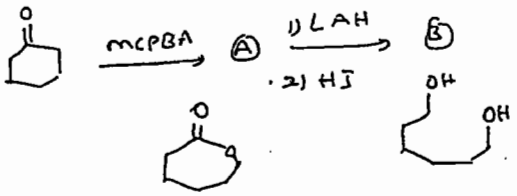


* In sidering db not probable to epoxidation

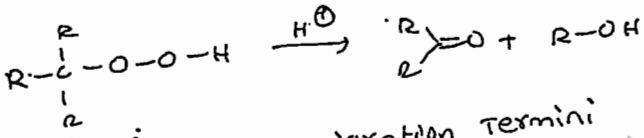
∴ used PBA.

B.V-oxidn - is predominate.

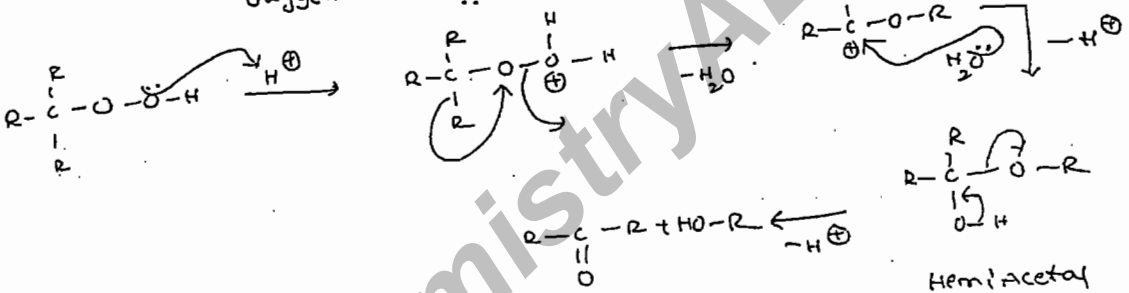




ALKYL HYDRO PEROXIDE REARRANGEMENTS :-

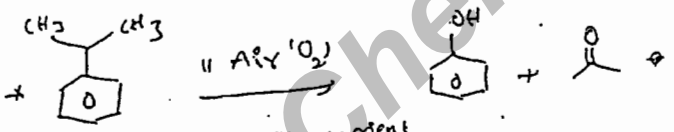


∴ Oxygen migration termini

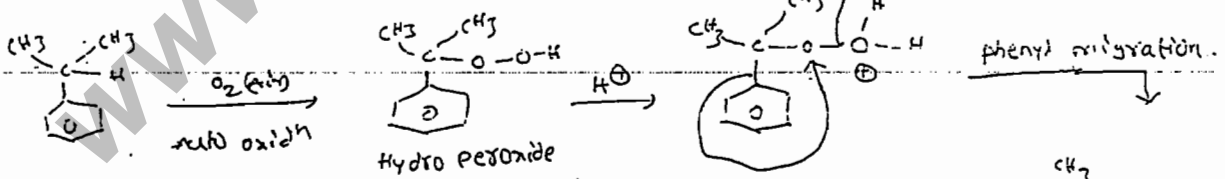


Hemi Acetal

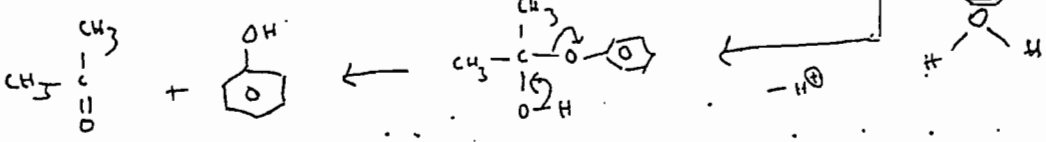
Unstable.

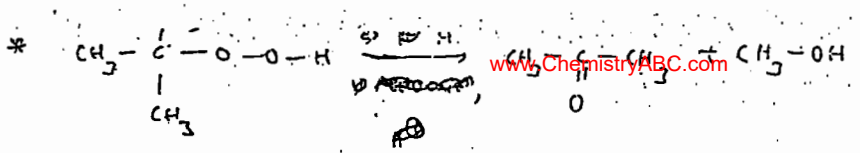


Industrial method to prepare phenol cheaper technique.



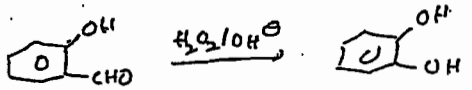
* No any oxidising agents used



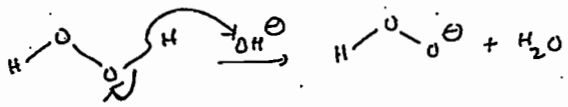


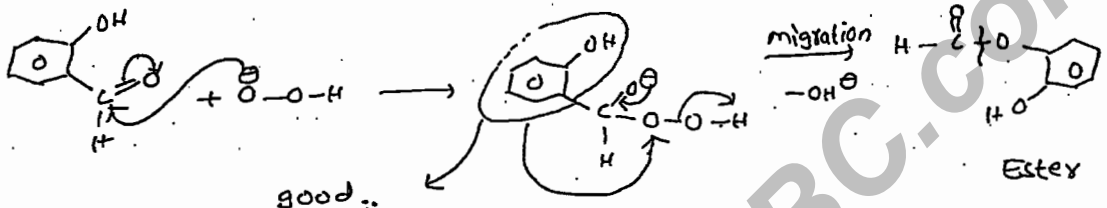
DAKINS - REACTIONS :-

conversion of ~~salicil~~ salicilaldehyde into catechol in presence of alkali H_2O_2

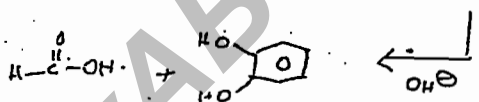


Mech :-





good migration aptitude than 'H'. Due to $\oplus$ E donating group on Aryl.



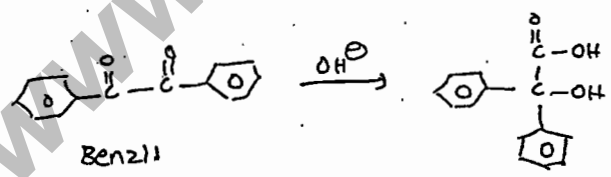
BASE CATALYZER MOLECULAR REARRANGEMENTS :-

1) Benzilic acid Rearrangement.

2) Favorski Rearrangement.

BENZILIC ACID REARRANGEMENT (OR) BENZIL - BENZILIC ~~ACID~~ ACID R.A :-

1,2 Di carbonyl compound $\xrightarrow{OH^\ominus}$ α - Hydroxy carboxylic acid.



Benzil

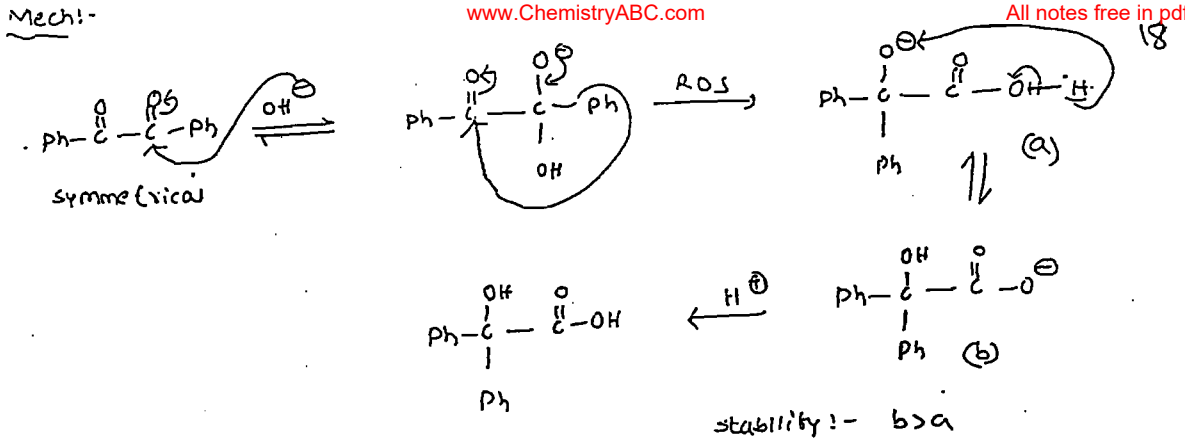
Benzilic acid (α - Hydroxy acid)

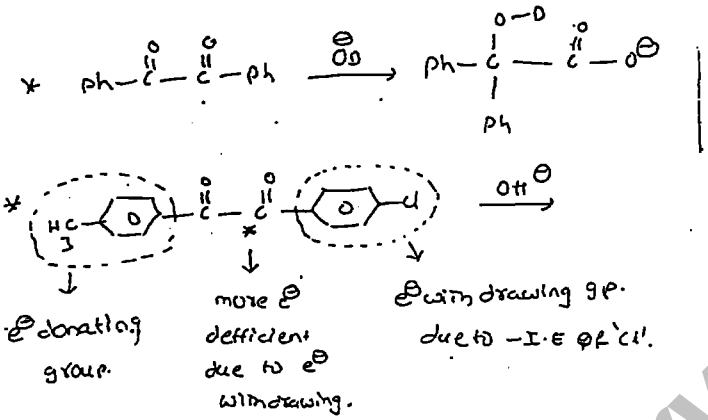
* 1,2 shift.

* $OH^\ominus$ act as Nu$^\ominus$ and base.

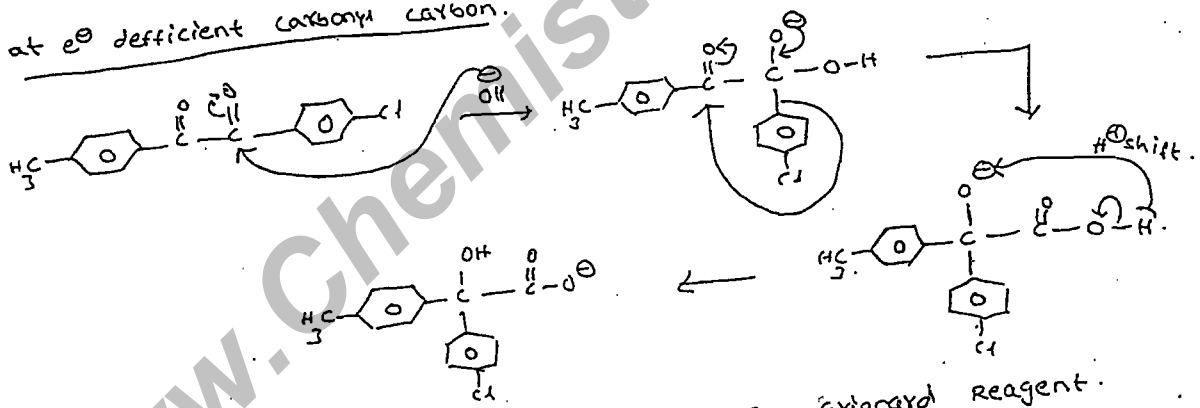
In this R.A $OH^\ominus$ Acts as Nu$^\ominus$.

Mech:-

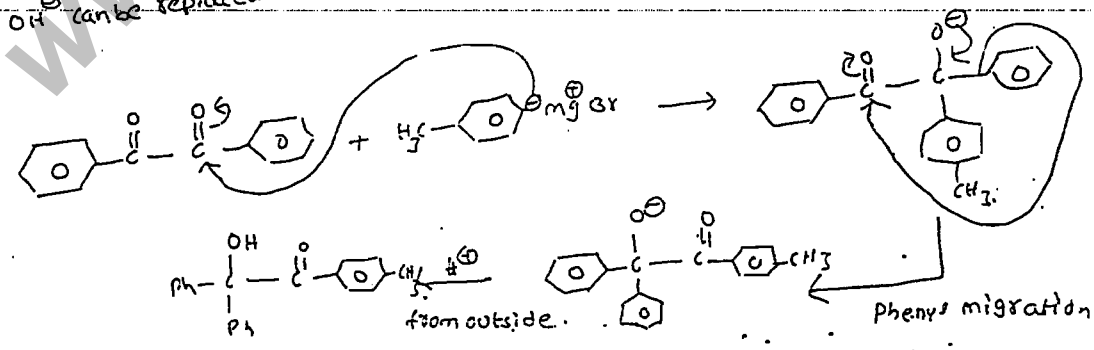




In the case of unsymmetrical 1,2- dicarbonyl compounds $OH^{\ominus}$ preferentially attacks at e⊖ defficient carbonyl carbon.

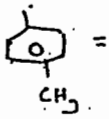


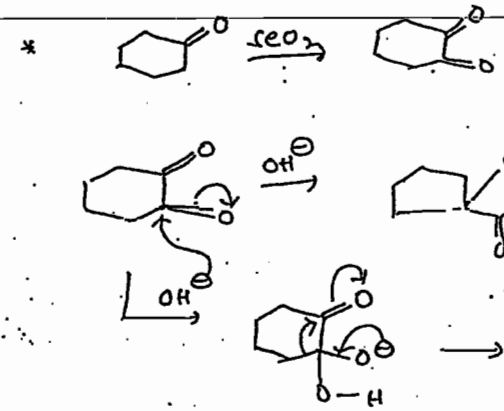
* $OH^{\ominus}$ can be replaced with other nucleophile. Ex:- Grignard Reagent.

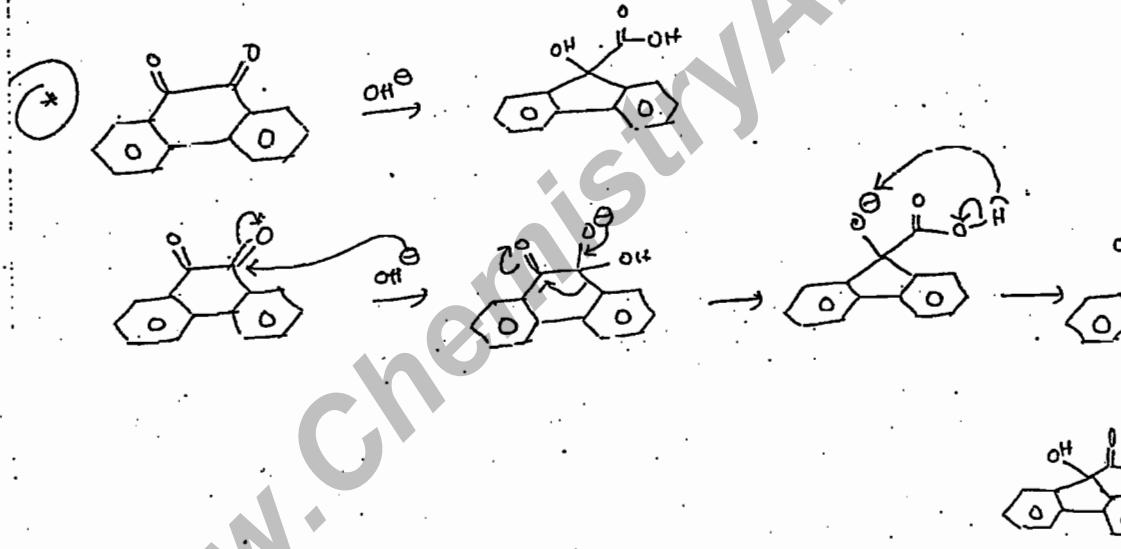


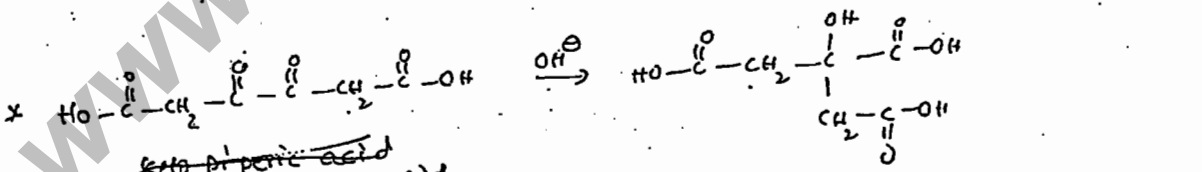
ph = old connecting group (prefer)

= new connecting & more stable.



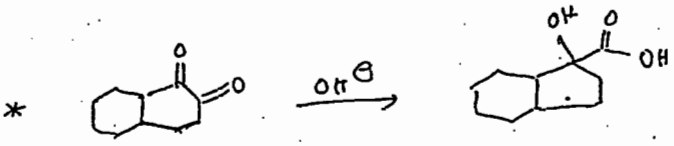






Ketopimic acid

citricacid.



FAVORSKII - REARRANGEMENT :-

ketone $\xrightarrow{\ominus OR}$ ester

$\xrightarrow{OH^{\ominus}}$ Acids

$\xrightarrow{NH_2^{\ominus}}$ Amide

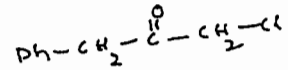
conversion of α-Halo ketones into esters in the presence of Alkoxide with change in carbon skeleton called Favorskii Rearrangement.

In the place of alkoxide use of Hydroxide or Amide.

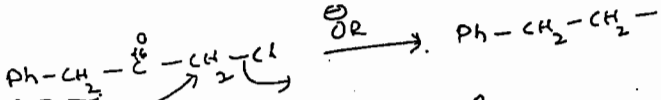
~~$OH^{\ominus}$ & $OR^{\ominus}$ as Nucleophile used~~

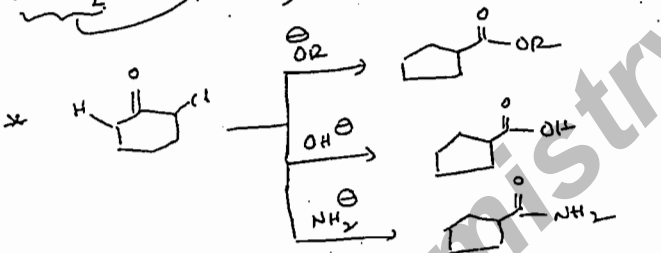
$OH^{\ominus}$ & $NH_2^{\ominus}$ as Nucleophile used products are Acid & Amide.

* Halo groups. Cl, Br, I can't 'F' Because 'F' is not good leaving group.



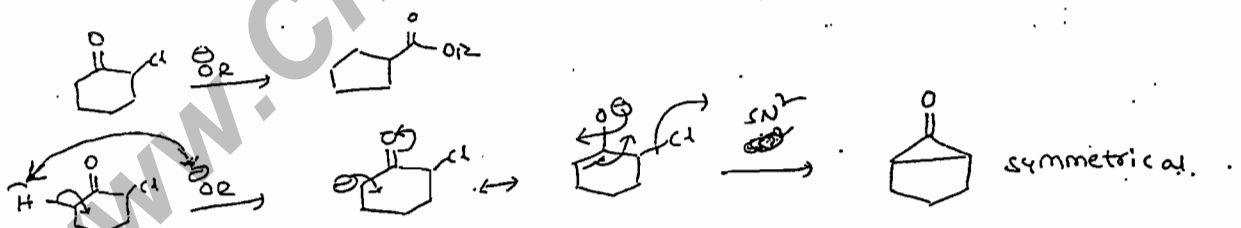
minimum one α'H to other side of $\overset{O}{\overset{\|}{C}}$ must, other wise No Rean.





"Ring contraction"

Mechanism :- proceeds Through cyclo propanone Intermediate.



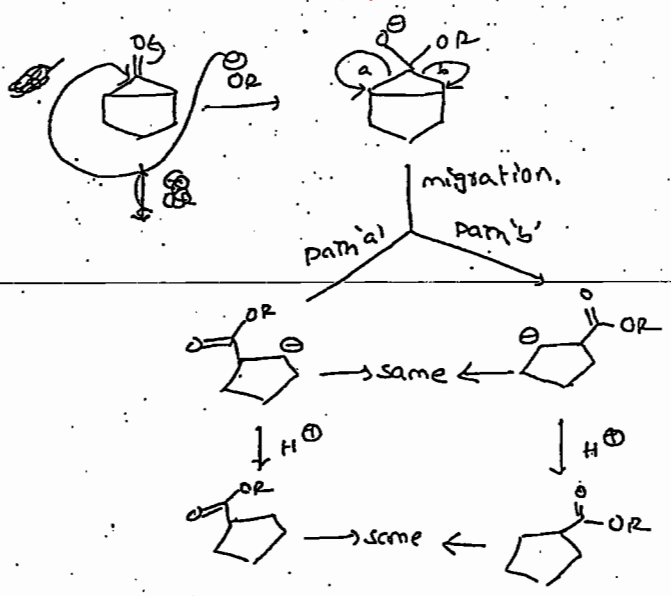
Act as Base

cyclo propanone Intermediate. unstable.

symmetrical.

* Non halo $H^{\oplus}$ can be removed.

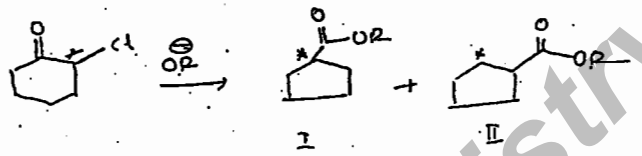
* In Rean $OR^{\ominus}$ acts as Base. and as well as Nu$^{\ominus}$.



EVIDENCE:-

For cyclo propanone formation:-

1) ISOTOPIC LABELLING:- ($C^{*} = C^{14}$)



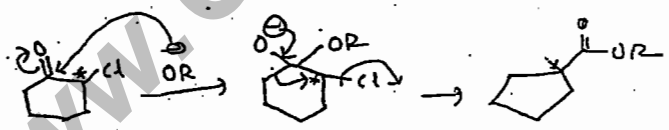
I II

Chemical theart features are same.

* products are differed in position of labelled carbon.

* These formation can be explained only with cyclo propanone. Intermediate.

another type mech:-



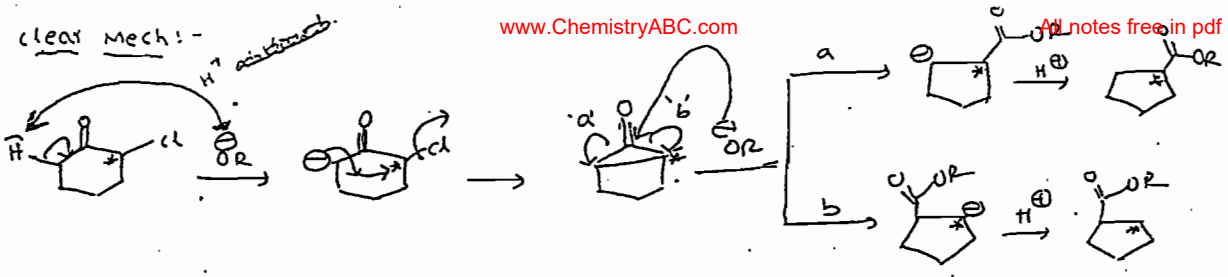
NO cyclo propanone formation. It's wrong mech. first mech. is clear mech.

It is proved.

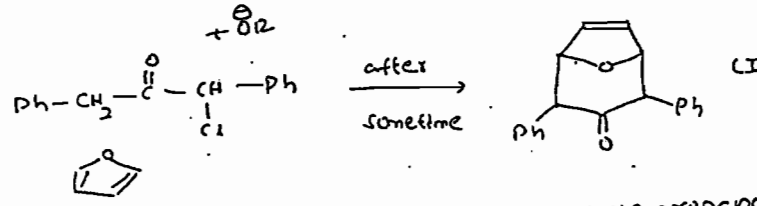
Without cyclopropanone Intermediate only one product is appear.

∴ the above mech is wrong.

clear Mech:-

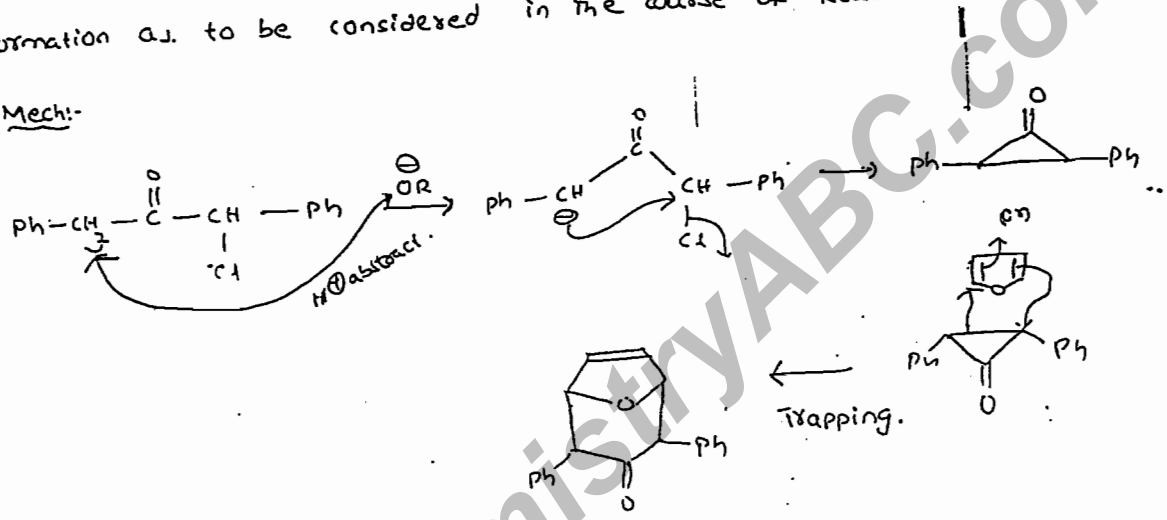


ii, TRAPPING OF CYCLOPROPANONE:-

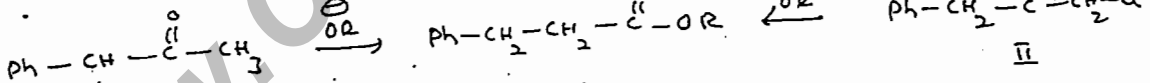


To explain formation of Isolated product cyclo propanone Intermediate formation as to be considered in the course of Reaction

Mech:-



Isolation of aduct indicating cyclo propanone intermediate. in Favorskii Rearrangement.

3) 

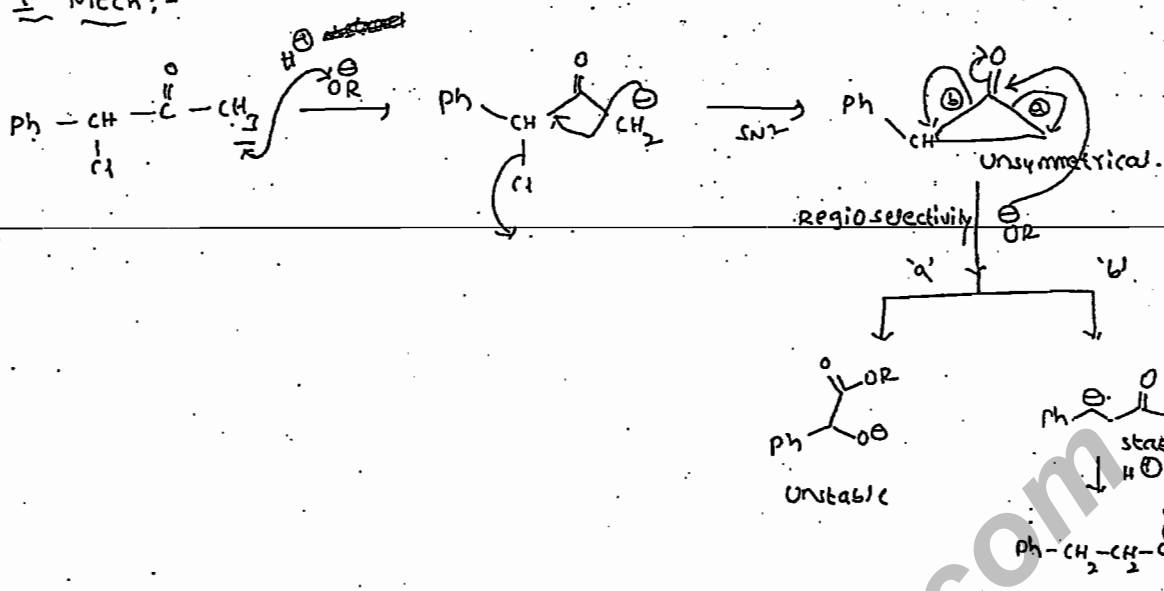
I II

Both Reacn produced same product.

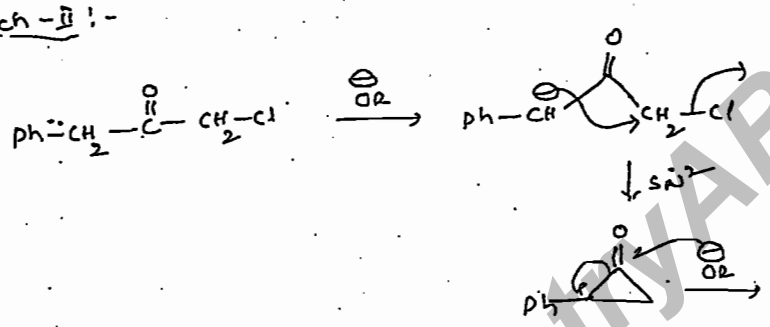
Formation of same product from these different reactant (I & II) can be shown only with cyclo propanone intermediate formation.

P.T.O.

I Mech:-

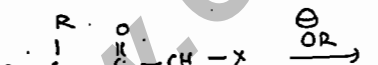


Mech-II :-



Both Ist & IInd rea^{n}s are proceeding through same an common ~~cyclo propanone~~ cyclo propanone intermediate. Therefore resulting products are same.

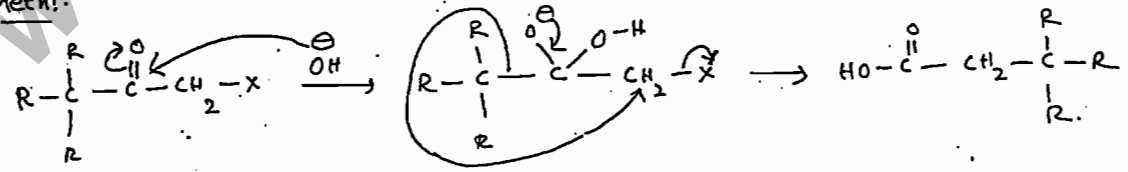
* 



NO 'α' H.

involved as Benzilic acid R.A.

Mech:-



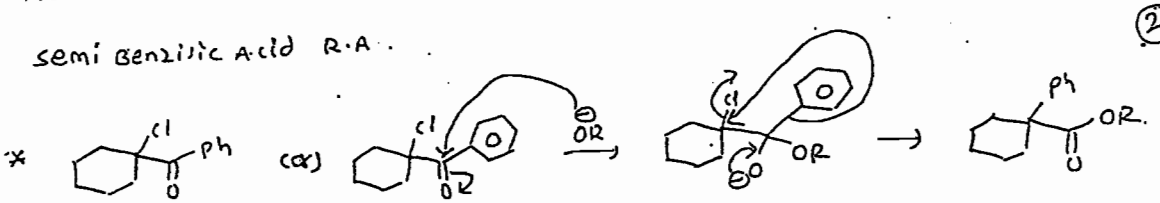
This mech is Benzilic acid ~~Rea~~ Type R.A.

∴ QUASIFAVORSKII (OR) SEMI BENZILIC ACID R.A.

At α-position of C-C if there is no proton follow Quasi Favorskii

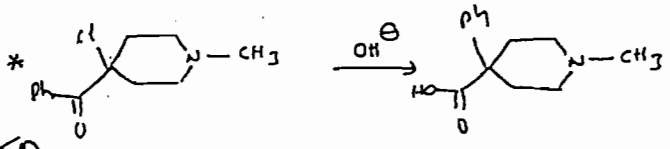
(21)

semi Benzilic Acid R.A.



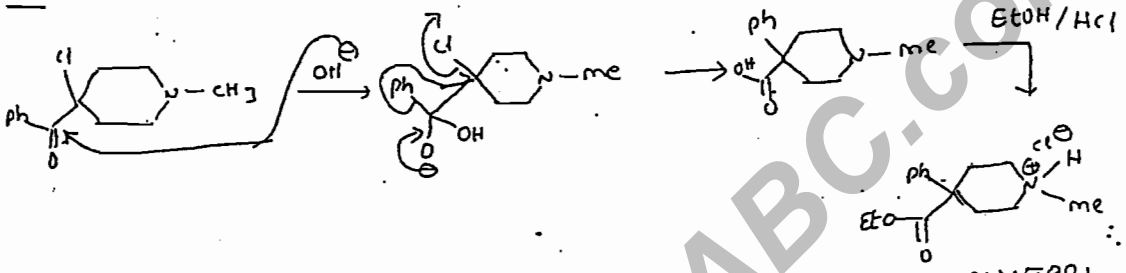
NO α-Hydrogen

semi Benzilic acid R.A.

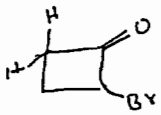


T.S

Mech:

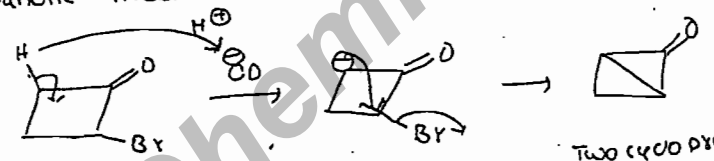


DIMEROL



There is a α-~~acid~~ proton still involve in semi Benzilic acid R.A. Because. Favorskii rearrangement develops highly strained cyclo propanone intermediate.

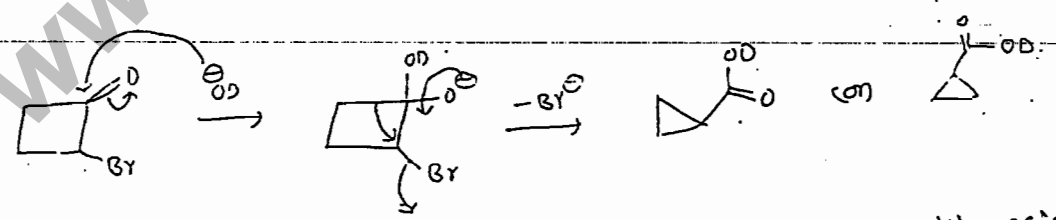
Mech:



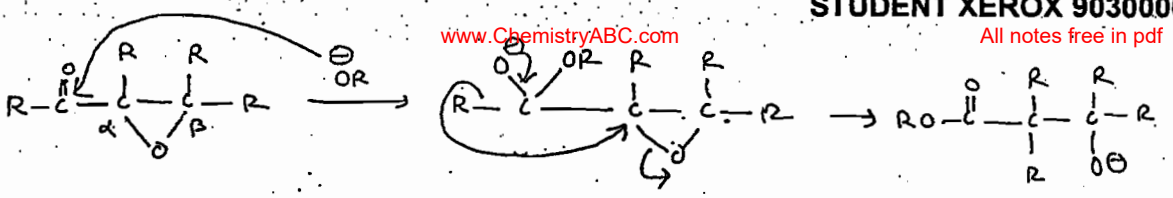
Two cyclo propane rings.

Highly strained intermediate.

∴ Not preferred Favorskii R.A. Taking alternate Pathway semi Benzilic Acid R.A.

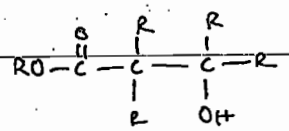


* α,β-Epoxy carbonyl compounds also may involve in semi Benzilic acid Type Rearrangement.



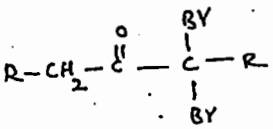
Quasi Favorskii or semi Benzilic acid

R.A.

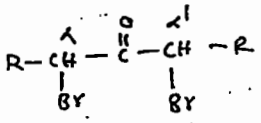


β-Hydroxy ester.

* Geminal, vicinal di halo C.C compounds stabilized as α, β-unsaturated ester, Acid etc.



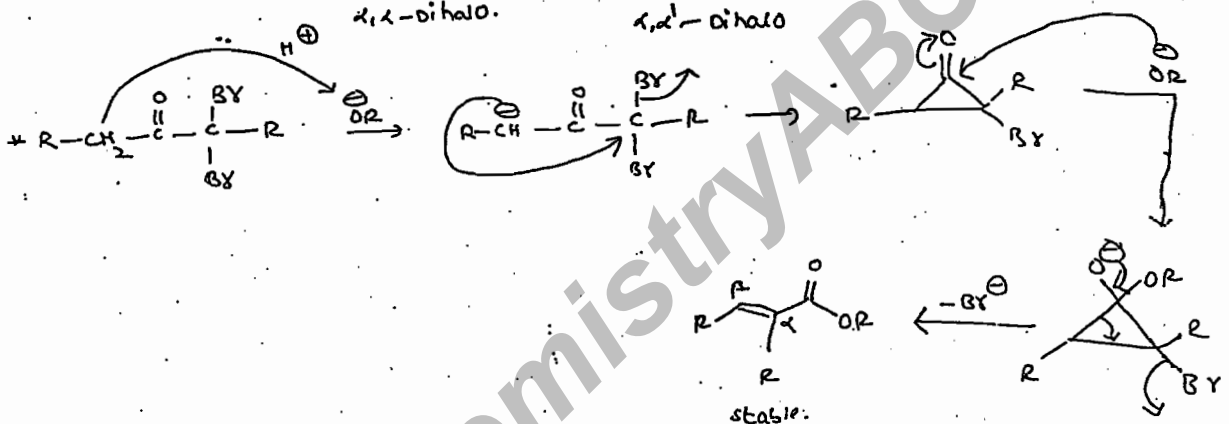
Geminal dihalo comp.



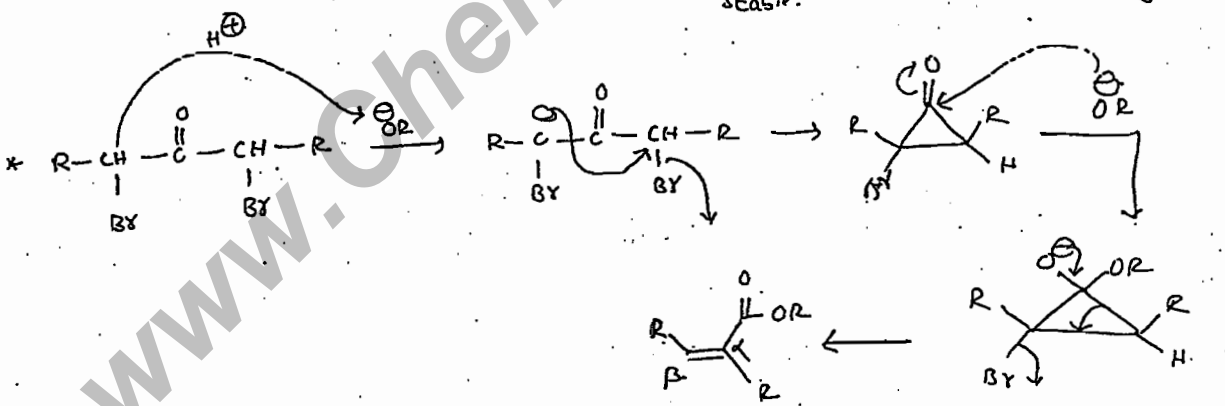
Vicinal dihalo

α,α-dihalo.

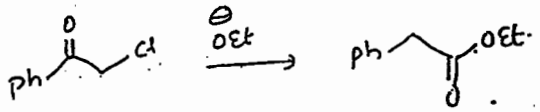
α,α'-dihalo



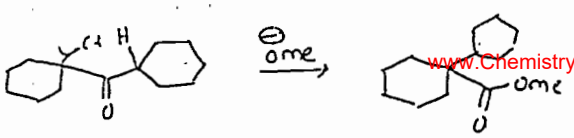
stable.



Examples:-

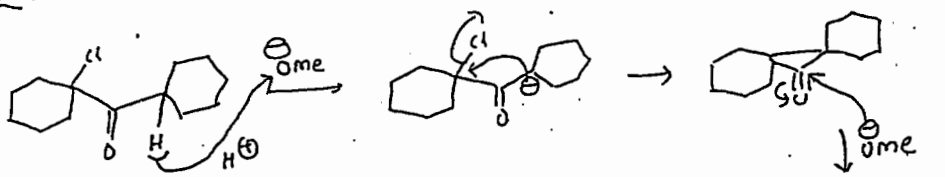


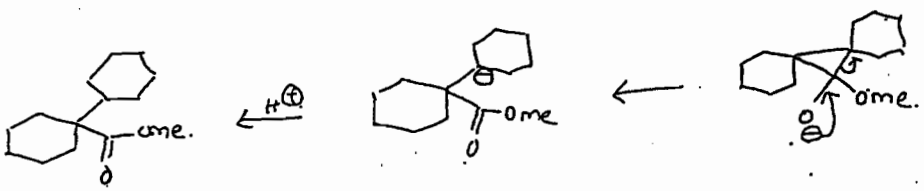
Quasi – Favorskii R.A

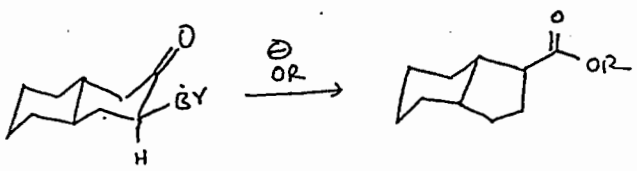


22

mech:-

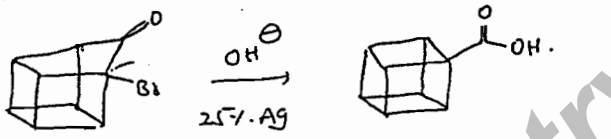


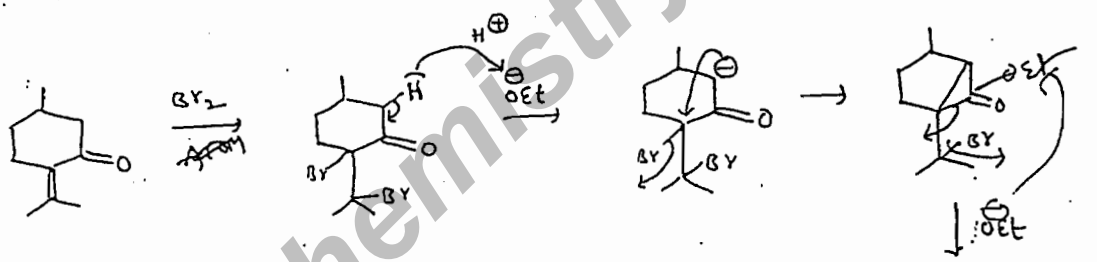


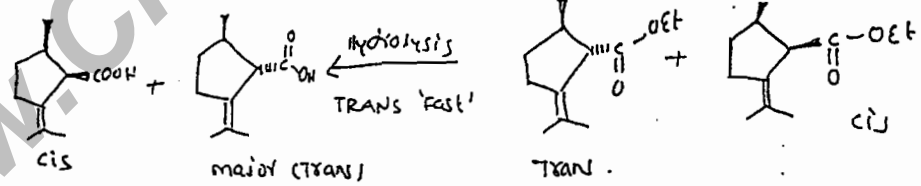


It Halo group at Axial position.

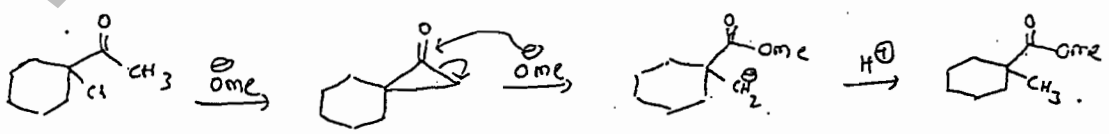
Favorskii R.A will not takes place.

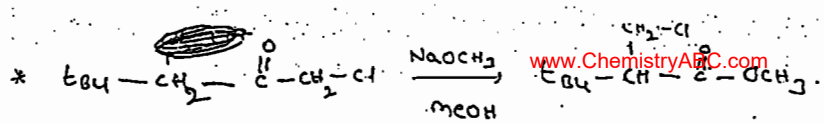


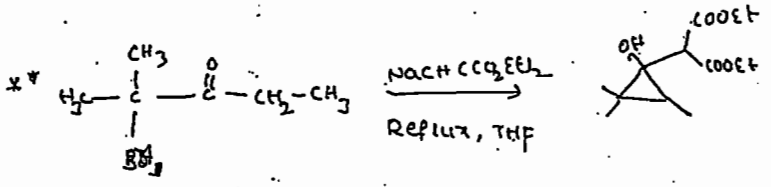


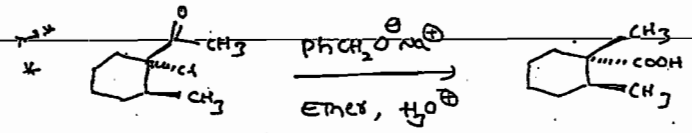


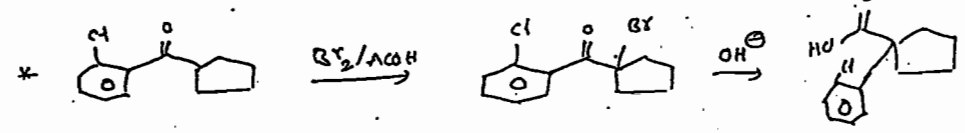
Trans-pulegenic acid

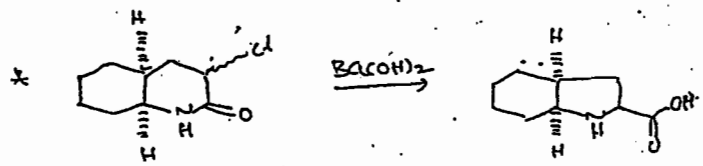




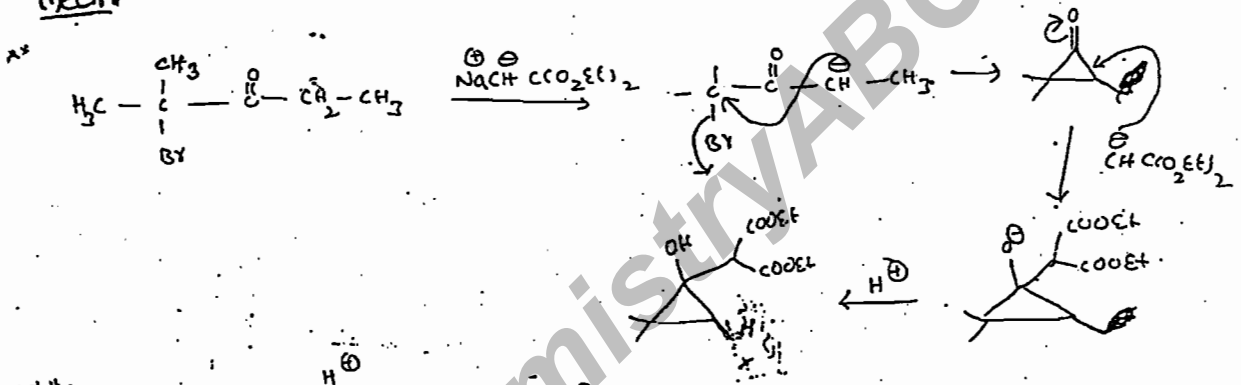


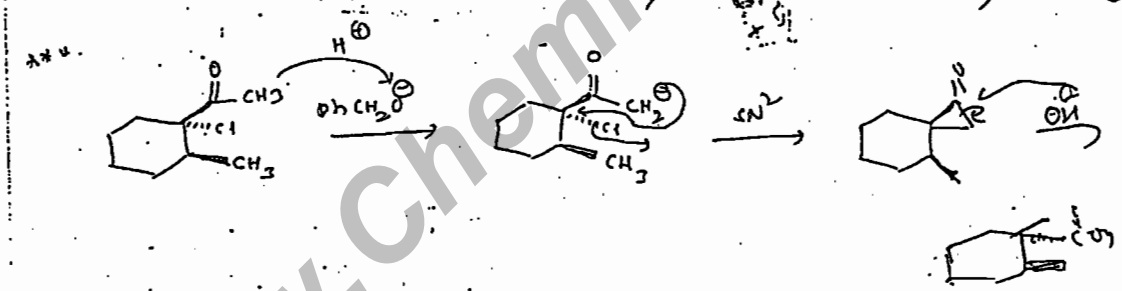


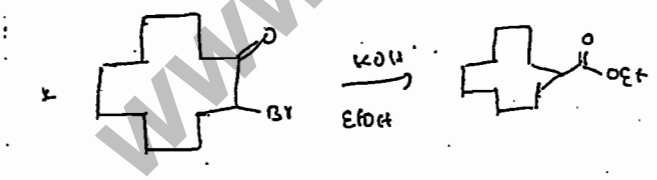


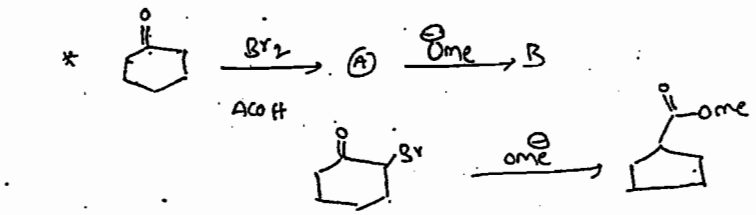


mech





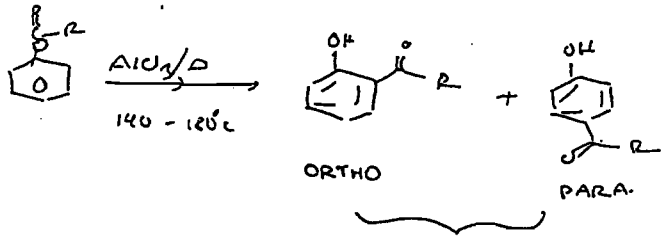




FRIES REARRANGEMENT :-

Rearrangement to Aromatic skeleton.

Inter convertable functional groups.

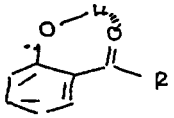


Unequal form

* major, minor Isomers formation depends on reaⁿ condⁿ.

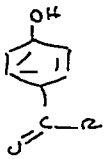
conversion of Aromatic Ester (Phenolic Ester) into Aromatic Hydroxy ketones in the presence of Lewis Acid ($AlCl_3$) called Fries Rearrangement

It is a thermal Rearrangement



Intra molecular H - Bond.

+ thermodynamically stable (Low B.P)



Inter molecular H - Bond (High B.P)

* IR is the Best spectroscopy to distinguish ortho, para Isomers.

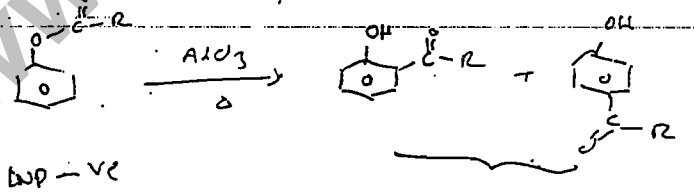
* Intramolecular H - Bonding Isomer B.p lesser.

Inter molecular H - Bonding Isomer B.p higher

Separation :-

Isomers are separated by steam distillation.

Chemical Test :-



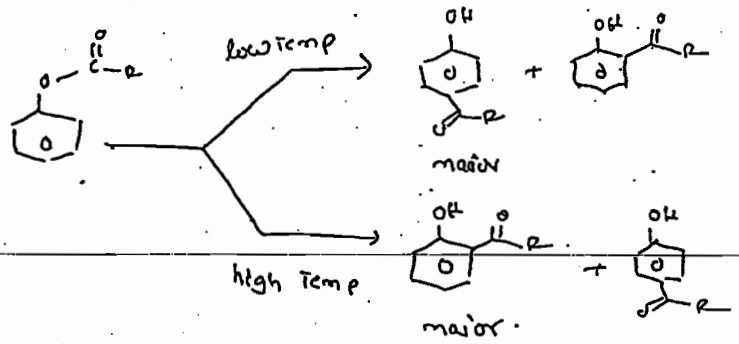
2,4, DNP - Ve

Neutral $FeCl_3$ - Ve

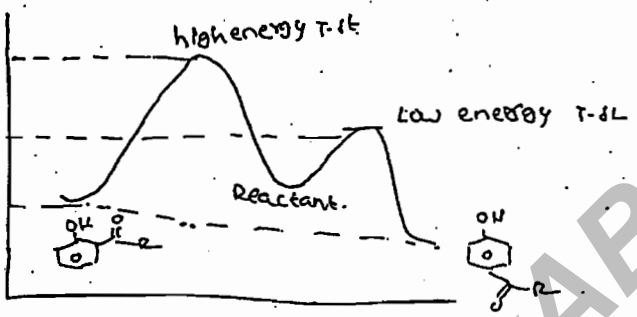
2,4 DNP +Ve (Test for carbonyl)

Neutral $FeCl_3$ +Ve (Test for phenolic)

STUDENT XEROX 9030000126



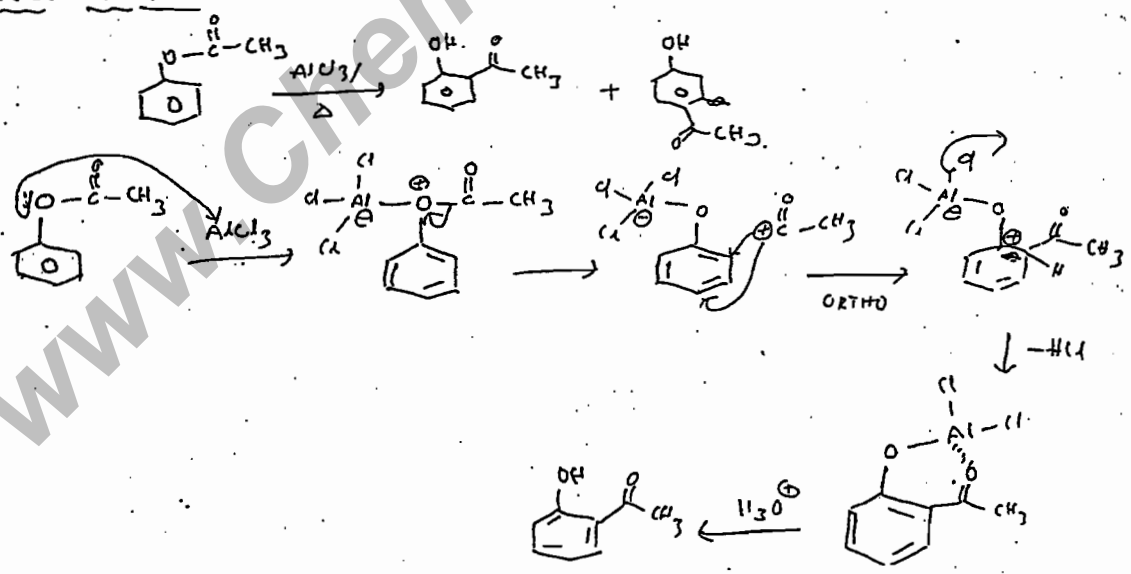
At higher Temp favouring thermodynamically stable product. Intramolecular H-Bonding participate and Internal energy less.



Mech:-

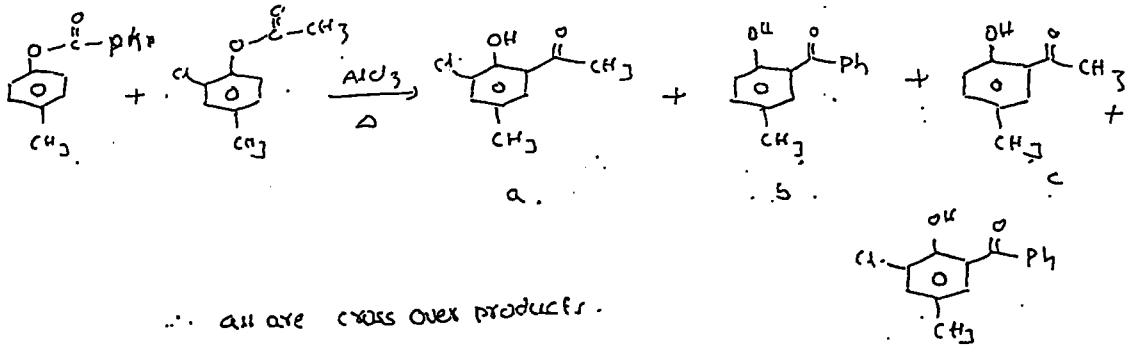
In general FRIES R.A are Intermolecular R.A. But even Intramolecular R.A also known

INTER M.R.A:-



EVIDENCE:-

CROSS OVER EXPERIMENTS:-



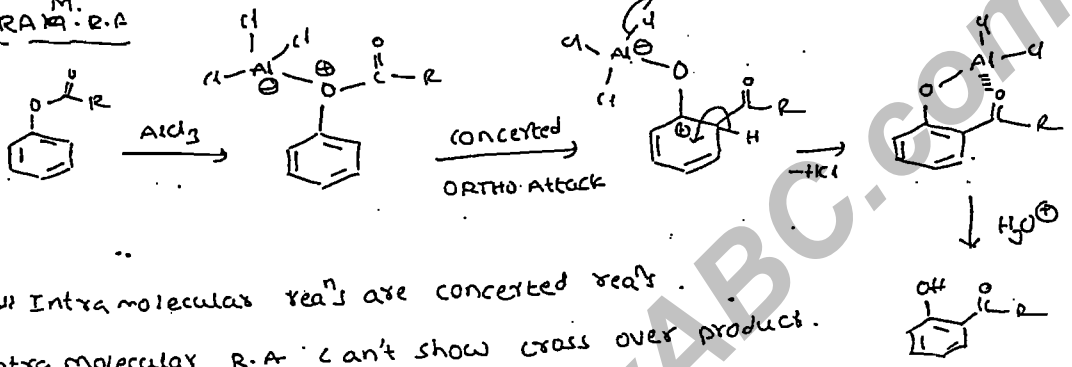
a. b. c.

d

∴ all are cross over products.

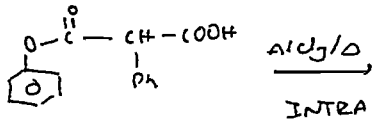
mechanism is inter molecular. R.A

INTRA M. R.A



* All Intra molecular rea^{n}s are concerted rea^{n}s.

¥ Intra molecular R.A can't show cross over product.



percentage of form^{n} of ORTHO – PARA Isomers depends on following condition.

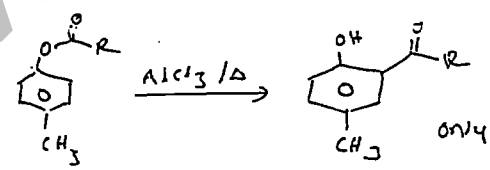
1) Temp:- Higher Temp major 'ORTHO'

Lower Temp major ~~PARA~~

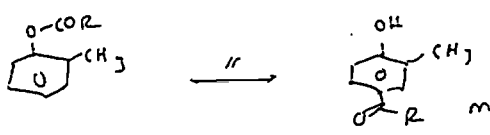
2) Amount of Catalyst:-

Increase in quantity of catalyst increases. percentage of ORTHO.

3) Nature of Reactant:-



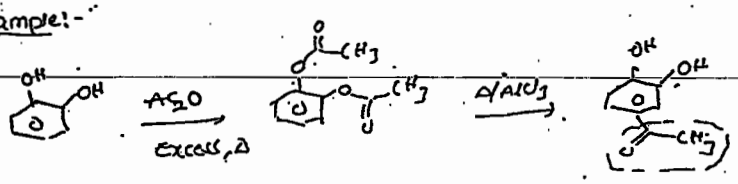
only ORTHO



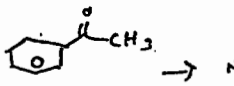
main. PARA

% of meta sub^n depends on Reaction condition.

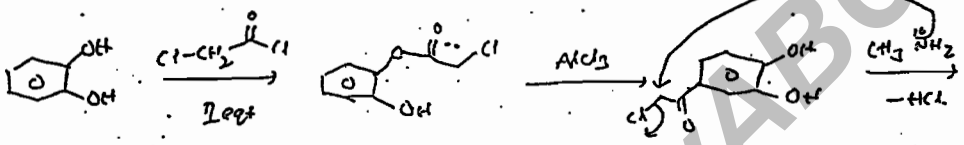
Example:-

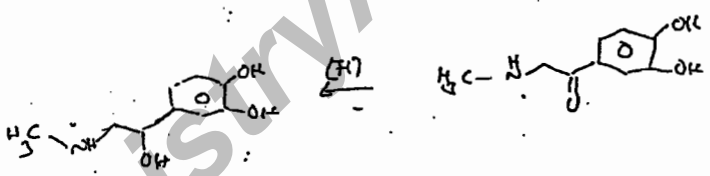


de activated phenyl group.
due to its $e^{\ominus}$ with drawing capacity.
∴ another Acyl cation will not attack an phenyl group.



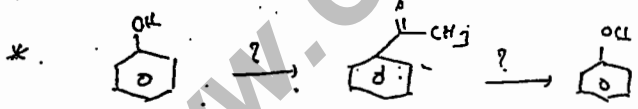
→ Not possible $e^{\oplus}$ sub^n on ring due to presence of $e^{\ominus}$ with drawing group.

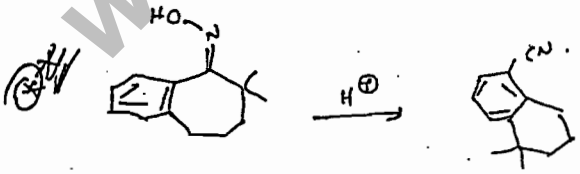


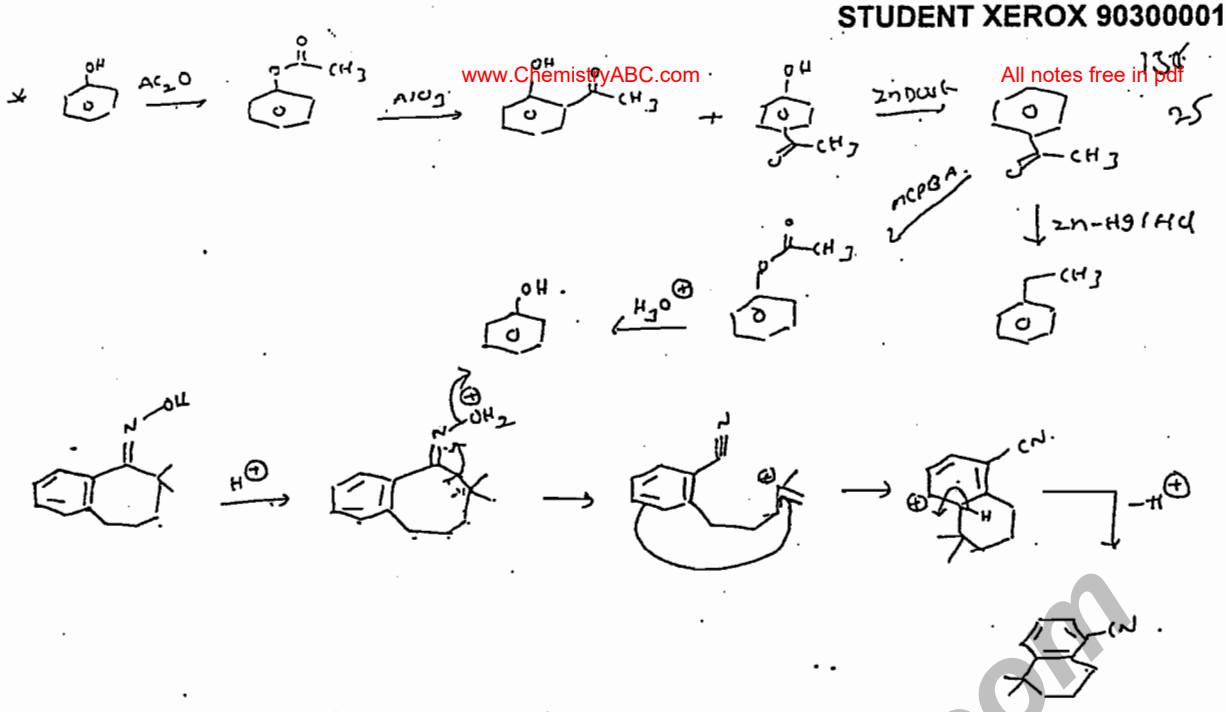


major

minor.





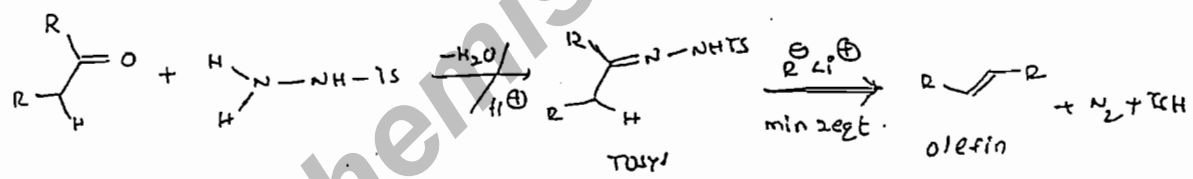


SHAPIRO REACTIONS

carbonyl compound $\xrightarrow{\text{condensation}}$ Tosyl hydrazones $\xrightarrow{\text{strong Bases}}$ olefins.

SHAPIRO Reaction.

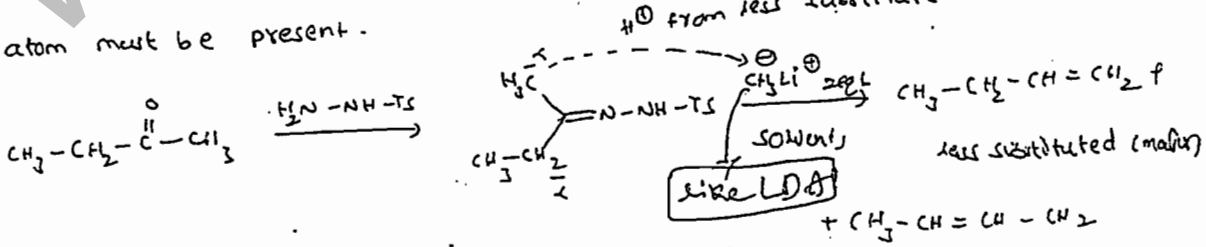
conversion of Tosyl Hydrazones of carbonyl compounds into olefins in the presence of excess strong Base. SHAPIRO Reaction.

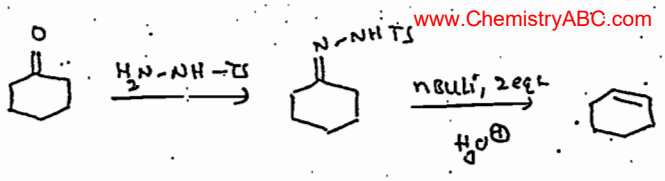


CARBONYL — OLEFIN

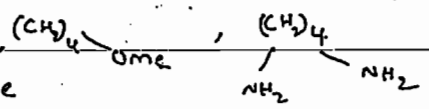
* min 1 Hydrogen at α-position of carbonyl compd (on α-position of Tosyl Hydrazone.

* At α-position of carbonyl compound or Tosyl-hydrazone min one H-atom must be present.

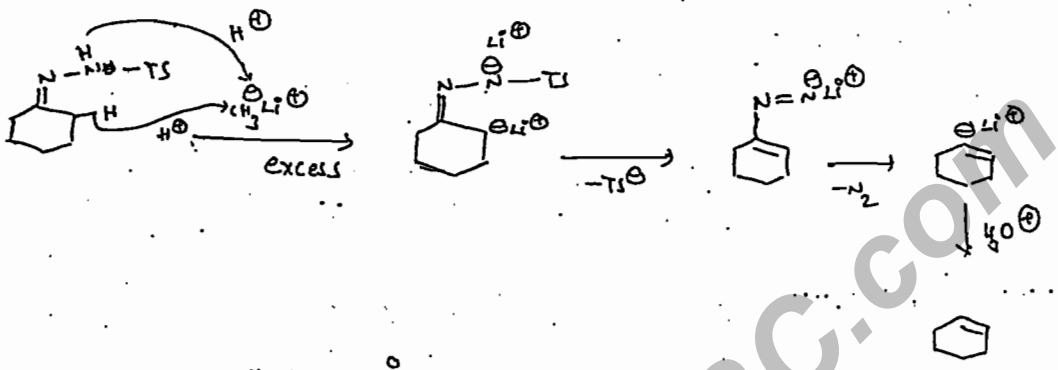


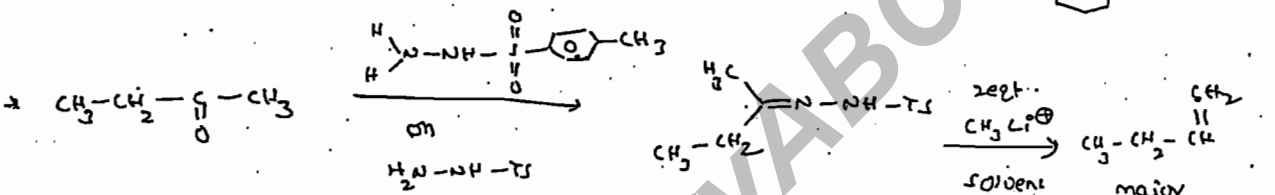


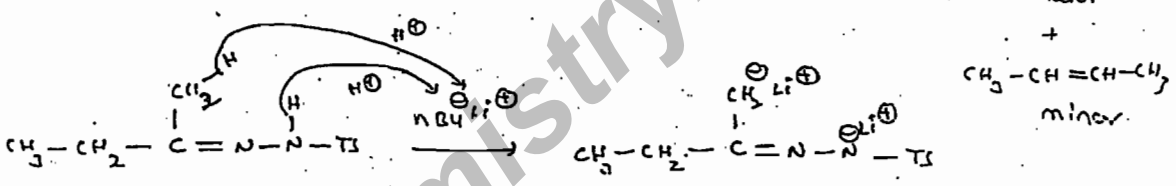
Solvent:

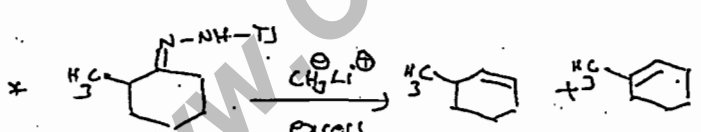


Mech.

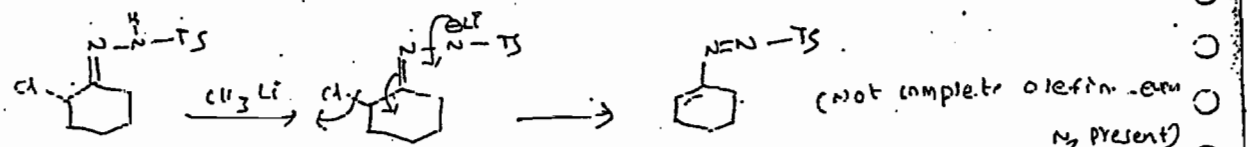


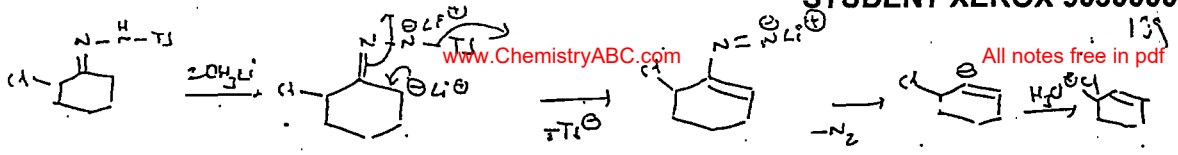




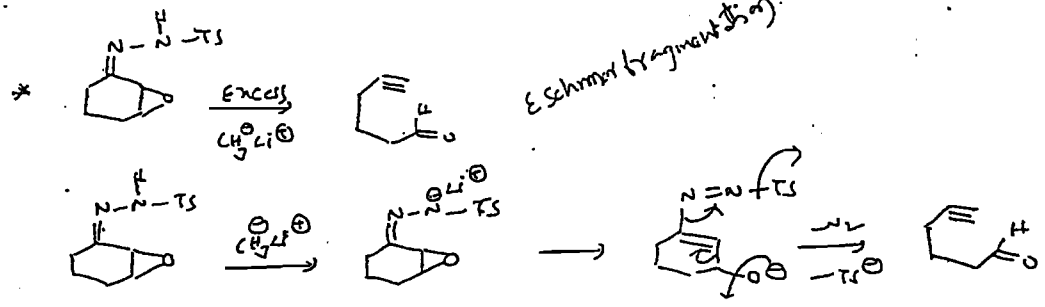


* If leaving group present at α- position

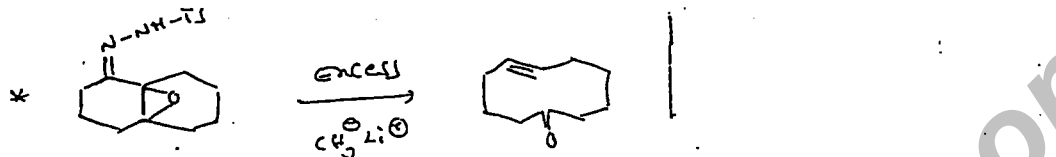


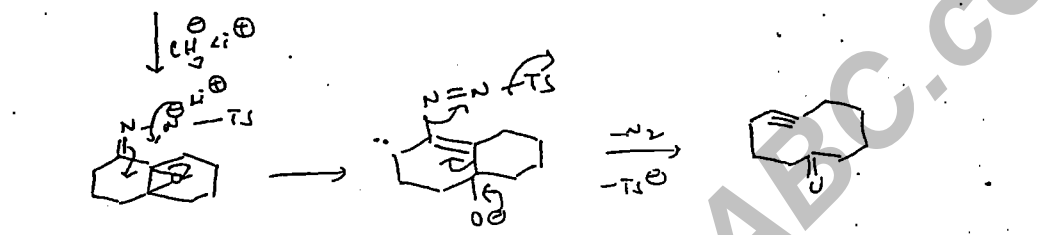


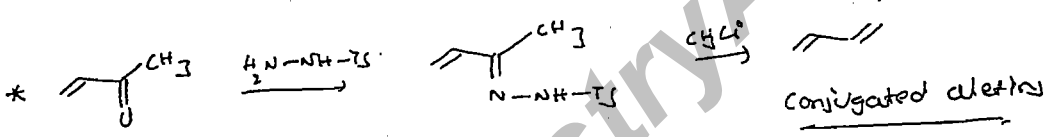
Dianion



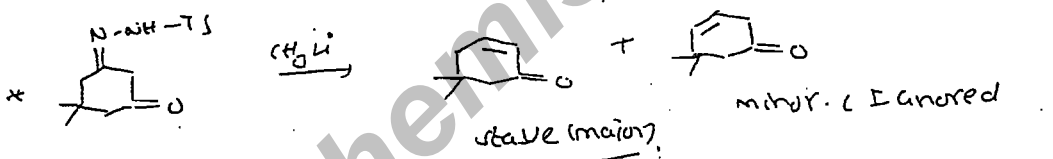
Eschenmoser fragmentation



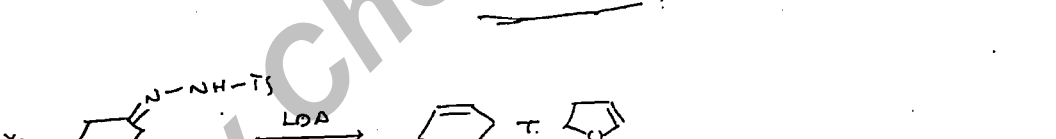


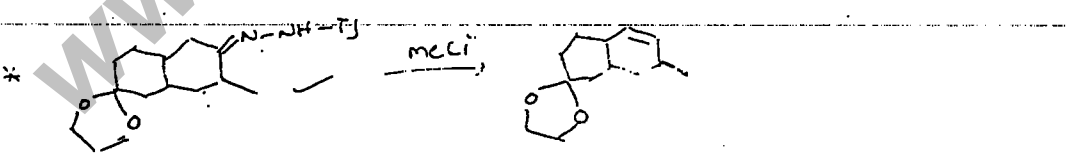


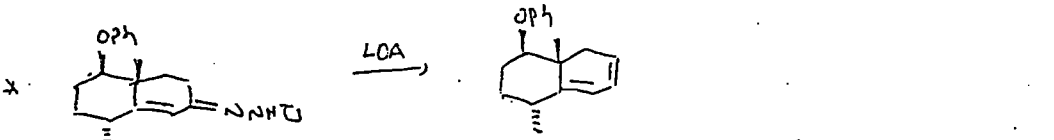
conjugated diene



major (Ignored)







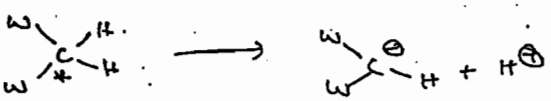
MICHAEL REACTION:-

Popular rea^{n} for C–C Bonding

* Addition of Active C-H group at activated α,β-unsaturated systems. called michael Reaction

* Active group which readily ionises into carbanion and proton is the active C-H group.

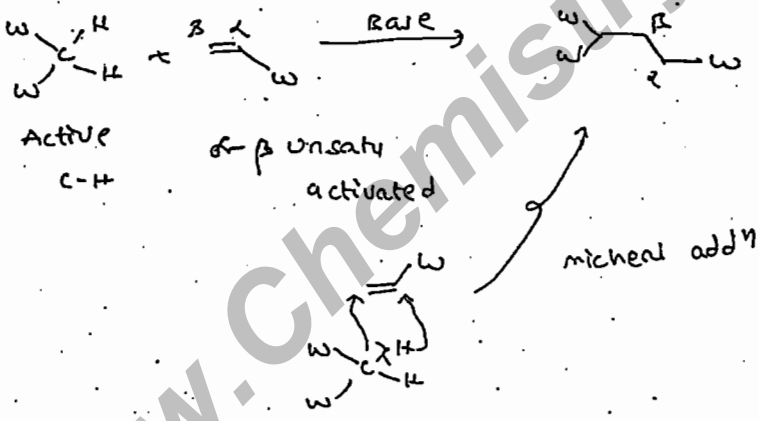
olefin which is attached to $e^{\ominus}$ withdrawing groups. Activated α,β-Unsaturation



Active C-H gp

Acidic


, Activated α,β unsaturation.

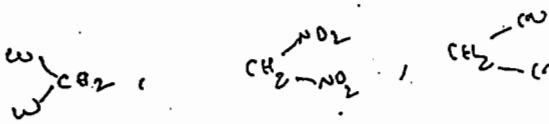


* new C–C bonding always at β- position of α,β-unsaturation activated

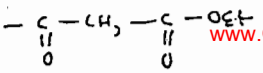
Example :-

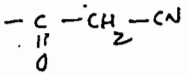
michael donor : $\omega-CH_3$

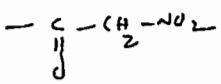
O_2N-CH_3, CH_3-CN, $CH_3-\overset{O}{\overset{\|}{C}}-R$, $CH_3-\overset{O}{\overset{\|}{C}}-OR$ etc

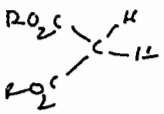


27

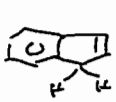
β-keto esters 

β-keto nitriles 

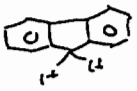
β-keto nitro 

diesters : 

Allylic & Benzylic position

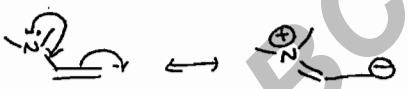


Indene

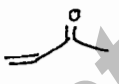


FLOURENE

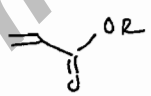
Enamines :- Amino function attached to olefin.

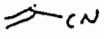
Enamine acting as M.D .. 

MICHAEL ACCEPTORS :- 

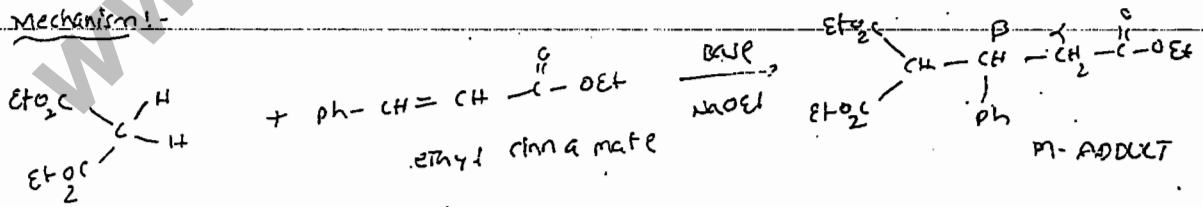
Ex:- α,β unsaturated C=C 

" Acids 

" esters 

Nitriles 

Mechanism :-



Diethyl malanoate

M. donar

ethyl cinnamate

M. Acceptor

M-ADDUCT

435

Bases:-

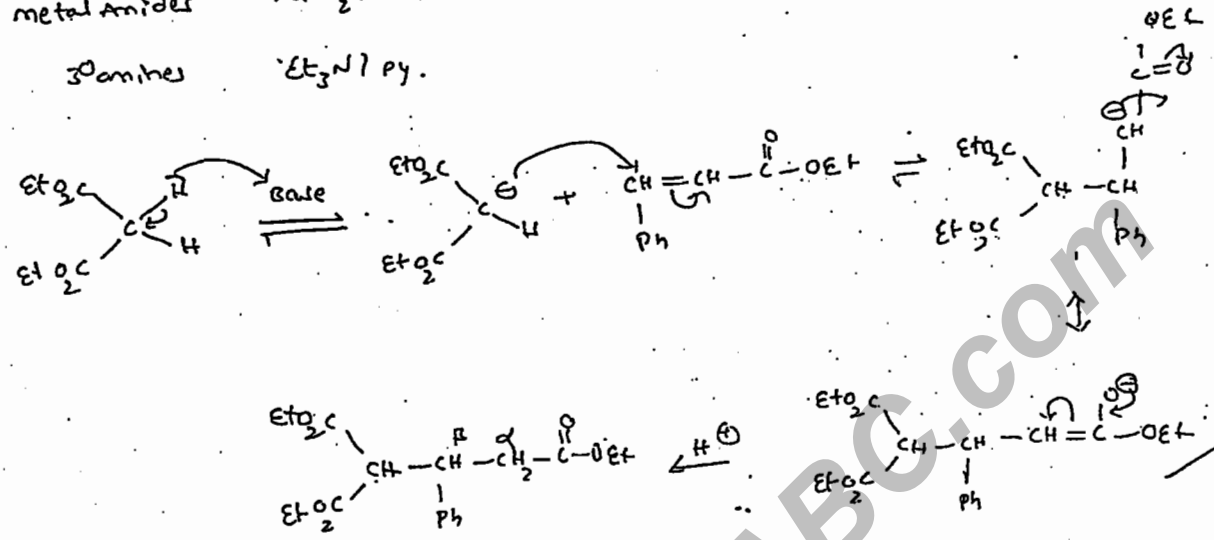
Hydroxides NaOH / KOH

Alkoxides $RO^{\ominus}Na^{\oplus}$ / $RO^{\ominus}K^{\oplus}$

metal hydrides NaH / KH

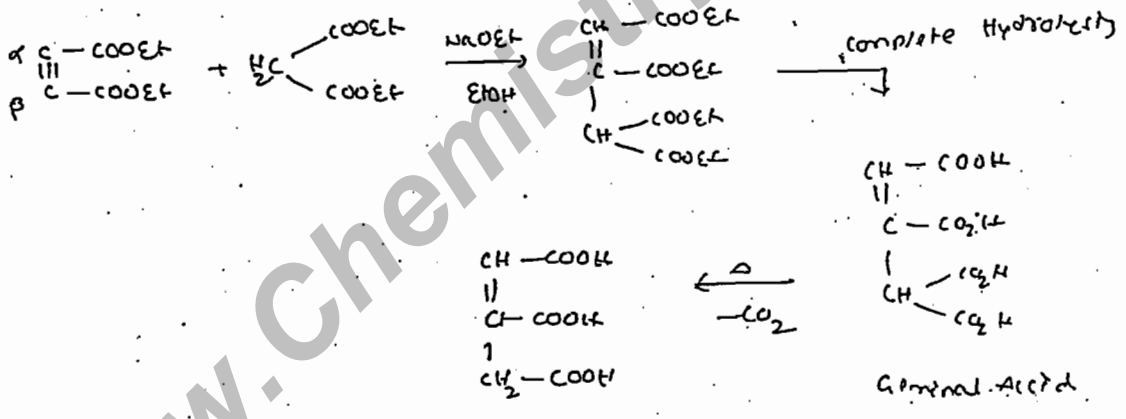
metal Amides $NaNH_2$ / KNH_2

3° amines Et_3N / Py.



APPLICATION:-

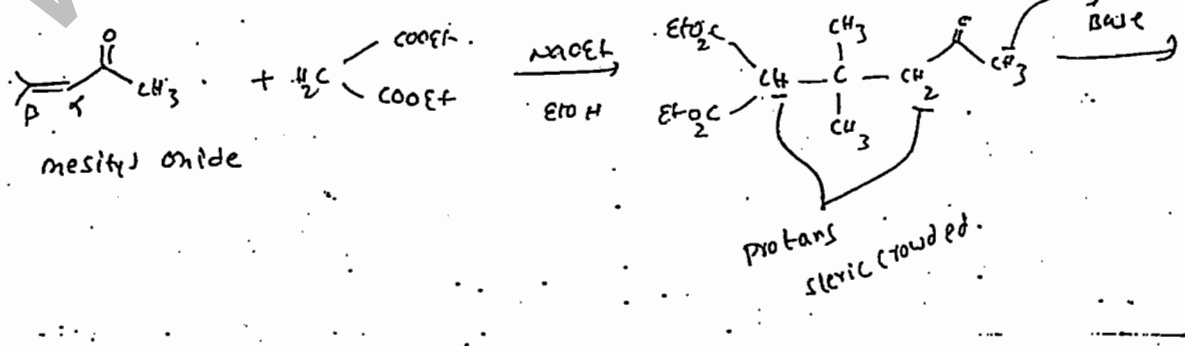
1) ACONITIC ACID



Citronal Acid

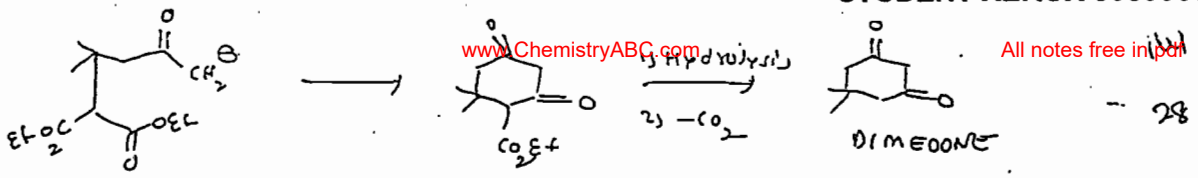
readily loss of CO_2

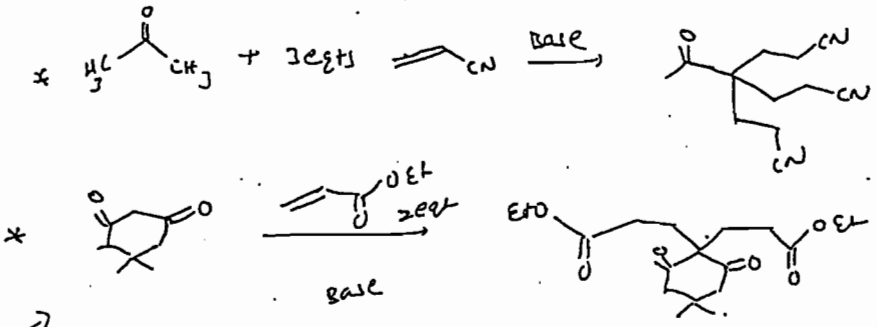
2) Prep^n of DIMEDONE :-



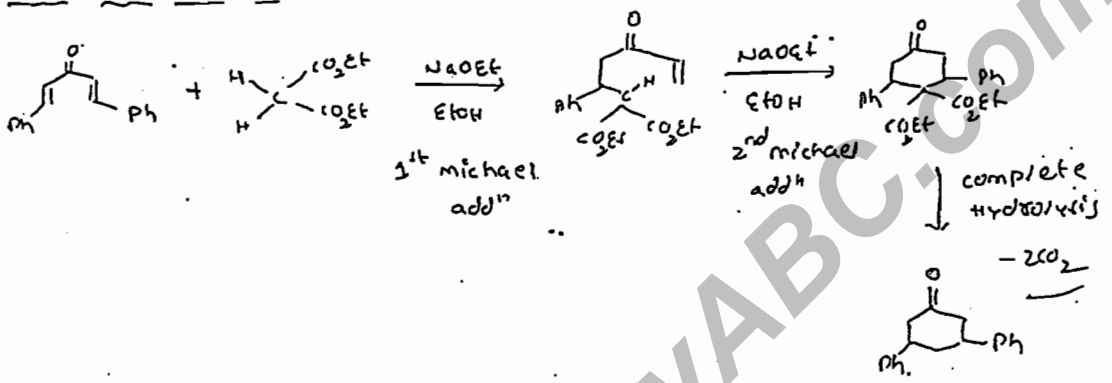
mesityl oxide

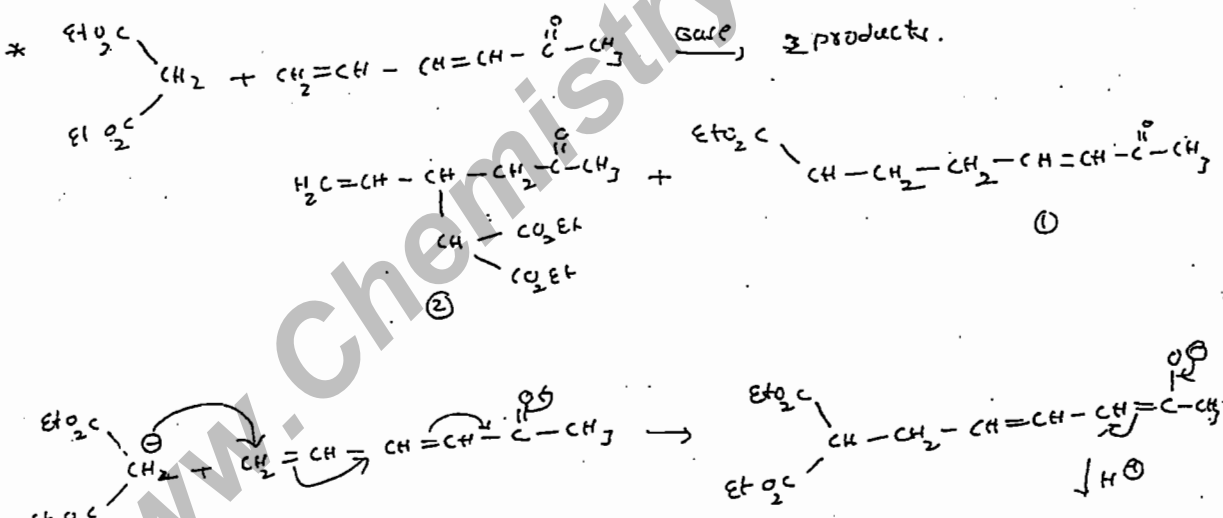
protons sterically crowded.

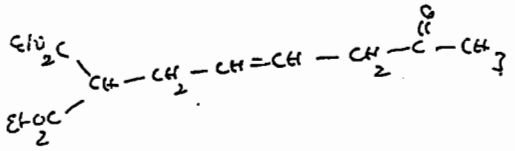




DOUBLE Michael Addⁿ:-







STORK ENAMINE REACTION:-

ENAMINE Analogus to Enol's ($=_{OH}$)

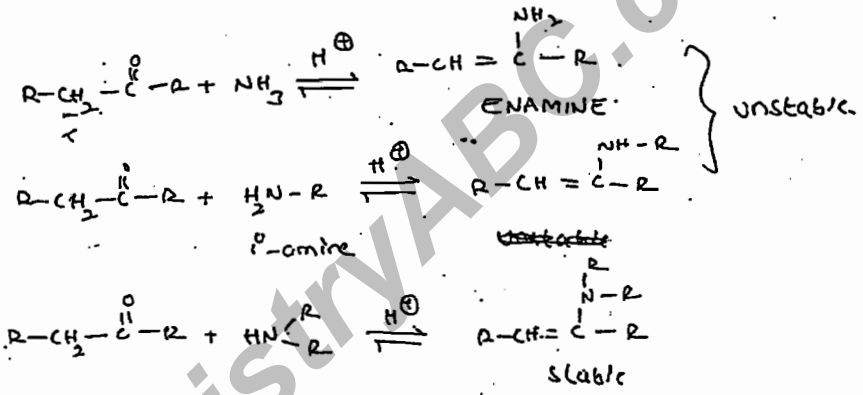
Preph of ENAMINES:-

Enamines are prepared from carbonyl compounds + Amines.

carbonyl compound + Amines NH_3, 1°, 2° $\xrightleftharpoons{H^\oplus}$ ..

↓

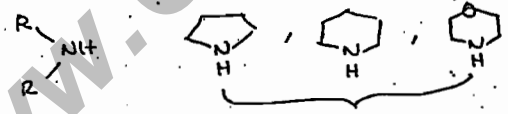
should have atleast one H-atom at α-position

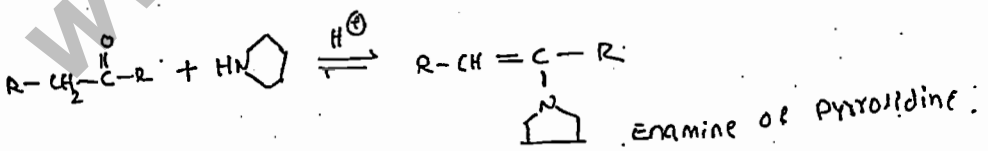


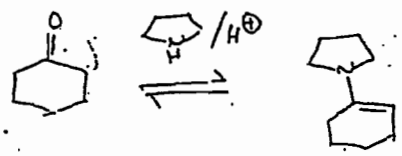
Enamines of NH_3 & 1°-amines – Unstable.

Enamines of 2°-amines – stable.

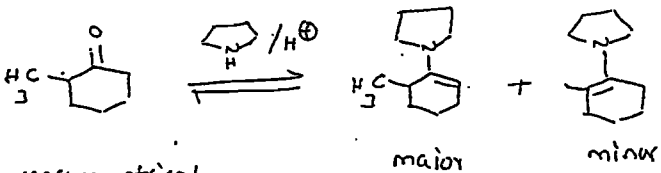
Secondary amines:- Acyclic or cyclic







REGIO SELECTIVITY :-



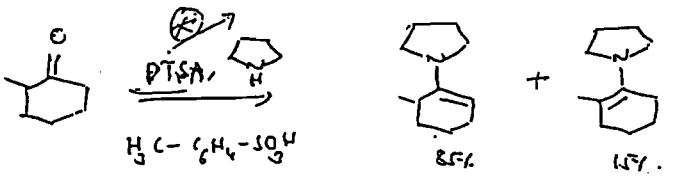
Unsymmetrical ketone

major

minor

Orientation of Db towards less substituted α position of carbonyl more favoured or prefered.

∴ Reason steric crowding.

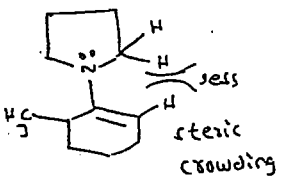


p-Toluene sulphonic acid

A

B

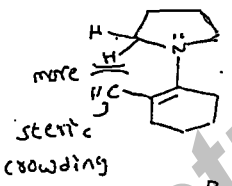
REGIO SELECTIVITY



less steric crowding

Both ring same plane

resonance is very easily



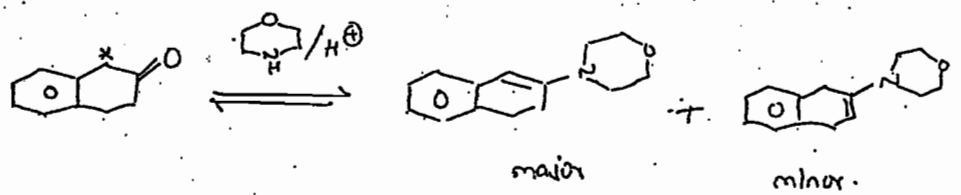
more steric crowding

Resonance energy more

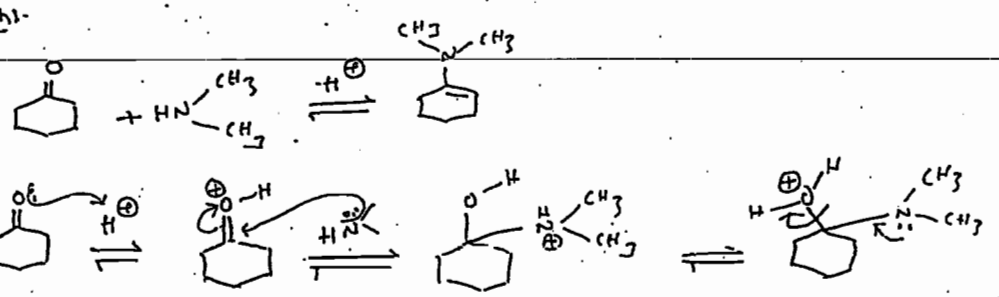
Both rings arrangement out of plane.

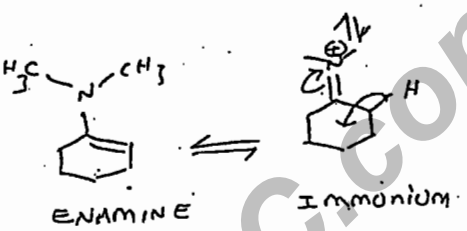
In 'B' compound there is a steric crowding b/w methyl of olefin and α-methylene group of amine. In order to reduce steric crowding Amine arrangement out of plane. with respective to cyclohexene hindered or high energy delocalisation of lone pair of Amine with π-e$^{\ominus}$s system destabilise. arrangement. Therefore form in low percentages.

ENAMINE a free from steric crowding Amine and π-system (cyclo Hexene) almost in the same plane, Free delocalisation stabilise arrangement. Hence it percentage of formation is high.

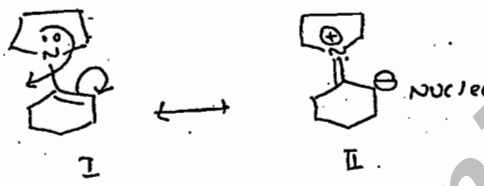


mechi.

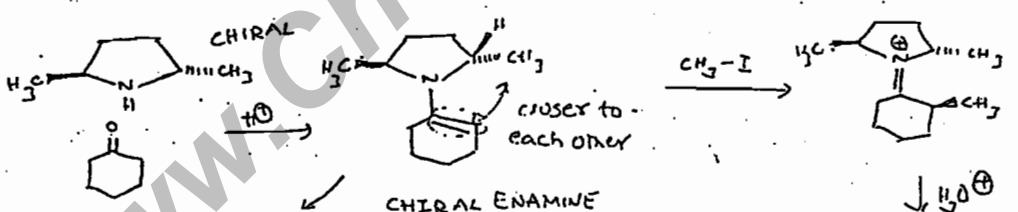




* ENAMINES on decomposition produces carbonyl compounds and Amines



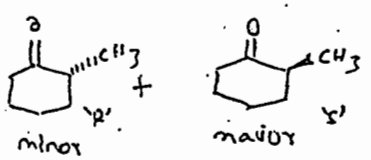
ASSYMETRIC STORK - ENAMINE REACTION:-

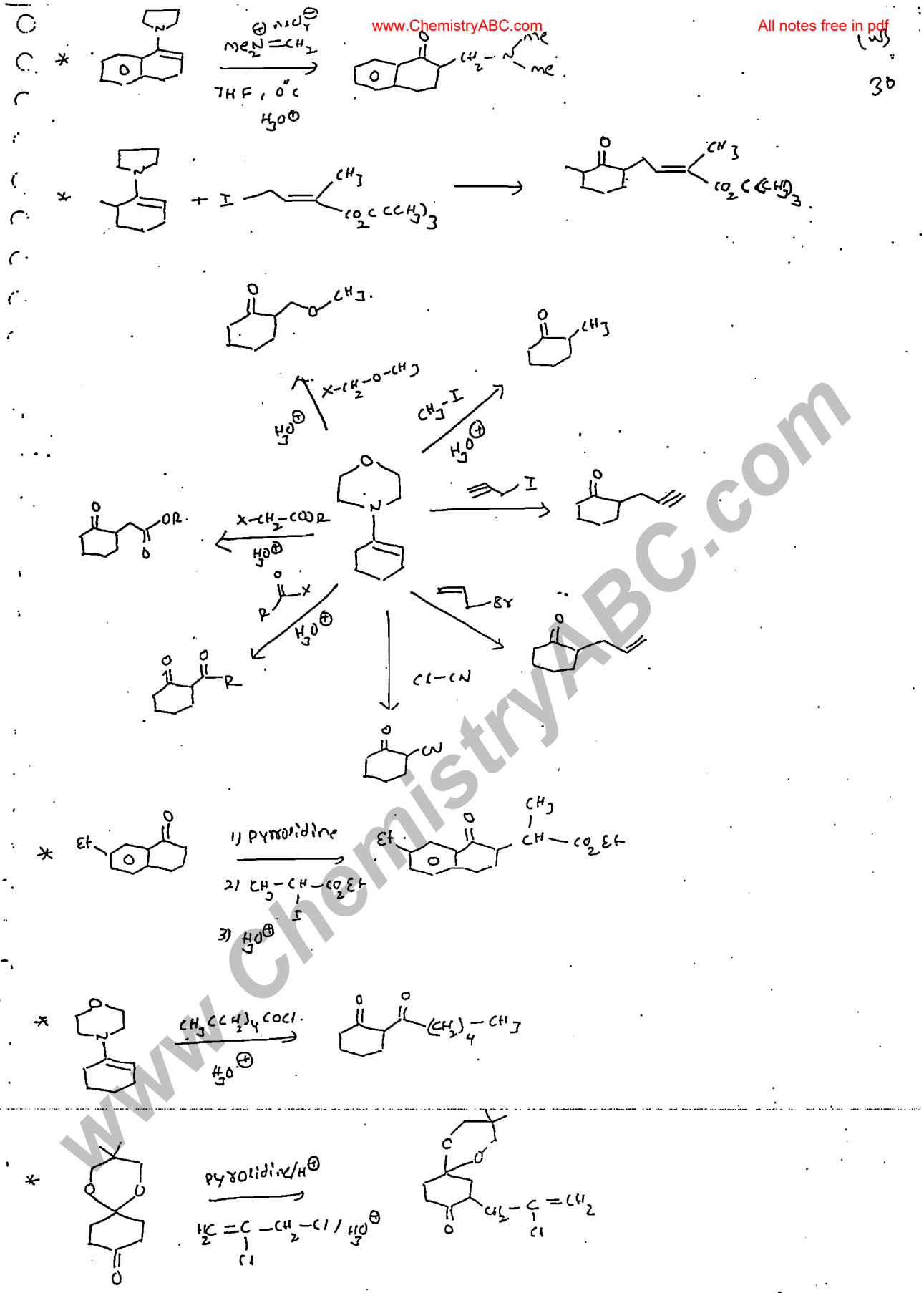


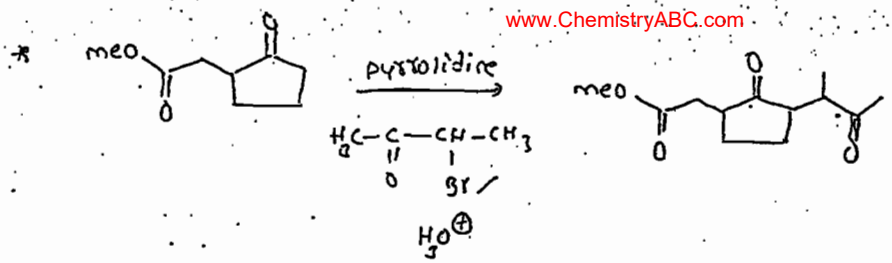
Back or Bottom face.
Sterically crowded due to
Orientation of Bulkier methyl
group of chiral centre at Backface.

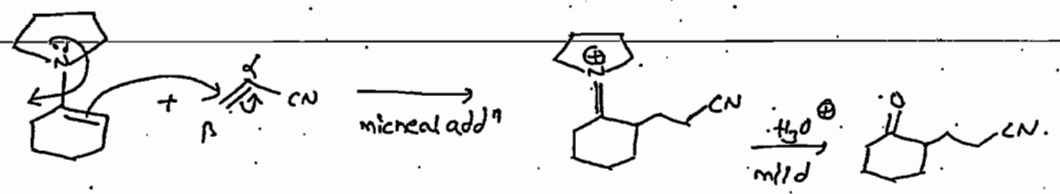
* Front or Top face sterically free

attacking $E^{\oplus}$ preferentially approaches Top or front.

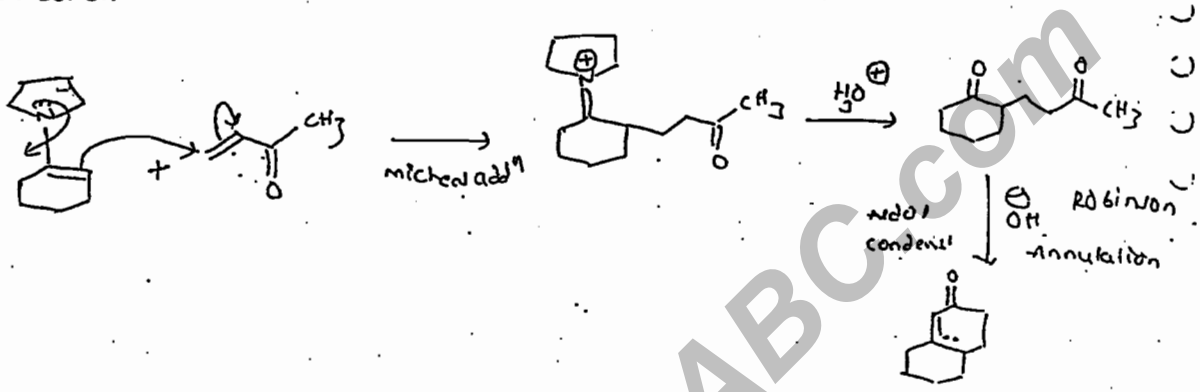






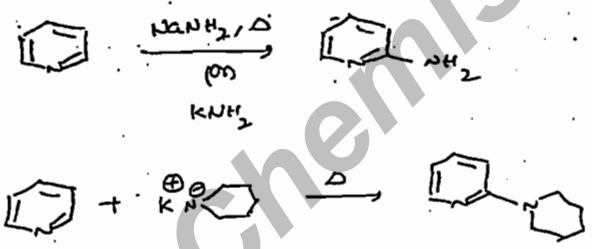


M. DONAR M-ACCEPTOR.

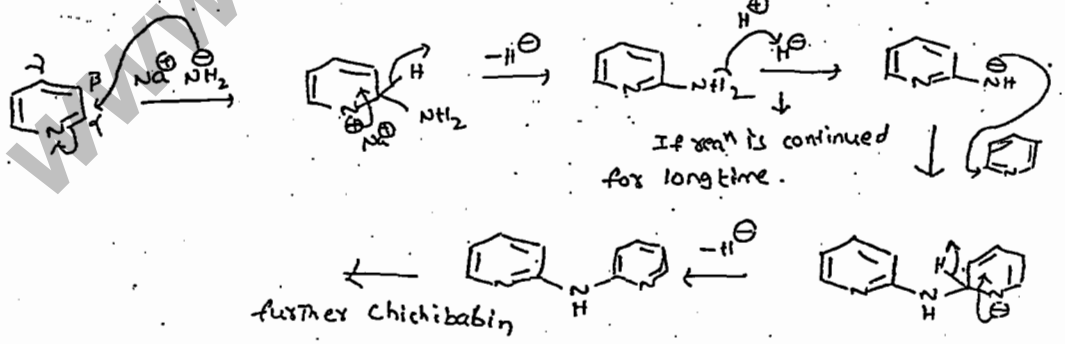


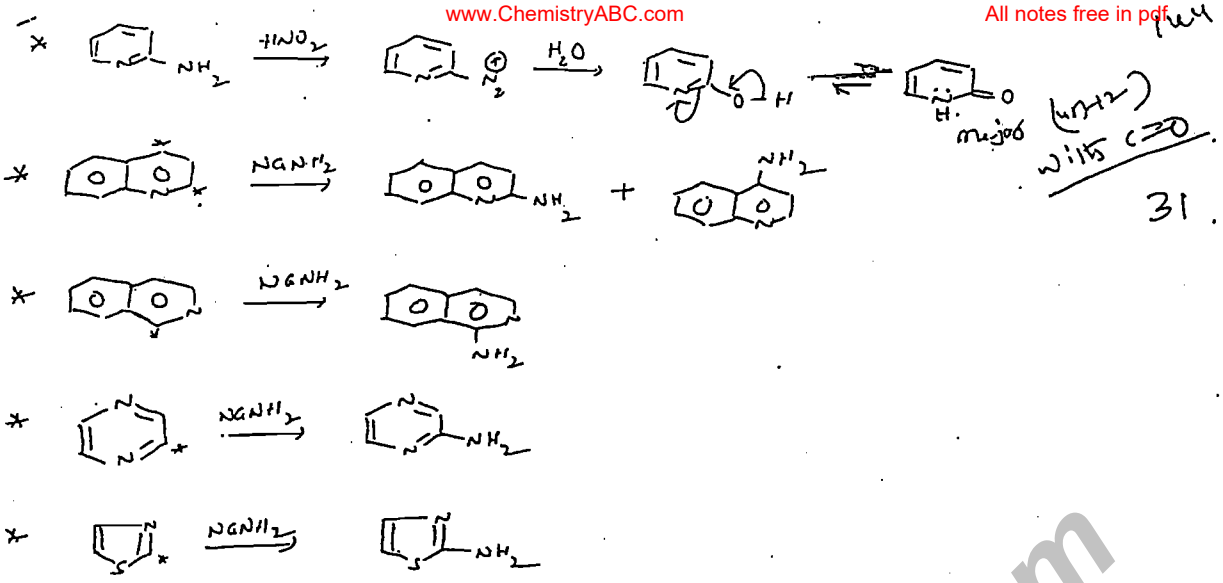
CHICHIBABIN REACTION:-

Amination of N-Heterocyclics with metal Amides at Higher temp.



Mech:- Nucleophilic substitution.





31.

WITTING REACTION :-

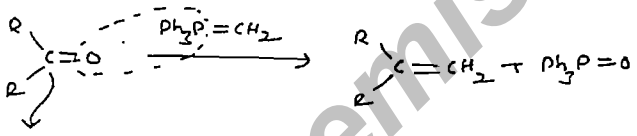
Conversion of carbonyl compound into olefins with phosphoranes / P-YLIDES.

Witting Reagent :- PHOSPHORANES / P-YLIDES

$Ph_3P=CH_2$ $Ph_3\overset{\oplus}{P}-\overset{\ominus}{C}H_2$ (charge separation at 1,2-position)

Carbonyl compound $\xrightarrow{\text{phosphorane}}$ olefin. (E/Z)

Aldehyde or ketone. (Aliphatic / Aromatic)



* Always the position of DB in resulting olefin is fixed at carbonyl carbon.

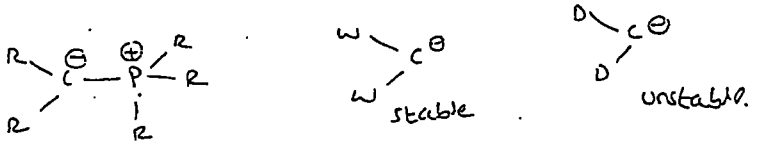
* Increase no of carbons & C–C Bond formation Reaction.

Advantage :-

* Easy to carry out, mild conditions.

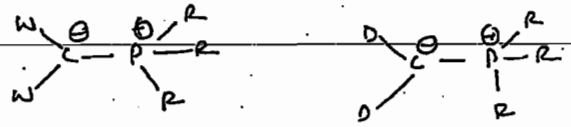
Anhydrous / Inert conditions has to be maintained.

Wittig reagent :-



* presence of with drawing gp at carbanion carbon Increases stability of witting Reagent.

* presence donating groups decreases stability of witting Reagent.



Stable. Unstable

Usually stable witting Reagent olefins are E-olefin.

Unstable " " " " Z-olefins

c.c + Unstable w.R → Z-olefin (major)

c.c + stable w.R → E-olefin (major)

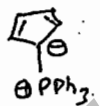
* stable w.R are slow in reaction with carbonyl.

If witting Reagent highly stabilize. Inert in witting Reaction.

Stability Increases ↓

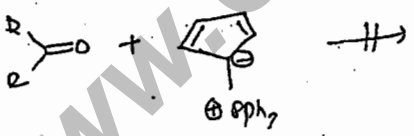
$H_3C-CH=PPh_3$ → more reactive in witting rea^n

$EtO_2C-CH=PPh_3$



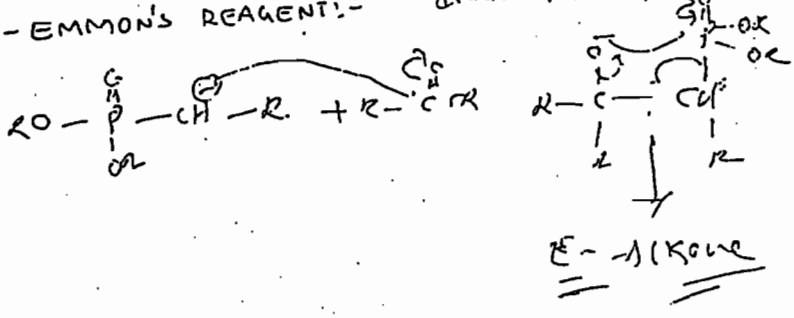
(Highly stable) due to aromatic character

↓ Inert in witting reaction



MODIFIED WITTING REAGENT:-

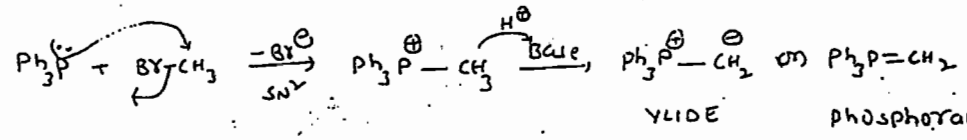
HORNER-WADSWORTH-EMMON'S REAGENT:- diester of phosphonic acid



E-Alkene

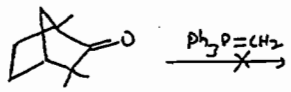
with this reagent if carbonyl connected to olefin.

simple wittig Reagent preparation:-



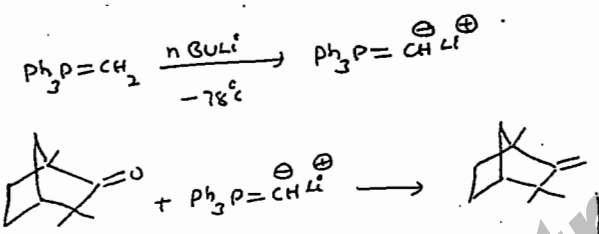
YLIDE phosphoranes.

Bases: LDA, NaH, $tBuO^{\ominus}K^{\oplus}$, $R^{\ominus}Li^{\oplus}$ ... etc.

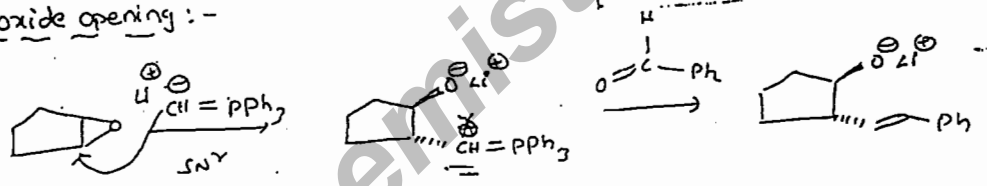


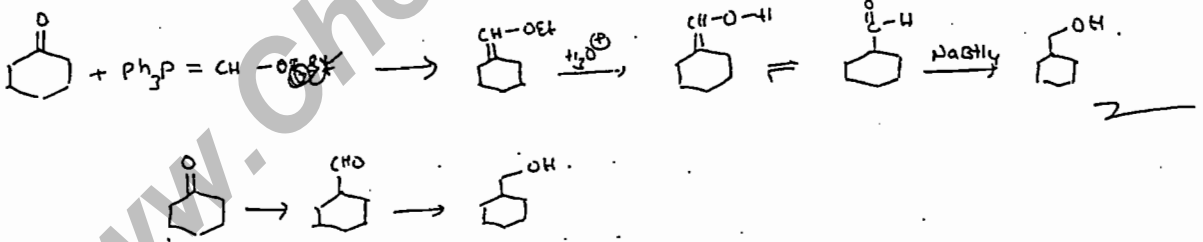
Carbonyl more sterically crowded . wittig Rea^n Not takes place.

* If Li Derivative of wittig reagent used carbonyl reacts and produces olefins

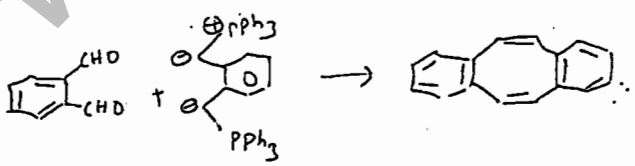


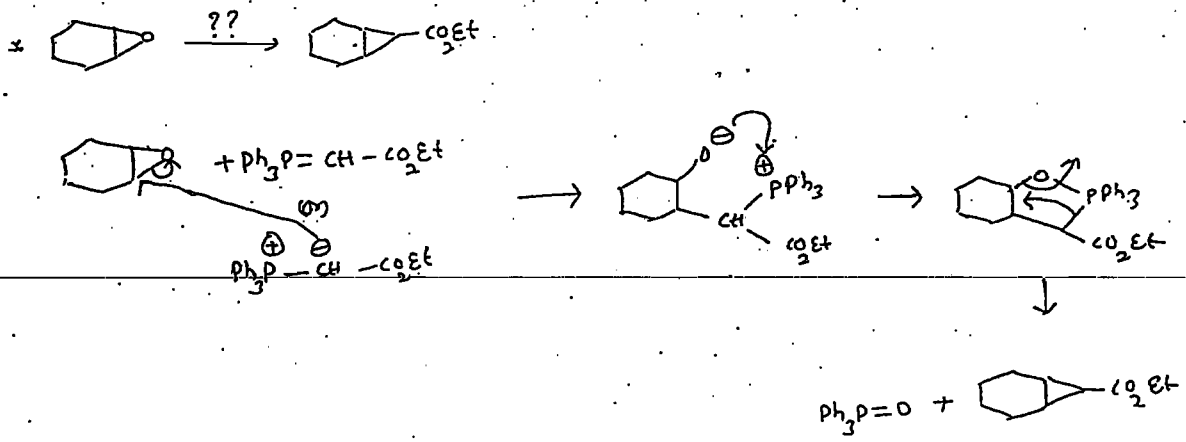
Epoxide opening :-





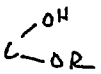
DOUble wittig rea^n:-

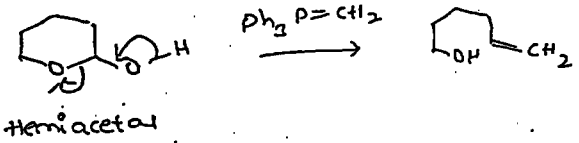




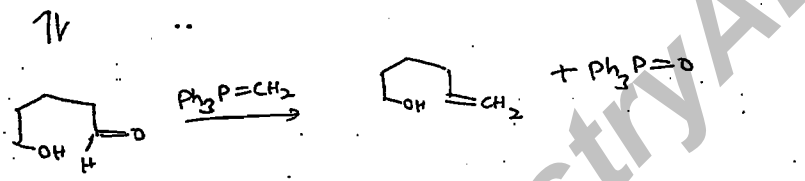
Hemi Acetal :-

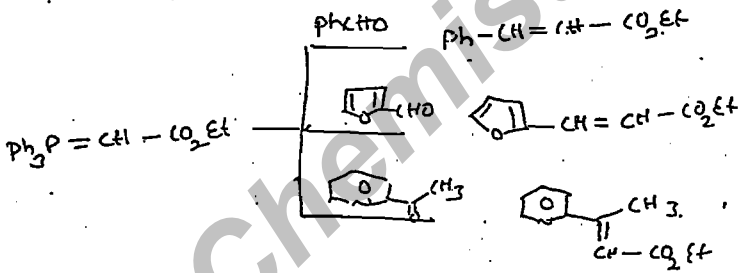
at a carbon one alcohol and one ether function.



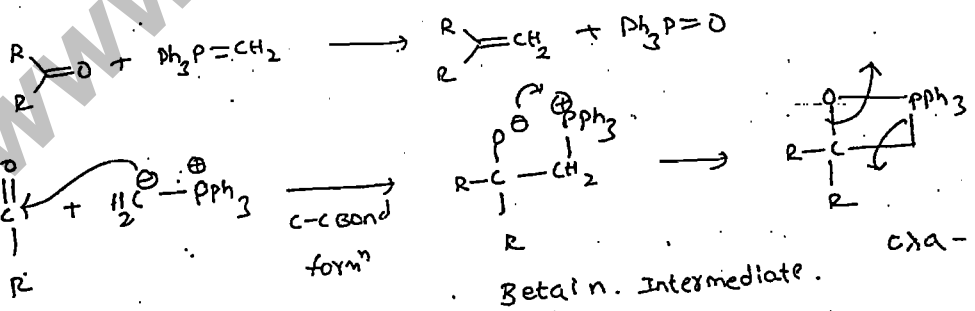


Hemiacetal





Mechanism :- ($C_2^{\pi} + \gamma^{\pi}$ type)



Betain. Intermediate.

1,4 position opp. charges.

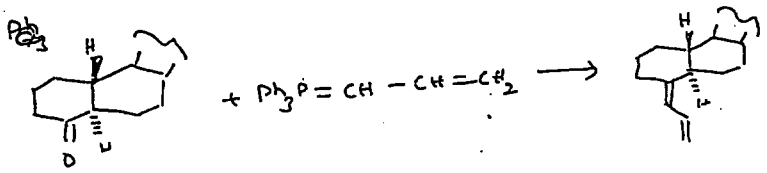
oxa-phosphetane.

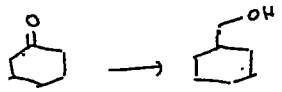
→ $R_2C=CH_2$ + $Ph_3P=O$

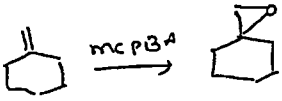
* In some of the Wittig reaⁿ. Betain form not observed.

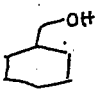
Ex!

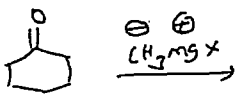
$Ph-CH=CH-\overset{H}{\underset{O}{C}}=O + Ph_3P=CH_2 \longrightarrow Ph-CH=CH-CH=CH_2 + Ph_3P=O$

* 

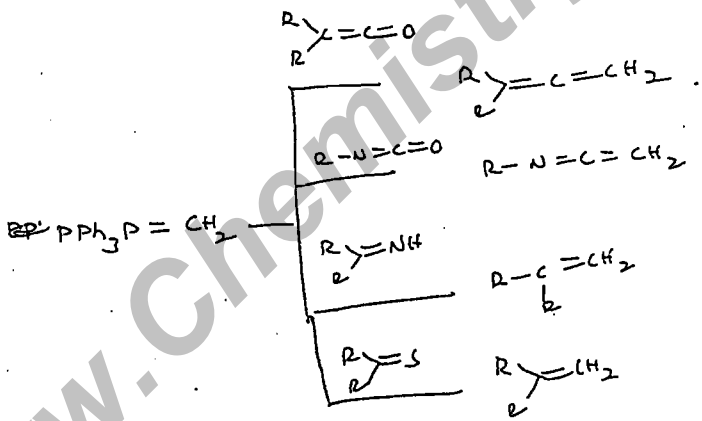
* 

$\xrightarrow{Ph_3P=CH_2}$  $\xrightarrow{mCPBA}$ $\xrightarrow{LAH}$ 

$\xrightarrow{B_2H_6 / H_2O_2/OH^\ominus}$ 

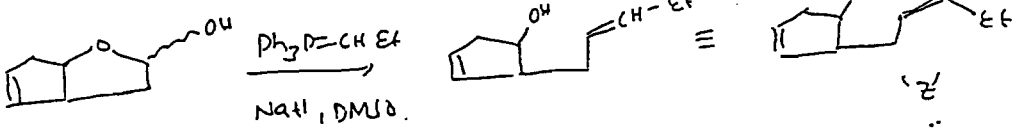
* 

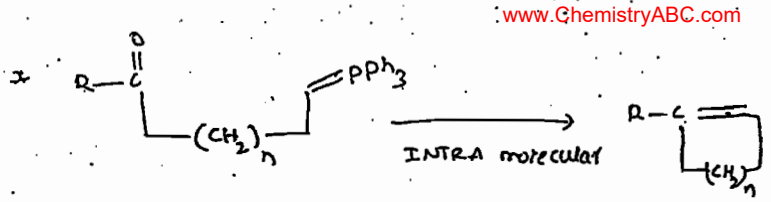
major

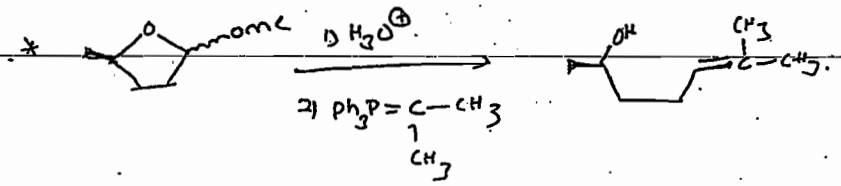


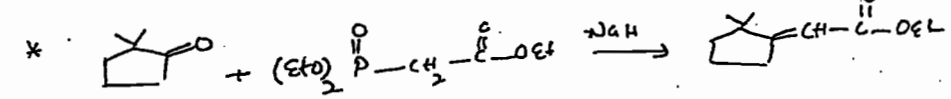
Ozonolysis

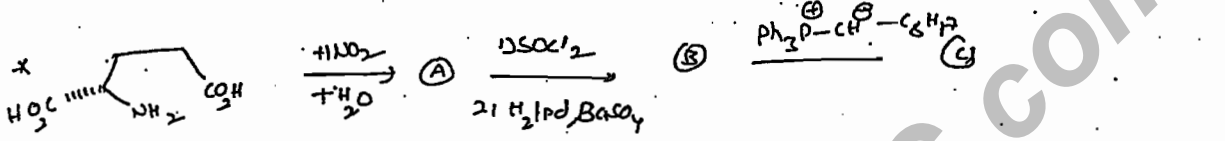
* $Ph_3P=CH-CH_3 \xrightarrow{O_3} Ph_3P=O + CH_3-CHO \xrightarrow{Ph_3P=CH_2} CH_3-CH=CH_2$

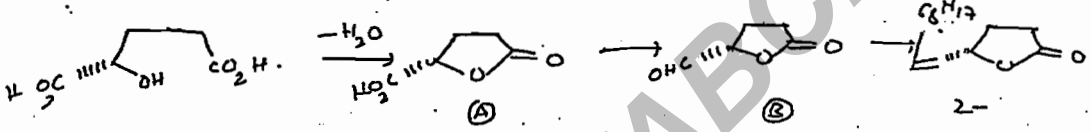
* 

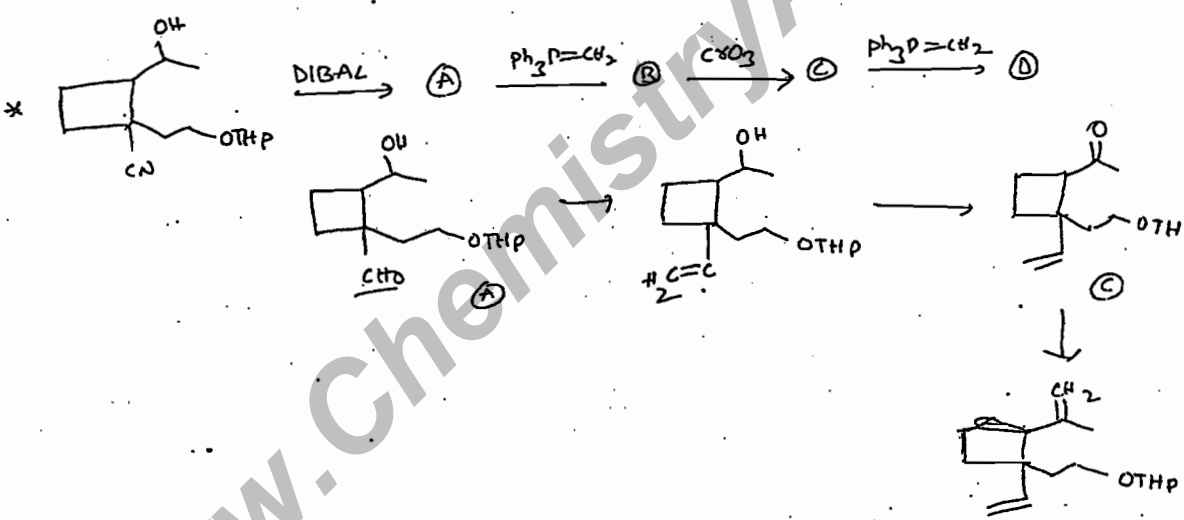


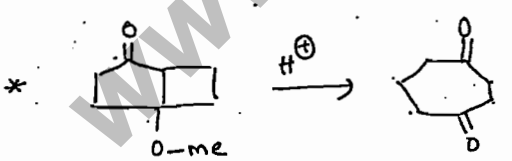


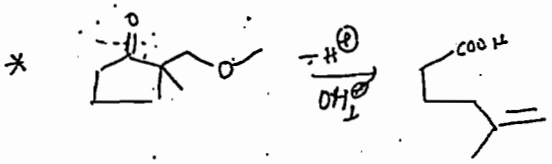












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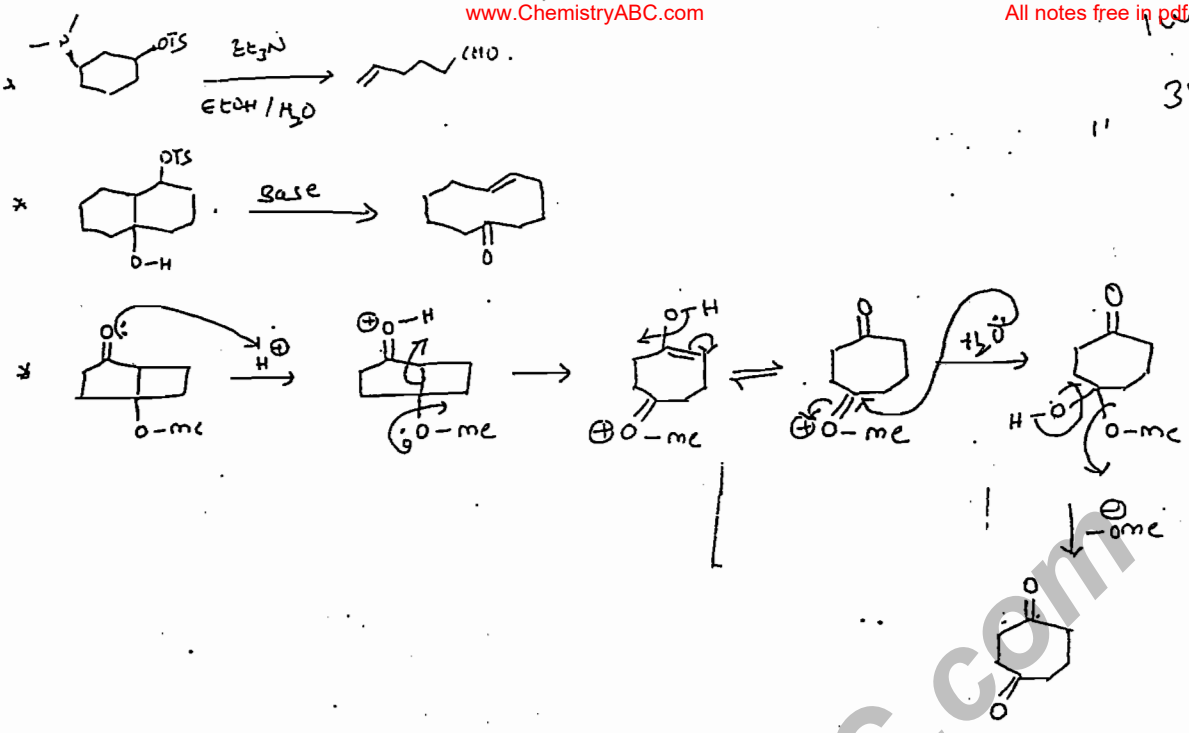
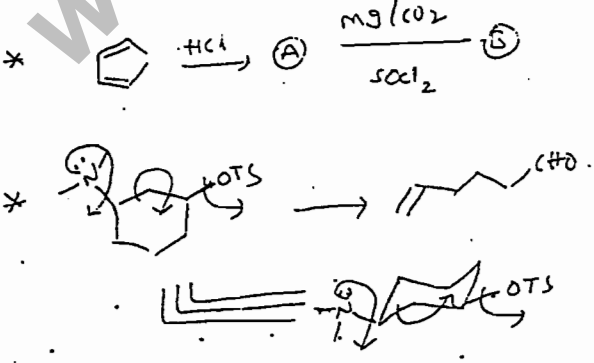
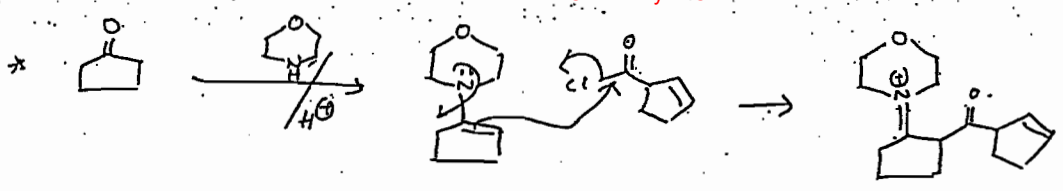
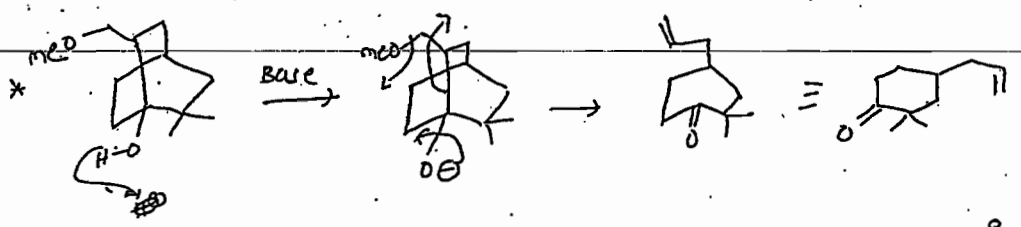
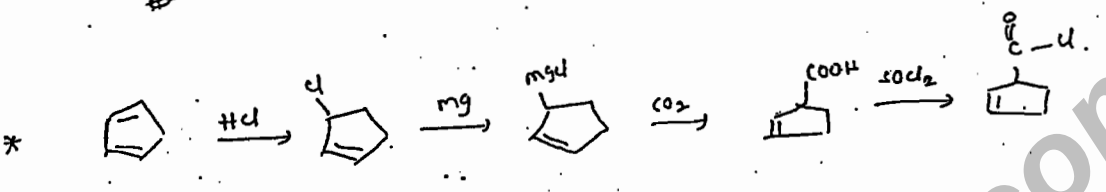


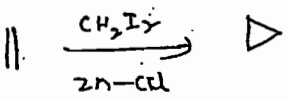








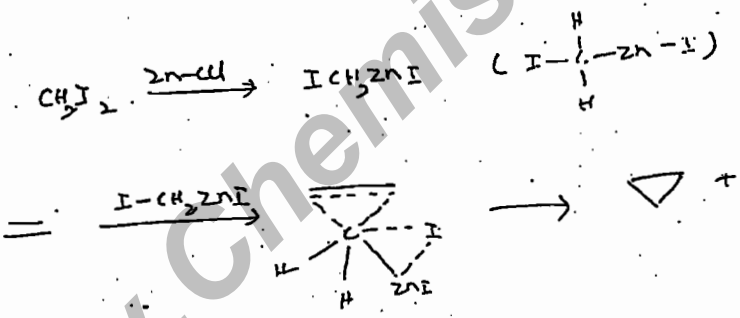
SIMMON'S SMITH REACTION :-

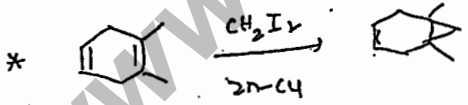


× concerted addition

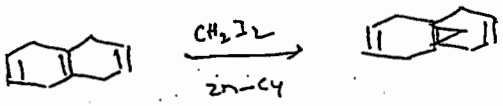
* no generation of carbene intermediate.

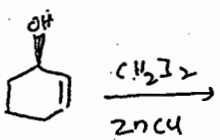
Mech!.

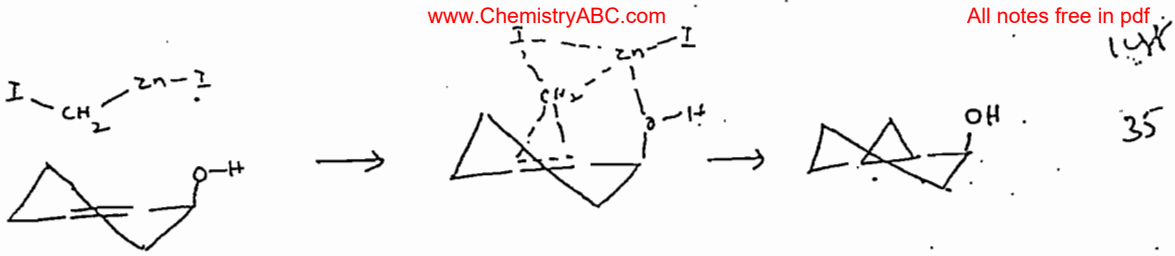




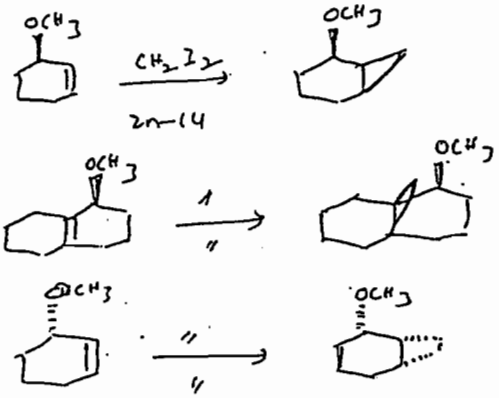
Highly alkylated olefin preferable



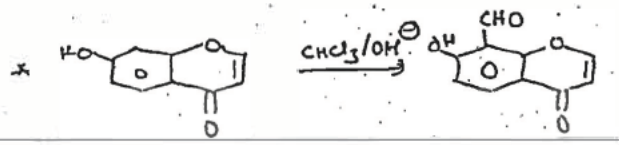


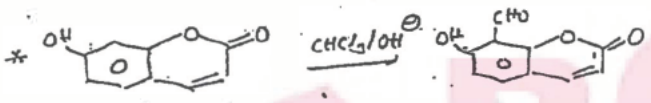


cyclo Hexane stable conformation half chair.



some more examples:-





coumarin