ORGANIC CHEMISTRY III

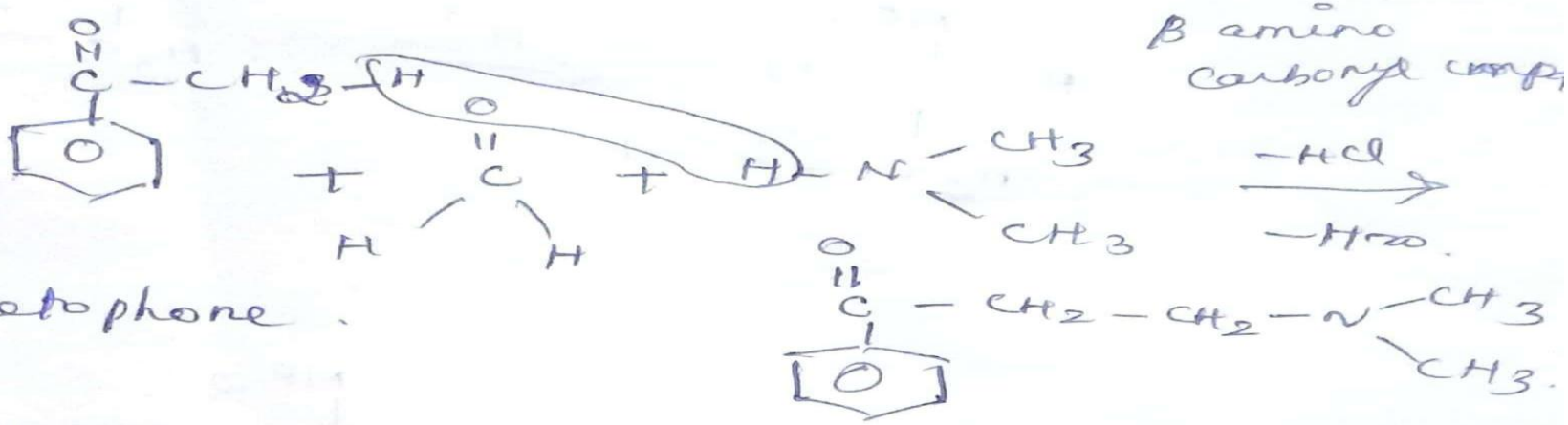
CODE : 18KP3CH09

UNIT – I

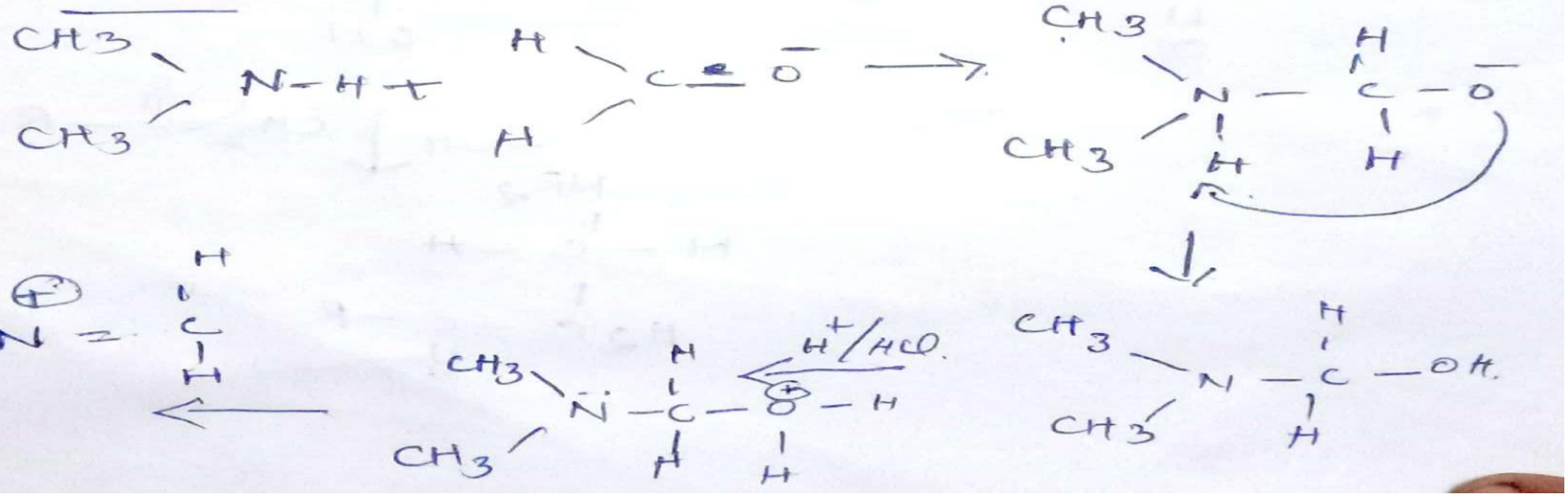
1. ADDITION AND ELIMINATION REACTIONS

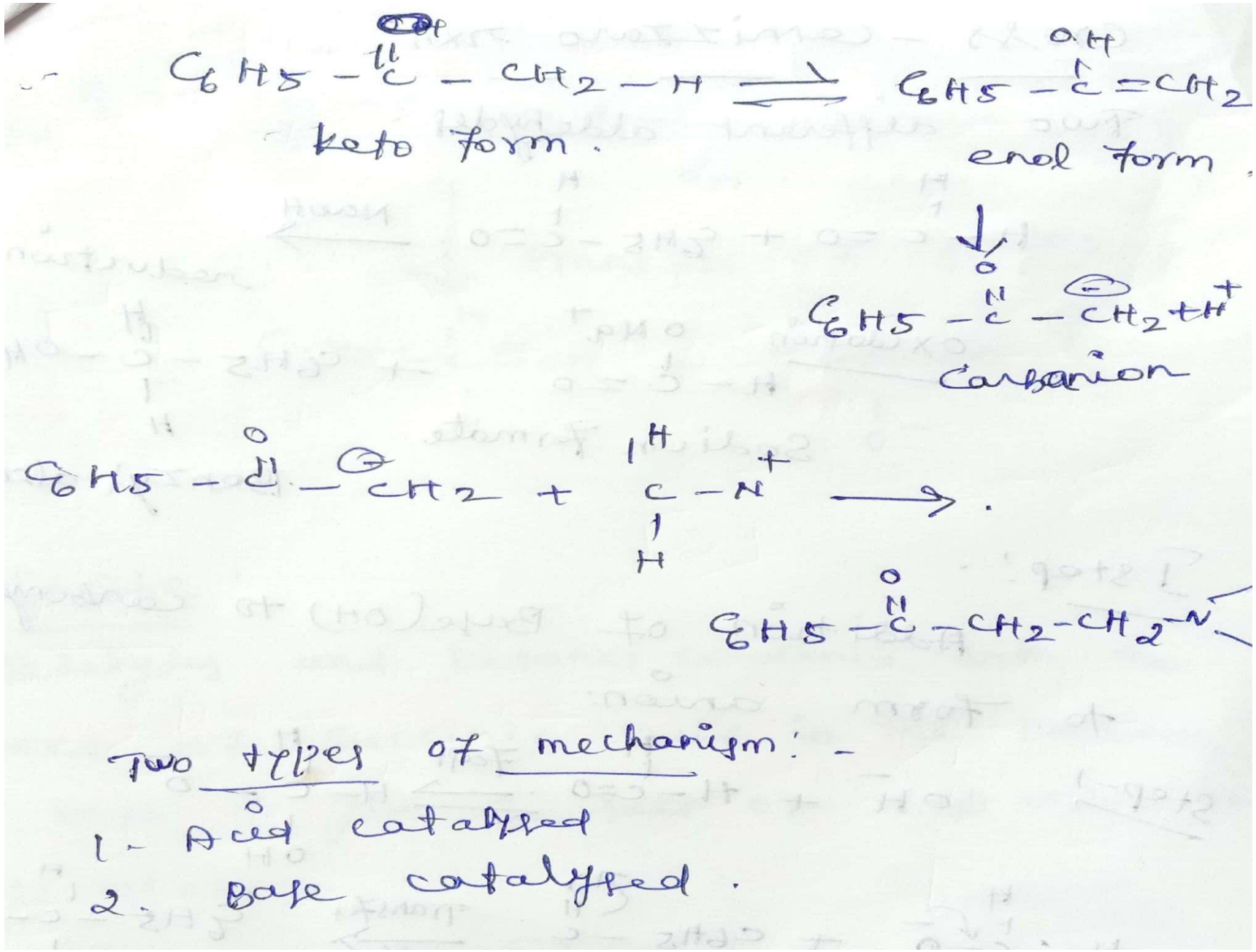
Mannich reaction :-

Ketone + Formaldehyde + 2° amine $\xrightarrow[-H_2O]{HCl}$ β amino carbonyl compound



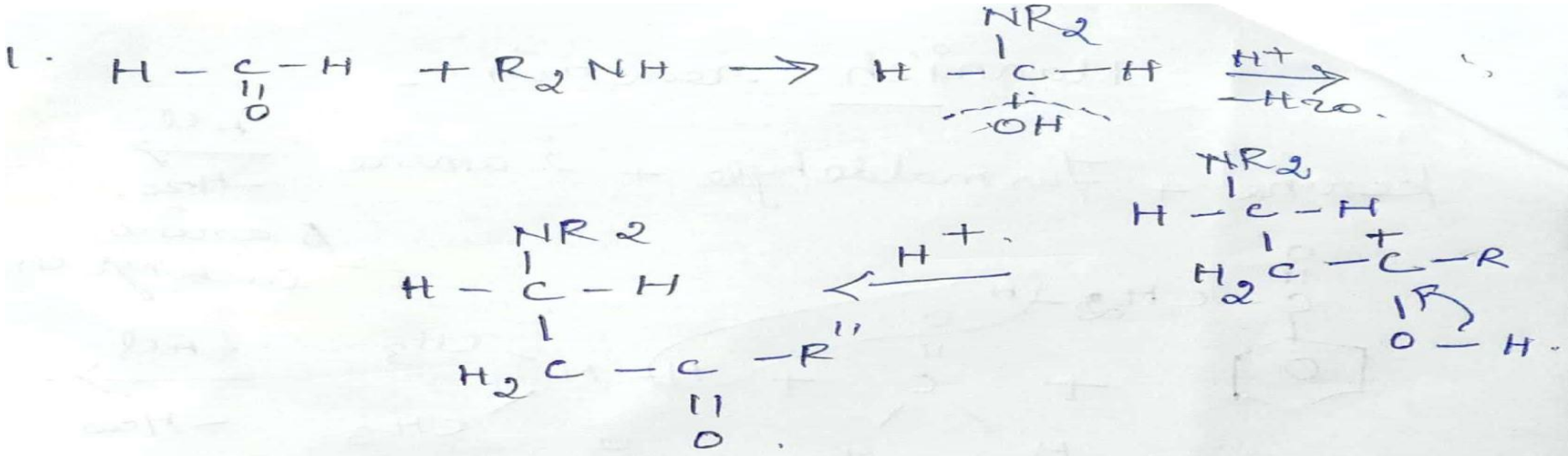
Mech :

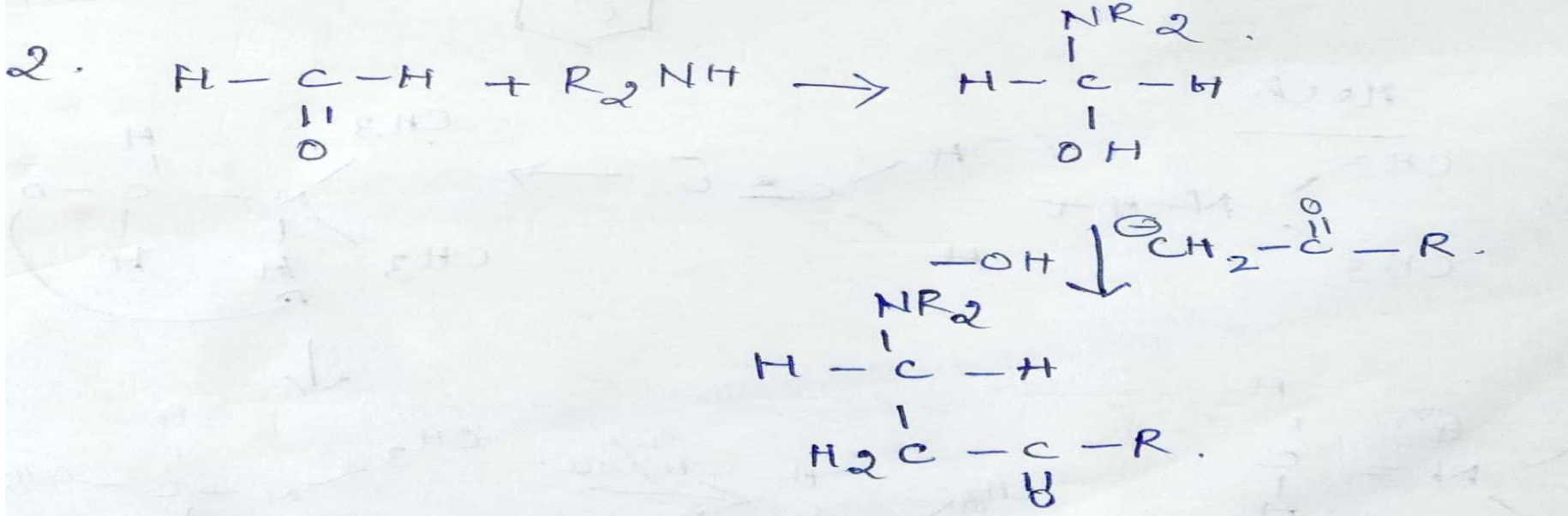




Two types of mechanism:-

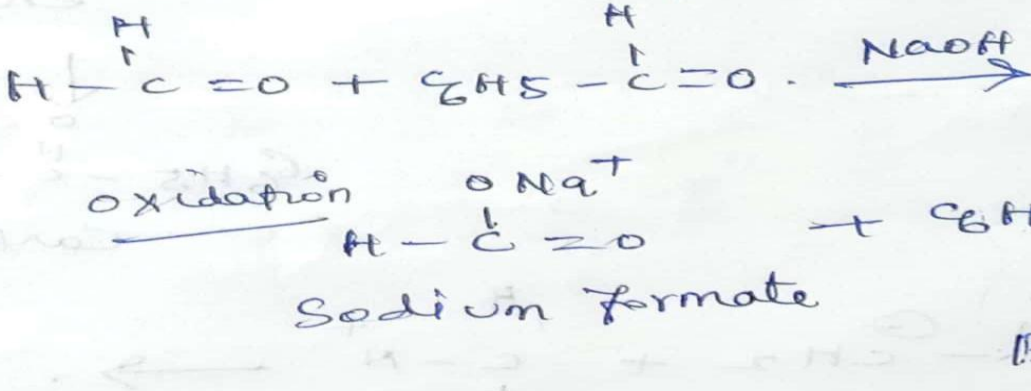
1. Acid catalyzed
2. Base catalyzed.

1. 

2. 

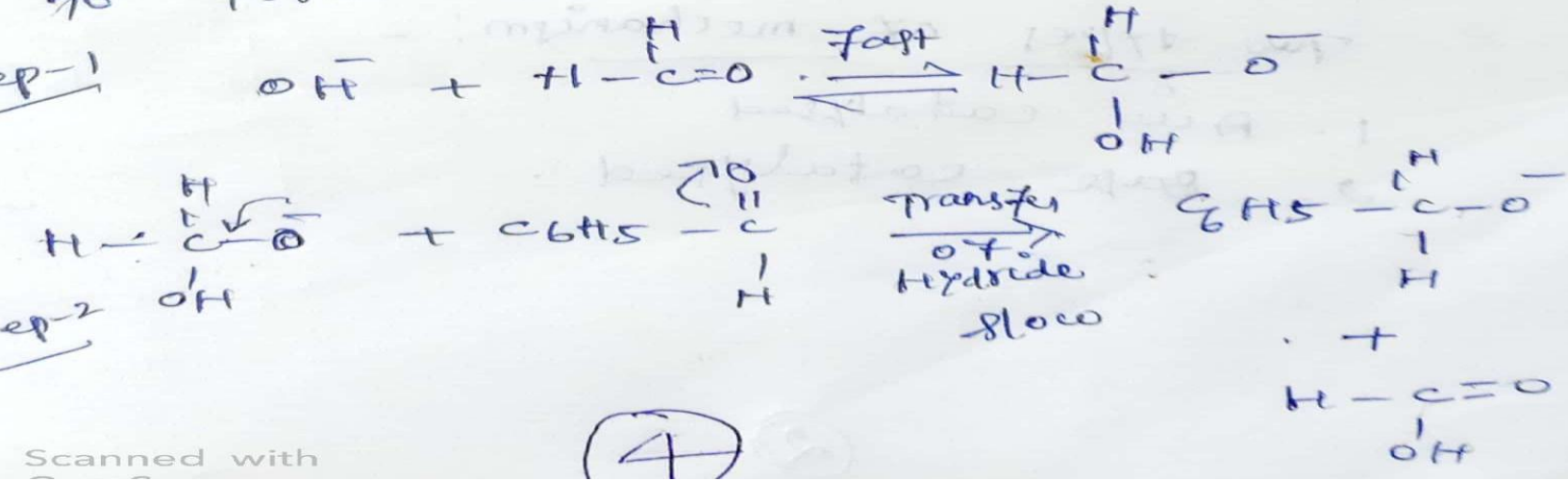
Cross - cannizzaro rxn.

Two different aldehydes.



I step:

Addition of Base(OH) to carbonyl gp to form anion.



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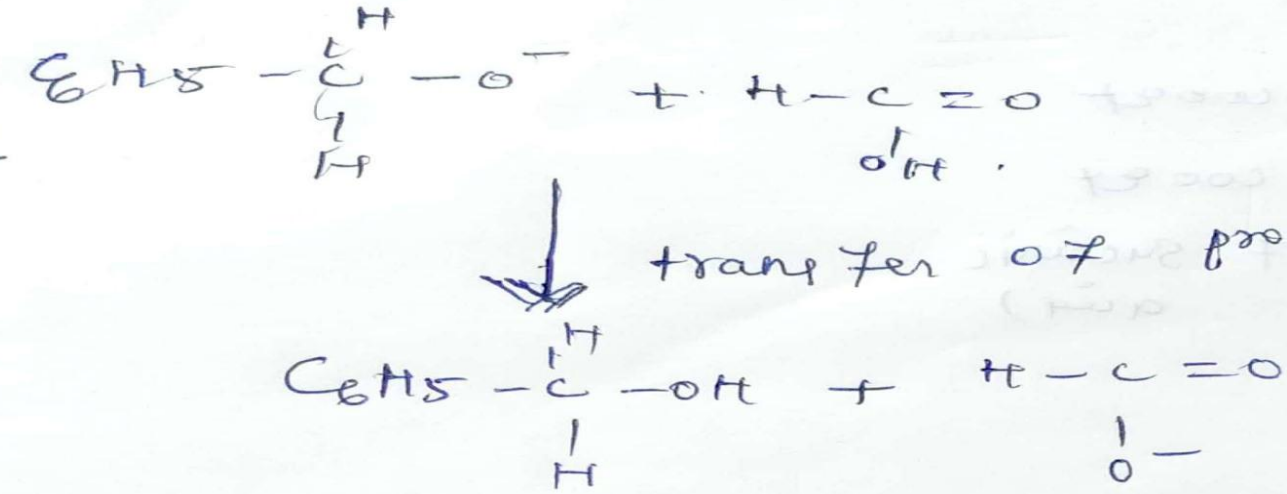
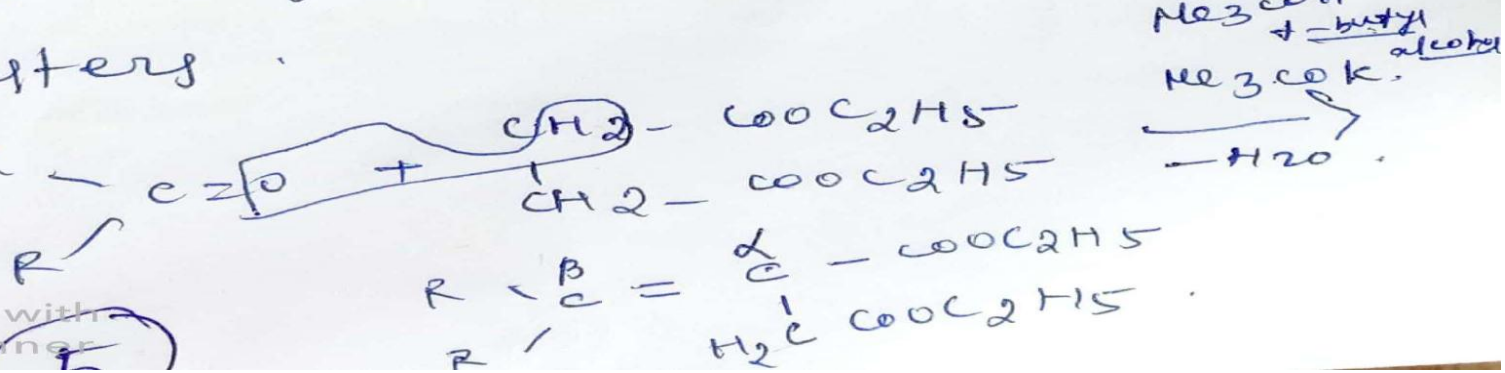
Step-3



Stobbe:

Aldehydes and ketones condense with the esters of succinic acid in the presence of base to give a salt of α-β unsaturated half esters.



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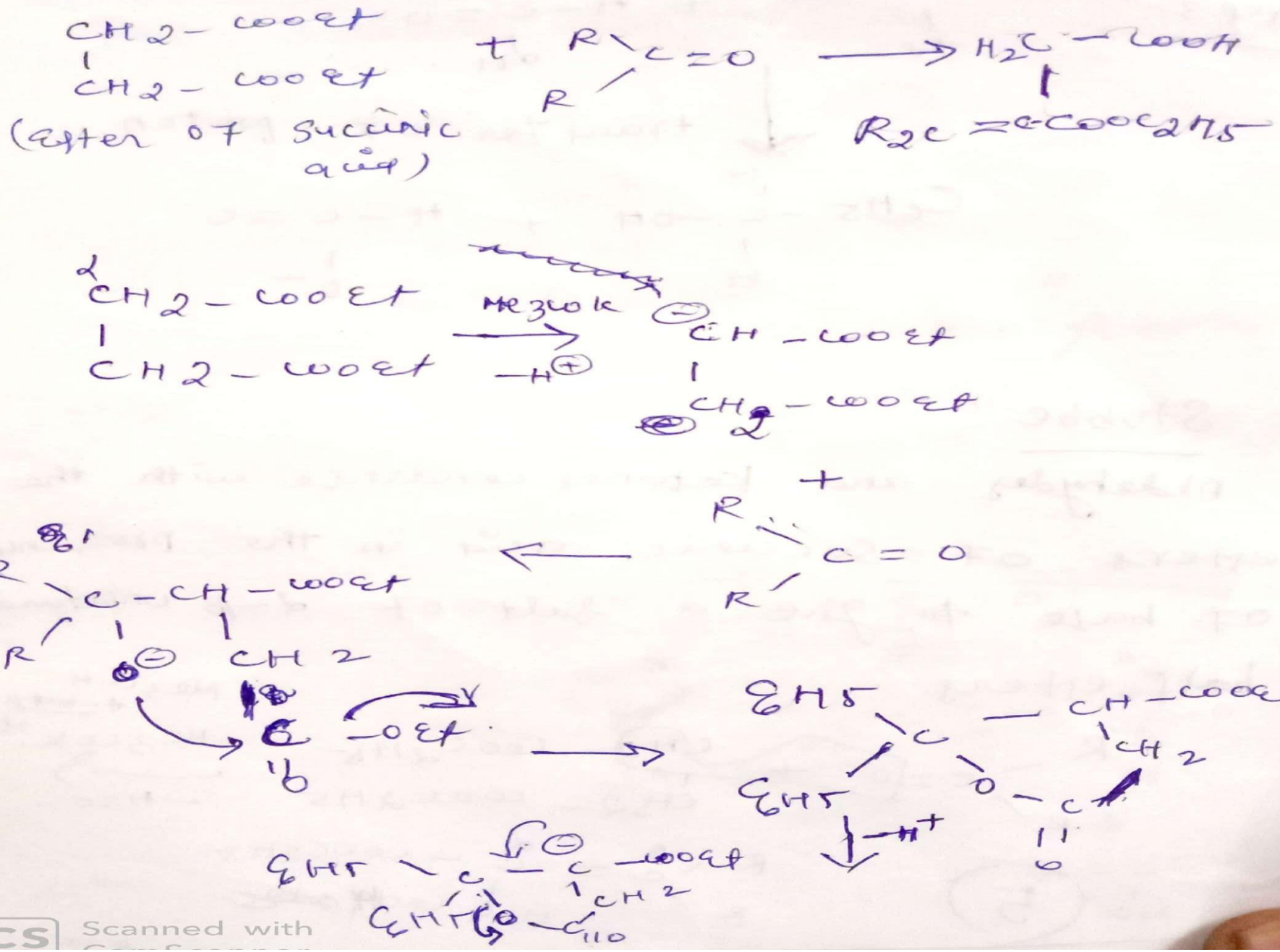
Mech:-



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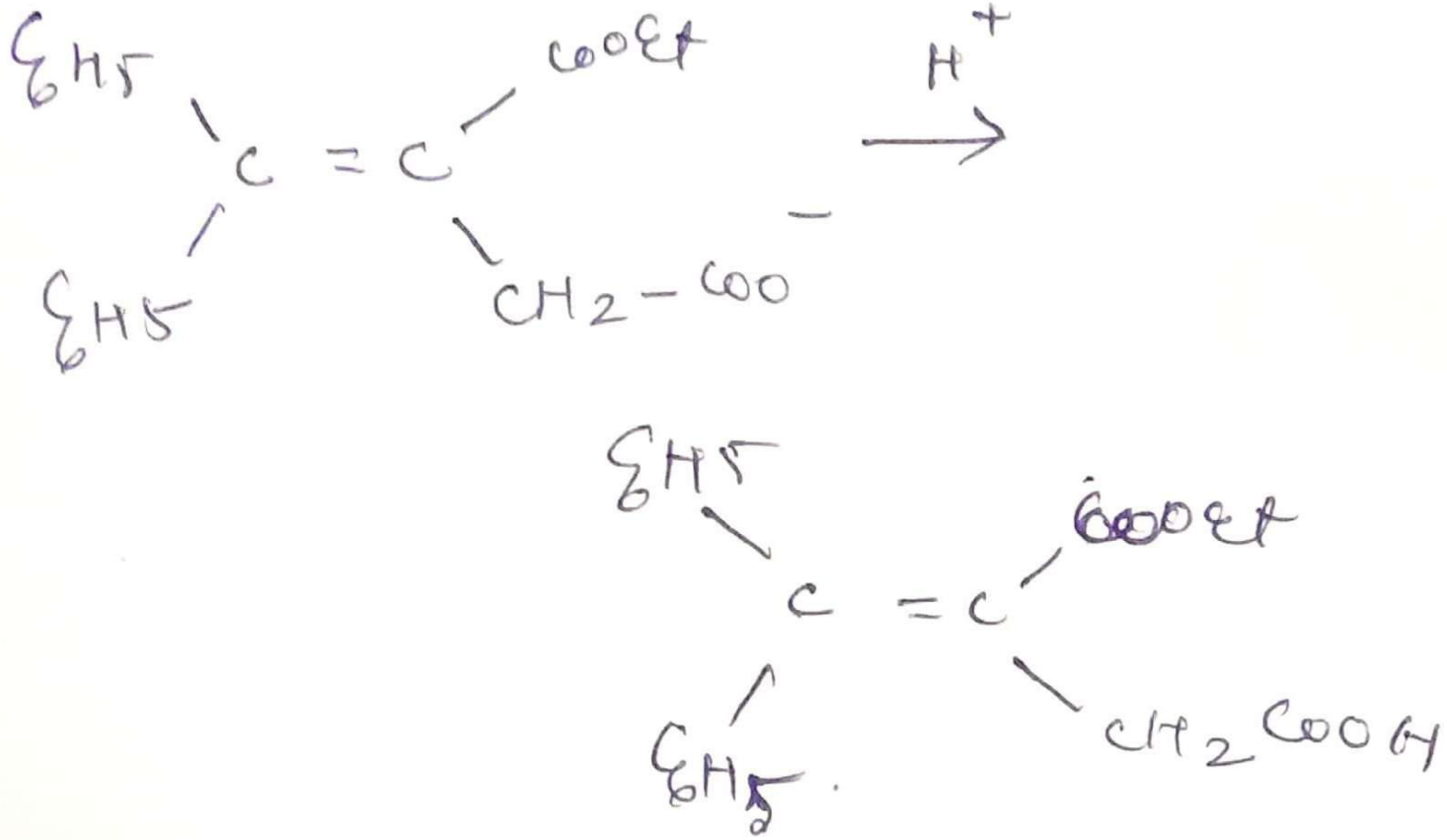
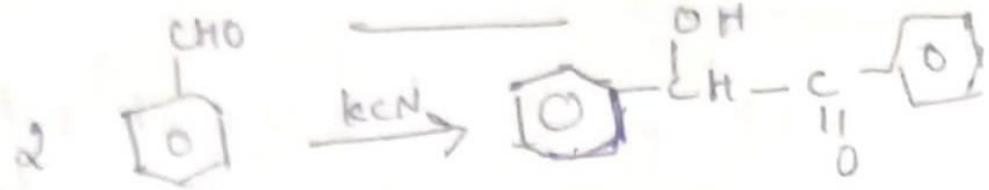

C6H5
C6H5
C = C
COOEt
CH2 - COO
H+
C6H5
C6H5
C = C
COOEt
CH2COOH

Benzoin



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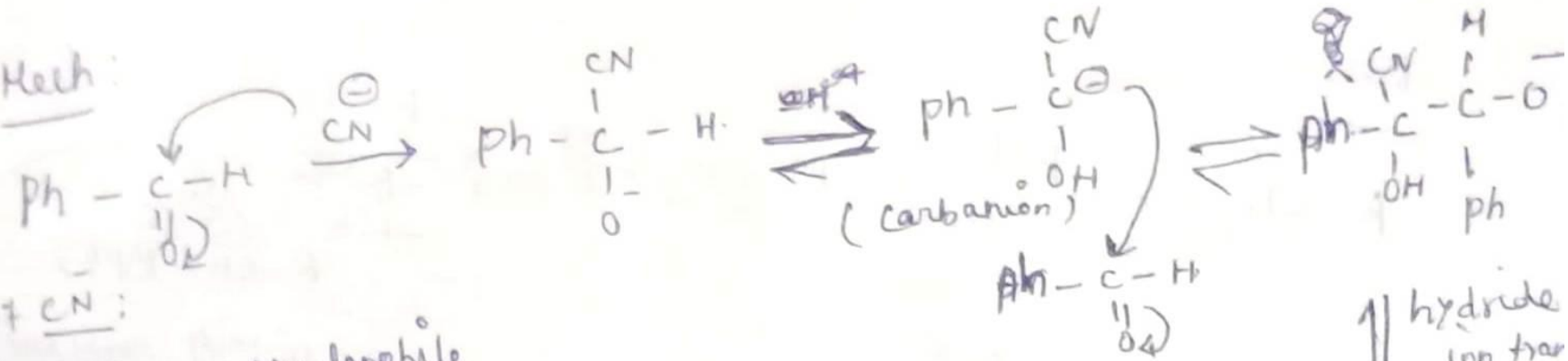
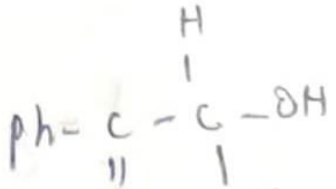


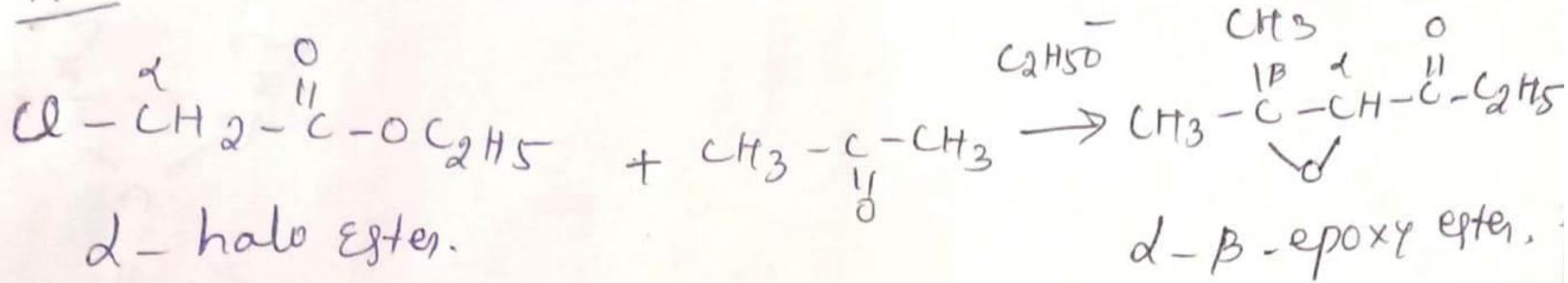
Role of CN:

1. as a Nucleophile
2. Stabilizer Carbanion
3. best leaving group



Darzen's glycidic ester.

RXN:



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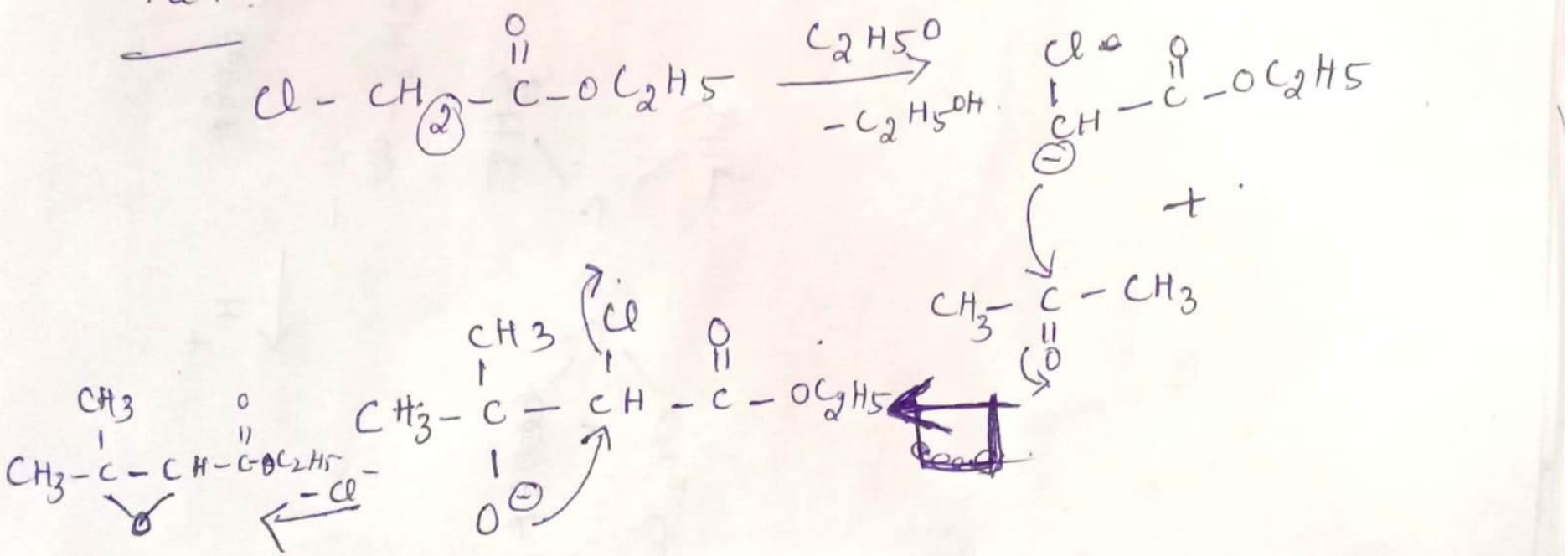
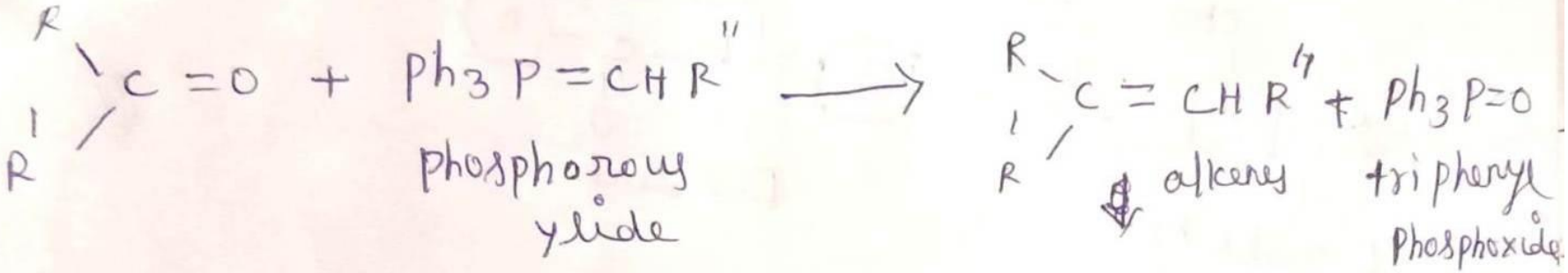


Wittig reaction



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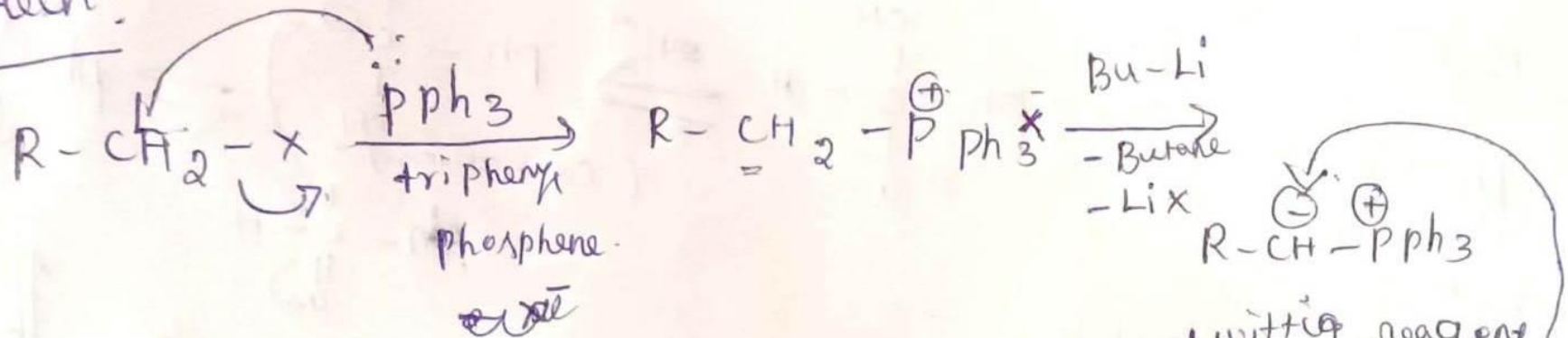
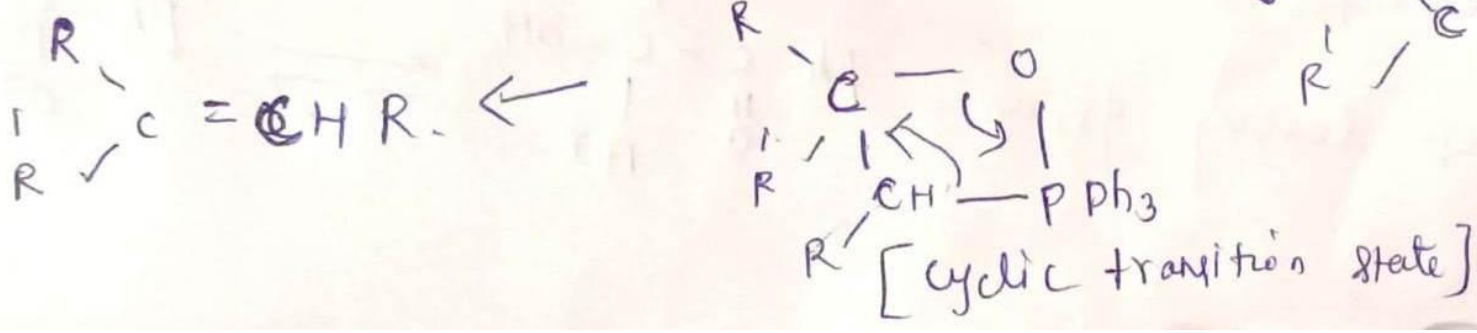
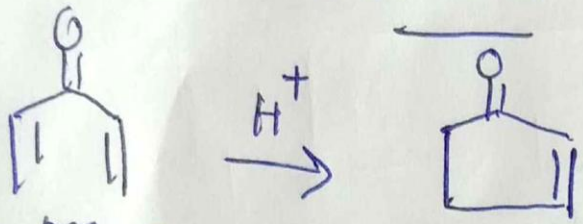




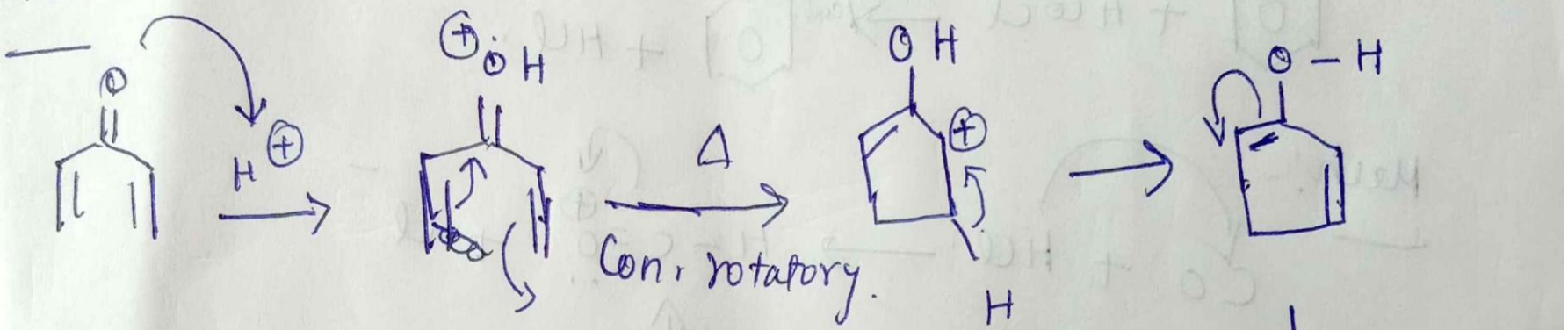
Nazarov cyclization reaction:-



$CH_2 = CH_2$

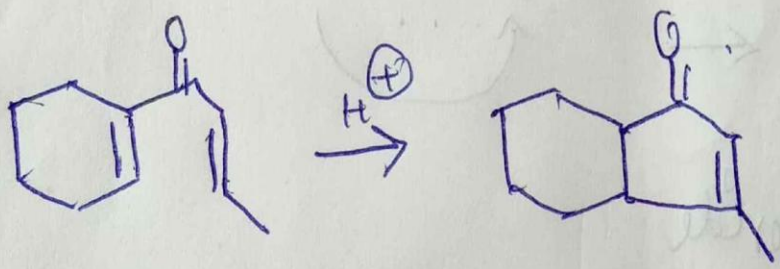
Divinyl pentanone. 2-cyclo pentanone.

Mech.



Tautomerism

eg.

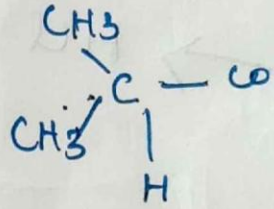


Koch-rxn.

Alkene + CO + H_2O $\xrightarrow{H^+}$ Acid.

$CH_2=CH_2 + CO + H_2O \xrightarrow[573-673^\circ]{H_3PO_4,\ \text{under Press}} CH_3-CH_2COOH$

1 carbon atom increased.

$CH_3CH=CH_2 + CO + H_2O \xrightarrow{\quad"\quad}$ 

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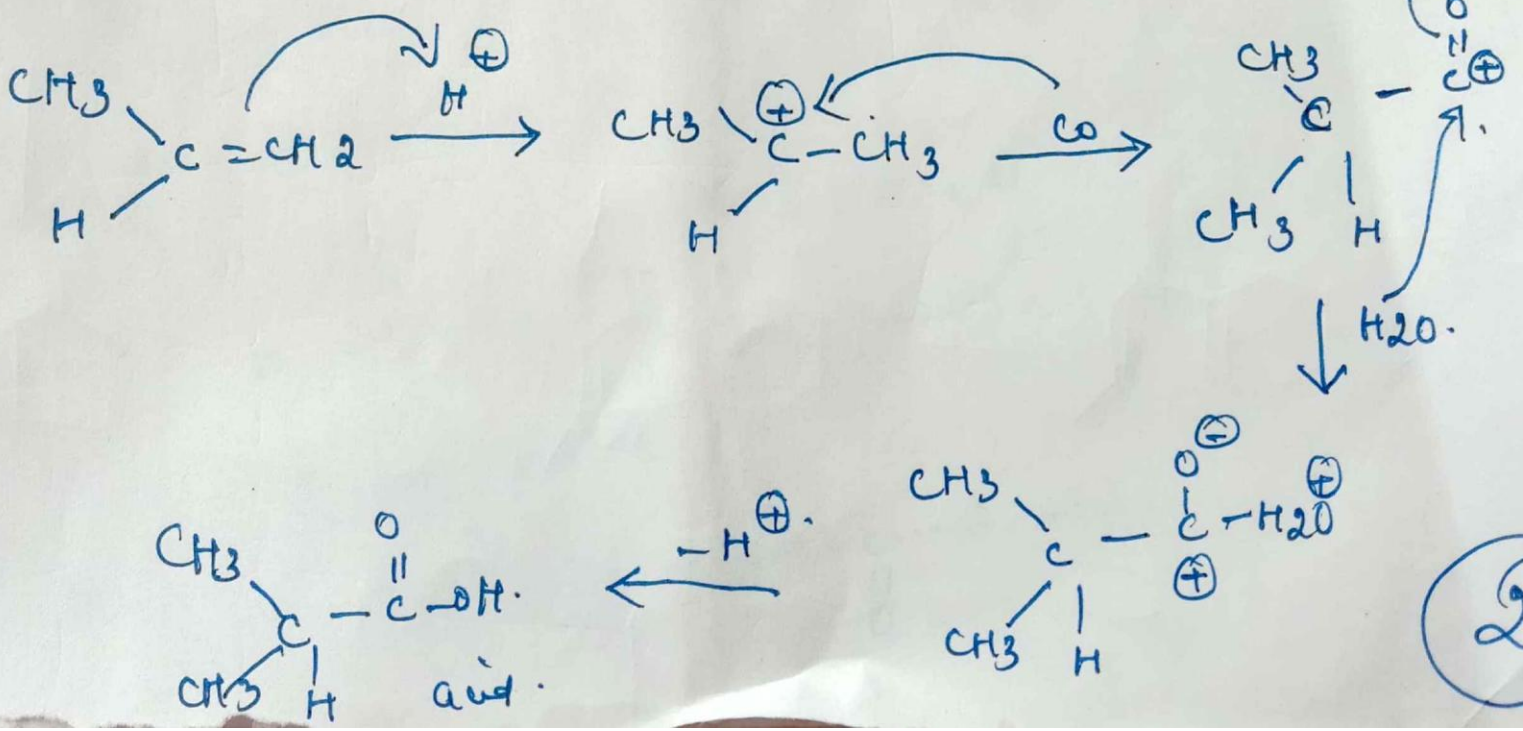

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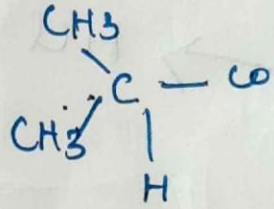
$CH_3CH=CH_2 + CO + H_2O \xrightarrow{\quad"\quad}$ 

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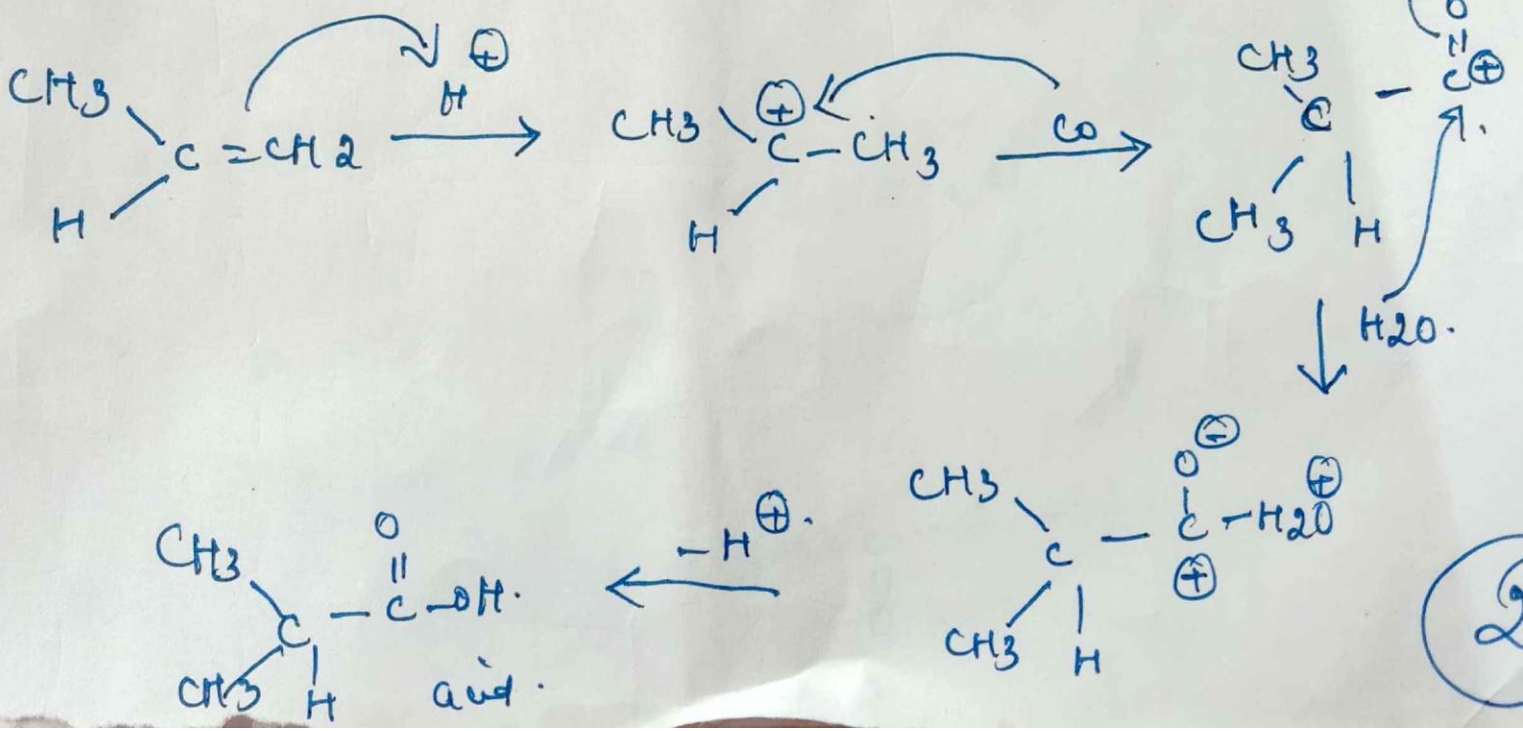

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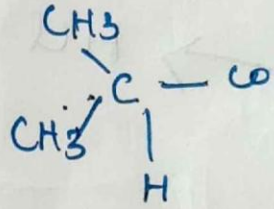
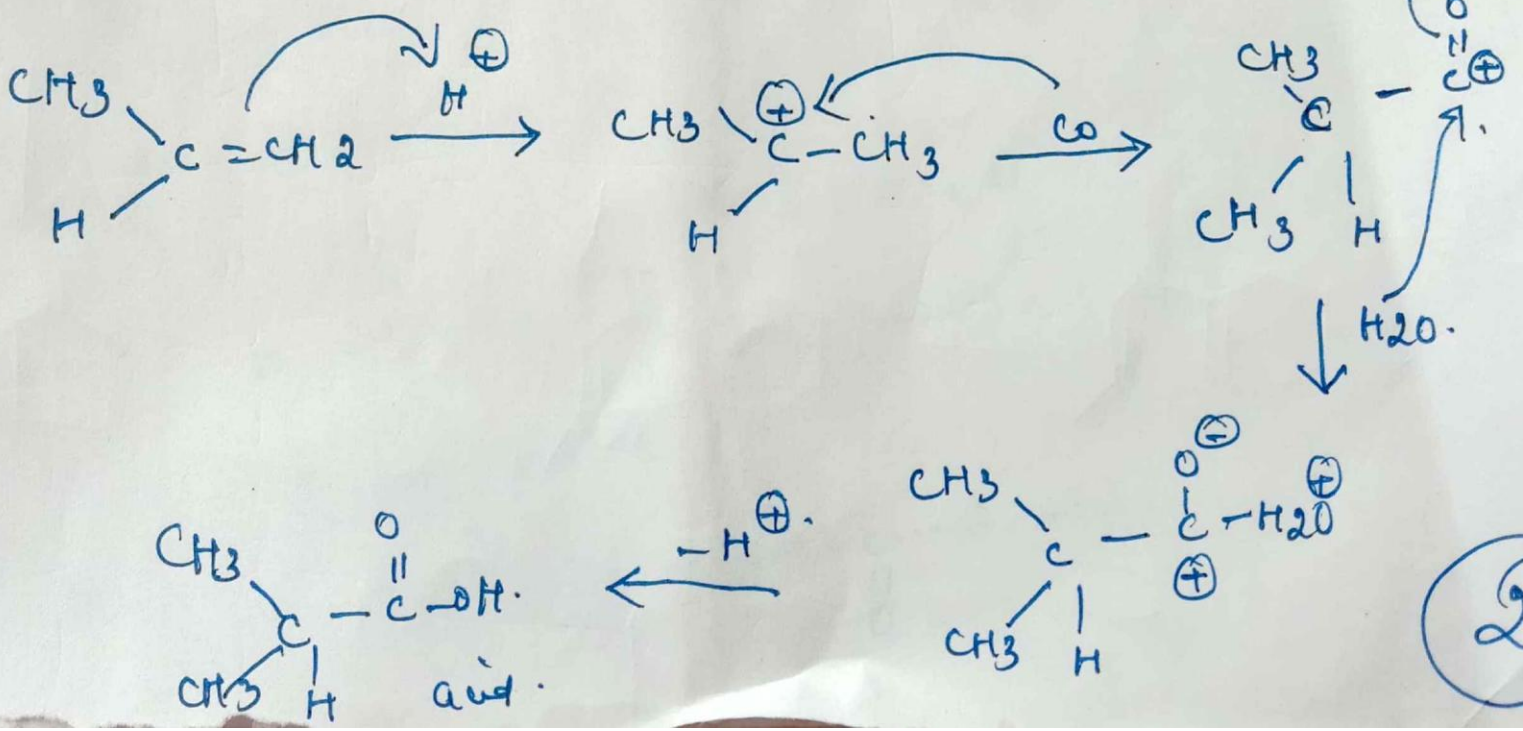
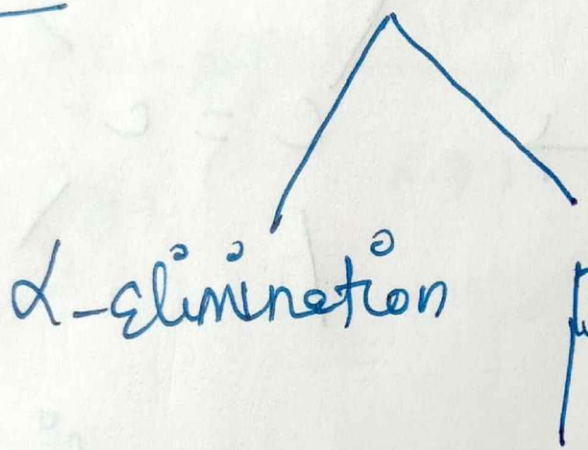
$CH_3CH=CH_2 + CO + H_2O \xrightarrow{\quad"\quad}$ 

Mech.



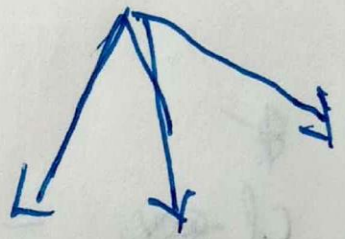
Elimination Reactions.

Removal of two atoms is known as elimination



α-Elimination

β-Elimination

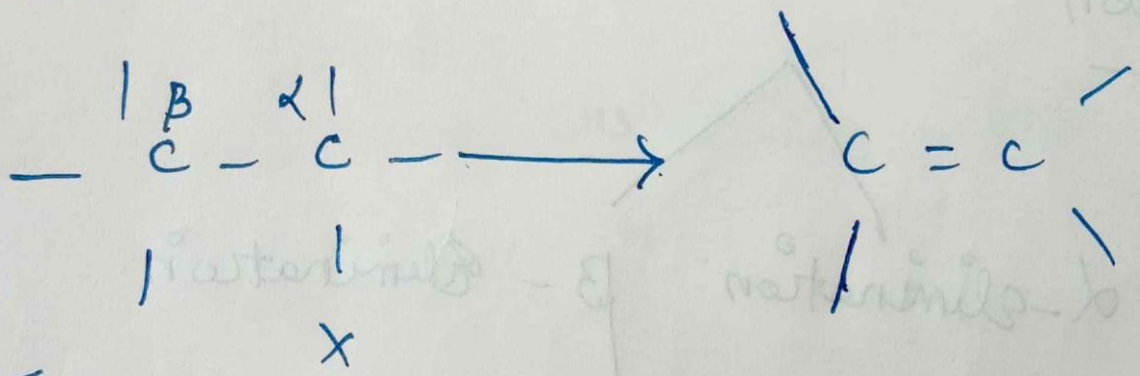


E_1 E_2 E_1CB.

α - Elimination :-

$$CHX_3 \xrightarrow{\text{Alc. KOH}} CX_2 + HX$$

E$_1$ Elimination :-



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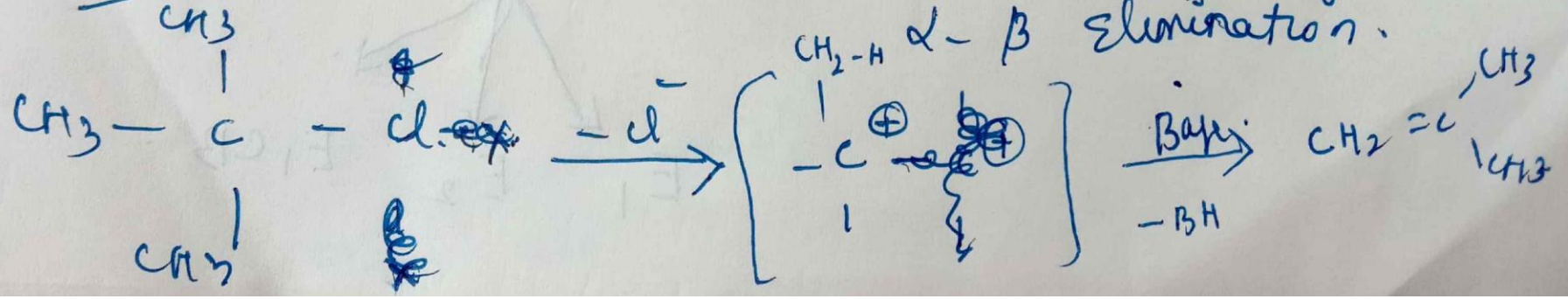
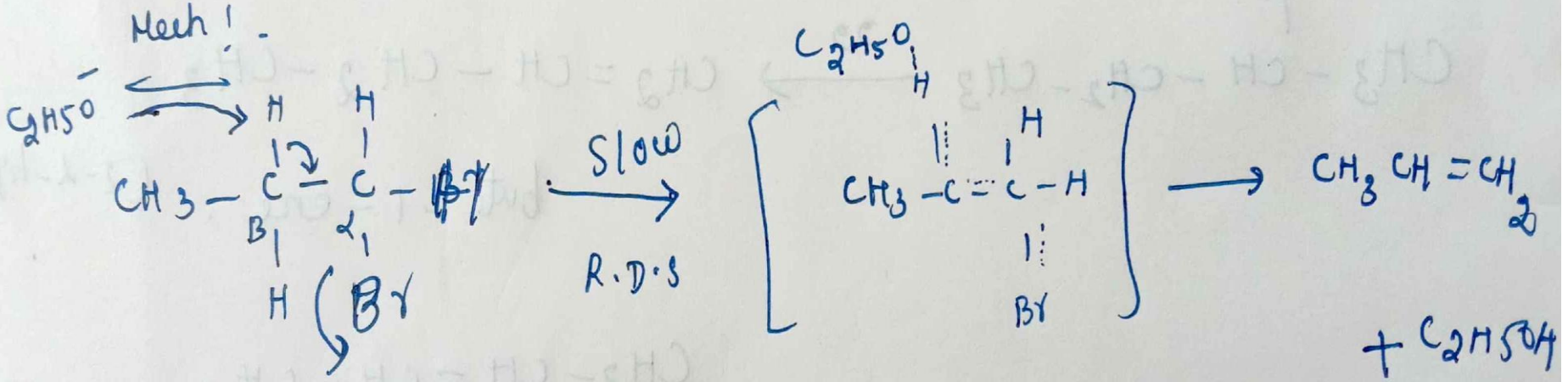


E2 :

C–X & C–H bond break simultaneously

$CH_3-CH_2-CH_2-Br + C_2H_5O^- \rightarrow CH_3-CH=CH_2 + C_2H_5OH + Br^-$

Mech! -



Saytzeff's rule & Hofmann rule.

$$CH_3 - \underset{\beta}{CH}(Cl) - \underset{\alpha}{CH_3} \xrightarrow{\text{Alc. KOH}} CH_2 = CH - CH_3.$$

$$CH_3 - CH(Cl) - CH_2 - CH_3 \xrightarrow{\Delta} CH_2 = CH - CH_2 - CH_3$$

but-1-ene. (2-α-hy

$$CH_3 - CH = CH - CH_3.$$ (b-α-hy

but-2-ene.

more α hydrogen is present in saytzeff's rule.

Less α hydrogen is present in Hofmann rule

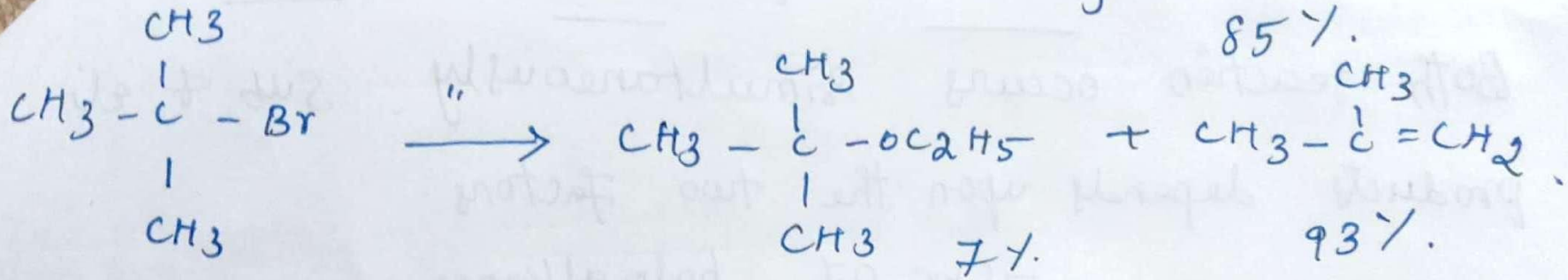
Competetion b/w Substitution & Elimination

Both reaction occurs simultaneously. Sub & eli products depends upon the two factors.

1. → Str of halo alkane
   → Base.

1. $CH_3CH_2CH_2CH_2Br$ (1° halo alkane.) $\xrightarrow[\text{alc NaOH}]{C_2H_5ONa}$ $CH_3CH_2CH_2CH_2OC_2H_5$.
   - NaBr.
   1 ethoxy butane. 90%.
   +
   $CH_3CH_2CH=CH_2$. 10%.

2. $CH_3CH(Br)-CH_2-CH_3$ (2° halo alkane.) $\xrightarrow{\text{''}}$ $CH_3-CH(OC_2H_5)-CH_2-CH_3$. 15%.
   +



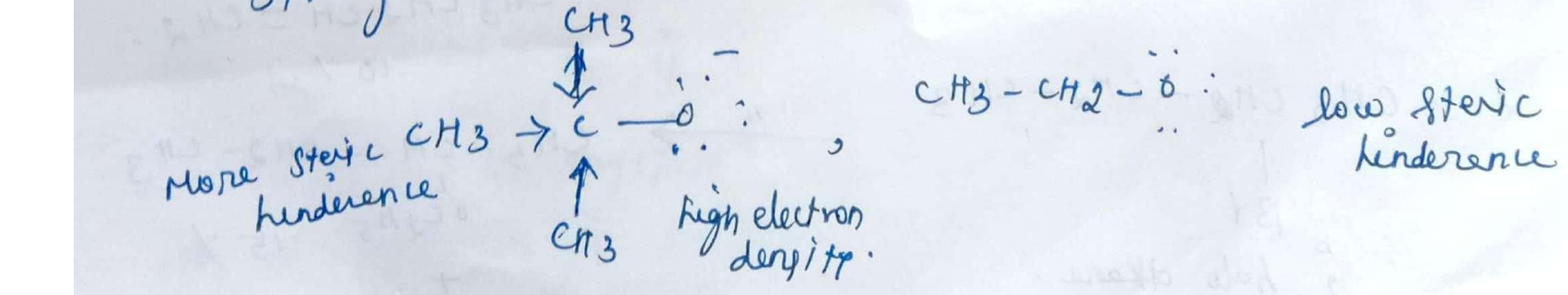
Order of reactivity in substitution & elimination

$3^\circ > 2^\circ > 1^\circ$ $\qquad$ $1^\circ < 2^\circ < 3^\circ$.

Base :

weak base favour the substitution

Strong base favour the elimination.



Chugaev reaction:-

Methyl xanthates are prepared by treatment of alcohols with NaOH and CS_2 to give RO-CS-SNa followed by treatment with methyl iodide.

$$R-CH_2-CH_2-OH \xrightarrow{NaH,\ CS_2,\ MeI} R-CH=CH_2.$$

Mech:

$$R-CH_2-CH_2-\bar{O}H^{+} \xrightarrow{NaH,\ CS_2} R-CH_2-CH_2-\bar{O} + C(=S)=S$$

$$R-CH_2-CH_2-O-\overset{\overset{S}{\|}}{C}-\bar{S} \xrightarrow{CH_3-I} R-CH_2-CH_2-O-\overset{\overset{S}{\|}}{C}-SMe$$

Xenthate ester.

$$R-\underset{\beta}{CH}-\underset{\alpha}{CH_2}-O-\overset{\overset{S}{\|}}{C}-SMe \xrightarrow{200^{\circ}C} RCH=CH_2 + \text{(H–S–C(=O)–SMe)}$$

$$\text{(H–S–C(=O)–SMe)} \longrightarrow MeSH + COS.$$

Dehydration of Alcohol.

Removal of water molecules is known as.

1. $R-\underset{\underset{H}{|}}{CH}-\underset{\underset{OH}{|}}{CH_2} \xrightarrow[180^\circ C]{conc\ H_2SO_4} R-CH=CH_2$.

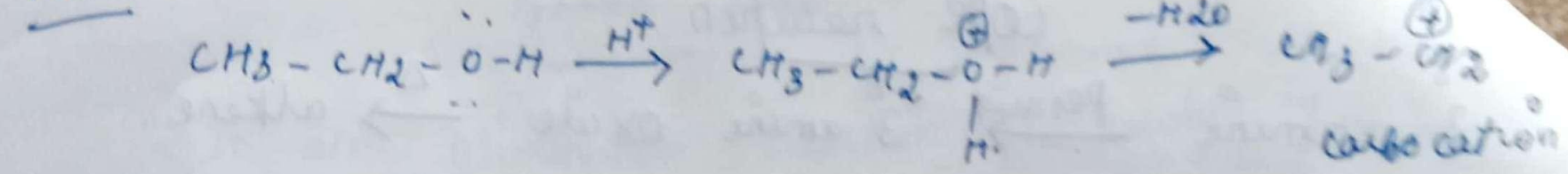
1° alcohol.

$R-CH_2-\underset{\underset{OH}{|}}{CH}-CH_3 \xrightarrow[100^\circ C]{60\%\ conc\ H_2SO_4} R-CH=CH-CH_3$.

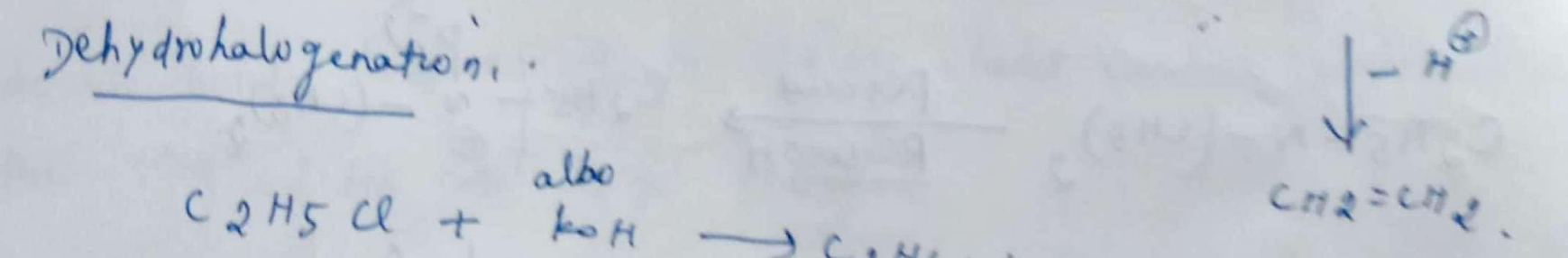
2° alcohol.

$CH_3-\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{C}}-OH \xrightarrow[85^\circ C]{20\%\ conc\ H_2SO_4} CH_3-\overset{\overset{CH_3}{|}}{\underset{\underset{CH_2}{||}}{C}} + H_2O$.

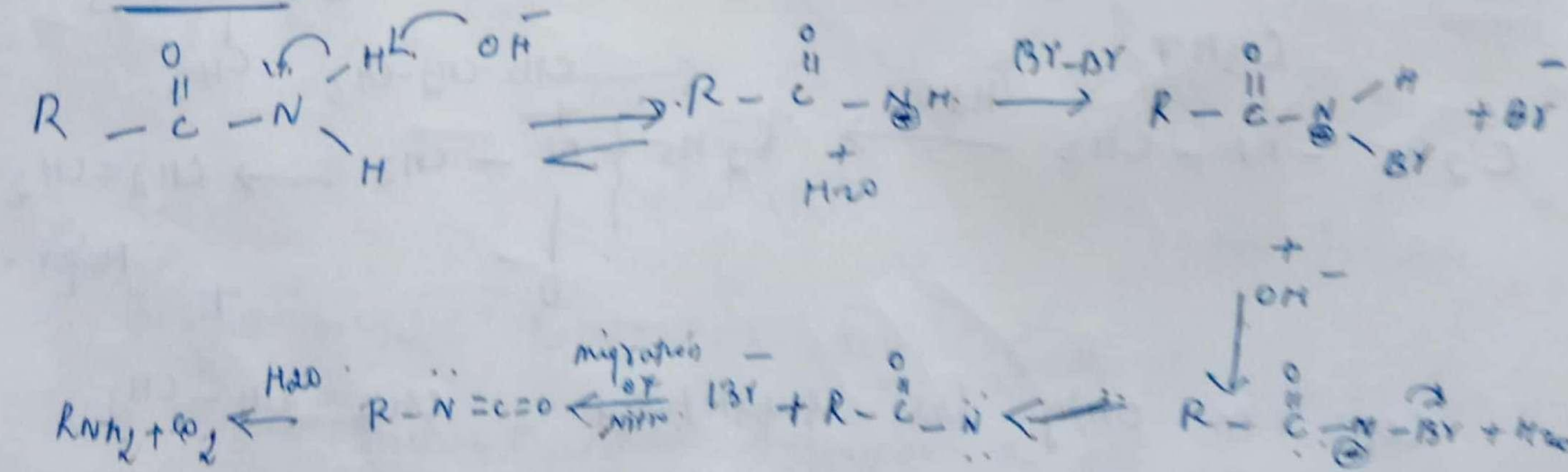
Mech:



Dehydrohalogenation:



Hoffman degradation:-



Cope reaction

3° amine $\xrightarrow{\text{Peracid}}$ 3° amine oxide $\xrightarrow{\Delta}$ alkene.

$C_2H_5-N-(CH_3)_2 \xrightarrow[R-COOH]{\text{peracid}} C_2H_5-\overset{\oplus}{N}(-O^{\ominus})-(CH_3)_2$

$\downarrow \Delta$

$CH_2=CH_2 + N(OH)-CH_3$

CH_3

$C_2H_5-N(C_3H_7)-CH_3 \xrightarrow{H_2O_2}$

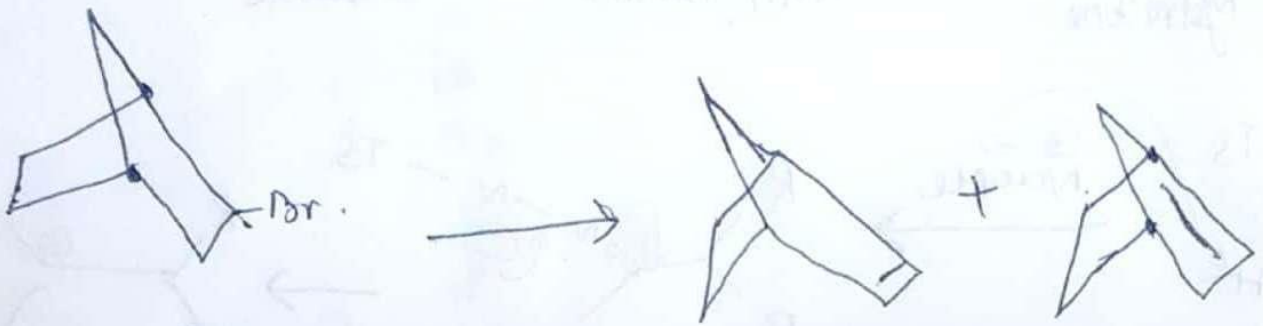
$C_2H_5-\overset{+}{N}(CH_2-CH_2-CH_3)(O^-)-CH_3 \longrightarrow CH_2=CH_2$ + Major.

Cope rxn only less substituted alkenes are major pdt.

$CH_2=CH-CH_3$.

Bredt's Rule

In an elimination reaction, the newly forming double bond does not go to bridge-head carbon unless the ring sizes are large enough.



(A) (B) C not possible

Bridged bicyclic compounds double bonds at the bridge head are impossible in small systems. the pdt (B) only is formed and not C.

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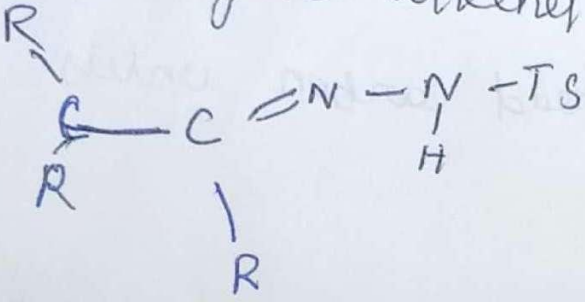
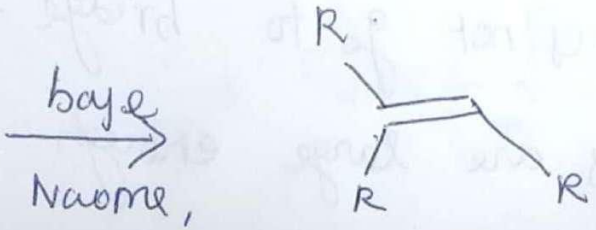
Bamford - Stevens reaction

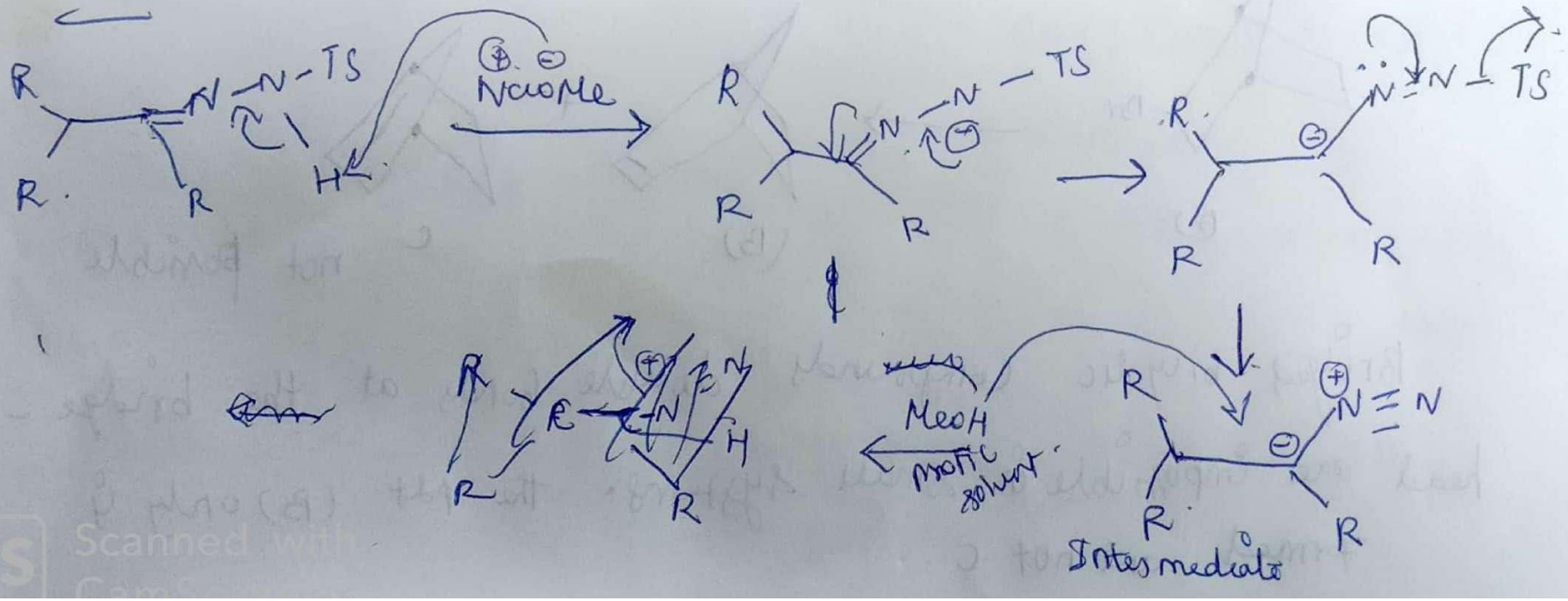
by the treatment of Tosyl hydrazone with mild base to give alkene:-

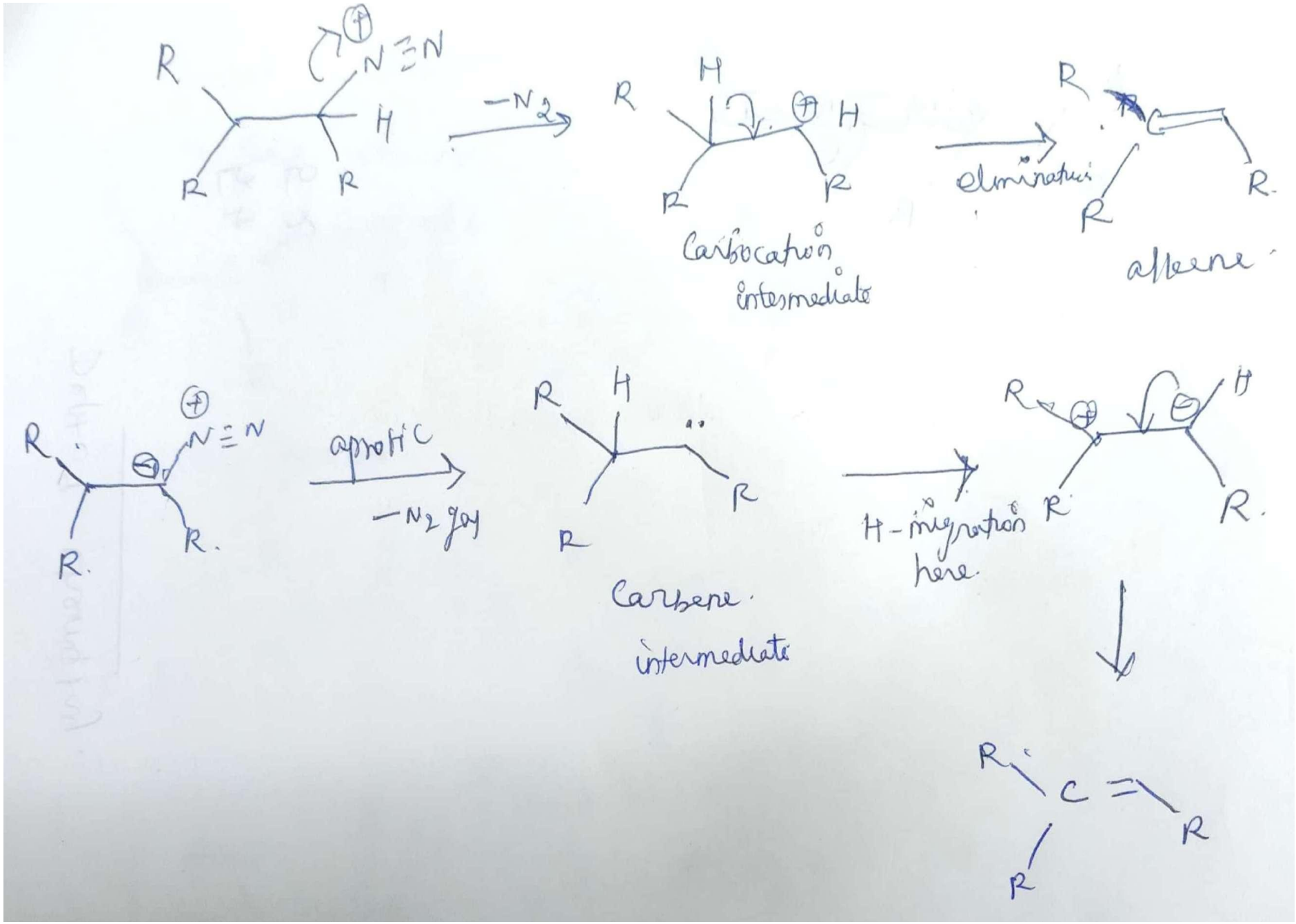


tosyl hydrazone.



Alkene.




R
N≡N
H
R
R
−N2
H
R
H
R
R
Carbocation intermediate
R
elimination
R
R
alkene
R
N≡N
R
R
R
aprotic
−N2 gas
R
H
R
R
Carbene intermediate
H-migration here
R
H
R
R
R
C
R
R

UNIT – II

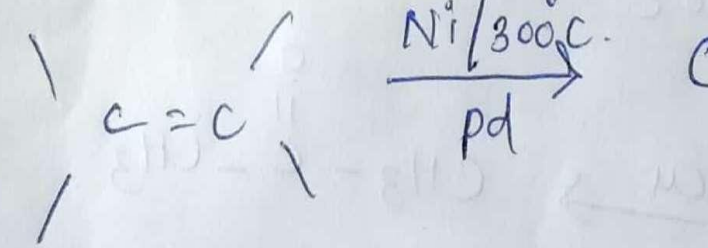
2. REAGENTS IN ORGANIC SYNTHESIS

2.1. REDUCTION

2.2. OXIDATION

Catalytic hydrogenation

Catalytic hydrogenation of a compound with (adding hydrogen) double or triple bond. It reduces the compound and leaves fewer bonds b/w the carbon. This proces utilizes a metal catalyst.



CH

Dehydrogenation:

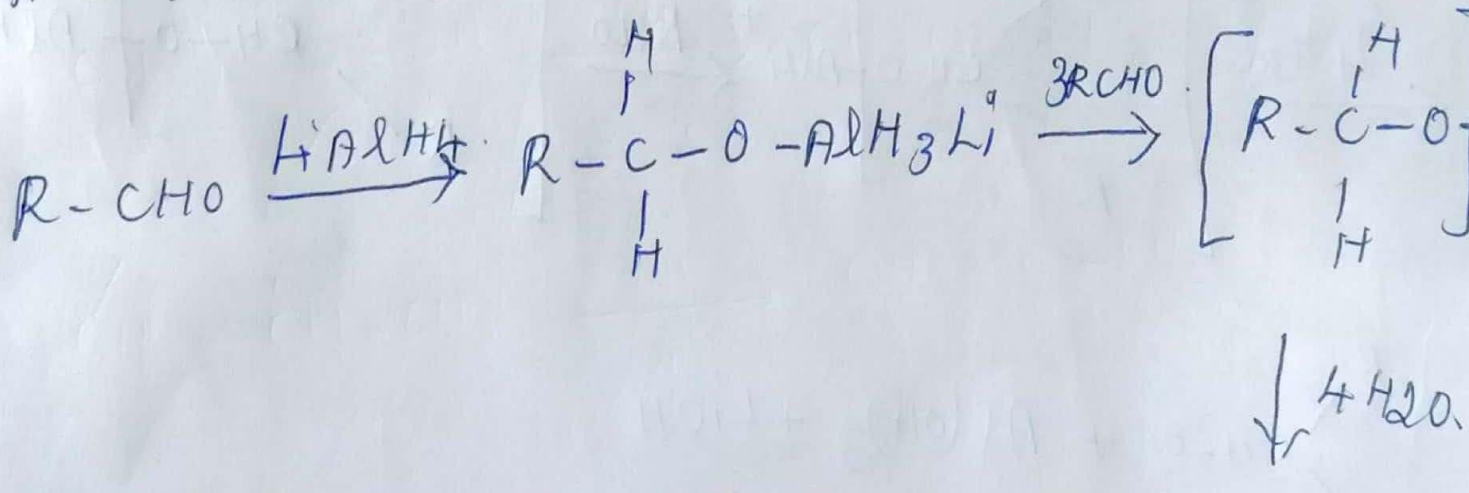
Dehydrogenation is a chemical reaction that involves the removal of hydrogen, usually from an organic molecule. Enzymes that catalyst.

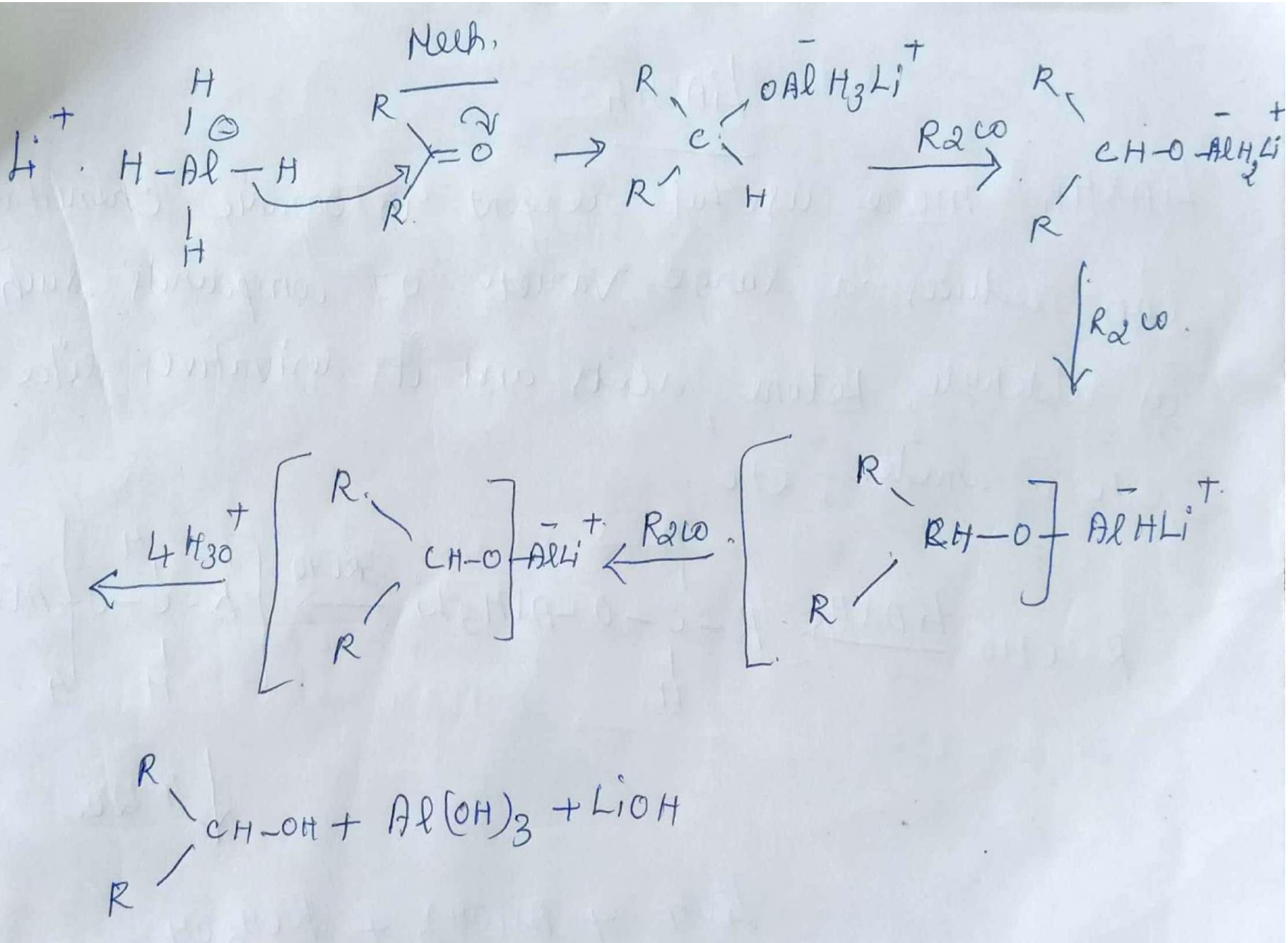
$$CH_3-CH_2-OH \xrightarrow[300^\circ C]{Cu} CH_3CHO + H_2.$$

$$CH_3-\underset{\displaystyle OH}{\underset{|}{CH}}-CH_3 \xrightarrow[\text{''}]{Cu} CH_3-\overset{\displaystyle O}{\overset{\|}{C}}-CH_3.$$

$LiAlH_4$.

$LiAlH_4$ more useful reagent in organic chemistry, can reduces a large variety of compounds such as aldehyde, ketone, acids and its derivatives like esters, amides, etc.





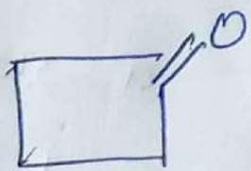
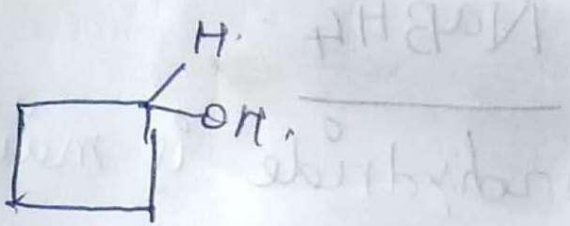
$$\begin{array}{l} R \\ \diagdown \\ \quad CH-OH \\ \diagup \\ R \end{array} + Al(OH)_3 + LiOH$$

eg- 1. $CH_3 \cdot CHO \xrightarrow{LiAlH_4} CH_3CH_2OH$.

2. $CH_3(CH_2)_5CHO \xrightarrow{4} CH_3(CH_2)_5CH_2OH$.

Ketones :-

1. $CH_3CH_2COCH_3 \xrightarrow{11} CH_3CH_2CHOHCH_3$.

2.  $\xrightarrow[H^+/H_2O]{LiAlH_4/ether}$ 

Acid

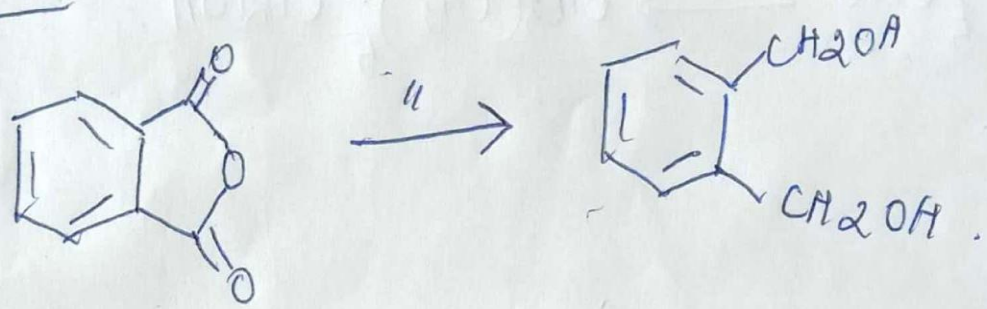
$RCH(NH_2)COOH \xrightarrow{4} RCH(NH_2)CH_2OH$.

Esters

$C_6H_5COOC_2H_5 \xrightarrow{11} C_6H_5CH_2OH$.

$C_6H_5CH=CHCOOC_2H_5 \xrightarrow{LiAlH_4} CH_3CH=CHCH_2OH$.

Anhydrides are reduced to diols:



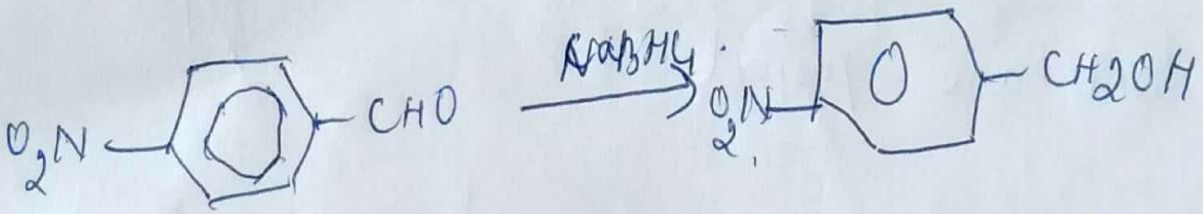
$NaBH_4$.

Sodium borohydride is mainly used as a reducing agent in ethanol. reduces only the ketones and aldehydes to the corresponding alcohols.

1. $CH_3COCH_2COCH_3 \xrightarrow{NaBH_4} CH_3CH(OH)CH_2CH(OH)CH_3$.

$CH_3CH=CHCHO \xrightarrow{NaBH_4} CH_3CH=CH-CH_2OH$.

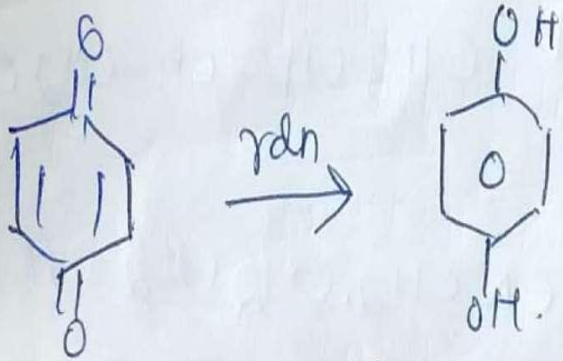
$CNCH_2CH_2CHO \xrightarrow{''} CNCH_2CH_2CH_2OH$.



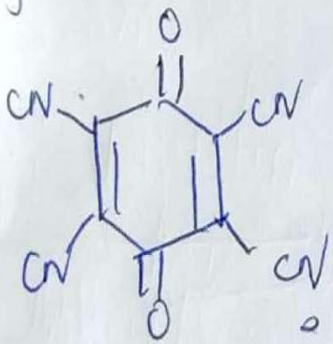
DDQ

Dichlorodicyanoquinone :-

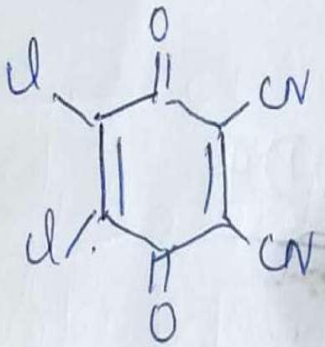
Quinones are powerful oxidizing agents. On reduction these are converted to more stable aromatic hydroquinones.



Quinones become especially powerful oxidizing agents. when $\bar{e}$ withdrawing substituents are present.



Tetra cyanoquinone



DDQ.

Gilman's Reagents

Lithium dialkyl cuprates are called the Gilman's reagents and provide a good method for coupling two alkyl fragments to give a large alkane. This reaction is called the corey-House reaction.

$$H_2C=CH-Cl + 2Li \xrightarrow[-LiCl]{\text{pentane}} H_2C=CH-Li \xrightarrow{CuI} (CH_2=CH_2)_2CuLi$$

Lithium divinyl cuprate.

$$CH_3CH_2CH_2CH_2Br + 2Li \xrightarrow[\text{"}]{\text{"}} CH_3CH_2CH_2CH_2Li \xrightarrow{CuI} (CH_3CH_2CH_2CH_2)_2CuLi$$

Lithium dibutyl cuprate

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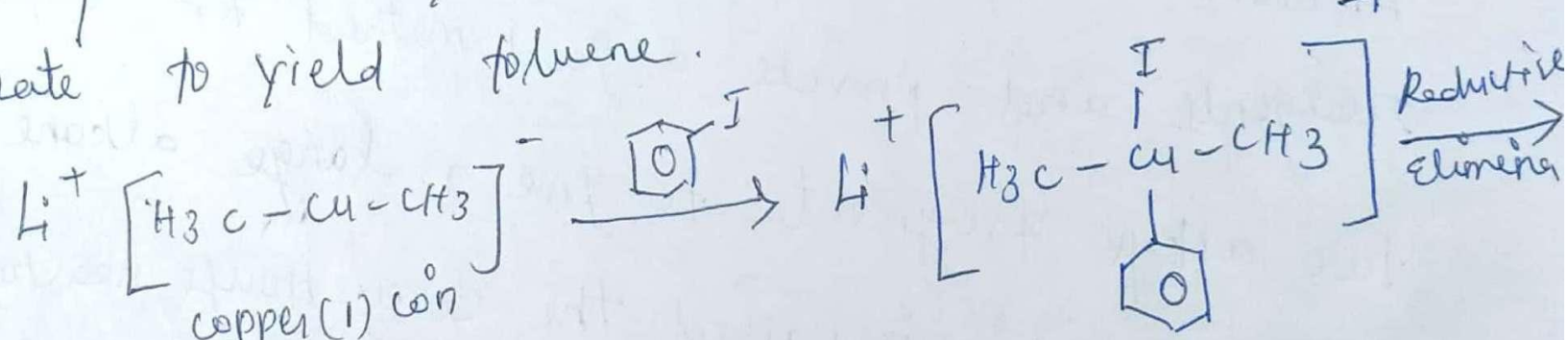
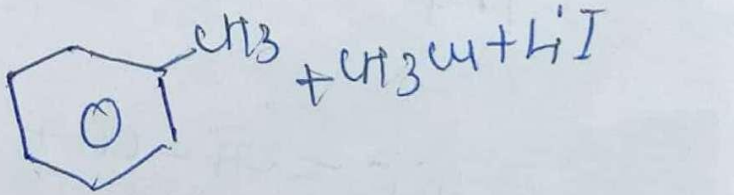
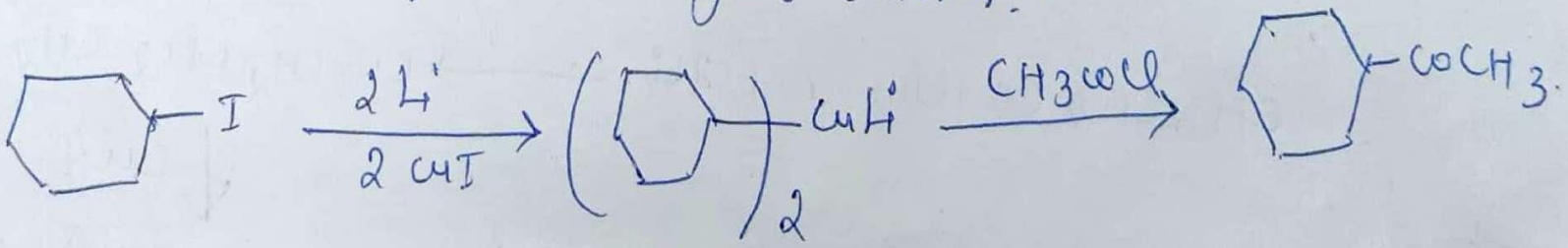
Mech!.

The mechanism of the rxn can be explained by considering the rxn b/w iodobenzene and lithium dimethyl cuprate to yield toluene.

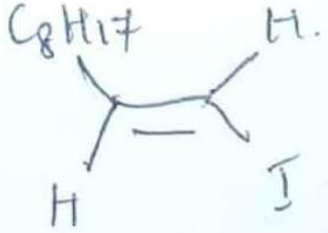




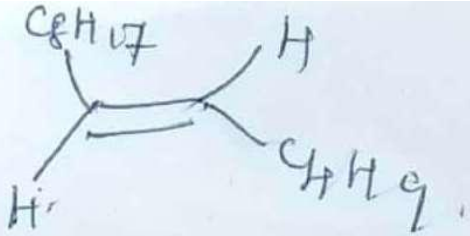
1. Reaction with acyl halides gives ketones!.



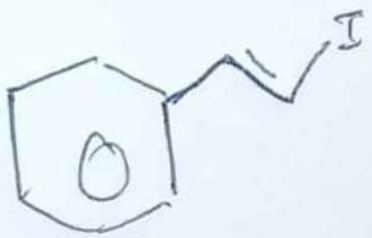
(ii.)



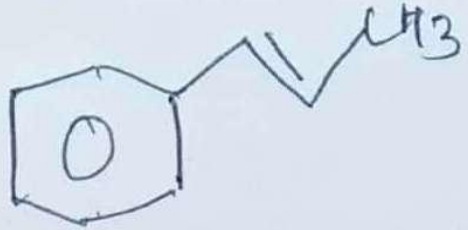
$(C_4H_9)_2CuLi$ →



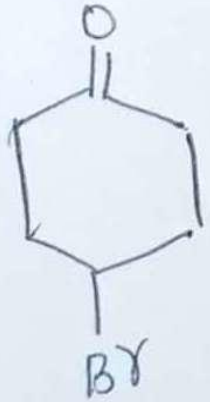
(iii)



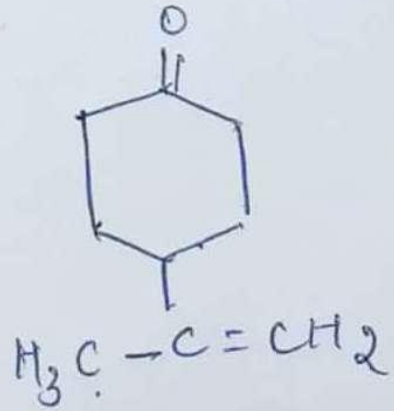
$(CH_3)_2CuLi$ →



(iv)

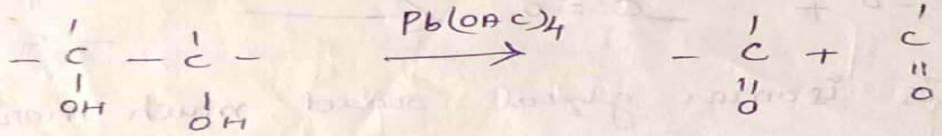


$(CH_2=CCH_3)_2CuLi$ →

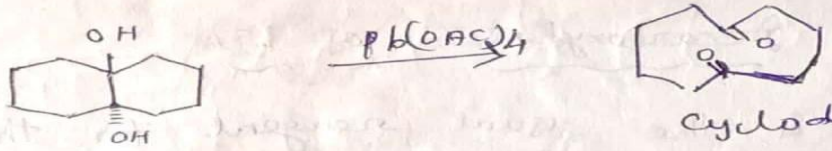


LEAD TETRA ACETATE ($Pb(OAc)_4$)

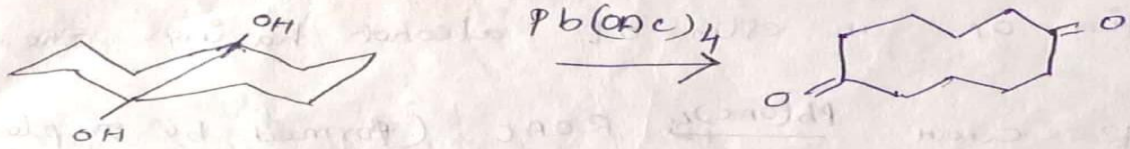
Lead tetra acetate is commonly used for the cleavage of 1,2 glycols. LTA is used in anhydrous solvent such as acetic acid under mild conditions. The cis isomer of this are more easily oxidised than the trans. This is explained on the basis of a five-membered cyclic intermediate



An 1,2 glycol need not necessarily be cis to undergo cleavage with lead tetra acetate. For eg trans-9,10-decalindiol undergoes cleavage to cyclodecane 1,2 dione.



Cyclodecane 1,2 dione

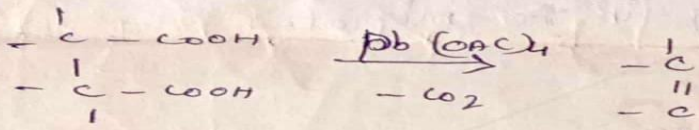


$\xrightarrow{-CO_2}$ $CH_3-\dot{C}H_2$ $\xrightarrow{Pb(OAc)_3}$ $Pb(OAc)_2 + CH_3-\overset{\oplus}{C}H_2 + AcO^-$

$\swarrow -H^{\oplus}$ $\qquad$ $\searrow AcO^-$

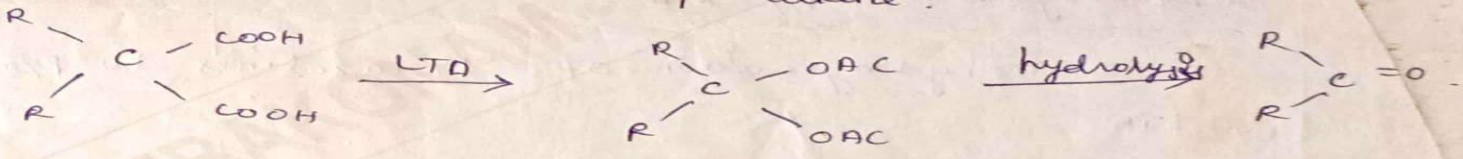
$CH_2=CH_2$ $\qquad$ CH_3-CH_2OAc

(iii) cis decarboxylation :

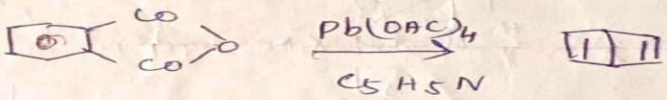


alkene.

(IV)

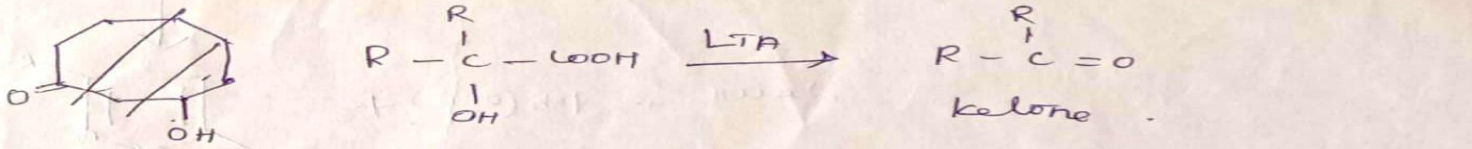


(V) This method is used for preparation of Dewar's benzene.



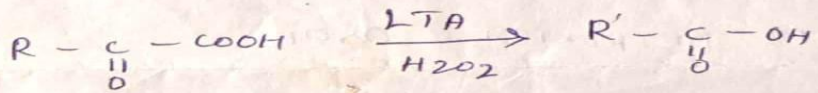
Dewar's benzene.

(VI)



α hydroxy acid.

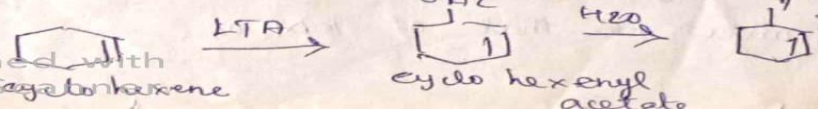
(VII)



α – keto acid

Oxidation of Alkene by LTA.

1)



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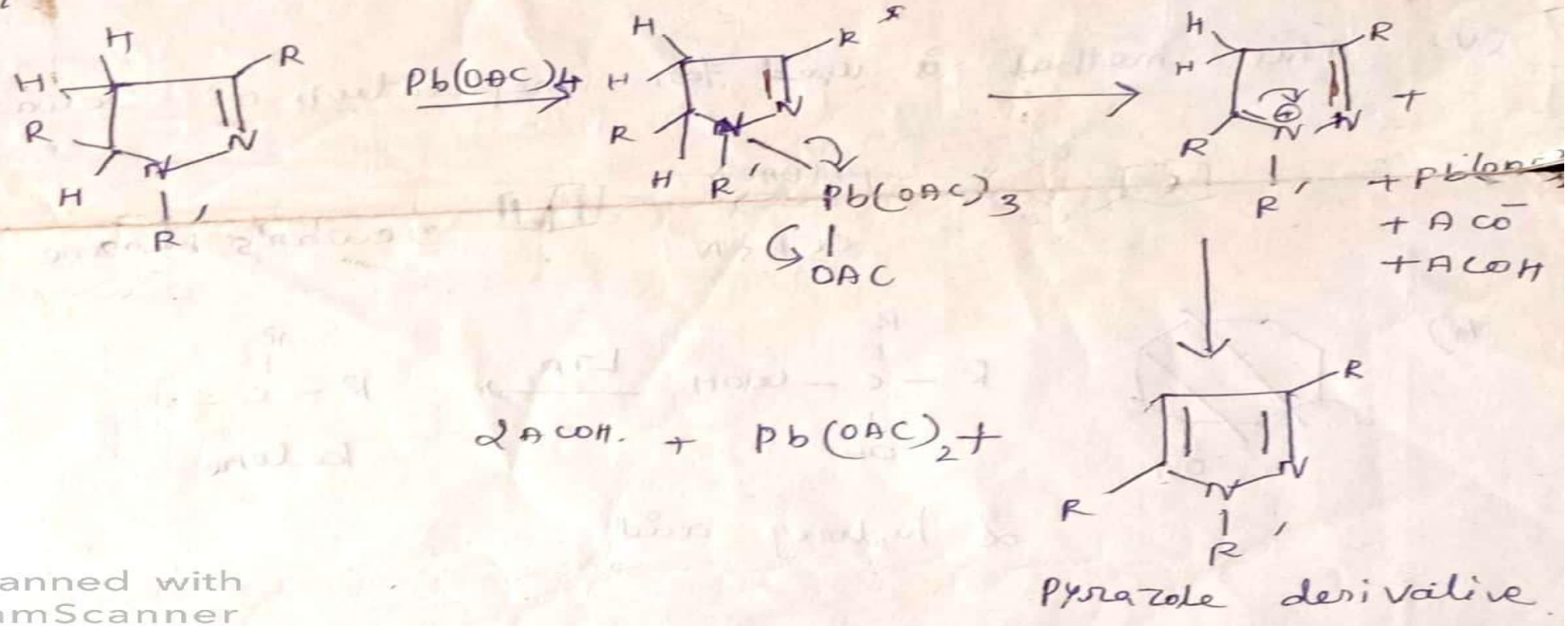
Oxidation of olefin with LTA generally produced by an addition to the double bond followed by elimination resulting in the migration of the double bond.

Dehydrogenation by LTA.

Dehydrogenation of Pyrazolines to Pyrazoles by LTA.



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Selenium Dioxide

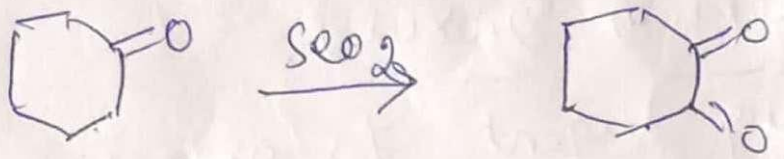
SeO_2 is an oxidising agent for organic compounds. It brings about the oxidation of reactive methyl or methylene groups, without affecting the carbonyl groups to dicarbonyl compounds. SeO_2 is employed for carrying out hydroxylation (or) dehydrogenation

$$CH_3CHO + SeO_2 \longrightarrow CHO\cdot CHO + Se + H_2O$$

glyoxal.

$$CH_3COCH_3 + SeO_2 \longrightarrow CH_3COCHO + Se + H_2O$$

$$C_6H_5COCH_3 + SeO_2 \longrightarrow$$

(IV) 

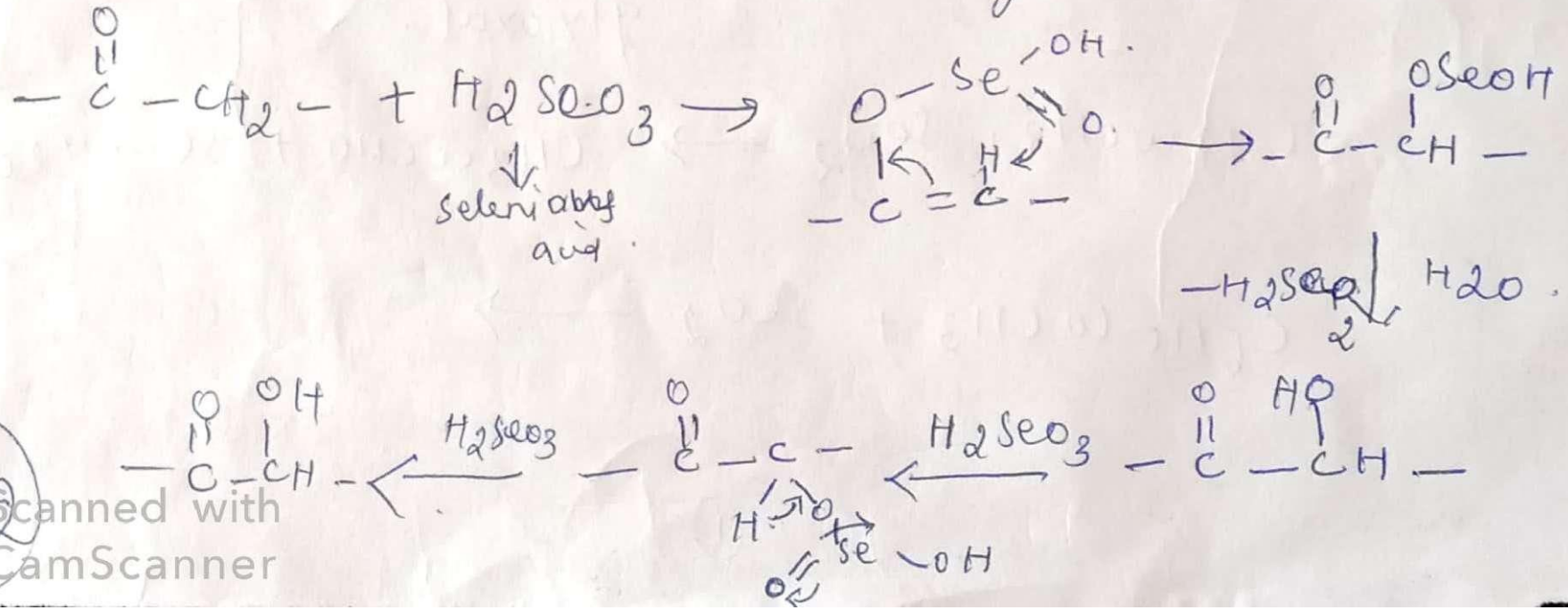
(V) $CH_3CH_2COCH_3 \xrightarrow{SeO_2} CH_3CH_2COCH_3 + CH_3COCOCH_3$

Major

(VI) $CH_2(COOC_2H_5)_2$ ⟶ $OC(COOC_2H_5)_2$

Ethyl malonate

Ethyl mesoxalate.



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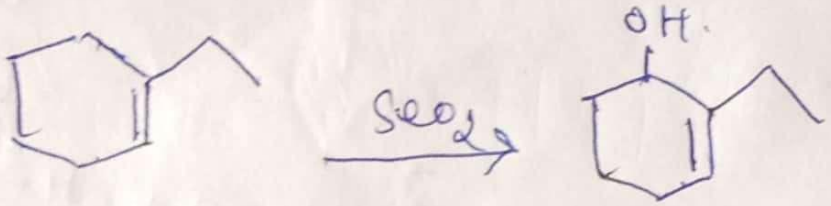
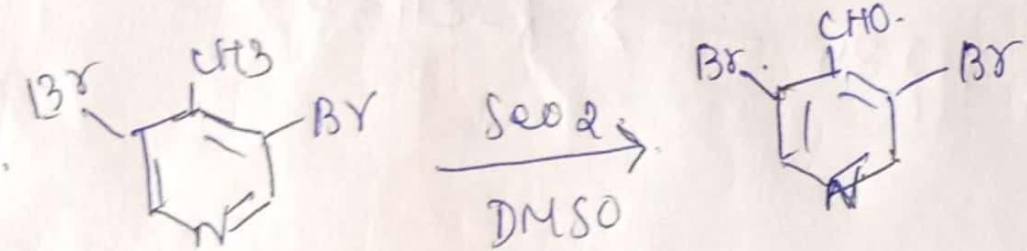
Oxidation of cyclic alkenes.

(a)

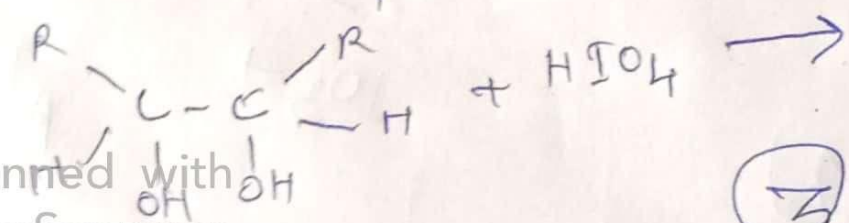


(b).



$HIO_4 \cdot 2H_2O$ (or) H_5IO_6.

The oxidative cleavage of C-C bond in vicinal glycols can also be achieved by HIO_4.



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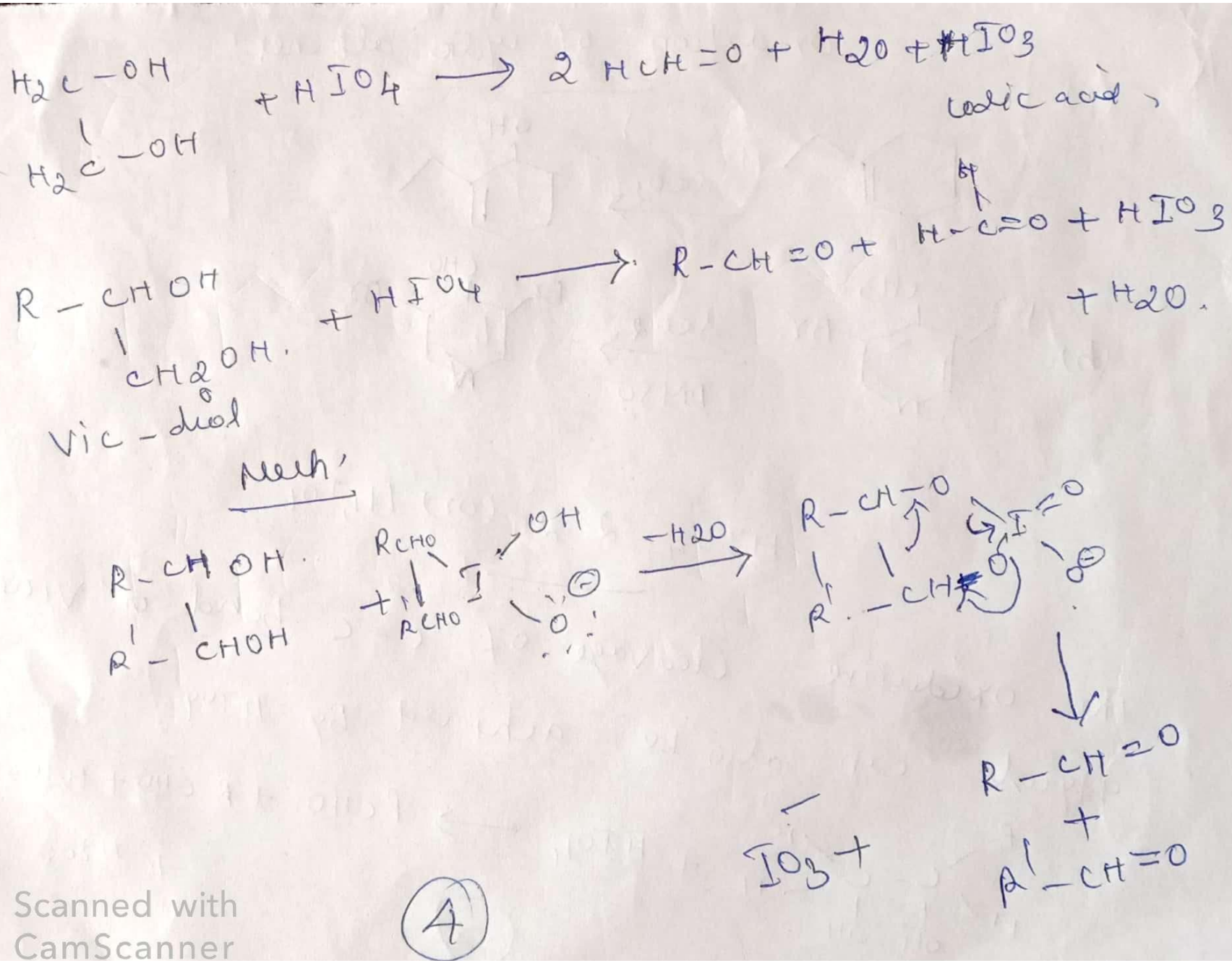

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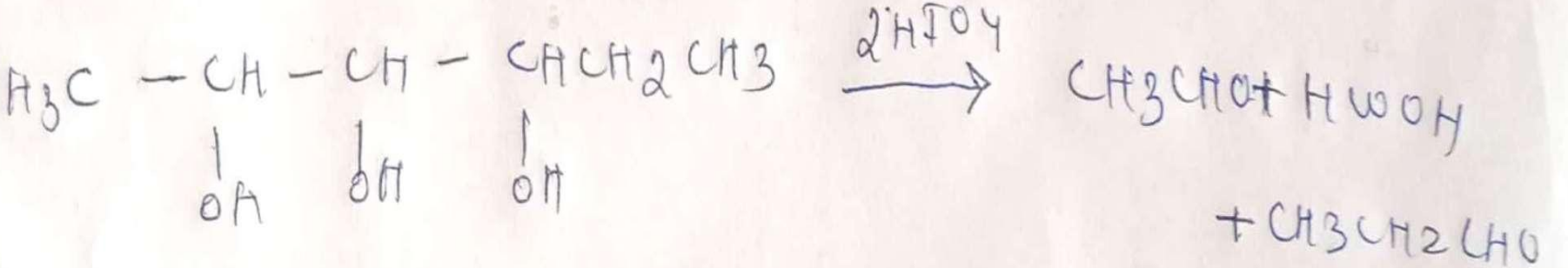
$$HOCH_2CH(OH)CH_2-CH_3 \xrightarrow{HIO_4} HCHO + CH_3CH_2CHO + HIO_3 + H_2O.$$

$$CH_3CH(OH)CH(OH)CH_3 \xrightarrow{HIO_4} 2\,CH_3CHO + HIO_3 + H_2O.$$



OsO_4:

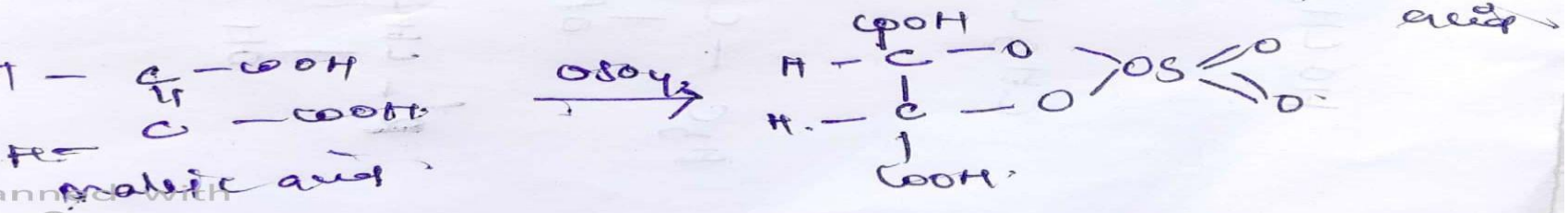
It is mainly used as valuable Hydroxylating agent in organic synthesis.

Preparation: —

$$Os + 2O_2 \xrightarrow[\text{in air}]{\text{Red hot}} OsO_4$$

1. **Formation of 1,2 diol:** —

2. **cis hydroxylation of maleic acid to meso-tartaric acid**



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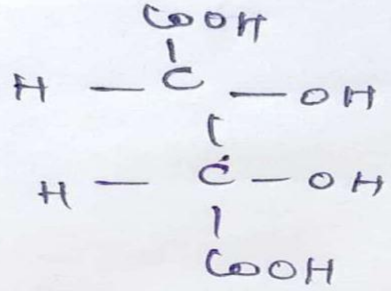
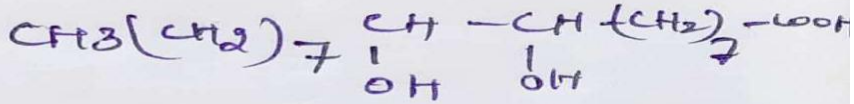
$\xrightarrow[H_2O]{NaClO_3}$



$+ OSO_4$.

(3) Oleic acid into 9,10 -dihydroxy stearic acid

$CH_3(CH_2)_7CH=CH(CH_2)_7COOH \xrightarrow{OSO_4, H_2O}$



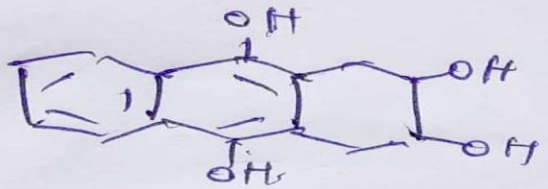
4) Acraldehyde is to Glyceraldehyde.

$H_2C=CH-CHO \xrightarrow{OSO_4} HOCH_2-CH(OH)_2-CHO$.

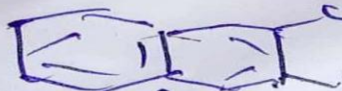
5)

phenanthrene.

$\xrightarrow{OSO_4}$



$\downarrow K_3Fe(CN)_6$,



Naphthalene 2,3 dicarboxylic acid.

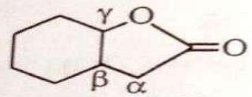
49.8. LITHIUM DIISOPROPYL AMIDE (LDA), $[(CH_3)_2CH]_2\ddot{N}^{\ominus}: Li^{\oplus}$

Preparation. Lithium diisopropylamide (**LDA**) is prepared in solution by addition of di-isopylamine in ether to a solution of **phenyl lithium** (prepared from bromobenzene in ether and lithium under nitrogen).

$$\underset{\text{Di-isopropylamine}}{[(CH_3)_2CH]_2\ddot{N}H} + \underset{\text{Phenyl lithium}}{C_6H_5Li} \xrightarrow{\text{Ether}} \underset{\textbf{LDA}}{[(CH_3)_2CH]_2\ddot{N}^{\ominus}: Li^{\oplus}} + C_6H_6$$

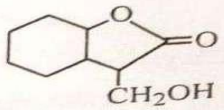
Application. (1) In a-hydroxymethylation of γ-and δ-lactones. For example,

(*a*)



trans-Cyclohexyl γ-butyrolactone

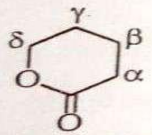
$\xrightarrow[(ii)\ CH_2O\ (N_2),\ -20°C]{(i)\ \text{LDA in THF at } -78°C}$



trans-α-Hydroxymethyl cyclohexyl γ-butyrolactone

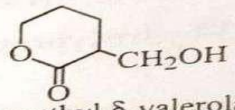
[THF = tetrahydrofuran]

(*b*)



δ-Valerolactone

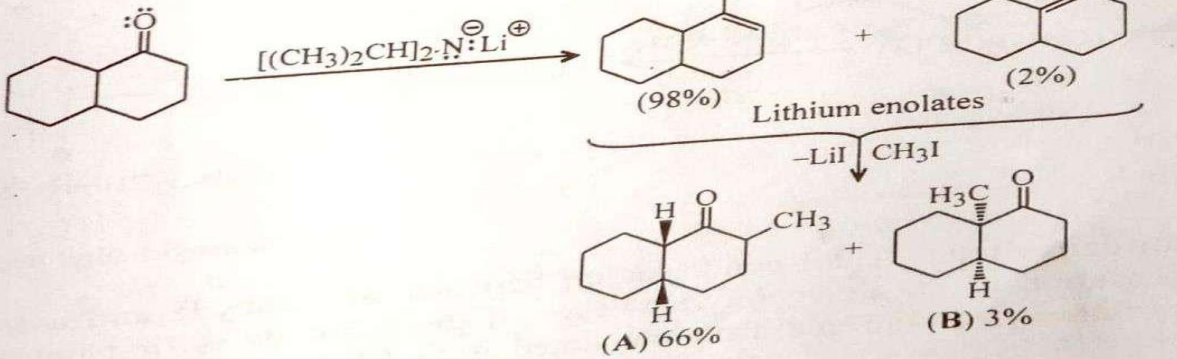
$\xrightarrow[(ii)\ CH_2O\ (N_2)]{(i)\ \text{LDA in THF}}$



α-Hydroxymethyl δ-valerolactone

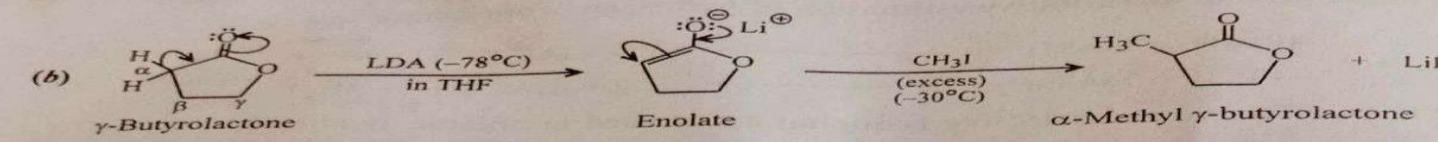
(2) In the formation of lithium enolates of unsymmetric ketones, which on **methylation** give ethylated ketones. For example,

(*a*)

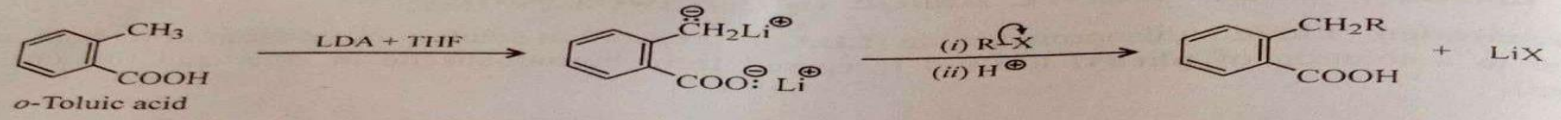


Methylation of the mixture with large excess of CH_3I gives mainly monoalkylated ketone (**A**). Thus

unsymmetric ketones can be alkylated at the **less hindered** position.

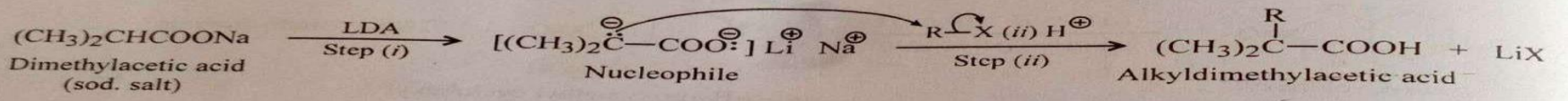


(3) In monoalkylation of toluic acid.



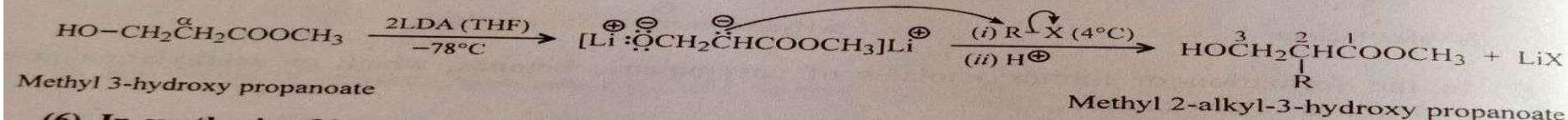
The order of reactivity being $o > m > p$.

(4) Alkylation of dialkyl acetic acid. In this reaction first step involves the formation of a carbanion which acts as a nucleophile for step (*ii*).

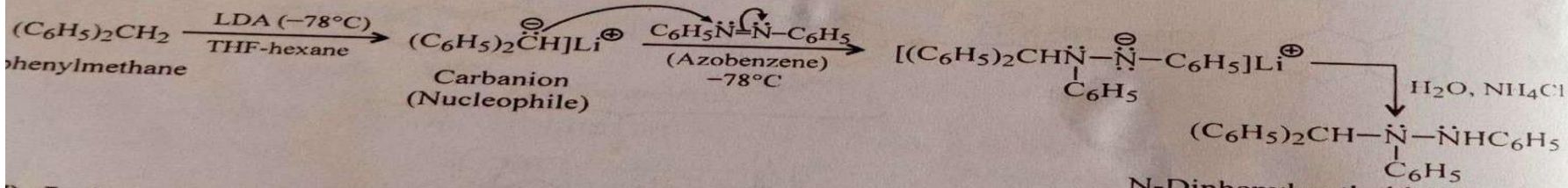


This provides a route for the synthesis of **sterically hindered carboxylic** acids.

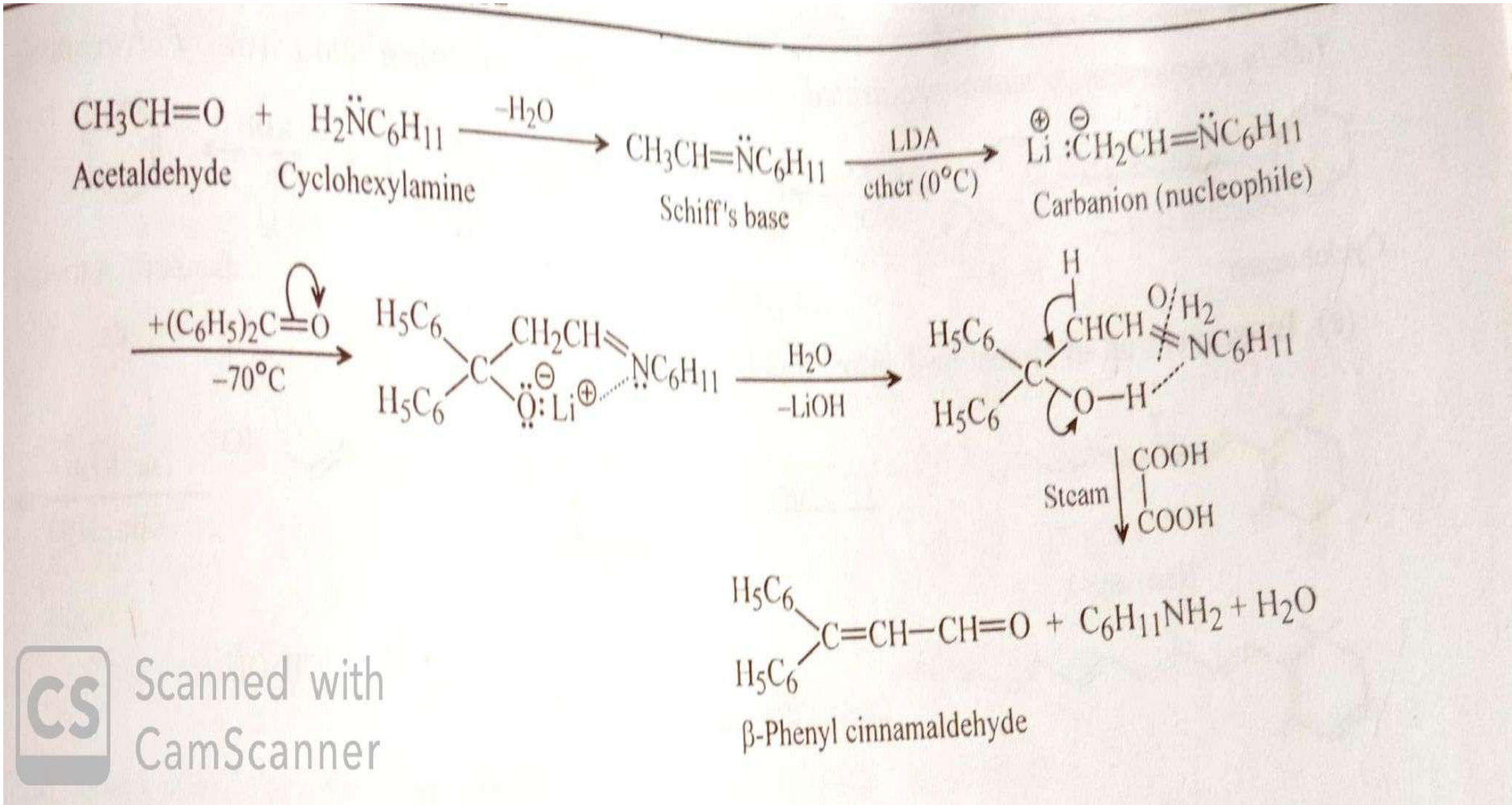
(5) In α-alkylation of methyl-3-hydroxypropanoate.



(6) In synthesis of hydrazobenzenes.



) Indirect aldol condensation. Aldol condensation between an aldehyde and a ketone is not e due to self condensation of an aldehyde. However, if the aldehyde is first converted into a **base** by using cyclohexyl amine and then metalated with **LDA**, aldol condensation can be d. For example,



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