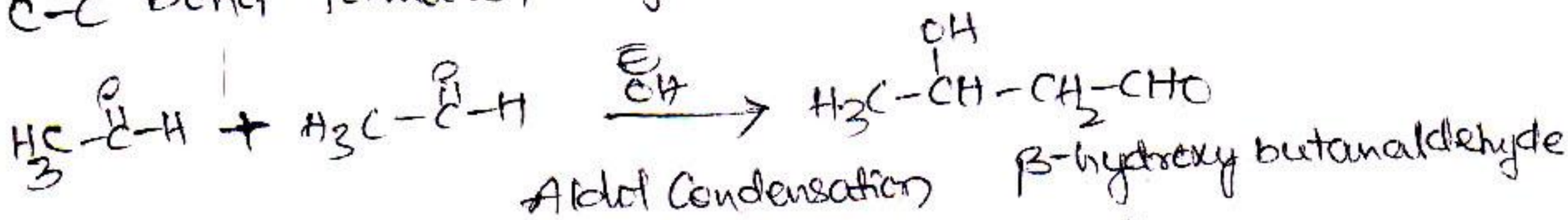
*. SYNTHETIC NAMED REACTIONS. (Synthetic Utility) *.

Importance of named reactions.

① C-C bond formation.



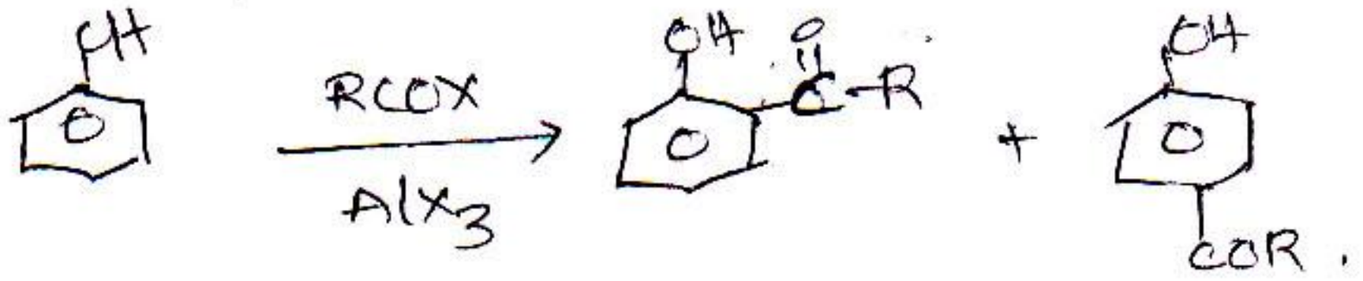
② C-C bond formation by interconversion of functional group.



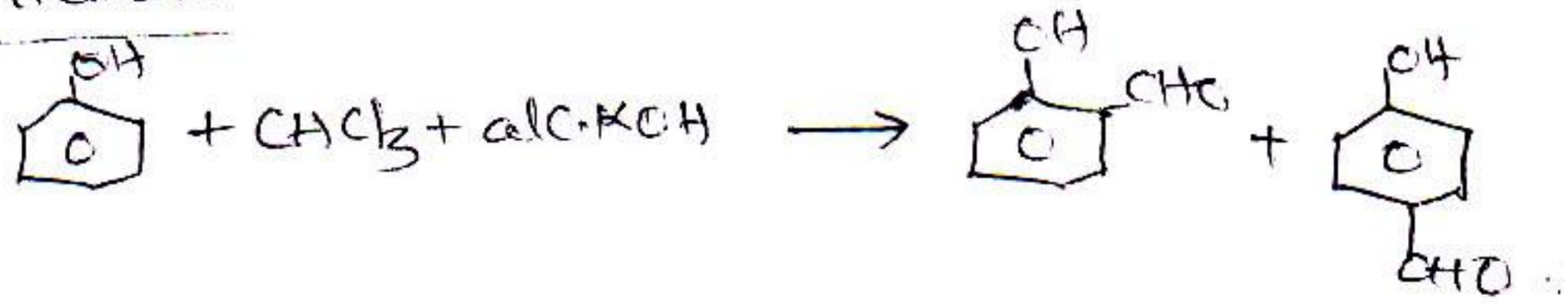
Aldol Condensation β-hydroxy butanaldehyde

③ C-C bond formation by F.G. addition.

eg: Friedal craft acylation.

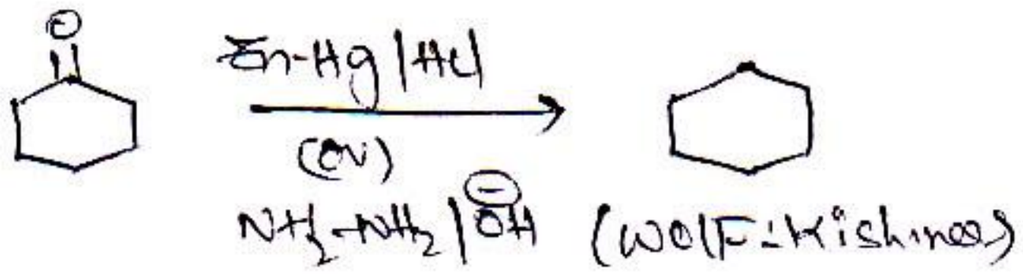


Riemer Tiemann

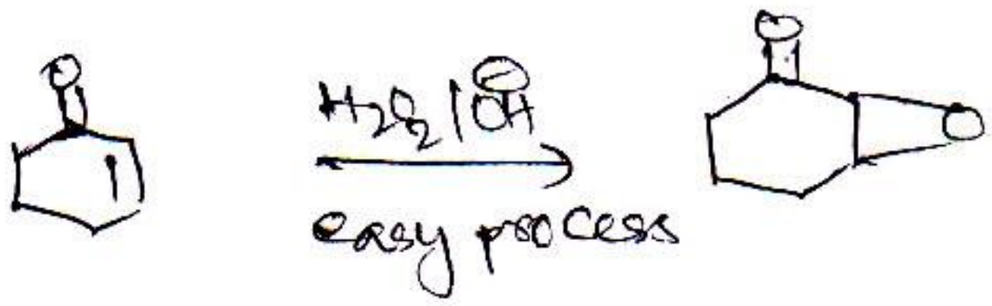


④ Functional group elimination.

eg: ① clemenson Reduction



⑤ F.G. interconversion.



⑥ C-C bonding followed by cyclisation.

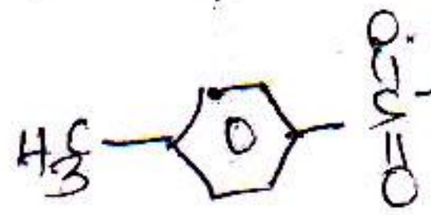
eg: Diels-Alder rxn



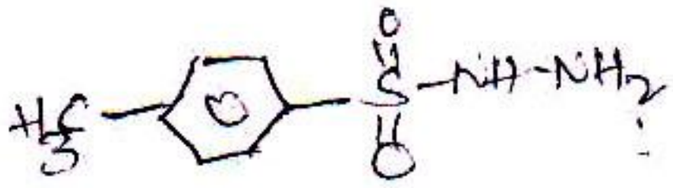
(1) SHAPIRO REACTION

In direct alternative to wittig reaction.

Tosyl hydrazene $Ts-NH-NH_2$: Ts = Tosyl ⇒ para toulyl sulfonyl



⇒ Tosylate

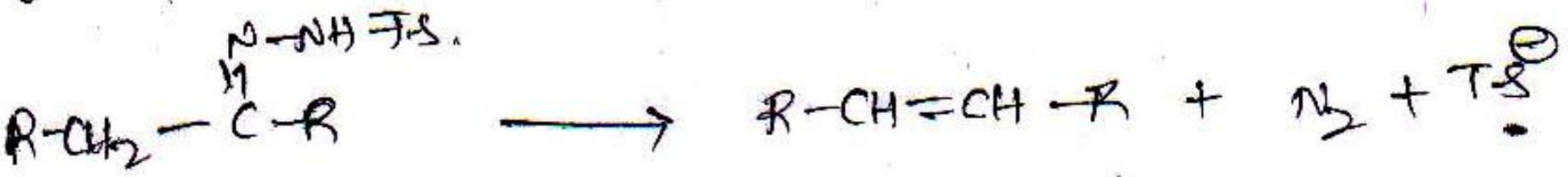


(Tosyl hydrazene)



Tosyl hydrazone

→ Conversion of Tosyl hydrazone of carbonyl compd having α H is into olefins in the presence of excess of 2 equalents strong bases alkyl lithium, LDA



Solvents :

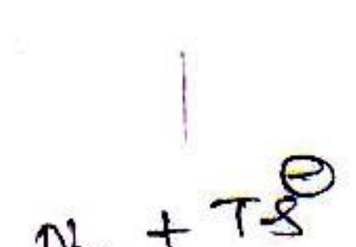
① TMEDA – Tetramethylene diamine

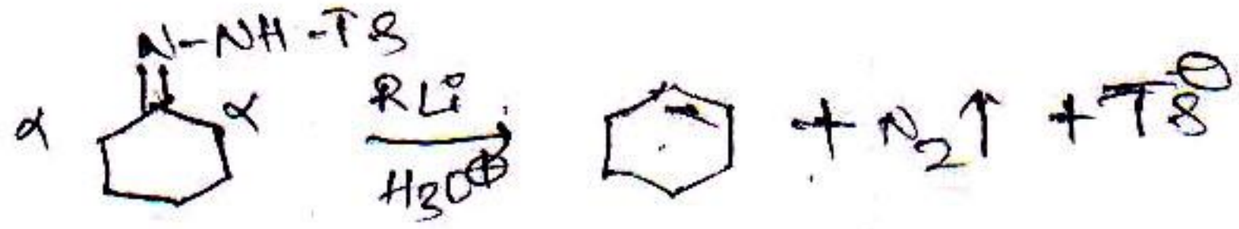
② Ethers

③ THF 

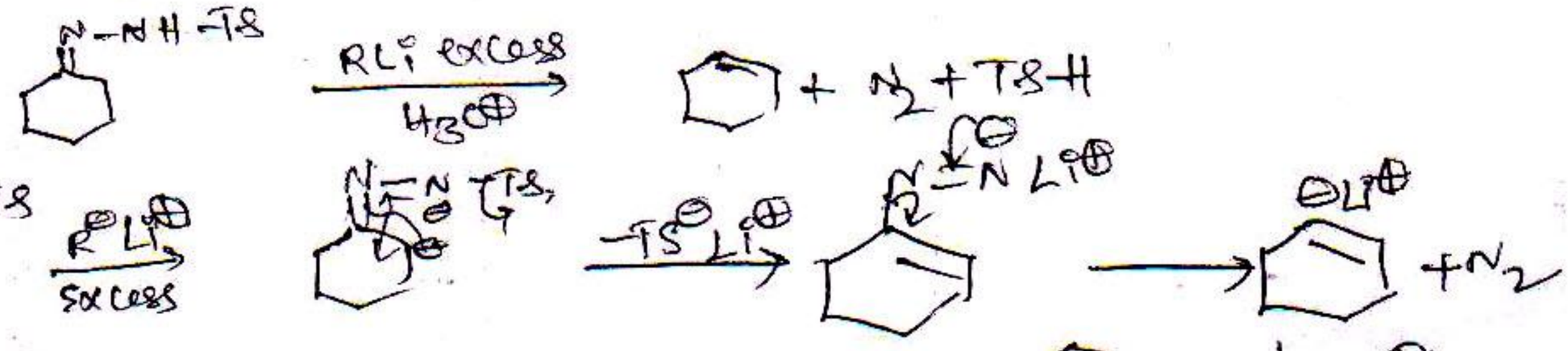
④ DME (Dimethoxy ethane) 

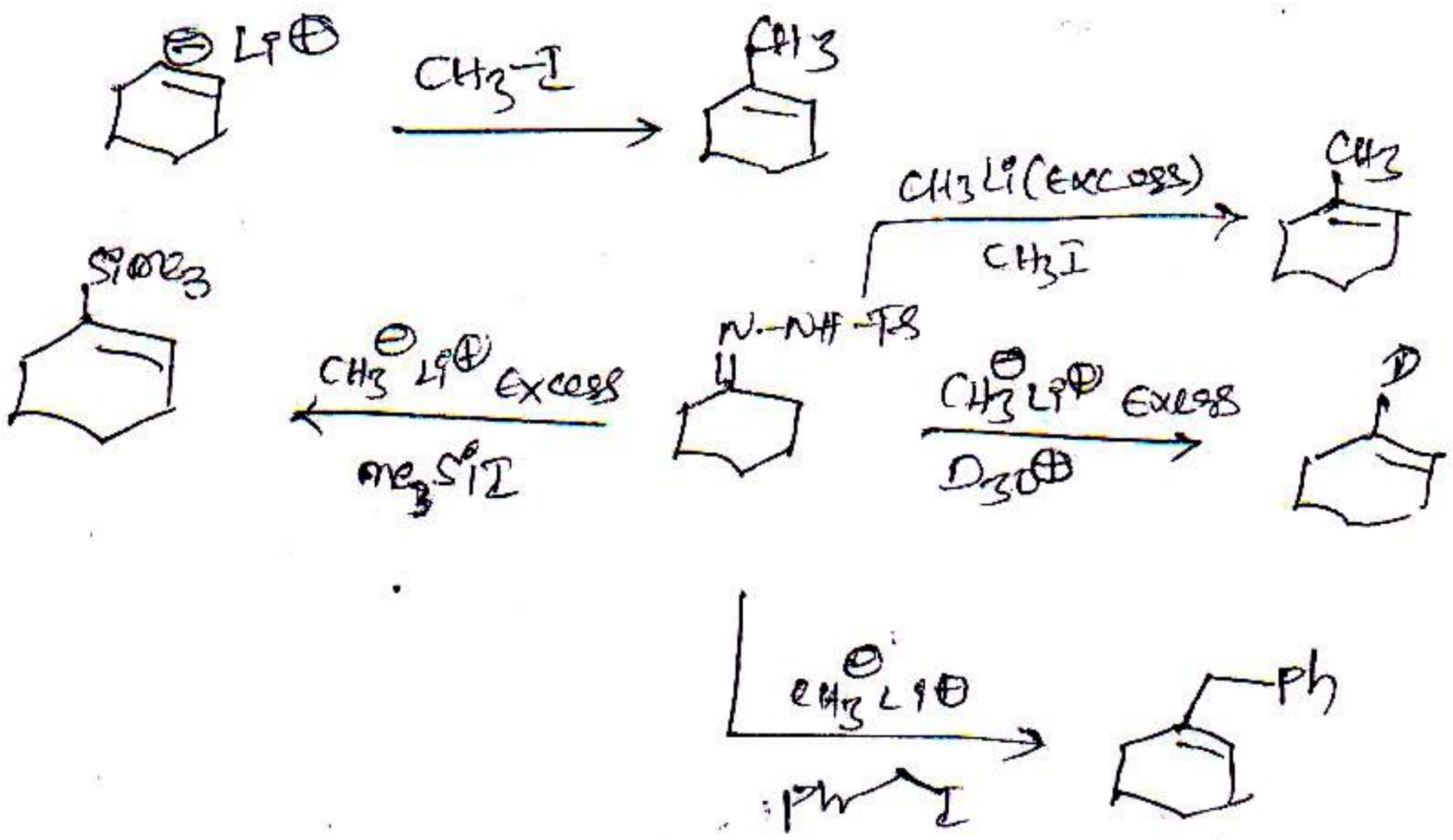
Bases ① RLi

② LDA (Lithium di isopropyl amine) 

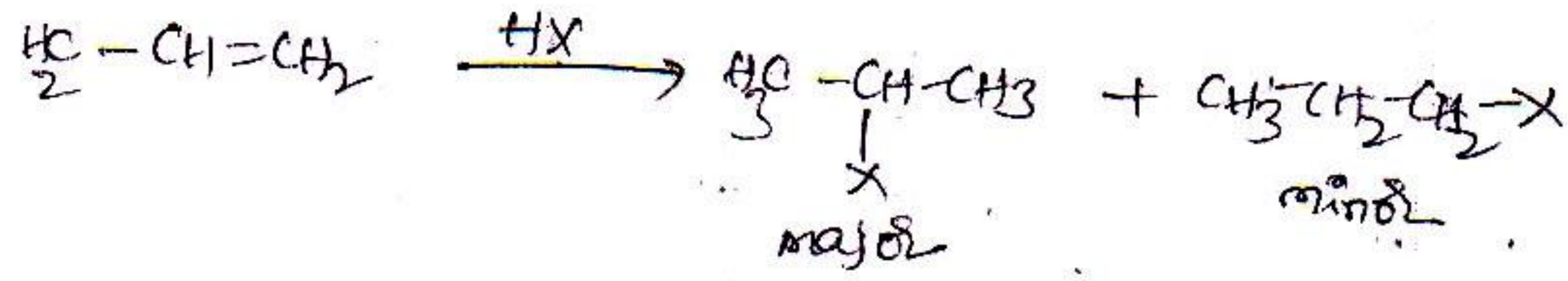


Mech's



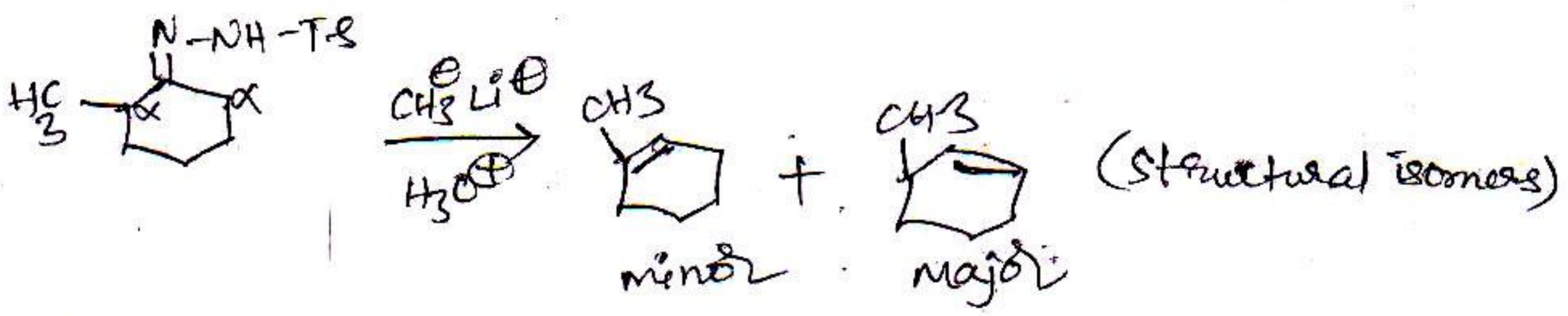


Regioselectivity :-

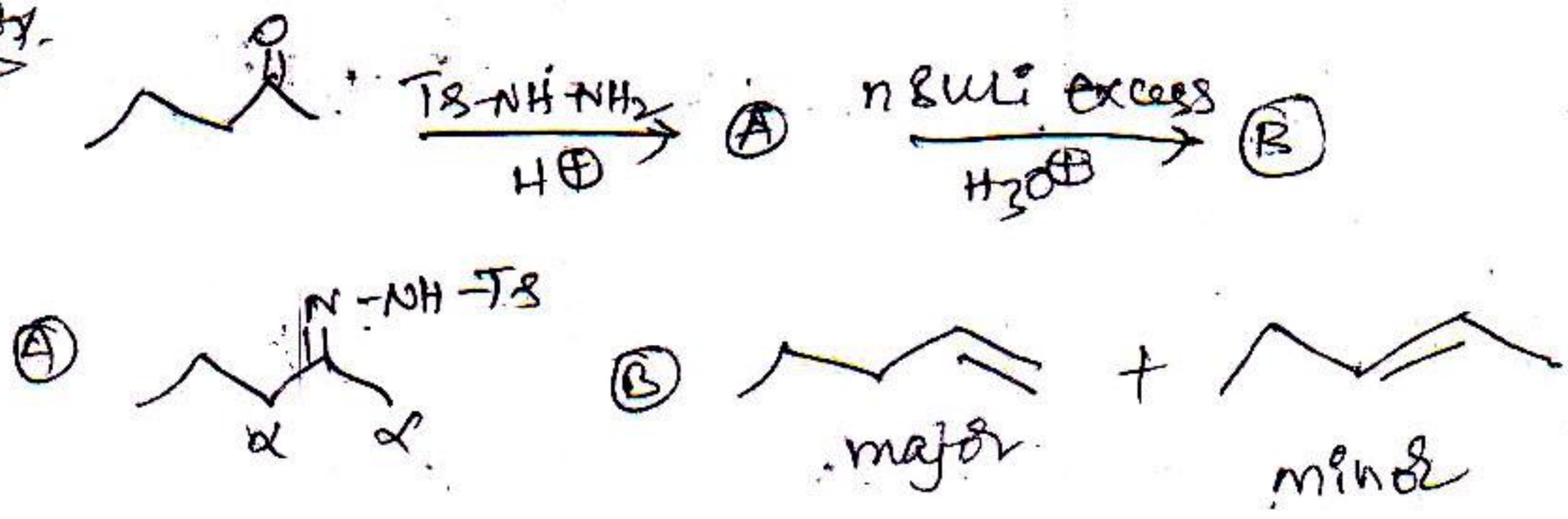


Def:- chemical reaction which produces unequal amounts of spectrum isomers called Regioselectivity.

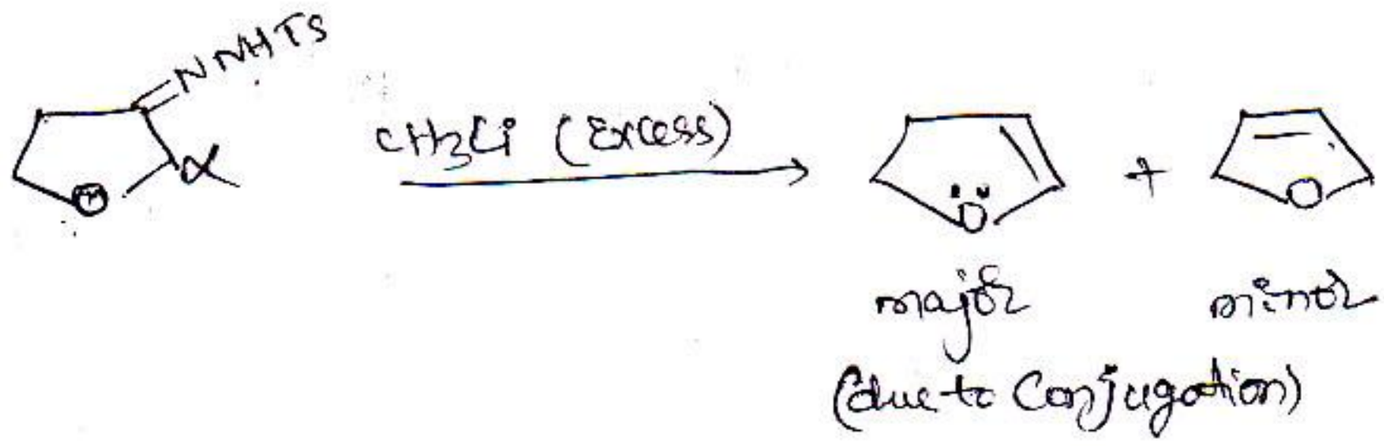
In the case of unsymmetrical Tosylhydrazones predominately double bond orients out. less substituted α-position.



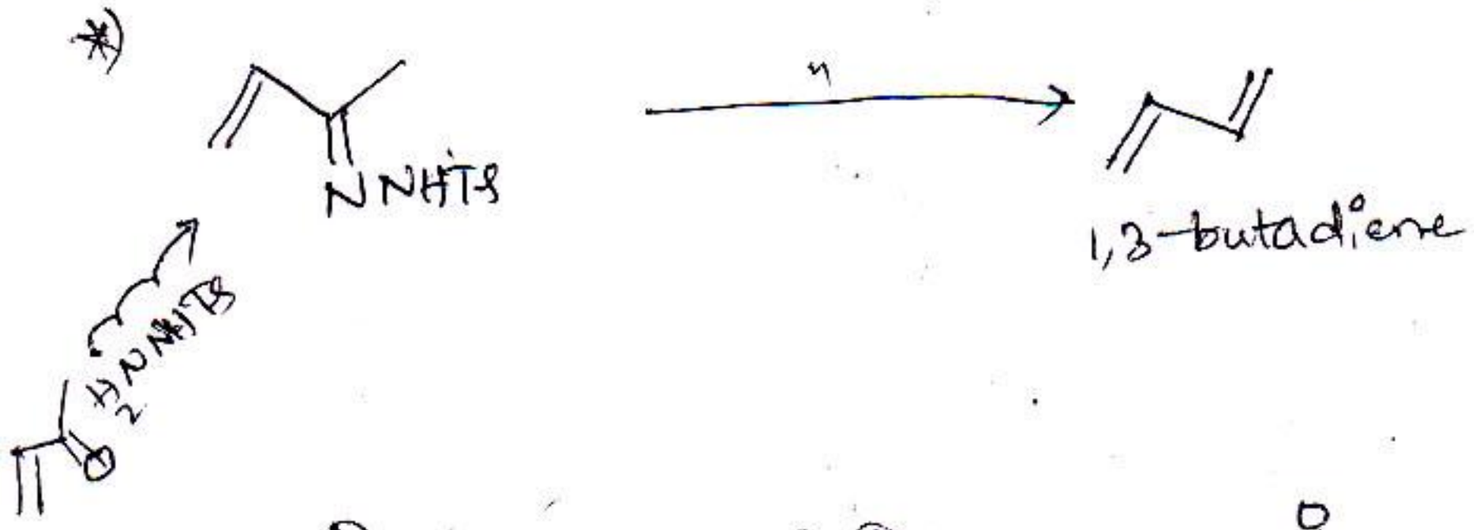
Ex.



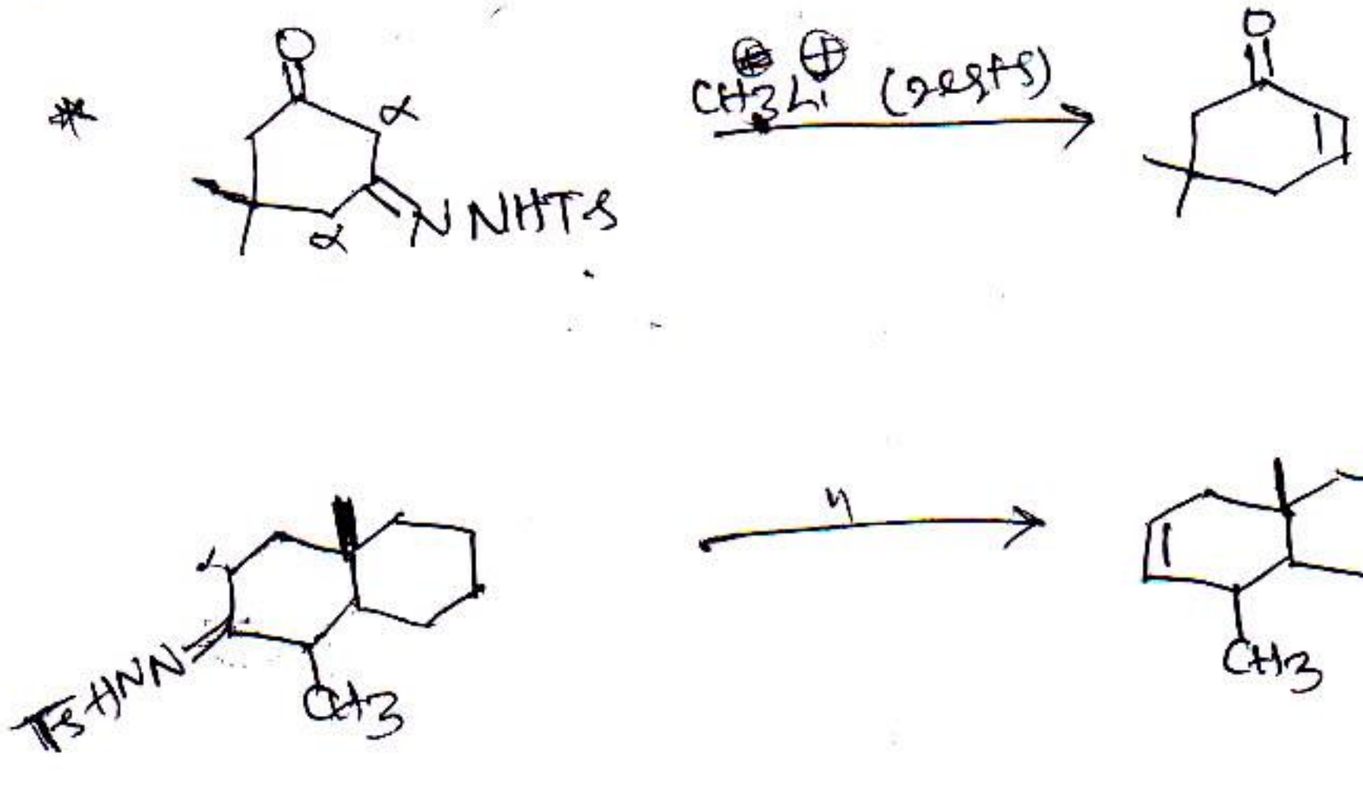
*



*)



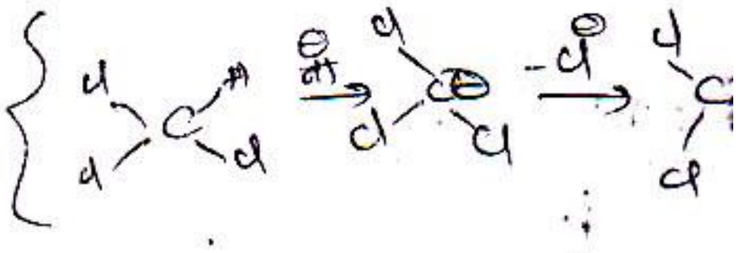
*



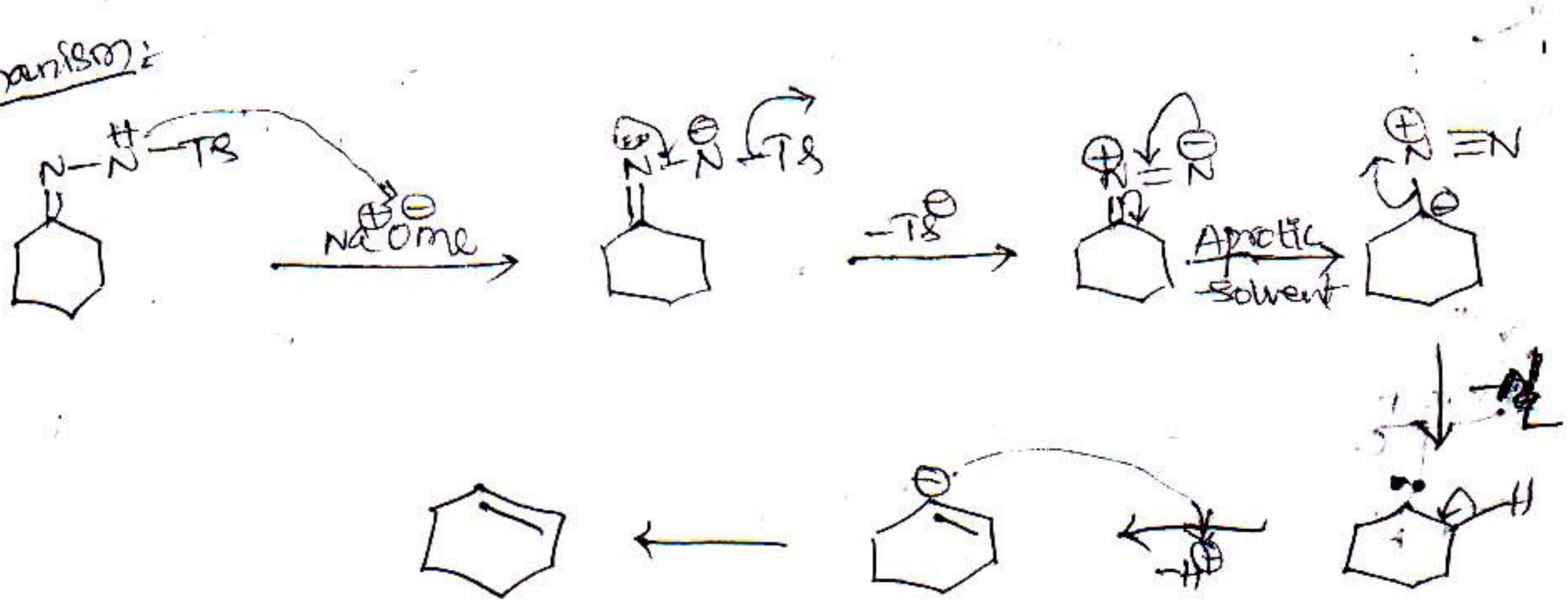
(*) BAMFORD - STEVEN'S - REACTION

Conversion of Tosyl hydrazone of carbonyl compds into olefins. In the presence less stronger bases, NaH, $NaNH_2$, NaOEt etc.. are called BAMFORD - STEVEN'S Rxn.





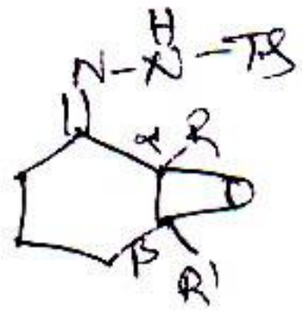
Mechanism:-



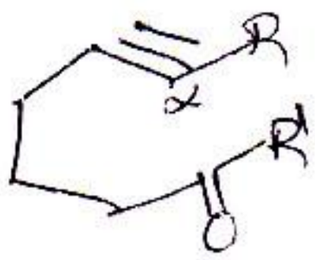
9) ESCHENMOSER - TANABE FRAGMENTATION :

Conversion of α,β-epoxy tosyl hydrazones into Alkynyl Ketones in basic or acidic or neutral conditions called ESCHENMOSER-TANABE fragmentation

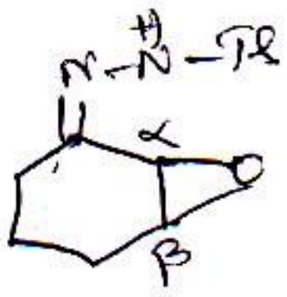
α,β-epoxy tosyl hydrazones of Carbonyl Compds $\xrightarrow[\text{(or) Heating}]{\text{Base (or) Acid}}$ Alkynyl Ketones. (Aldehydes)



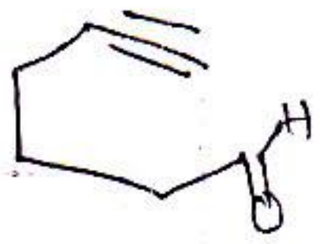
Base / Acid



$+ N_2 + Ts^{\ominus}$

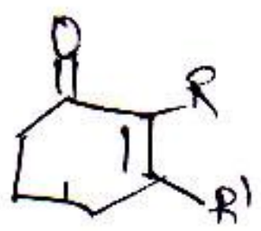


η

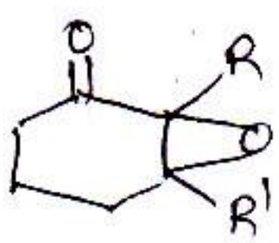


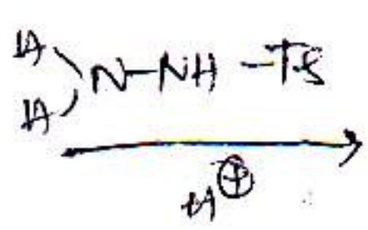
[No substitution at α & β in reactant]

(ii)

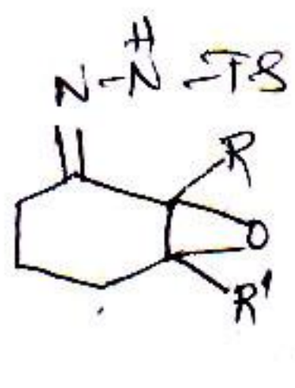


$H_2O_2 \,|\, \overset{\ominus}{O}H$

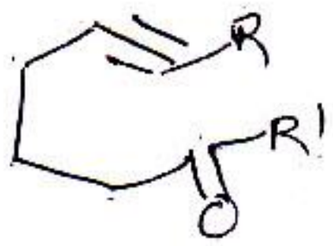




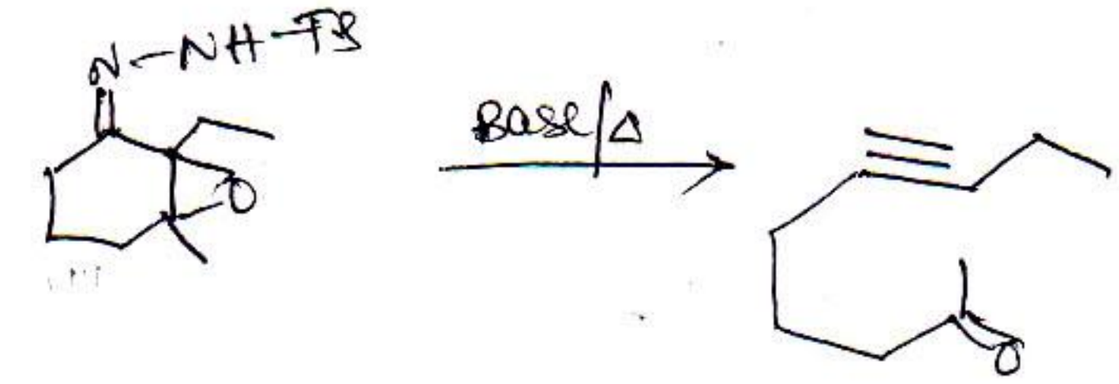
$H^{\oplus}$

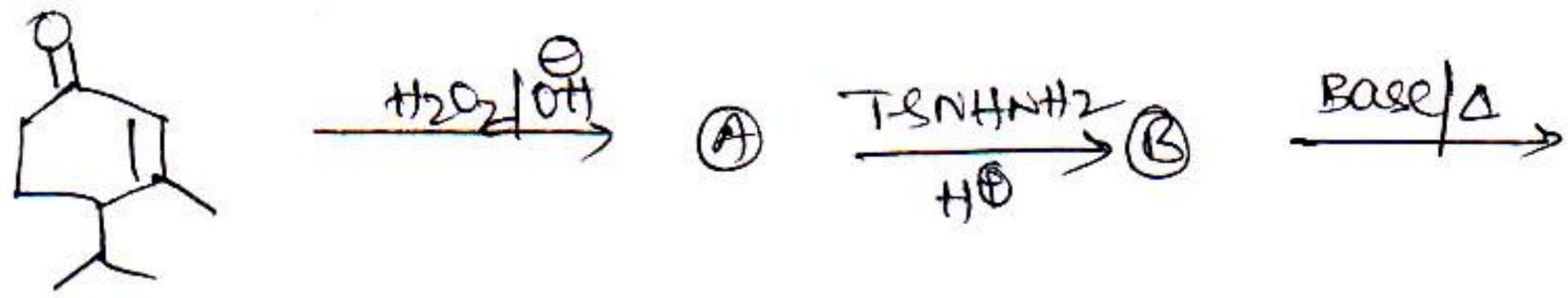


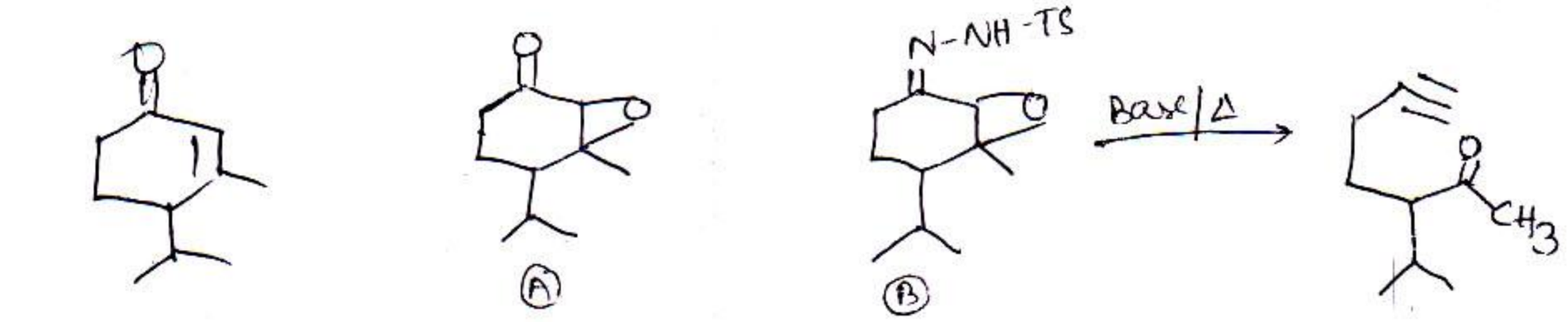
Base

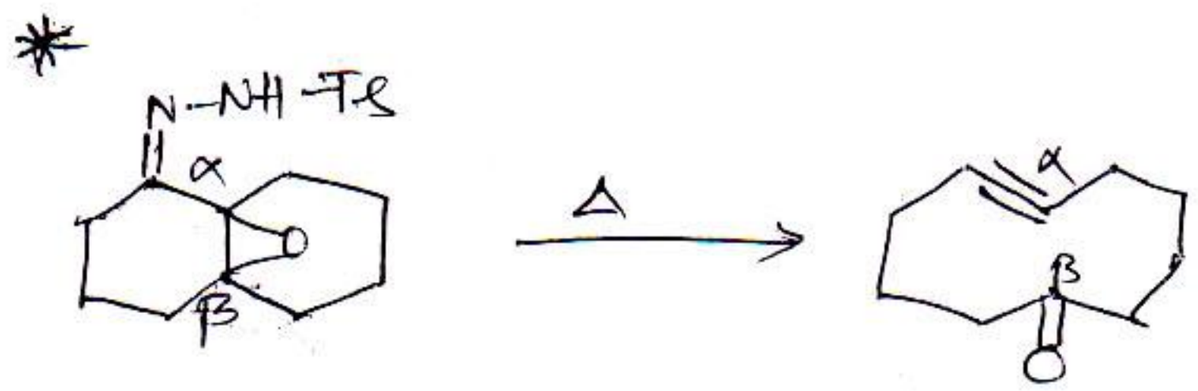


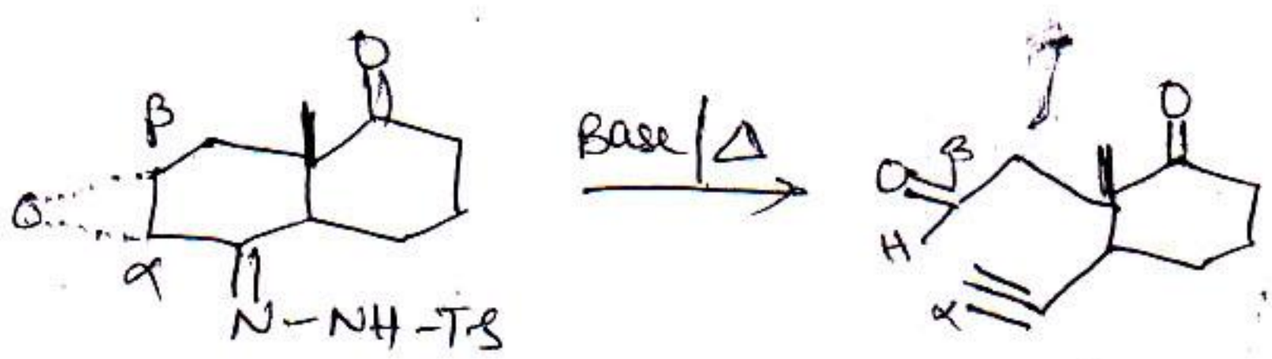
Mech:-

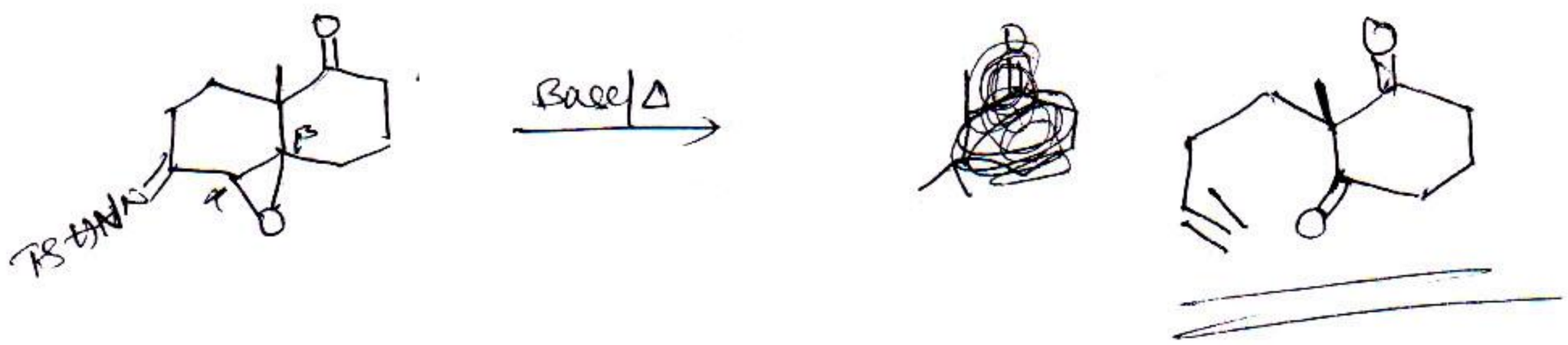




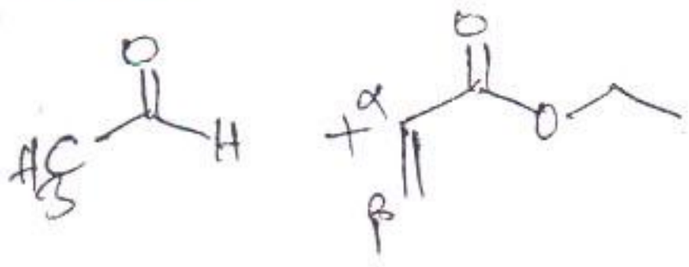






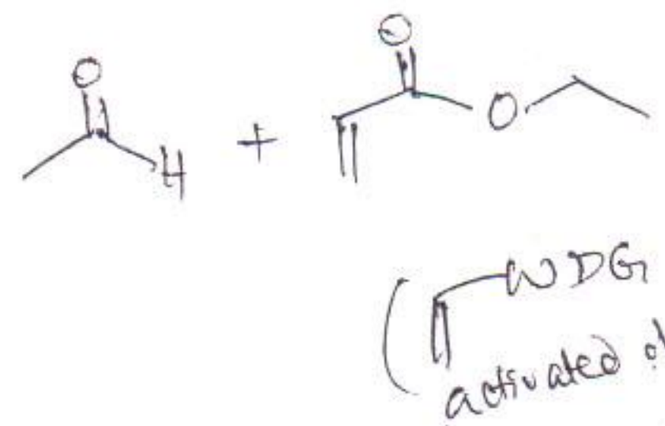


BAYLIS-HILLMANN REACTION (MORITA) 1968 (V)

① 

(MORITA)

< 27%

② 

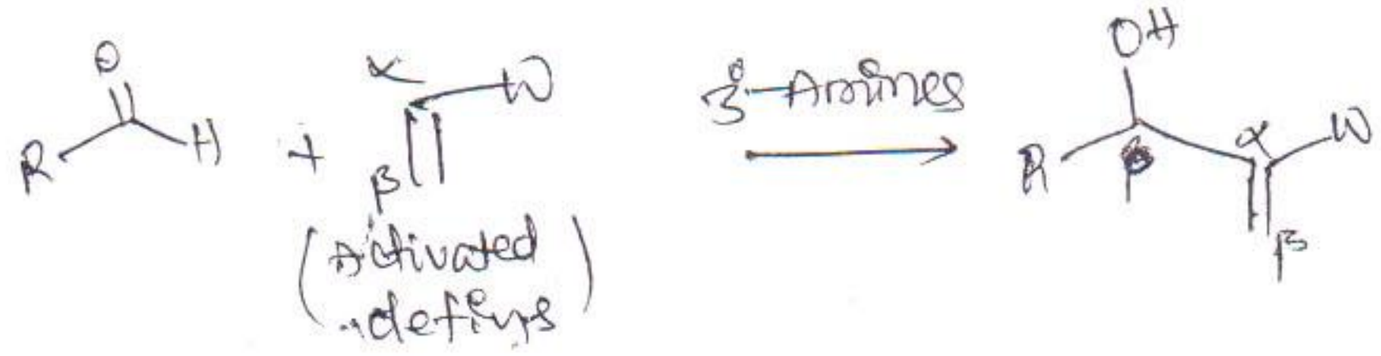
(BAYLIS-HILLMANN)

80%

In 1968, MORITA developed following rxn —① The disadvantage of this rxn is low % yeilds (< 27%).

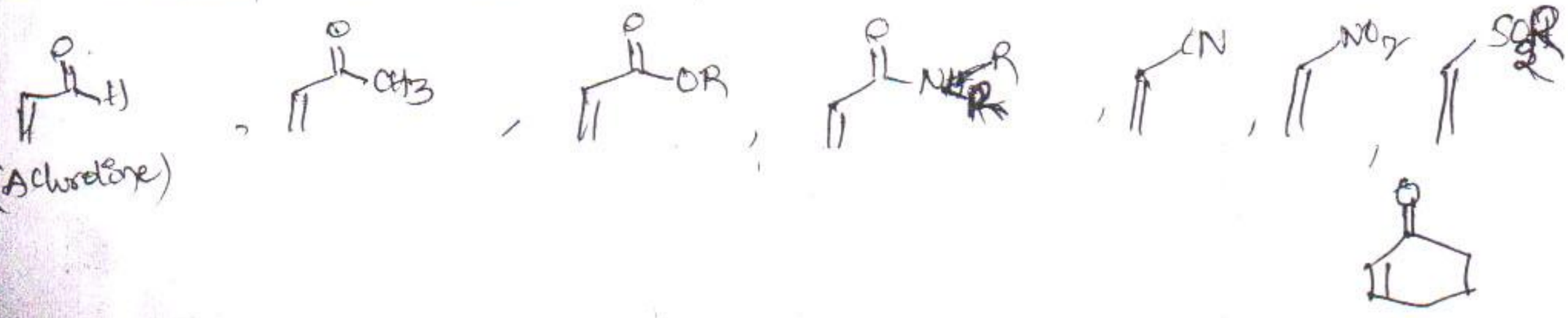
~~BAYLIS~~-HILLMANN modified MORITA rxn, the replacing 3° poshpines with 3°-Amines, the % yeilds of products are increased. —②

Conversion of activated olefins into Hydroxy alkenyl adducts by developing a new C–C bonding at α-position of olefin and carbonyl 'C'. in the presence of 3°-Amines called BAYLIS-HILLMAN rxn. —②



olefine attached to WDG called activated olefins.

Eg:



Aldehyde :-

~~ALDEHYDE~~ : ~~ALIPHATIC~~ / ~~AROMATIC~~ (Ketenes less common)

3°-Amines :-

~~Amines~~ : Et_3N, DABCO, QUINUCLIDNE,

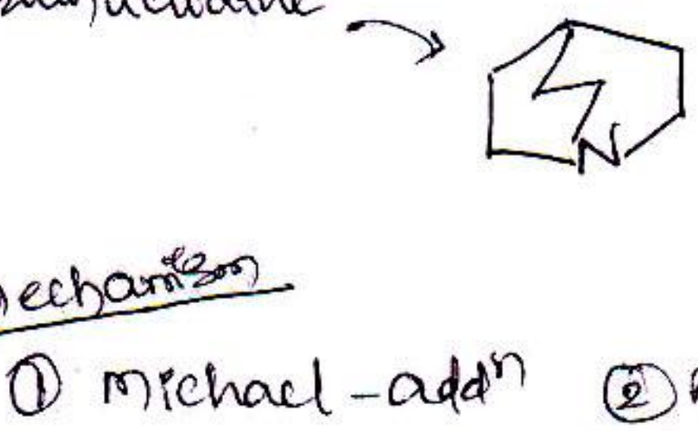
more Common in BAYLIS-HILLMANN

DABCO



1,4 diaza bicyclo [2 2 2] octane

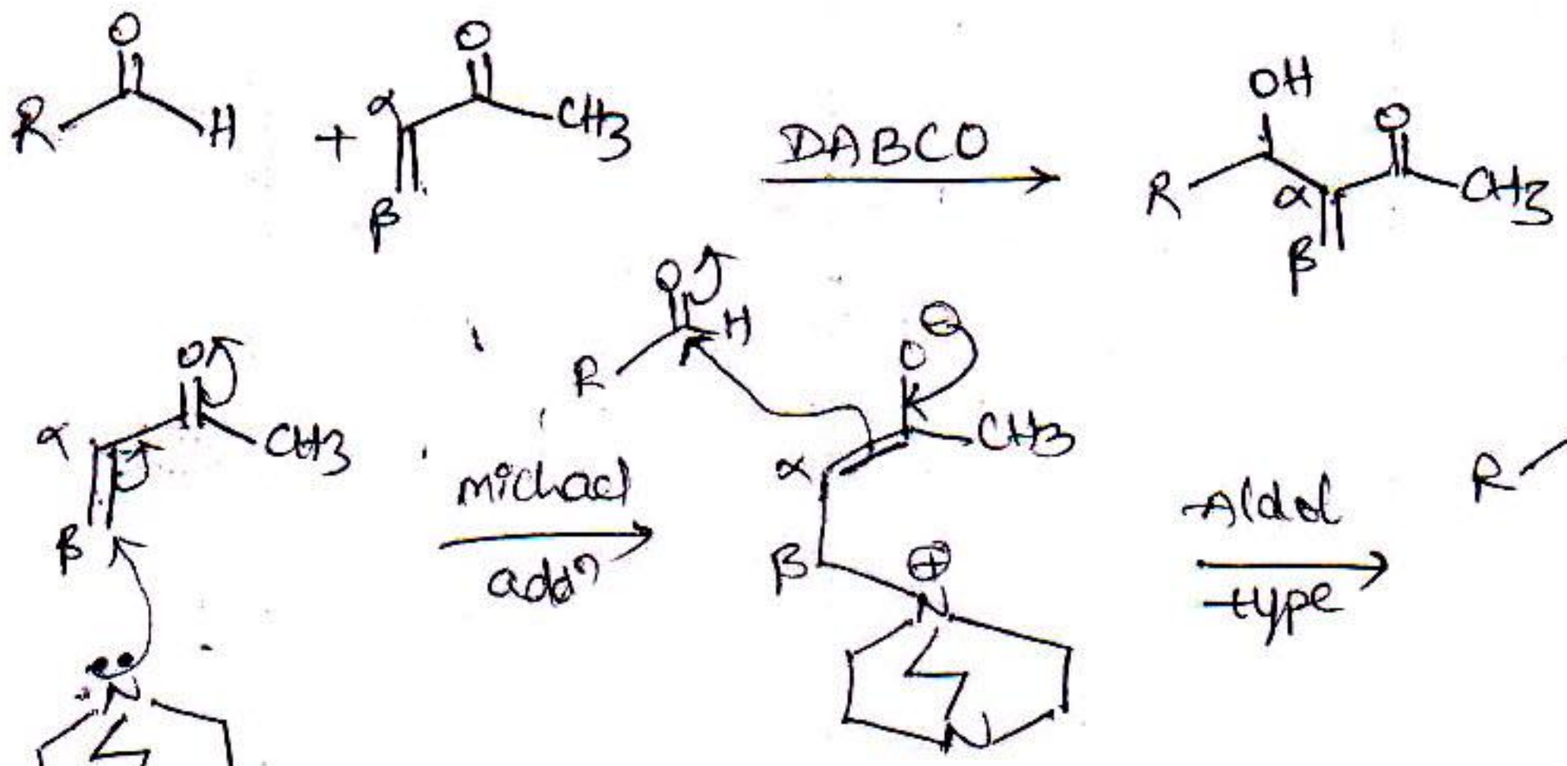
Quinuclidine →



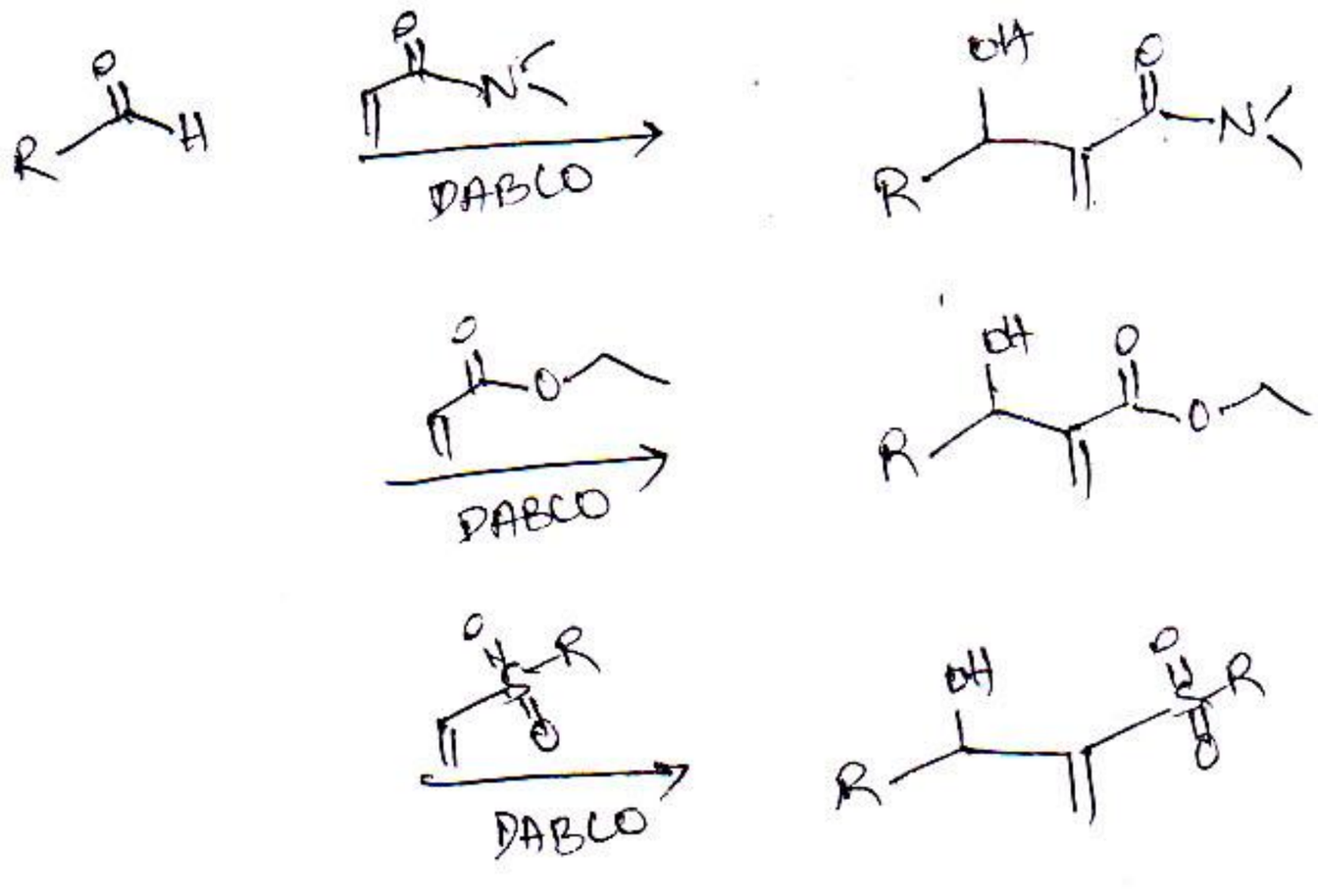
Mechanism

① Michael-addⁿ ② Aldol type ③ Elimination.

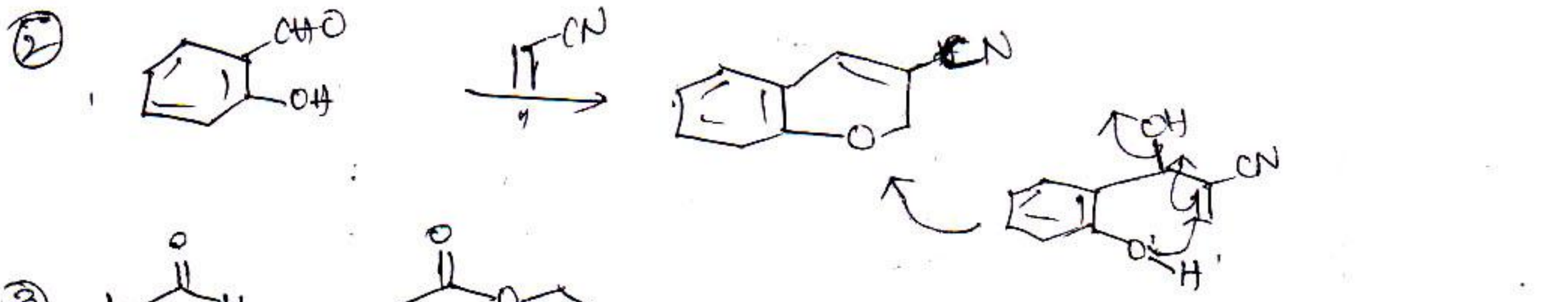
3° Amines, (DABCO, Quinuclidine) are nucleophilic catalyst

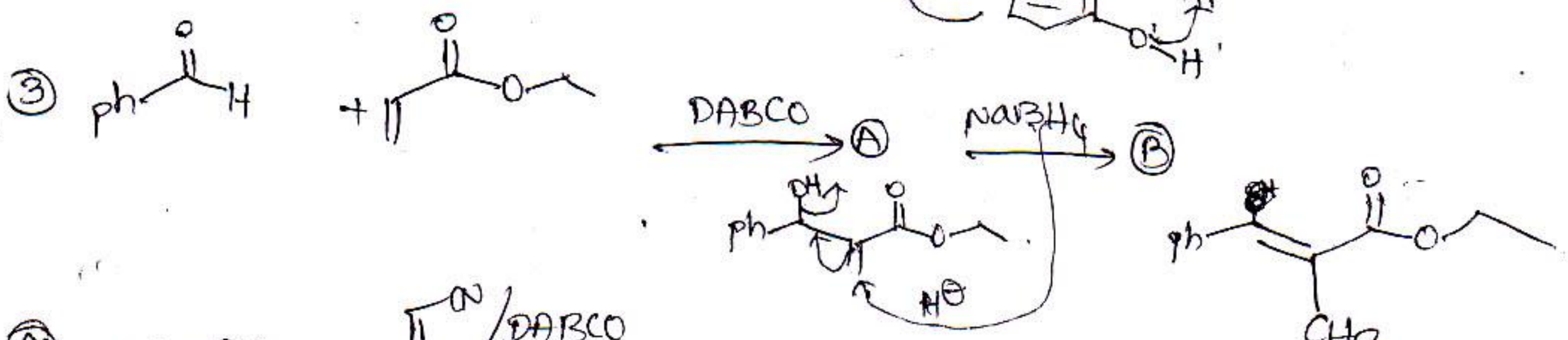


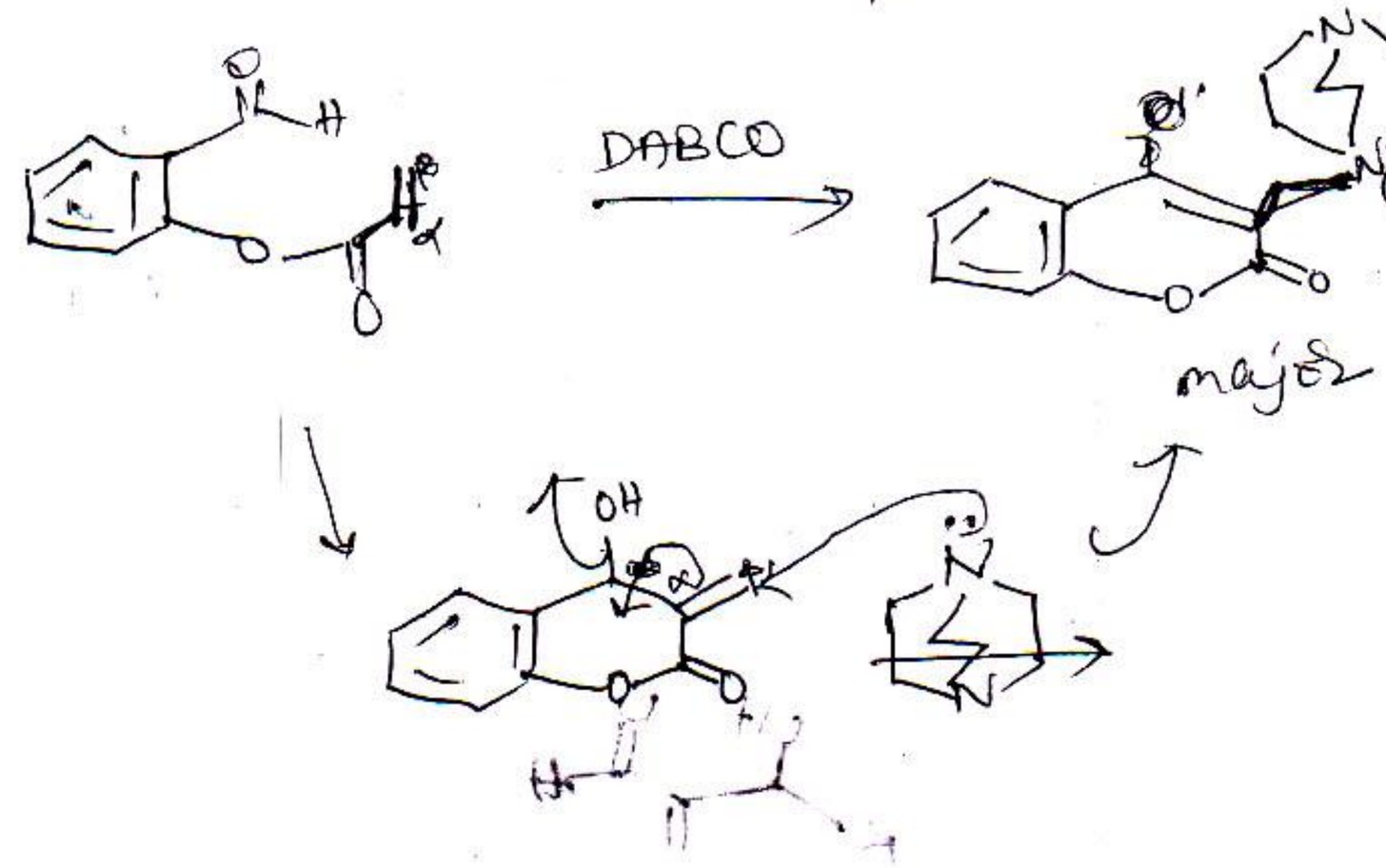



DABCO
DABCO
DABCO


DABCO
CN


DABCO
CN
CN
OH
CN
O
H


DABCO
NaBH4
A
B
CH3
CN/DABCO
Ac2O
Ac2O
CN
OAc
CN

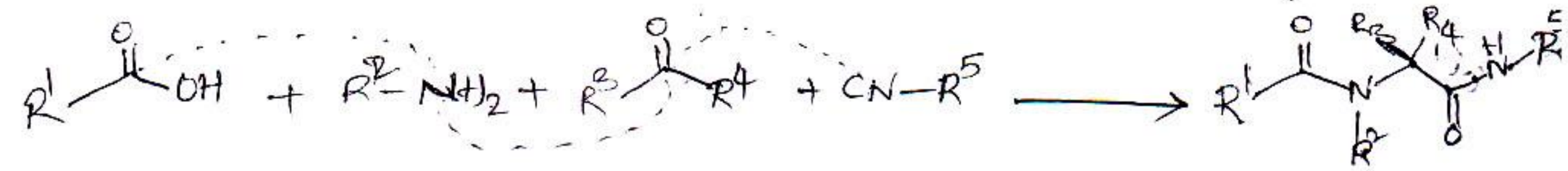

DABCO
major
OH

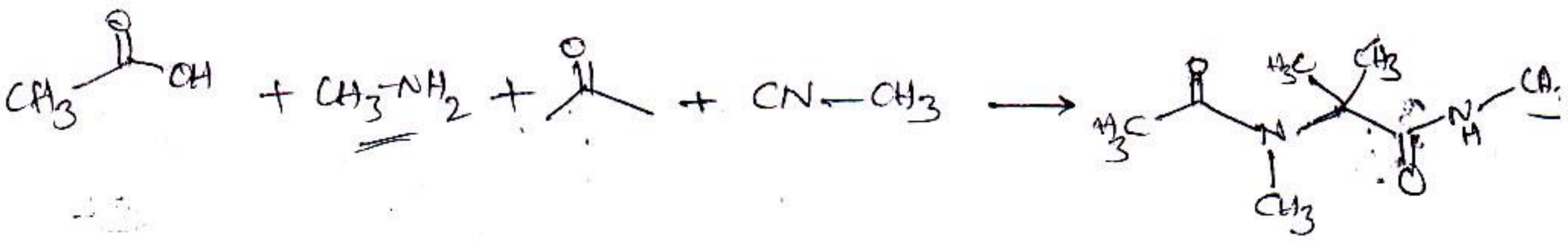
UGI-REACTION (U-4CR)

UGI-Rxn is one POT synthesis without isolating intermed in multistep rxn. It completed at onestep by taking all the appropriate starting material called one pot synthesis.

UGI rxn is 4 component one pot synthesis.

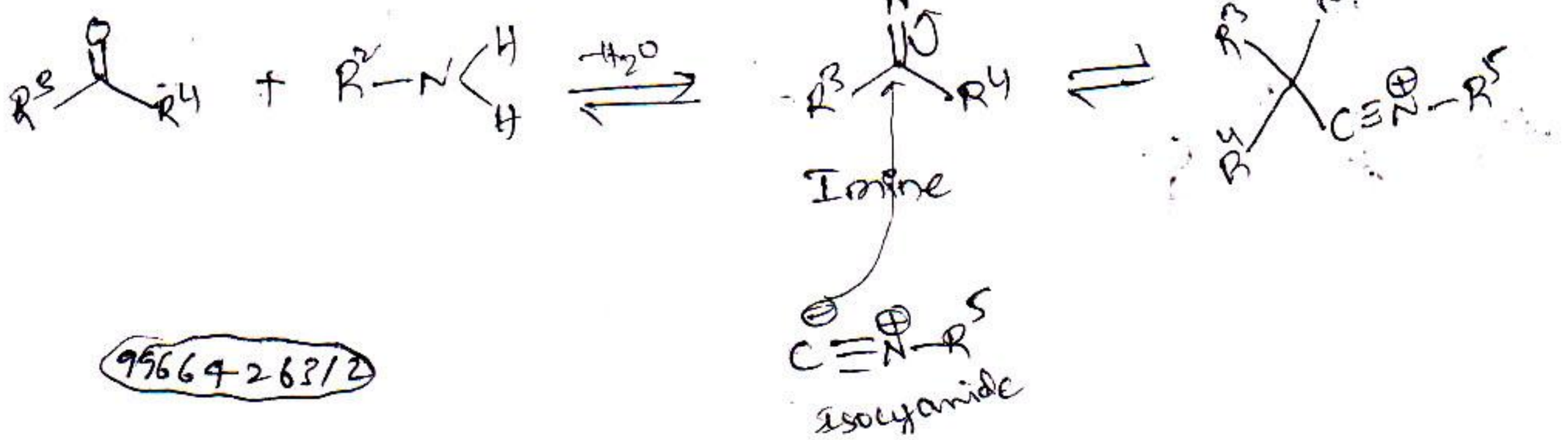
U-4CR Rxn.
4 Component



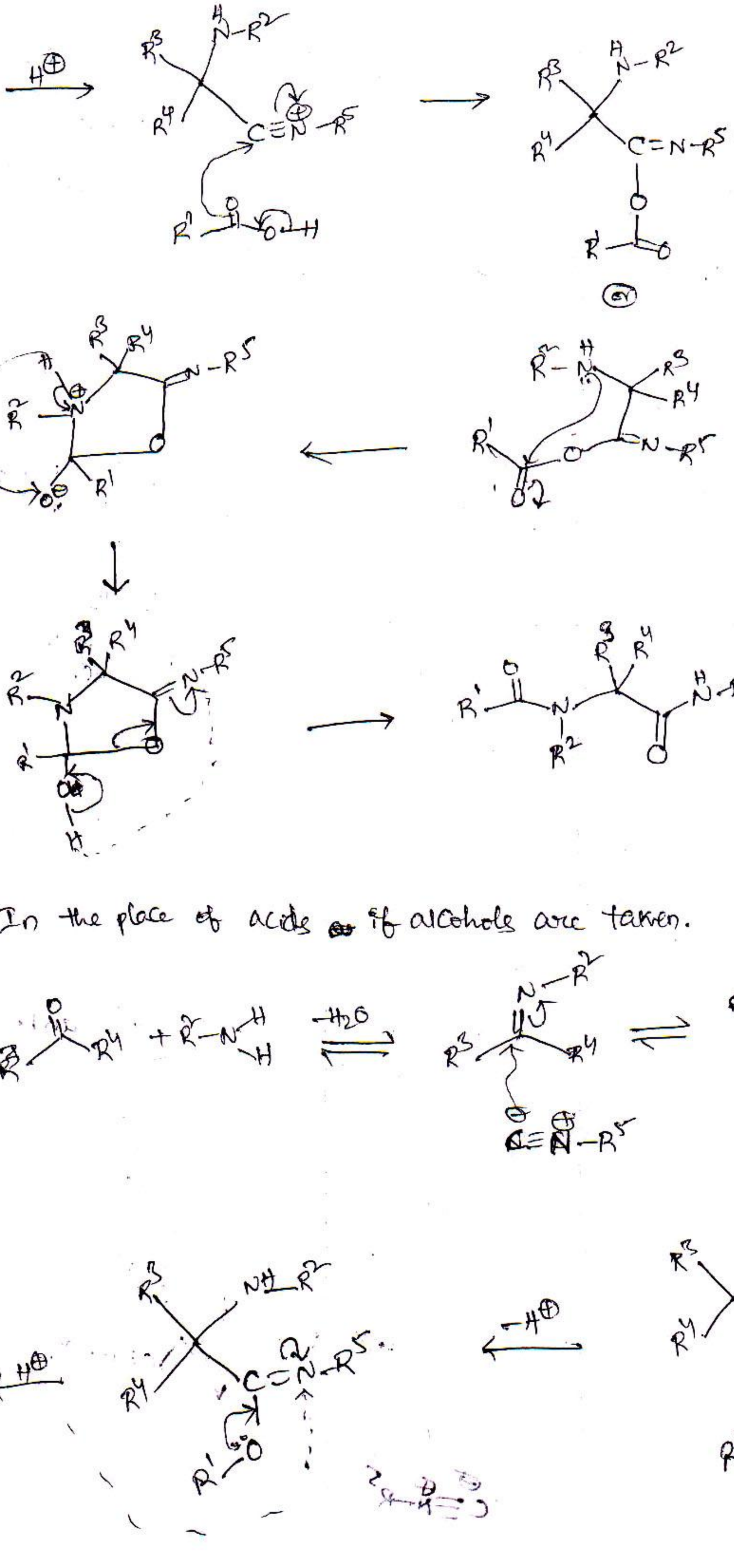


* Easy to carry out.
* Temp -80°C to 80°C.
* Amines may be 1° or 2° amine
* All types of isocyanides
* carbonyl Compd may be aldehyde or ketone.
* Carboxylic acid is nucleophilic partner, even others can be used eg:- H_2O, alcohols, $R-NH_2$, $R-N=C=O$, HN_3 etc..
* It takes minutes to days.

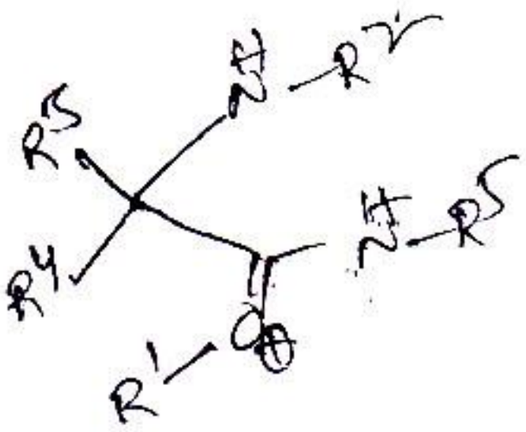
mechanism :-

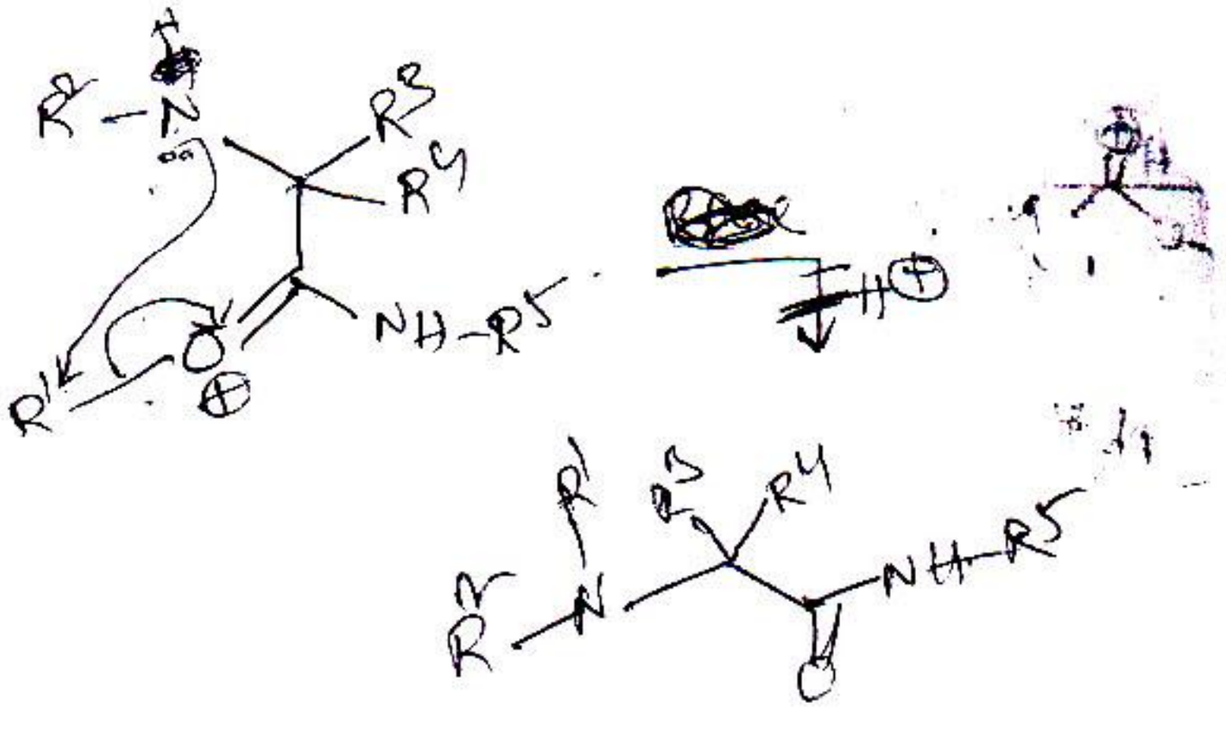


9566426312

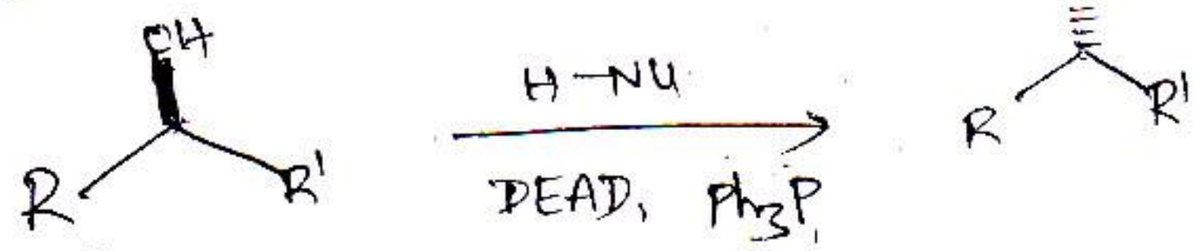


In the place of acids if alcohols are taken.





MITSUNOBU RXN :- (V)



2° alcohol.

Nucleophilic Sub^{n} of 1°, or 2°-alcohols by using weakly acidic NU$^{\ominus}$ DEAD, Ph_3P with inversion of Configuration is called MITSUNOBU RXN.

*) Alcohols - 1° or 2°.

*) No rxn with 3°-alcohols.

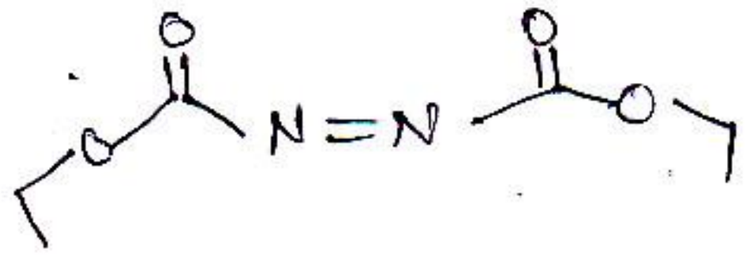
*) weakly acidic Nucleophiles. R-$\ddot{O}$-H, R-$\ddot{S}$-H, R-$\ddot{N}$H$_2$, R-COOH, HN$_3$, Imine ....etc

*) Solvents to do rxn are ethers,  (DME)

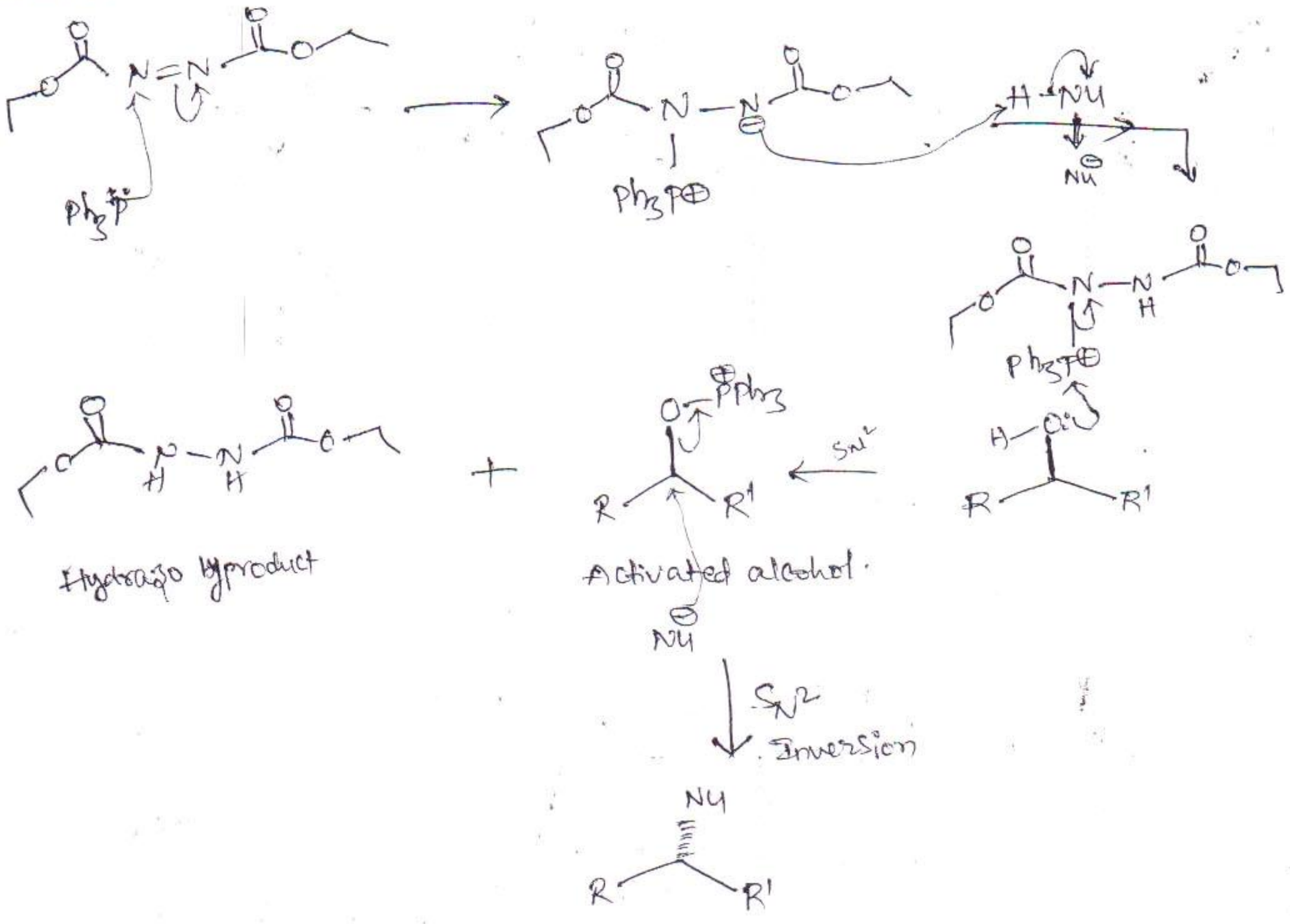
*) Temperature 0°-25°C.

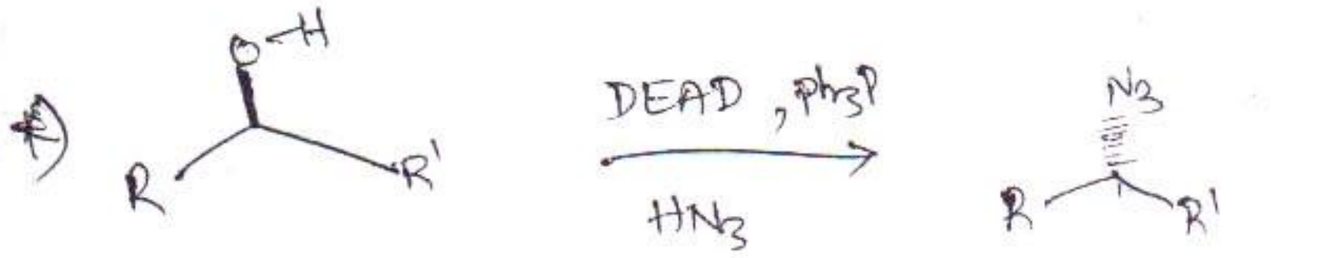
*) Rxns are S_N2 type.

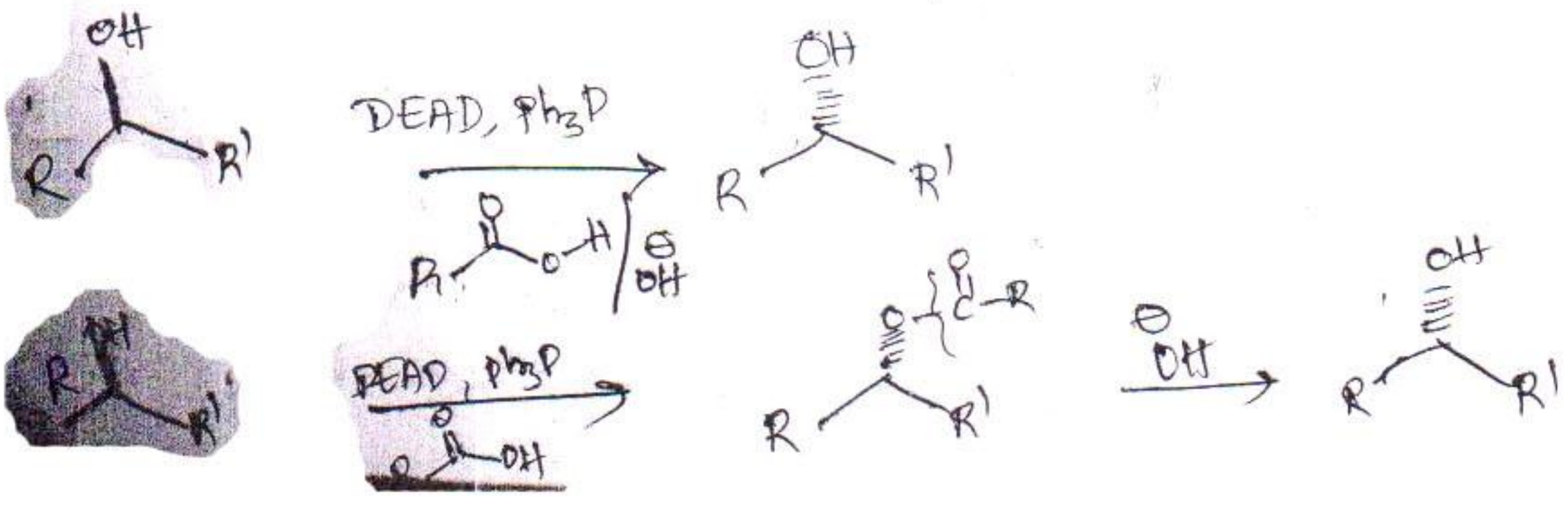
DEAD (Di Ethyl AZO Dicarboxylate)



Mechanism :-


Ph3P
Ph3P⊕
NH⊖
Ph3P⊕
Hydrazo byproduct
SN2
Activated alcohol.
NH⊖
SN2
Inversion
NH
R
R'


DEAD, Ph3P
HN3
N3
DEAD, Ph3P
ph-OH
O-ph
DEAD, Ph3P
ph-SH
S-ph
DEAD, Ph3P
W
W
W = -CN, -CO2Et, -CHO
CO2Me
CO2Me
R
R'

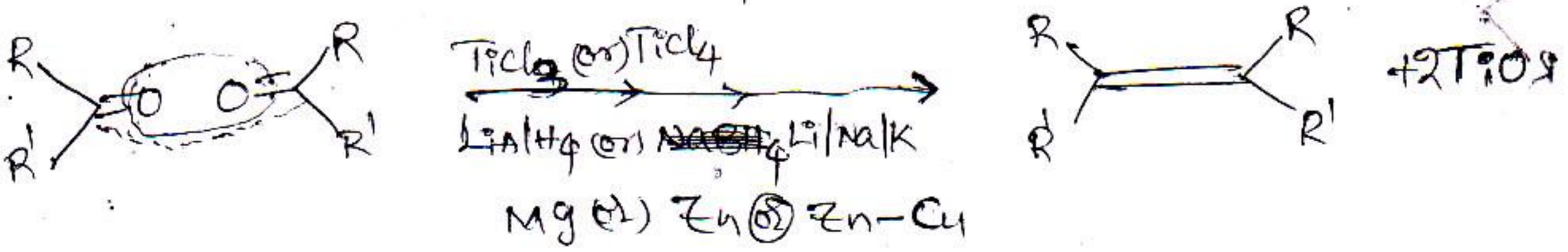

OH
DEAD, Ph3P
OH
DEAD, Ph3P
OH
R
R'

* OLEFINS - FORMATIONS :- ① Mc MURRY - COUPLING

② JULIA - LYTHGOE - OLEFINATION

③ PETERSON'S OLEFINATION.

① McMURRY COUPLING :- (V)



This is Reductive coupling of carbonyl Compds into olefins with $TiCl_3$ & $TiCl_4$ and reducing agents called McMurry coupling

*) Solvents - THF, DME, 1,4-DIOXANE

*) At low temp. Competative products pinacols.

*) Highly substituted olefines easy to prepare (Compare to mono) tri, or tetra Subted - - .

*) poor selectivity in olefin formation (Easer selectivity very poor)

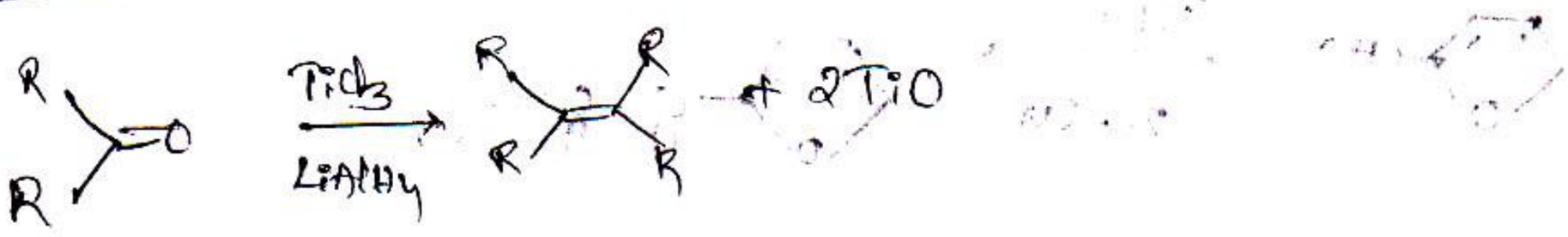
*) Both aldehydes & ketones undergo MCMURRY coupling but aldehyde are fasters than ketones.

To molecule having aldehyde & keto function selectively aldehyde involving in MCMURRY COUPLING, Chemoselective given.

*) Reducing agents are - $LiAlH_4$, Li/Na/K, Mg, Zn, Zn-Cu Coupl

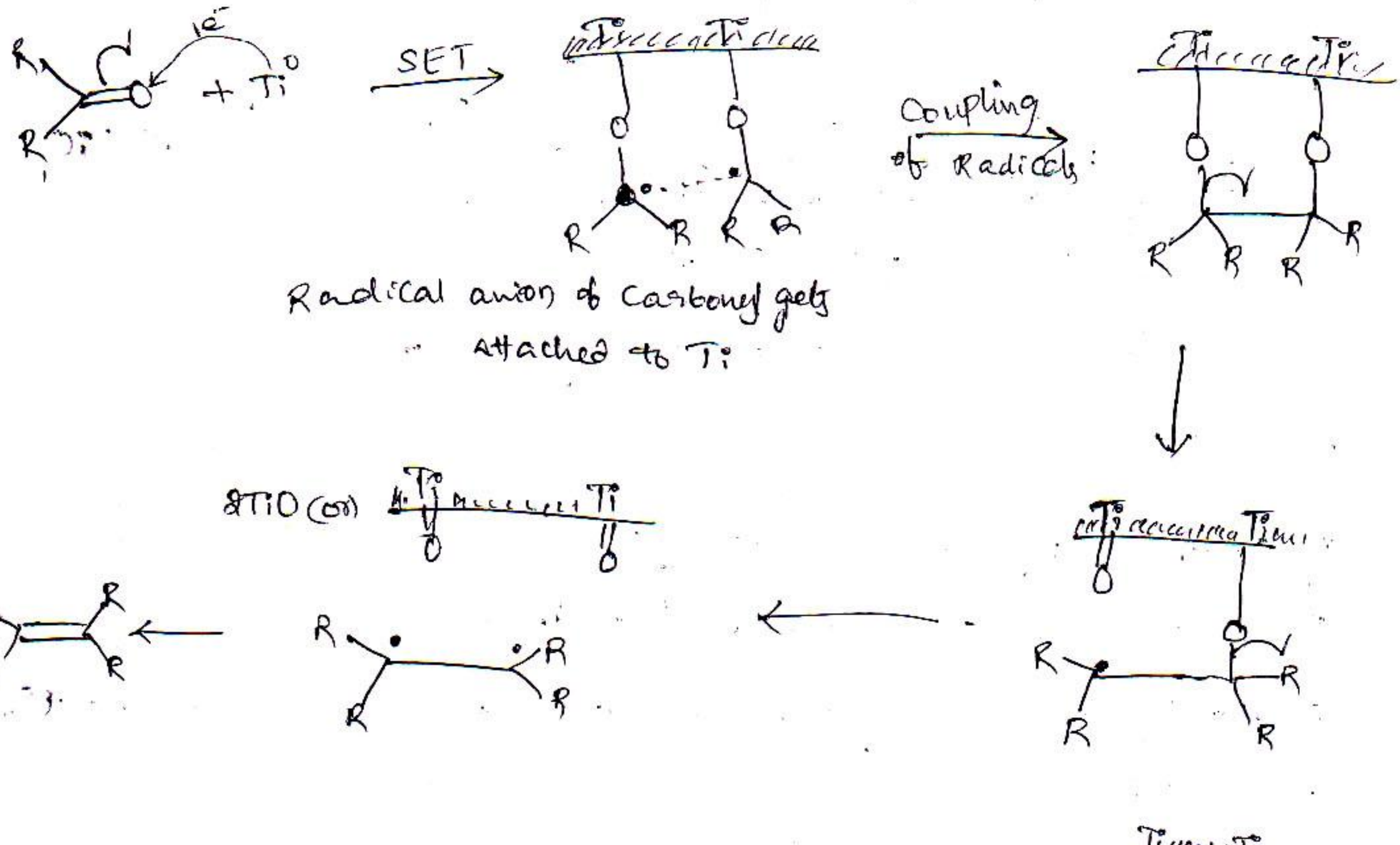
*) Zn-Cu, LAH are more common in this given.

Mechanism :-



$TiCl_3 + LiAlH_4 \longrightarrow Ti^0$ Low valent Titanium

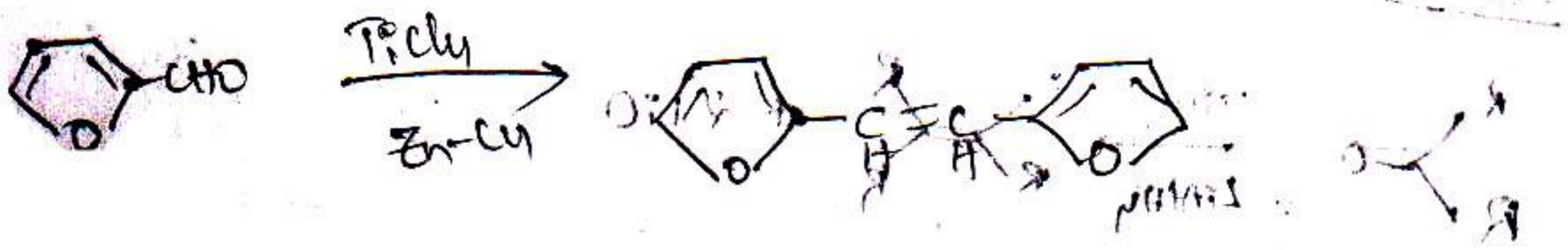
Reducing agents convert Titanium halides into low valent Ti which is reactive species in conversion of C=C into olefine

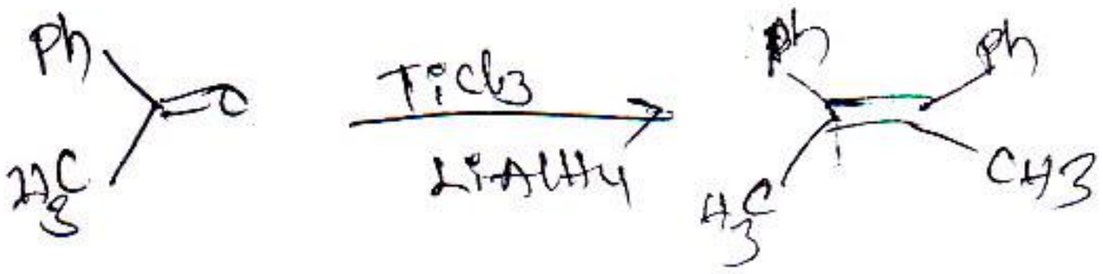


*) Not only identical. even non identical carbonyl functions also involve in this mixing coupling called cross Coupling.

eg: $Ph-CHO \xrightarrow[LiAlH_4]{TiCl_3}$  $Ph-\underset{H}{C}=\underset{H}{C}-Ph$

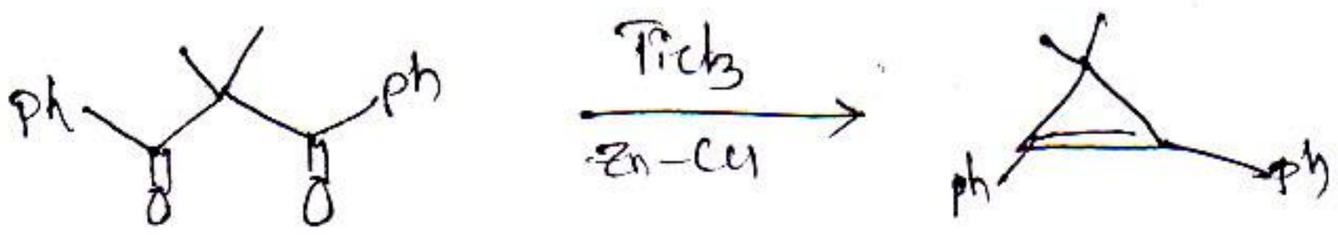




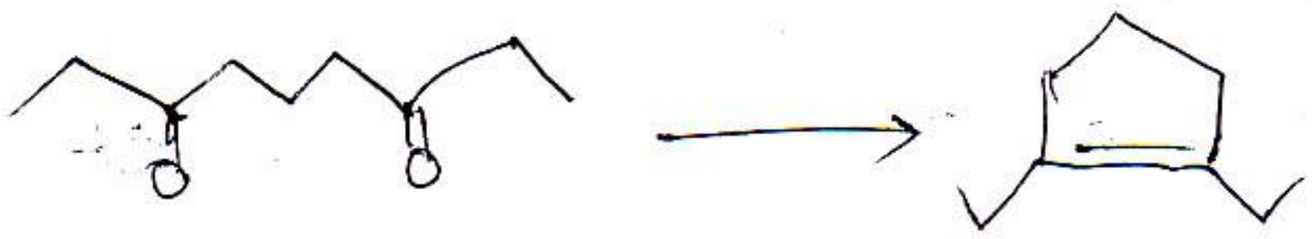




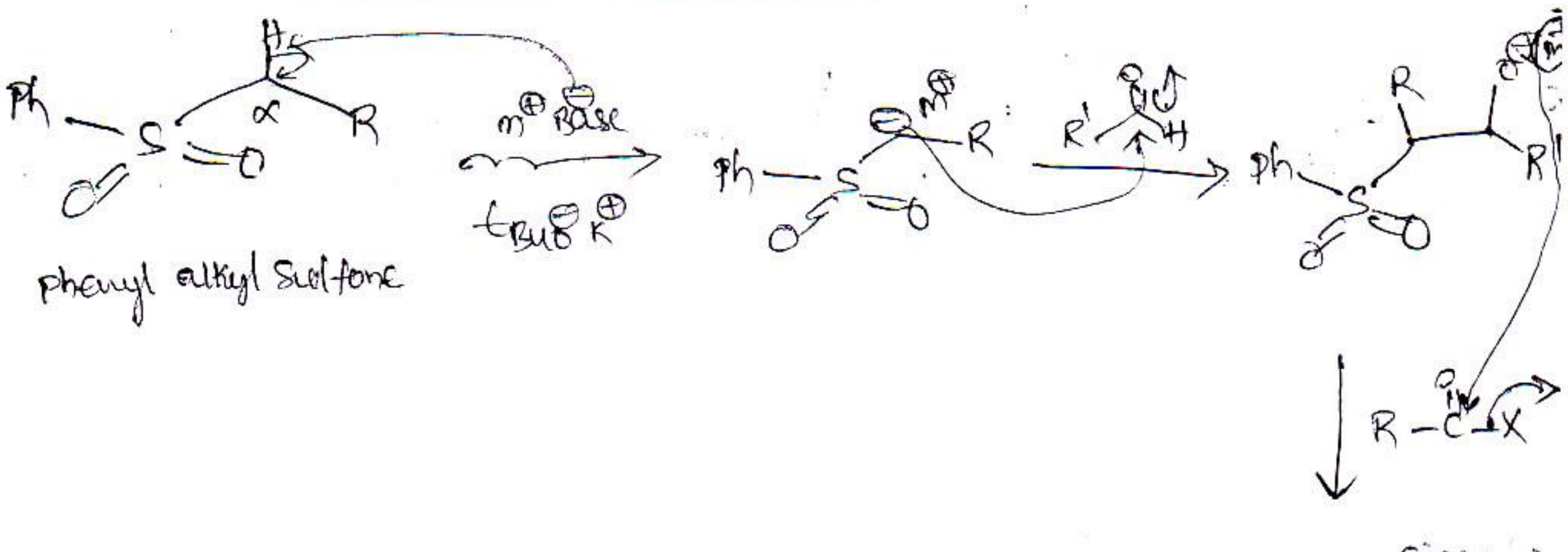
Intramolecular Mc Murry couplings are known.

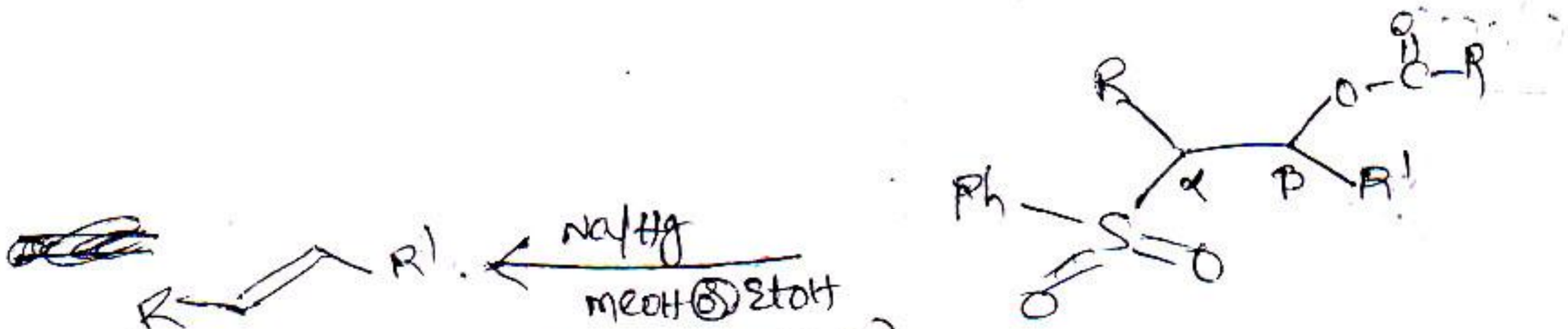


Intramolecular coupling products are cyclic olefins. 5, 6 membered cyclic olefins formation is faster.



JULIA - LYTHGOE - OLEFINATION :-

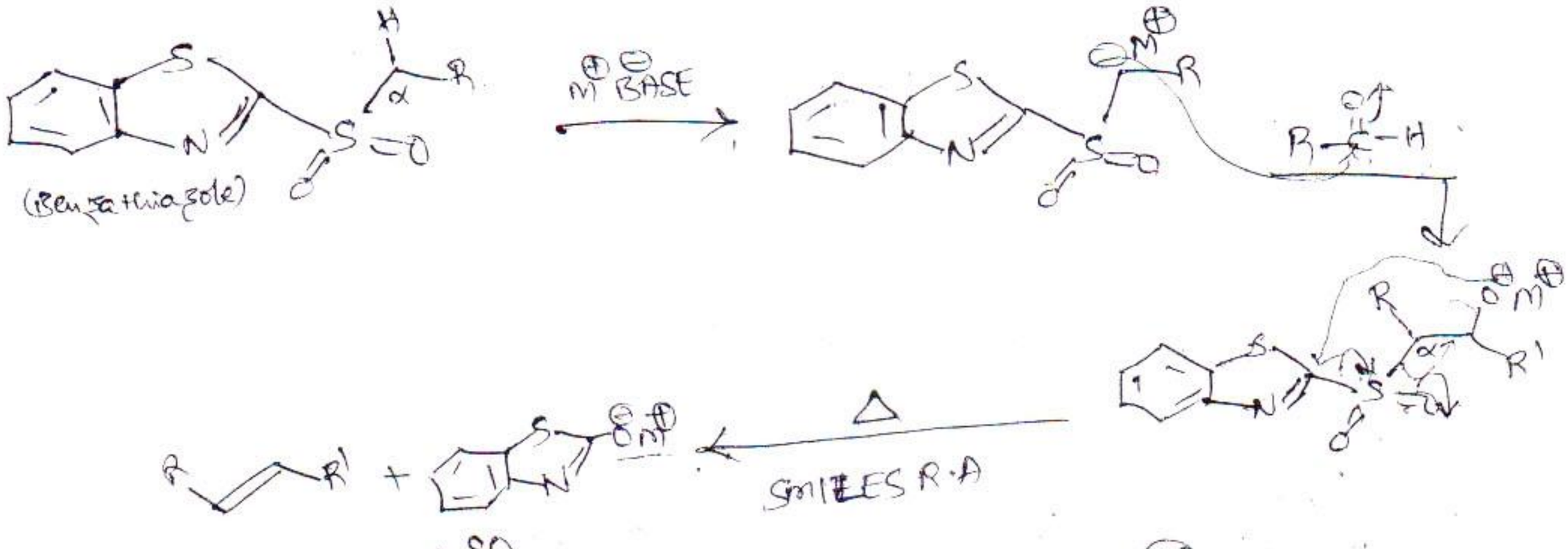




Classical Julea-Lythgoe Rxn.

Conversion of β-acyloxy sulfones into olefins in presence of Na/Hg & EtOH & DME

Modified (ONE-POT SYNTHESIS) Julia-Lythgoe :—

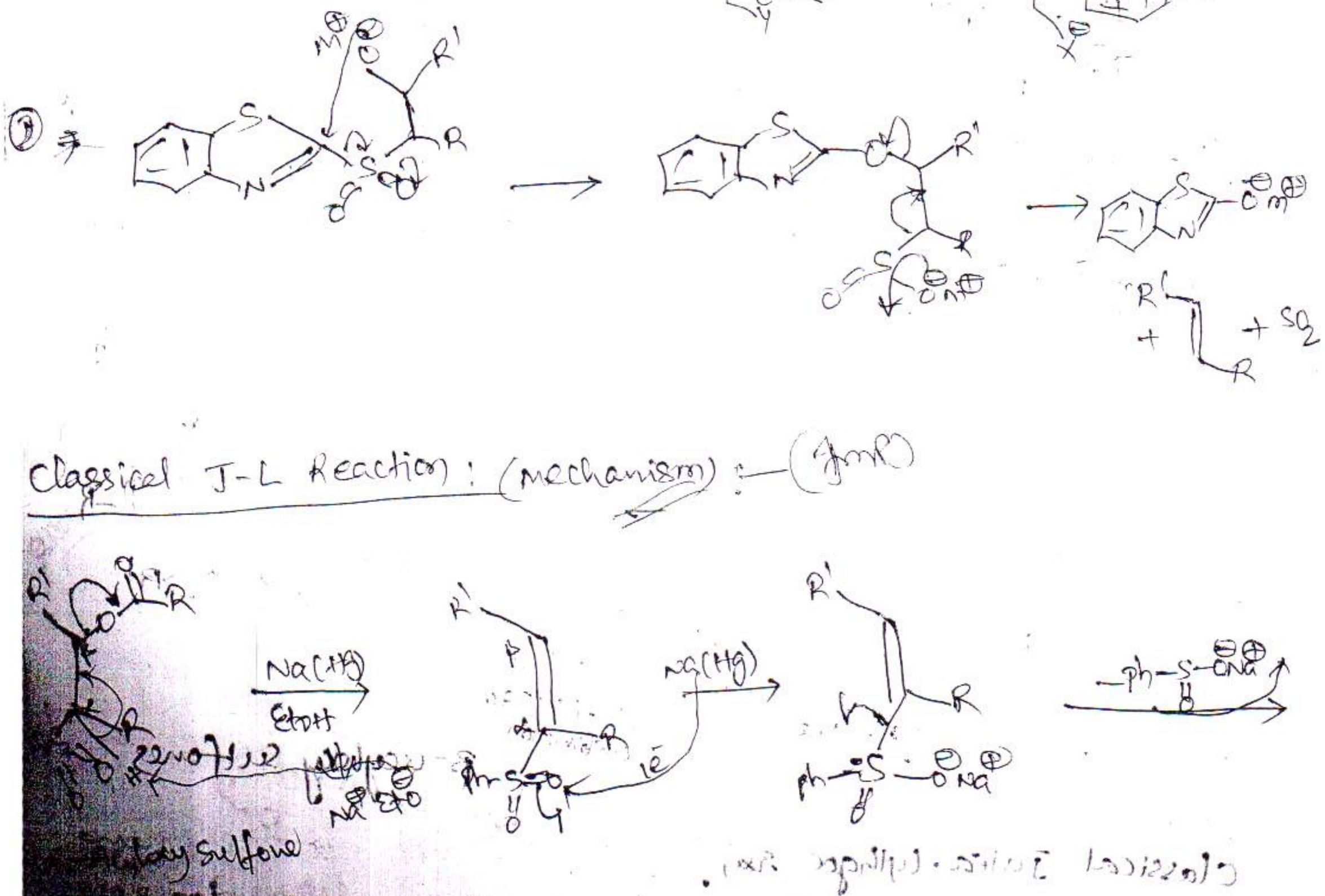


(II)

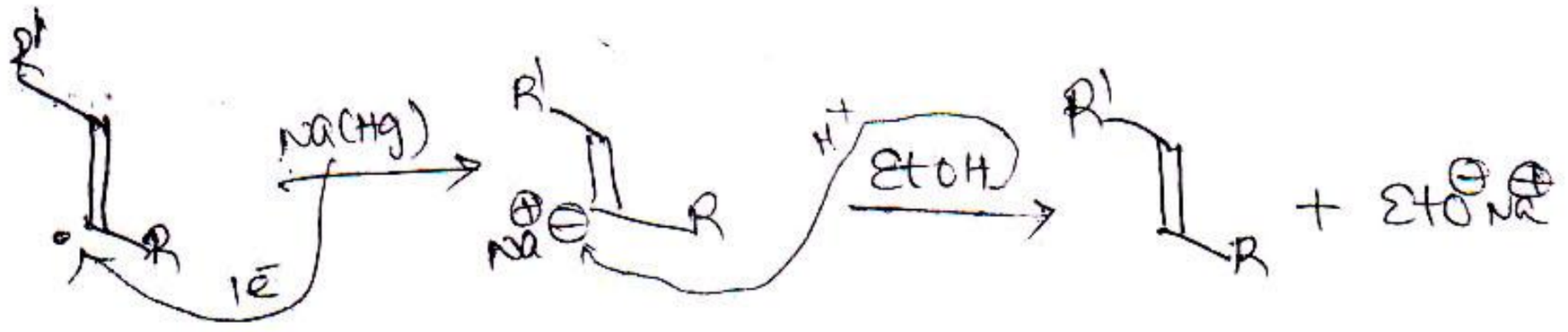
*) Highly E-Stereo selective reaction

*) With increase in branching at alkyl gps in olefins E-selectivity increases

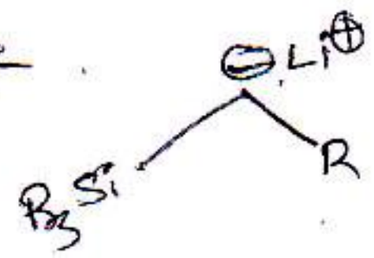
*) Nature of gps on β-Acyloxy sulfones will not influence E-selectivity in the reaction. (E-product only dominating)



Classical J-L Reaction: (mechanism) :— (Imp)

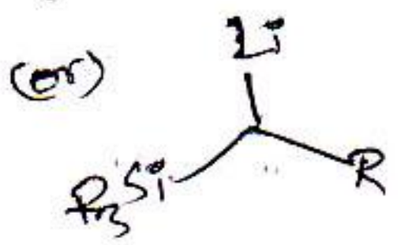


(✓) PETERSON'S OLEFINATION :-



(Lithium derivatives of Silates)

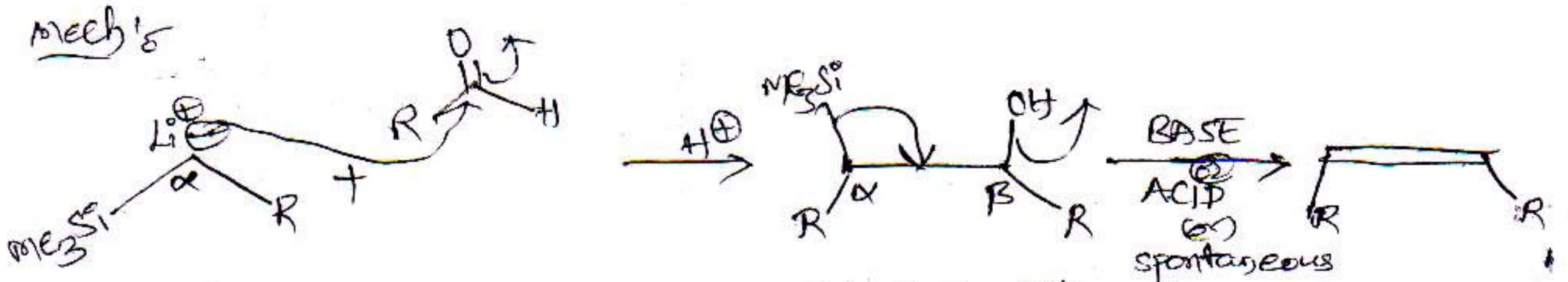
(or)



Conversion of Carbonyl Compds into olefins by treating with Lithio & magnisio derivatives of Silane are called PETERSON'S olefination



Mech's



β-hydroxy Silane, decomposition intermediate.

+ Me_3Si-OH

Trimethyl Silanol.

$Me_3Si-O-Si-Me_3$.

Hexamethyl disiloxane

Low boiling liquid

Easy to remove from rxn mixture.

Basic (Syn elim)

Three → Trans.

Erythro → cis

Acidic (Anti elim)

Threo → cis

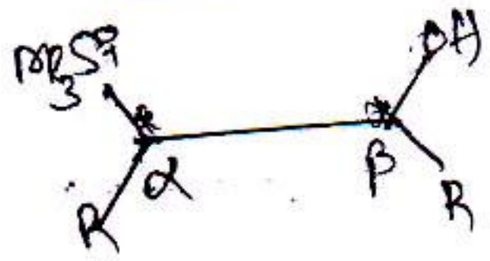
Erythro → Trans.

In peterson's defination ~~Hexa~~methyl disiloxane is low boiling liquid. easy to remove from rxn isolating defin in pure form easier. But in Wittic rxn, the biproduct $Ph_3P=O$ (Triphenyl phosphorous oxide) insoluble in water, difficult to remove from rxn mixture.

Ran intermediate is β-hydroxy silane which decomposes in basic or acidic or spontaneously into olefins.

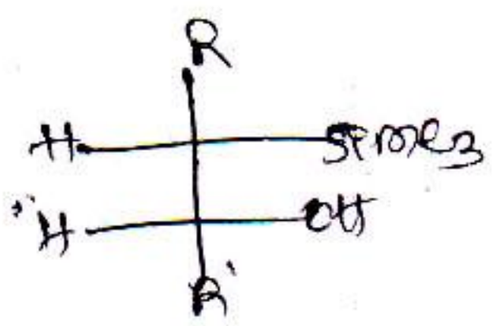
The stereo selectivity of resulting olefin depends on nature of diastereomer of β-hydroxy silane intermediate and rxn conditions. (that means whether acidic or basic)

stereo selectivity in peterson's olefination

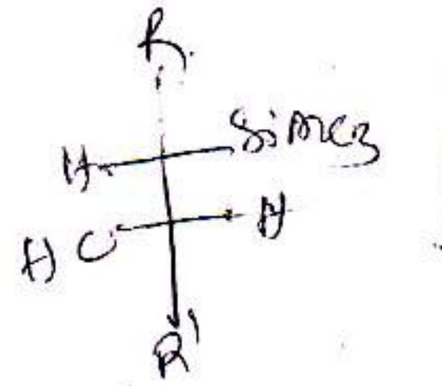


α,β Carbons ⇒ Constitutionally assymetric.

(diastereomers)



Erythro



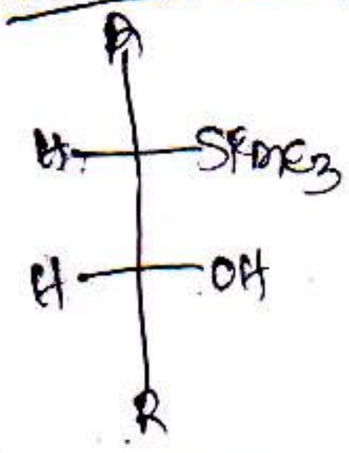
Threo

two diastereomers.

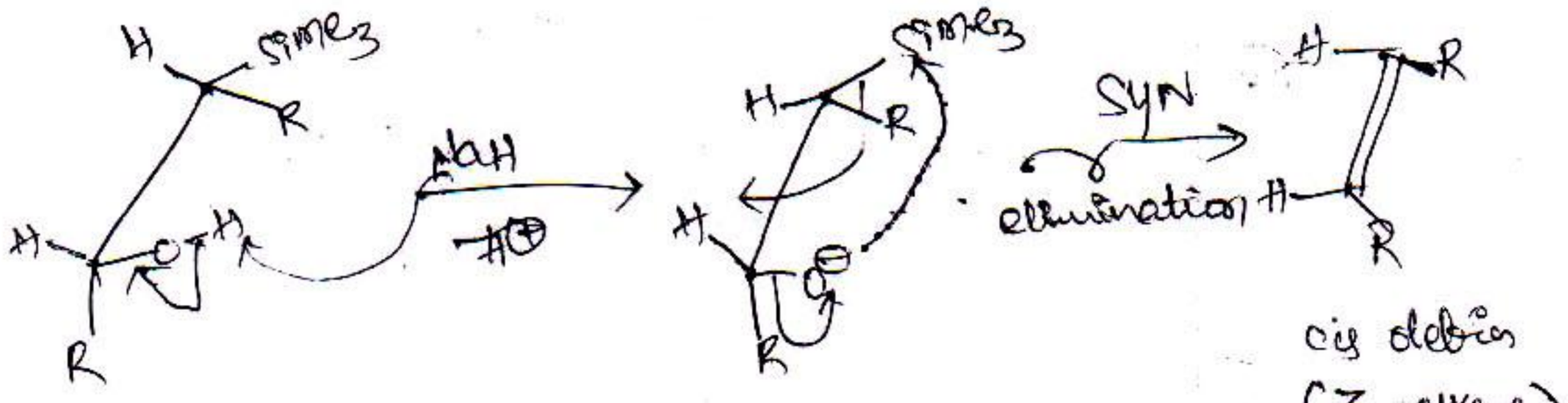
In basic medium syn elimination predominates.

In Acidic ↑ anti elimination predominates. (E_2-elimination rxn)

① BASIC MEDIUM ELIMINATION OF ERYTHRO



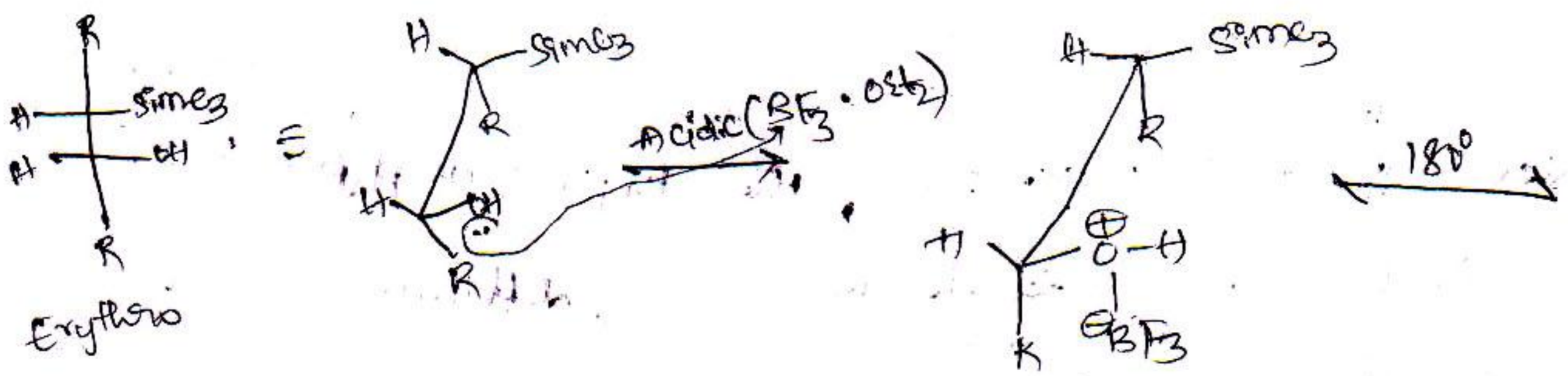
ERYTHRO

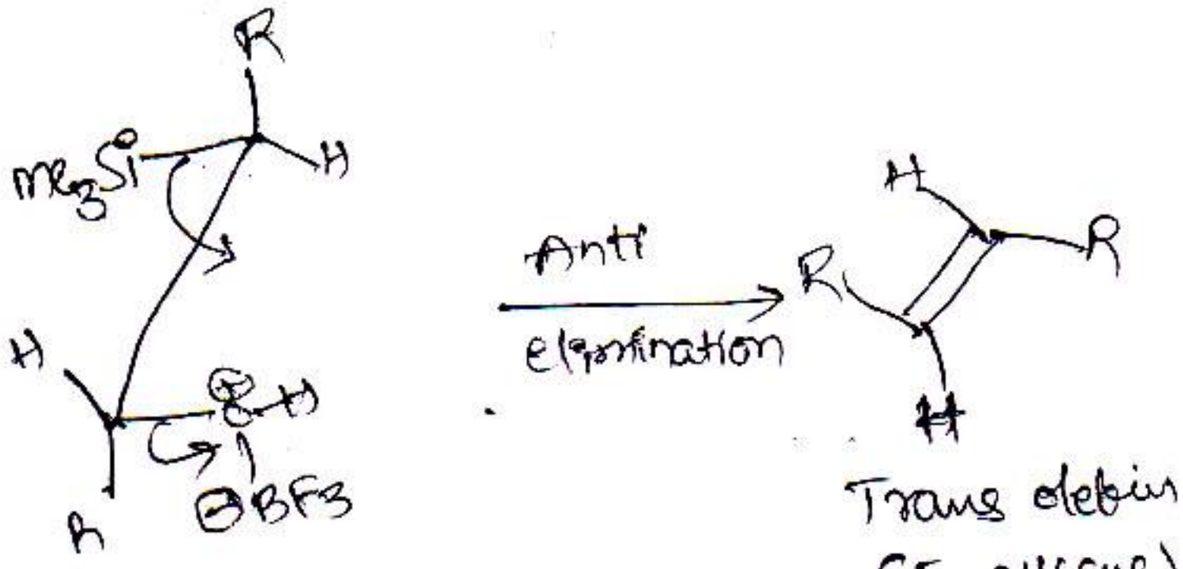


$Me_3-Si-OH$ ⟵ $H^{\oplus}$ ⟵ $+ Me_3Si-O^{\ominus}$

Trimethylsilanol.

ACIDIC MEDIUM ELIMINATION OF ERYTHRO



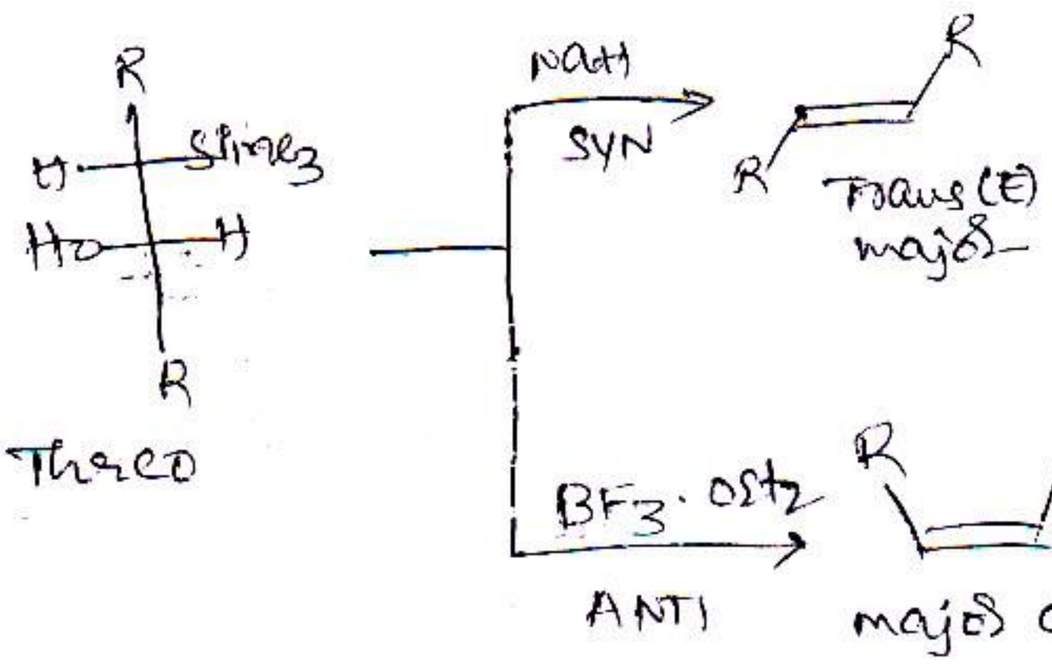


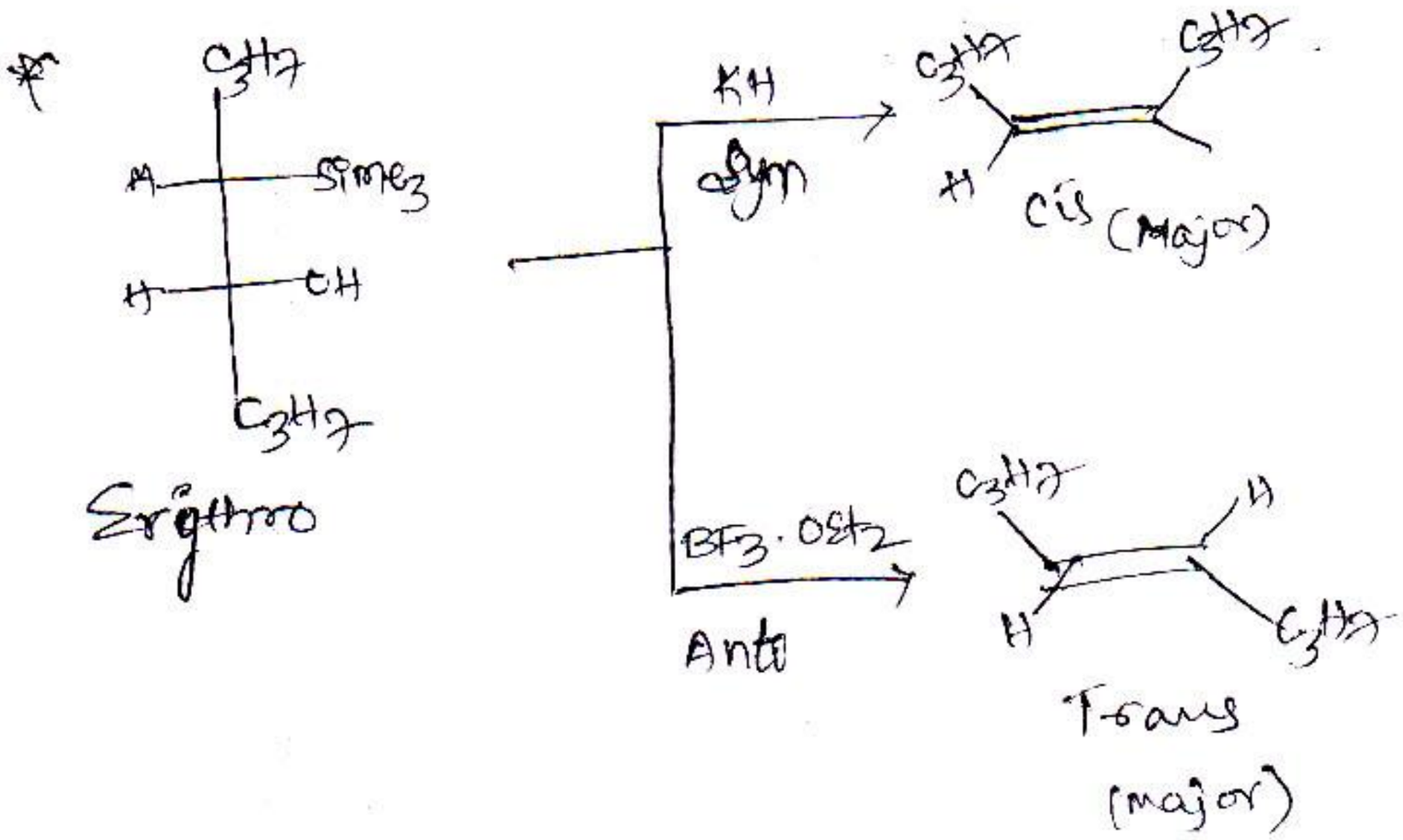
Anti-periplanar
Transition state.

* From Erythro in basic medium cis & Z-isomer major.

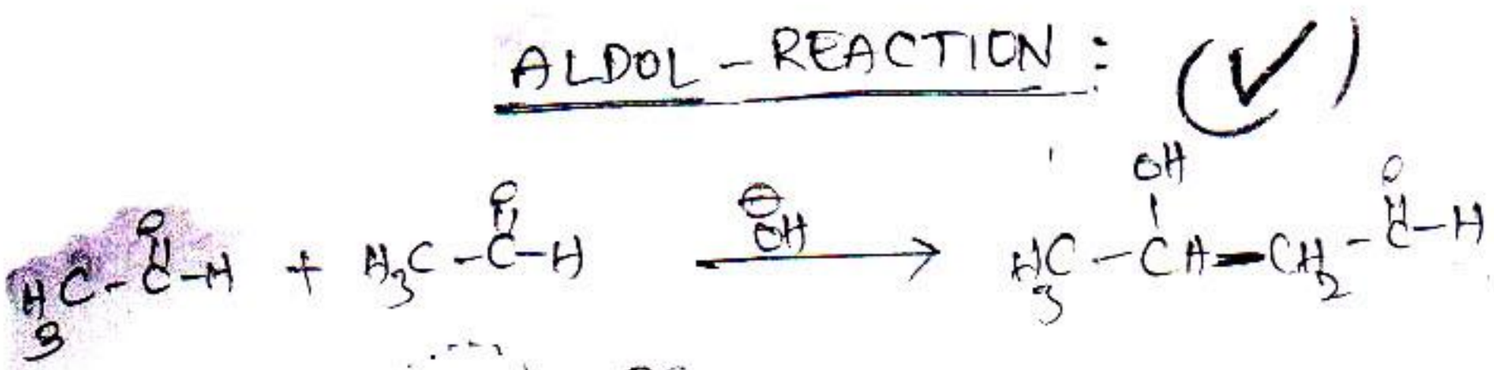
In Acidic medium trans & E-isomer is major.

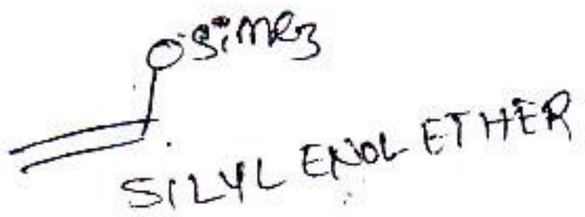
* THREO DIASTEREOMER



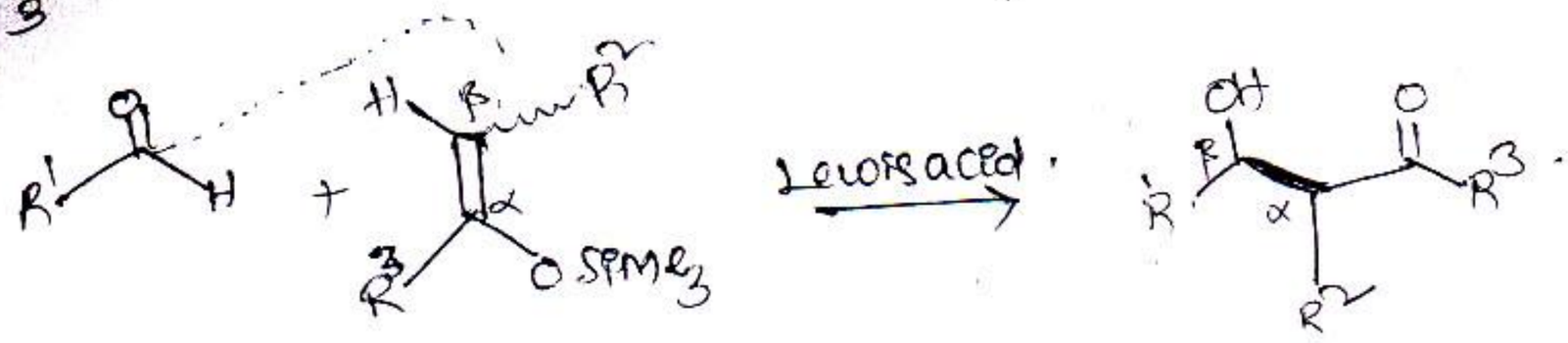


ALDOL - REACTION : (V)





SILYL ENOL ETHER

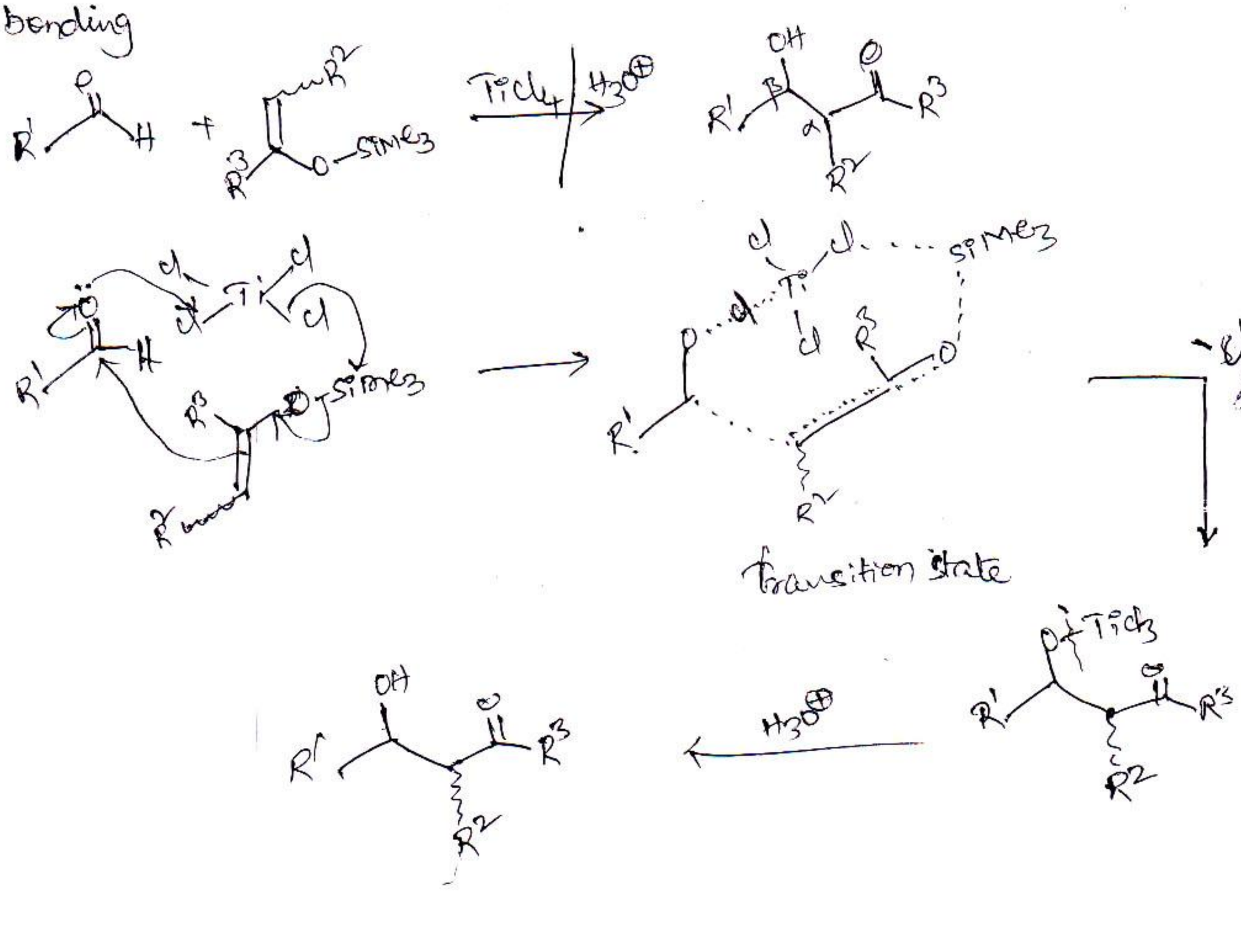


Silyl enol ethers

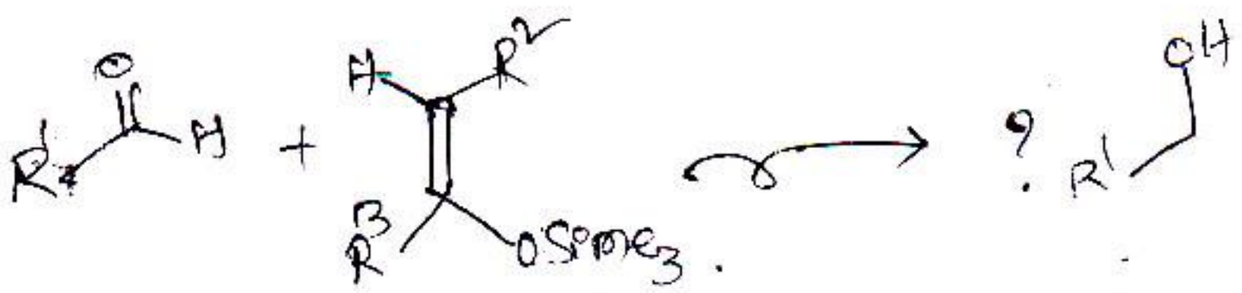
Rxn b/w, Aldehydes and Silyl enol ethers in the presence of lewisacids. is called MUKAIYAMA ALDOL Reaction. The resulting products are β-hydroxy carbonyl compds with new C-C bond formation.

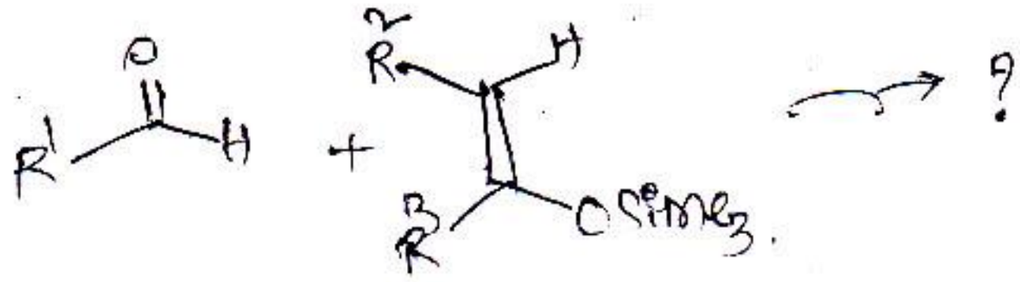
The Commen Lewis acids for rxn $TiCl_3$, $TiCl_4$ & BF_3 but other lewis acids $AlCl_3$, $SnCl_2$, $SnCl_4$, $ZnCl_2$, $FeCl_3$ and $InCl_3$, clay (one kind of sand type act as acid.) also can be used.

Lewis acid activates carbonyl function and develops faster C-C bonding



Stereochemistry :-





∴ E-

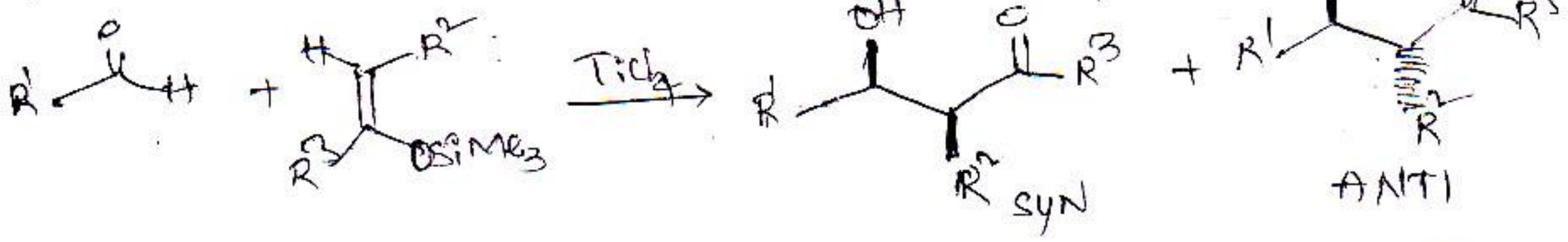
The resulting products will have diastereomers syn and anti.

Diastereoselectivity of stereochemical outcome in the MUKAIYAMA ALDOL reaction depends on type of substituents on the silyl Enol ethers (steric crowding) whether silyl enol ether with Z- & E- stereoisomeric relationship.

RULE:- R^3 bulkier, R^2 small on silyl enol ether. → anti diastereomer major

R^2 bulkier, R^3 small on " → syn diastereomer major

Z-SILYL-ENOL-ETHER



R^3 = BIG = MINOR

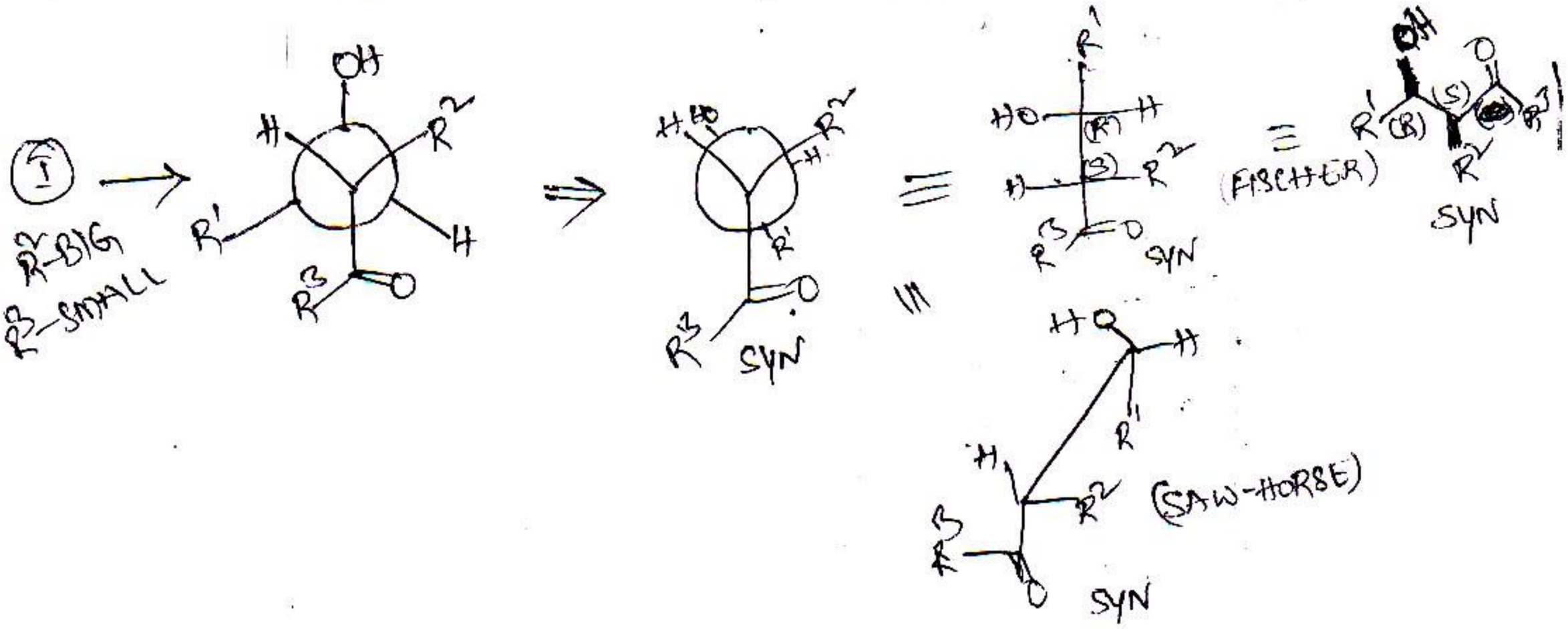
R^3 = BIG = MAJOR

R^2 = BIG = MAJOR

MINOR.

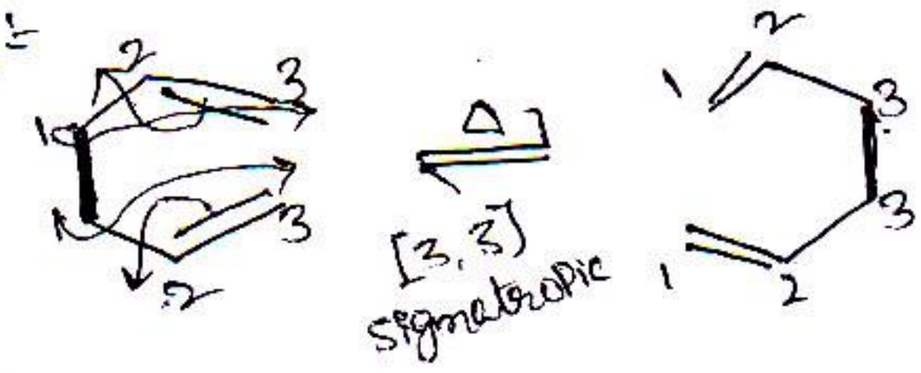
R^3 is bulkier, (II) is favoured and stable

R^2 is bulkier, (I) is favoured and stable.

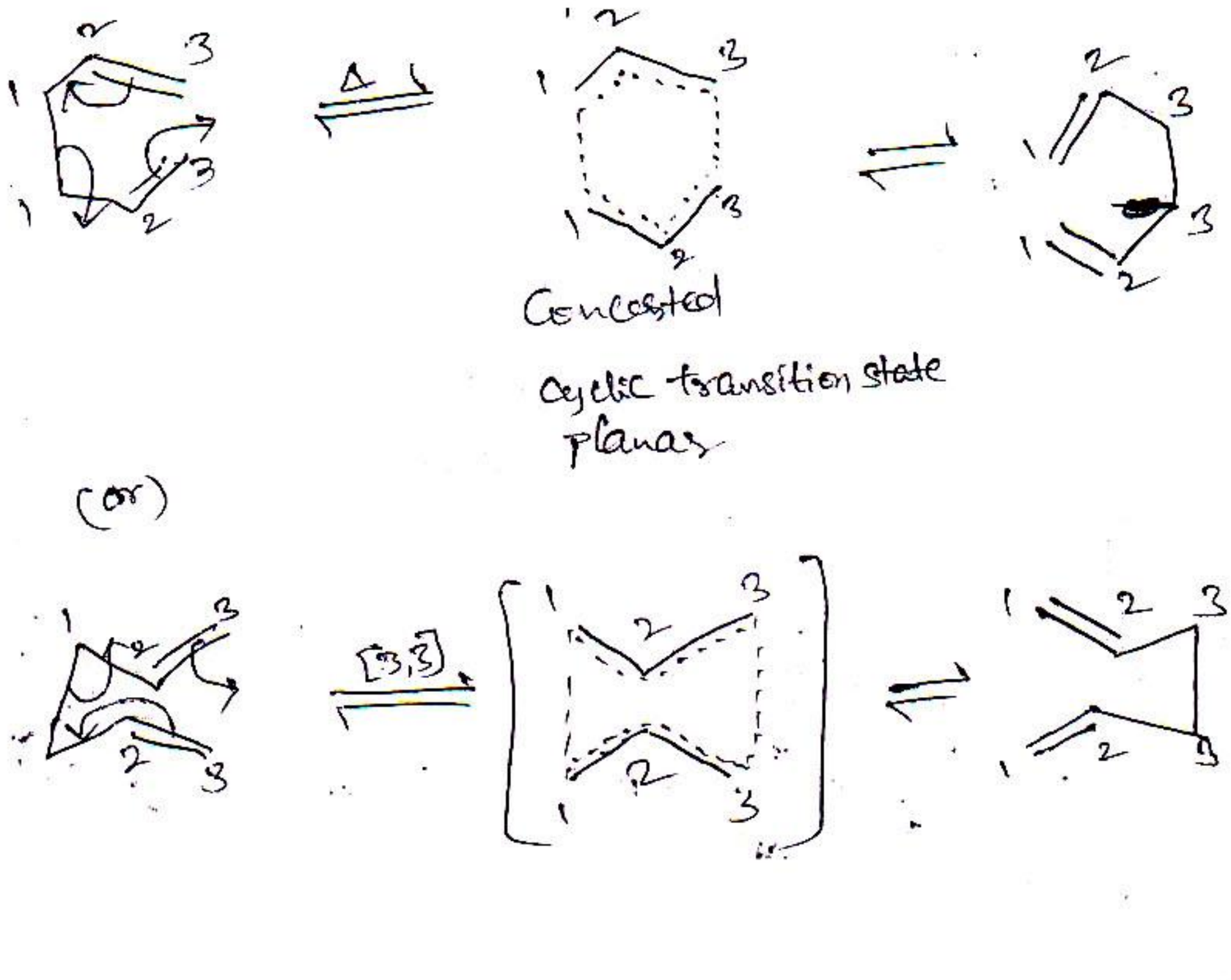


AZA-COPE REARRANGEMENT :-

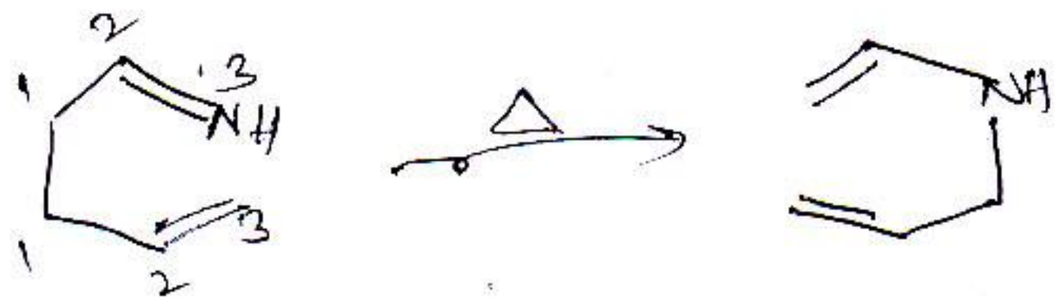
COPE R.A :-



[3,3] Sigmatropic Shift of 1,5-dienes under thermal Conditions called COPE REARRANGEMENT.

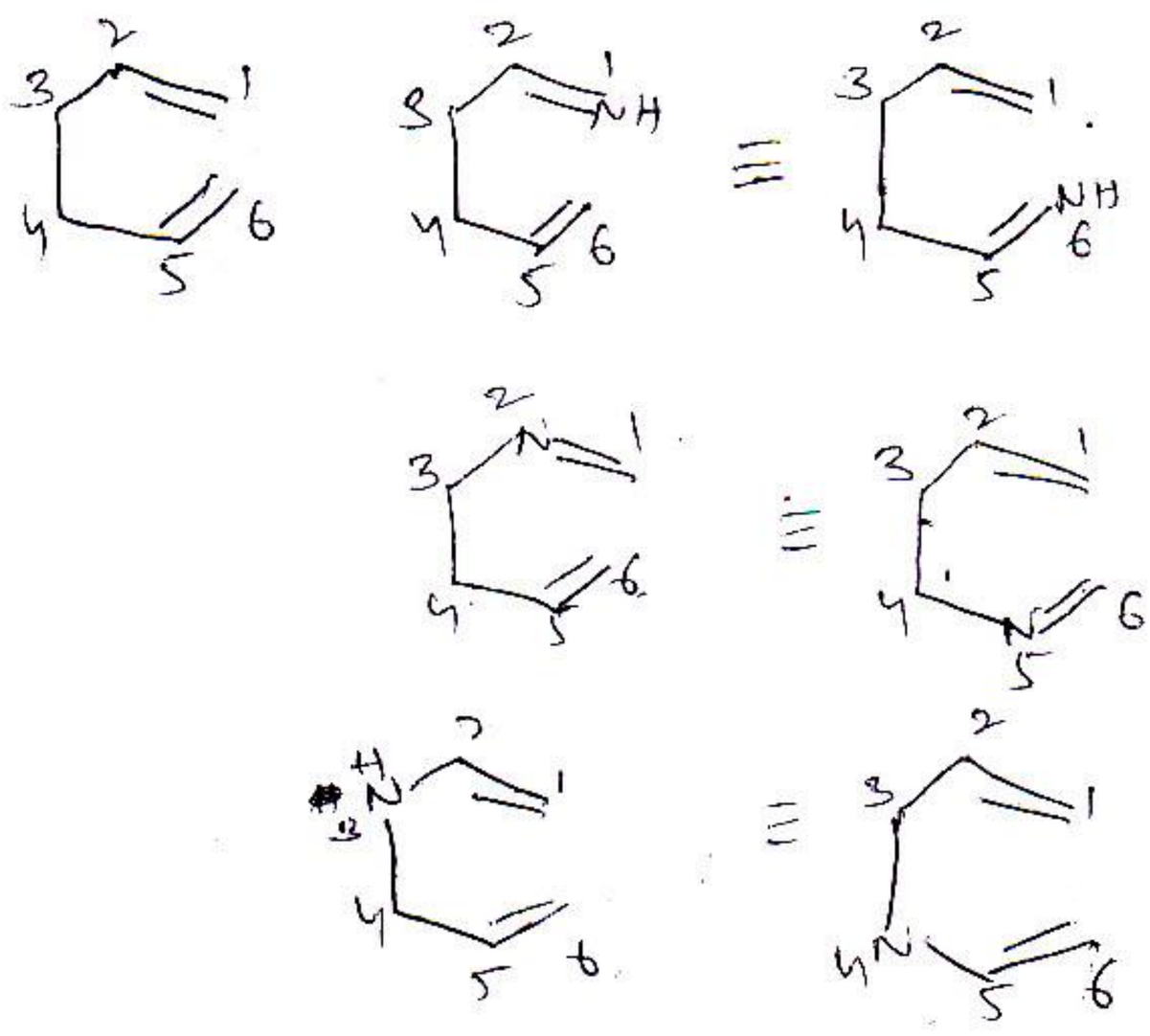


Aza Cope R.A:- (Imp)



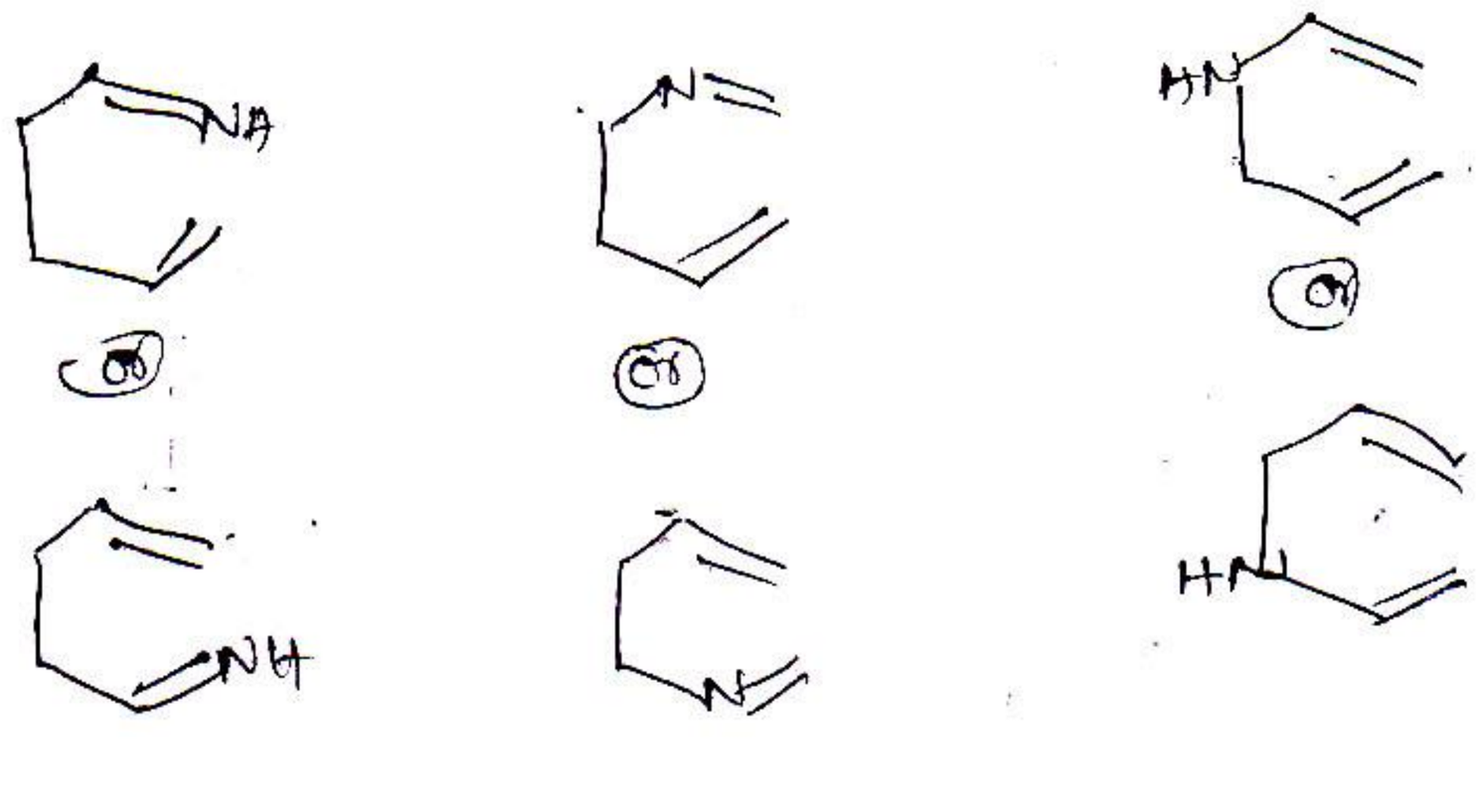
N-Substituted
1,5-dienes

N-Substituted 1,5-dienes [3,3] Sigmatropic Shift under thermal Conditions Called Aza cope R.A.

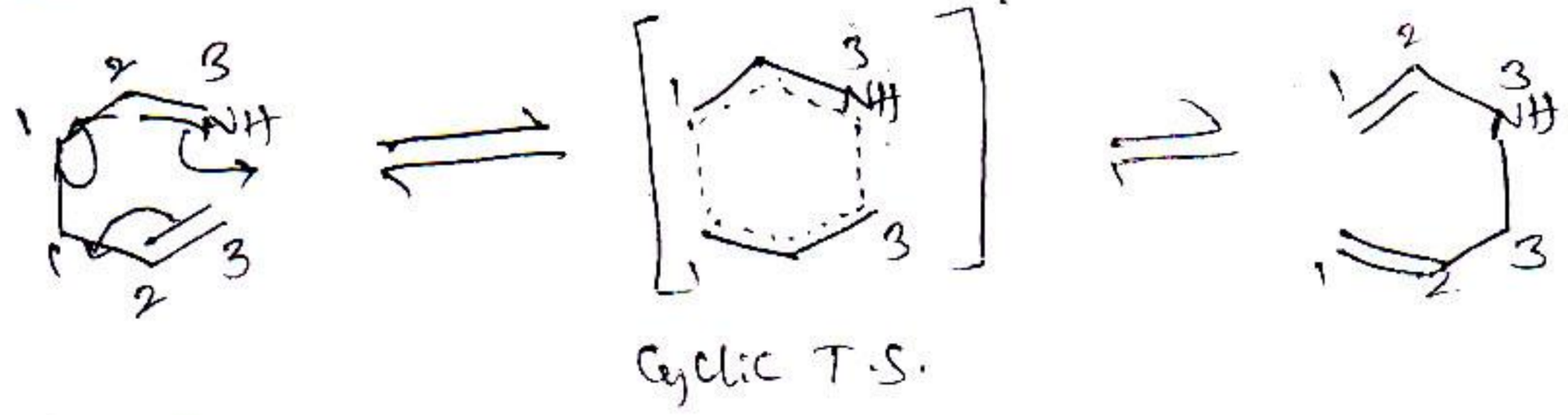


Aza cope R.A. 3 types.

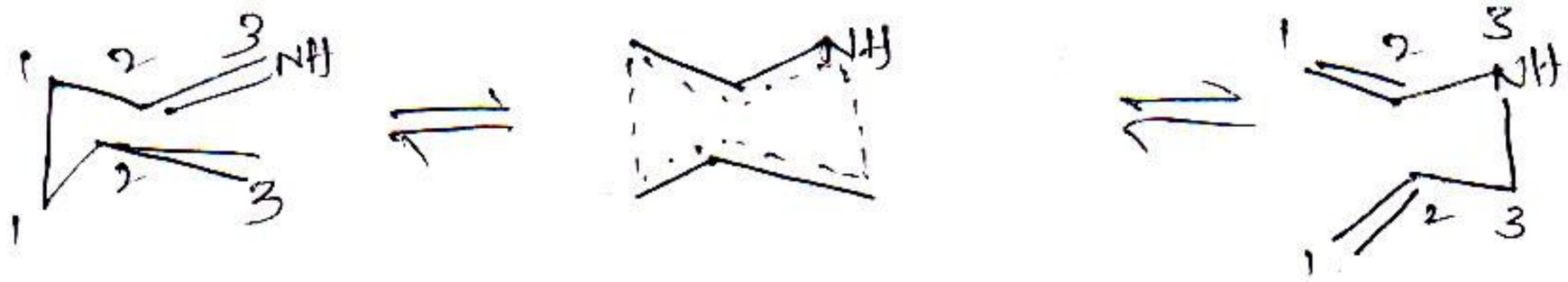
- 1-Aza Cope R.A.
- 2-Aza Cope R.A
- 3-Aza Cope R.A..



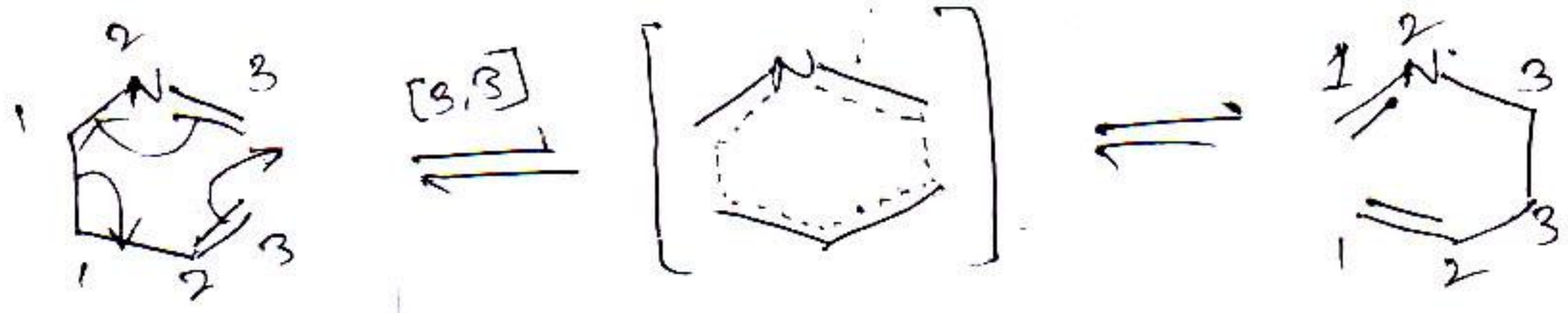
1-Aza Cope R.A



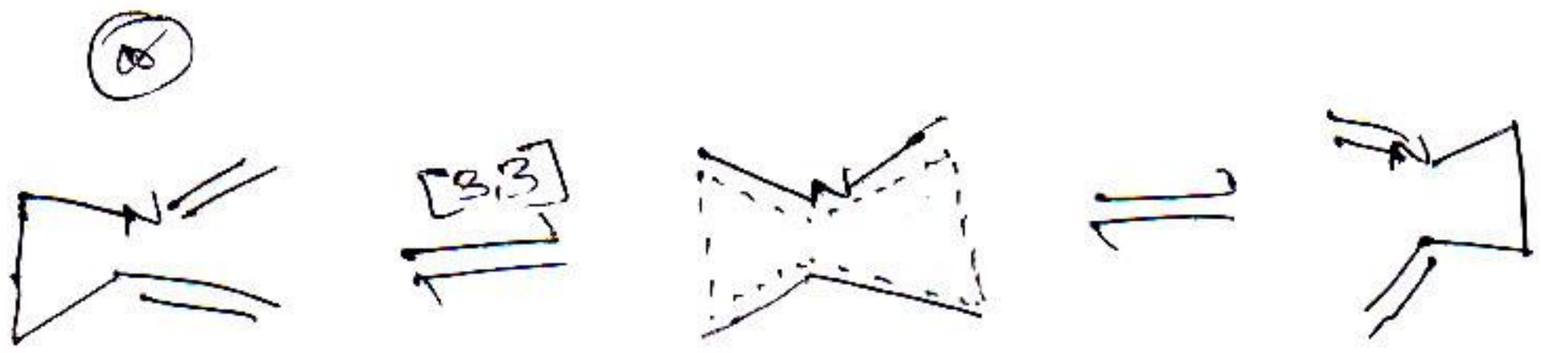
(a)



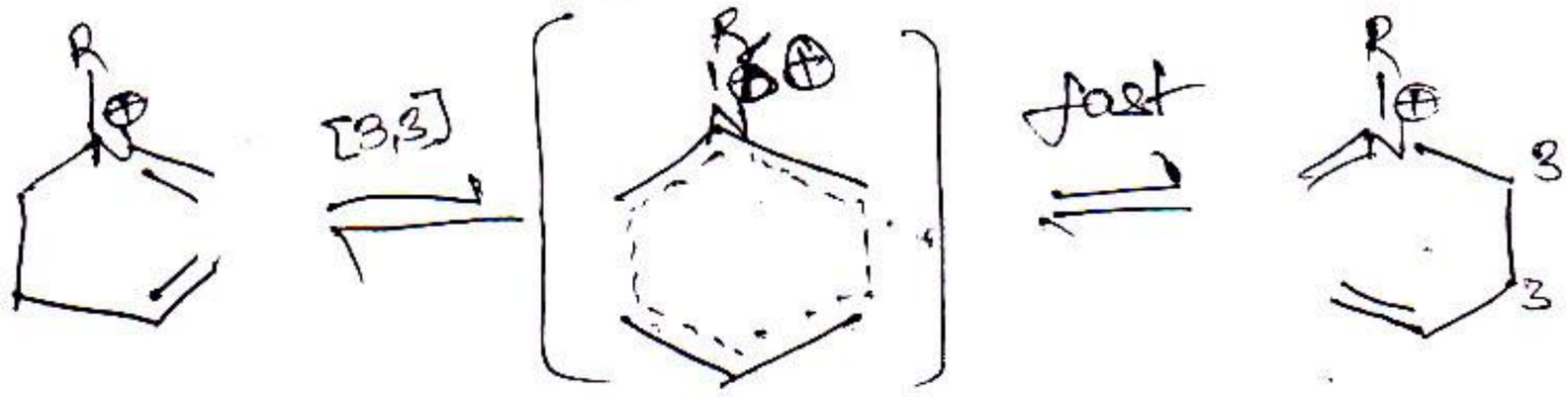
2-Aza Cope R.A :-



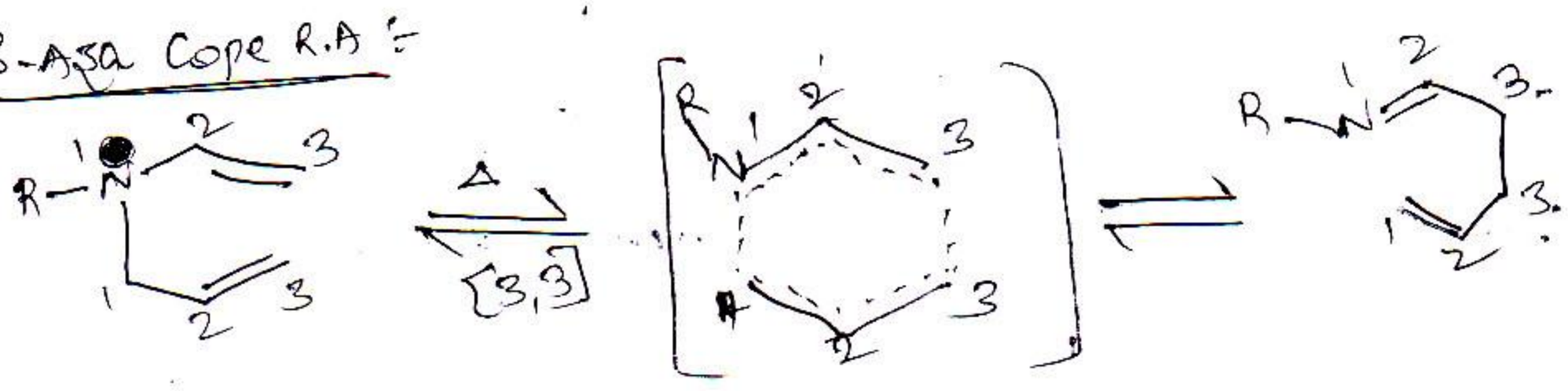
(b)



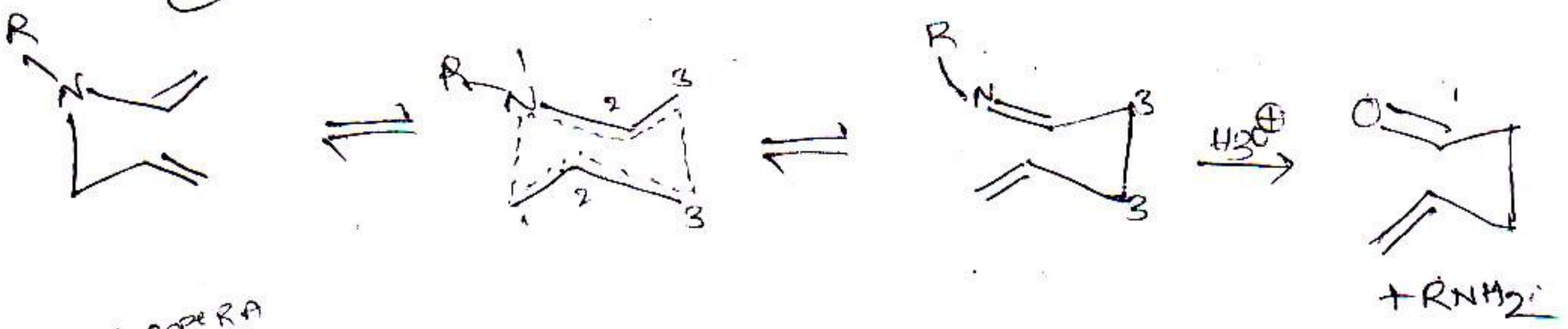
It 'N' carries charge rate of rxn increases due to decrease in transition state energy.



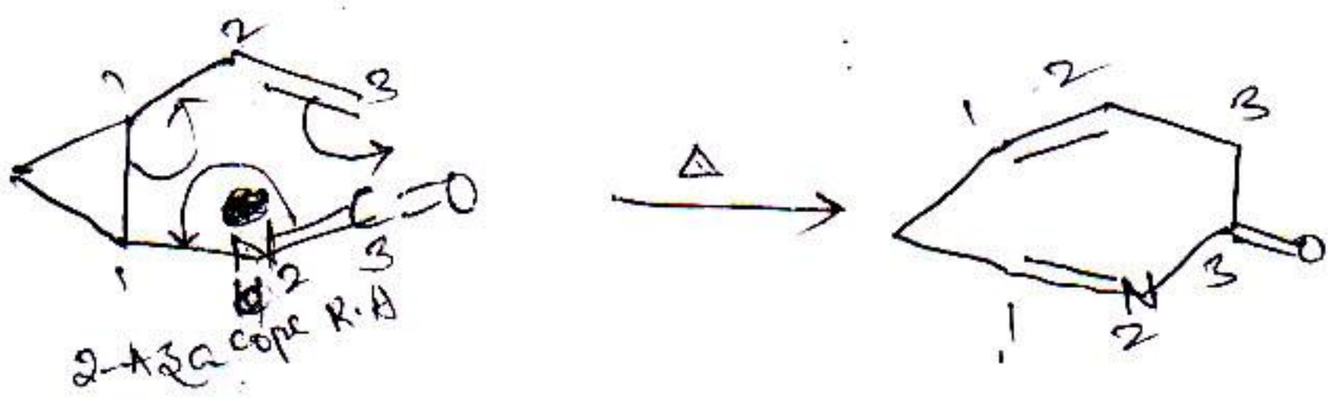
3-Aza Cope R.A :-



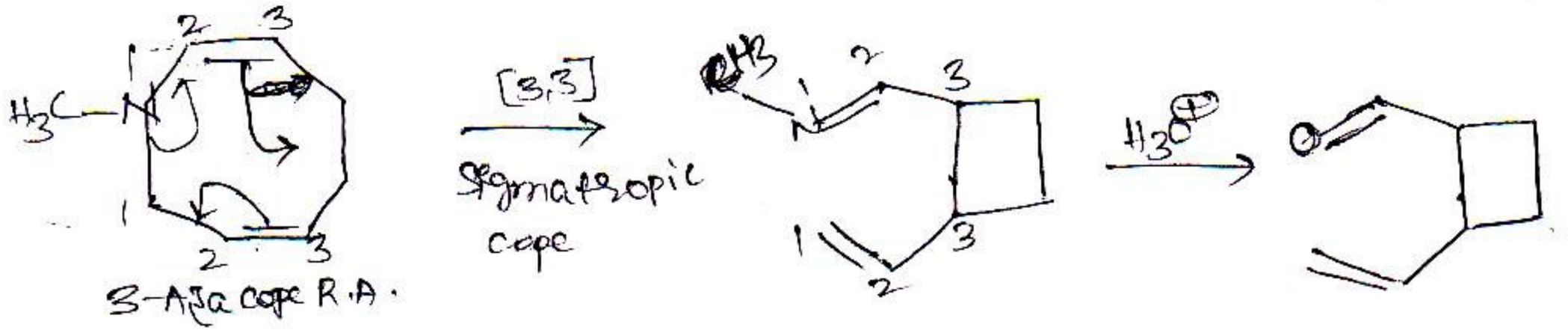
(or)



1-Aza cope R.A



2-Aza cope R.A

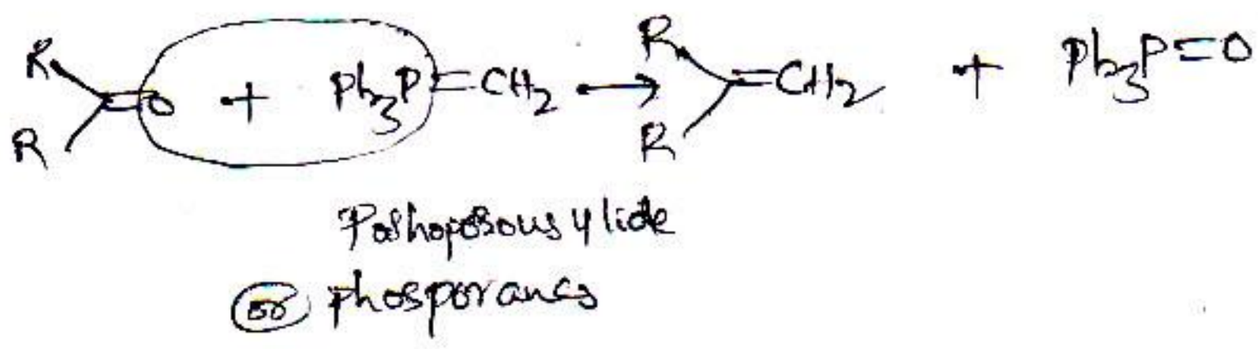


3-Aza cope R.A.

3-Aza Cope R.A is also called as Aza Claisen R.A.

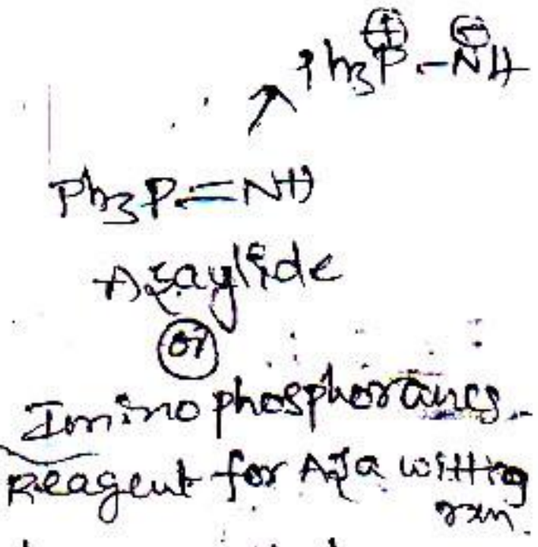
AZA-WITTIG RXN :- (✓)

WITTIG RXN



Posphorous ylide

(or) phosporanes



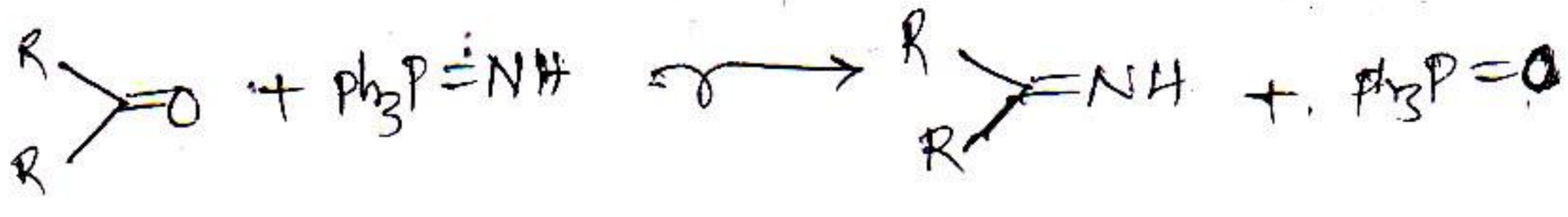
Azaylide

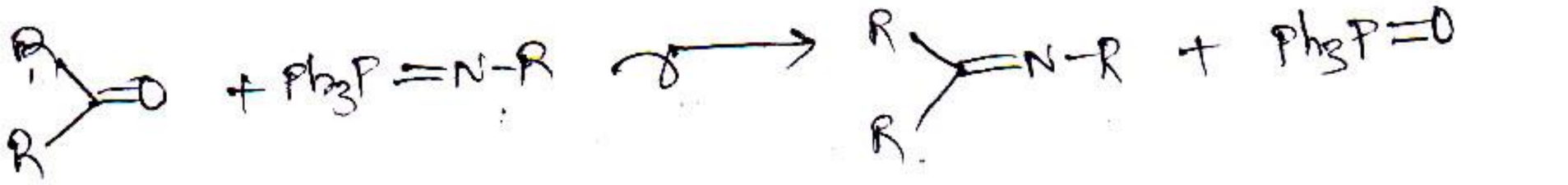
(or)

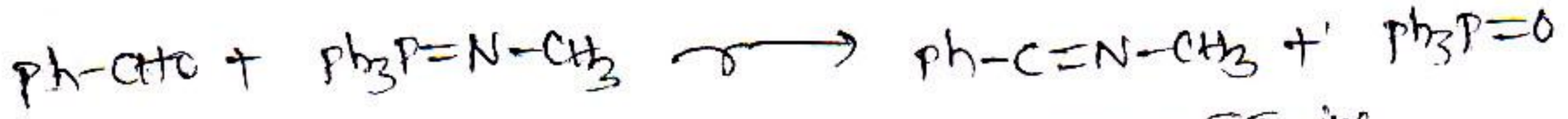
Imino phosphoranes.

Reagent for Aza wittig rxn.

Conversion of carbonyl compds into Imines or Schiff's bases called as .. with Imino poshoranes or Azaylides called Aza wittig rxn.

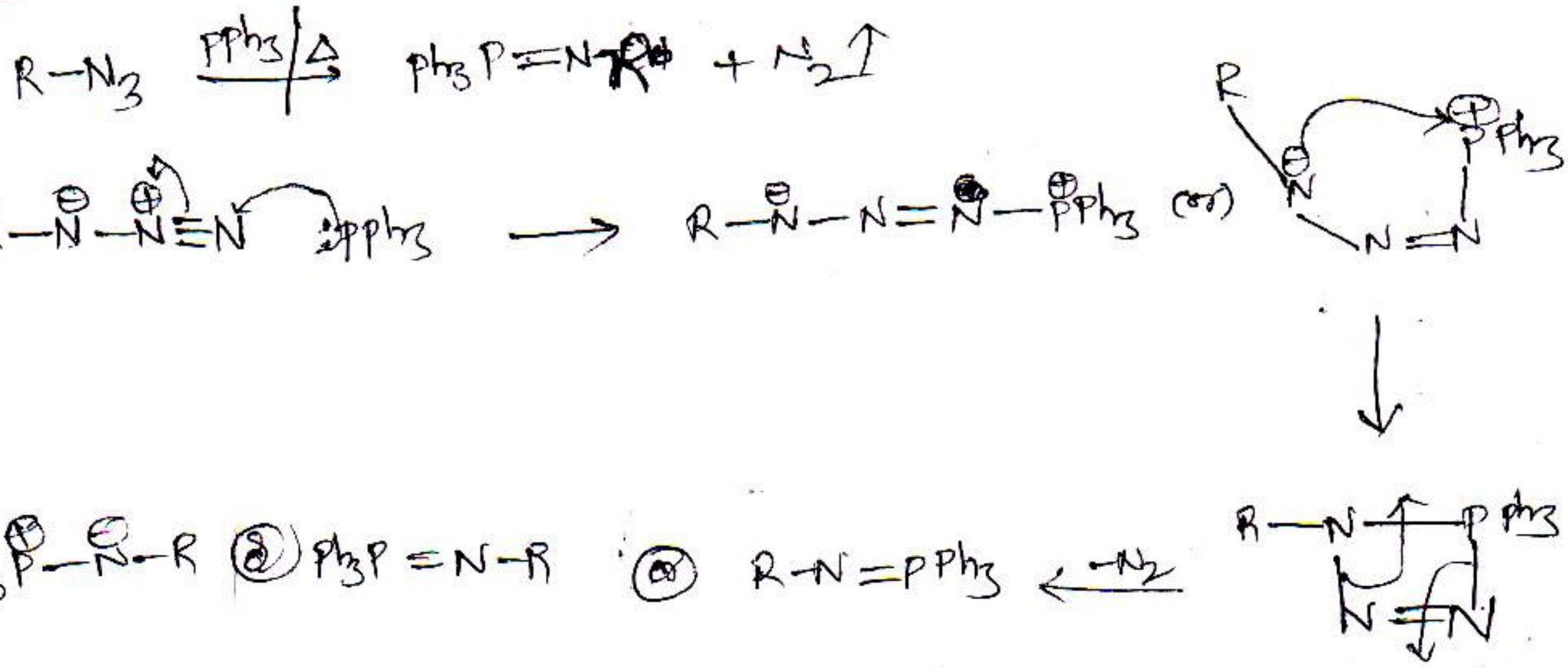




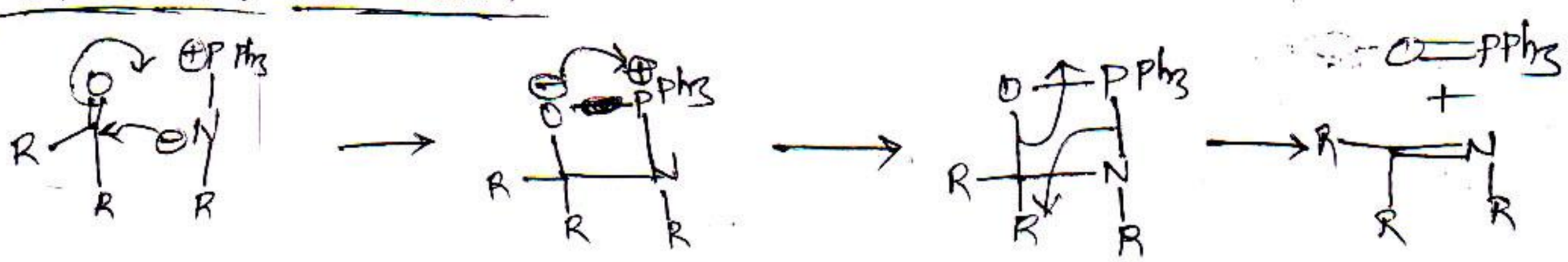


Schiff's base (or) Imine

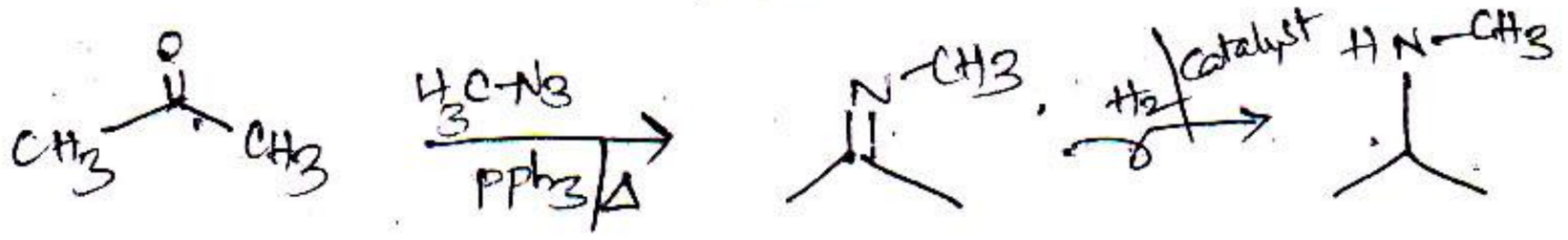
PREPARATION OF AZA YLIDE :



AZA-WITTIG MECHANISM

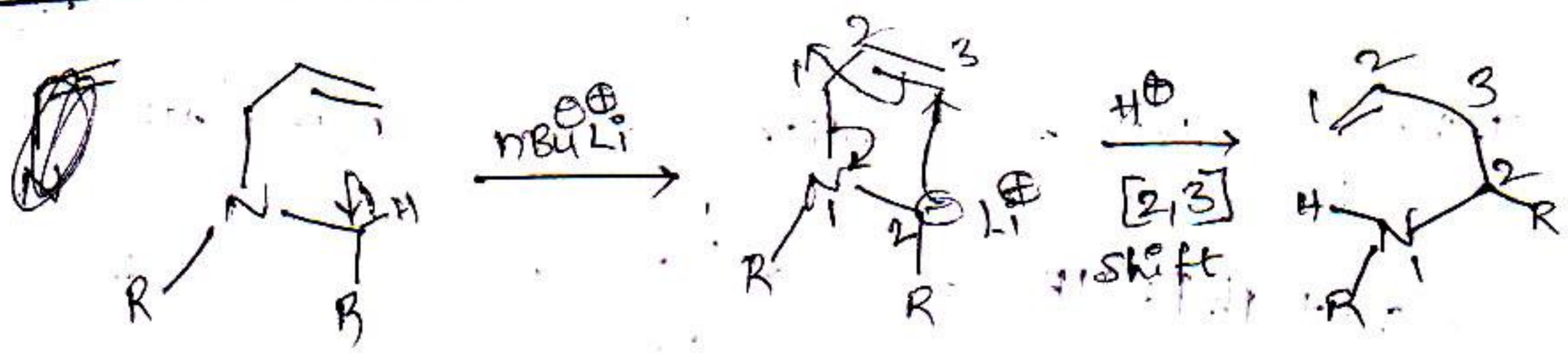


Zwitterion
Intermediate formation.

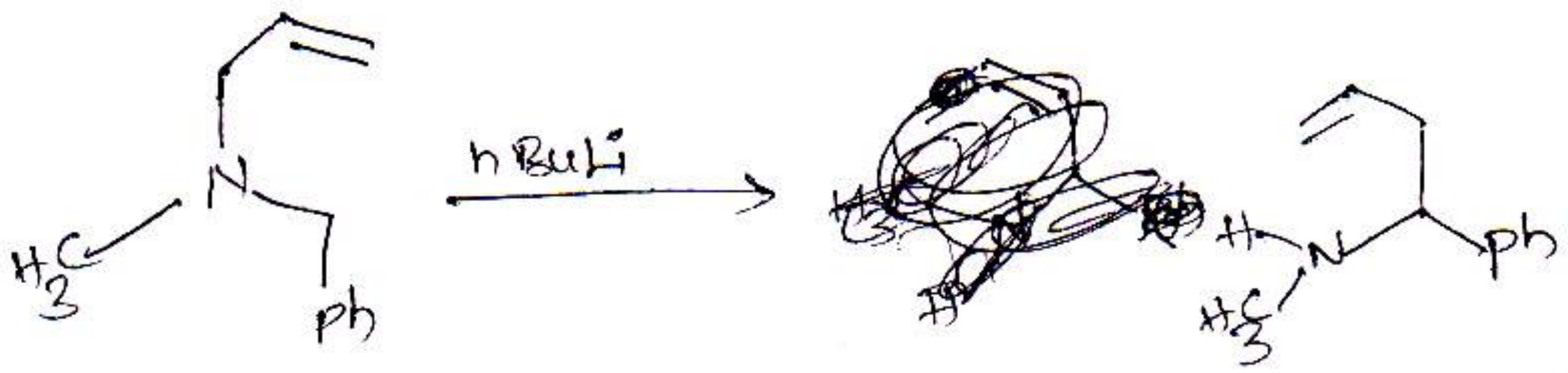


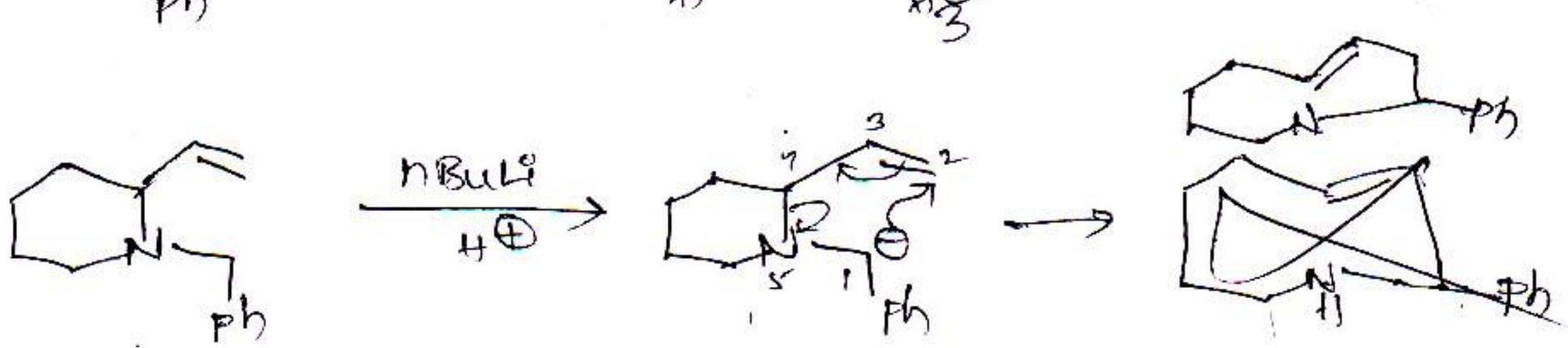
~~[2,3] Aza wittig shift~~

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



[2,3] Sigmatropic Shift allyl alkyl 3° amines into allyl amines in basic medium called [2,3] Aza wittig rearrangement.





Pd-COMPLEXES BASED NAME REACTIONS

Pd^0, Pd^{II} Complexes are widely used for organic synthesis.

Pd^0 $\xrightarrow{OXD}$ Pd^{II} $\xrightarrow{RED^N}$ Pd^0

Pd^{II} $\xrightarrow{OXD}$ Pd^{IV} $\xrightarrow{RED^N}$ Pd^{II}

Pd^0 & Pd^{II} Complexes involved in organic synthesis in oxidations & red^{ns}

By transfesing two $\bar{e}$s. (two $\bar{e}$ transfer pd-rxns)

pd Complexes are used for C–C, C–N, C–O bonding and.

Cleavage of C–C, C–N, C=C, C=O

These are used for Hydrogenolysis.

These are used for Regio, stereo, chemoselectivity.

* SUZUKI-COUPLING/RXN (✓)
* HECK-COUPLING/RXN (✓)
* STILLE- " /" (✓)
* BUCHWALD-HARTWIG/" (✓)
* SONOGISHIRA COUPLING (✓)

$Pd^{0}L_n$

n = no of ligand.

ligand

eg: $Pd^{0}(PPh_3)_4$

Tetrakis (Tri phenyl phosphine) Palladium (0)

② $Pd_2(dba)_3$ dba = dibenzylidine acetone

Tris (dibenzylidine acetone) di palladium (0).

⊛ $Pd^{II}L_n$

eg: $Pd^{II}(OAc)_2$ Palladium diacetate.

$[Pd^{II}(PPh_3)_2Cl_2]$

Palladium Complexes are versatile species (widely used).

palladium complexes are catalytic medium in organic Synthesis.

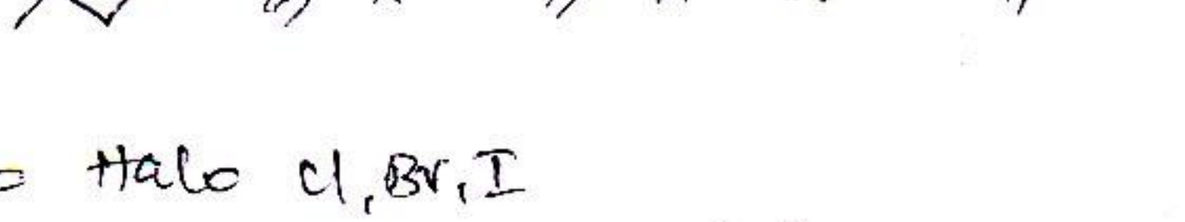
SUZUKI-COUPLING.

$R-X + R-X \rightarrow R-R$ (Self Coupling)

$R-X + R'-X \rightarrow R-R'$ (Cross coupling)

$$R-X + R'-BY_n \xrightarrow[Pd^{0}L_n \,|\, Base \rightarrow solvent]{Pd^{0},\ LIGANDS} R-R'$$

R = Alkyl, Alkynyl, Alkenyl, Aryl, Allyl



X = Halo Cl, Br, I

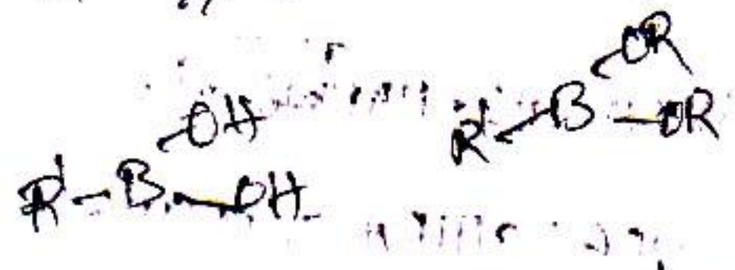
X = OTf = Triflate  (Trifluoromethane Sulfonate)

R' = Alkyl, Alkenyl, Alkynyl, Aryl, Allyl



Y = −OH, −OR

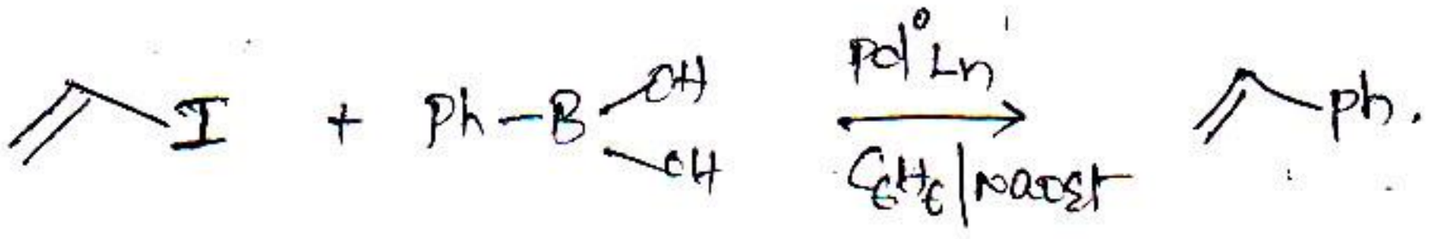
n = 2



Boronic acid, Boronate esters

Solvents = Ethers or Benzene

BASE = Na_2CO_3, Cs_2CO_3, KOH, $NaOEt$ etc...



Reactivity:- R–Cl < R–Br < R–I

Characteristics

① All the starting materials are readily available & cheaper

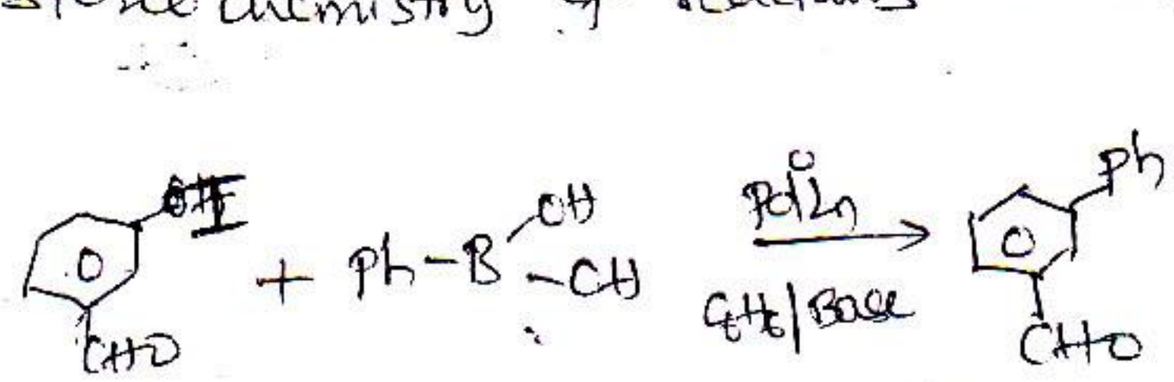
② All the components are non toxic, easy to handle.

③ High % yields (80 to 90%)

④ Easy to remove biproducts.

⑤ Stereo chemistry of reactants retained in the product

⑥

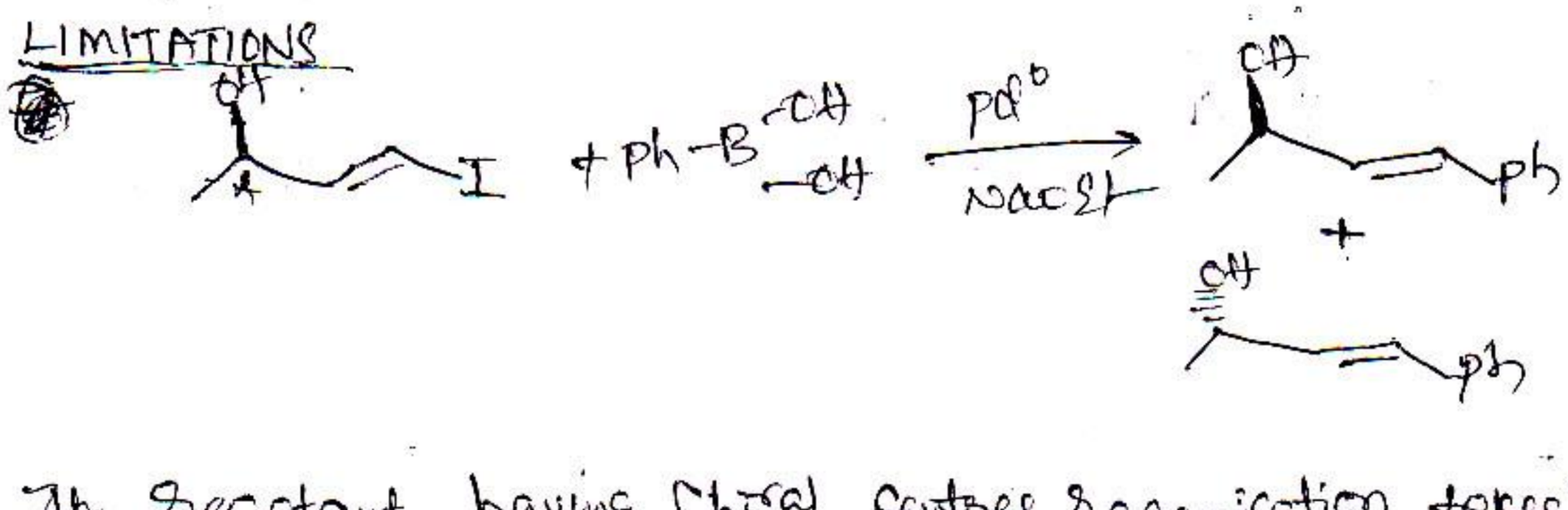


The reactant Halo Coupd are triflet or may be acetate with other variety of functional gps

–OH, –CHO, –COOH, –COOR etc.., are uneffected.

LIMITATIONS

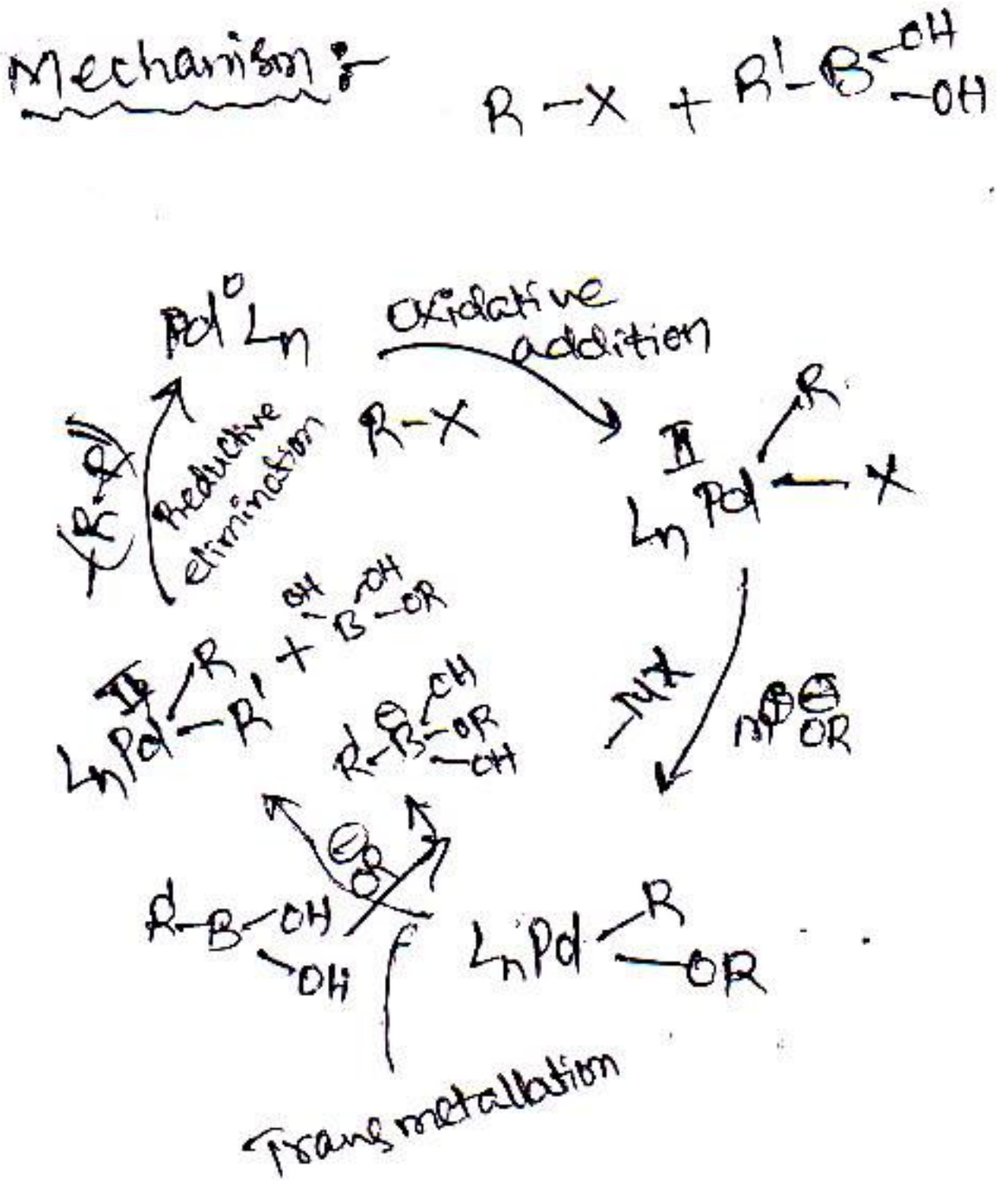
①



If reactant having Chiral centres Racemisation takes place due to presence of base.

* Aryl Halides are sluggish in SUZUKI COUPLING (Slowly Sm)

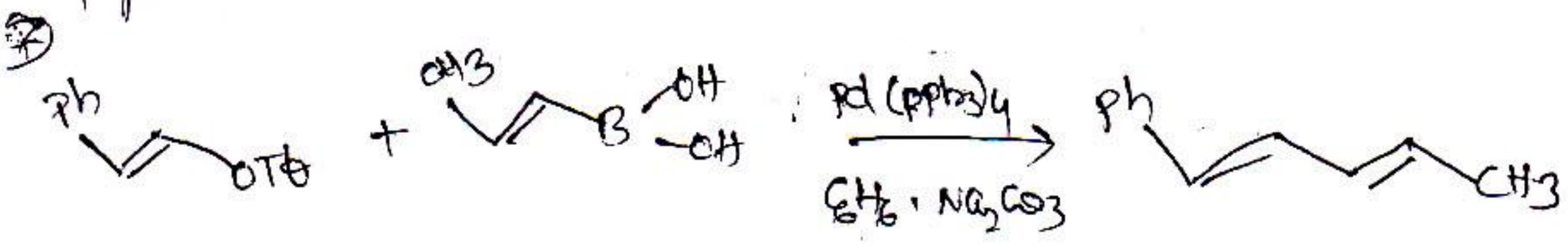
Mechanism:-

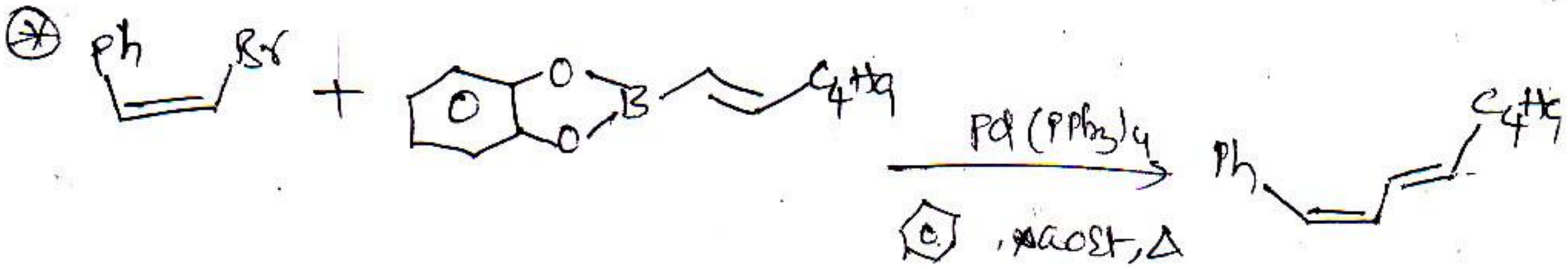


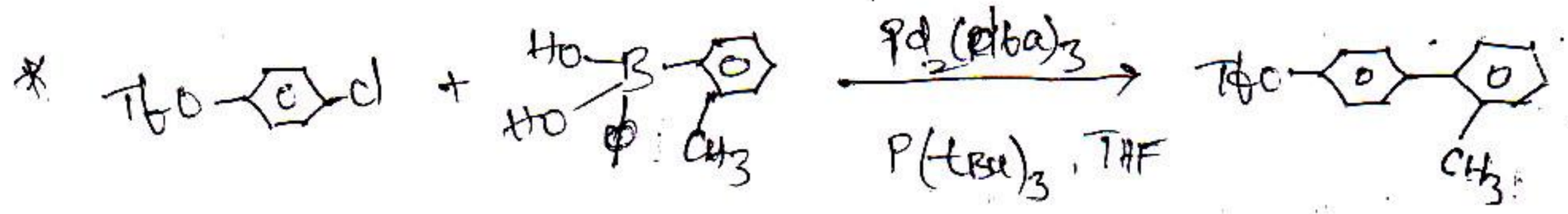


Soluble in water, easy to remove.

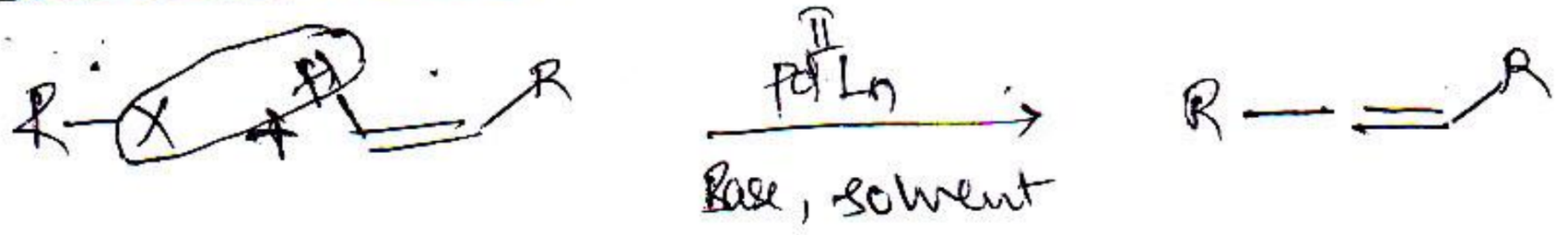
Regeneration of Initial Palladium Complex







* HECK - COUPLING :-



monodentate & bidentate ~~ligands~~ phosphines  to enhance rate of the rxn.

Formation of C—C bonding by halo organic compds & organotrifla eg. and debins with palladium complexes and base called HECK RXNS.

- X = Cl, Br, I R = Any organic group
- X = OTf

one of R = donating & withdrawing.

R = E.D gp = olefin becomes ē deficient

RXNS are faster.

Presence of phosphine ligand also enhances rate of rxn. by reducing Pd(II) to into Pd(0)

By HECK rxns Pd(0) complexes insitive generation from Pd(II) complexes.

It is very good for alkenyl.

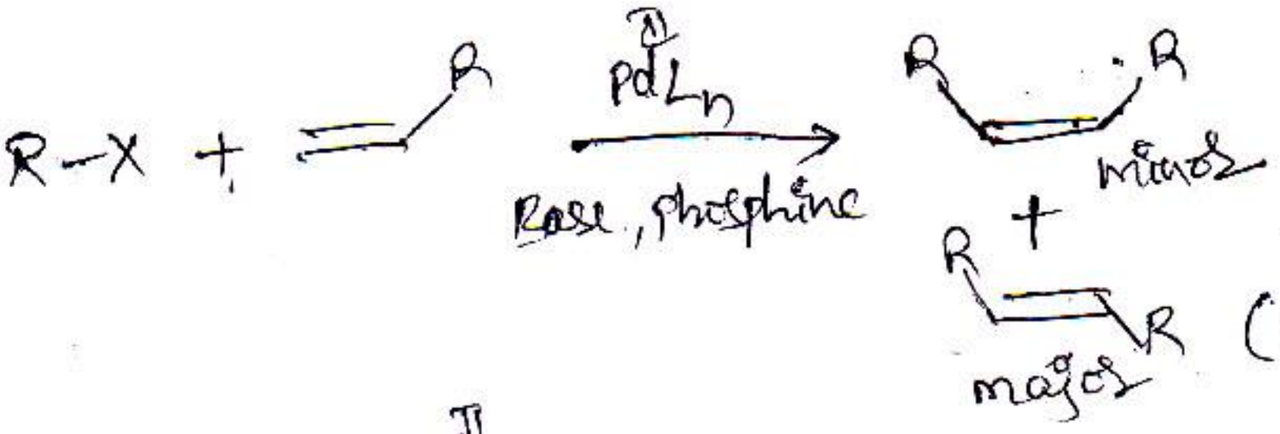
LIMITATIONS

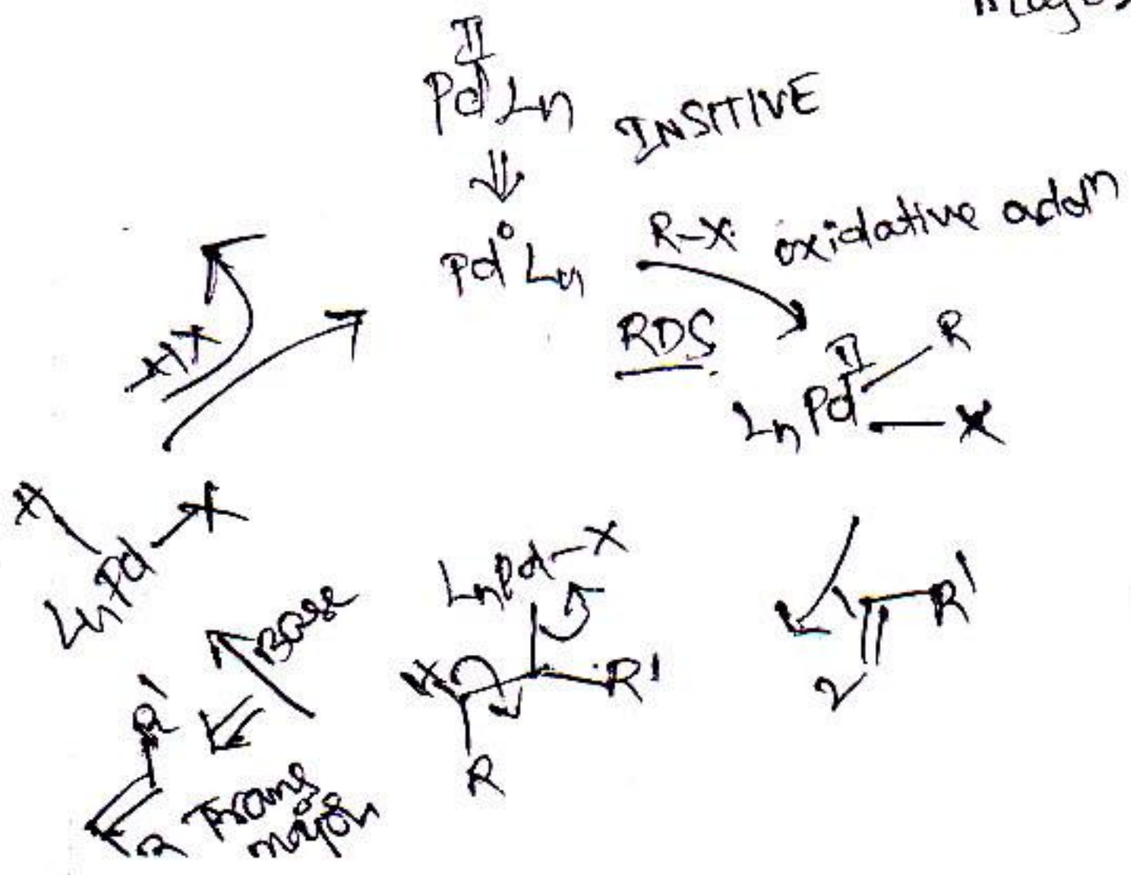
1) Starting materials are little expensive

2) In the case of alkene, & alkynes & aromatic compds taken rxn almost inert.

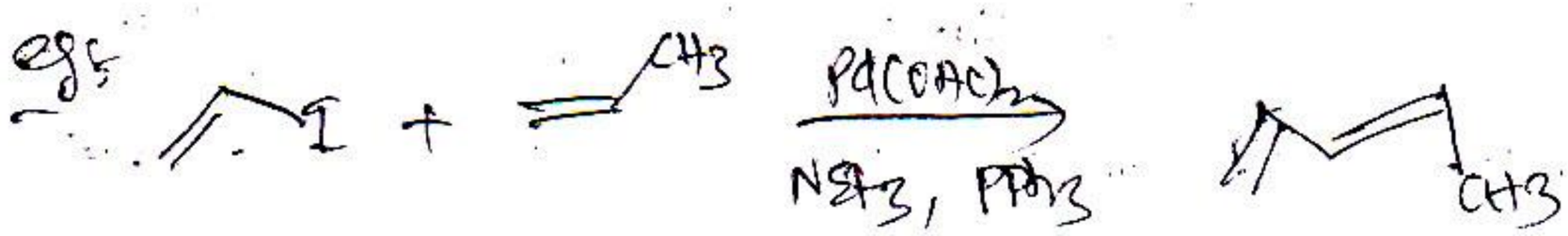
3) Aryl Halides are slow in rxn.

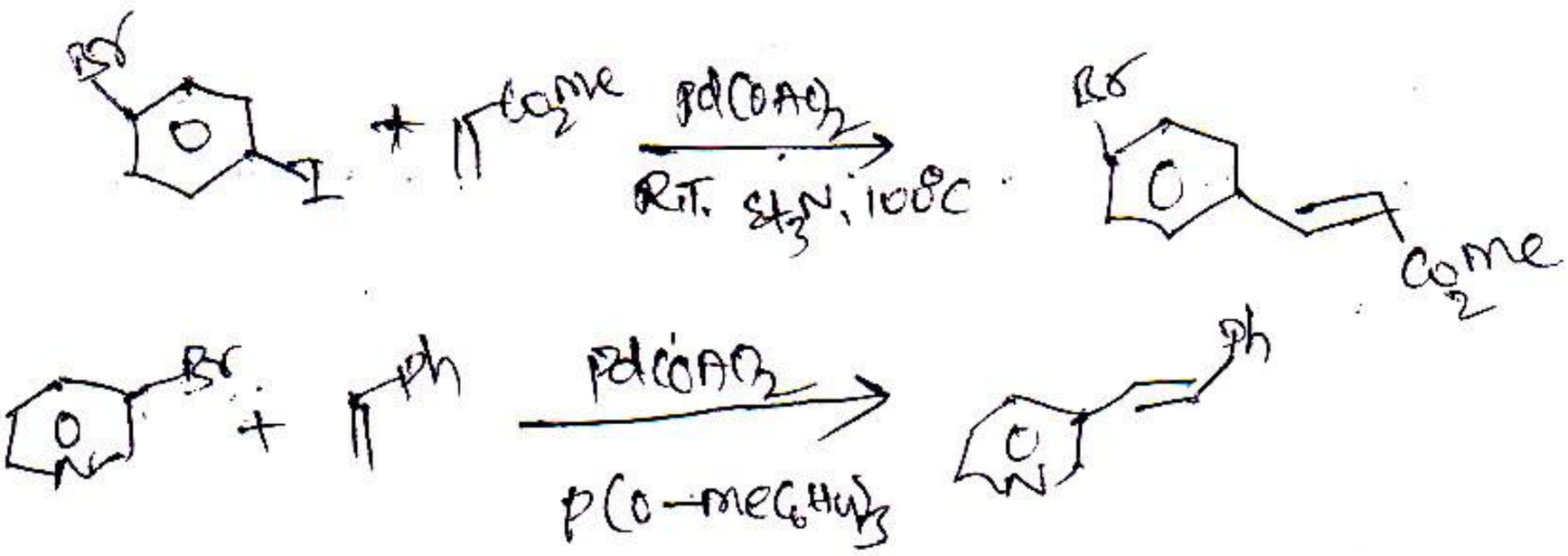
MECH:

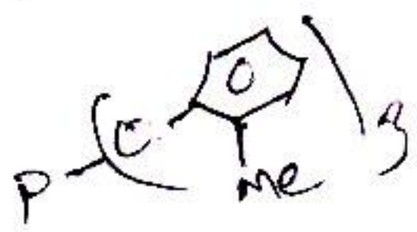




eg:-







tri Tollyloxi phosphine

STILLE - COUPLING :-



STANNANES

i

R = Alkyl, Alkenyl, Aryl, Allyl,

X = Halo (-Cl, -Br, I), OTf

R' = Alkyl, Alkenyl, Aryl, Allyl

→ Easy to do reaction

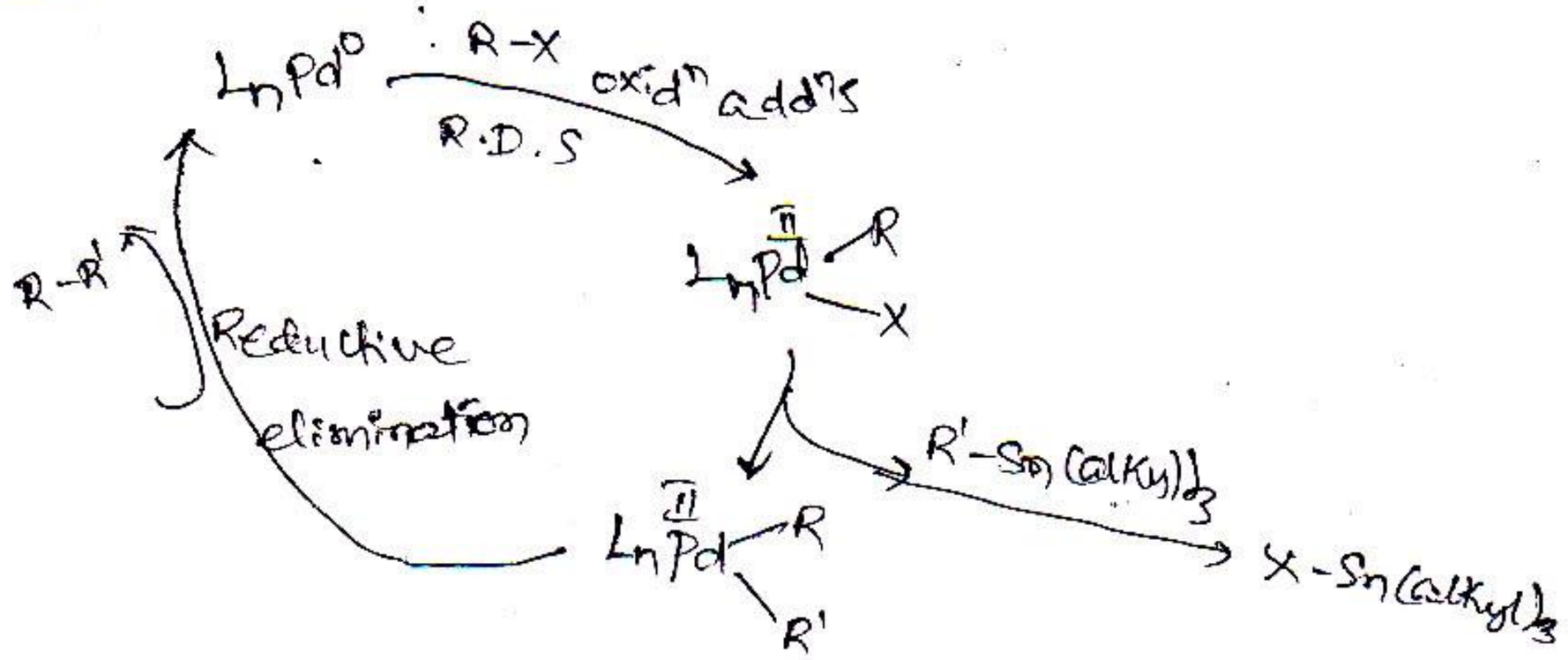
→ Easy to remove biproducts

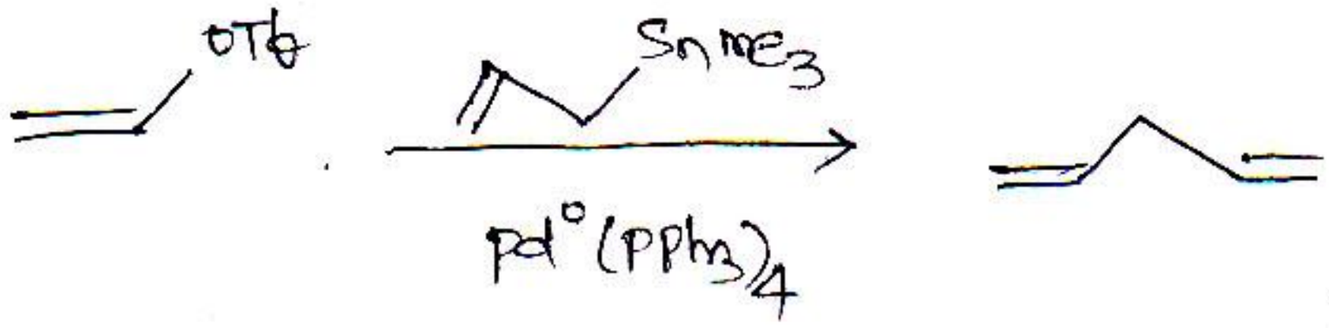
→ Good % of yeilds

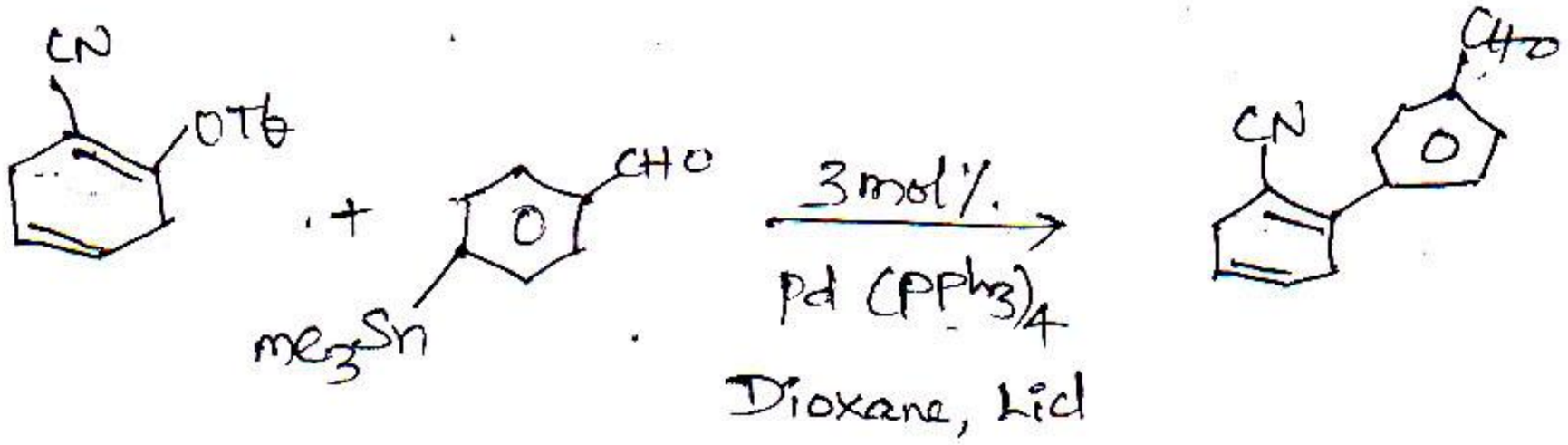
→ presence of any other function (-OH, -NH2, -CHO, -C(=O)-) will not influence on reaction.

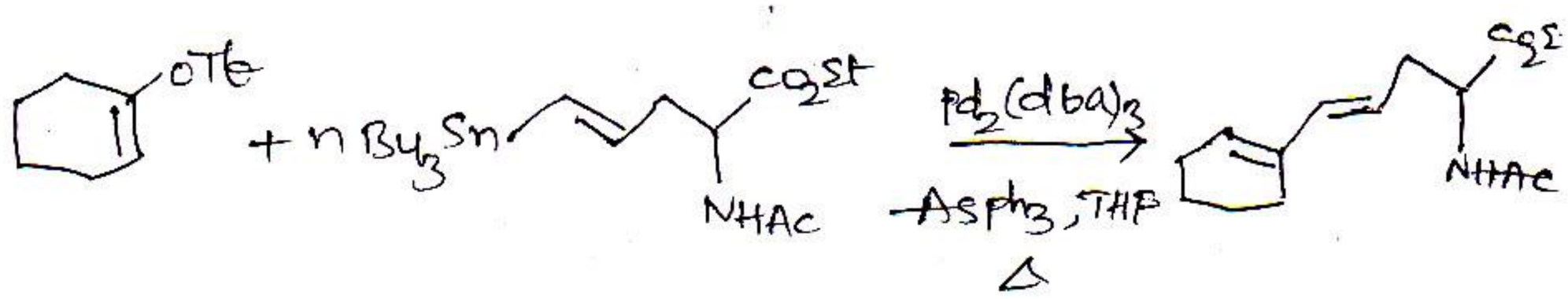
→ STANNANES are little toxic and drawback of Stille-coupling

Mechanism :-

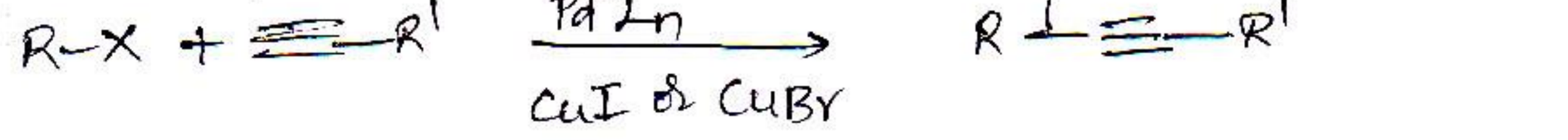


*) 

*) 

*) 

SONOGHASHIRA - COUPLING



CuI & CuBr

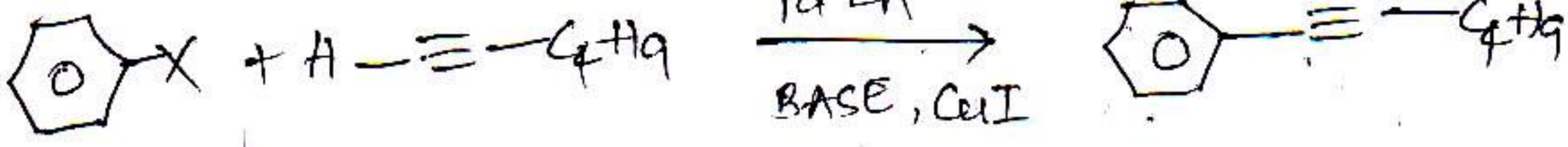
(OR)

Cu^{I}, SALTS, Solvent

R = Alkyl, Alkenyl, Aryl, Allyl

X = Hclo, OTf

R' = Alkyl, Alkenyl, Aryl, Allyl

(*) 

→ Easy to do reaction

→ Easy to remove by product.

→ Good % of yields

→ with inverse in size of substituent on the alkyl the rate of reaction decreases.

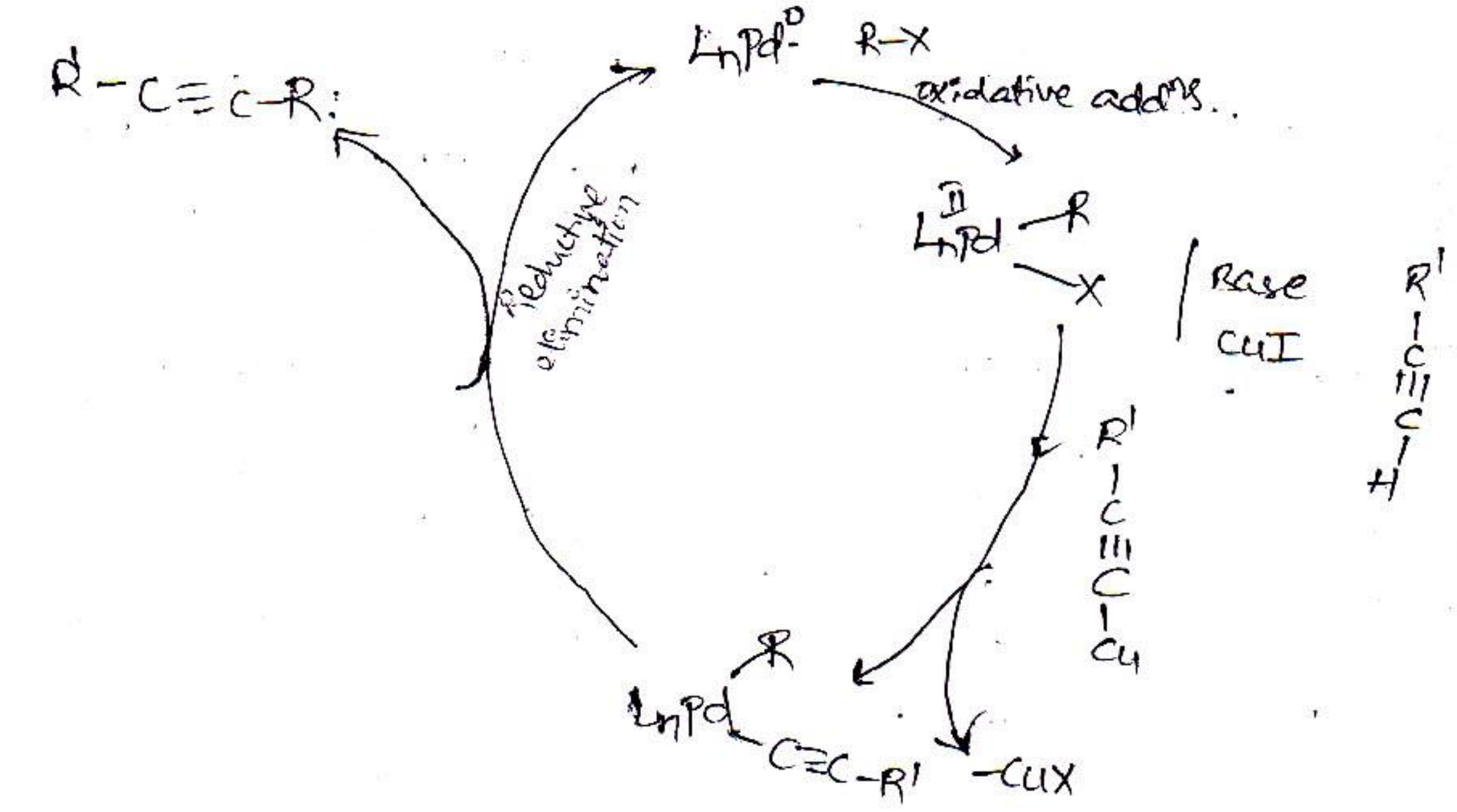
→ presence of any other functions (-OH, $-NH_2$, -CHO, -ester, etc..) will not influence reaction.

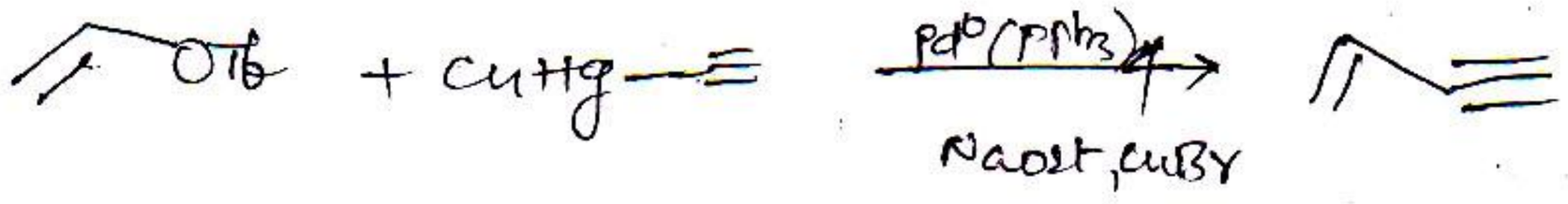
→ Internal alkynes will not undergo coupling



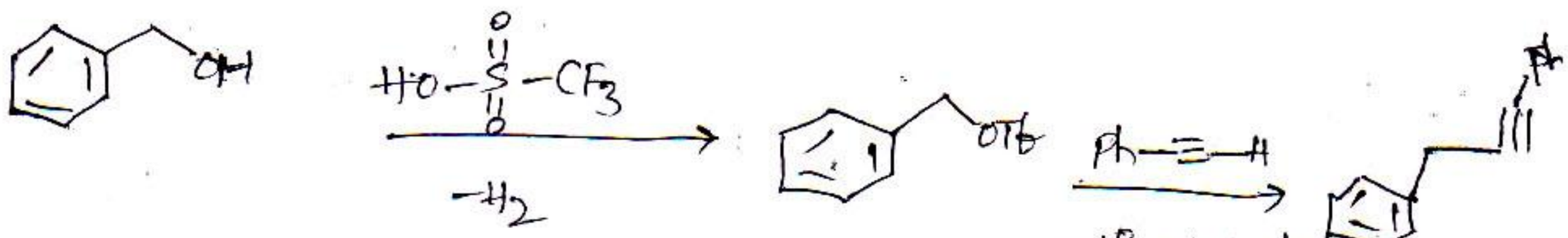
Copper ylide.

Mechanism:-

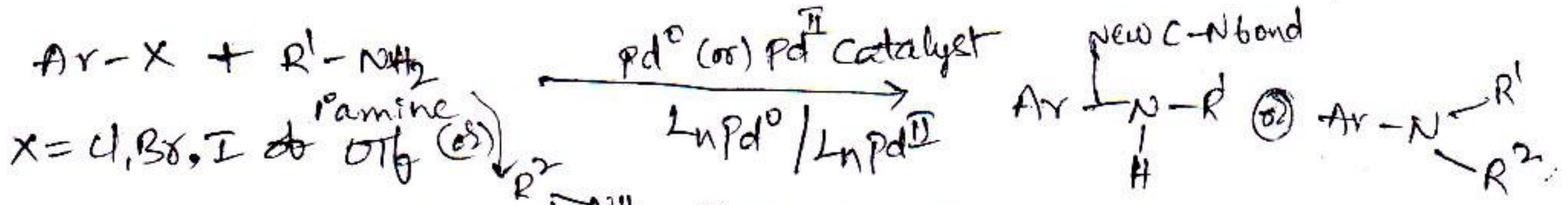


(*) 

f)



BUCHWALD – HARTWIG – COUPLING REACTION :- C–N, C–O reactions.



(or)



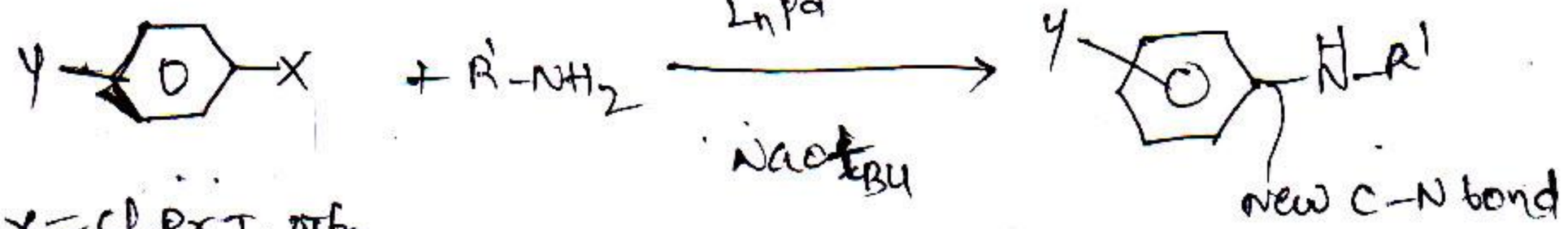
R, R' = Alkyl, Alkenyl, Aryl, Allyl, benzyl.

Base = Highly bulkies base, NaO^tBu ($tBuO^-Na^+$, $LiN(SiMe_3)_2$ (Hexamethyl disilazide)

→ Formation of new C–N bonding b/w aryl halides & triflates and 1° (or) 2° amines.

(or).

formation of new C–O bonding b/w aryl halides & triflates and Alcohols or phenols in the presence of Pd-catalyst and base called "Buchwald-Hartwig Coupling.



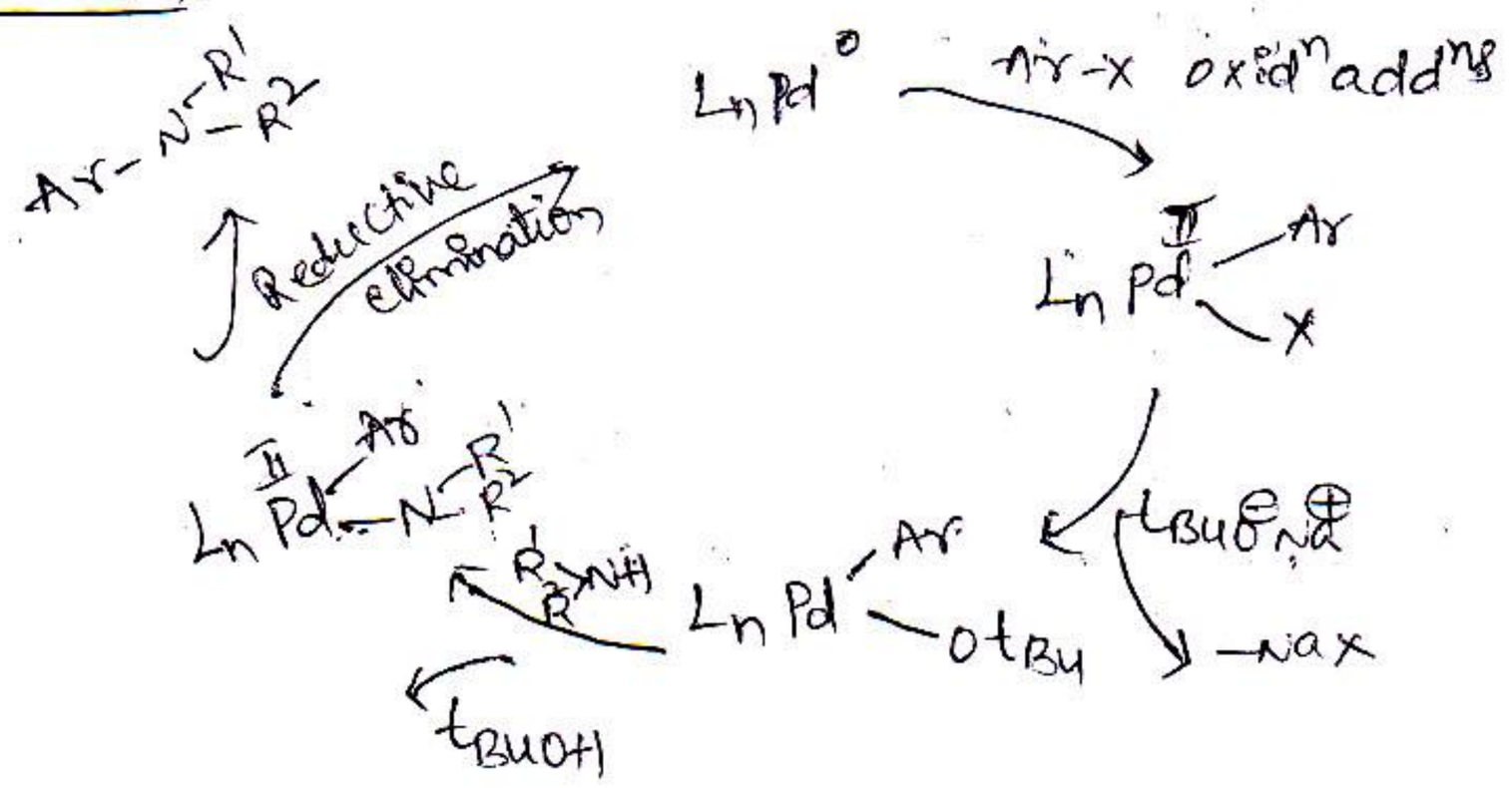
X = Cl, Br, I, OTf

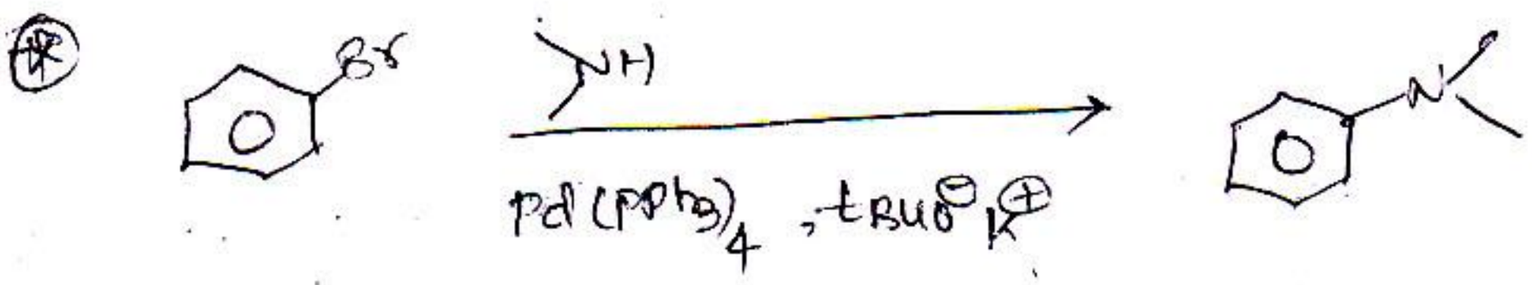
Y = o/m/p-Substituents

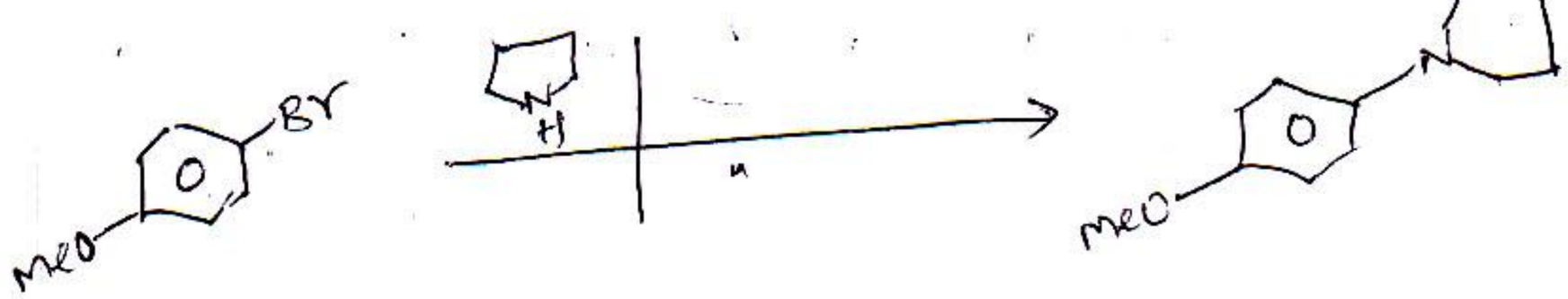
Alkyl, amine, etc

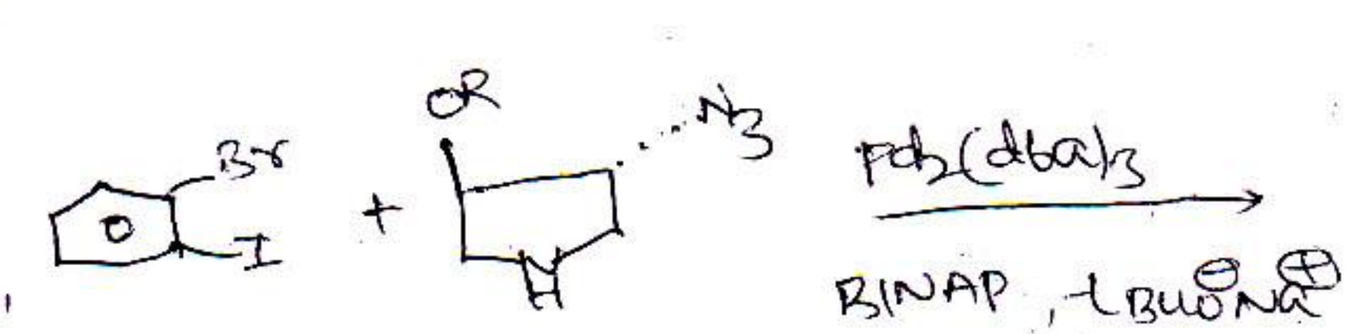


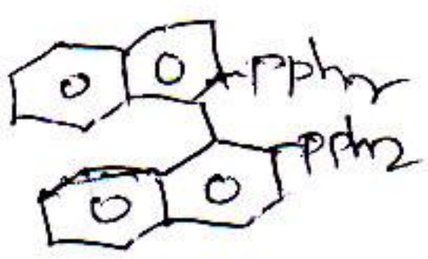
Mechanism



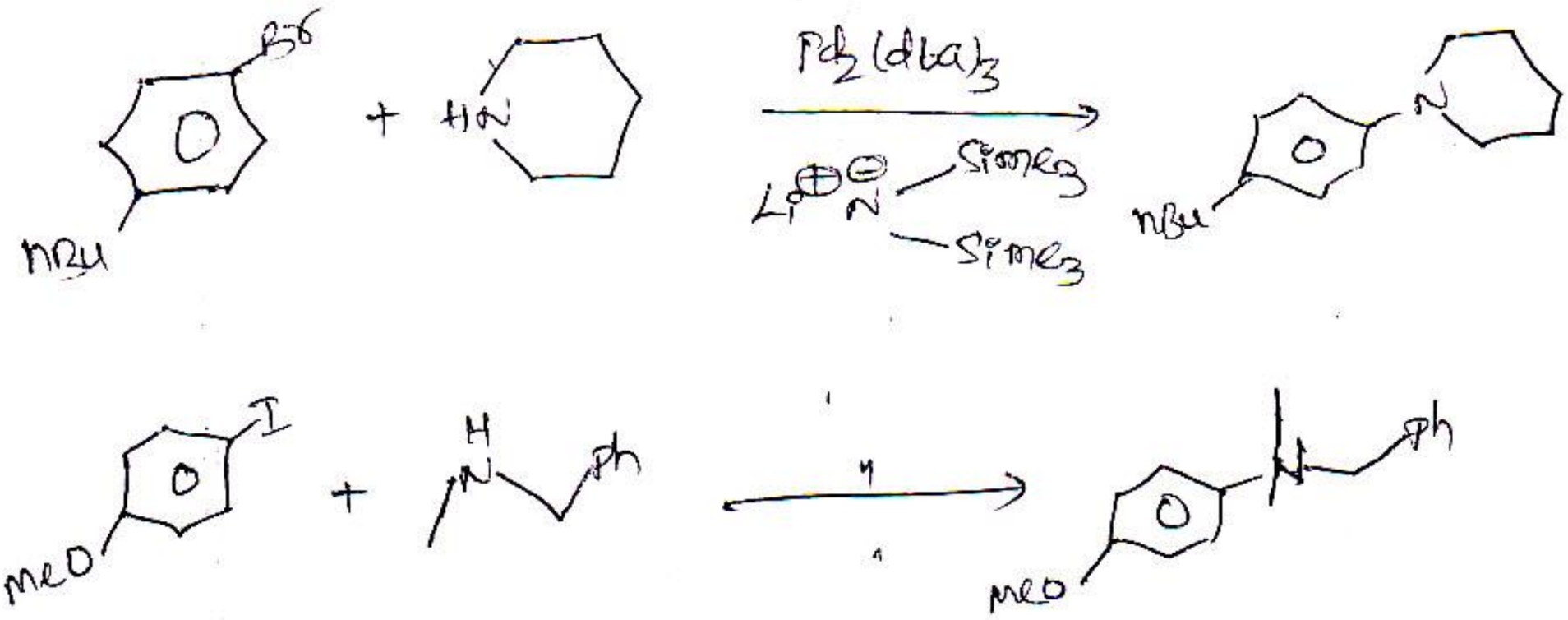








BINAP


Pd2(dba)3
SiMe3
SiMe3
nBu
MeO
Ph
Pd(PPh3)4
tBuO Na, K2CO3
Bn
Pd°-catalyst
tBuO Na
R
SUZUKI
Base
R-X + R'-Byn
HECK
Base
R-X + =-R
STILLE
R-X + R'-Sn(alkyl)3
Pd/Pd
SONOGHASHIRA
R-X + R'-≡-H
Cu(I) salts, Base
⇒ R-R'
R'-=-R
R'-≡-R
BUCHWALD
HARTWIG
Base.
Ar-X + R'-NH2
Ar-NH-R'
Ar-N(R')-R2
R'-CH
Ar-OH
Ar-OR'

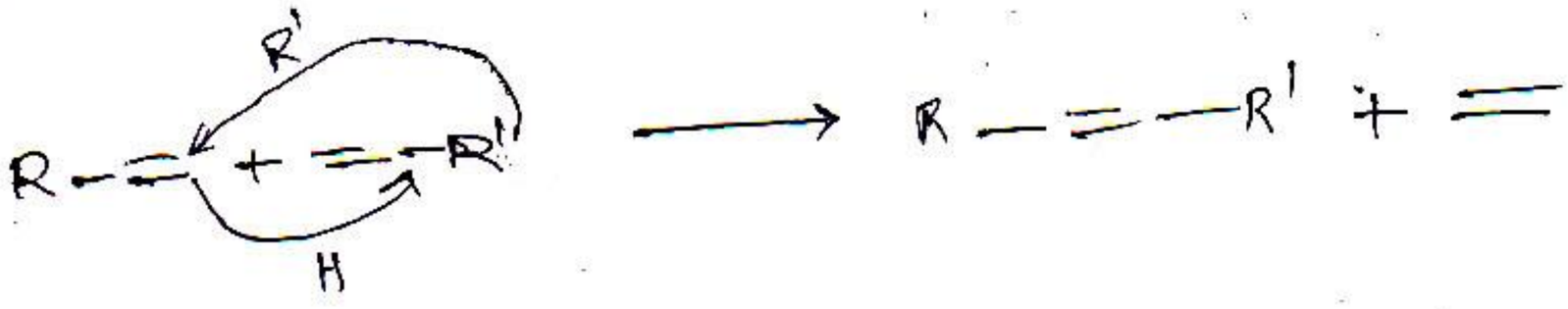
OLEFINE - METATHESIS

debin metathesis



-trans alkylinidation.

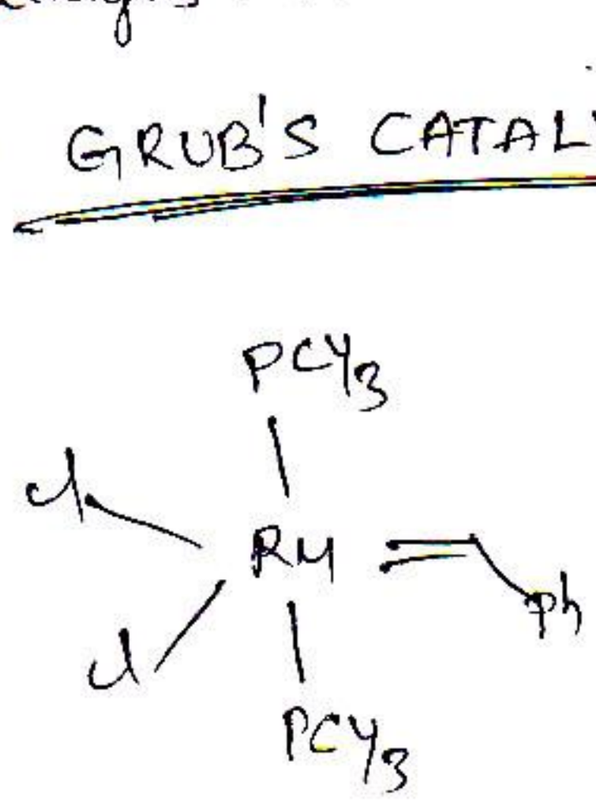
* (mutual) natural transfer of groups b/w different olefins called olefin - metathesis (or) Trans - alkylinidation.



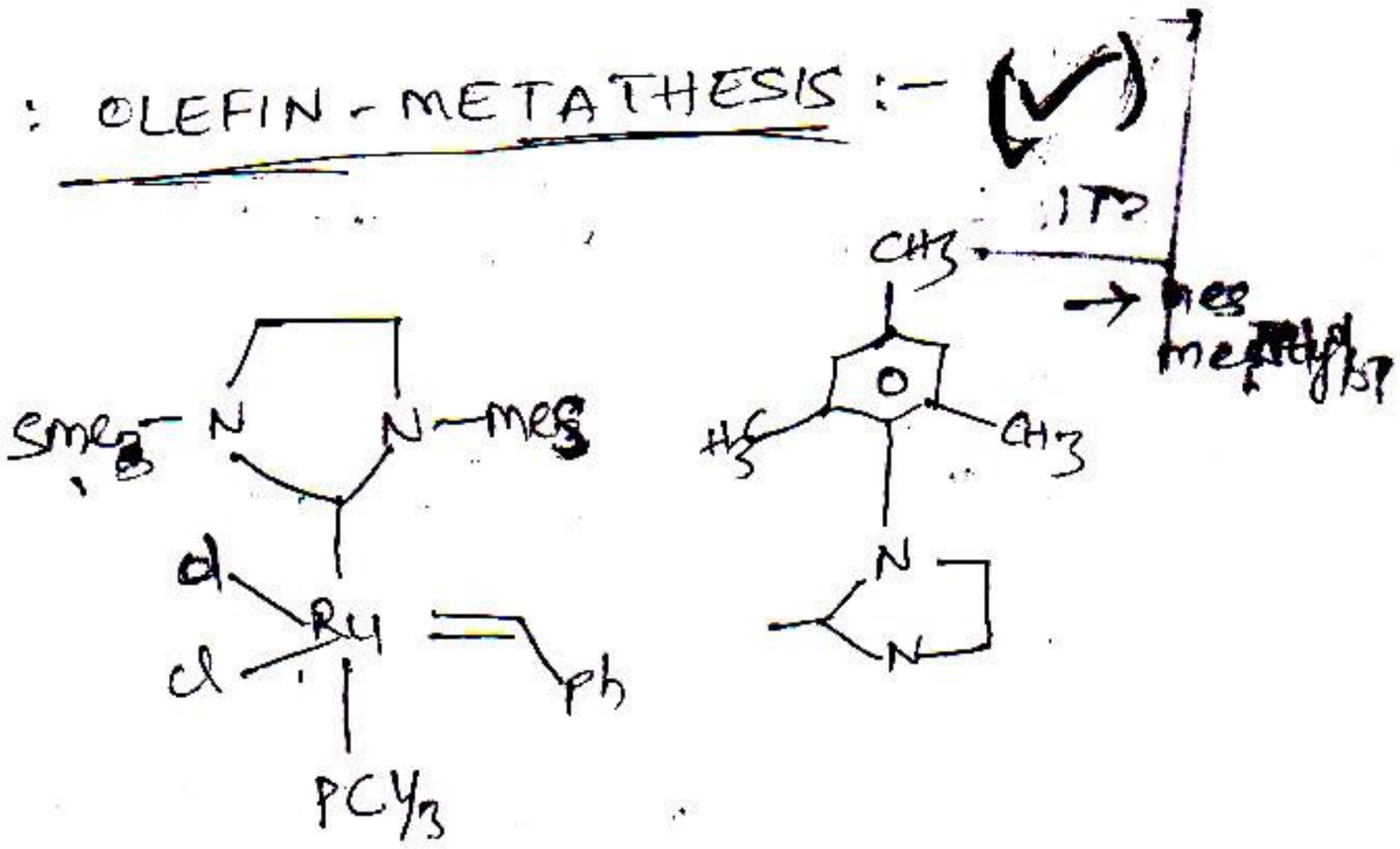


for olefin-metathesis Ru-catalysts are popular compare to Mo, Pd catalysts. etc...

* GRUB'S CATALYST : OLEFIN - METATHESIS :-



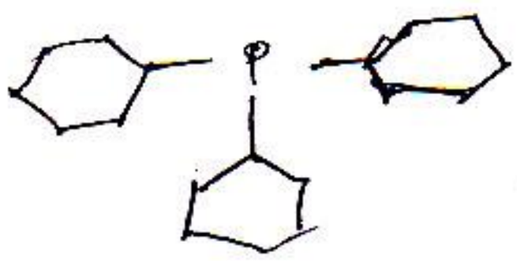
First generation Grub's catalyst



Second-generation Grub's catalyst

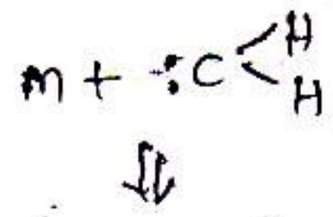
Cy = cyclohexyl

PCy3 =

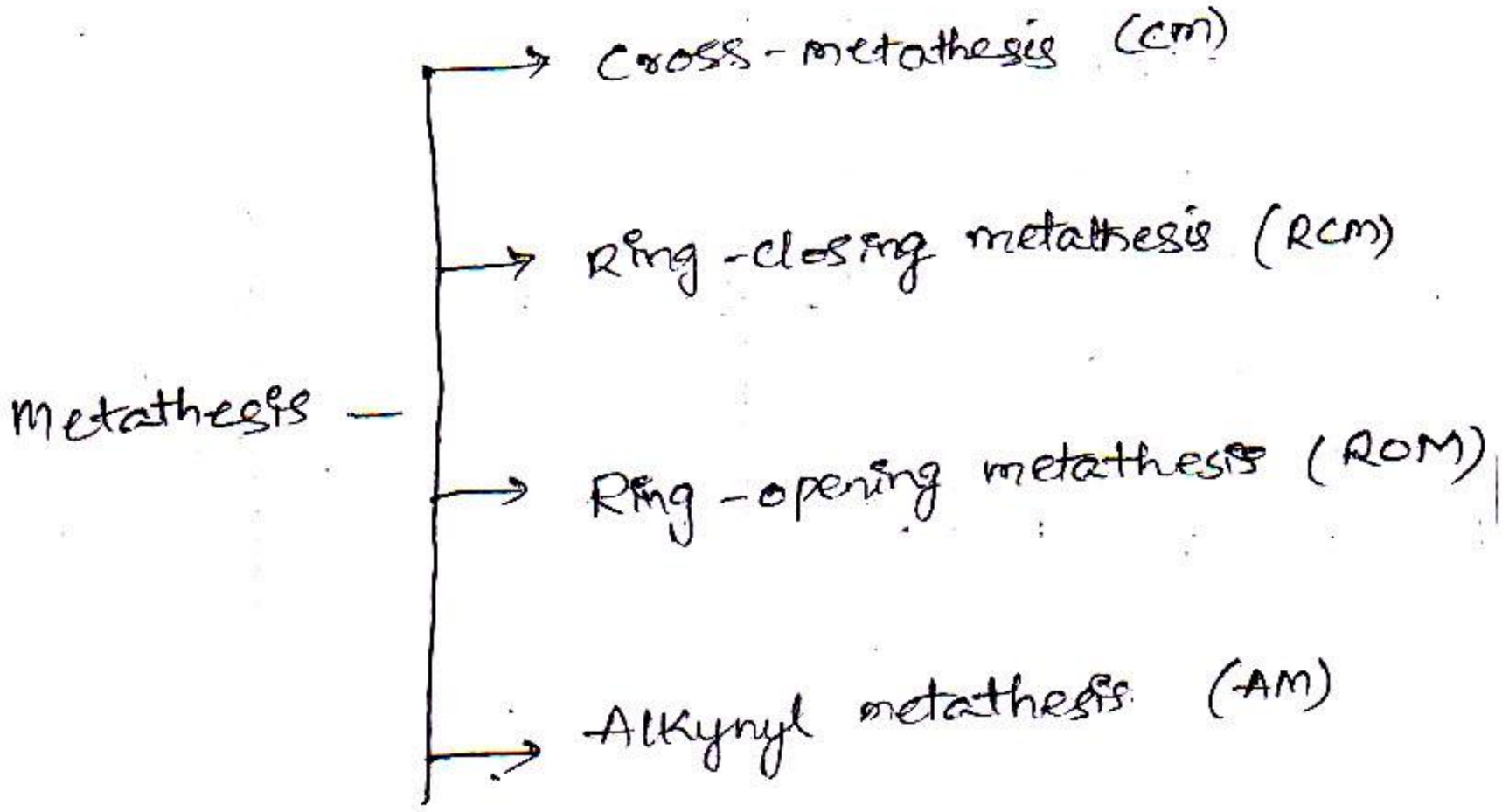




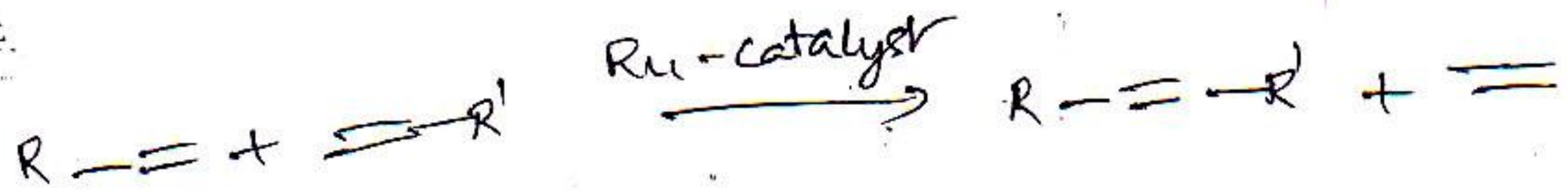
Simplified Grubb's catalyst



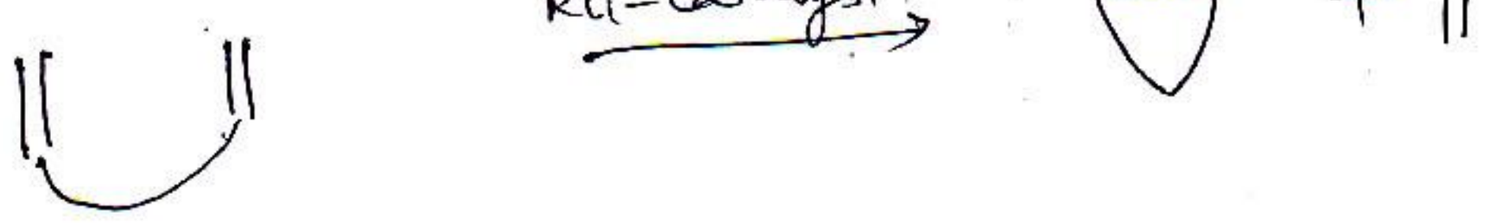
Metal bound carbene



CM :-



RCM :-



ROM :-



AM :-



* RCM are very common for organic synthesis
→ Easy to do rxn
→ All the other functions allowed to keep will not influence reaction

→ High % of yield

→ various types of olifinic groups can be developed (cyclic, acyclic

→ Good method for preparation of medium size cyclic olefins

[7,8 membered olefins etc ...]

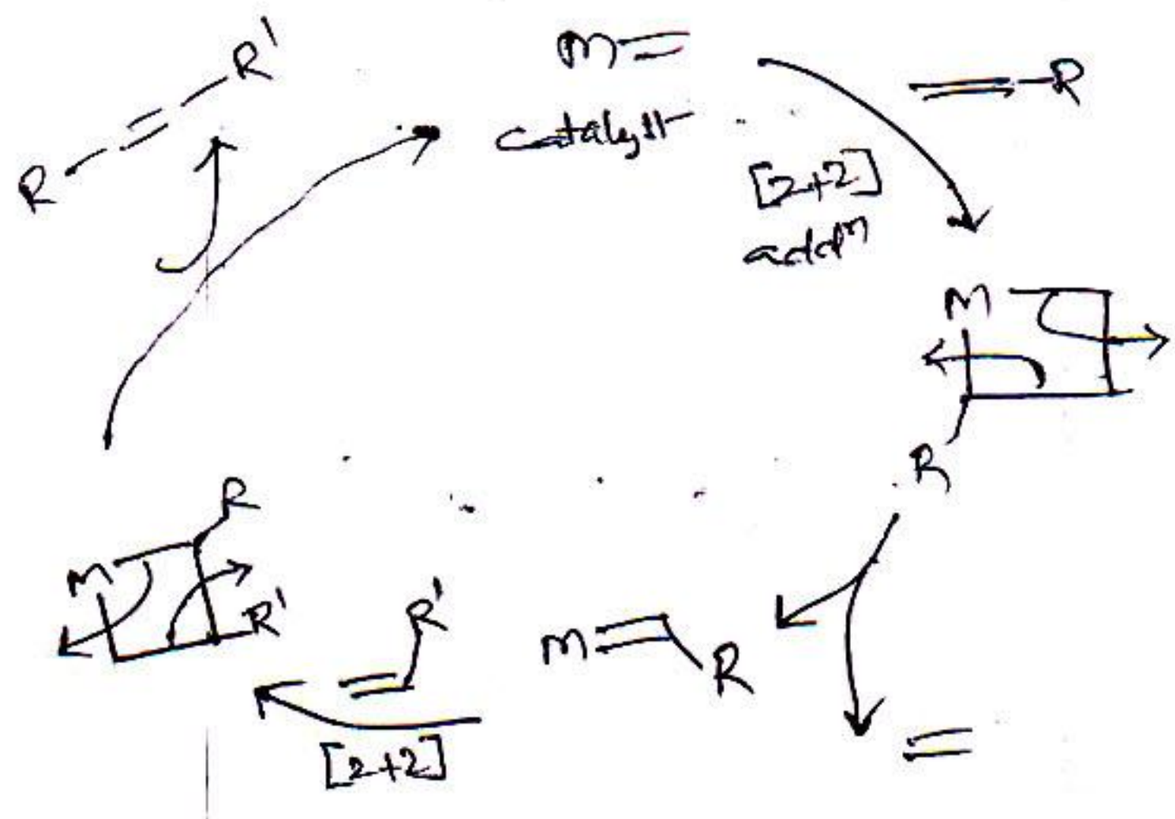
→ easy to handling all the components

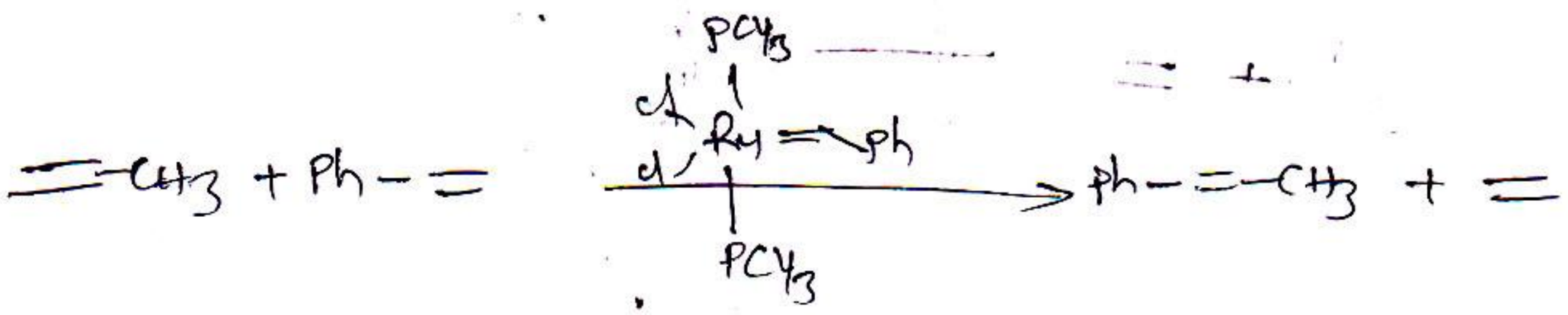
→ not influence by AIR or MOISTURE or WATER WET

CM:-

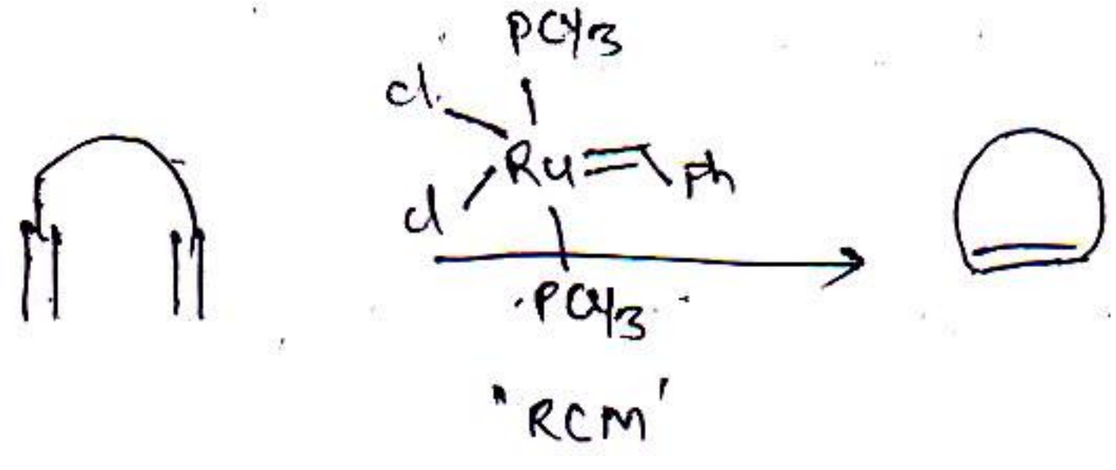








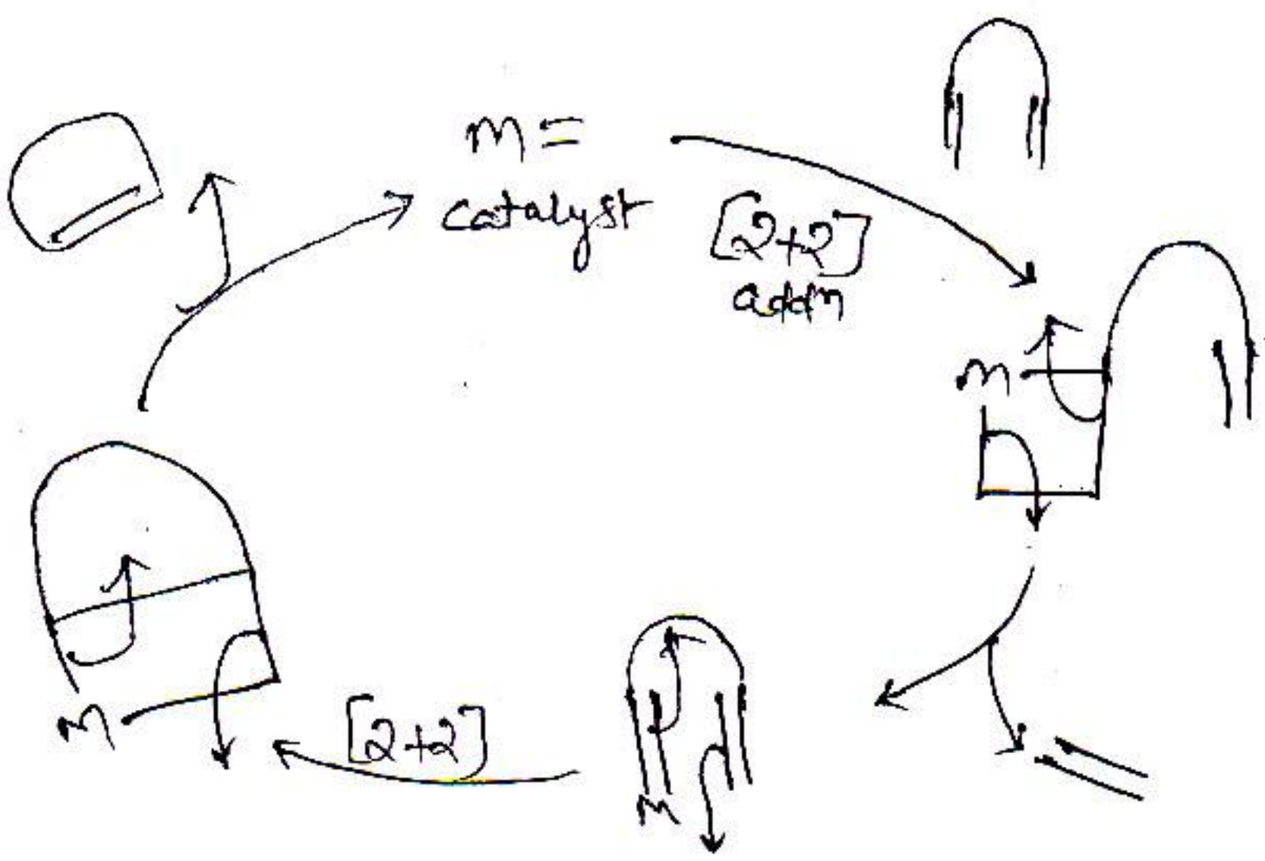
RCM (Ring closing metathesis) :-



"RCM"

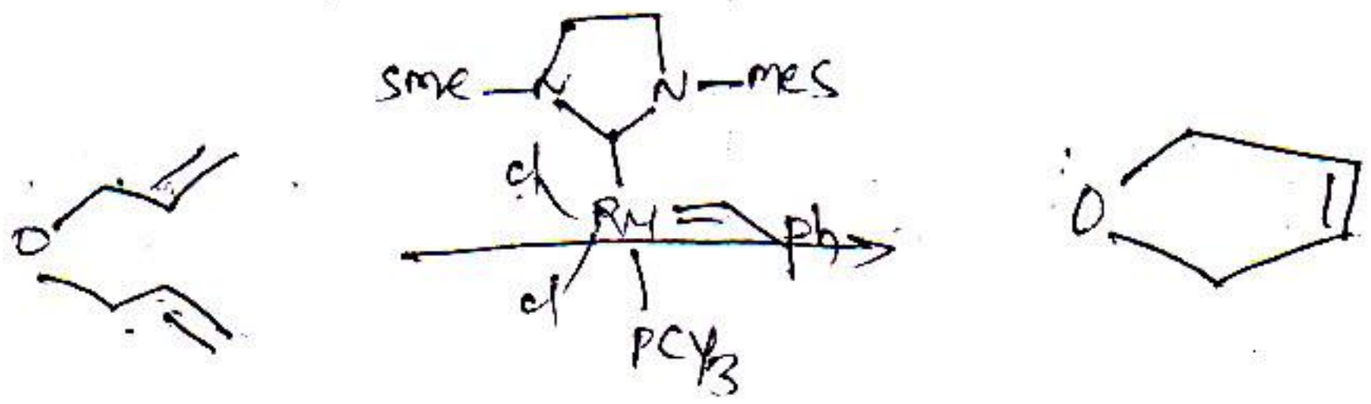


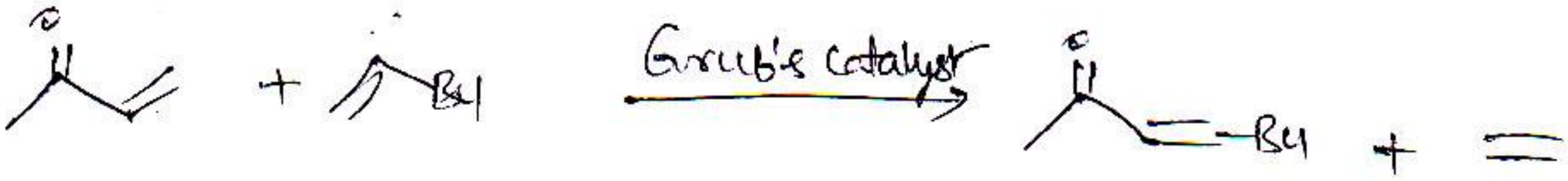
mech:-

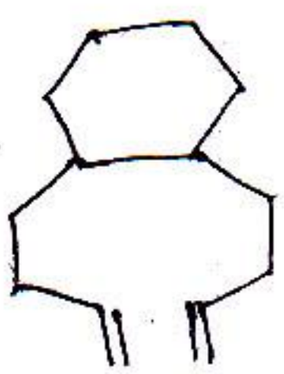


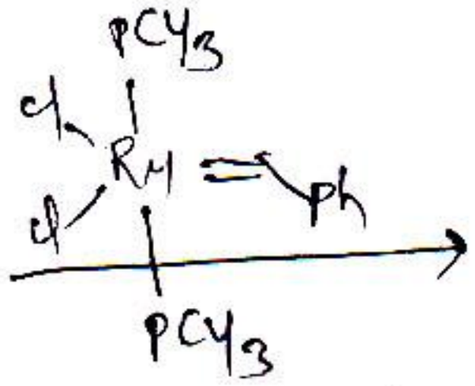
[2+2] addn b/w olefins and catalyst followed by elimination leads to formation of olefins with cyclisation.

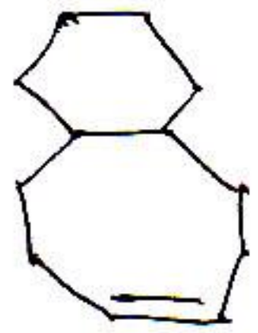
eg:-



* 



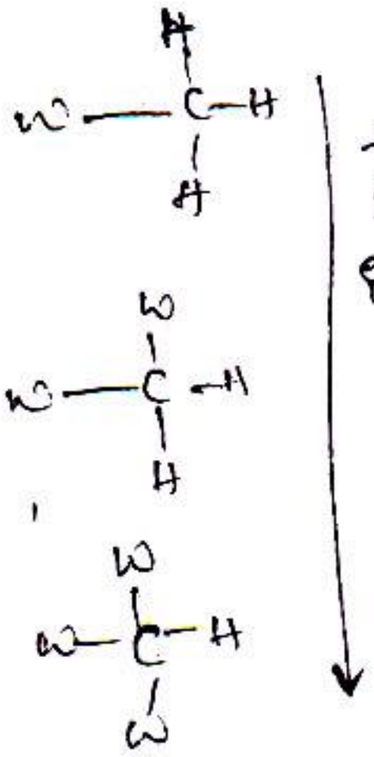




MANNICH REACTION :-

- Acidic group & carbon group which can be ionised H/w carbanion and H^+, called active C–H group

→ carbon group attached to withdrawing gp called Acidic/Active



Acidic Strength increases

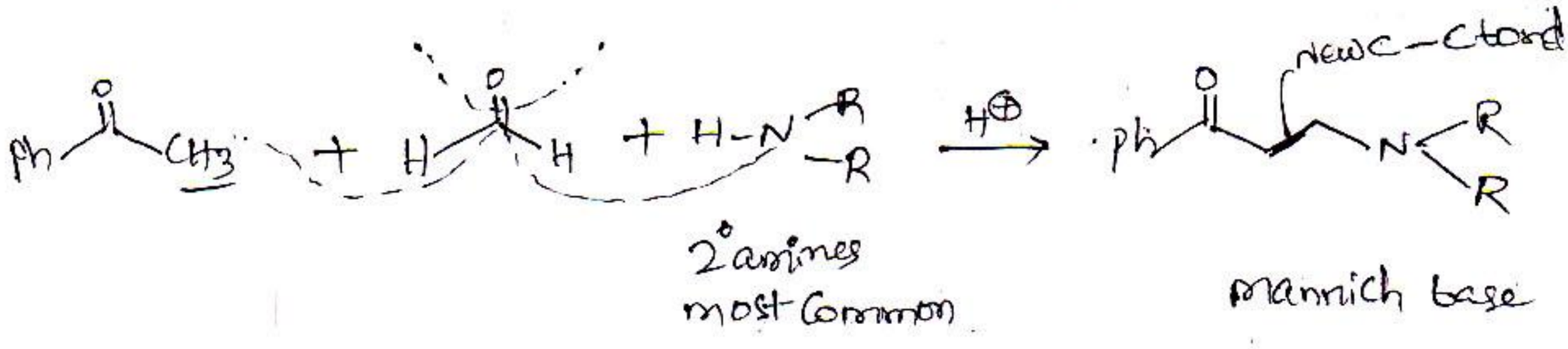
$H_3C-\overset{O}{\overset{\|}{C}}-H$, H_3C-CO_2H , $H_3C-\overset{O}{\overset{\|}{C}}-R$, H_3C-CN , H_3C-NO_2

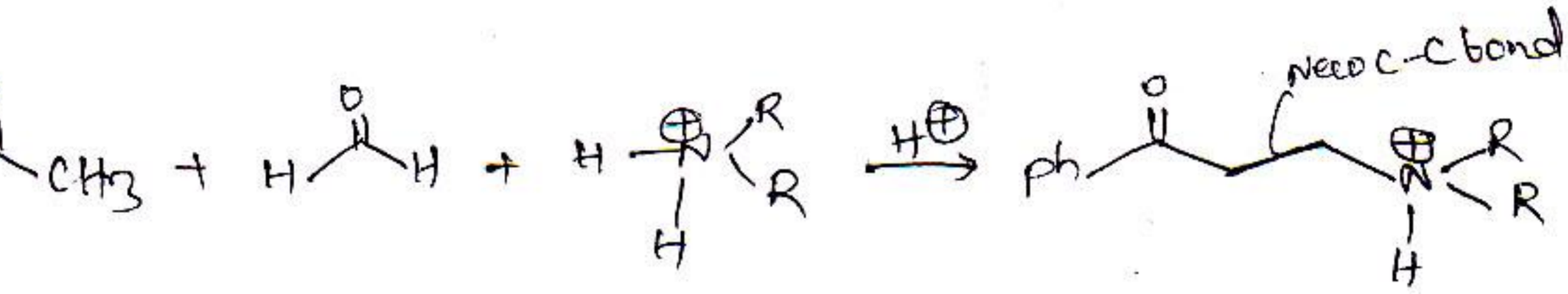
- Amino methylation of active C–H functions using formaldehyde and amines ' MANNICH RXN"

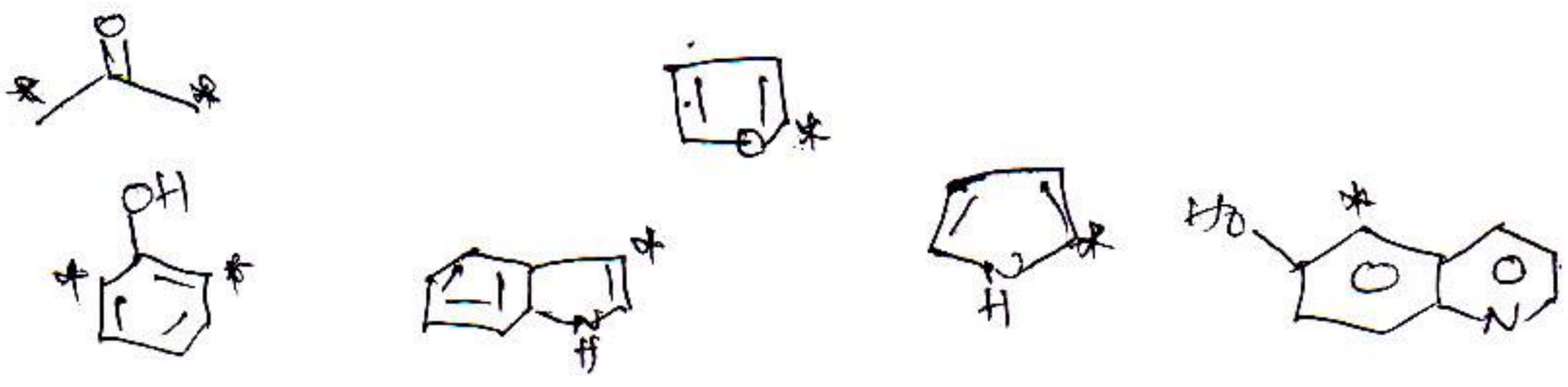
Compd having active C–H + HCHO + Amines $\xrightarrow{H^+}$ Mannich Base

(or)

Compd having active C–H + HCHO + Salt of Amine $\xrightarrow{H^\oplus}$ mannich salt

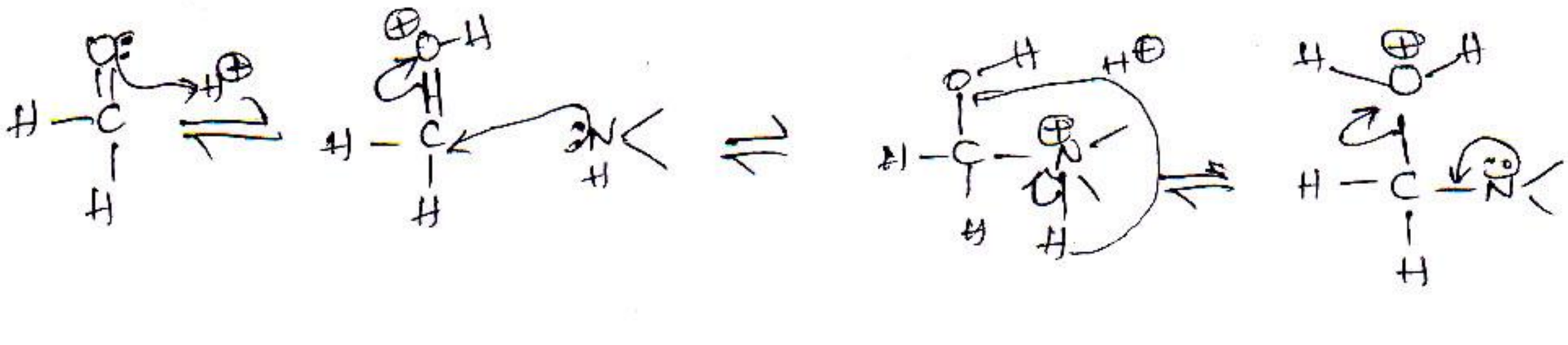






Mechanism:-

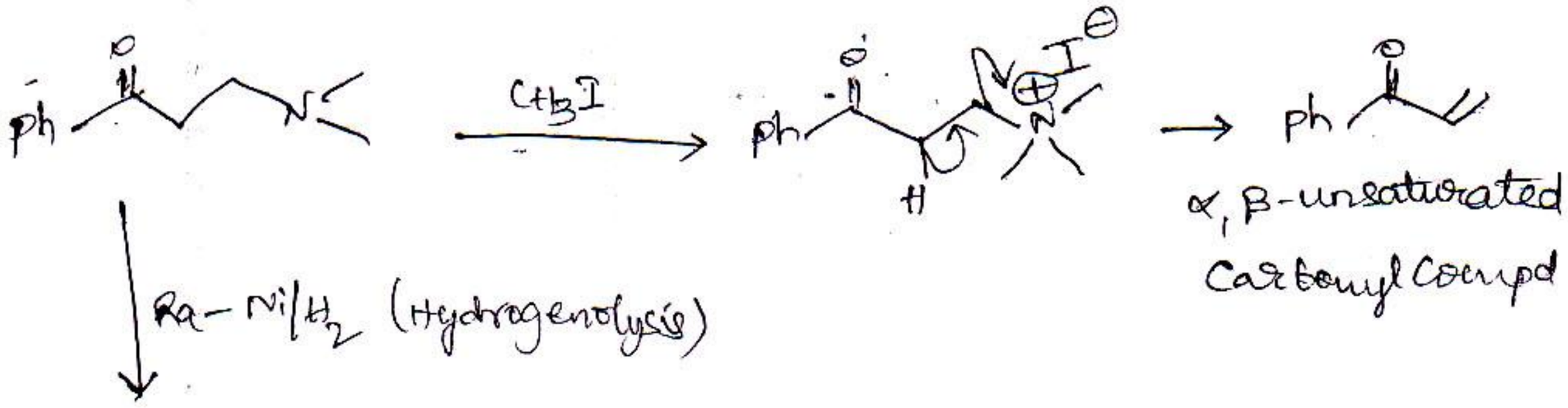


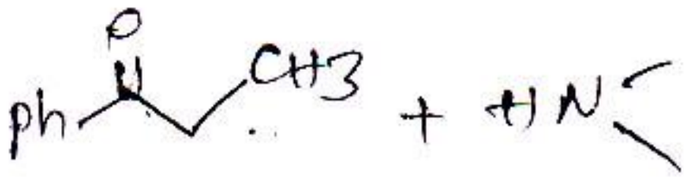




Immonium ions, con) Immonium ions

Enol





Secondary amine may be cyclic



Pyrrolidine



Piperidine

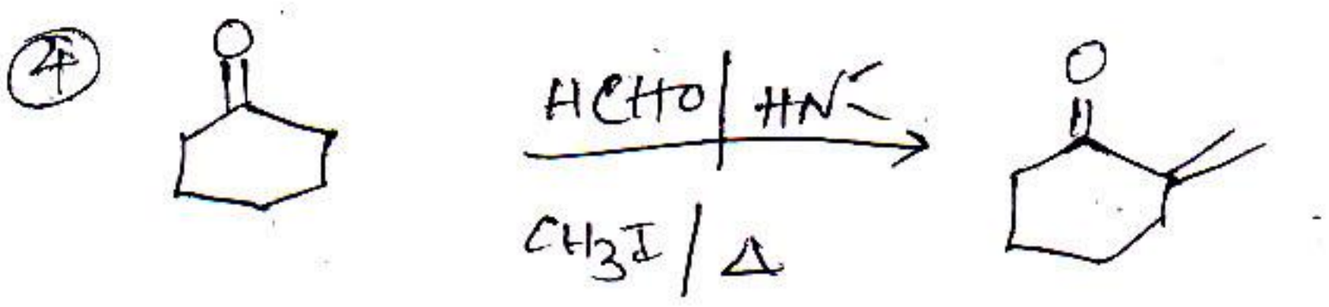


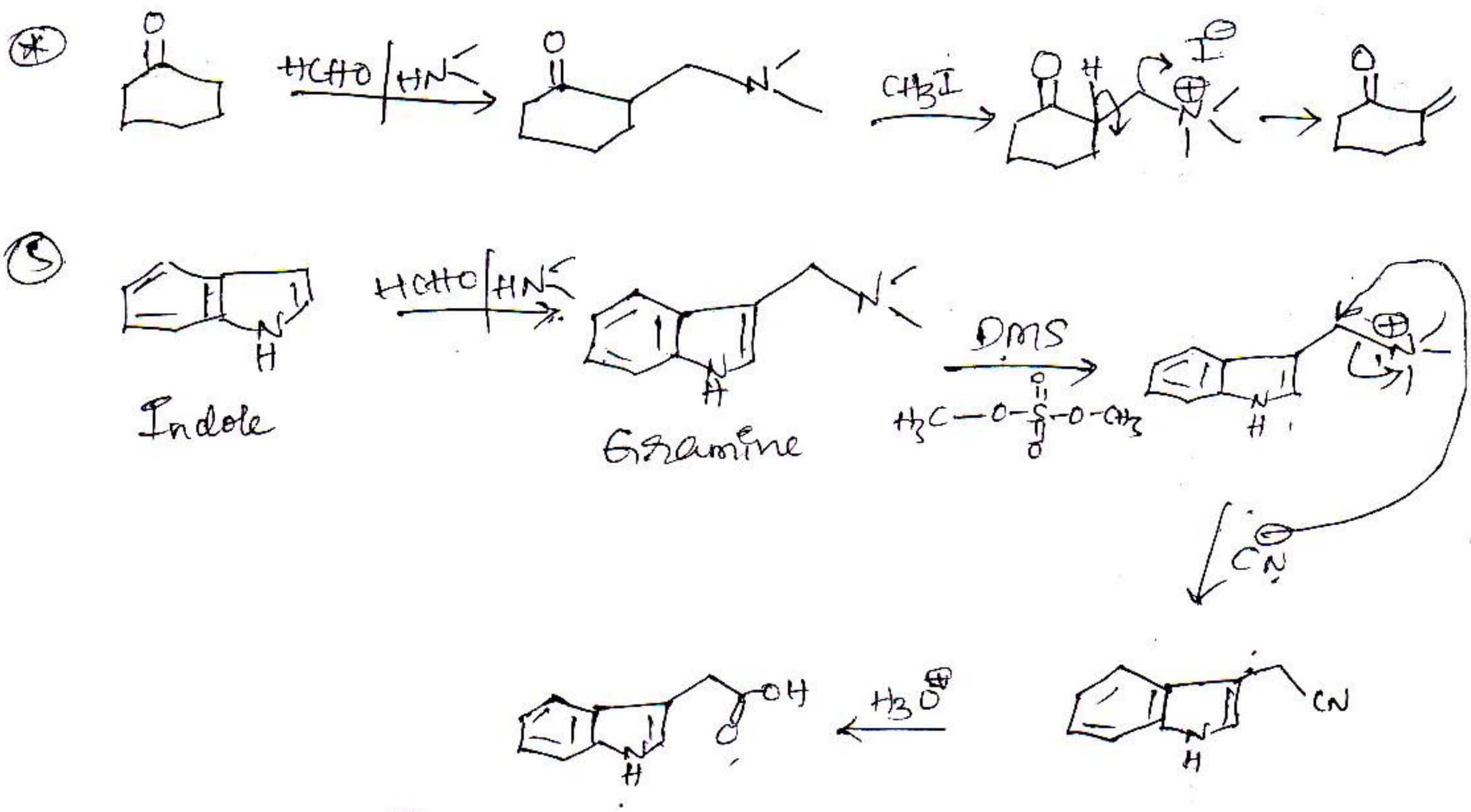
morpholine

① 

② $H_3C-C\equiv C-H \xrightarrow[HCHO]{HN<} HC-C\equiv C-CH_2-N<$ (3)

③ 

④ 

⑤ 

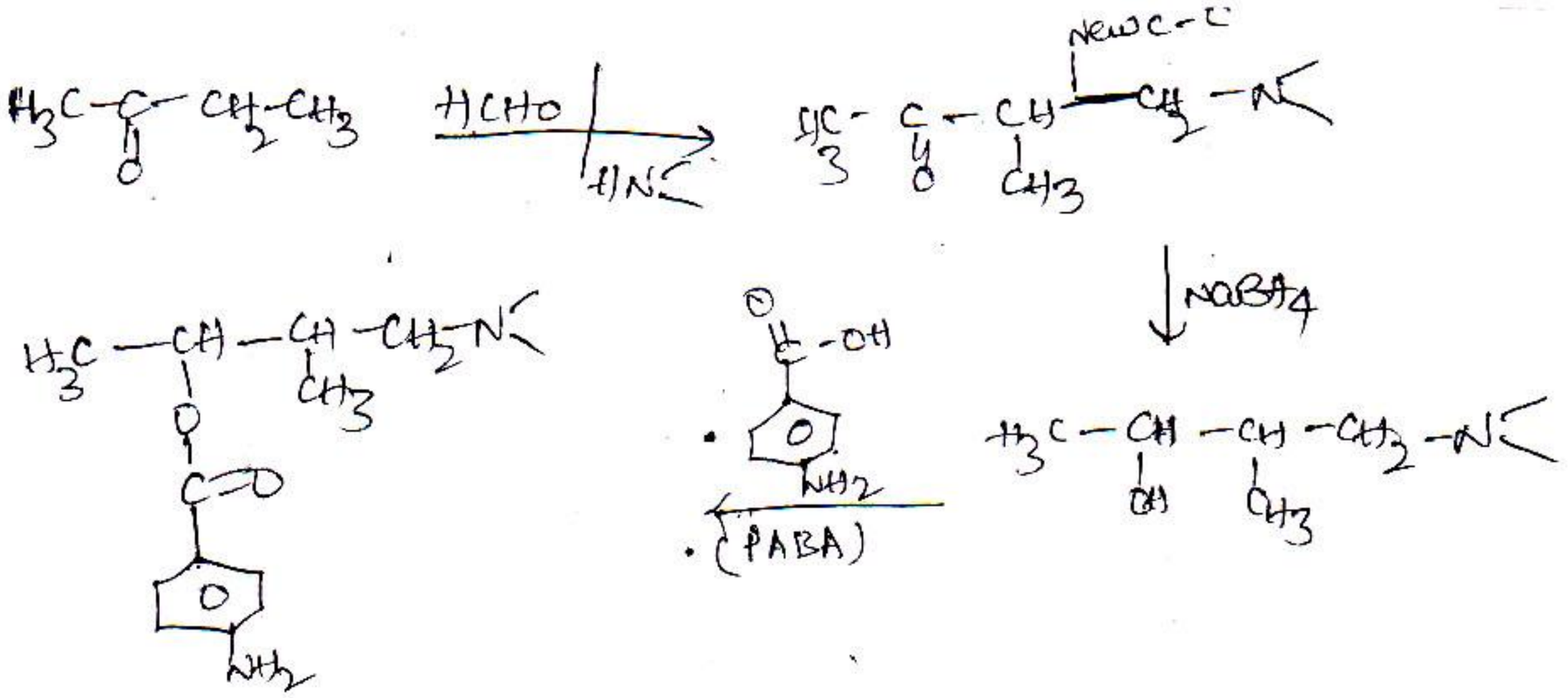
Indole

Gramine

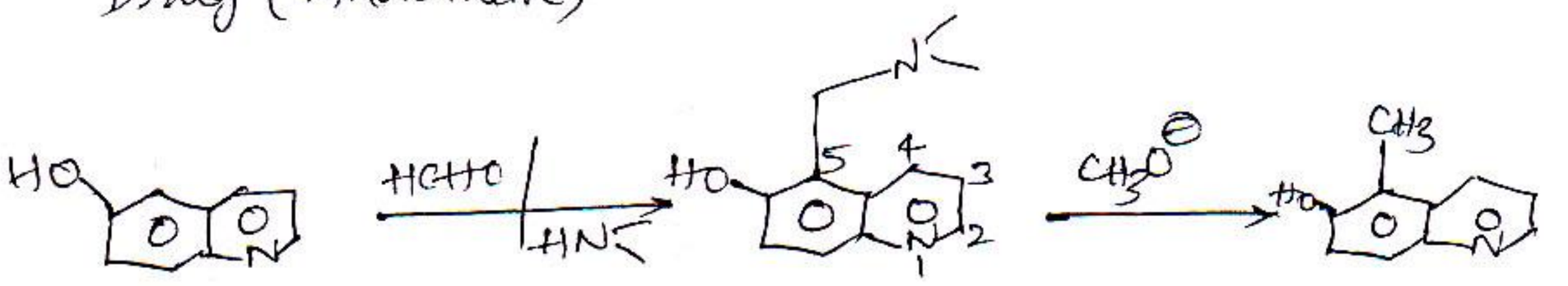
Indole-3-aceticacid

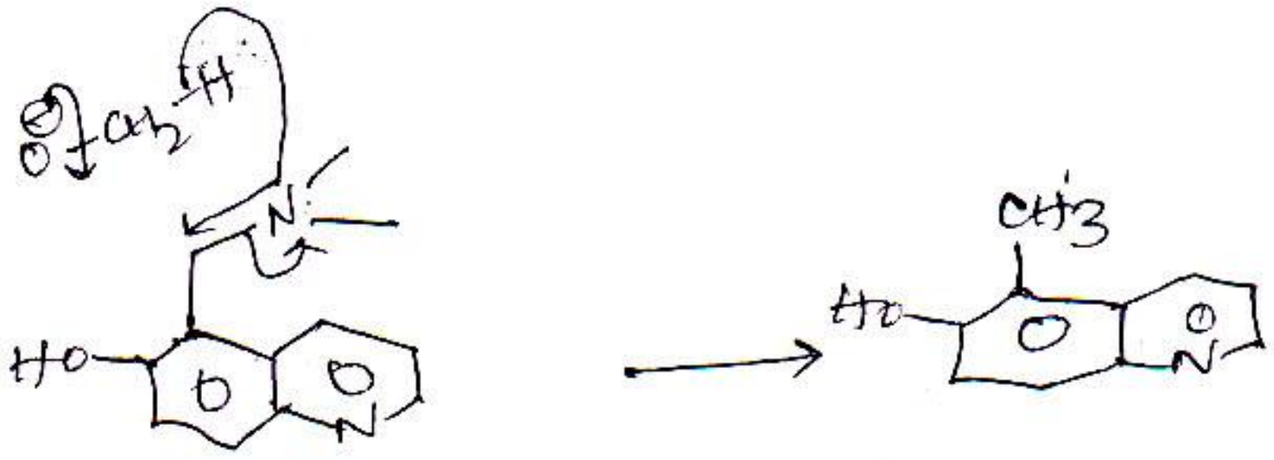
(or)

Heteroauxine

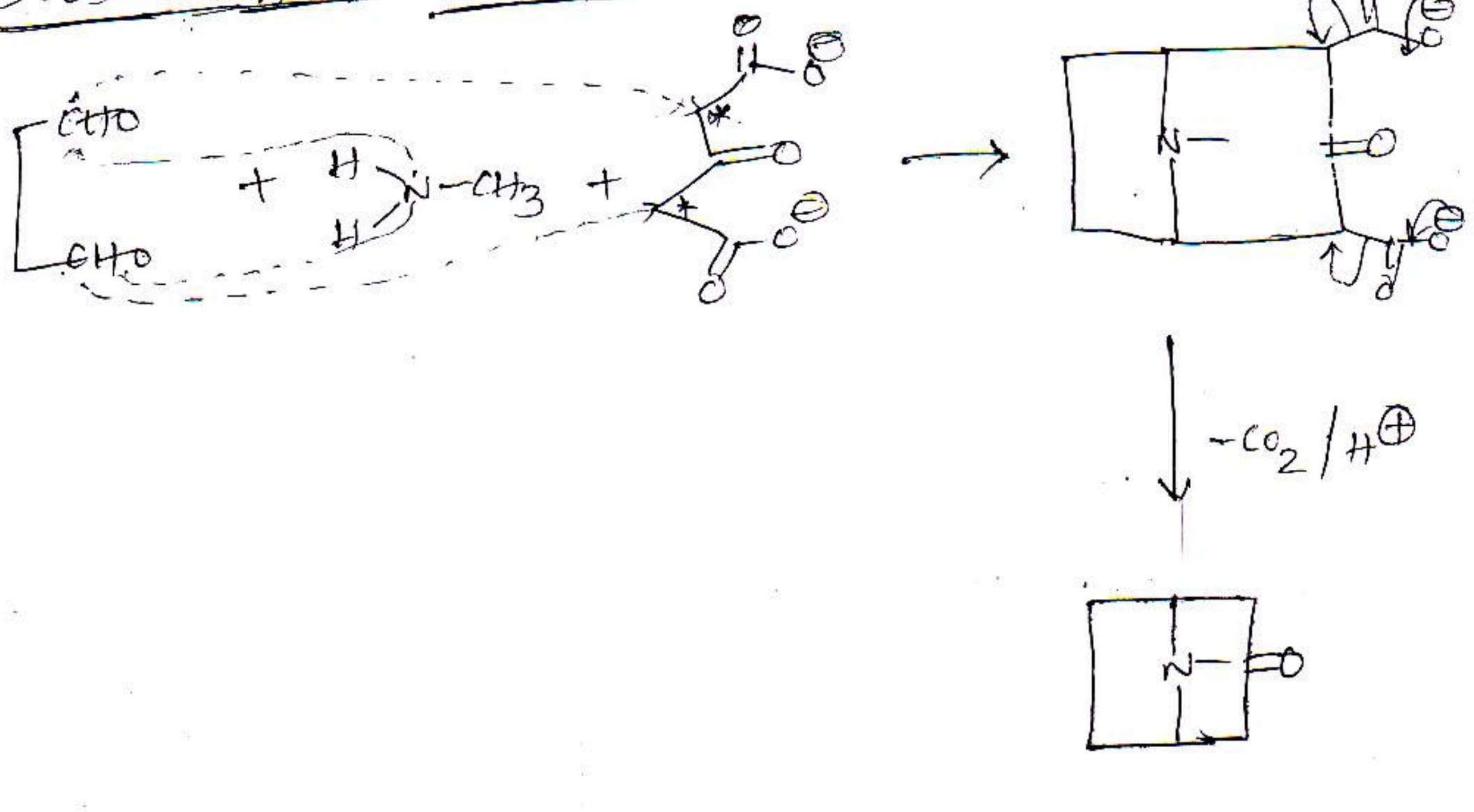


Tutocain ಎಂಬ ಔಷಧ
Drug (Anasthetic)





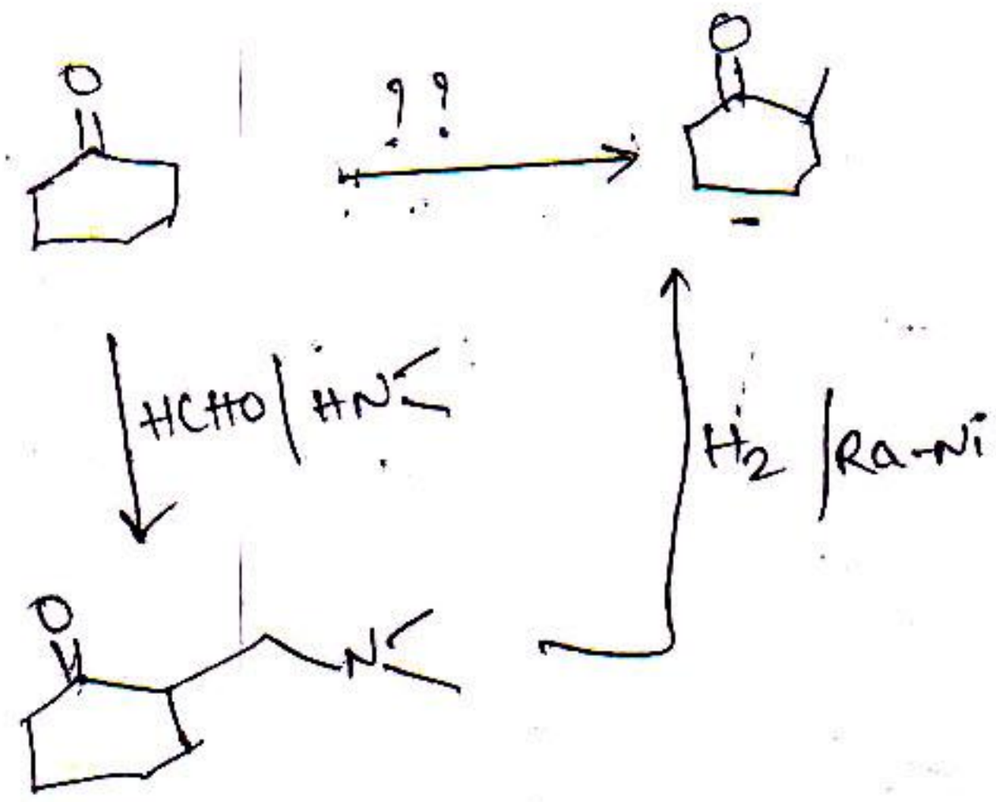
DOUBLE - MANNICH REACTION :-



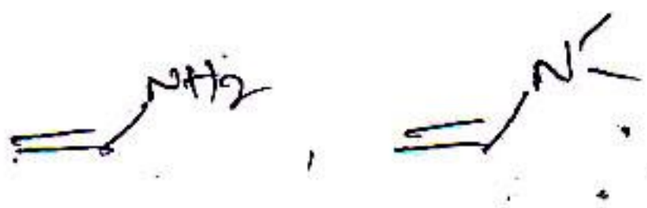


INTRAMOLECULAR MANNICH RXN





STORK-ENAMINE REACTION

ENAMINE:  , ENOLE

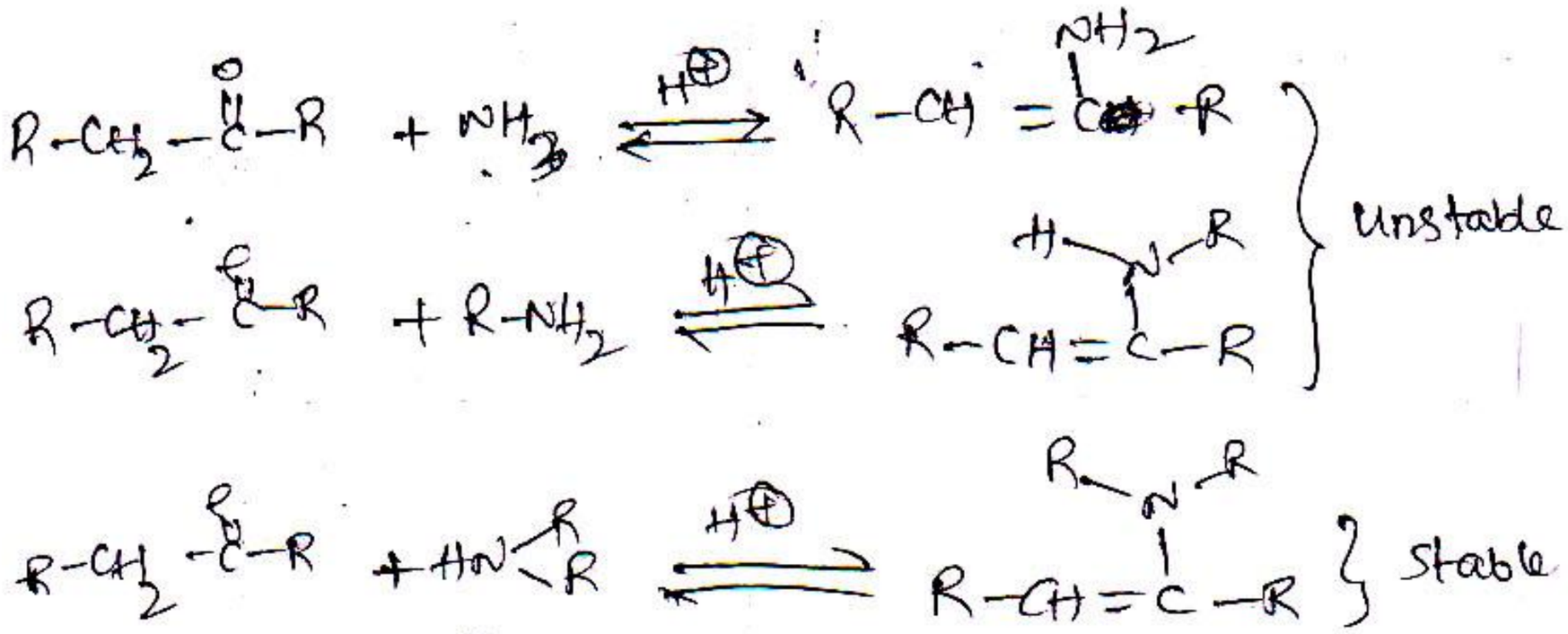
* Amino alkenes are Enamines

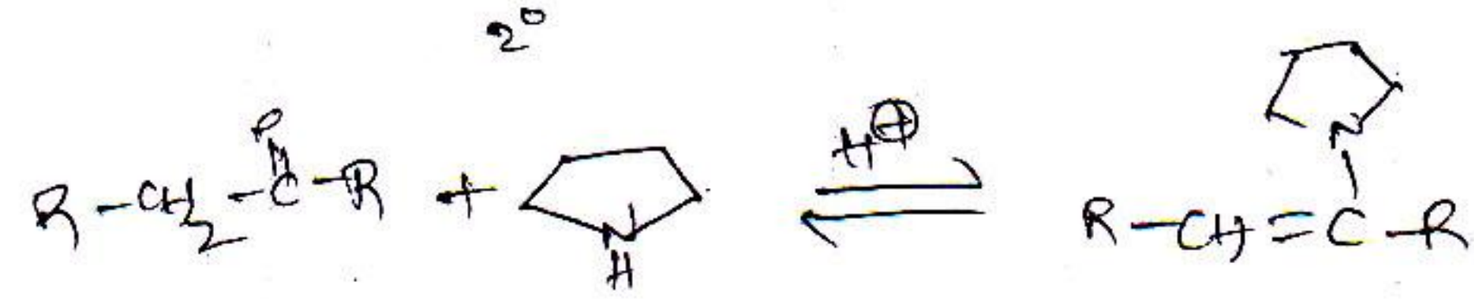
prepn of Enamines

Carbonyl Compds having α, –CH functions on reacts with amines in acidic medium produces Enamines

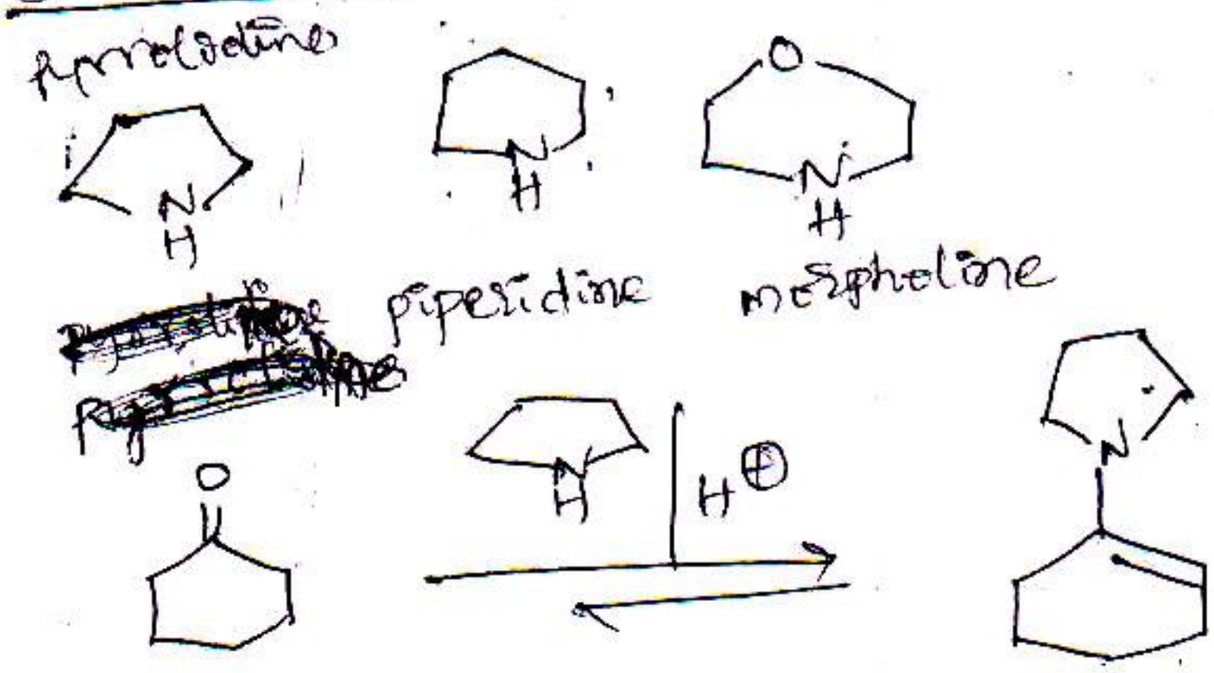
→ Enamines of 2°-amines more stable than enamines of 1°-amines

(or) ammonia.

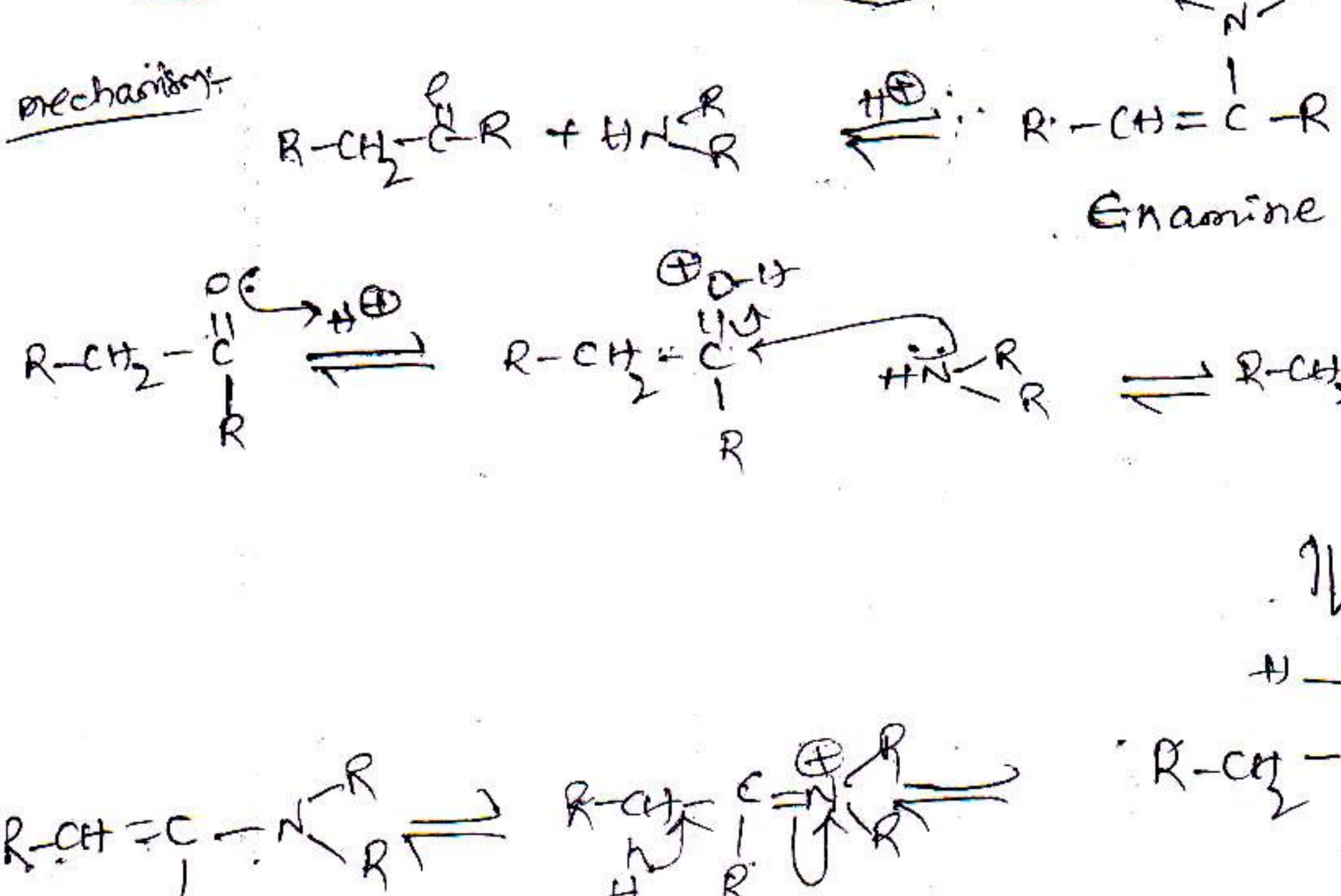




Cyclic amines :-



Mechanism :-

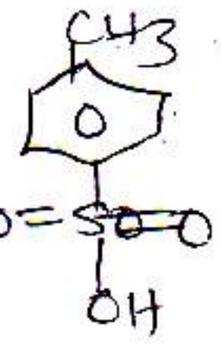


ENAMINE

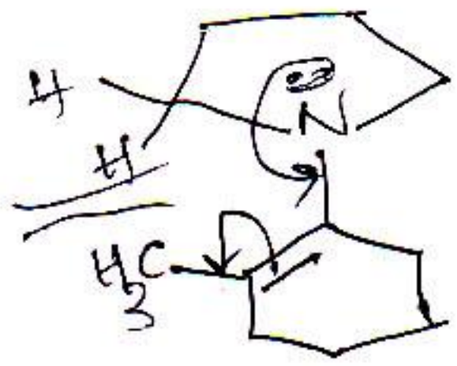
Regioselectivity in formation of Enamines



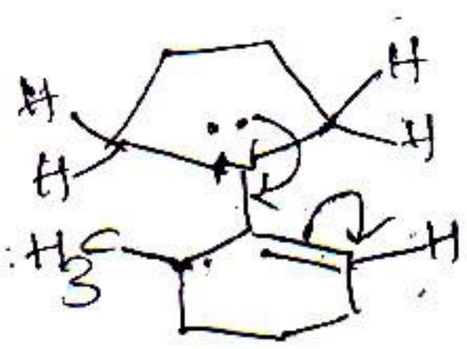
PTSA = P-Toulenesulphonic acid



In the case of unsymmetrical ketone, orientation of db predominately at less substituted α-position, resulting product is major (or) less substituted enamine as major.



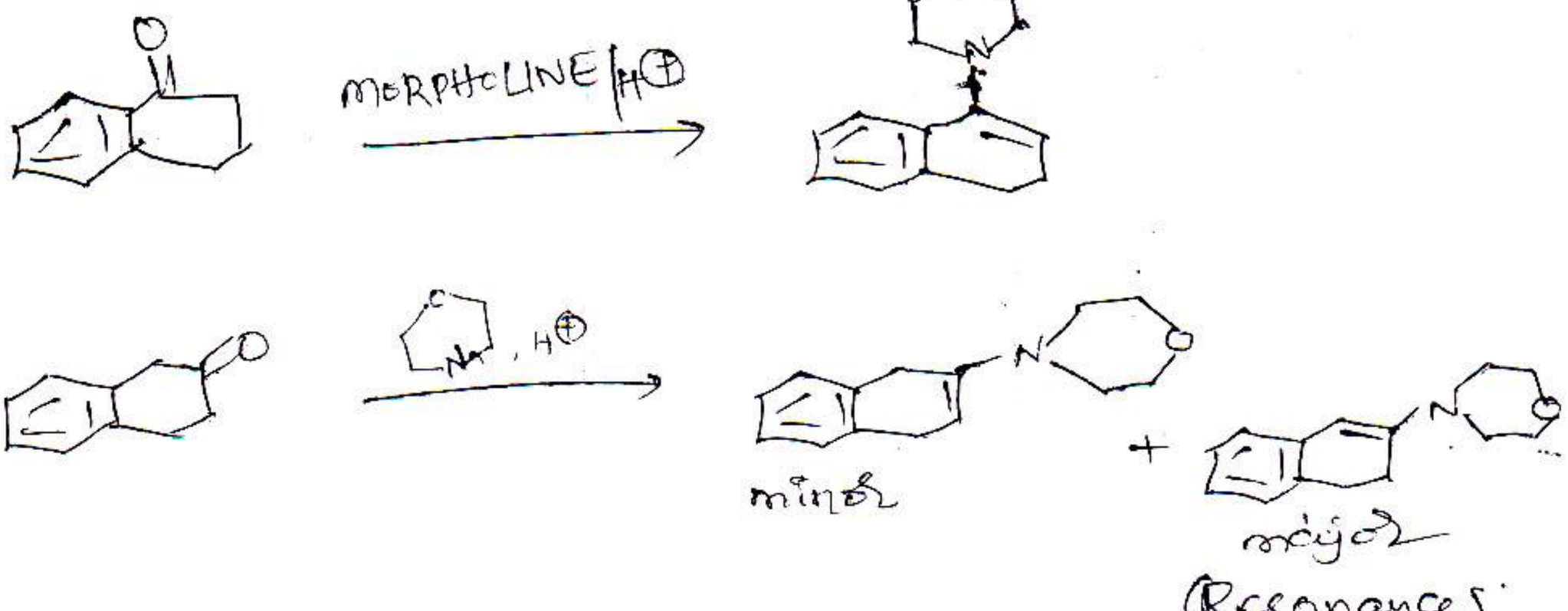
I

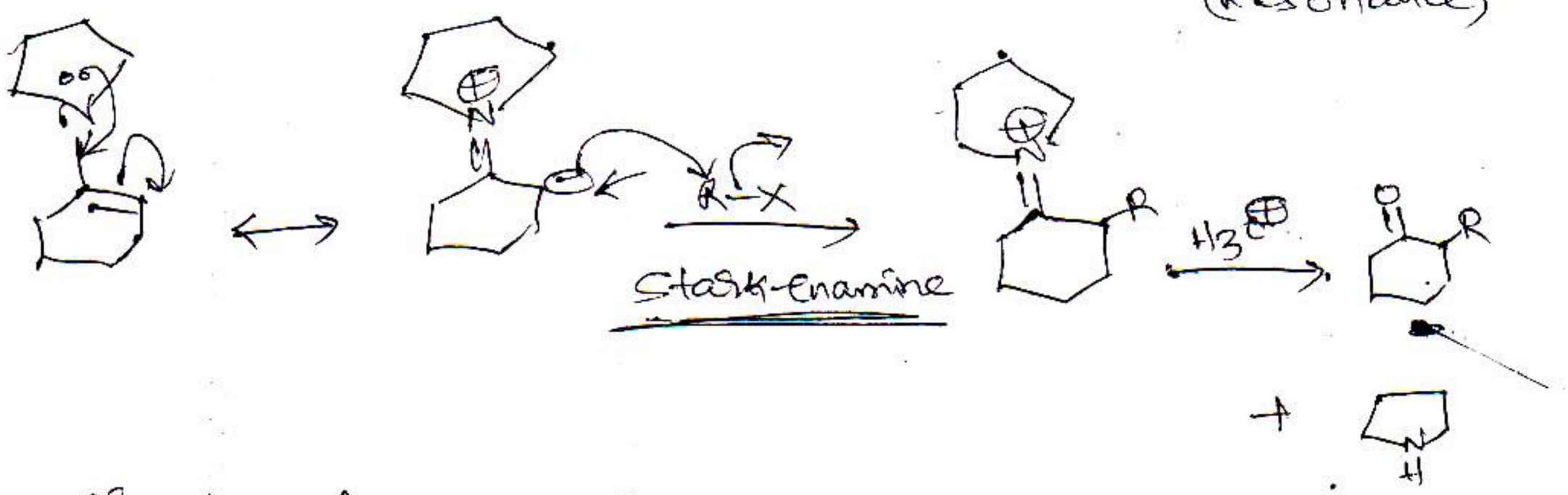


II

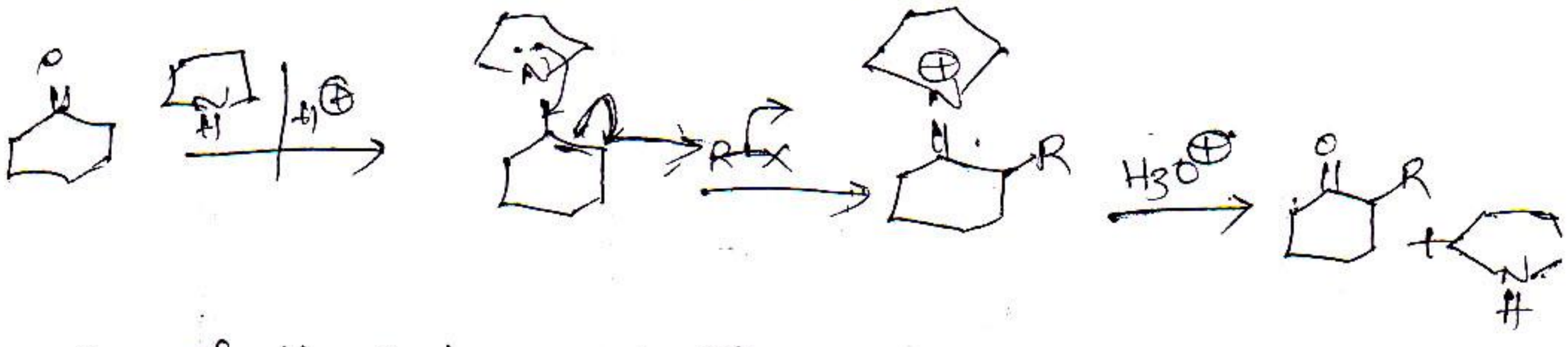
In Ist isomer steric crowding blw $\alpha-CH_2$ of amine and $-CH_3$ group of olefin hindered resonance is stabilized isomer % of formation loco.

In IInd isomer free from steric crowding, in plane arrangement of amino & olefin groups free delocalisation Stabilized isomer, high % of formation

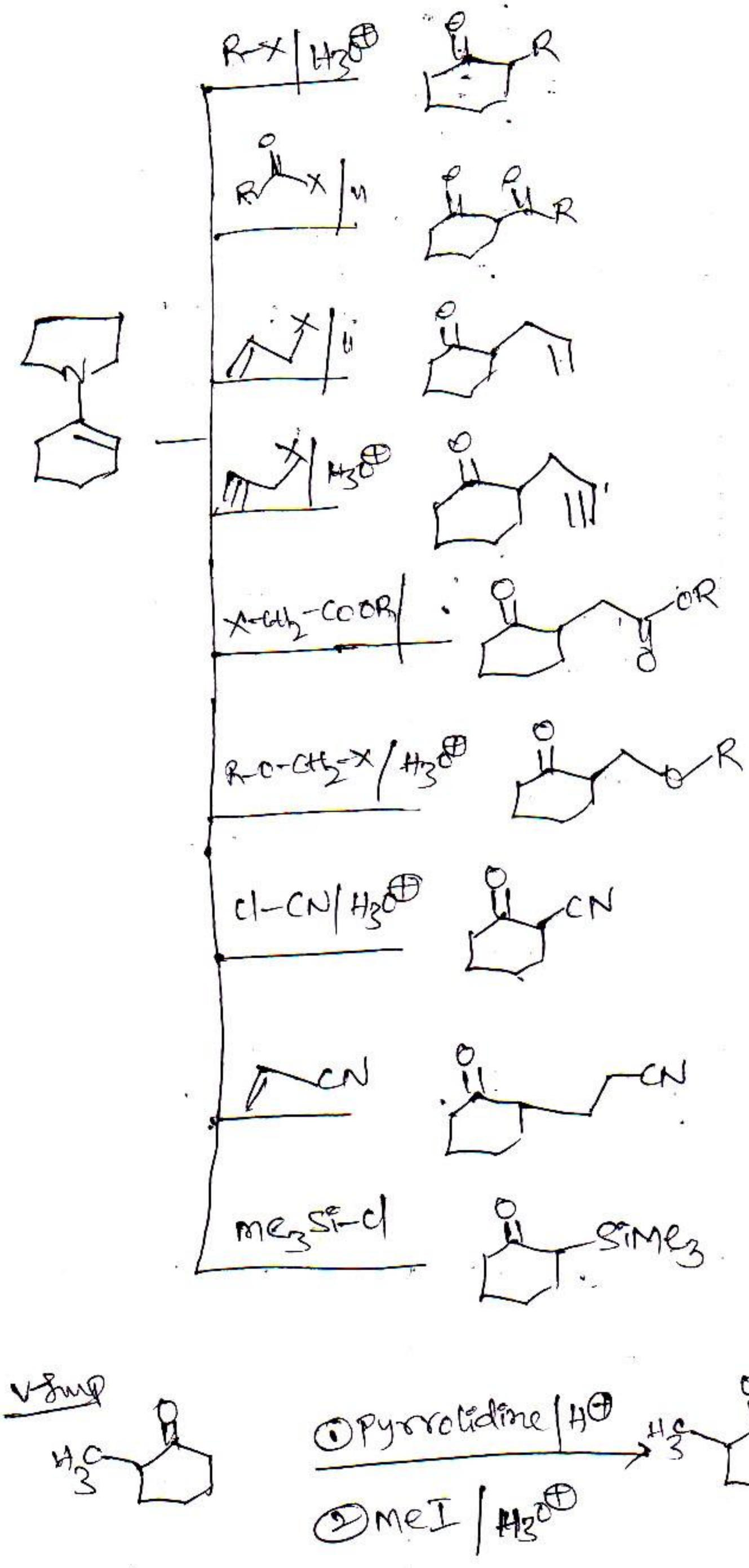




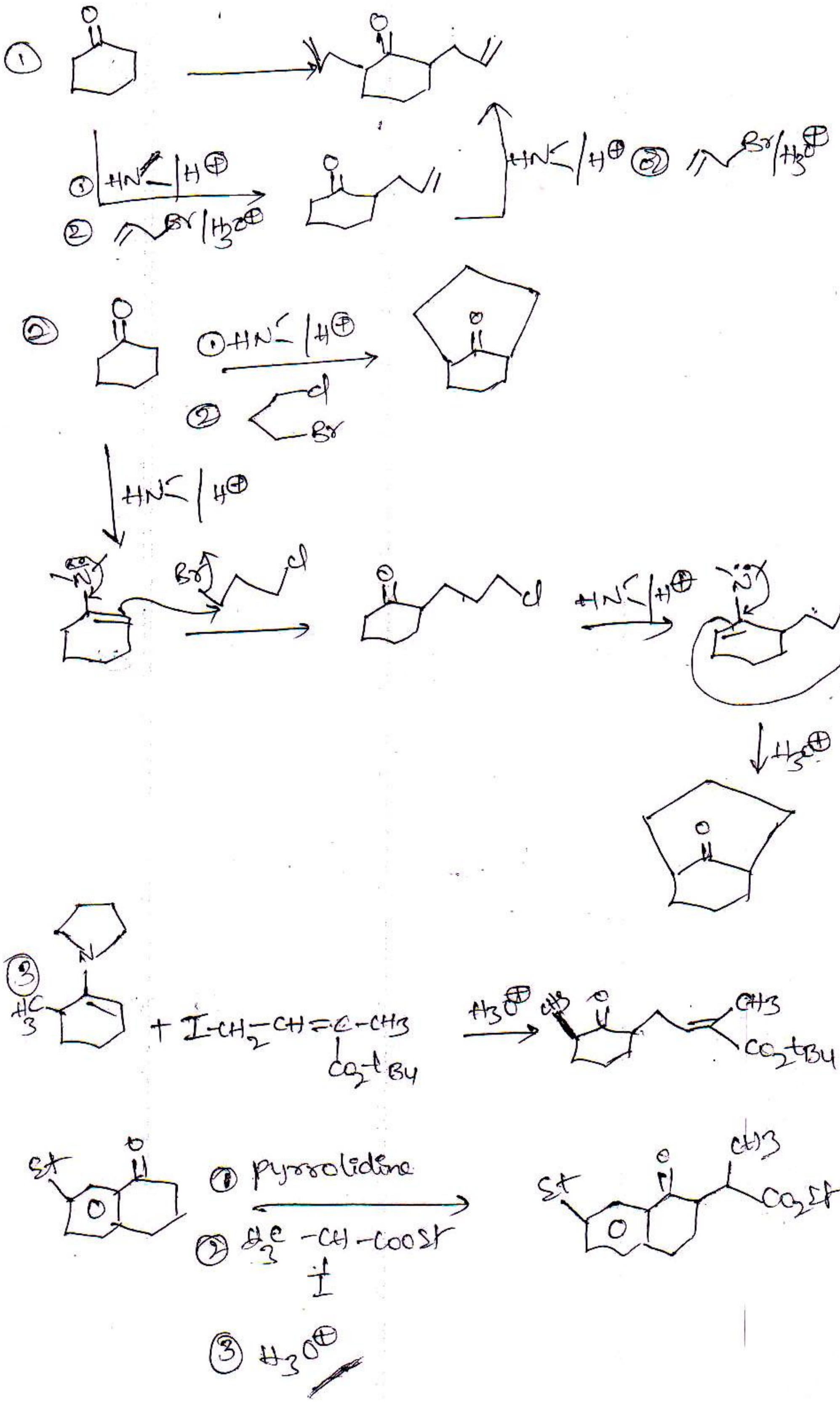
→ formation of C-C bonding by attacking electrophillic groups & Enamine, STORK-ENAMINE RXN.

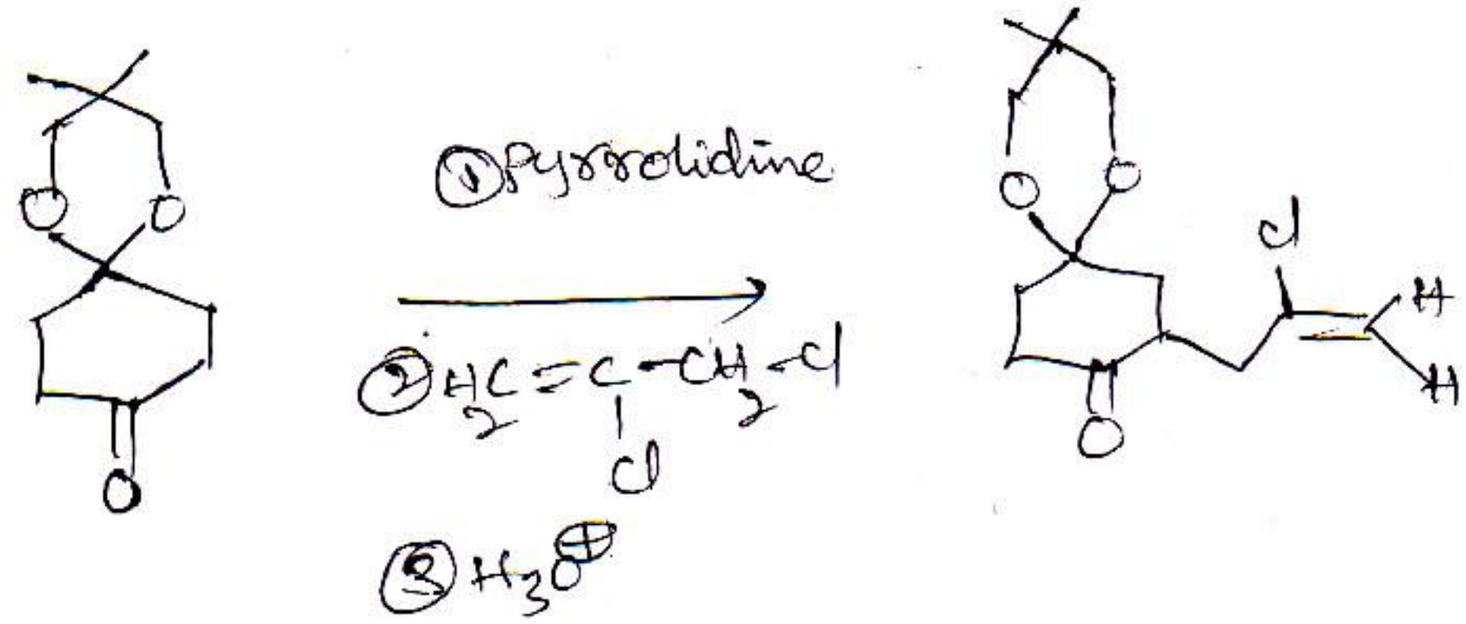


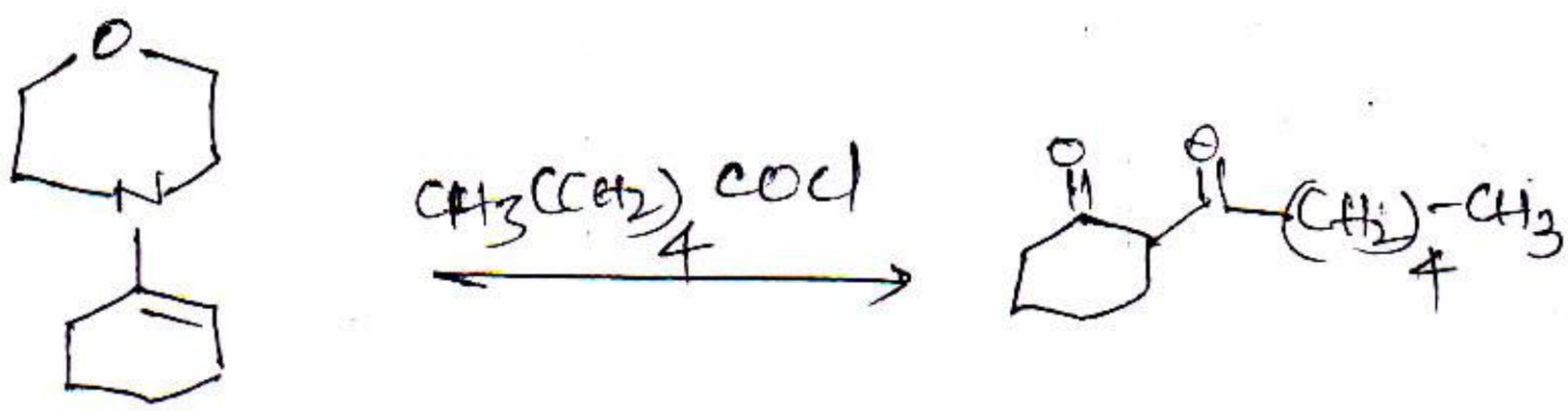
→ One of the best method for alkylation of C.C at α-position.

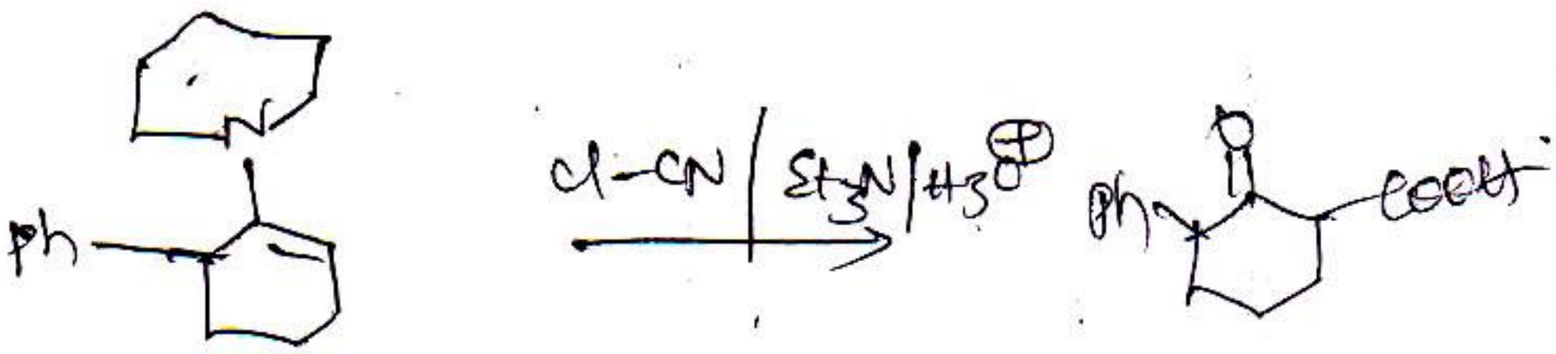


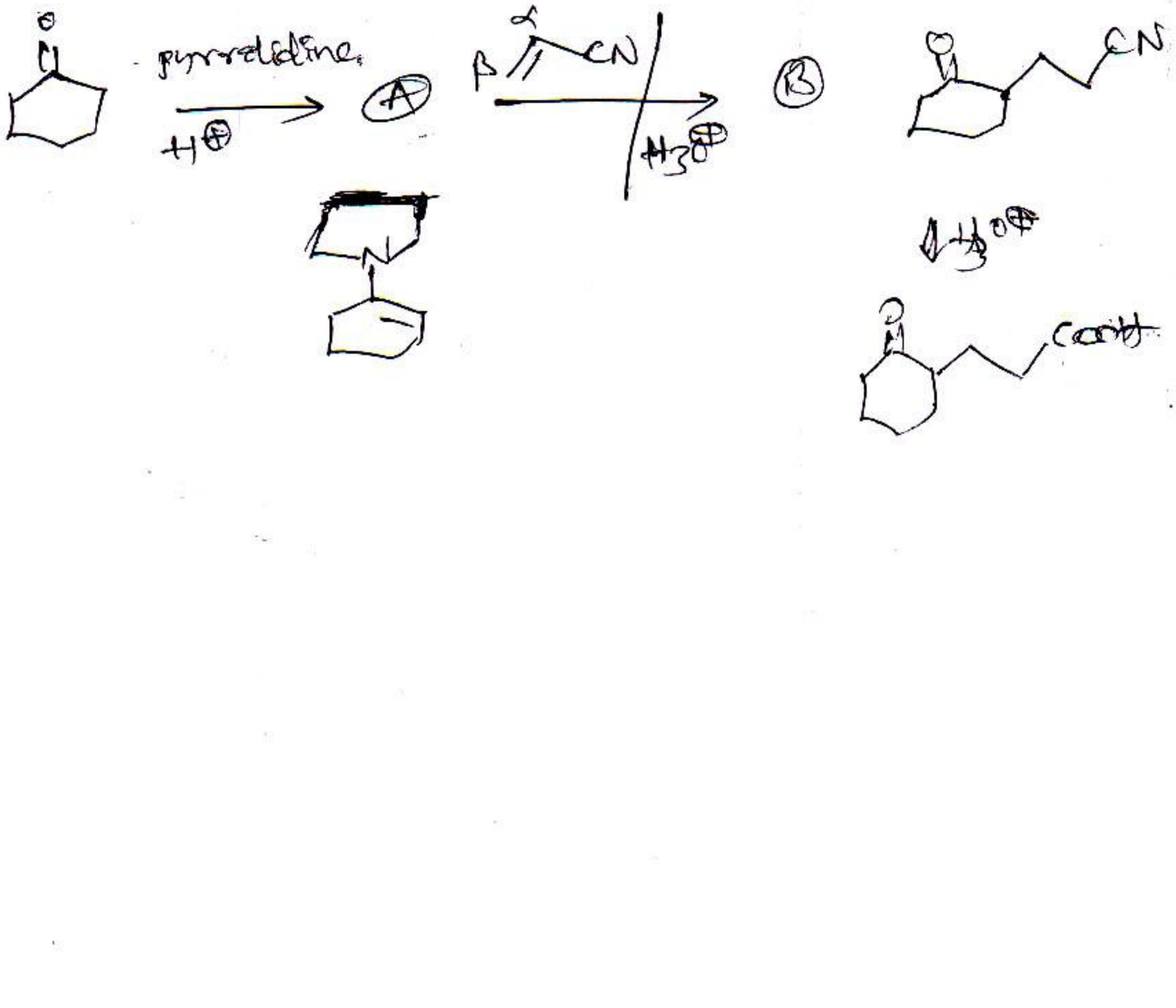
In unsymmetrical Ketones predominately alkyⁿ at less substituted α-position


①
①HN⁻ / H⊕
②
②HN⁻ / H⊕
①
②
HN⁻ / H⊕
Cl
Br
HN⁻ / H⊕
Br
Cl
HN⁻ / H⊕
H3O⊕
③
+ I-CH2-CH=C(CO2tBu)-CH3
H3O⊕
CH3
CO2tBu
①
Pyrrolidine
②
H3C-CH-COOEt
I
③
H3O⊕
Et
CH3
CO2Et


① Pyrrolidine
② H2C=C(Cl)-CH2-Cl
③ H3O⊕


CH3(CH2)4COCl

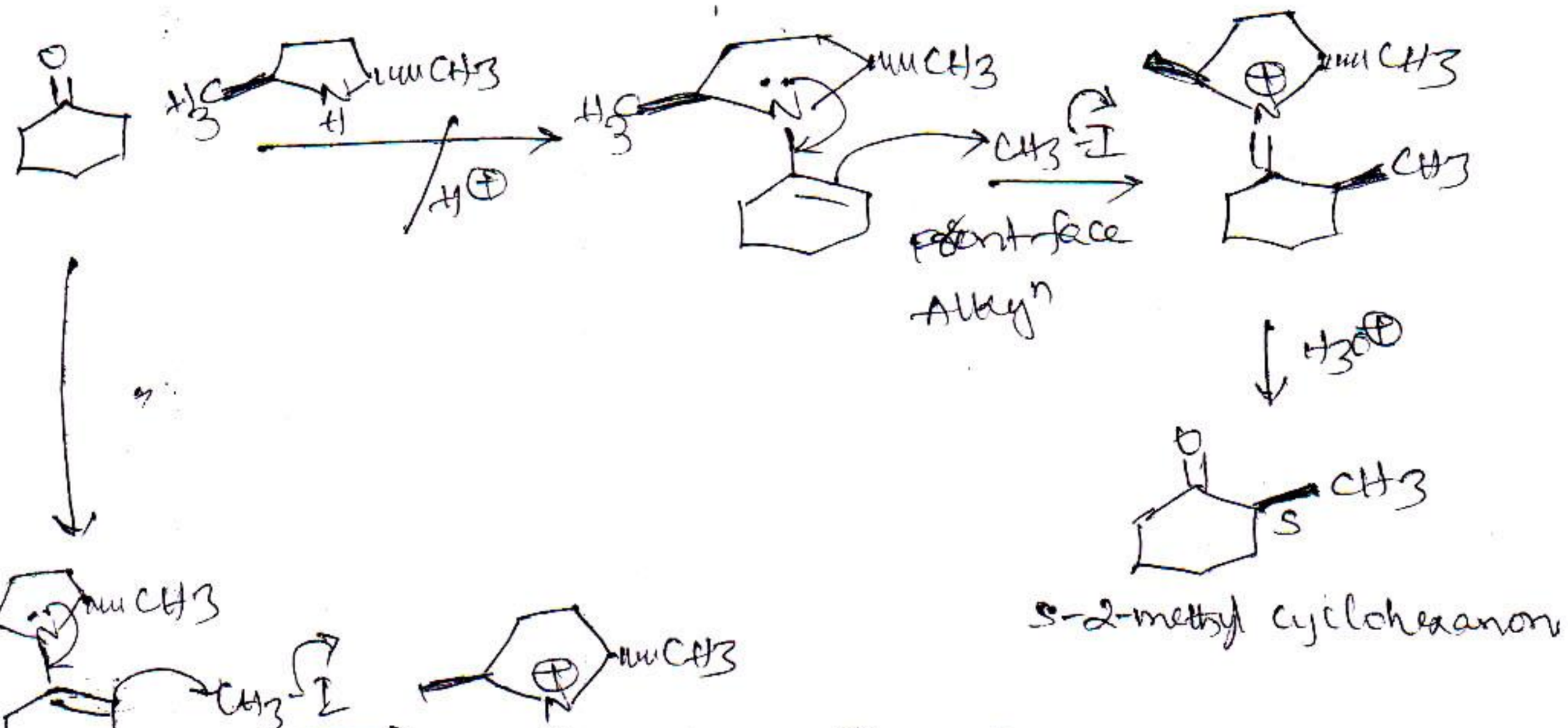

Ph
Cl-CN / Et3N / H3O⊕
Ph
COOH


pyrrolidine
H⊕
A
β
α
CN
H3O⊕
B
CN
H3O⊕
COOH

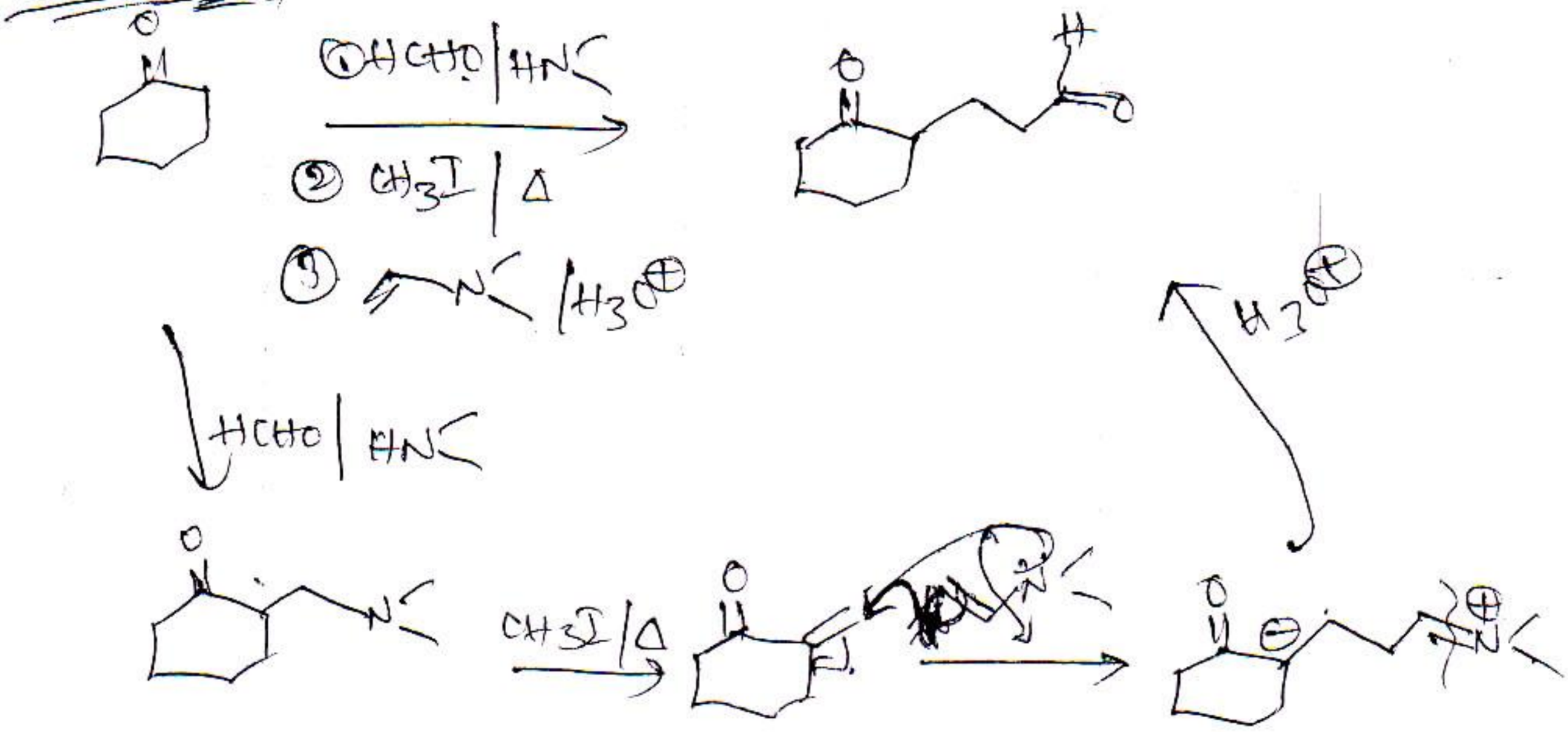
Assymmetric Stork enamine synthesis



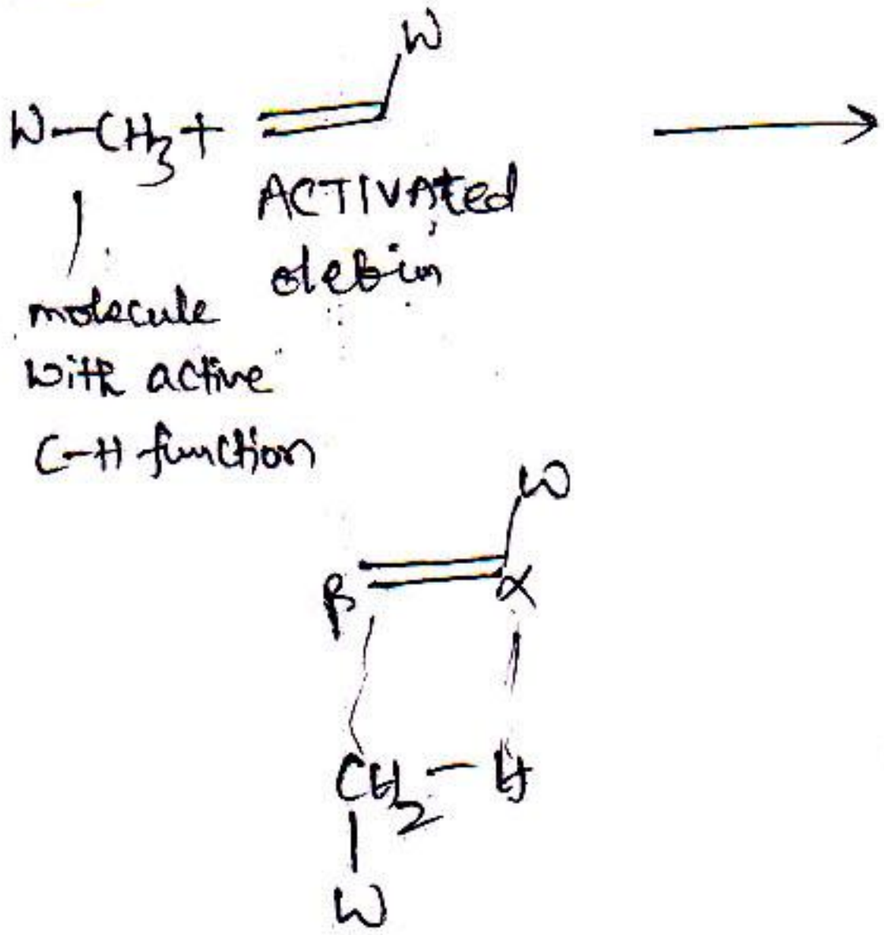
CHIRAL
2° - amine



Mannich rxn's



MICHAEL-ADDITION| REACTION



Conjugative addition of active C-H function to activated olebin in basic medium called michael addition develops new C-C bonding at β-position of activated olefin.

Activated olefin:- olefin attached to EWG with drawing group ($\overset{W}{=}$)

Active C-H function:- Acidic C-H & group ionisable into carbanion and $H^{\oplus}$.

Compound with active C-H + Activated olefin $\xrightarrow{\text{Base}}$ Michael adduct.

Compound with active C-H → Michael donar

Activated olefin → Michael acceptor

BASE = NaOH | KOH , NaH, KH, $RO^{\ominus}Na^{\oplus}$ | $RO^{\ominus}K^{\oplus}$, 3° amine.

EWG → M-donar



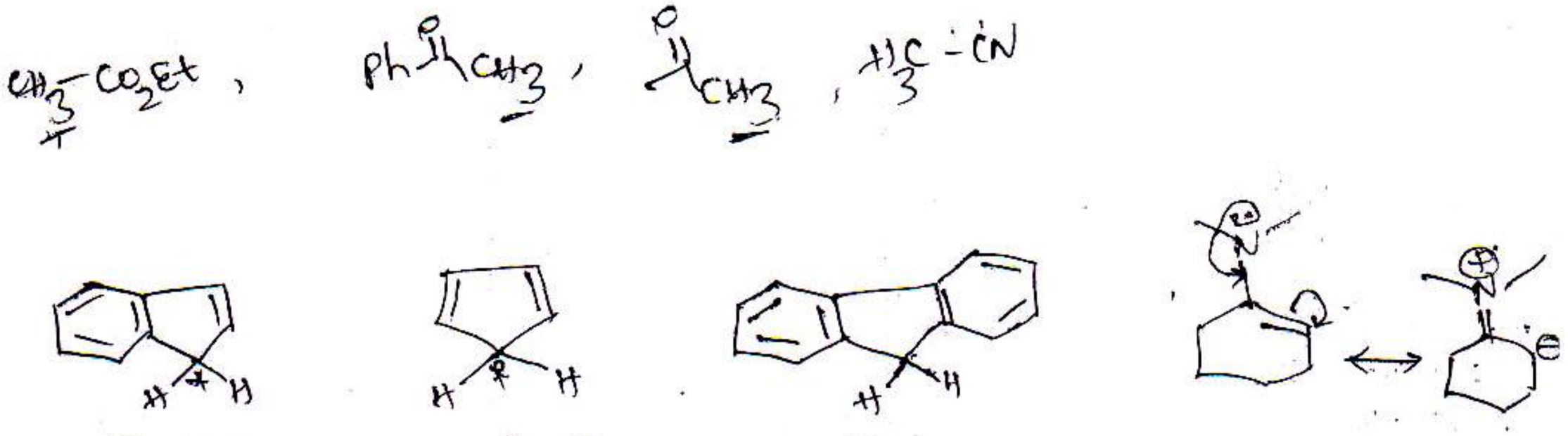
β-Keto ester $R-\overset{O}{\overset{\|}{C}}-CH_2-CO_2R$

β-diketones $R-\overset{O}{\overset{\|}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-R$

β-Ketoamides $R-\overset{O}{\overset{\|}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-N$

β-Keto cyano $R-\overset{O}{\overset{\|}{C}}-CH_2-CN$

β-Keto Nitro $R-\overset{O}{\overset{\|}{C}}-CH_2-NO_2$



Michael acceptors : (C=C=O)

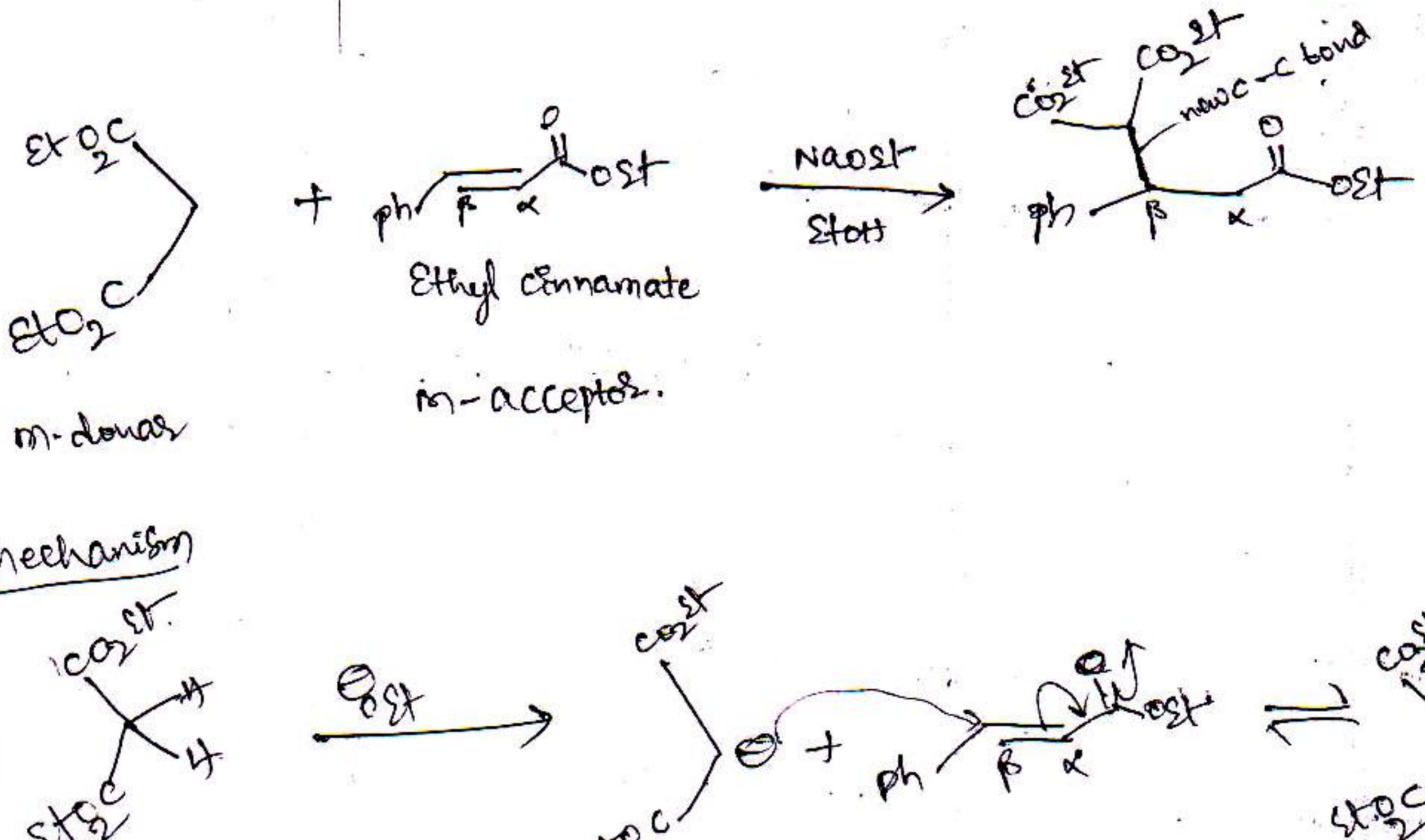
① α,β unsaturated ester

② " " ketone MVK (methyl vinyl ketone)

③ " " Amide

④ " " cyano

⑤ " " NO_2

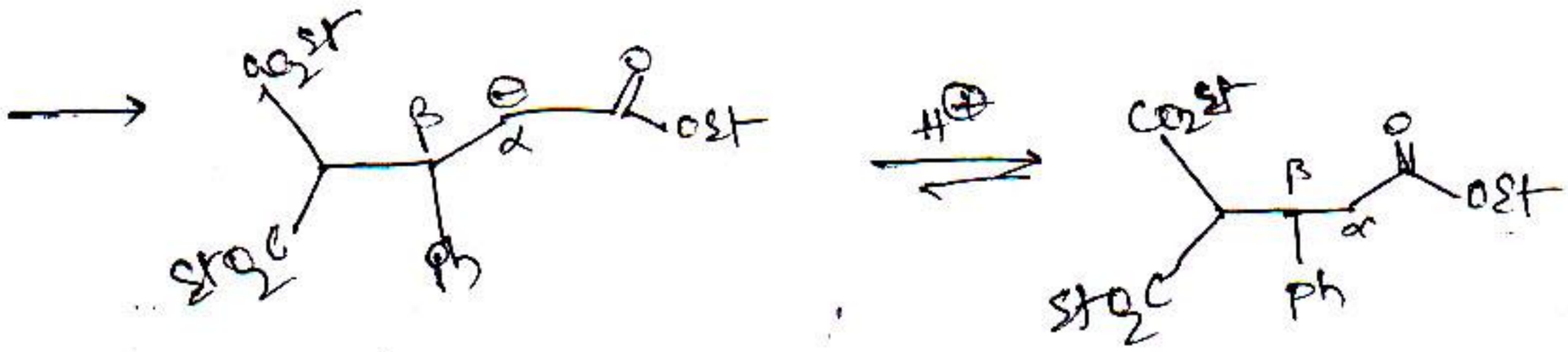


m-donar

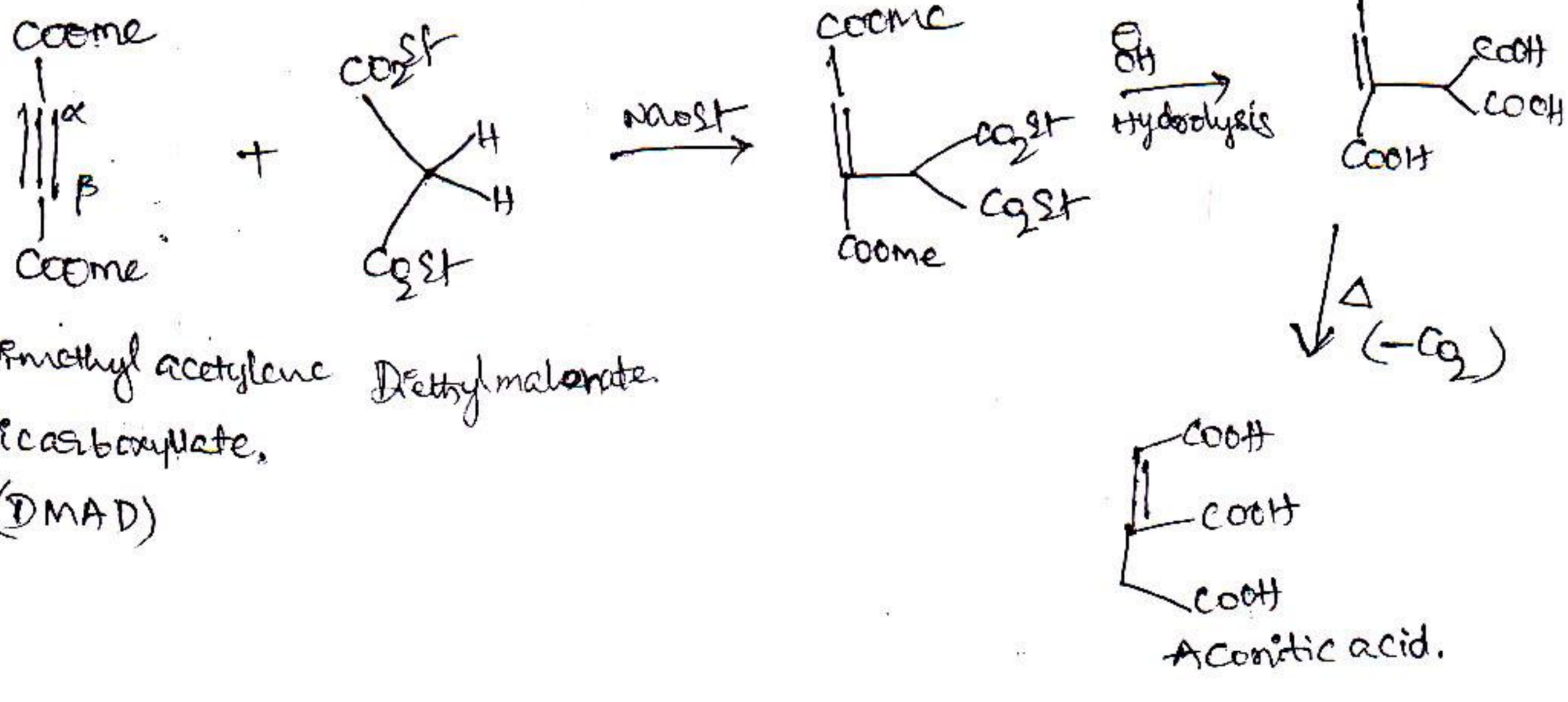
Ethyl cinnamate

m-acceptor.

Mechanism



*) ACONITIC-ACID

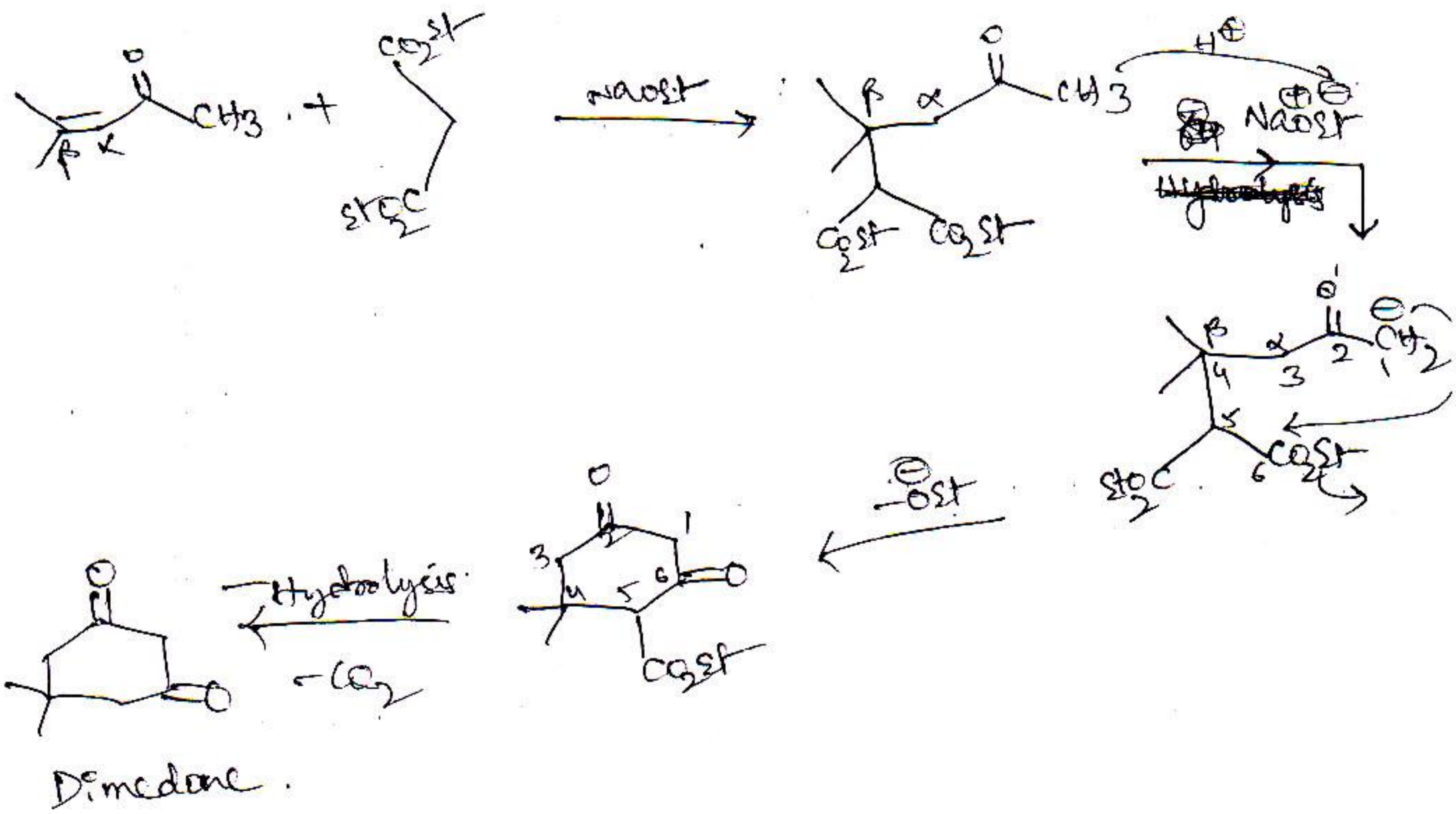


Dimethyl acetylene dicarboxylate. (DMAD)

Diethyl malonate.

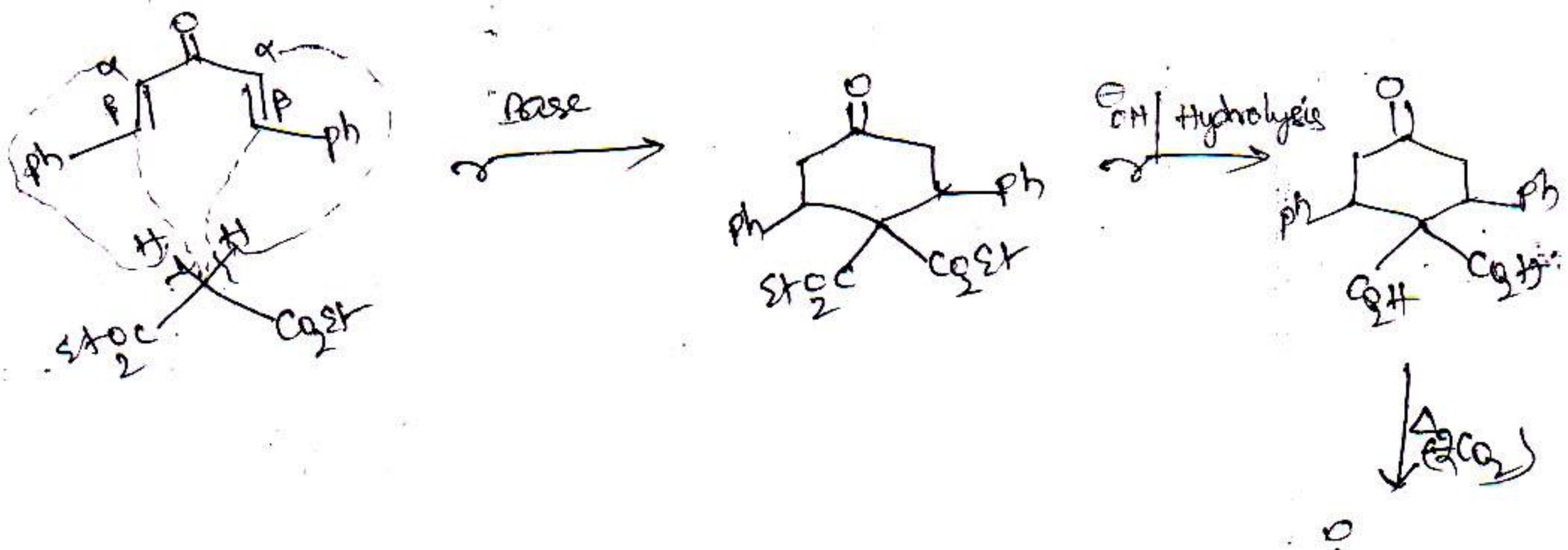
Aconitic acid.

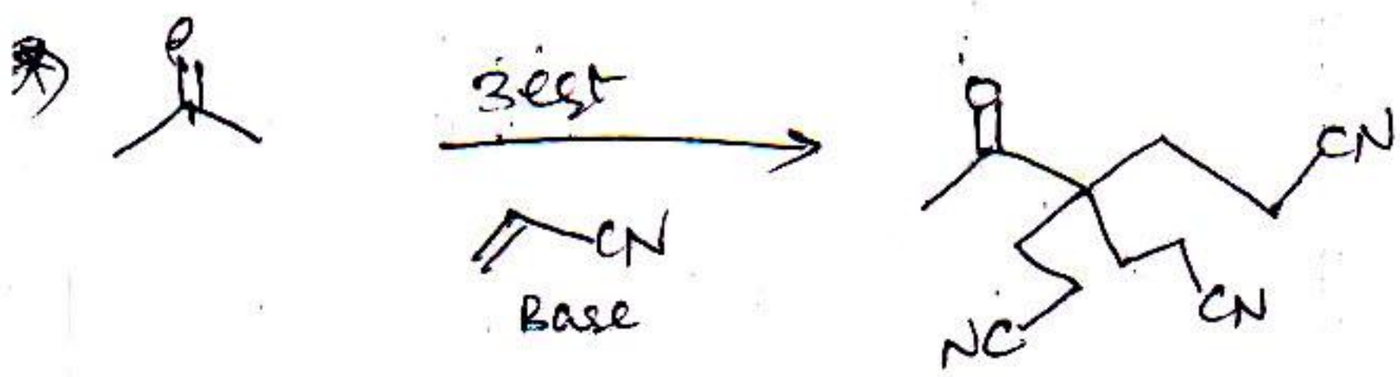
*) DIMEDONE

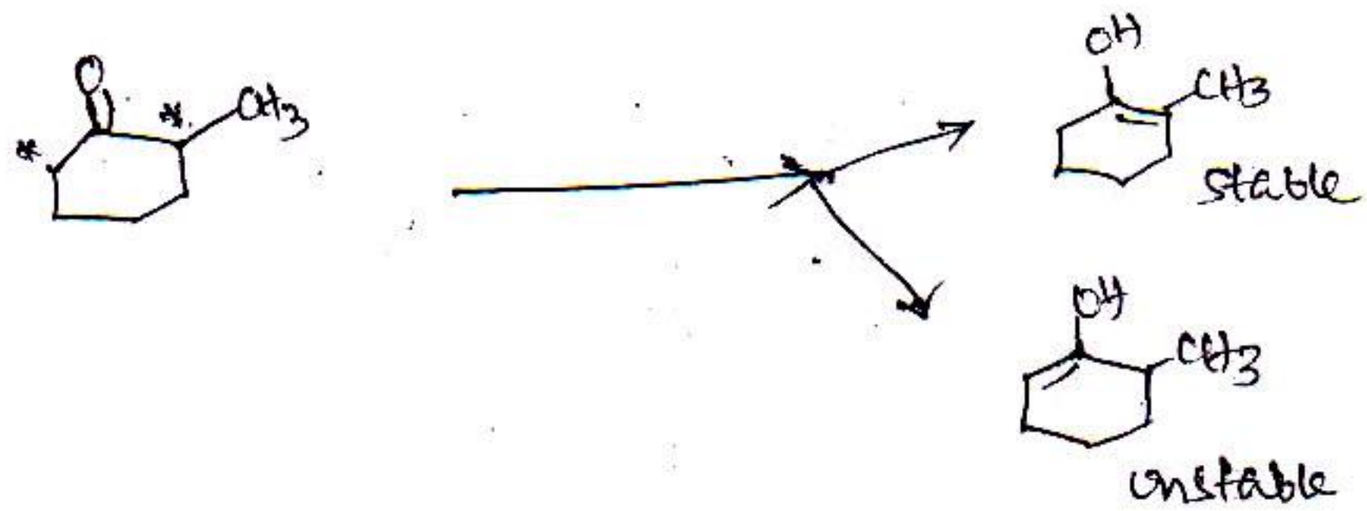


Dimedone.

DOUBLE - MICHAEL ADDITION :-





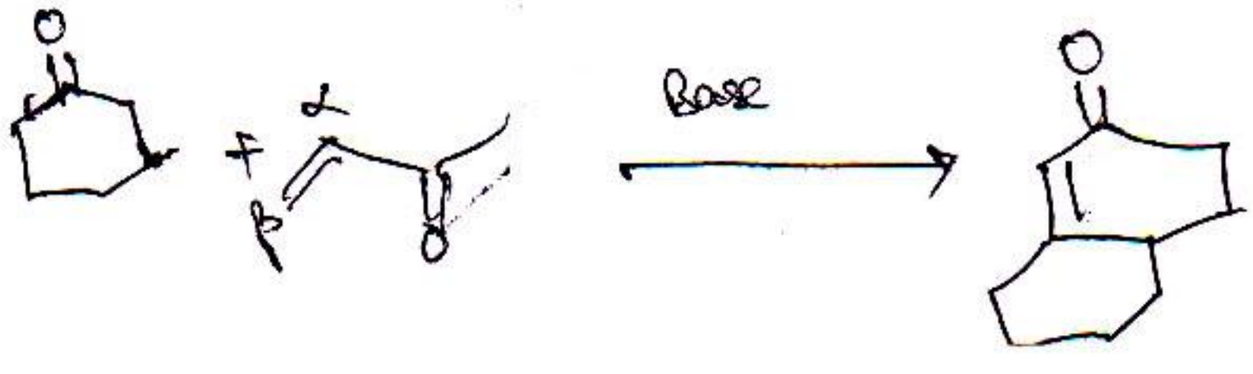


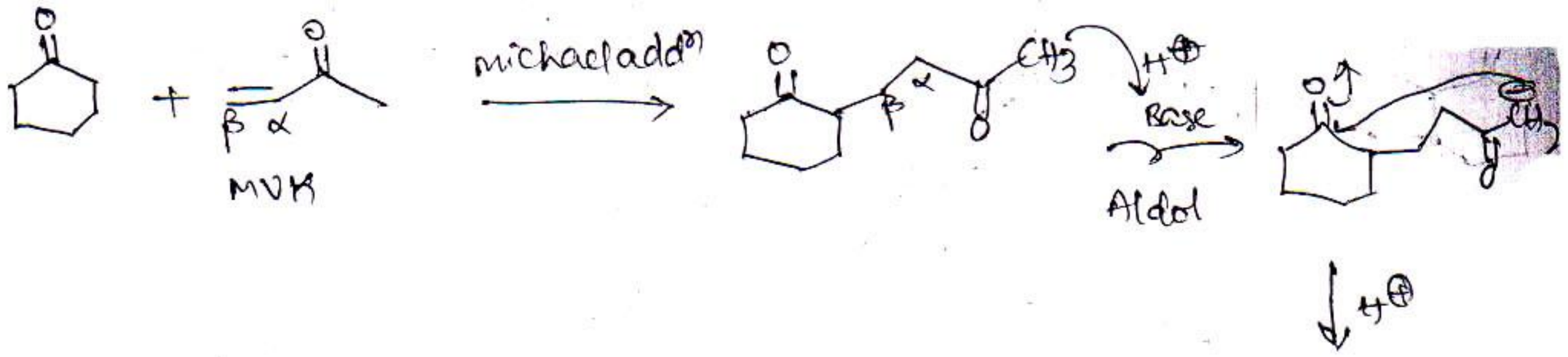
(∵ Saytzeff's rule)

ROBINSON - ANNULATION :-

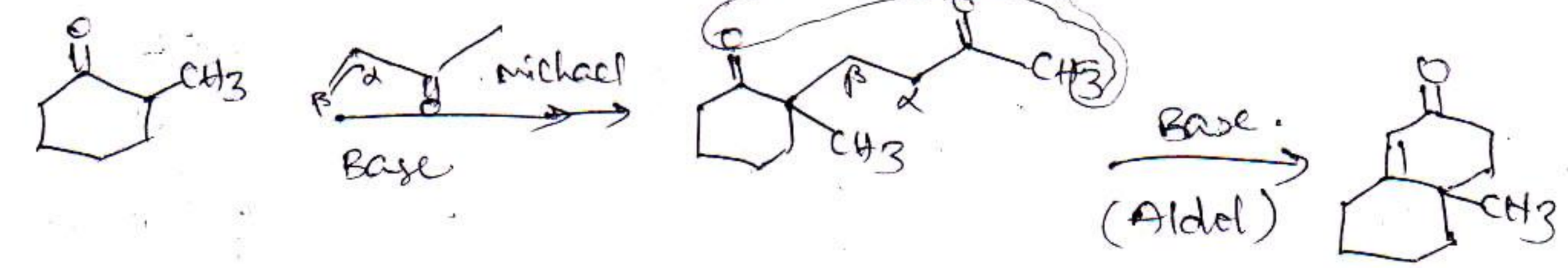


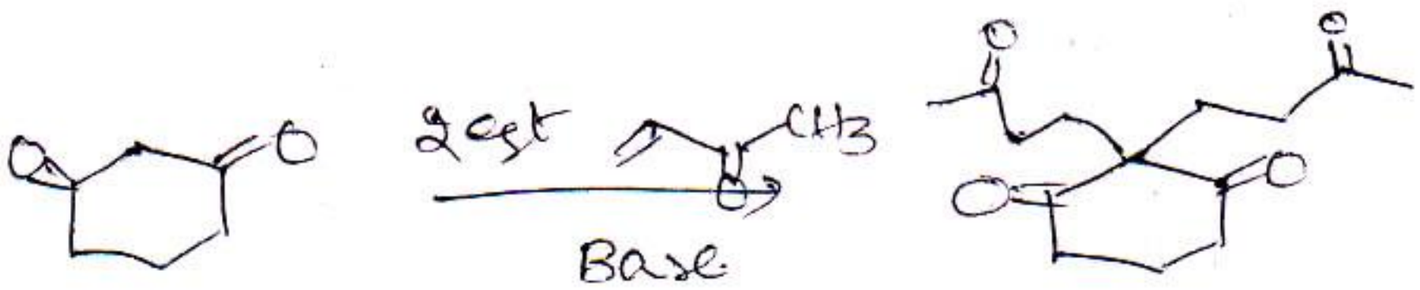
Robinson annulation is combination of Michael addn and aldol condensation



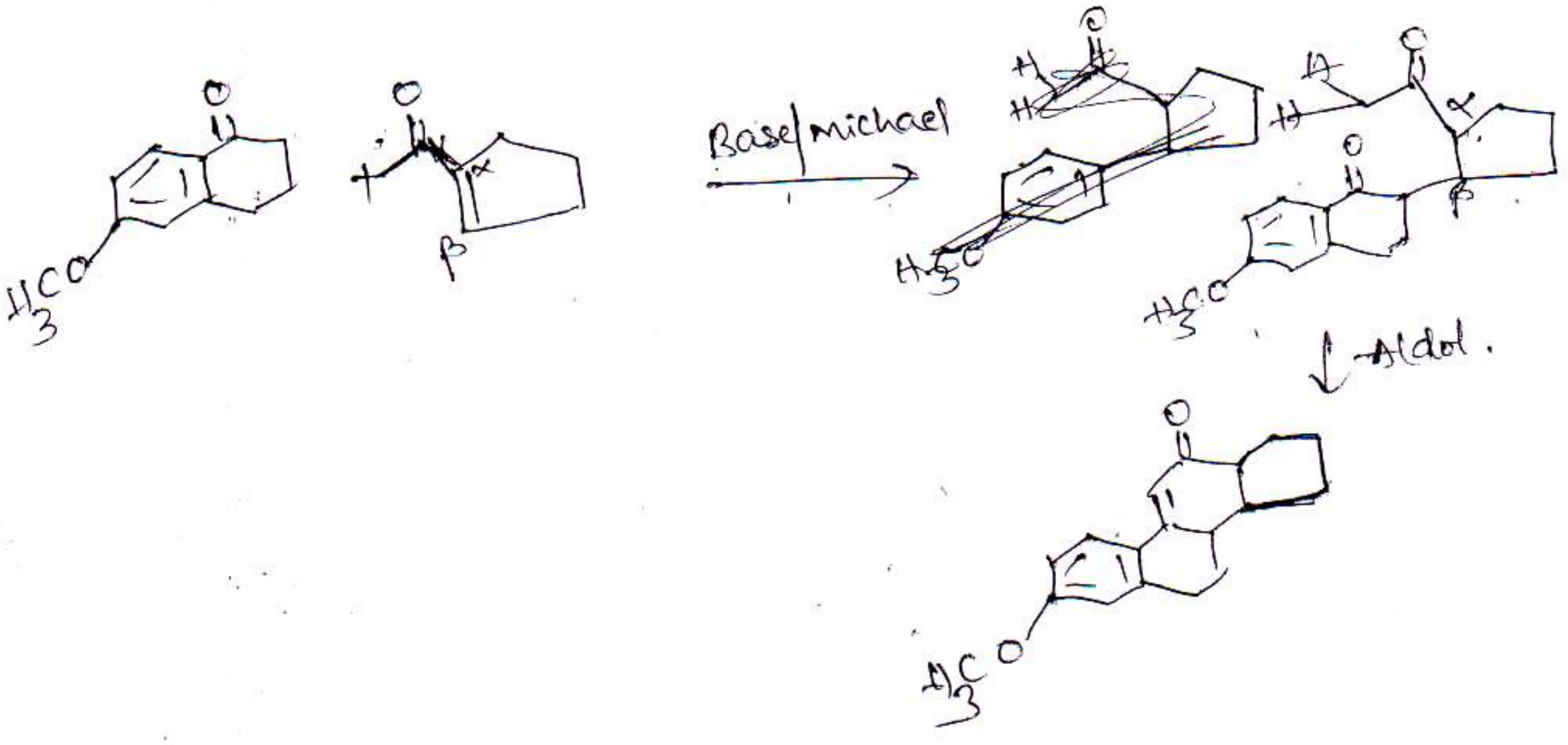


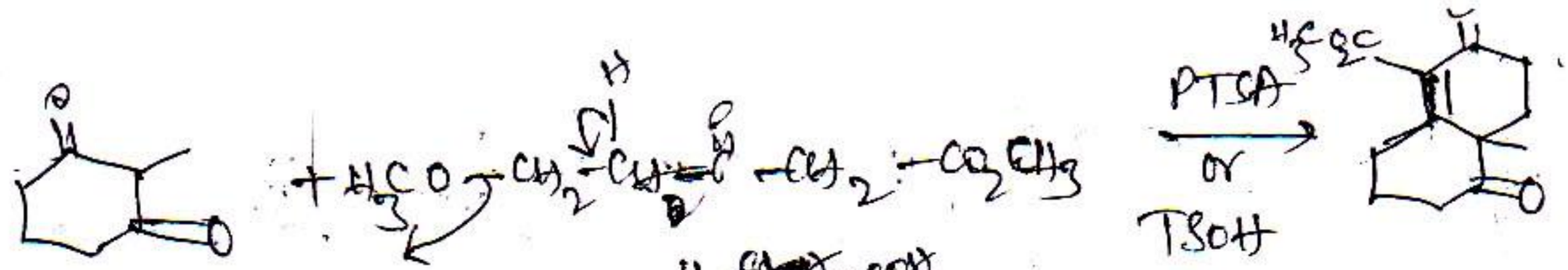
In the case of unsymmetrical ketones Robinson's annulation takes place at more substituted α-positions due to formation of stable enol.

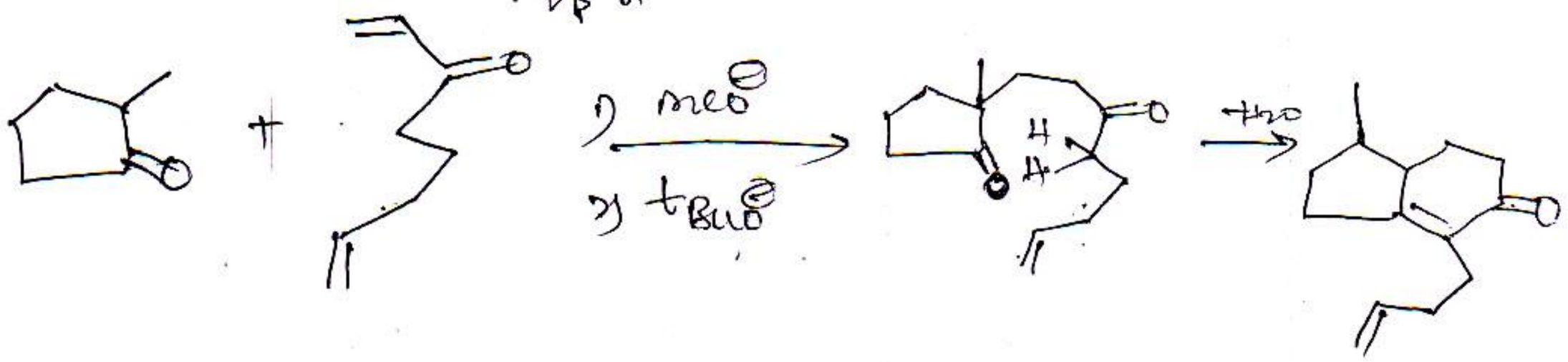


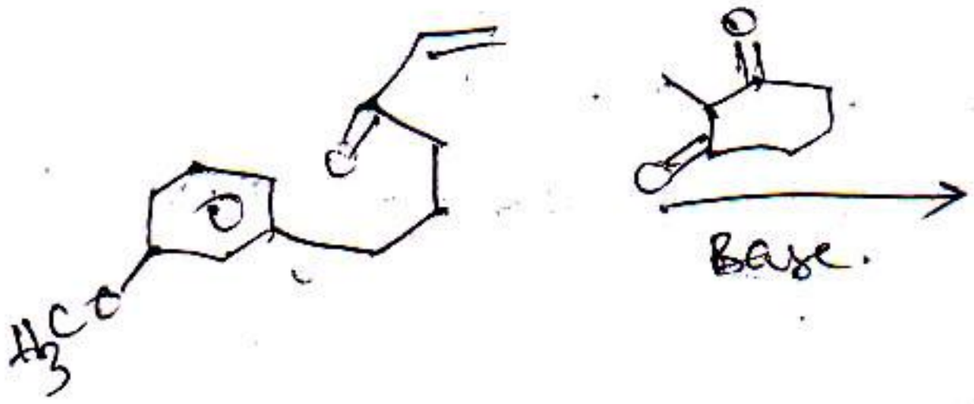


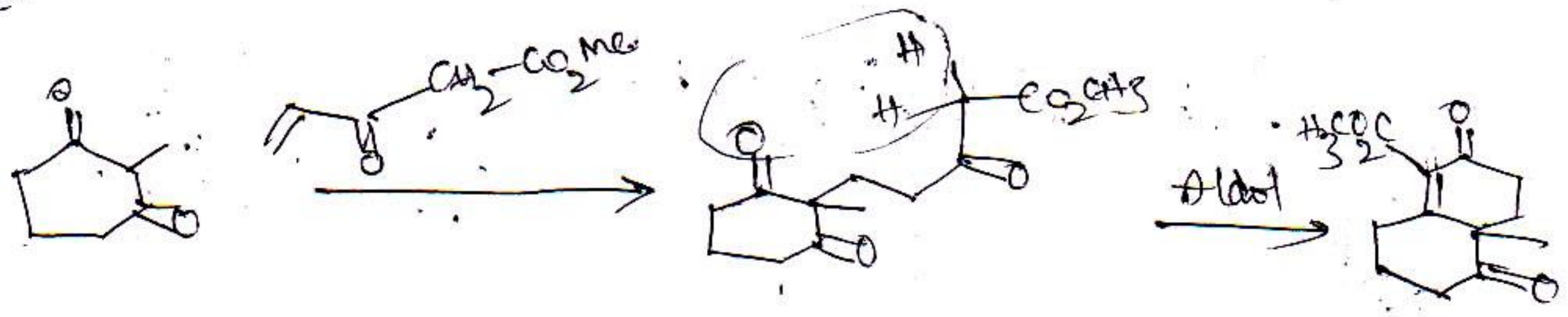
No Robinson ann due to steric hindrance



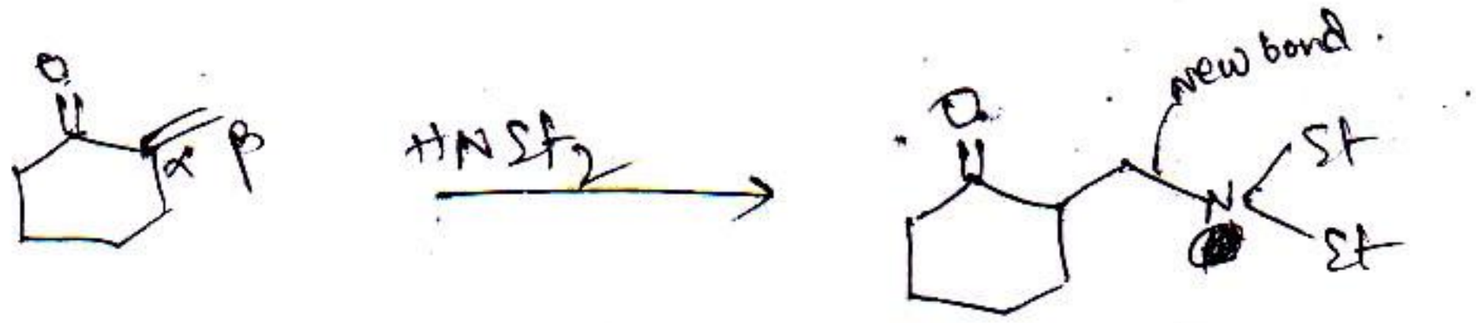

PTSA
or
TSOH
MeOH

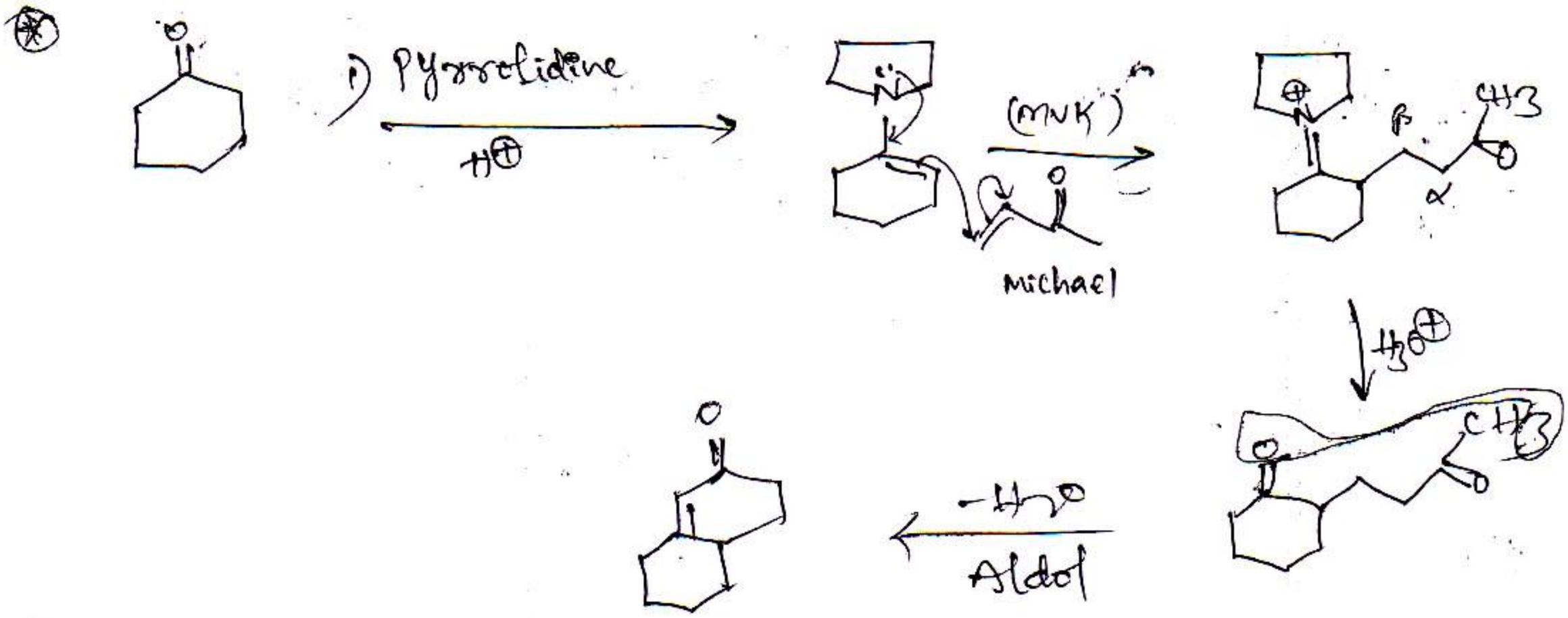

1) MeO⊖
2) tBuO⊖
H2O

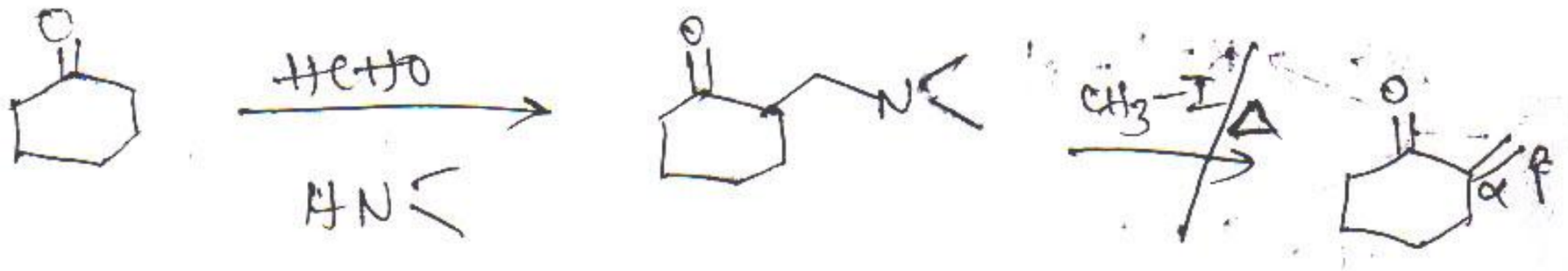

Base.
mechi


Aldol

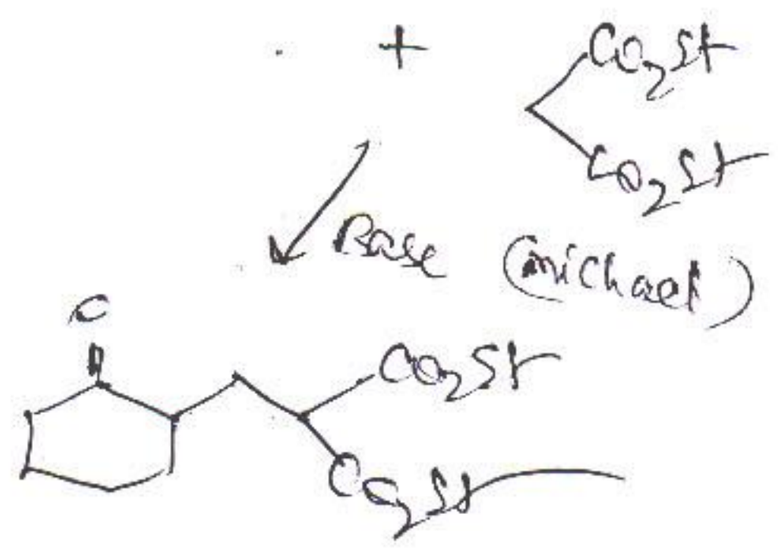
(K)

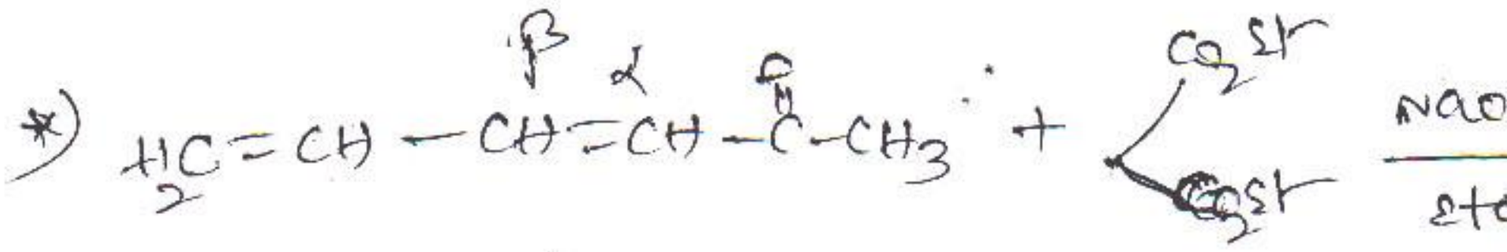

HNEt2
new bond


1) Pyrrolidine
H⊕
(MVK)
Michael
H3O⊕
-H2O
Aldol

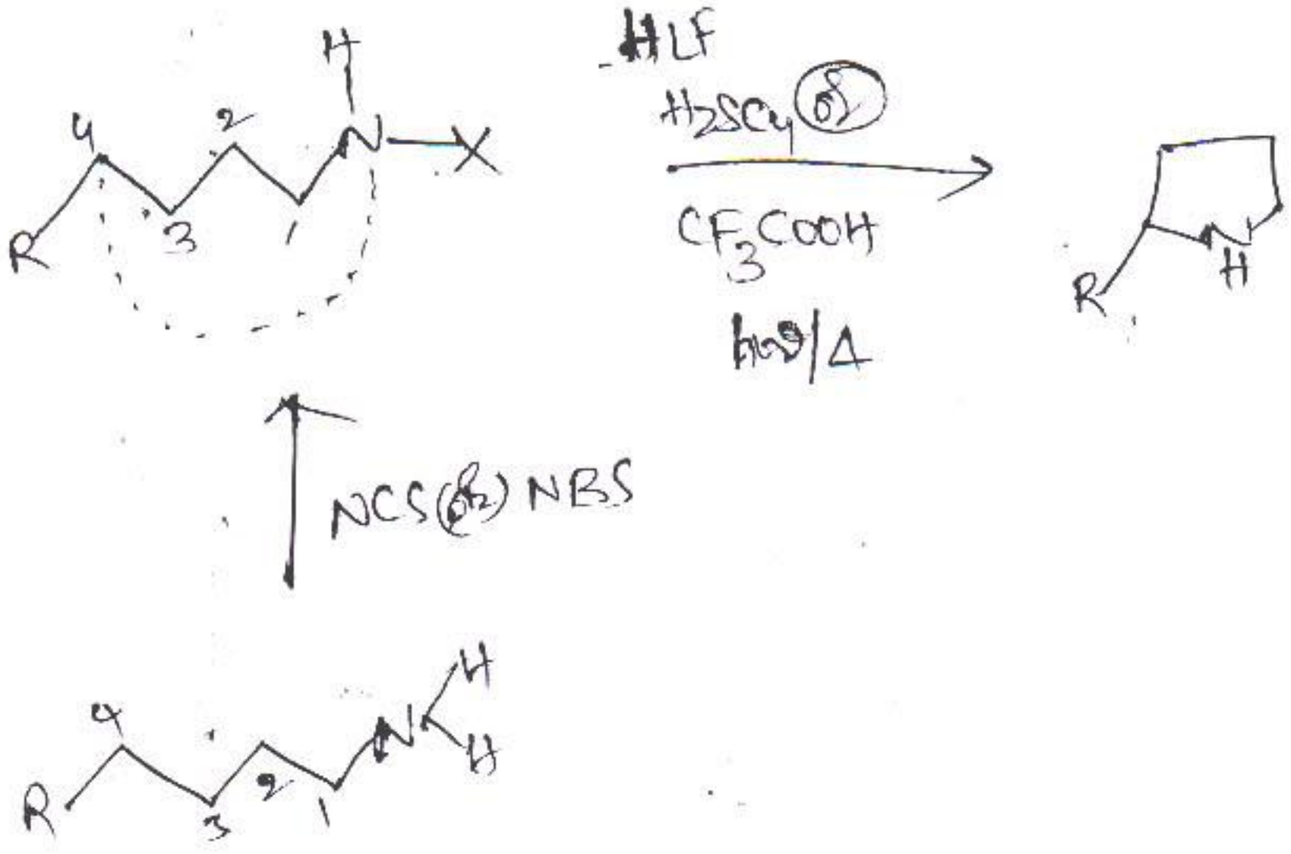


α,β-Unsaturated acrolein.



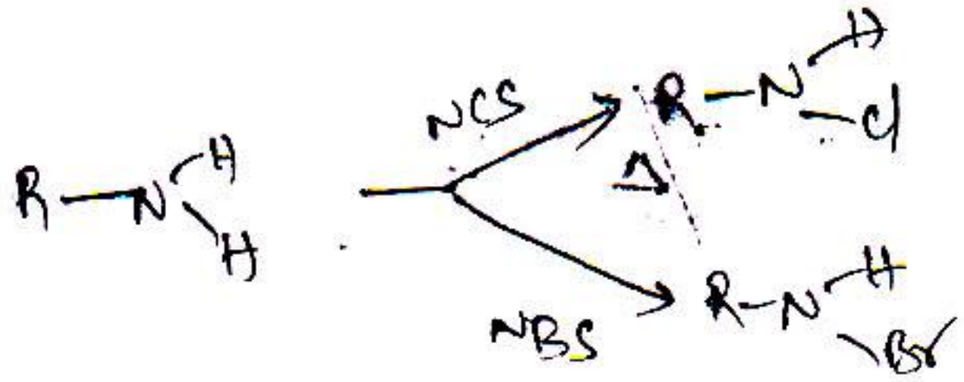


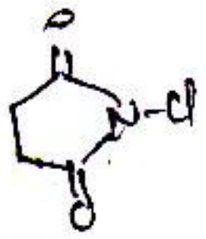
HOFMANN-LOEFFLER-FREYTAG REACTION / HLF-Reaction.

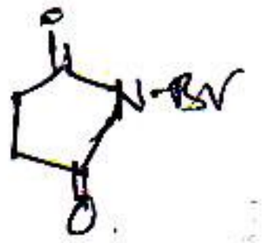


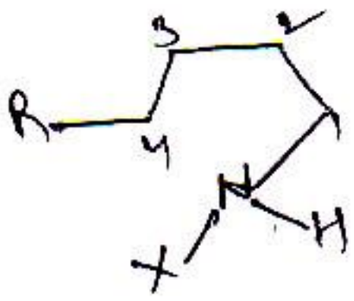
Conversion of N-Haloamines having C_4-H & C_5-H into 5 or 6 mem-ed Nitrogen Heterocyclic with H_2SO_4 & CF_3CO_2H under photochem or thermal Condition is called HLF Rxn.

N-Haloamines are prepared from amines by treating with NCS, NBS



NCS: N-chloro succinamide 

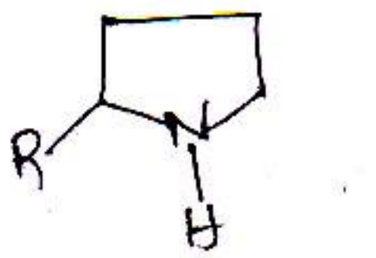
NBS - N-Bromo : 



Cu·H2SO4 ⑥ CF3COOH

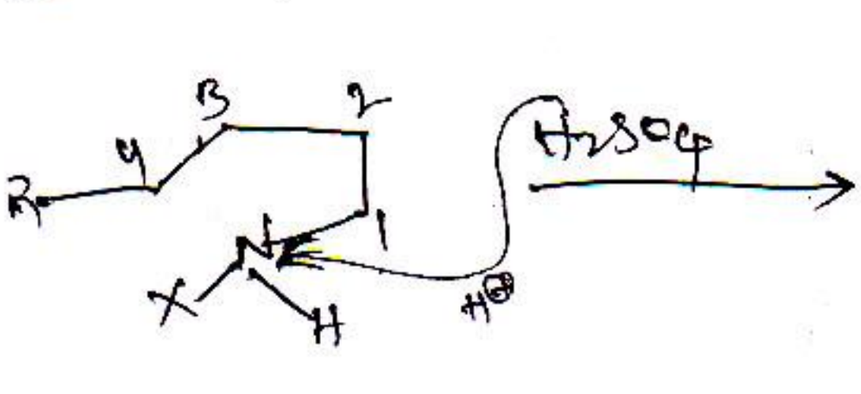
·hν ⑤ Δ

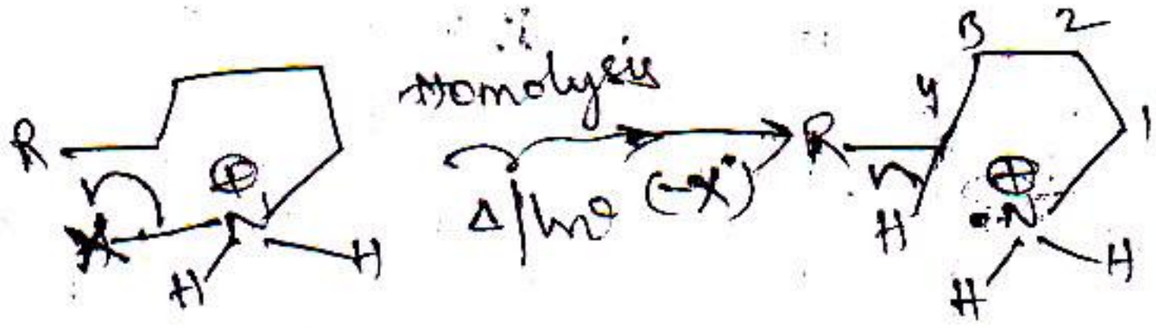
NaOH

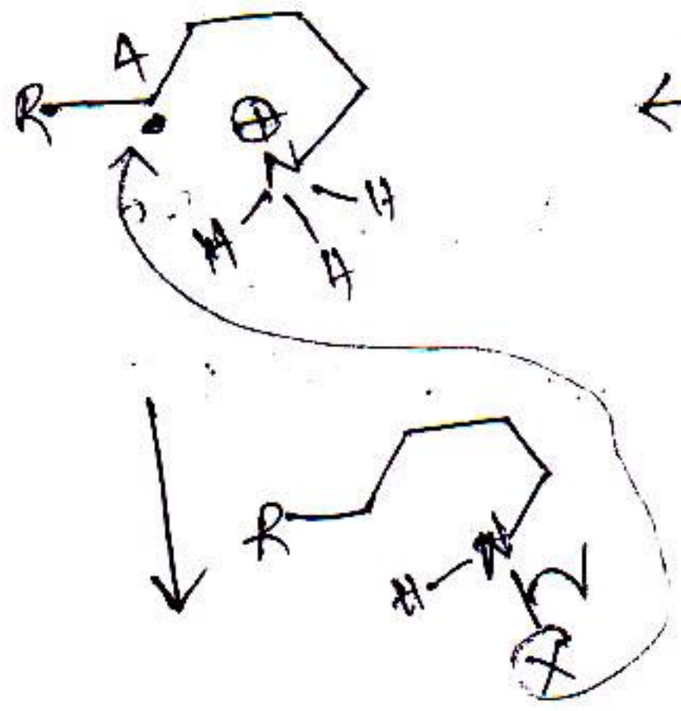


Pyrrolidine

Mechanism :- (5 mp)

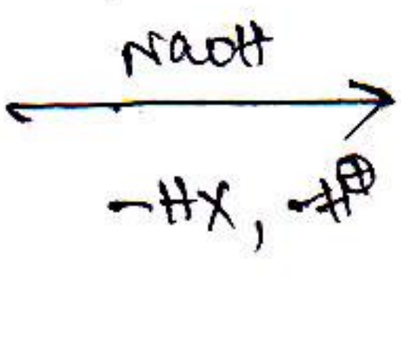


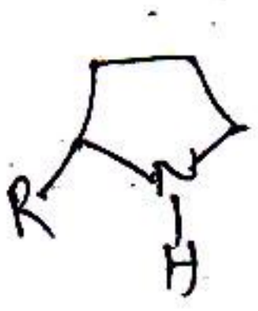




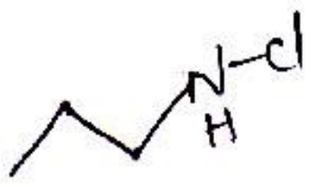








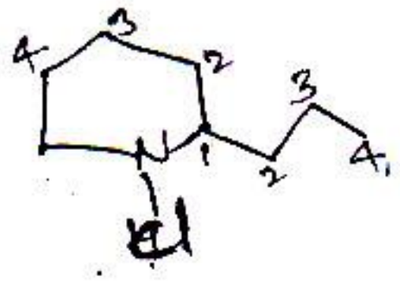
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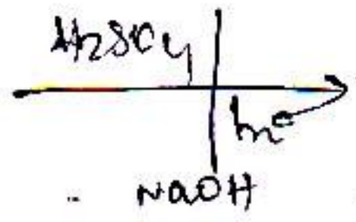


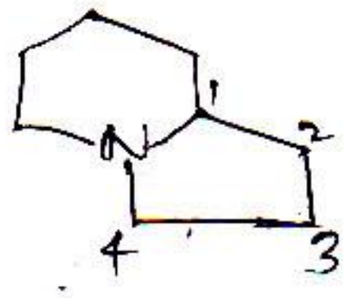
HLF Rxn.



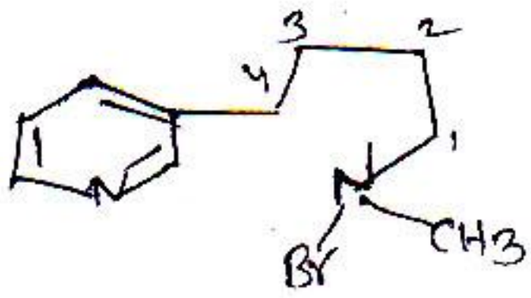
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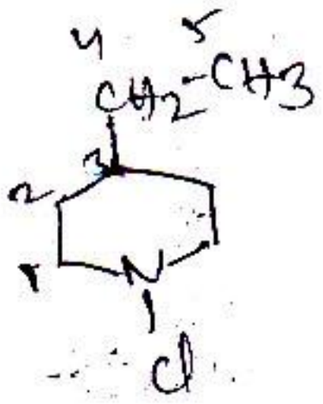


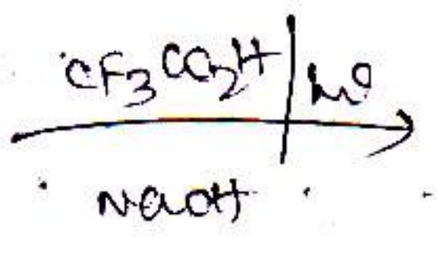




Nicotine

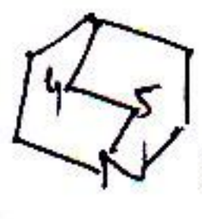
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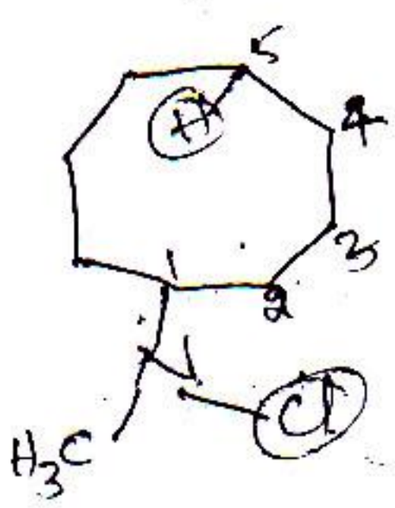


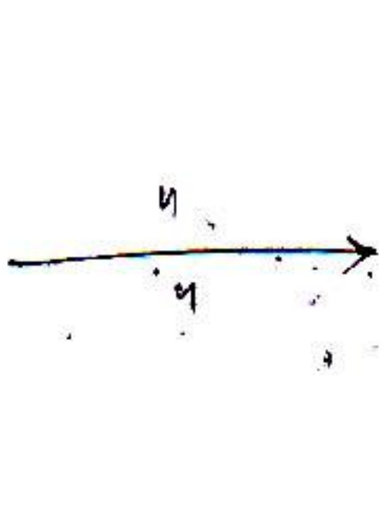
Quinuclidine

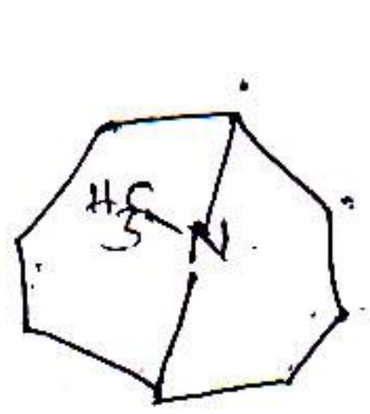
C4 Product

C5 product

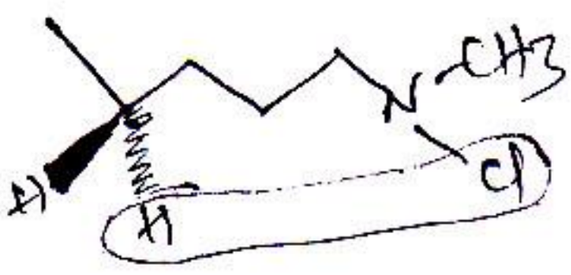
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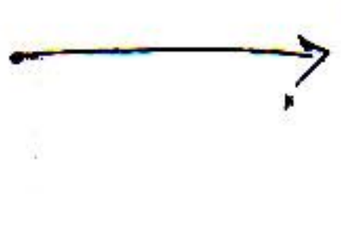


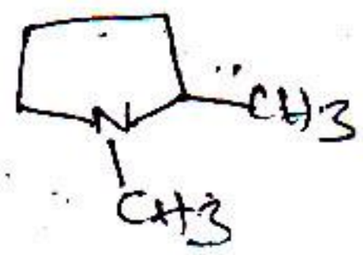


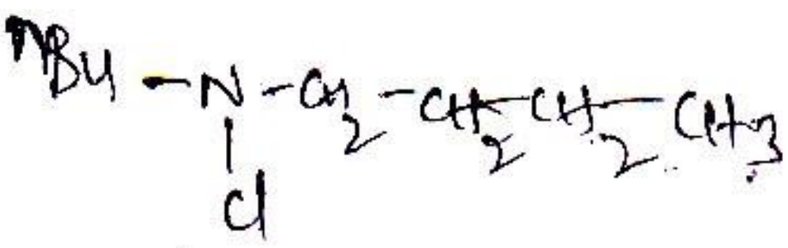


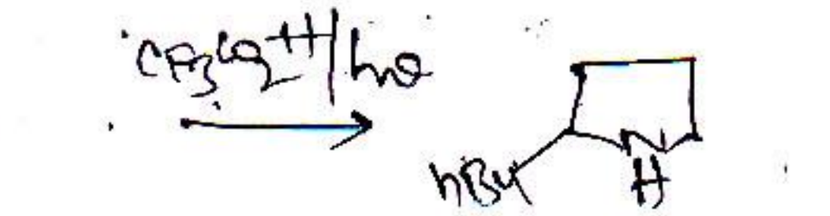
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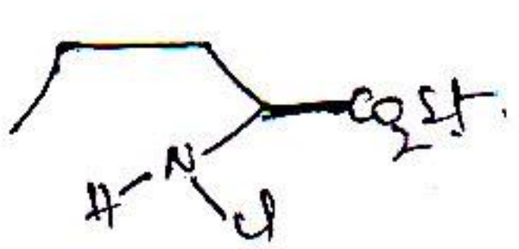


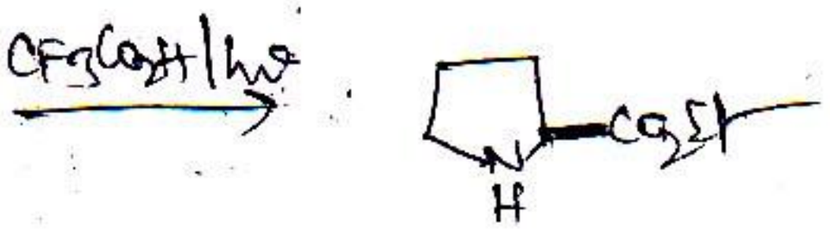


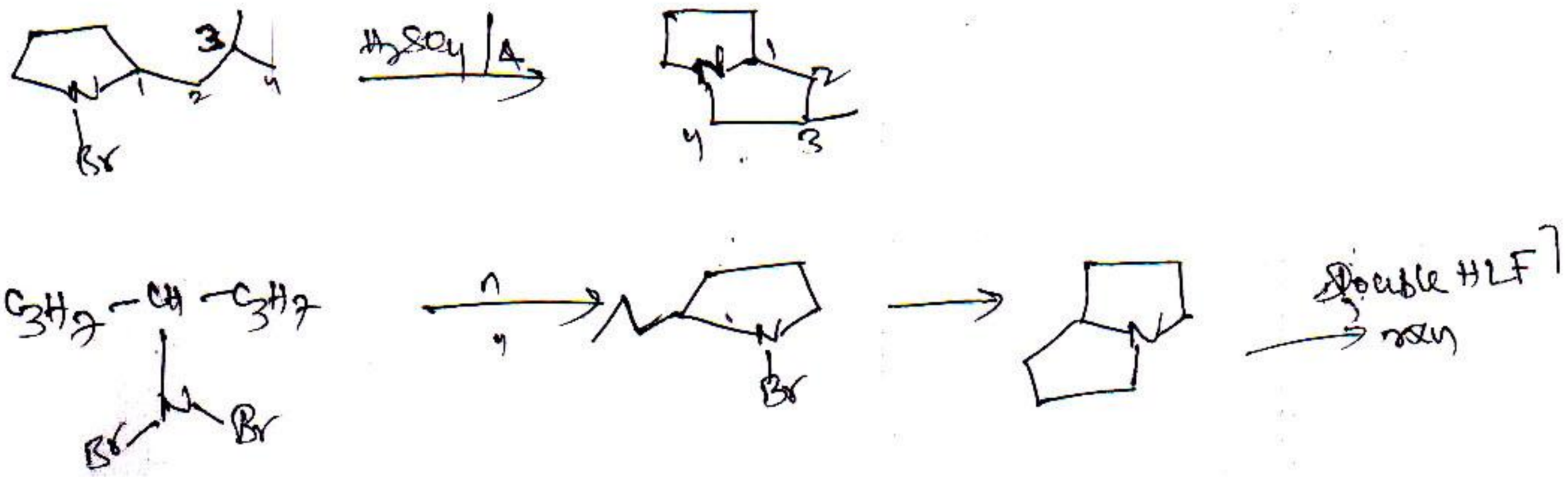


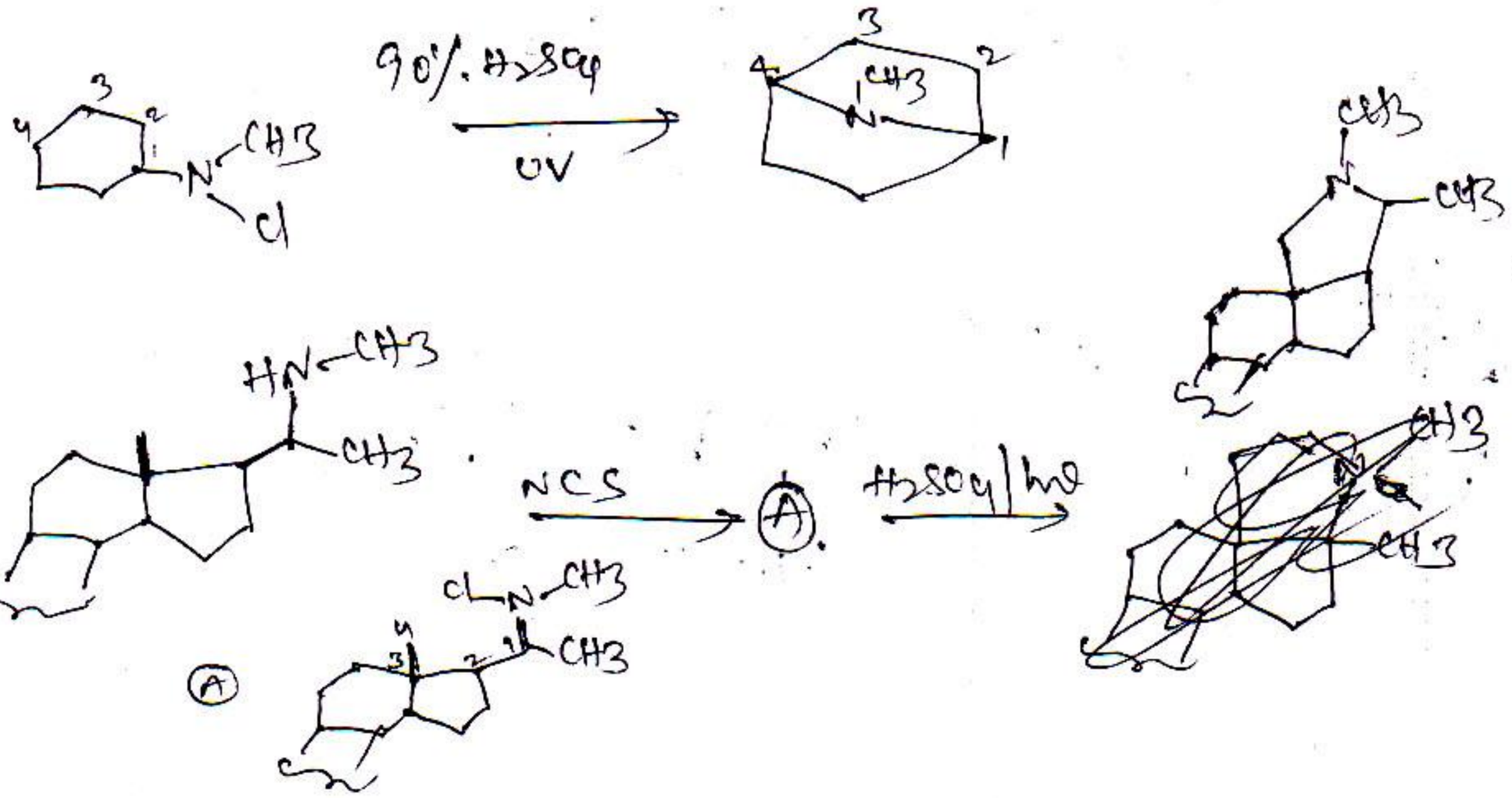


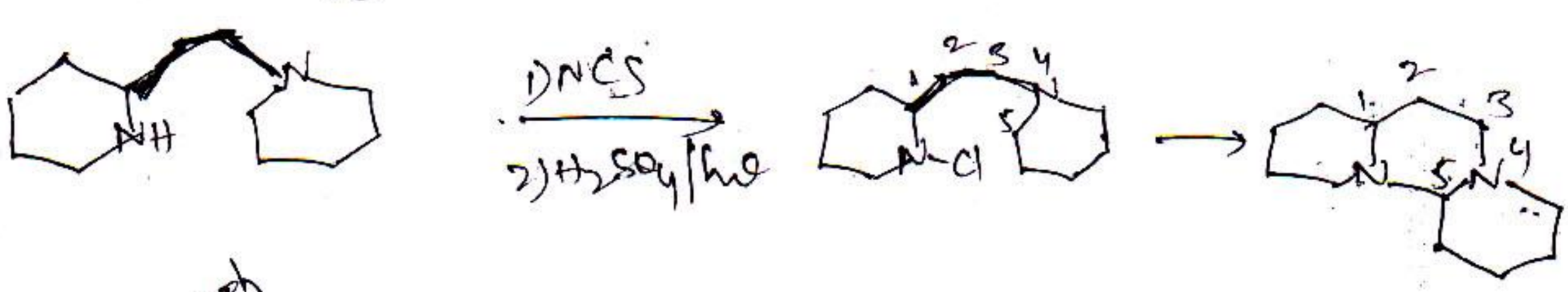


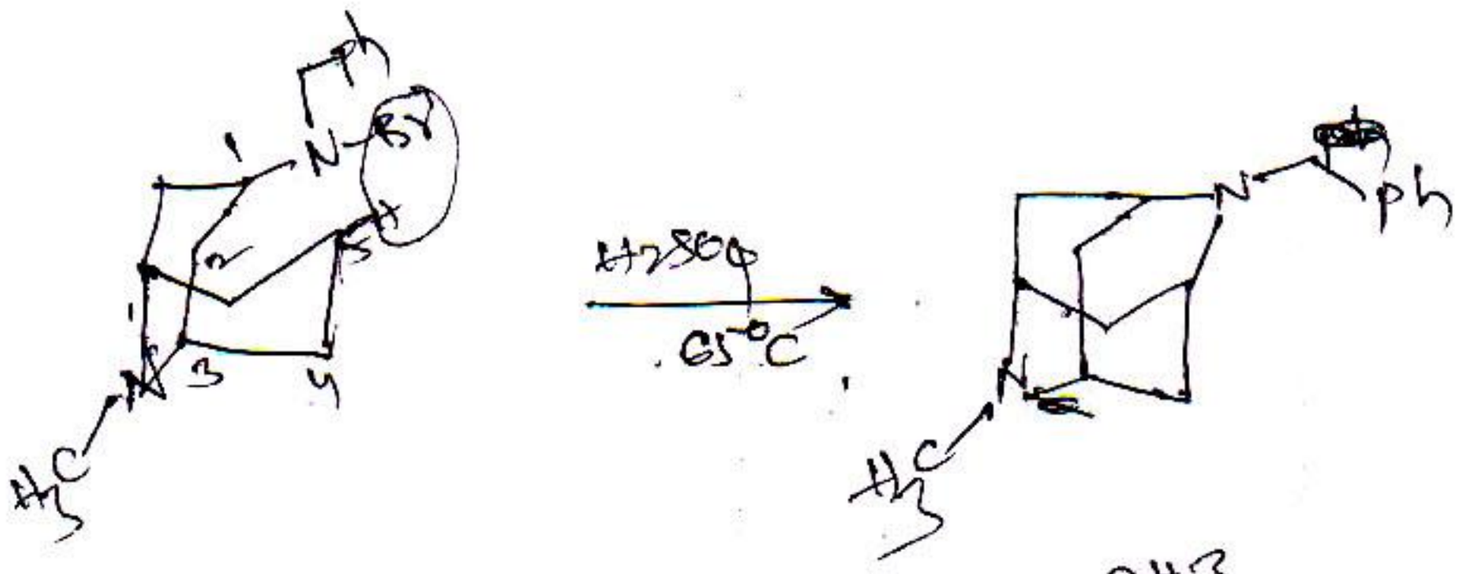


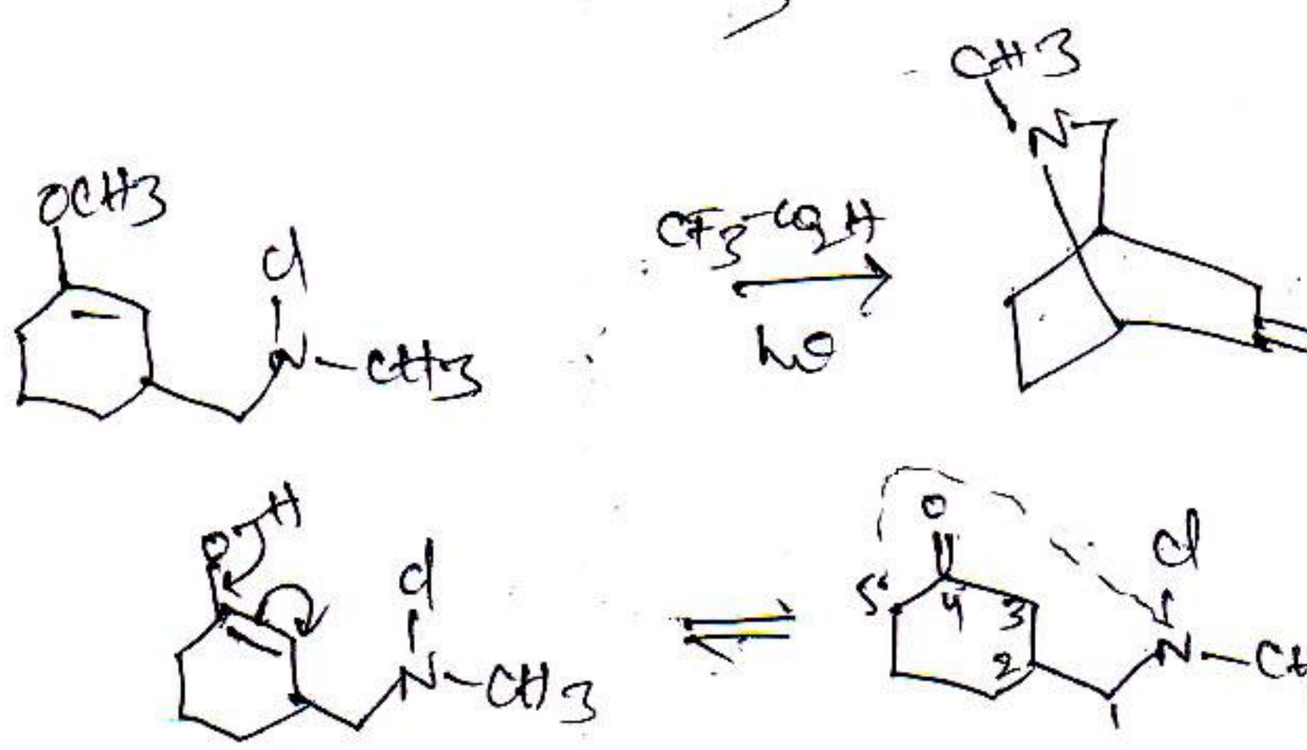



H2SO4 / Δ
Br
C3H7 – CH – C3H7
Br
Br
hν
Double HLF
rxn


90% H2SO4
UV
CH3
Cl
HN – CH3
CH3
NCS
(A)
H2SO4 / H2O
CH3
CH3
CH3
CH3
(A)


NH
1) NCS
2) H2SO4 / H2O
N – Cl


Ph
N – Bz
H2SO4
65°C
H3C
Ph


OCH3
Cl
N – CH3
CF3 – CO3H
H2O
CH3
N
O
O
Cl
N – CH3

WITTING Reaction:-

$$C{=}O \xrightarrow[\text{phosphoranes}]{\text{P-ylide (or)}} \text{olefins} + \text{P-oxides}.$$

Conversion of carbonyl compds into olefins with phosphorous ylide (or) phosphoranes is called Wittig rxn.



(i) C-C Bonding reaction:-

(ii) mild reaction

(iii) Good % of yields

(iv) Easy to prepare mono, di, trisubstituted olefins from the str. of carbonyl easy to predict location of double bond resulting product, always new double bond develops at carbonyl carbon.

LIMITATION

① Not easy to prepare tetra substituted olefins

② By product phosphorous oxides insoluble in water. ∴ ~~Different to~~ ∴ ~~Difficult~~ difficult to remove rxn mixture.

* Not easy to isolate olefin in pure form.

* Stereo selectivity in olefin formation unpredictable depends upon several factors.

* Nature of solvent, Nature of intermediate, Nature of reactant, Nature of Rxn Conditions.

Solvents: Dry ethers, Et_2O, DME, THF

Inert Conditions

in the absence of oxygen or we take $N_2/Ar_2/He$ medium

C.C $\xrightarrow[\text{Anhydrous}\ \&\ \text{inert}]{\text{P-ylide}}$ olefins

Aliphatic aldehydes / Ketones.

Aromatic aldehydes / "

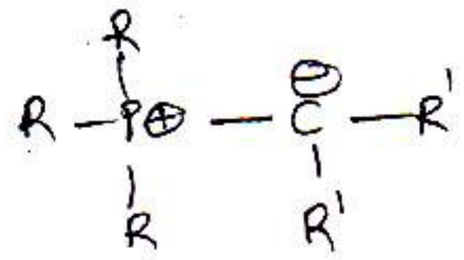
Conjugative " / "

Heterocyclic " / "

Allylic " / "

Reagent:- P-ylide (or) phosphoranes.

(opposite charges adjacent is called ylide)



R = alkyl, Aryl = phenyl

R = phenyl very common.

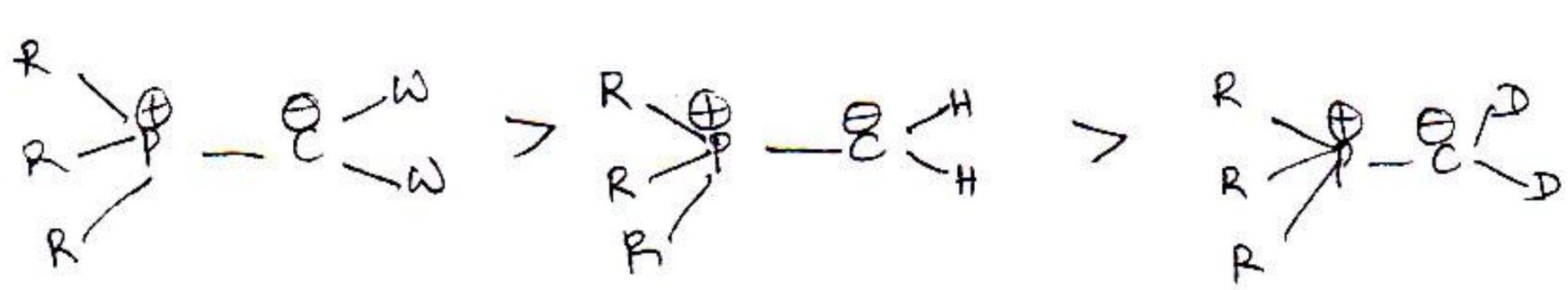
R' = Donating & withdrawing, Alkyl, Aryl.

Stability:- $\overset{\ominus}{C}-W > \overset{\ominus}{C}-H > \overset{\ominus}{C}-D$

W = withdrawing, D = Donating

Stability of P-ylide depends mainly on nature of groups at carbanion.

* withdrawing gp stability - increases
* Donating gp stability - decrease.



Stability of ylide controles Stereo selectivity in olefin formation

∴ Unstable ylide ⇒ Z-olefin major

Stable ylide ⇒ E-olefin

Semistable ylide ⇒ Z+E mixture

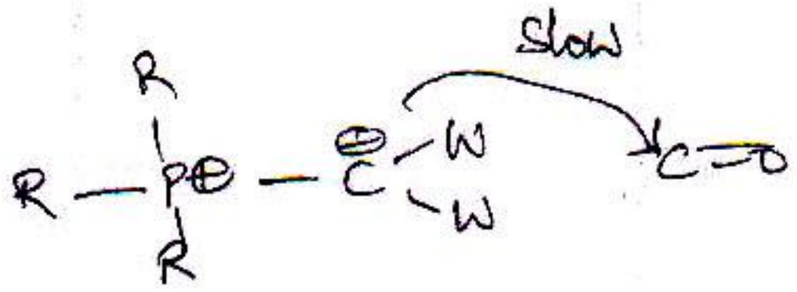
L.D.A 

In wittig rxn Li bases are used.

Eg: n BuLi, LDA
Lithium Hexa methyl di silazile (LDA) favours E-olefins

→ If other than Li bases used wittig rxns are

Eg: NaH, KH, $tBuO^{\ominus}K^{\oplus}$ these W.R. are Li-salt free wittig rxns — favours Z-olefins.



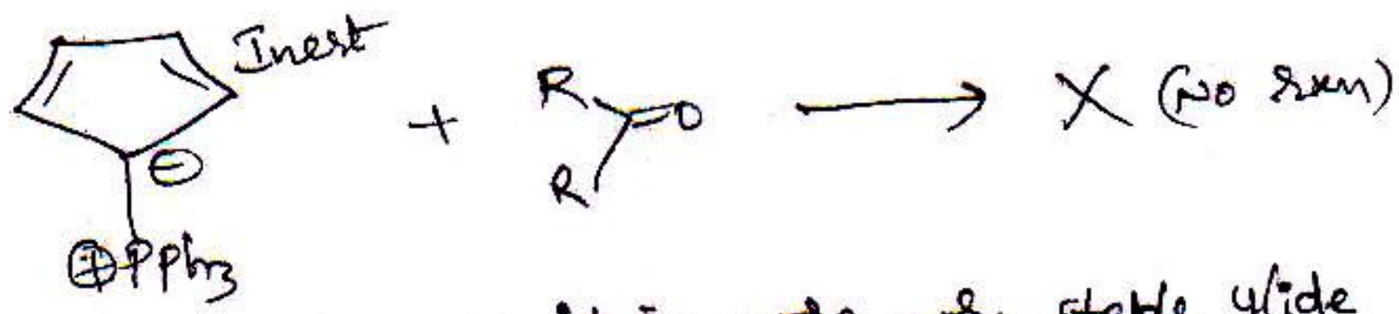
Stable ylide slow in Rxn with carbonyl compound.

Unstable wittig ylide fast in rxn with carbonyl compound.

more stable ylide ⇒ Less reactive

Less stable ylide ⇒ more reactive



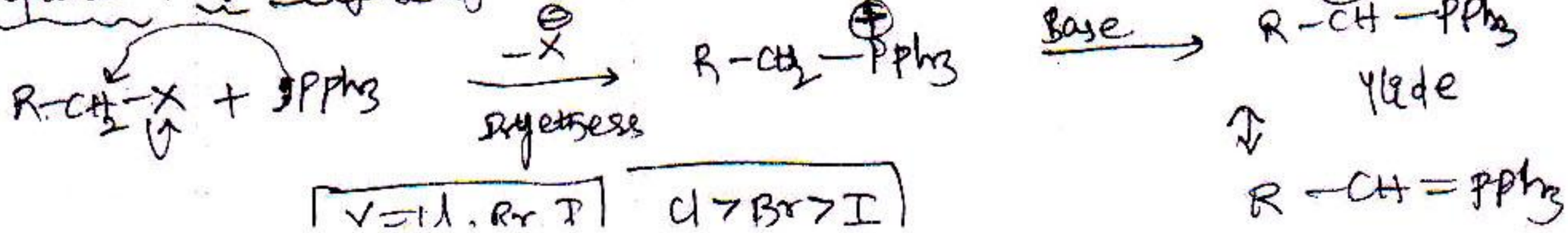
Ex: 

└ Because it is more more stable ylide

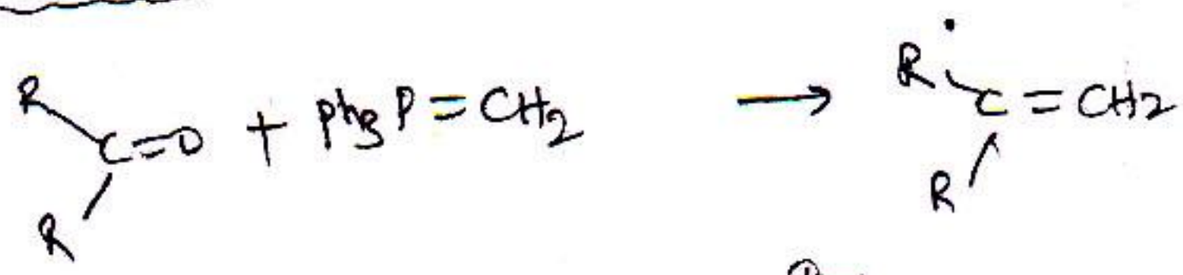
Highly stable ylide are inert in witting rxn

Highly stable, inert because of Aromaticity.

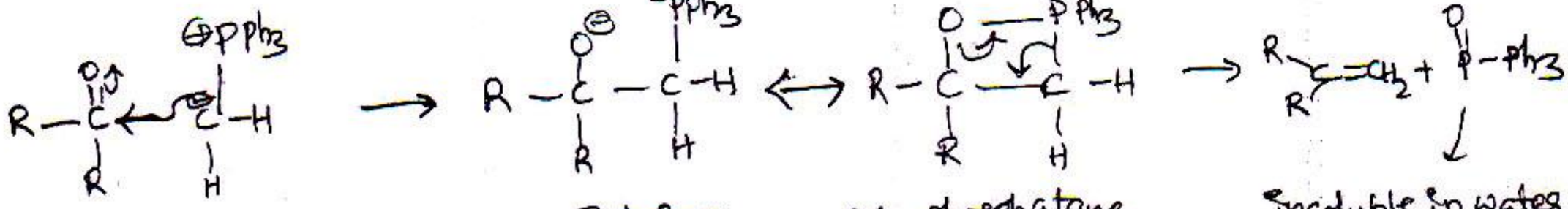
Preparation of wittig-Reagent:



Jittig Mechanism:-



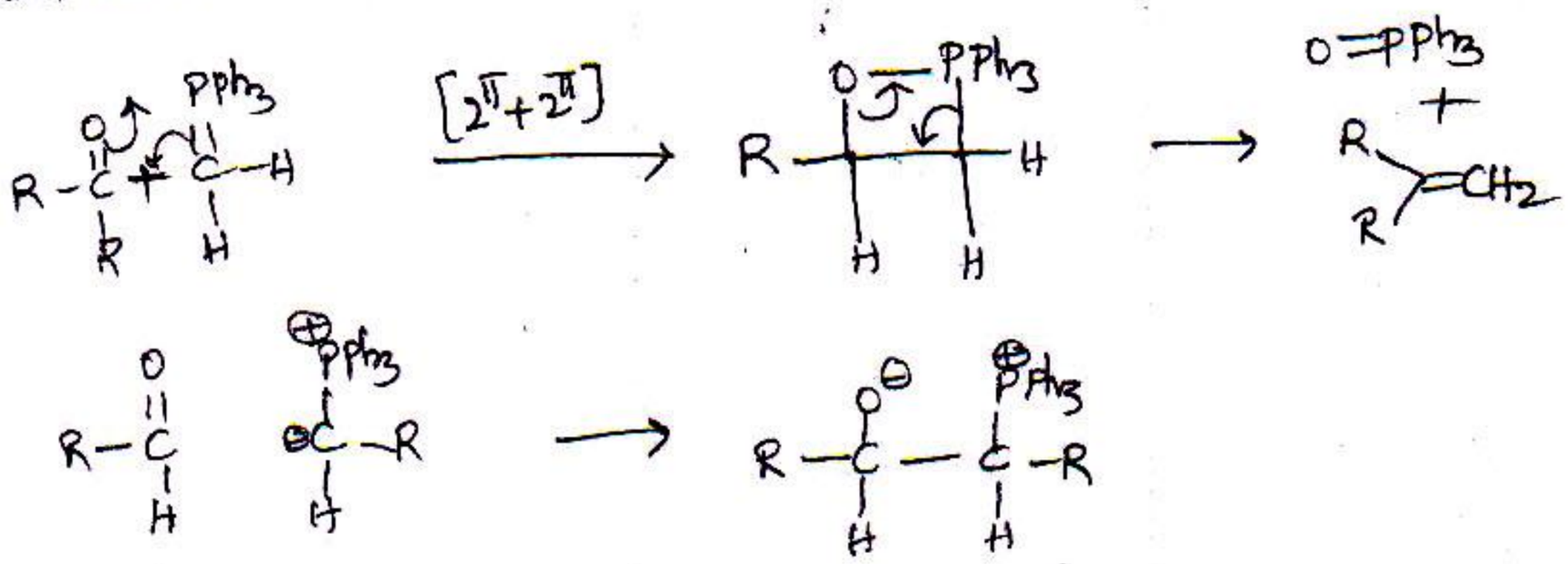
mech:-



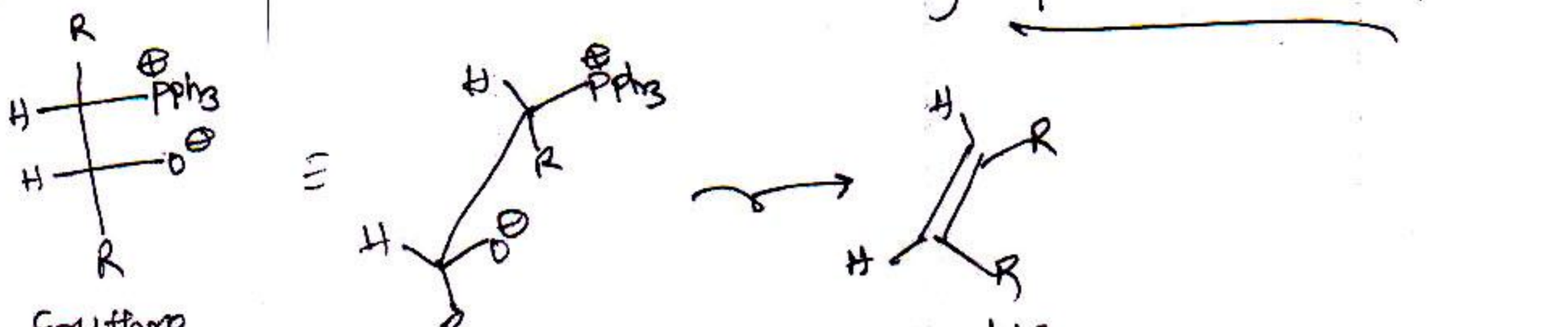
P- Having good attraction forming P=O bond.

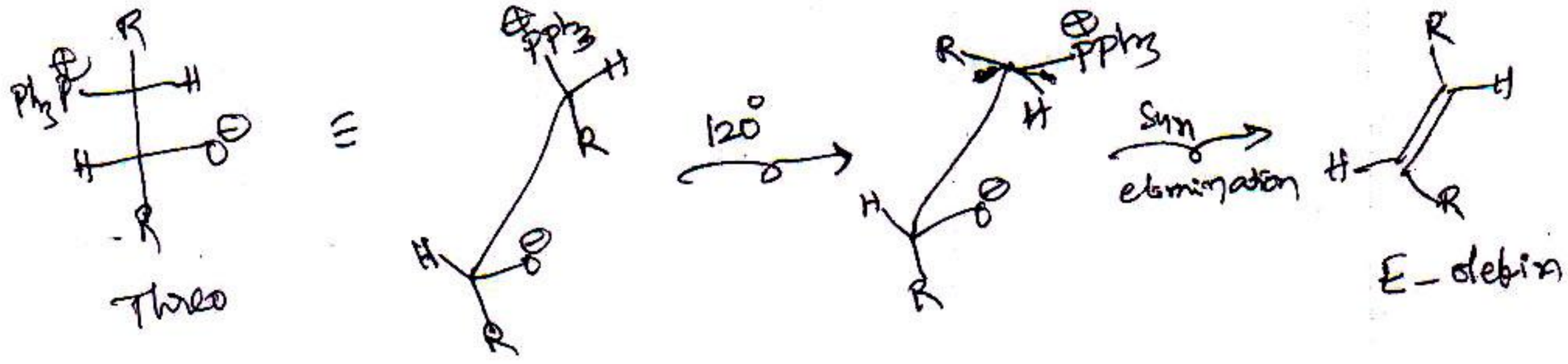
Betain' form' not observed in all wittig rxns. Some of the wittig rxns directly produces oxa-phosphatane without prepare betaine.

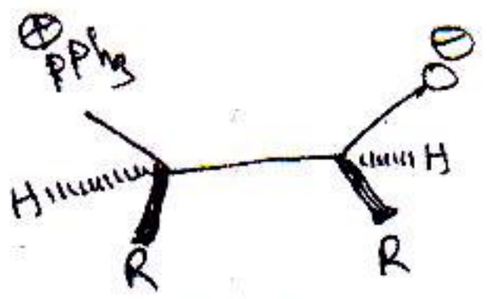
Whenever Betain is formed can be isolated from rxn mixture.



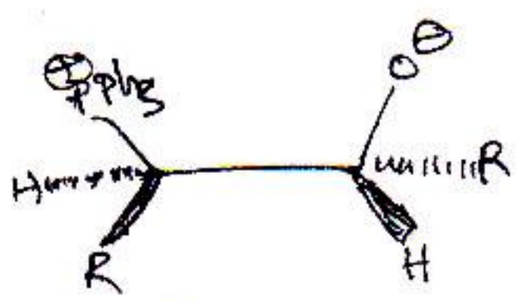
There are two chiral centres in the betain can have stereo isomers, erythro threo there are its decomposition in olefin depends on nature of stereo isomer of Betain syn Condn usually syn eliminations preferred.



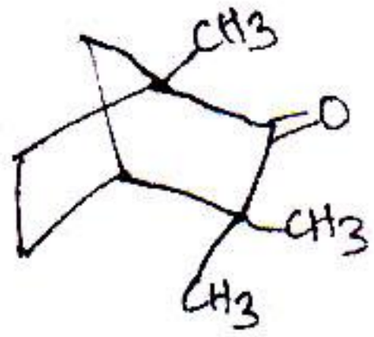




Erythro



Threo



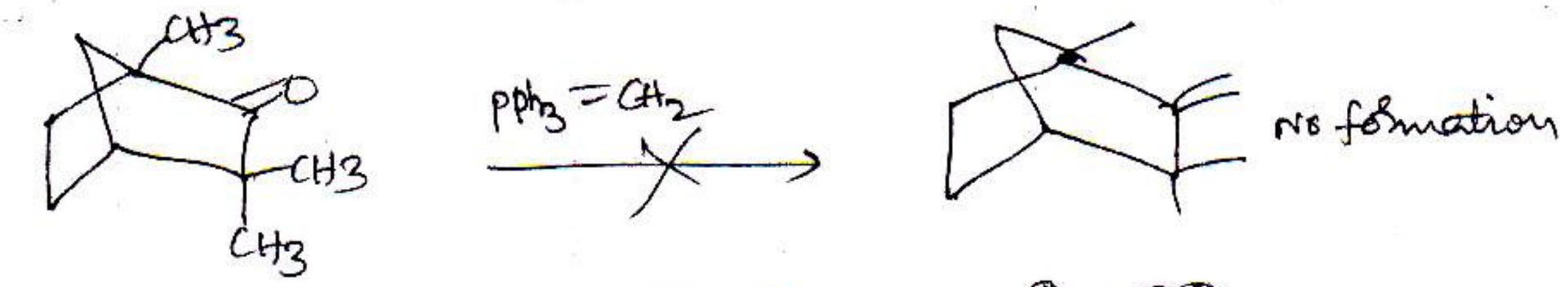


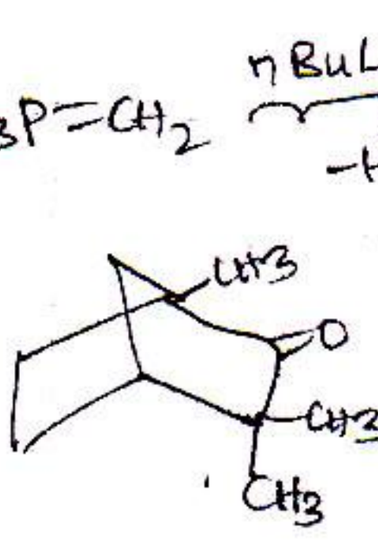
→ No rxn.

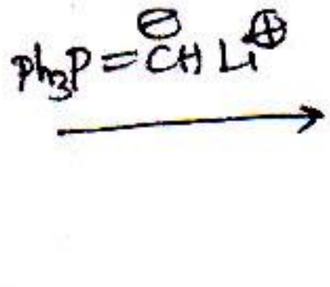
(Due to steric crowding)

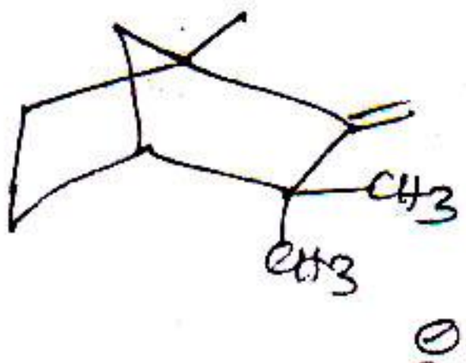


Some of the carbonyl Compds inert in wittig rxn with simple ylide, due to high steric crowding at carbonyl function to overcome steric crowding anion of phosphoranes (or) dianion of P-ylide are used.

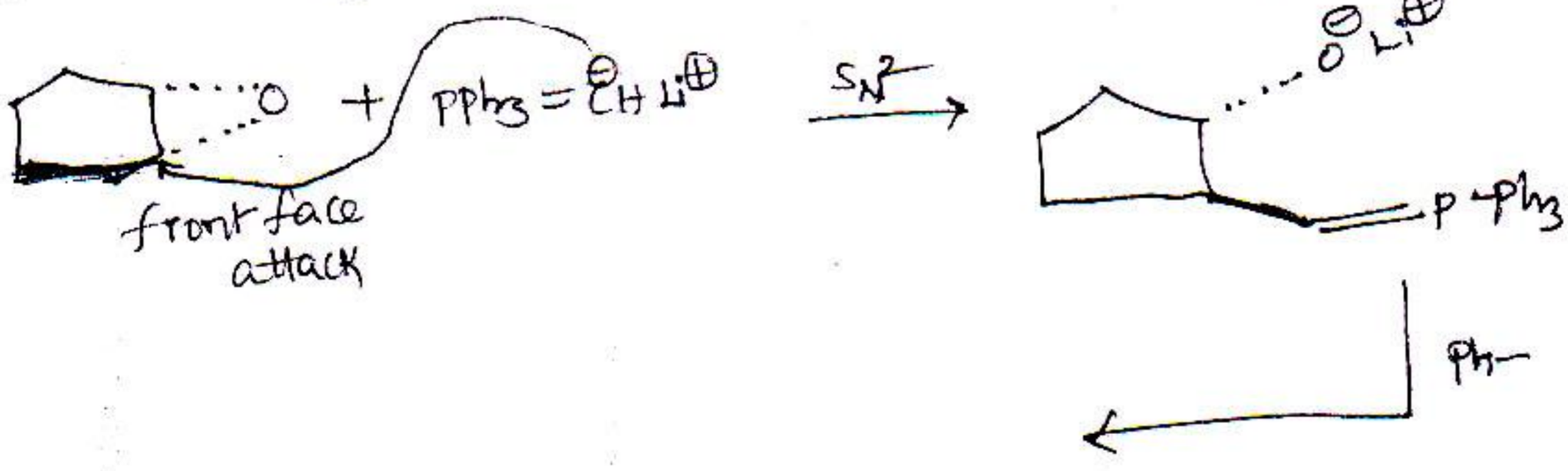




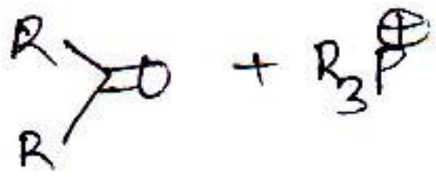




Ex:



HARDWORTH-EMMON'S REACTION :- (or) HORNER-EMMONS OLEFINATION

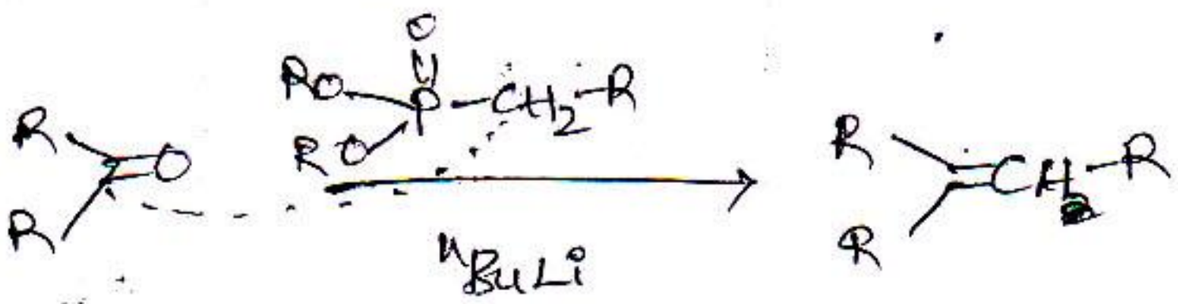


Wittic rxn have some debects in order to correct these defects WORD WORTH-EMMON'S rxn developed by modifying wittic reagent.

Simple wittic reagent phosphorane.

modified wittic reagent phosphonates 

C.C converted into olefins by using phosphonates is called HARDWORTH-HORNER-EMMON'S rxn.



Advantages

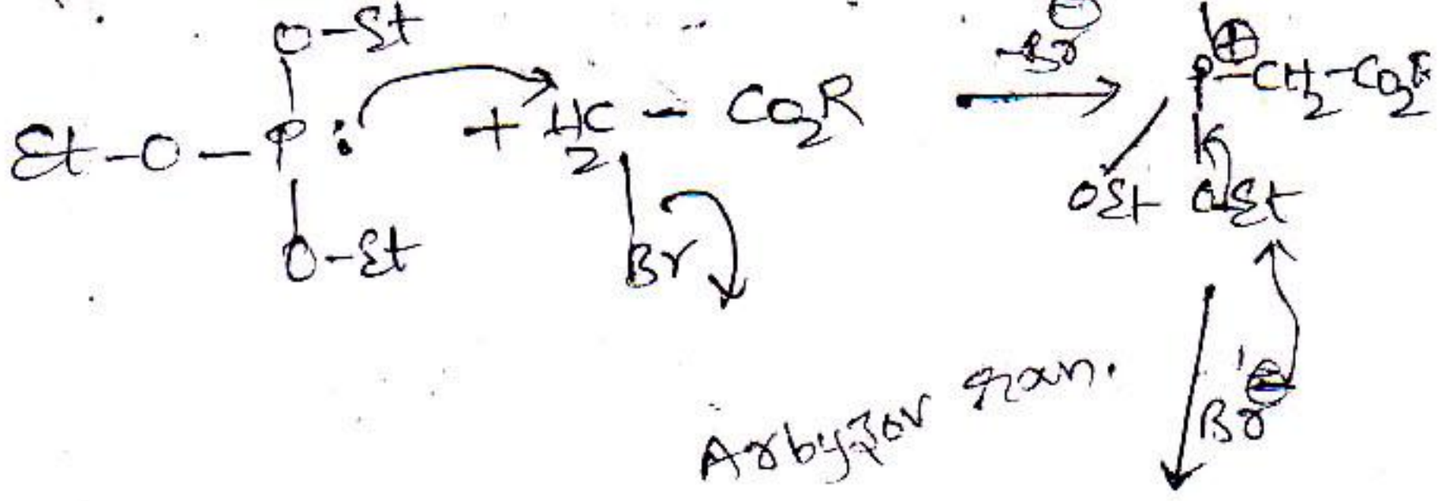
① By products are easily soluble in water ∴ Easy to remove from rxn mixture.

② E-selective rxn.

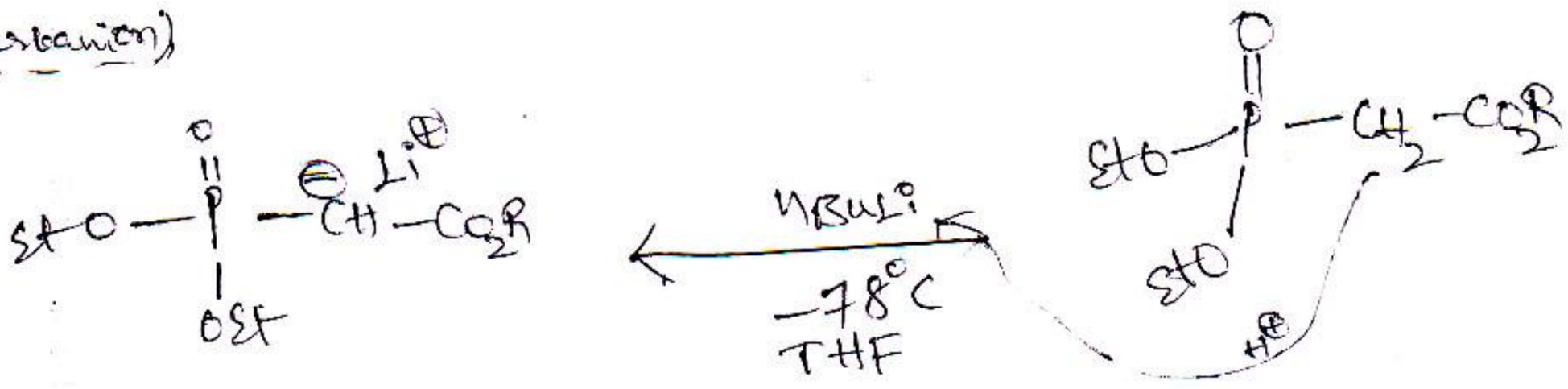
③ Even tetra substituted olefins also can be prepared.

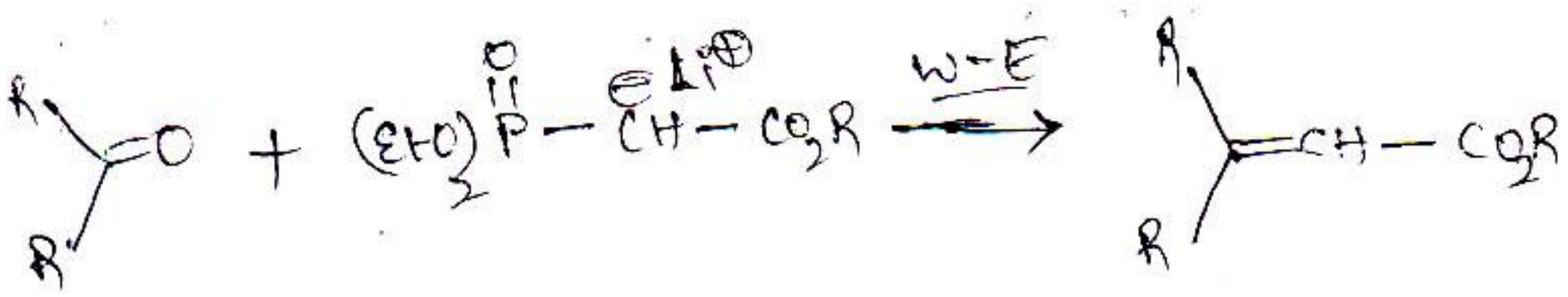
PHOSPHONATES PREPARATION:-

Alkyl phosphites $(RO)_3P$

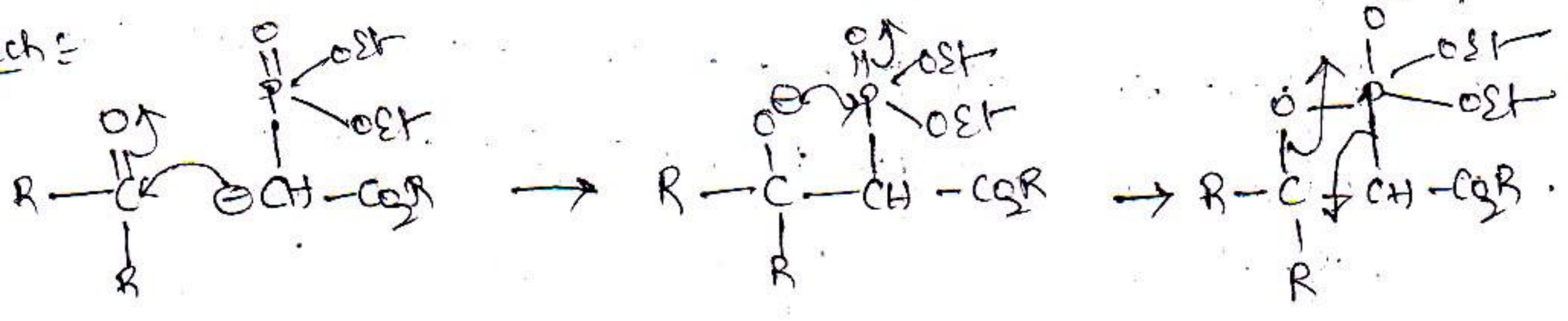


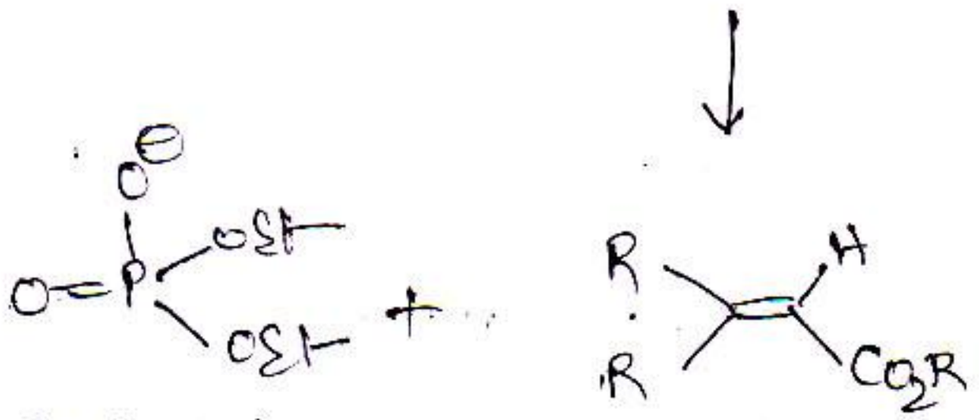
(Good carbanion)





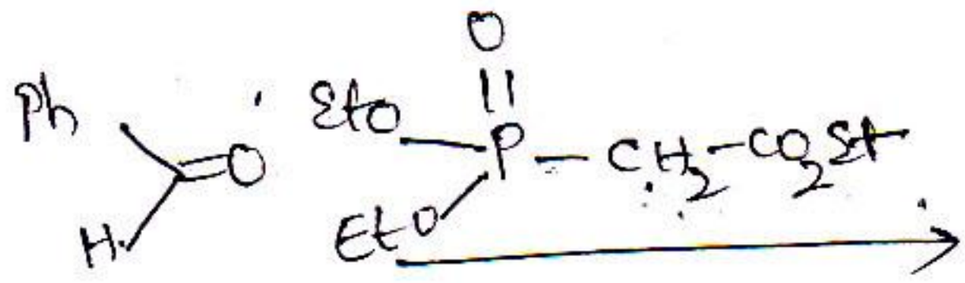
Mech :-





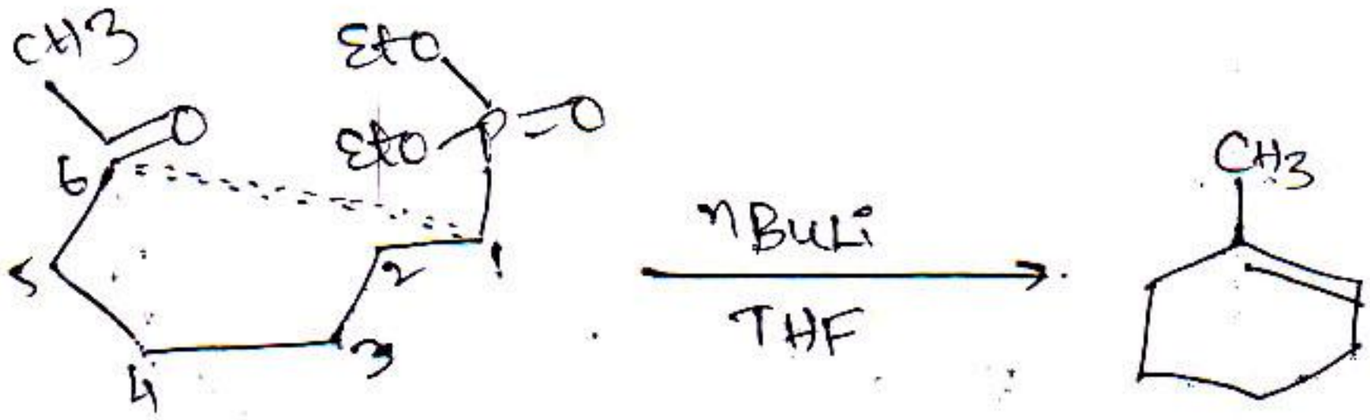
Easily soluble in water
so easy to remove.

(*)

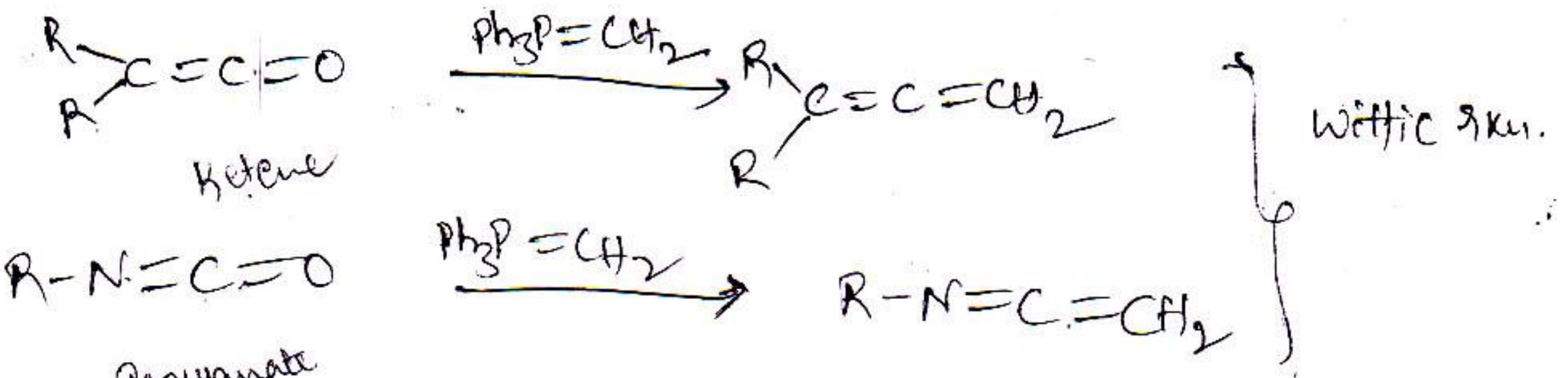


Trans (major)
Ethyl cinnamate:

(*)



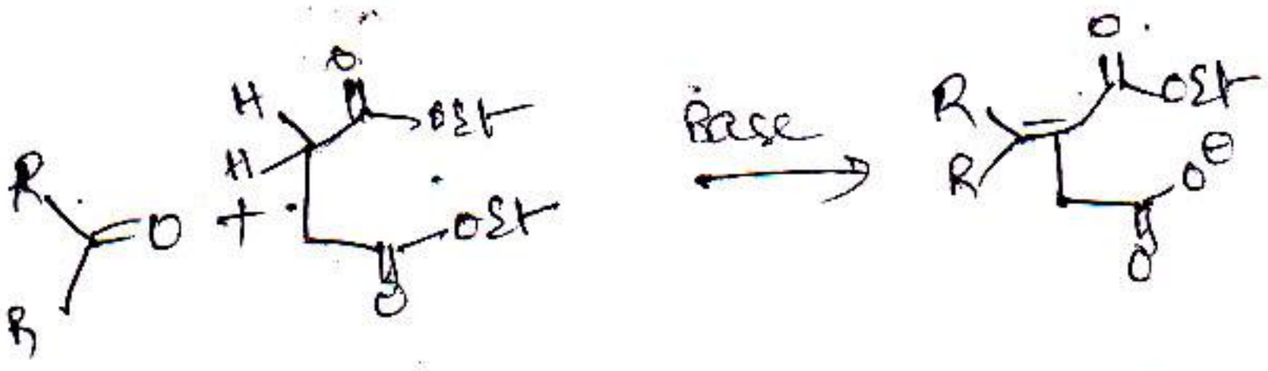
Intramolecular Wadsworth-Emmons ran





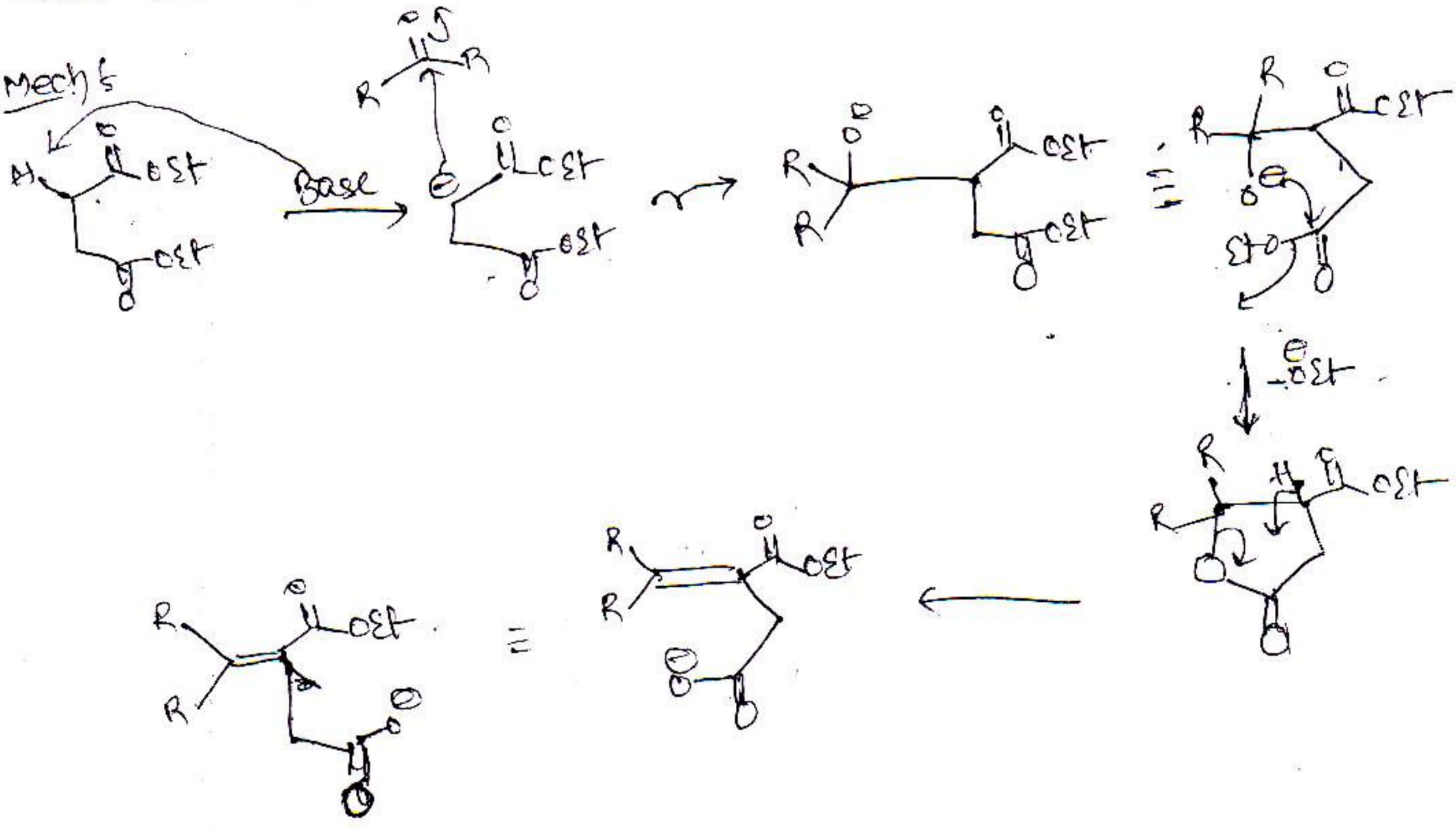
Wittic reagents can undergo ozonolysis.

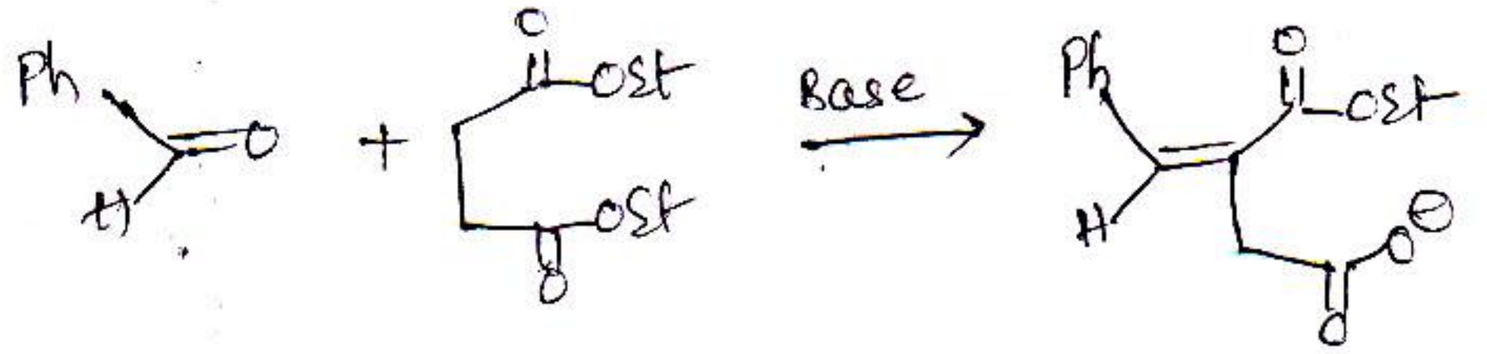
STOBBE - CONDENSATION :- (Diethyl Succinate)



Condensation of diethyl succinate & C.C in the presence of base called Stobbe Condensation one of the ester gets hydrolysed.

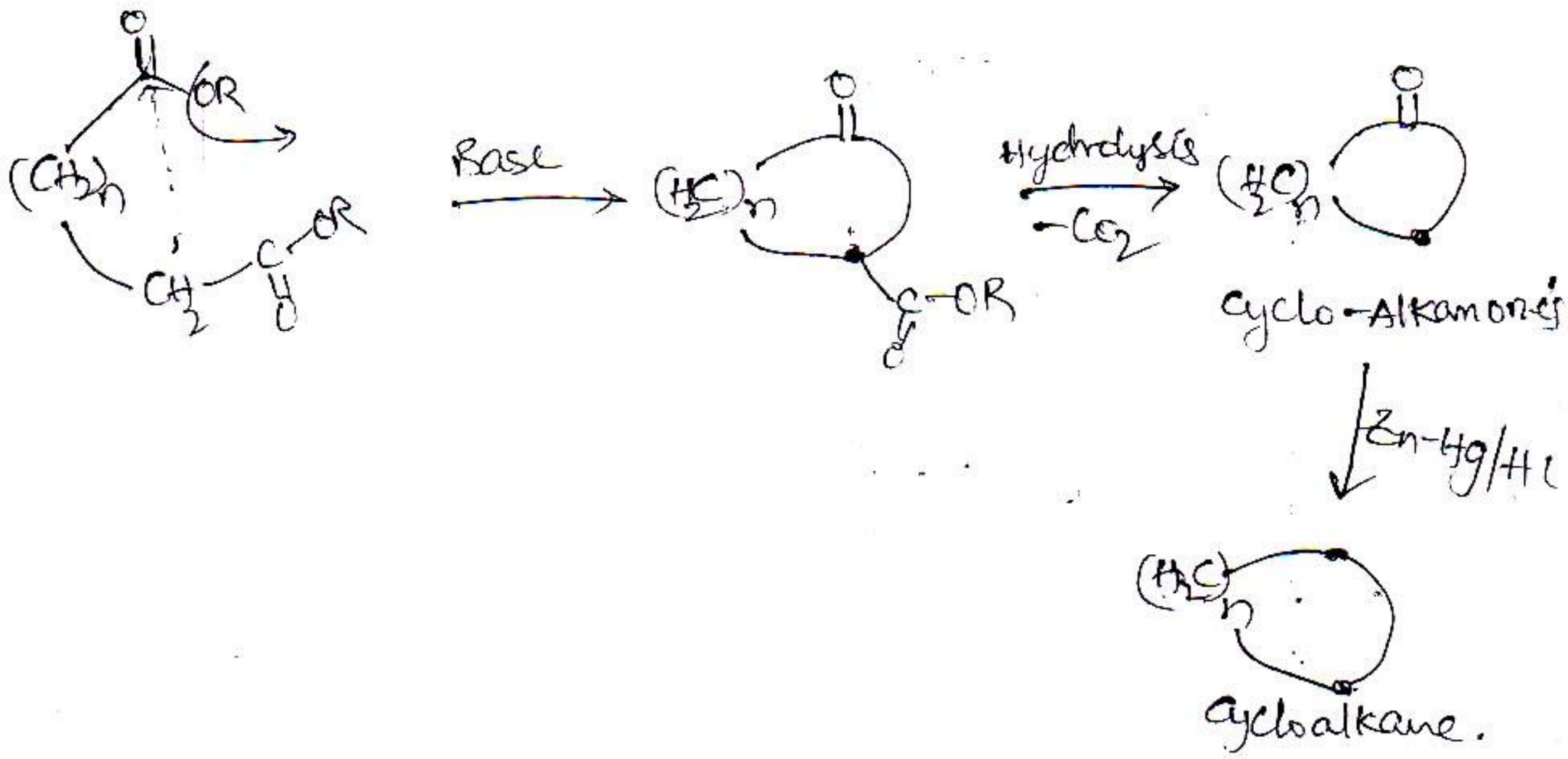
Mech :-





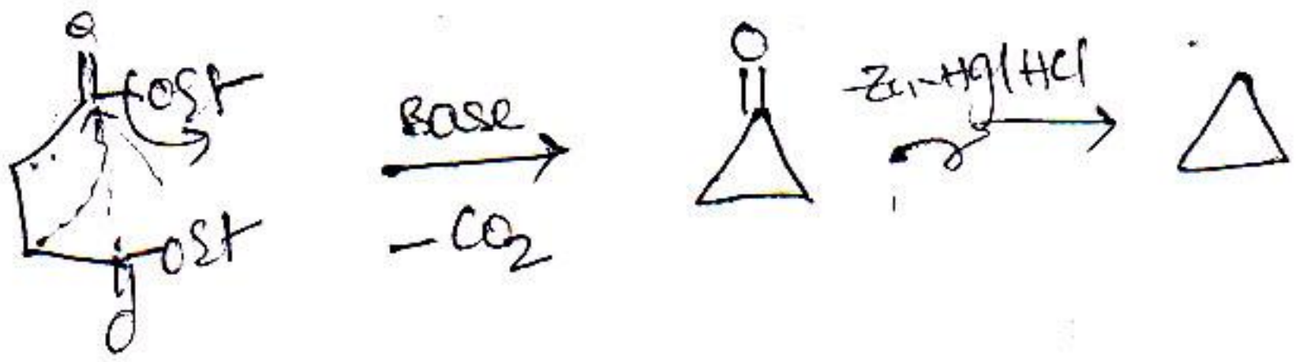
DIECKMAN'S-CYCLIZATION :-

Intramolecular cyclization of diester in base is Dieckman cyclization

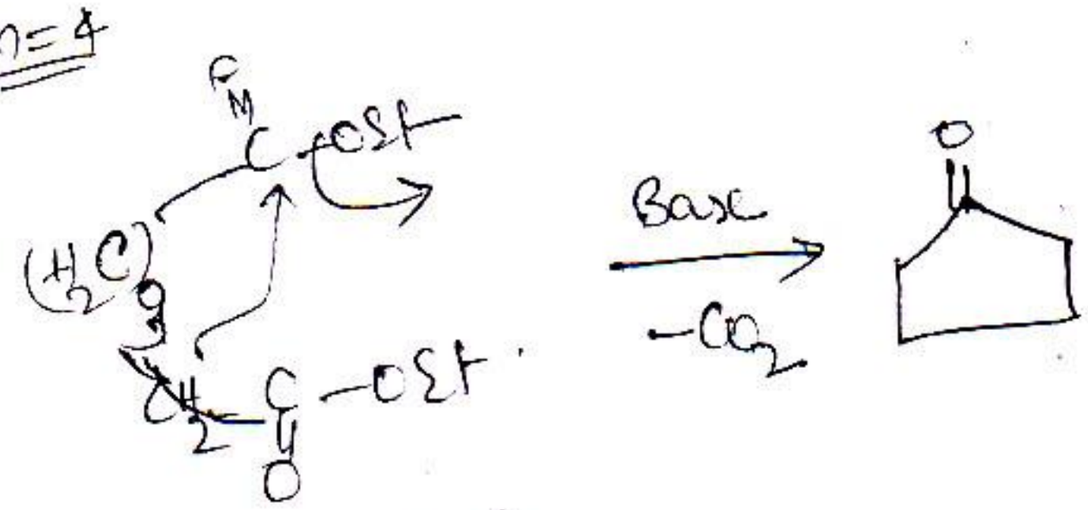


Diethyl-Succinate

$n=2$

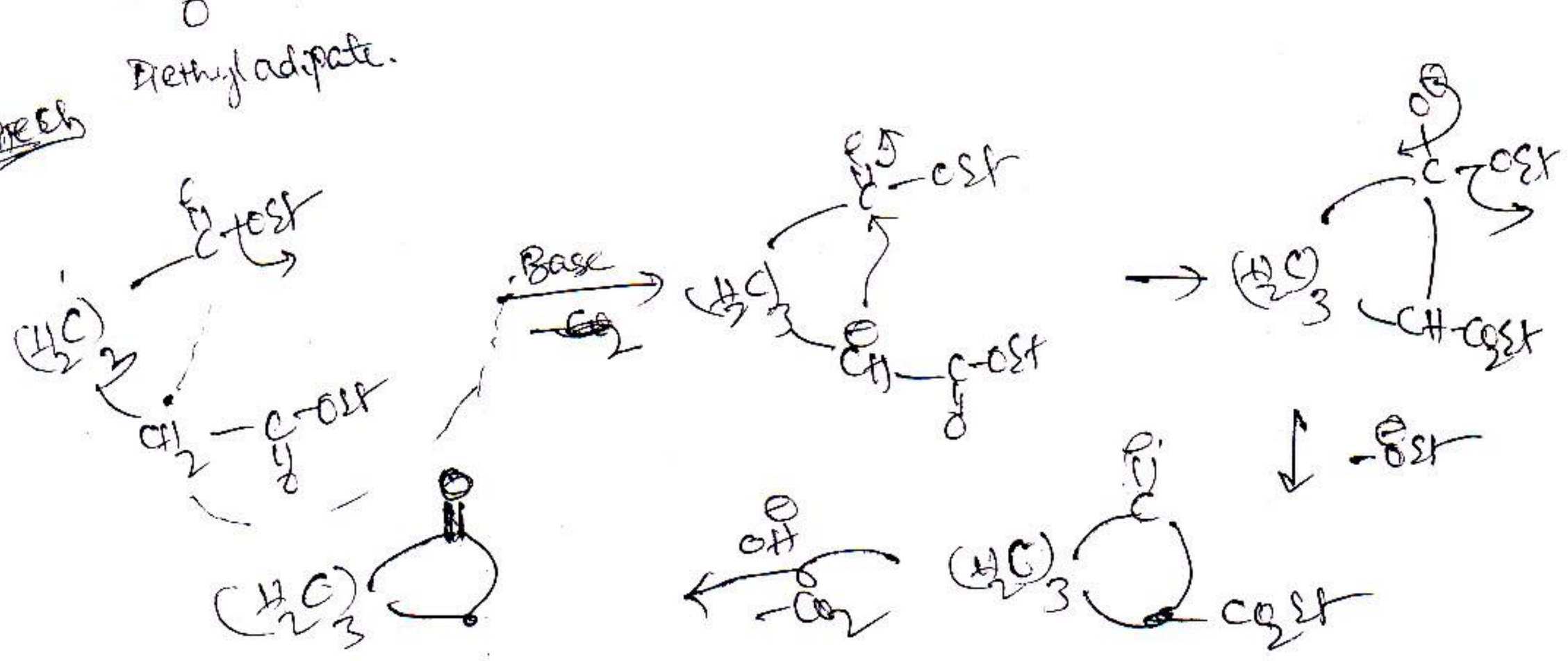


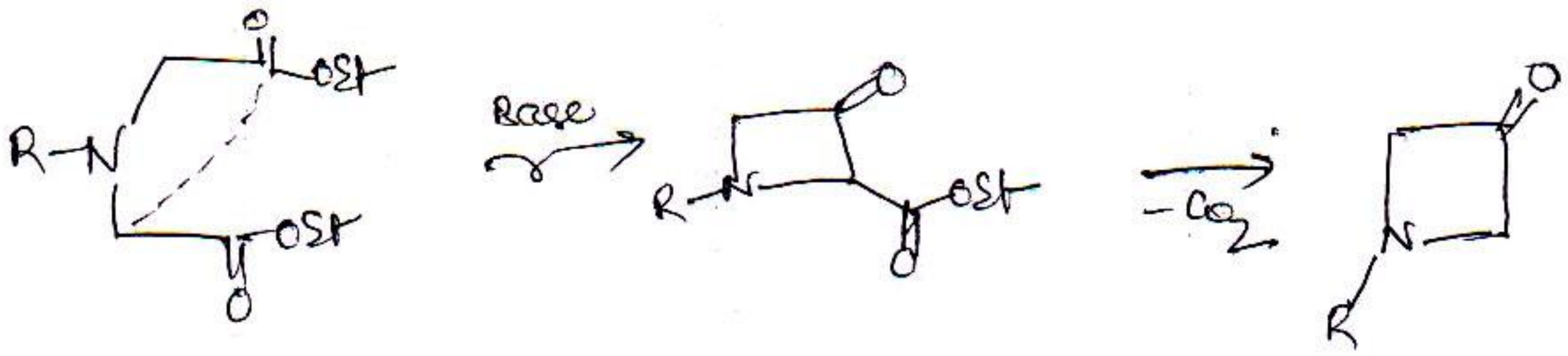
$n=4$



Diethyl adipate.

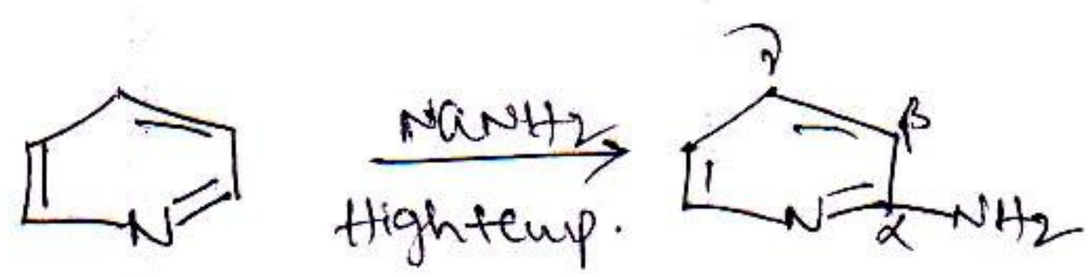
Mech





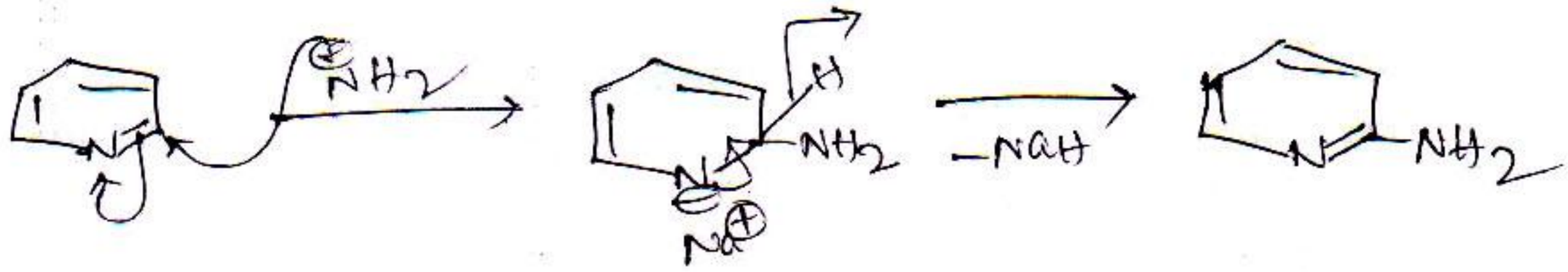
Base catalysed, carbanion intermediate, new C–C bonding intra molecular method for prepn of cycloalkanones & cycloalkanes.

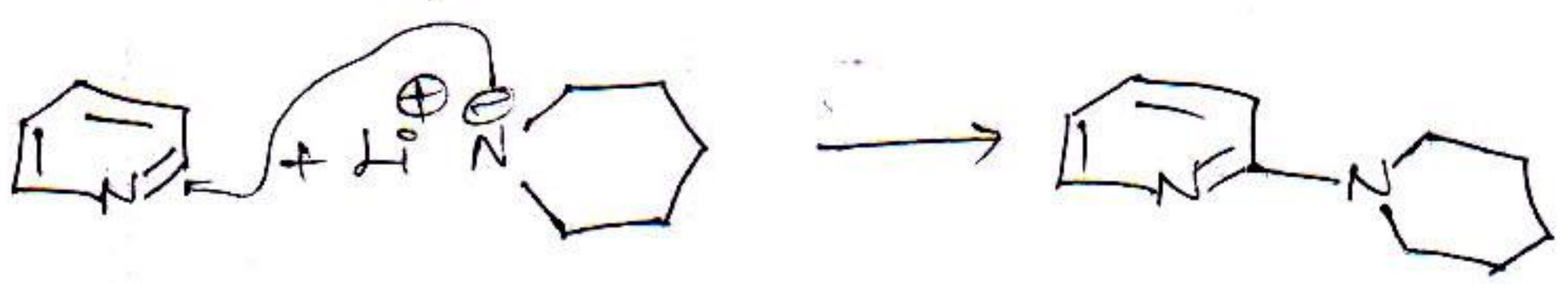
CHICHIBABIN REACTION:- Amination of Nitrogen Heterocyclics

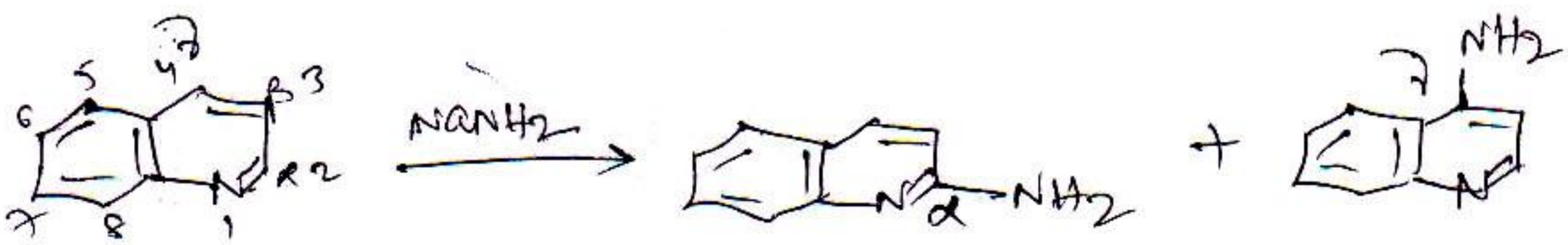


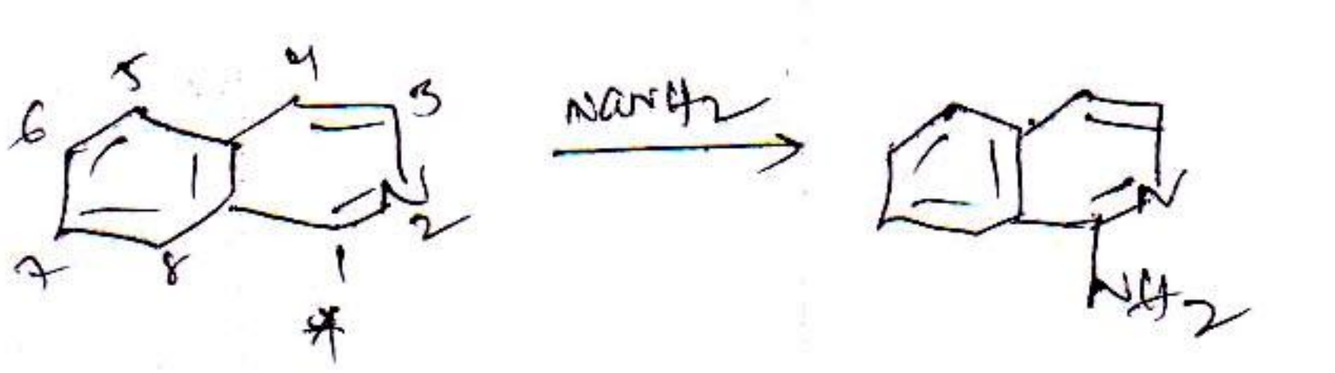
Mech:-





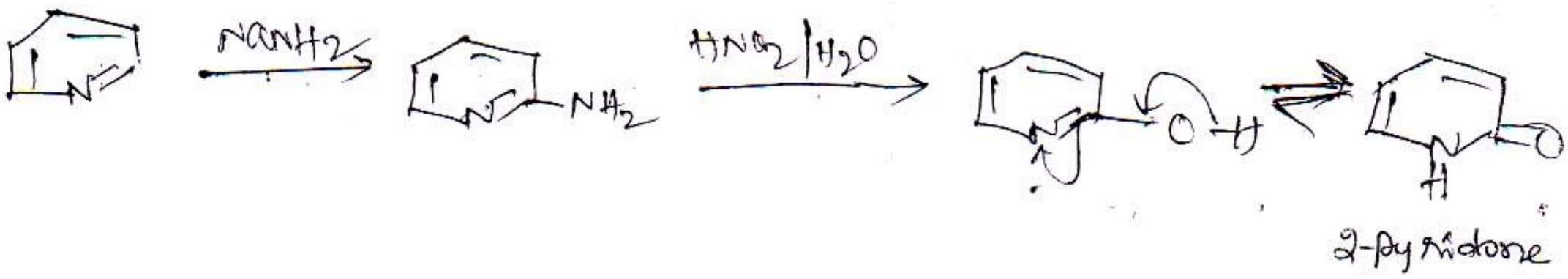






1-amino isoquinoline





2-Pyridone