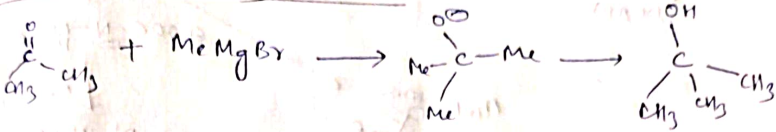
# Unit-3 : C-C and C=C bond formations reactions

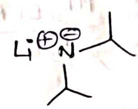
## C-C Bond Forming Reactions



Aldol condensation → enolate + benzaldehyde.

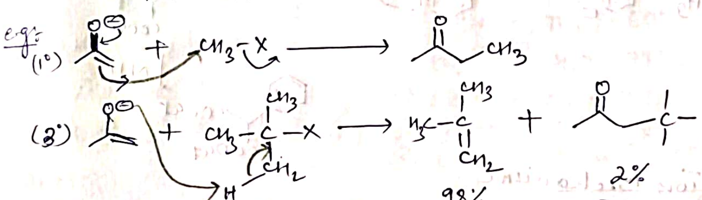
Enolates

α-H containing carbonyl compd + Base } → Enolate
↓ Alkylating agent
C-C bond

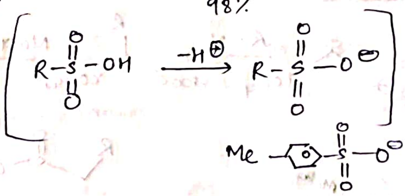
- Different types of bases used are
  - NaOEt / EtOH
  - NaOH
  - NaH
  - LDA (Lithium diisopropyl amine) 

- Alkylating agent used are
  1. Alkyl halide
     1°, 2° → Reaction occur
     but 3° → Does not occur.

e.g.:



2. Sulphonate

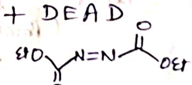


3. Alcohols

$R-OH \xrightarrow{H^{\oplus}} R-\overset{\oplus}{O}H_2$

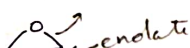
Mitsunobu RxN

$PPh_3$ + DEAD



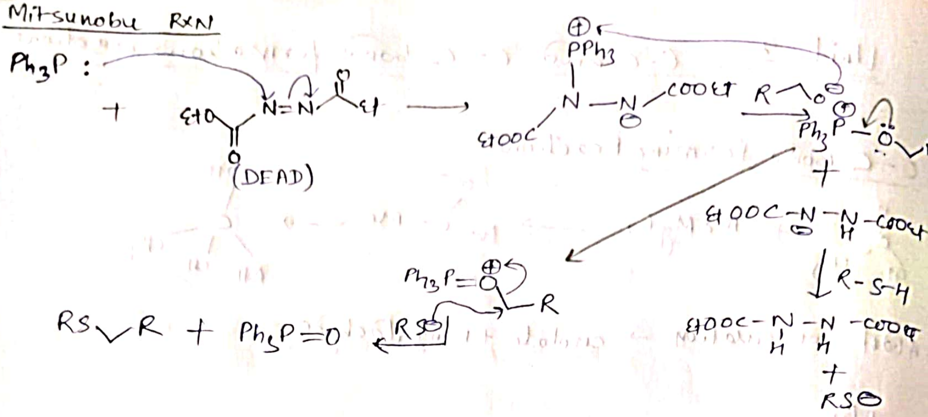
Diethylazodicarboxylate.

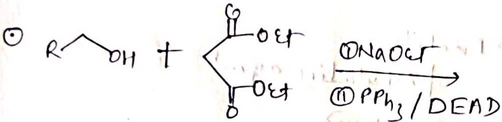
4. Epoxides



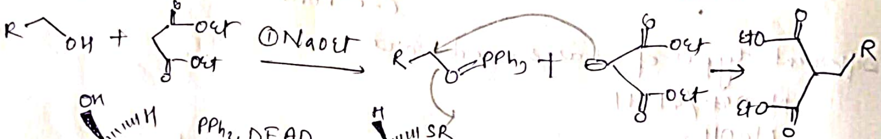
strained system.

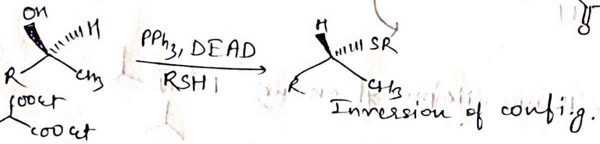
Mitsunobu RXN

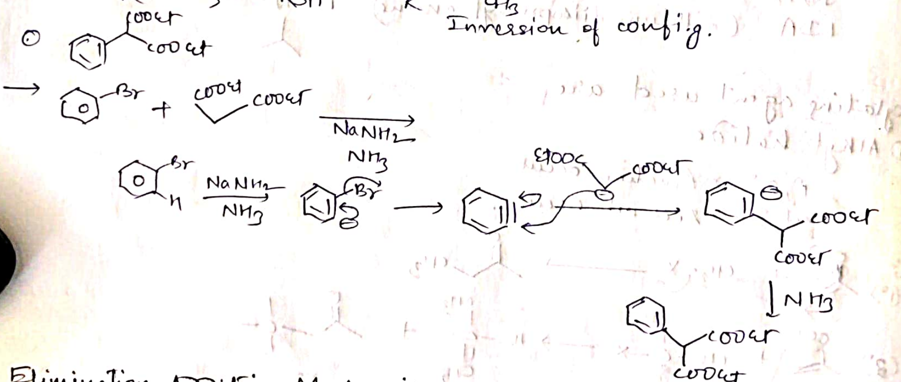




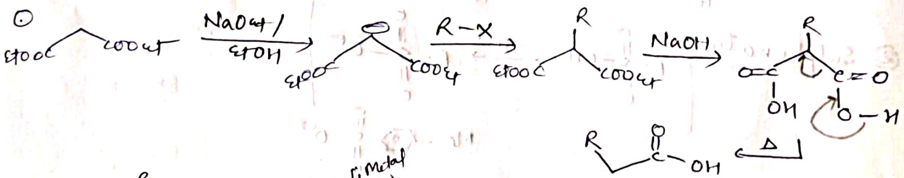
Ans :

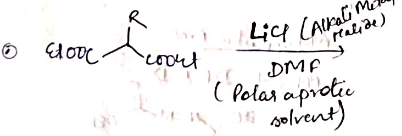


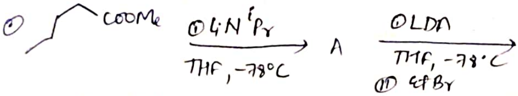


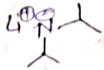



Elimination Addition Mechanism

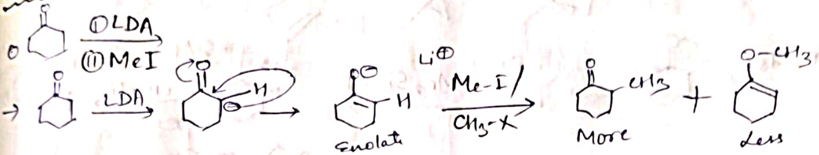


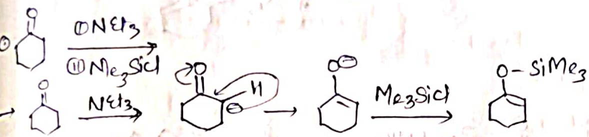




LiN$^i$Pr (Non-nucleophilic)  = LDA

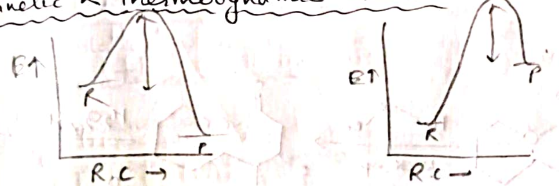
## Enolates

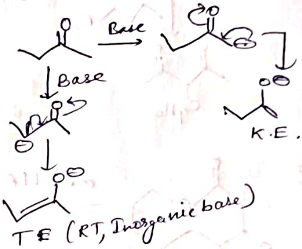



- O-Si >>> O-C bond
  S-F bond is also strongest bond.

## Kinetic & Thermodynamic Enolates



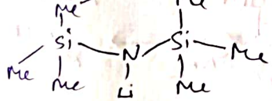

### Thermodynamic Enolate

Bases: (i) NaOEt / EtOH
(ii) KOH / EtOH
(iii) t-BuO$^-$K$^+$ / t-BuOH

### Kinetic Enolate

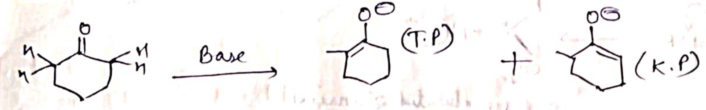
(i) LDA / THF / -78°C
(ii) LiHMDS / THF / -60°C
(iii) $Ph_3C^-Na^+$ / $Et_2O$ / -78°C
(iv) LiCA / THF / -78°C
(v) LiTMP / THF / 0°C
(vi) LiCA (Lithium isopropyl cyclo hexyl amide)

(i) LiHMDS

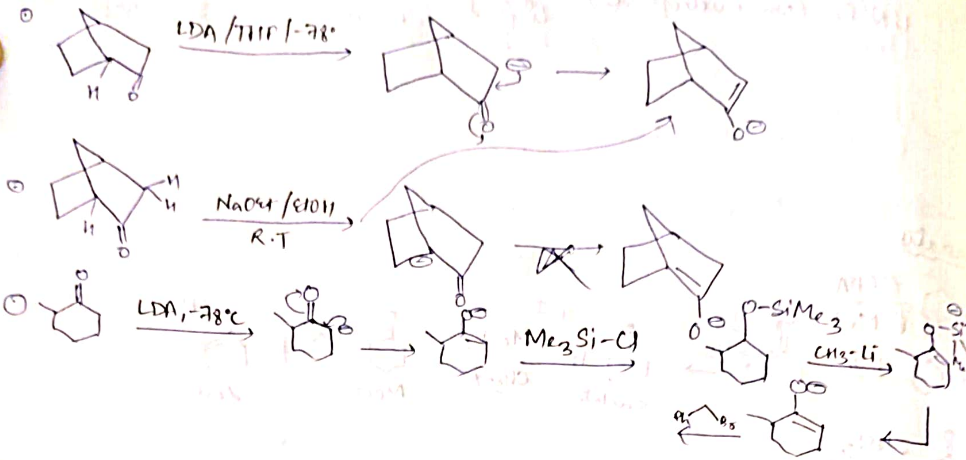


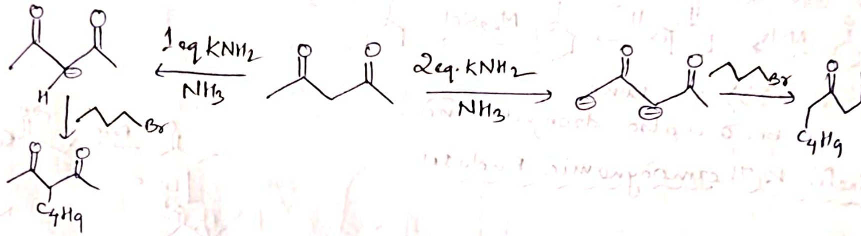

Lithium bis(trimethylsilyl amide)

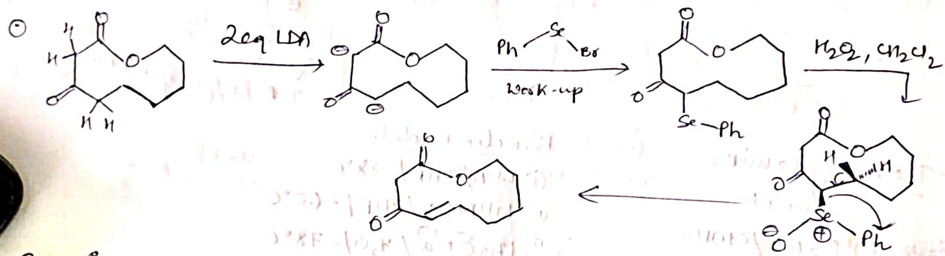
(vii) LiTMP [Lithium (tetramethyl piperidide)]




| | T.P | K.P |
|---|---|---|
| LDA, DME = -78°C | 1% | 99% |
| $Ph_3CLi$, DME = -78°C | 9% | 91% |
| $Ph_3CLi$, DMF | 90% | 10% |
| t-BuOK, t-BuOH | 93% | 7% |

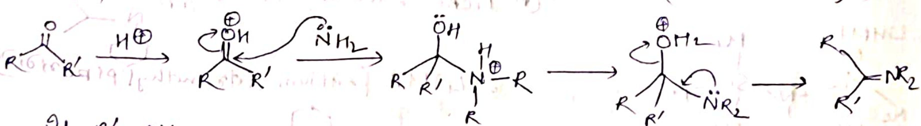


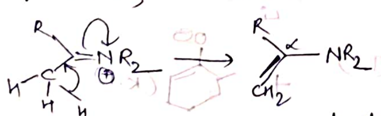




## Enamines

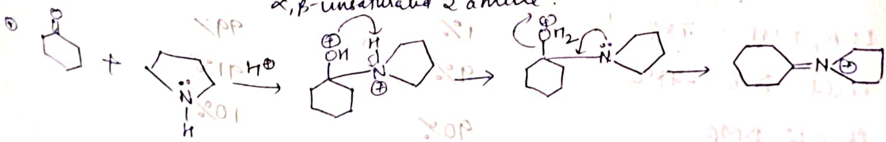
Aldehyde/Ketone + 2° Amine $\xrightarrow{H^\oplus}$ Enamine : $\left( CH_2=\overset{NR_2}{\overset{|}{C}}-R \right)$

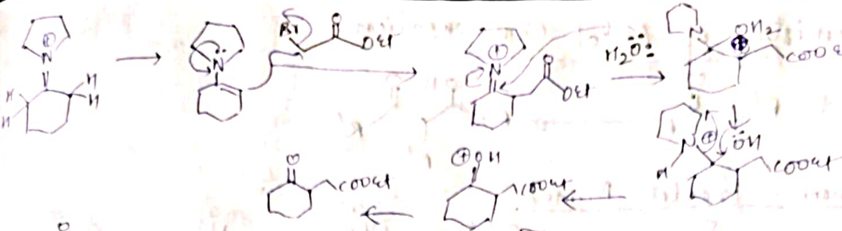


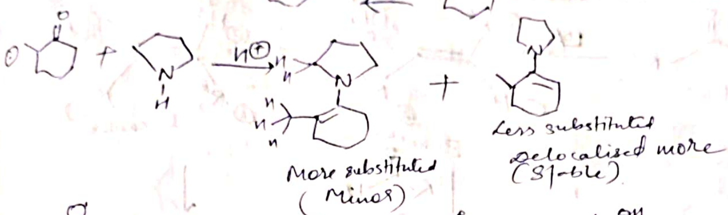

If $R' = CH_3$

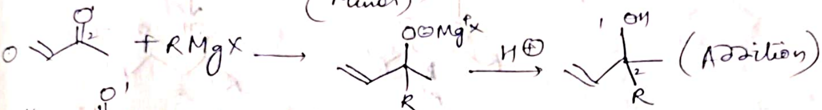


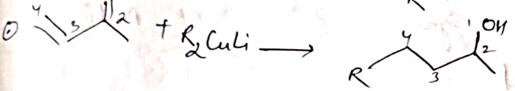
α,β-unsaturated 2° amine







Hard Nu$^{\ominus}$ ⟶ 1,2-Addition.

**Michael Addition**

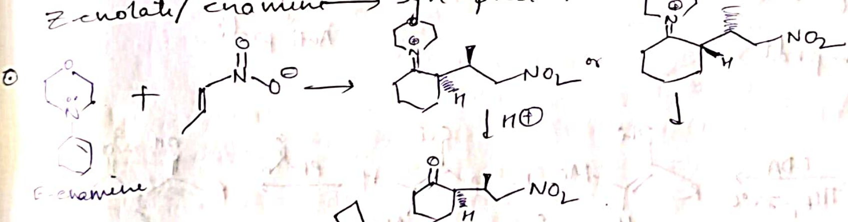
E-enolate/enamine ⟶ Syn prodt (E2)

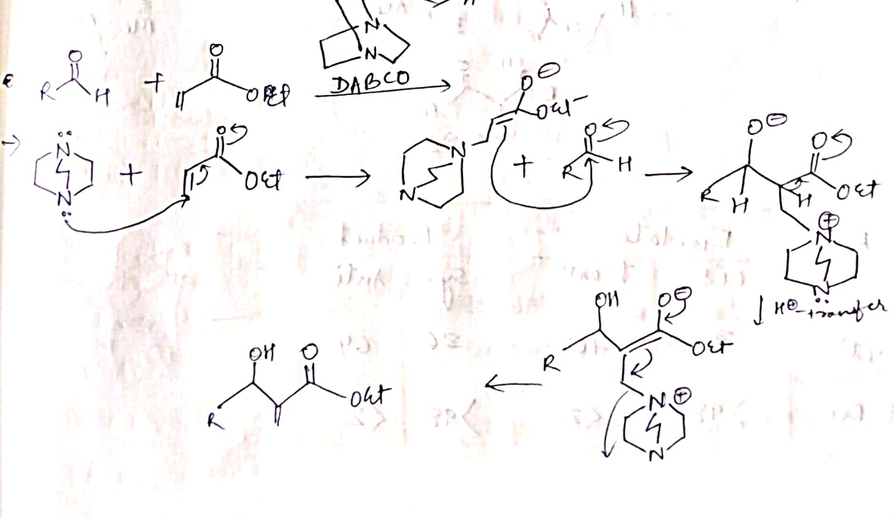
Z-enolate/enamine ⟶ Anti prodt

**Aldol Condensation**

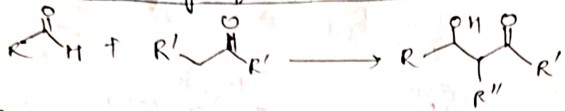
E-enolate/enamine ⟶ Anti prodt (MES)

Z-enolate/enamine ⟶ Syn prodt.

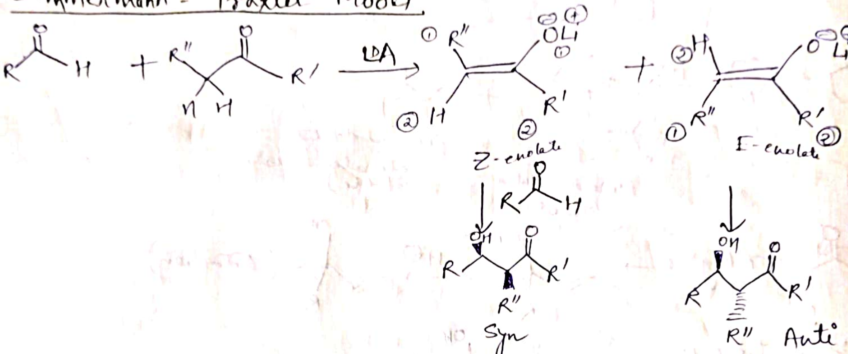


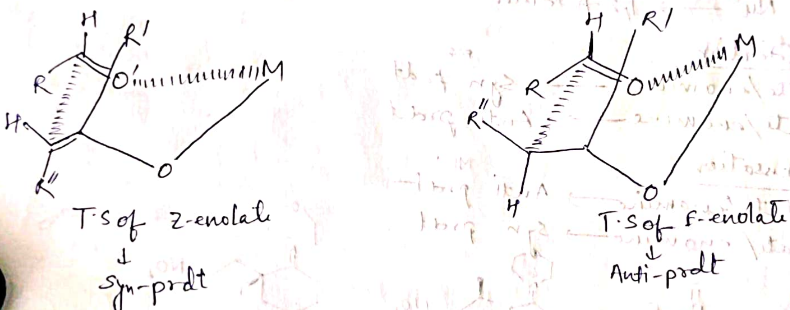
# Stereochemistry of Aldol Condensation

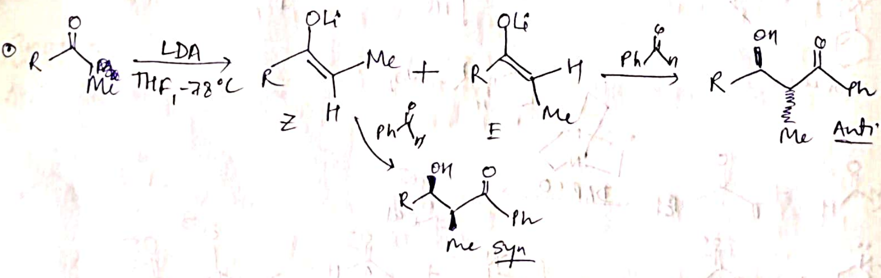


## Zimmermann-Traxler Model

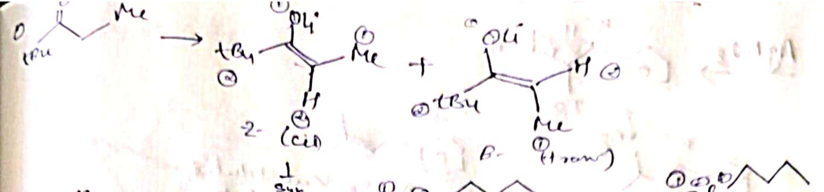


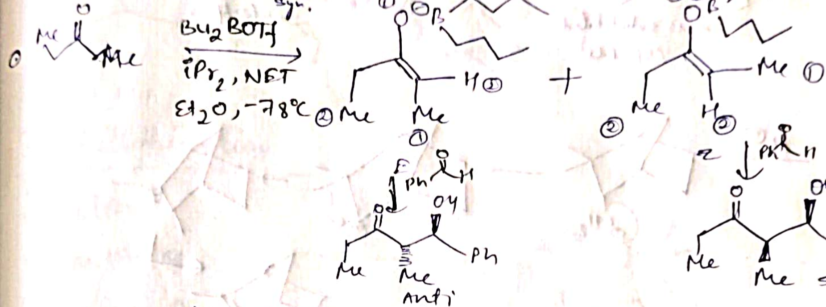

## Transition State of Z-T Model

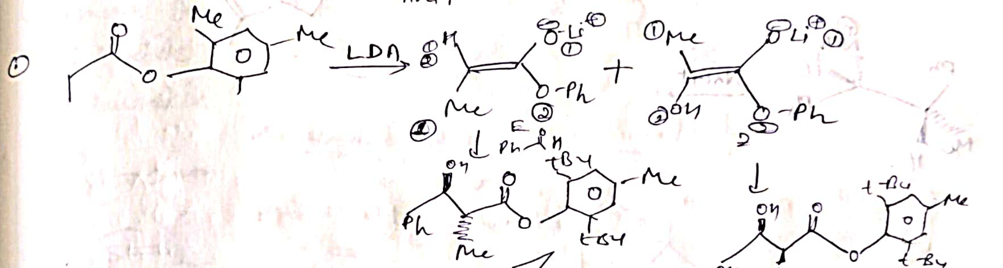


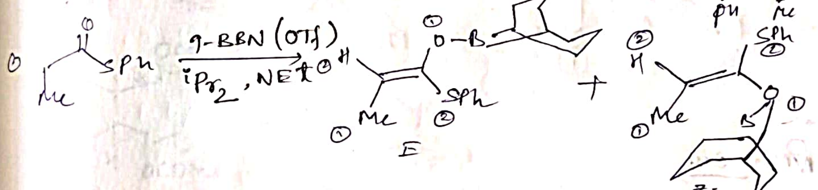




| R | Enolate | | Product | |
|---|---|---|---|---|
| | cis | trans | Syn | Anti |
| Et | 30 | 70 | 36 | 64 |
| t-Bu | >98 | <2 | >98 | <2 |



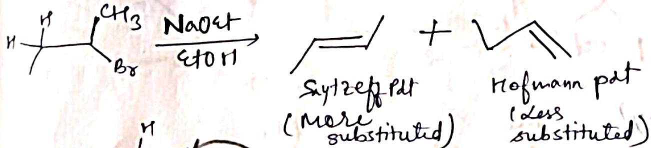

## Formation of C=C Bond

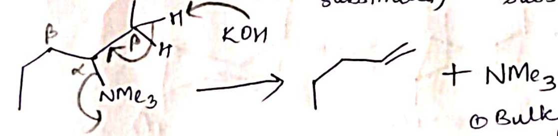
β elimination

(i) $E_1$

(ii) $E_2$

(iii) $E_1CB$

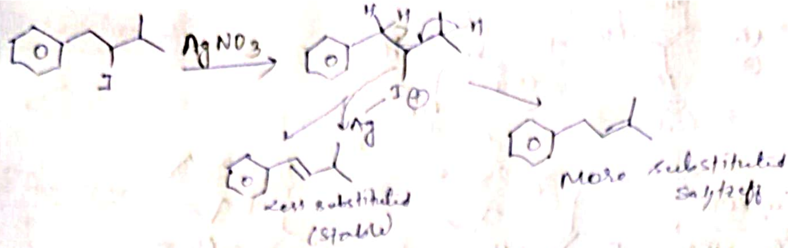


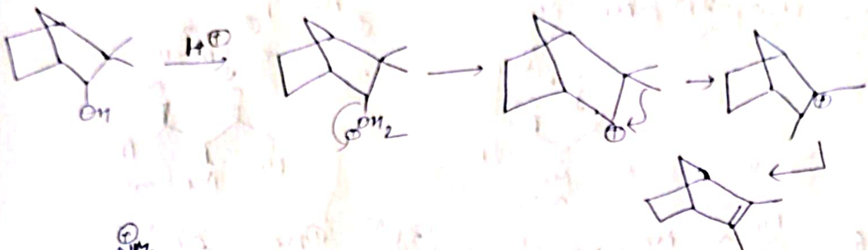



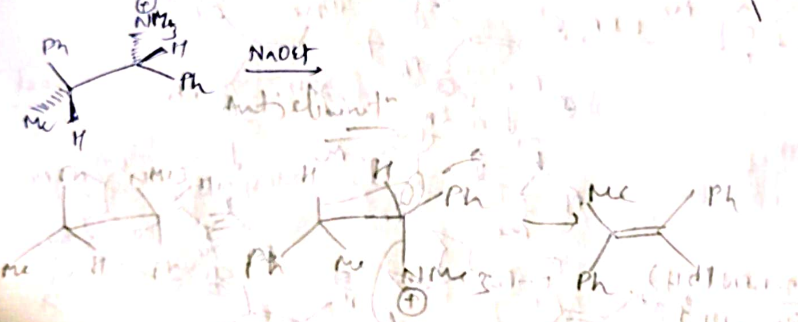

① Bulky substrate

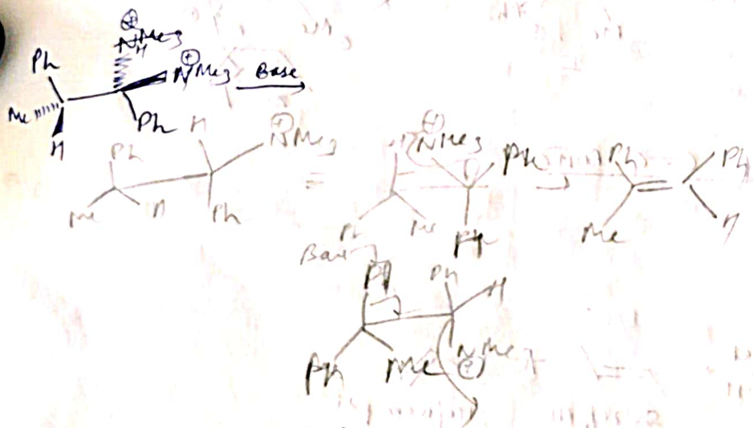
② Quaternary ammonium salt

③ Additional conjugation

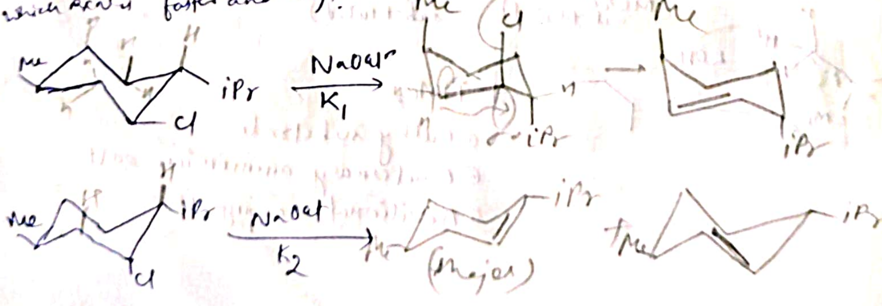


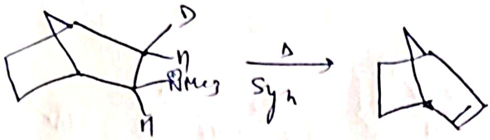




Which RXN is faster and why?

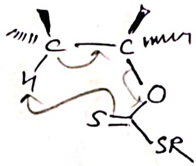


$K_1 <<< K_2$ .

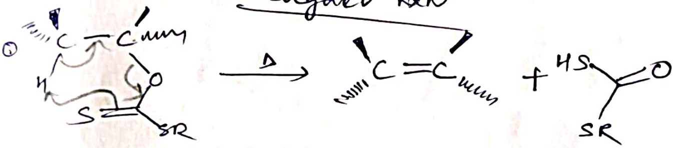


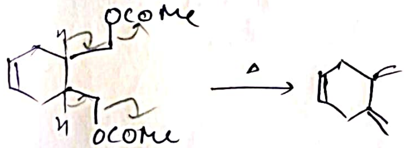

## Syn - Elimination

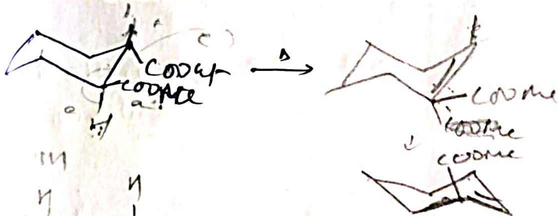
(i) Esters
(ii) Xanthates
(iii) Amine Oxide
(iv) Sulfoxide
(v) Selenoxide .

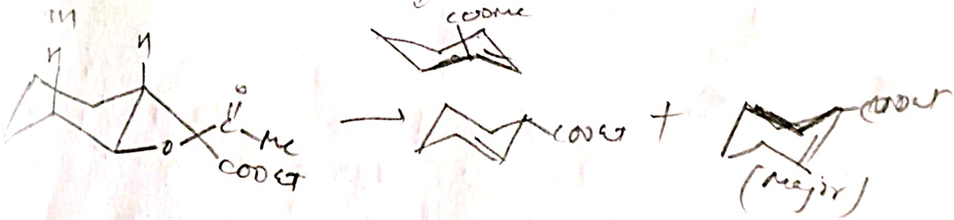


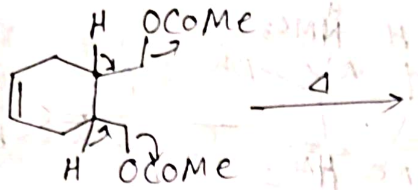

Chugaev RxN



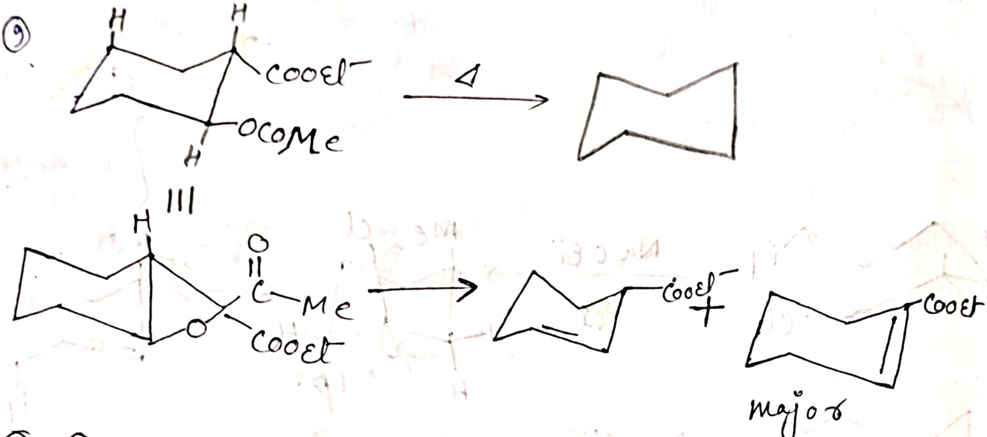



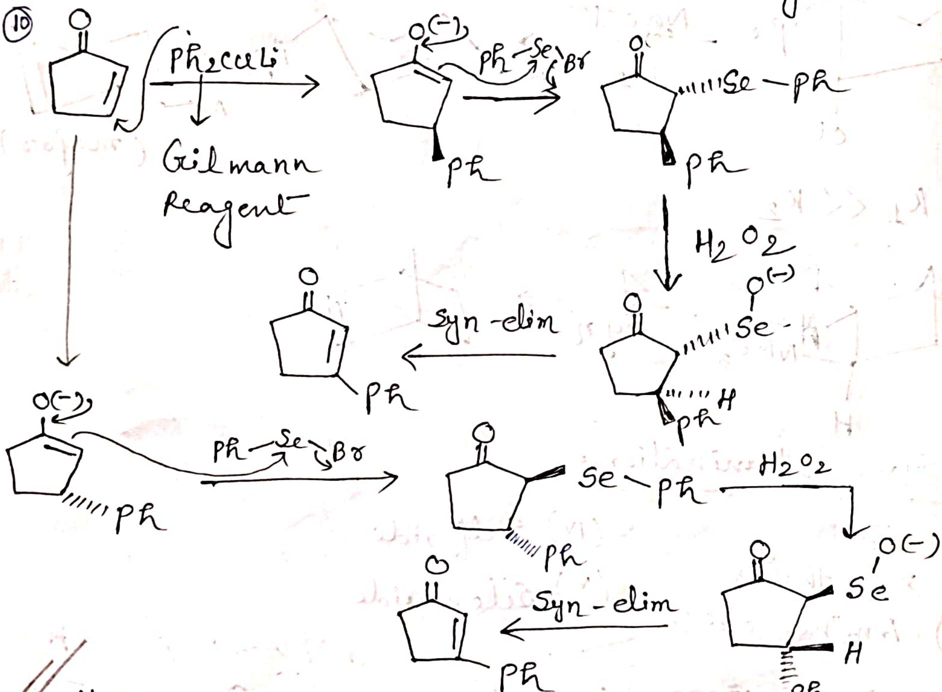




H OCOMe
Δ
H OCOMe

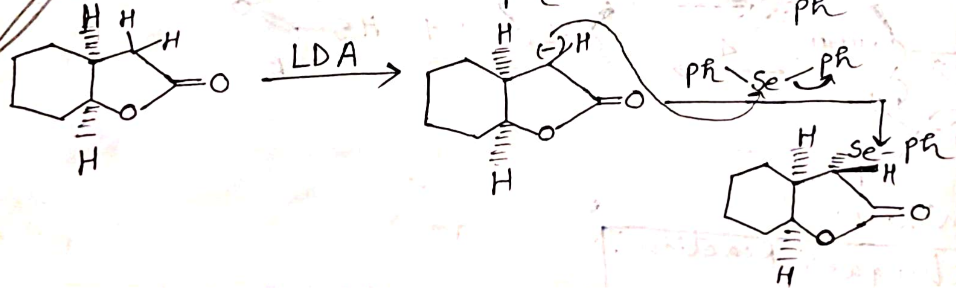
*) 9

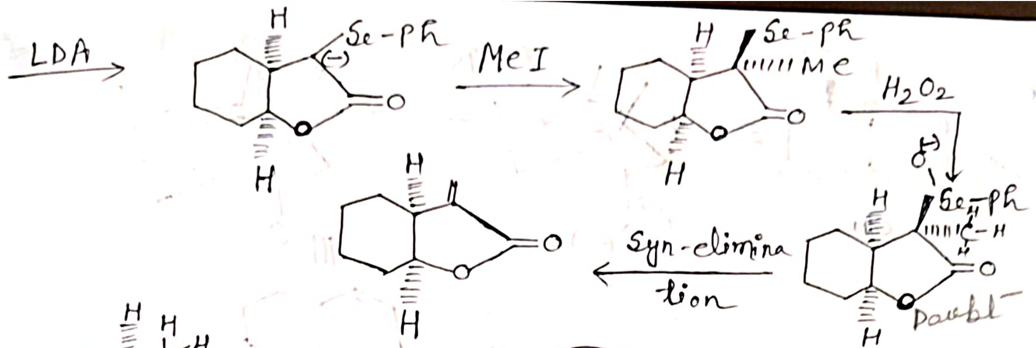

H
H
COOEt
OCOMe
H
Δ
H
Me
COOEt
COOEt
+
COOEt
major

*) 10

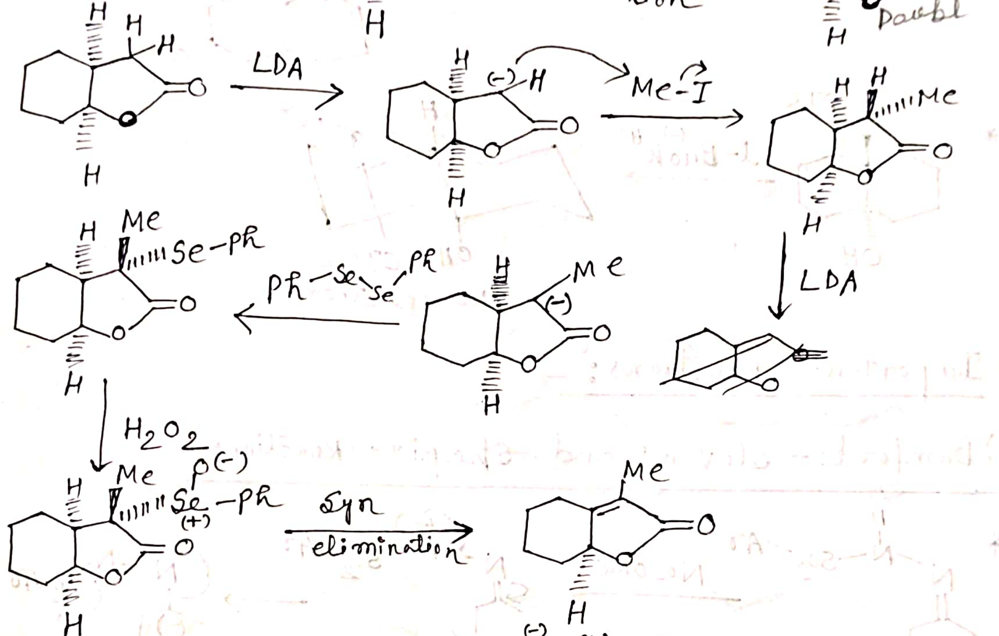

Ph2CuLi
Gilmann Reagent
Ph–Se–Br
Se–Ph
Ph
H2O2
Syn-elim
Se
H
Ph
Ph–Se–Br
Se–Ph
H2O2
Syn-elim
Se
H
Ph

*)

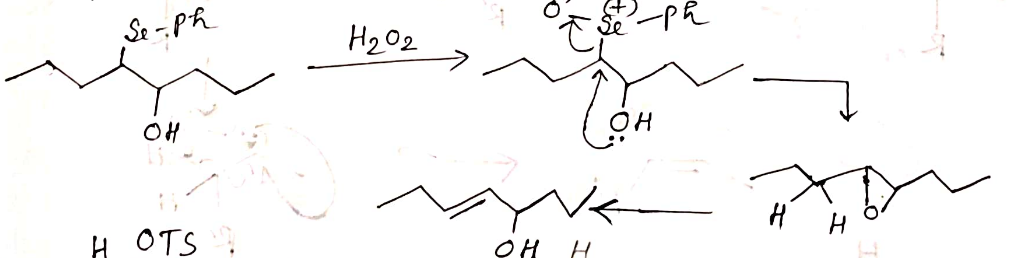

H H
H
O
H
LDA
H
(–) H
O
H
Ph–Se–Ph
H
Se–Ph
H
O
H


LDA
Se-Ph
MeI
Se-Ph
Me
$H_2O_2$
Syn-elimination
Double

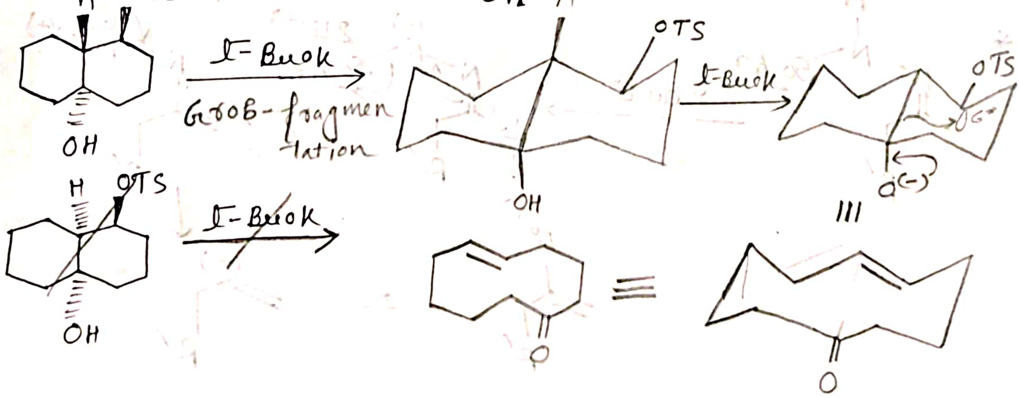
*)

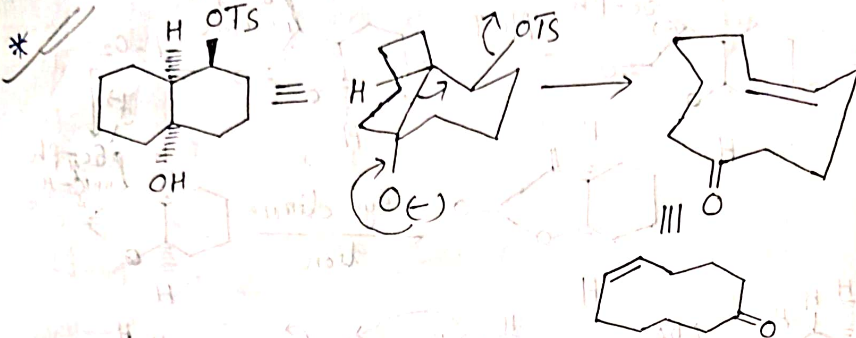

LDA
Me-I
Me
LDA
Ph-Se-Se-Ph
Me
Se-Ph
$H_2O_2$
Me
Se-Ph
Syn elimination
Me

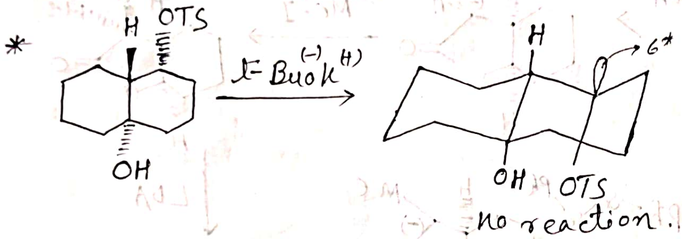
*)


Se-Ph
OH
$H_2O_2$
Se-Ph
OH
OH

*)

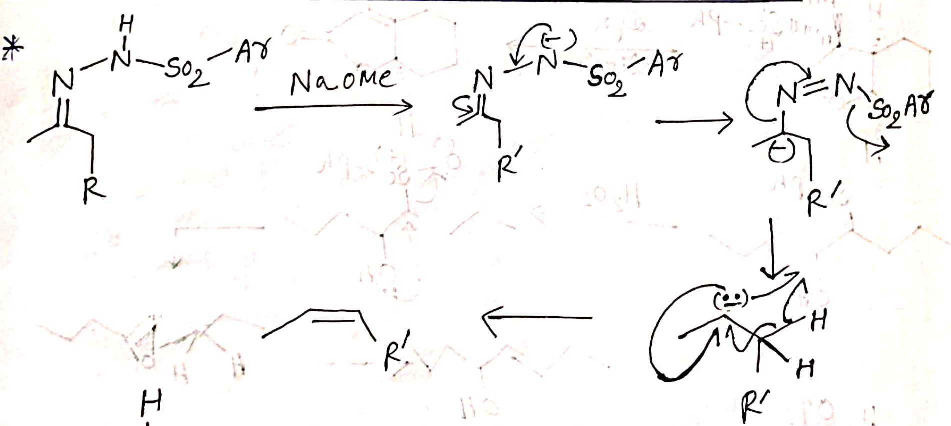

H OTS
OH
t-BuOK
GROB-fragmentation
OTS
OH
t-BuOK
OTS
H OTS
OH
t-BuOK

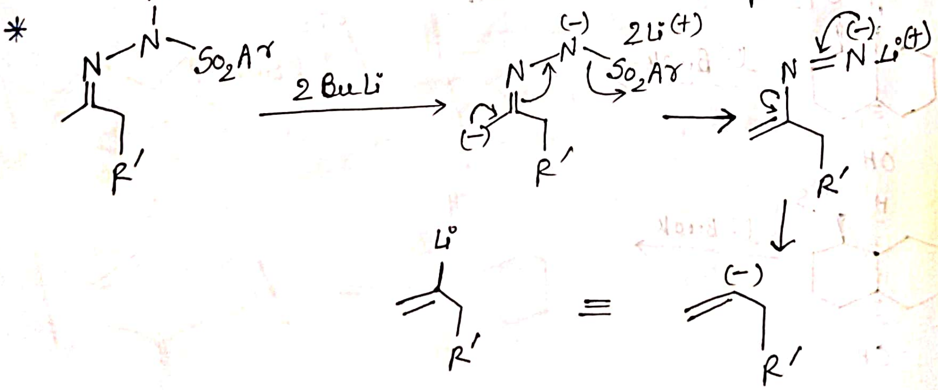


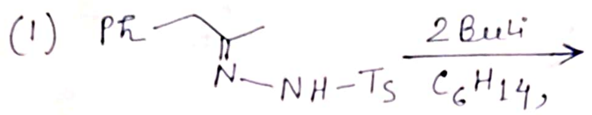

Important Reactions:-

(1) Bamford - Stevons and Shapiro Reaction:-



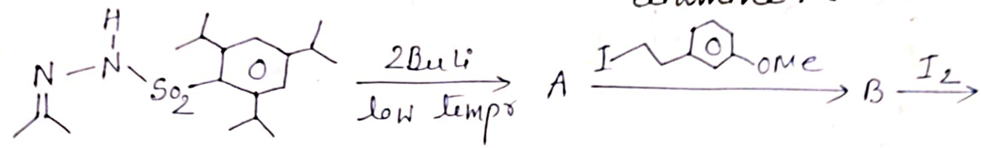



H.W (1)

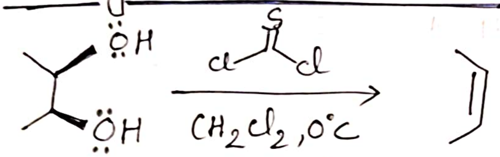


TMEDA → Tetramethyl ethylene diamine.

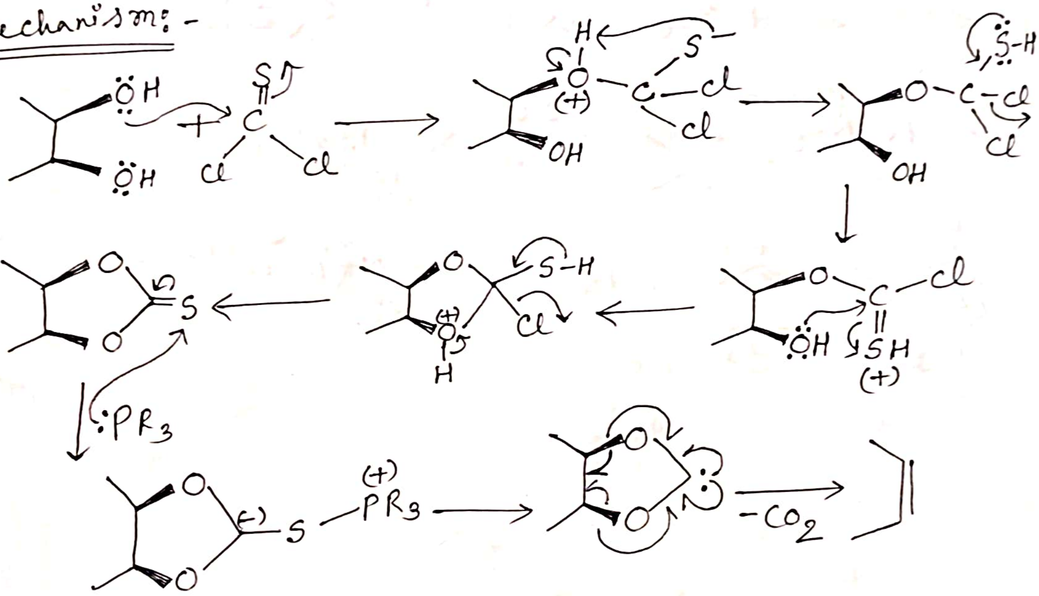
(II)

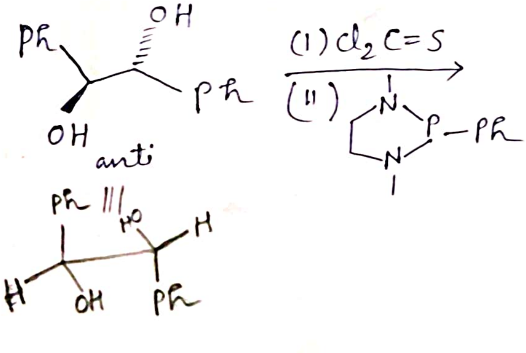


# Corey - Winter Reaction :-

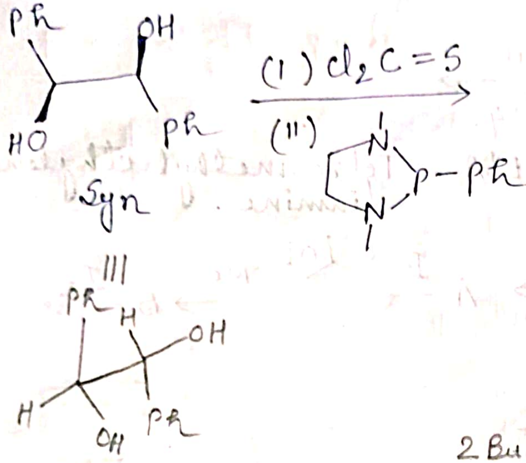


mechanism :-



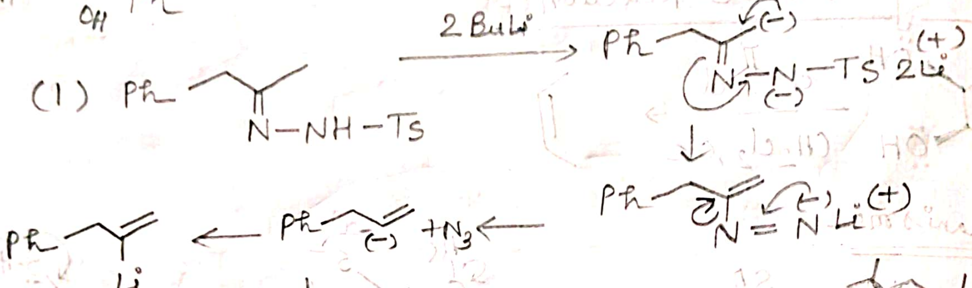


anti



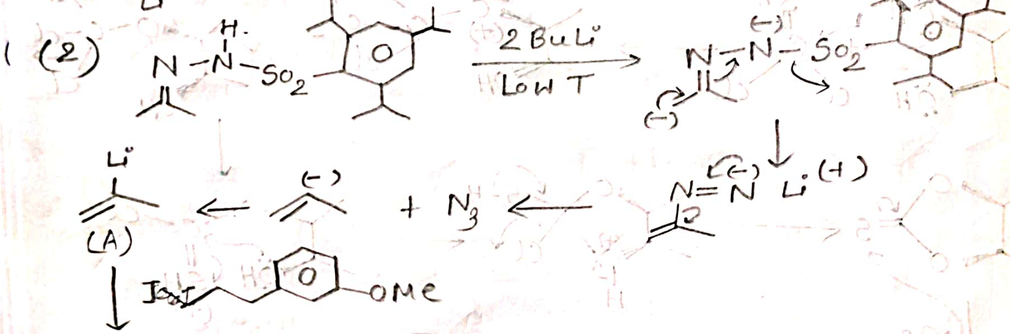
Ph
OH
HO
Ph
Syn
(I) $Cl_2C=S$
(II)
P-Ph
Ph
H
OH
H
OH
Ph


(1)



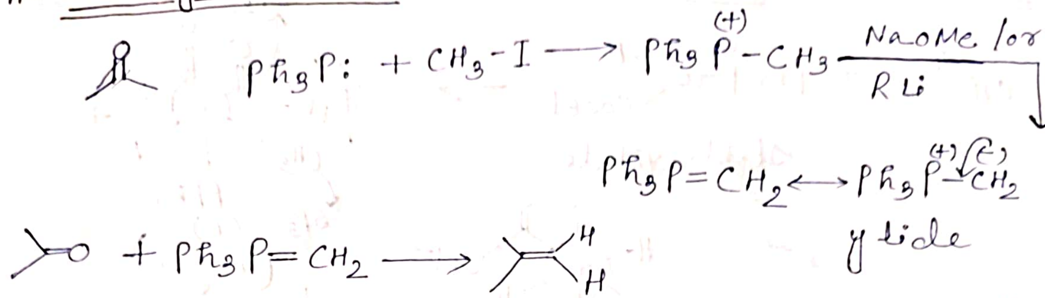
Ph
N-NH-Ts
2 BuLi
Ts 2Li(+)
Ph
N=N Li(+)
Ph
$+N_3$
Ph
Li

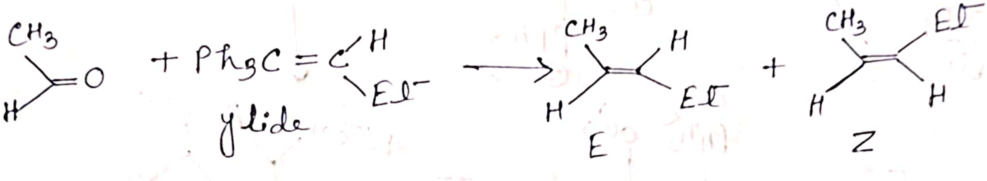

(2)



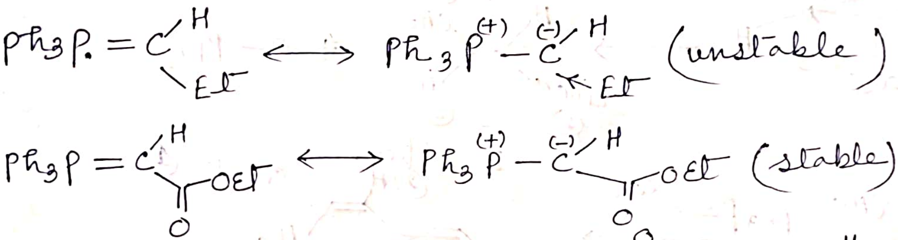
H
N-N-$SO_2$
2 BuLi
Low T
N-N-$SO_2$
N=N Li(+)
+ $N_3$
Li
(A)
I
OMe

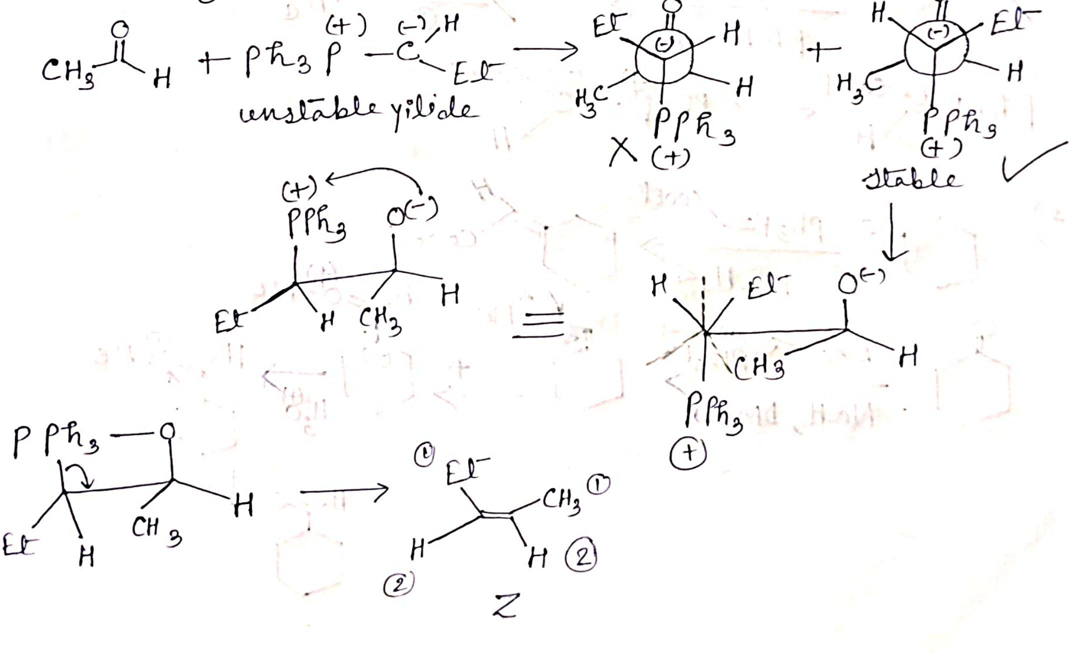
# Wittig Reaction :—



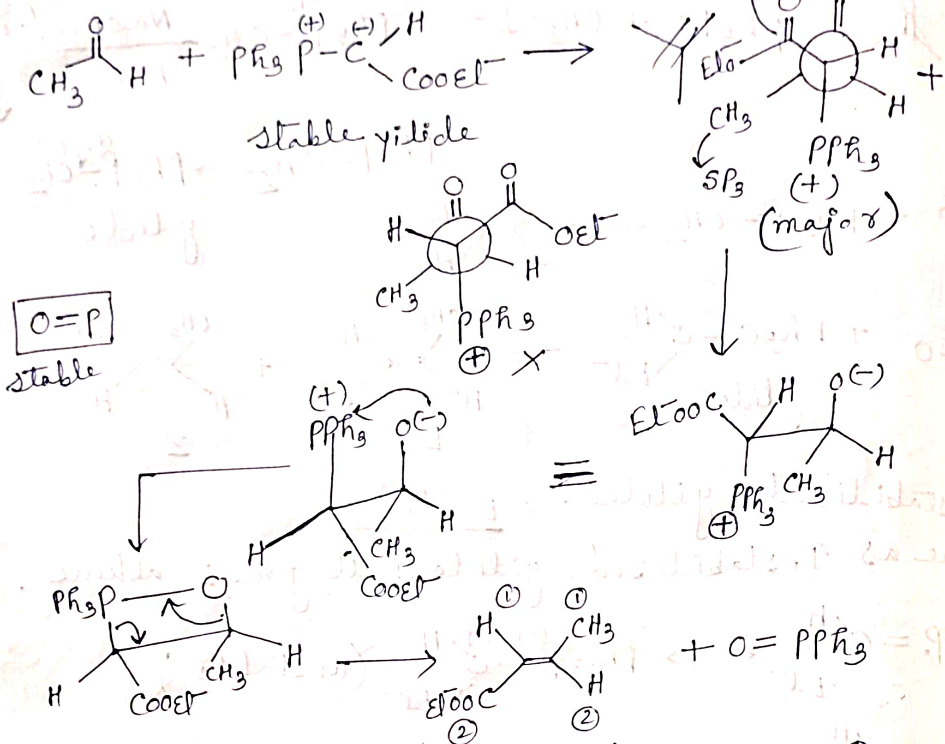




stabilizede ylide → E-alkene
where as Destabilized ylide will give Z-alkene.

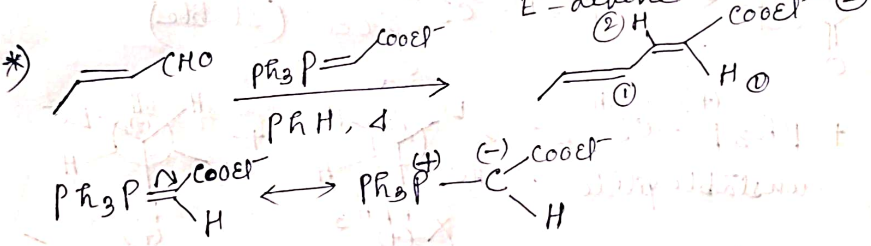


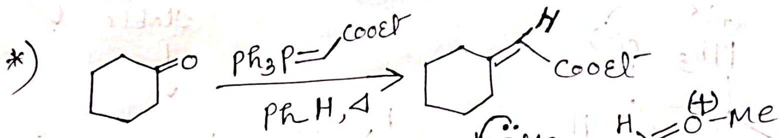



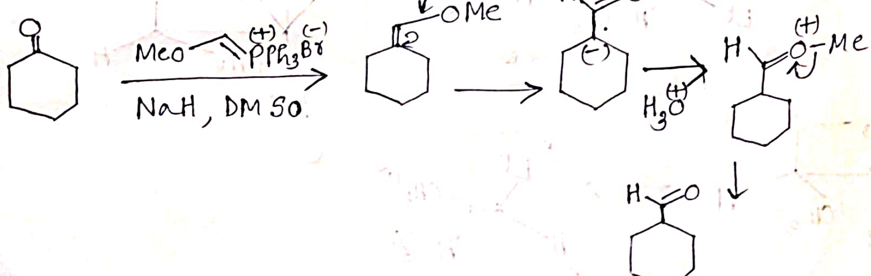
## For stable ylide:-



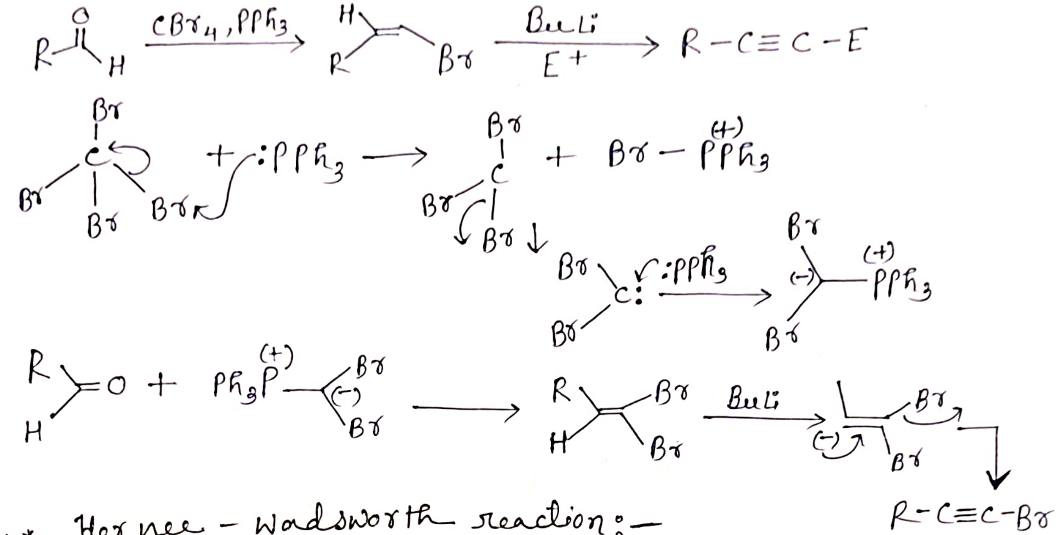

E-alkene



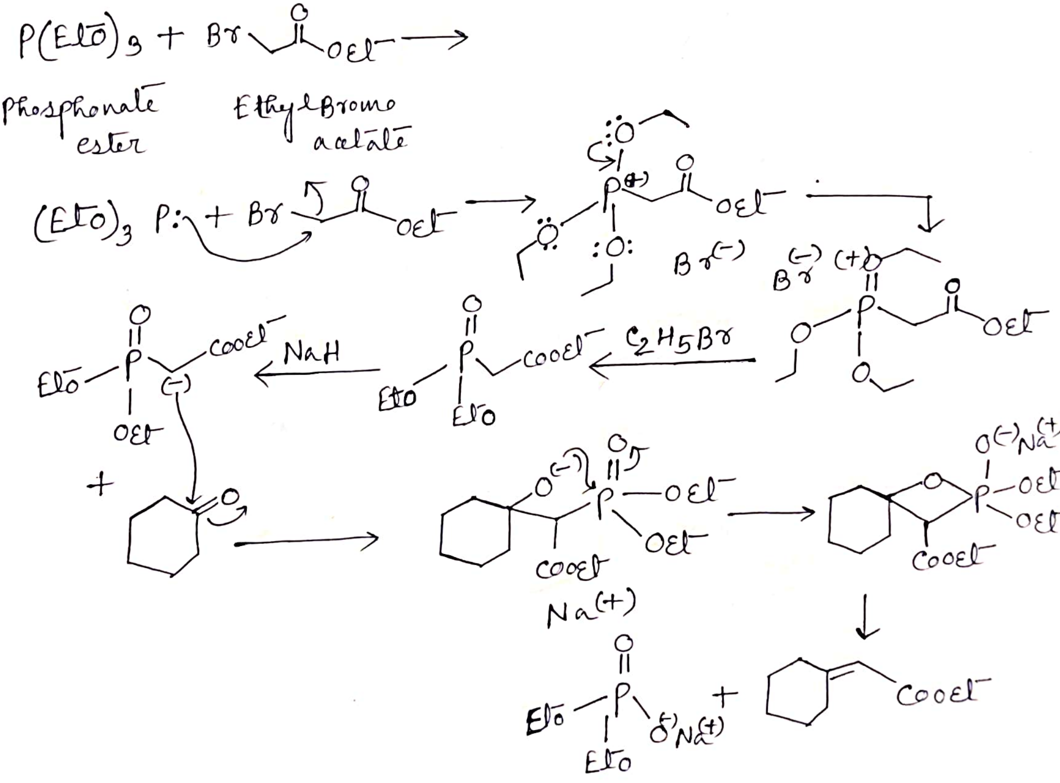



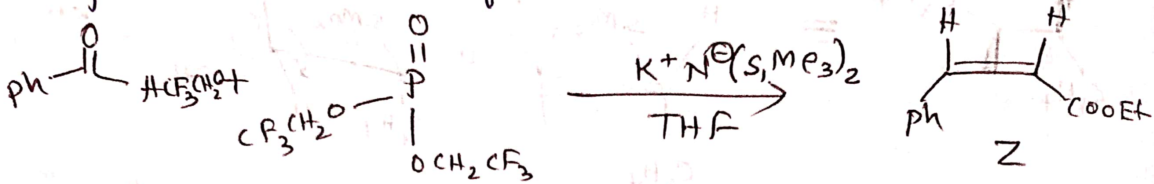
# Corey Fuch's Reaction :- (varient of witig rxn)



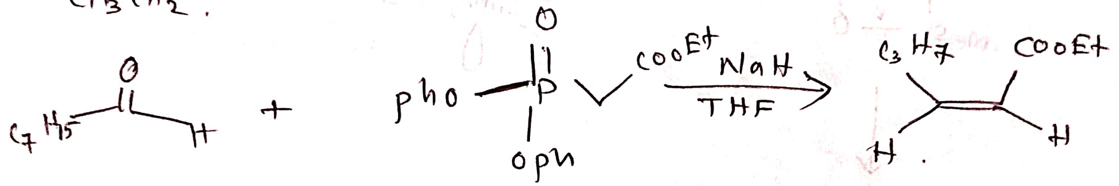

## ** Horner - Wadsworth reaction :-



Exceptional cases of H.W.E Rxn:-



$$\frac{CF_3CH_2}{CH_3CH_2}$$



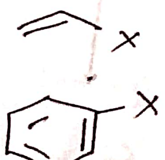
Coupling Reaction 19/09/25

Heck coupling

R − X + alkene $\xrightarrow{\text{Pd-catalyst}}$

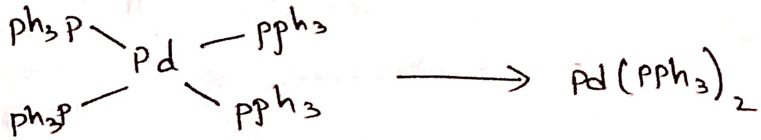
alkyl gp that contain $sp^2$ e⁻

X = Good L.G.



* alkene can be either e⁻ rich or e⁻ poor or neutral molecule.

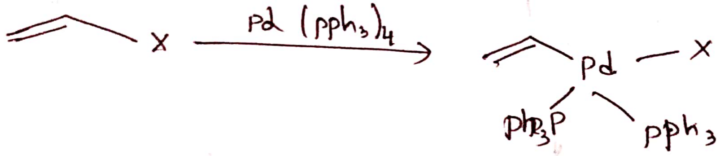
* Both intramolecular and intermolecular coupling possible.



For a $Rx^n$ take place, the $Rx^n$ is to bulky so two $PPh_3$ are remove from it to make it reactive

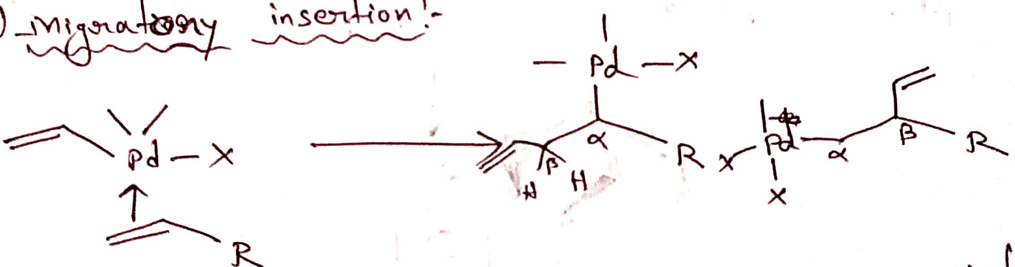
## Mech$^n$!

① oxidative addition



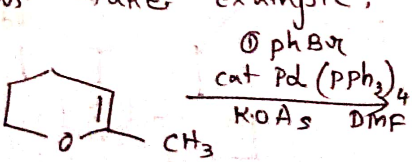
(ii) Addition of olefin.

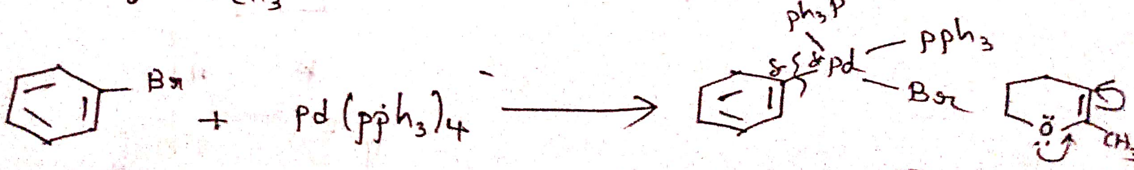
(iii) Migratory insertion !-

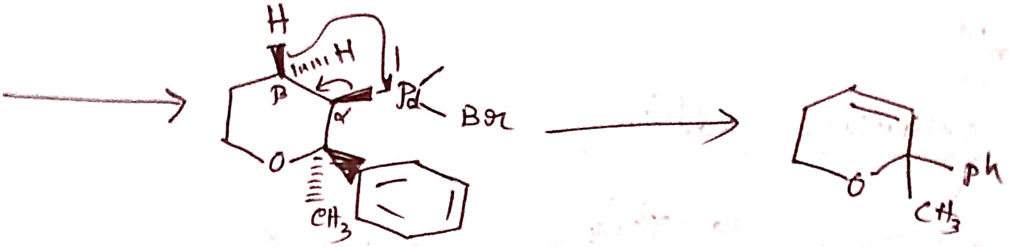


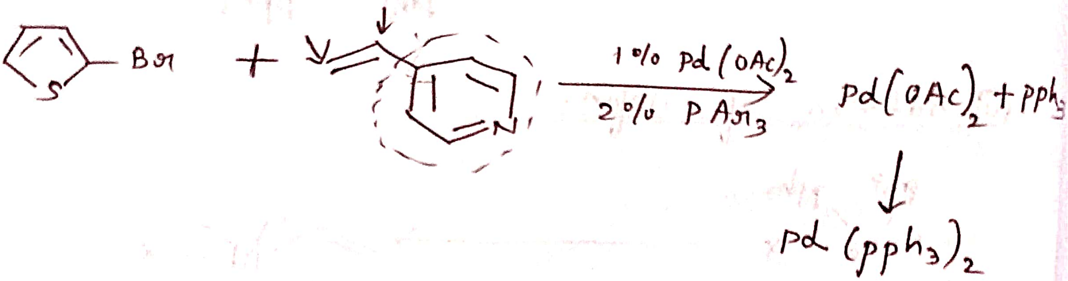
(iv) β-elimination !- The metal and the β-Hydrogen must be in syn geometry

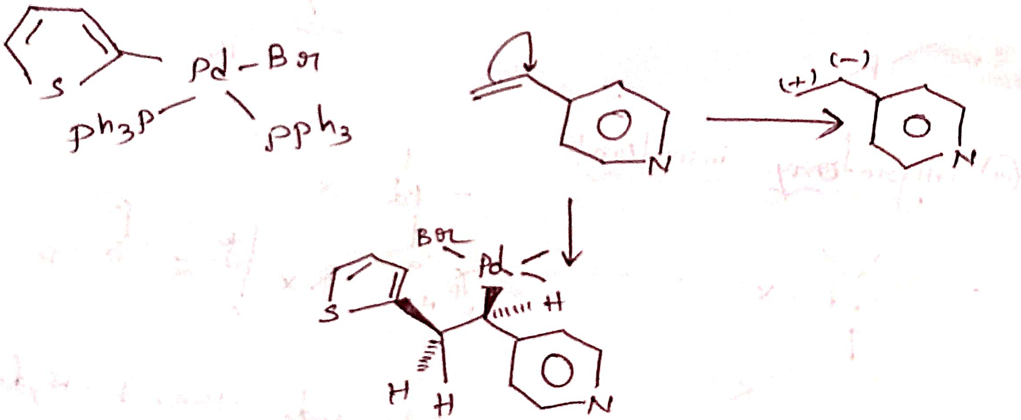
Let us take example,

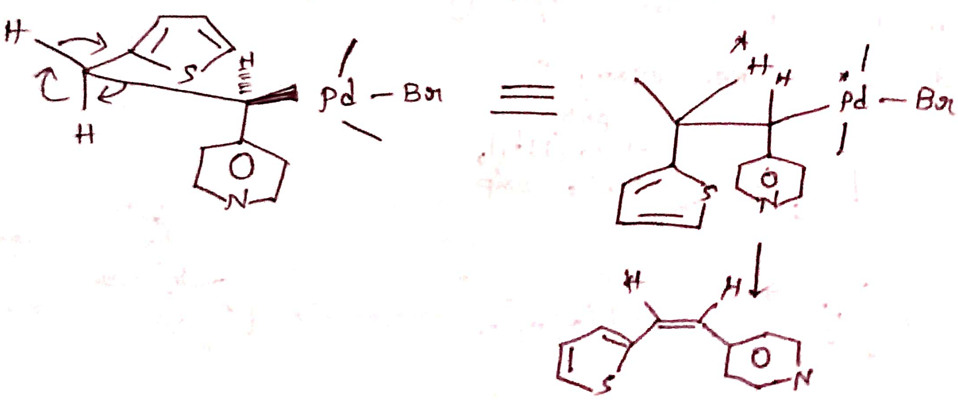




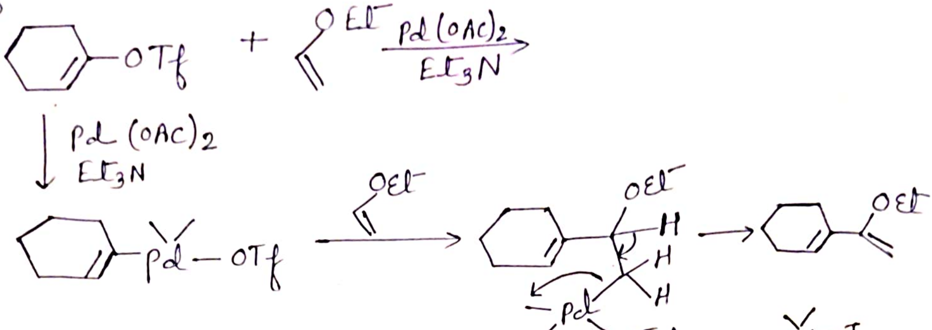

H
H
β
α
Pd
Br
O
CH3
ph


Br
S
+
N
1% Pd(OAc)2
2% P Ar3
Pd(OAc)2 + PPh3
Pd (PPh3)2

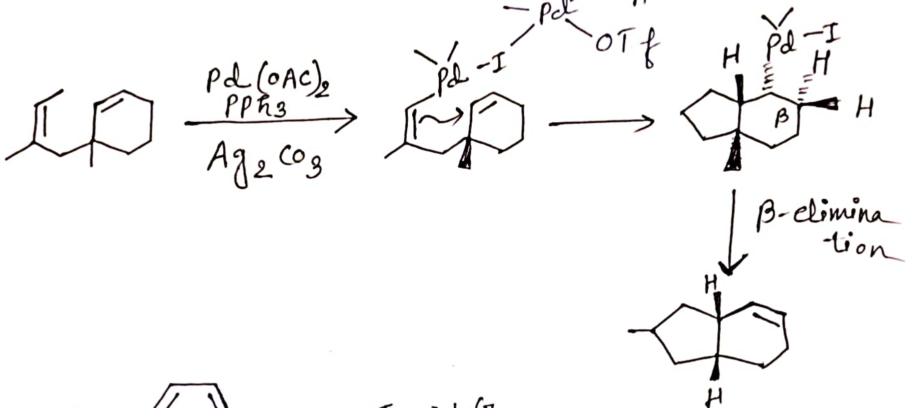

Pd – Br
S
Ph3P
PPh3
N
(+)
(–)
Br
Pd
H
H H


H
H
H
S
Pd – Br
N
≡
H H
Pd – Br
H
H

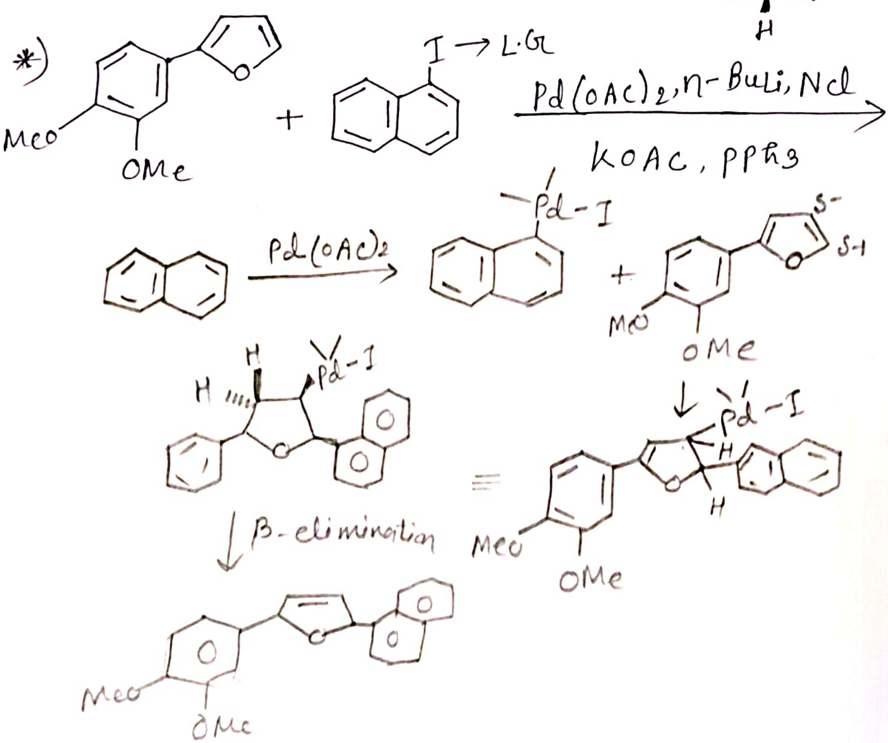
*)


OTf
OEt
Pd (OAc)2
Et3N
Pd (OAc)2
Et3N
Pd — OTf
OEt
OEt
H
H
H
Pd
OTf
OEt

*)


Pd (OAc)2
PPh3
Ag2 CO3
Pd - I
H
Pd - I
H
H
β
β-elimination
H
H

*)


MeO
OMe
I → L·G
Pd (OAc)2, n-BuLi, NCl
KOAC, PPh3
Pd (OAc)2
Pd - I
MeO
OMe
H
Pd - I
H
β-elimination
Pd - I
H
H
MeO
OMe
MeO
OMe

$$R-X + R'-M \xrightarrow{Pd^{(0)}} R-R'$$

$M = Si \longrightarrow$ Hiyana coupling

$M = B \longrightarrow$ Suzuki Coupling

$M = Zn \longrightarrow$ Negishi Coupling

$M = Cu \longrightarrow$ Sonogashira Coupling.

$M = Sn \longrightarrow$ Stille Coupling.

$X = I, Br, Cl, OTf, OTs$

# Suzuki Coupling:-