

Midterms scanned and returned to you electronically

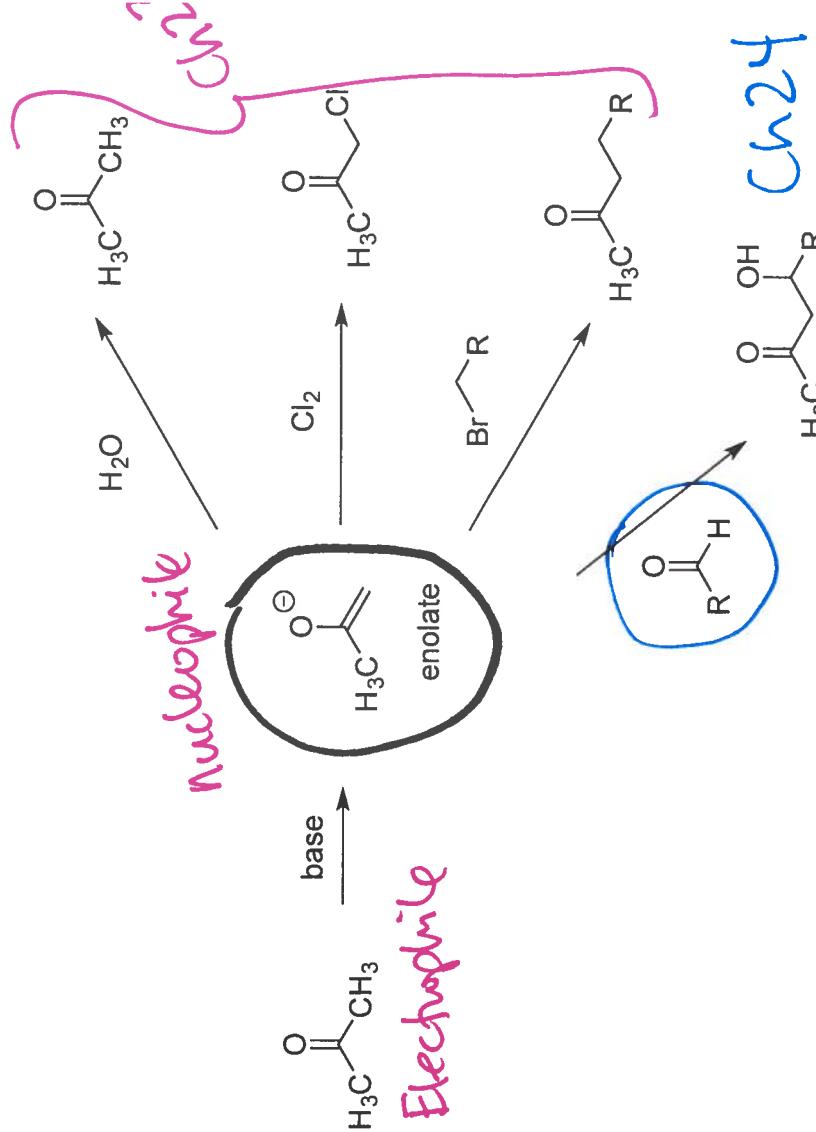
Lecture 17: Ch 24 Aldol reactions!

Secret Agent Man (Johnny Rivers)
They give you a number and take away your name

We took away a proton from a carbonyl to make an enolate. Now it is a nucleophile, not an electrophile. It can attack an electrophilic carbonyl now.

Nucleophile

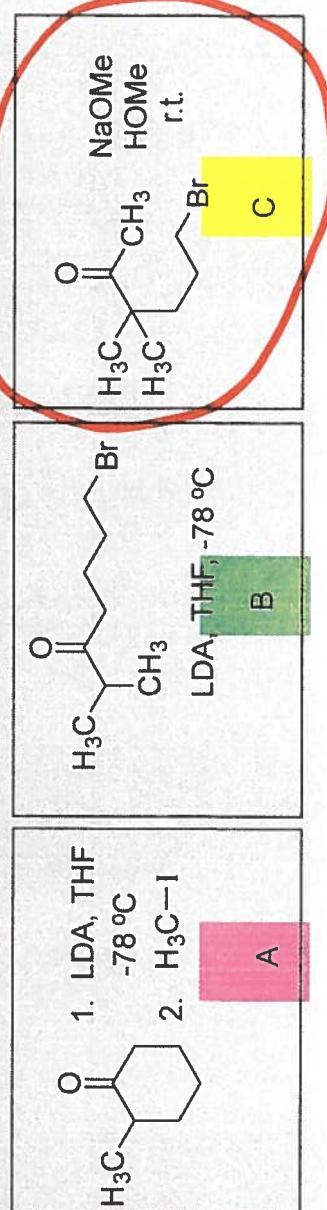
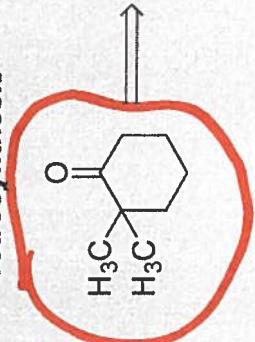
Electrophile



alcohol

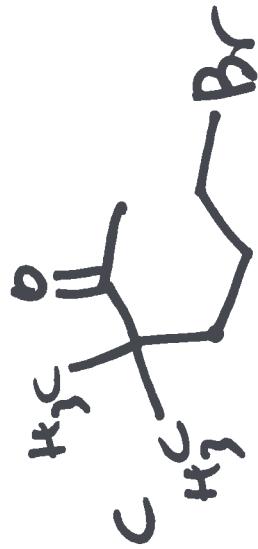
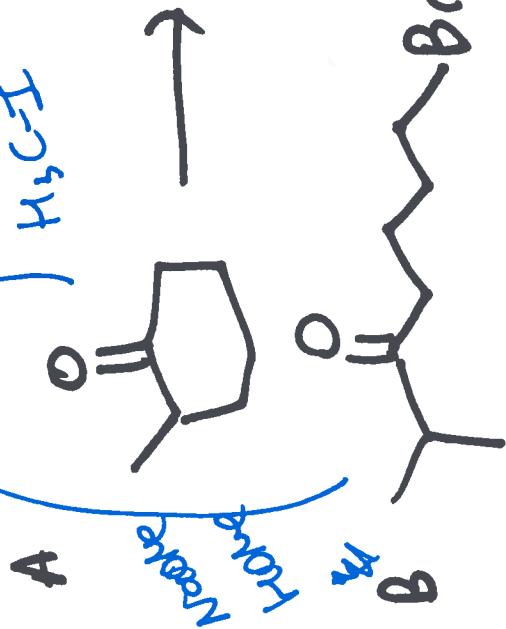
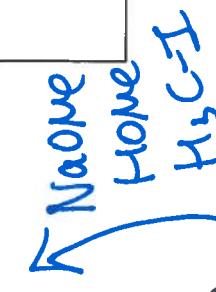
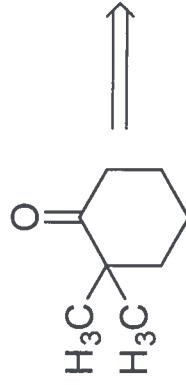
Capercard question:

Complete the retrosynthesis

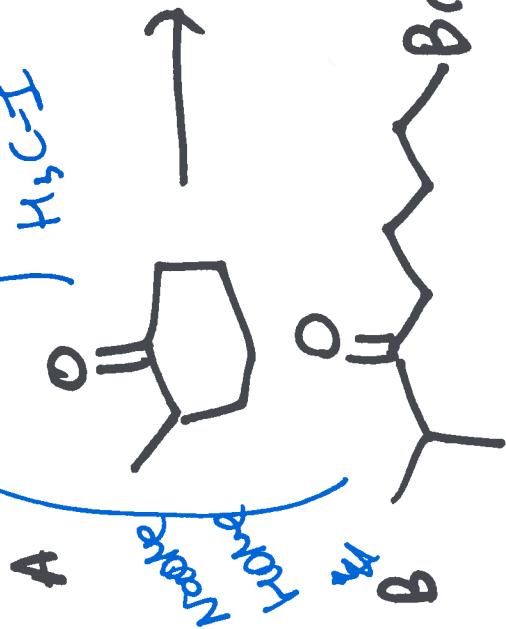
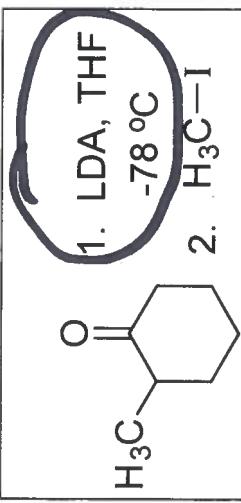


Capercard question:

Complete the retrosynthesis



Kirchner



$$\text{CH}_3\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{Br} + \text{NaOMe} \xrightarrow{\text{r.t.}} \text{CH}_3\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{COCH}_3$$

$$\text{CH}_3\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{Br} + \text{LDA, THF, } -78^\circ\text{C} \rightarrow \text{CH}_3\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{COCH}_3$$



C

CC(C)(C)C(=O)CCBr

CC(C)(C)C(=O)CCBr

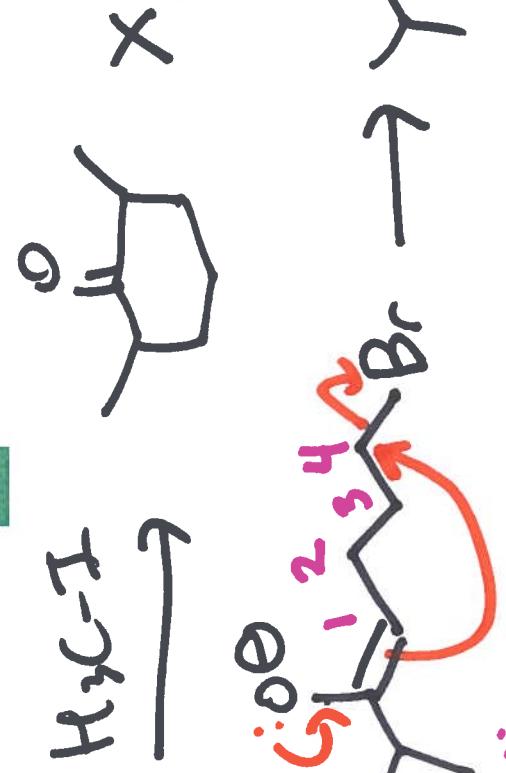
NaOMe HOMe
r.t.

B

CCCCBr

CCCCBr

THF, -78 °C



C

CC(C)(C)C(=O)CCBr

CC(C)(C)C(=O)CCBr

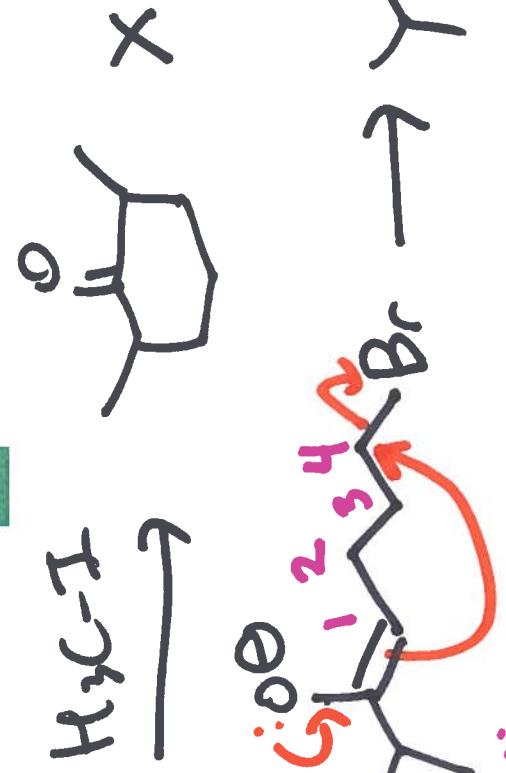
NaOMe HOMe
r.t.

B

CCCCBr

CCCCBr

THF, -78 °C



Ch 24:

aldol reaction:

Nucleophile
electrophile

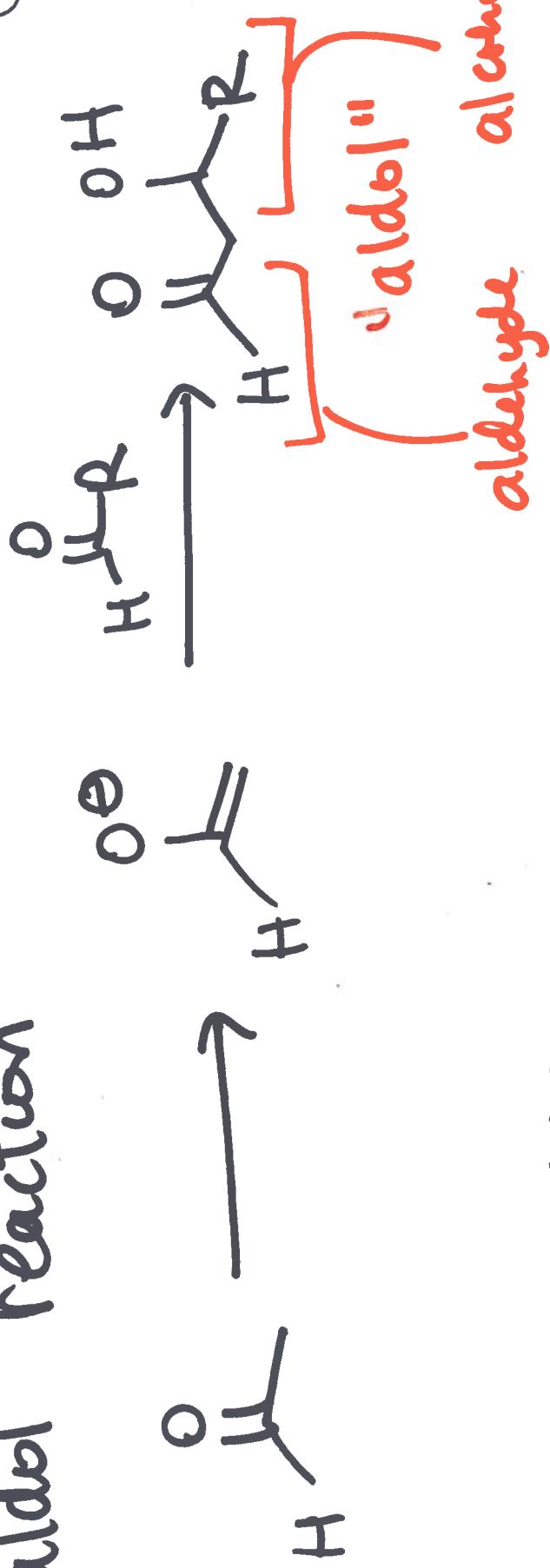
Enolate
aldehyde
Aldol

Claisen
ester
intra ester
Dickemann
condensation
 α, β -unsaturated
ketone / aldehyde
Michael
Rohm &
annulation
imine
Enolate
Enolate
Enolate
Enolate
Enolate
Enolate
Enolate
Enolate

Essentially
the
same!

(4)

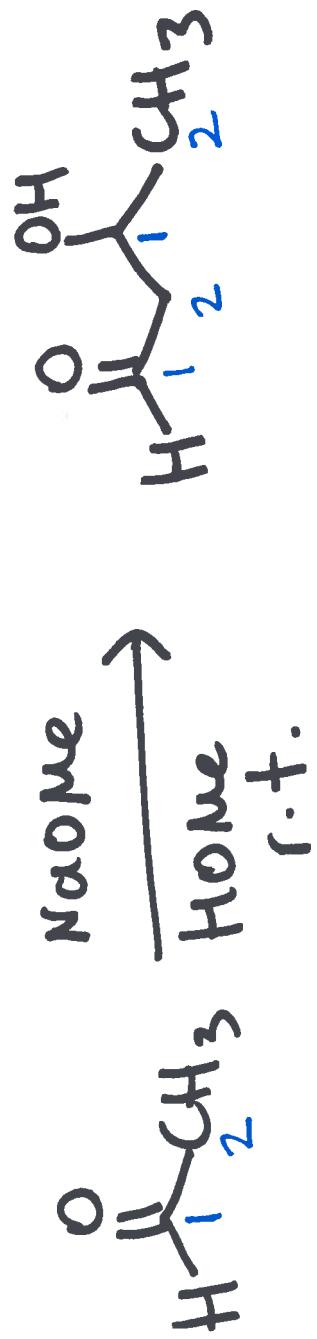
alcohol reaction



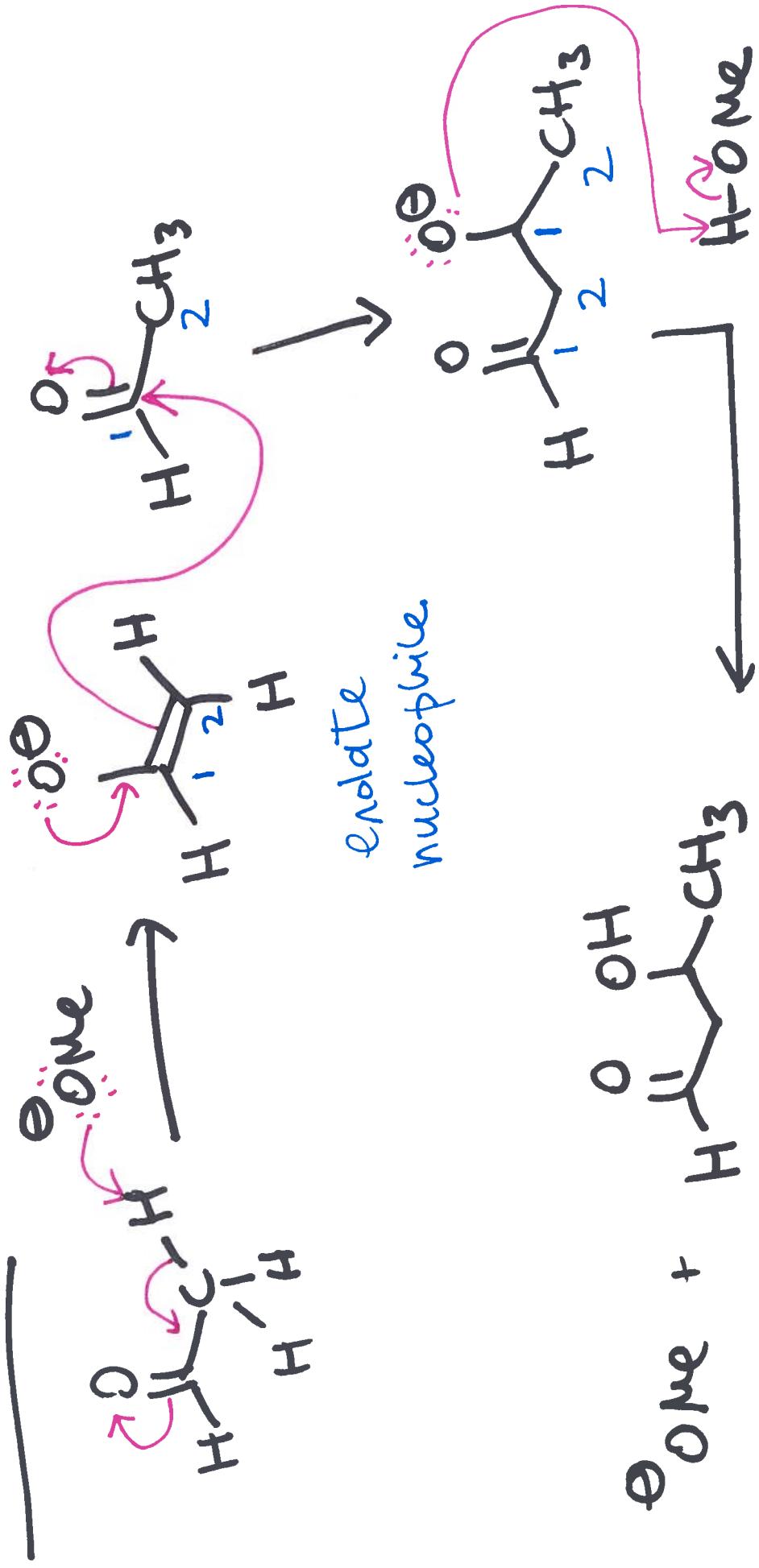
alcohol: aldol syn
versus aldol condensation

- crossed aldol reactions
(2 different aldehydes)
- directed aldol reactions
(modern chemistry) (LDA)
- intramolecular versions.

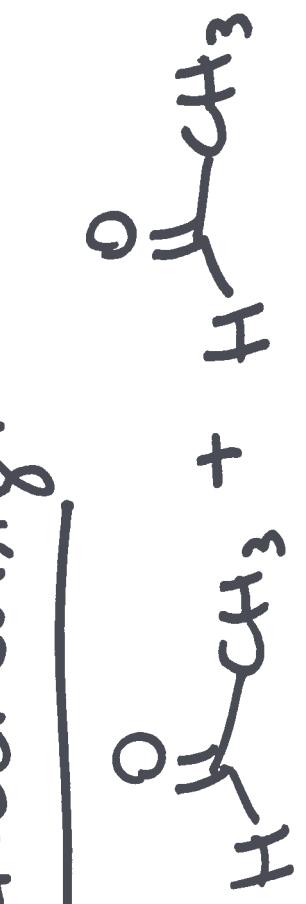
(5)



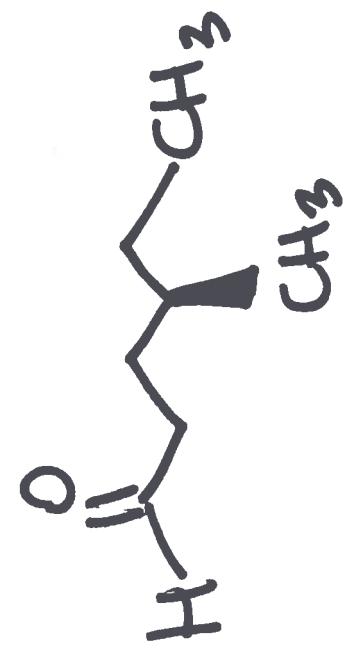
Mechanism:



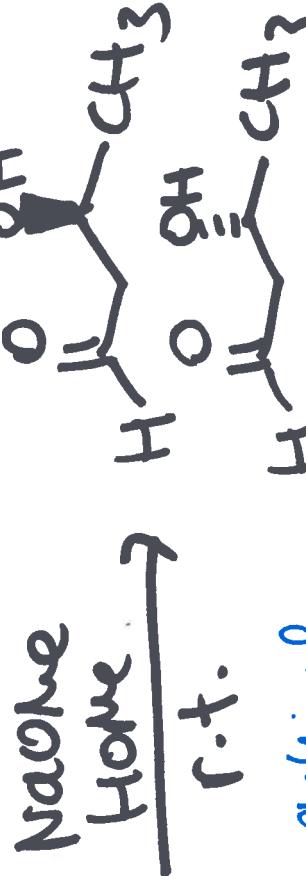
Stereochemistry:



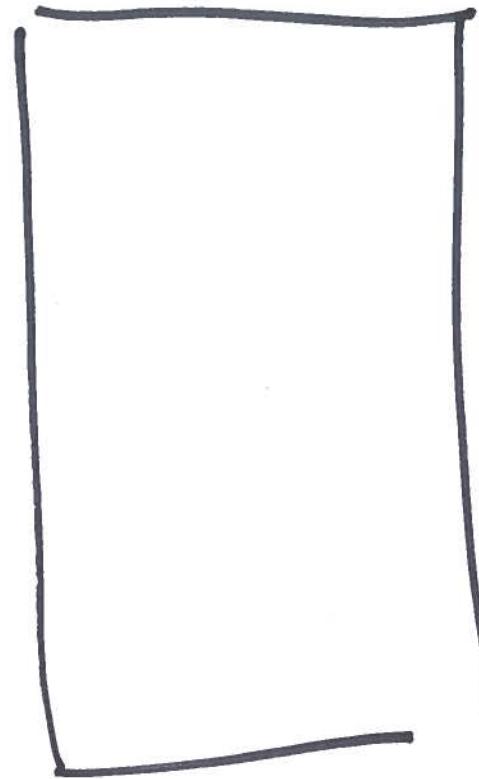
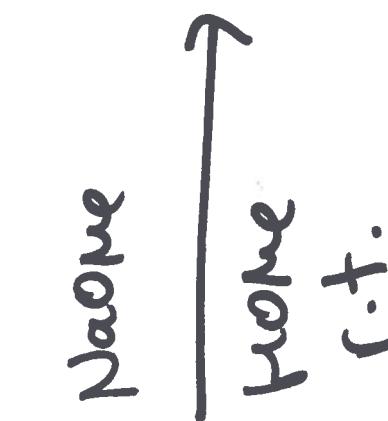
achiral



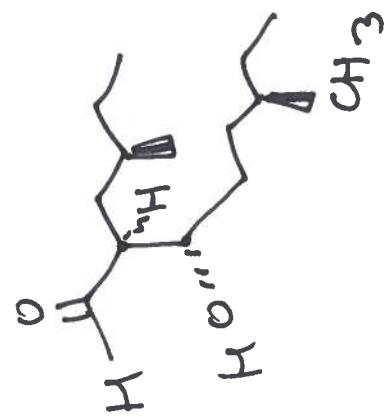
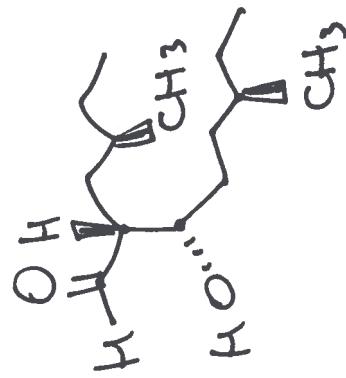
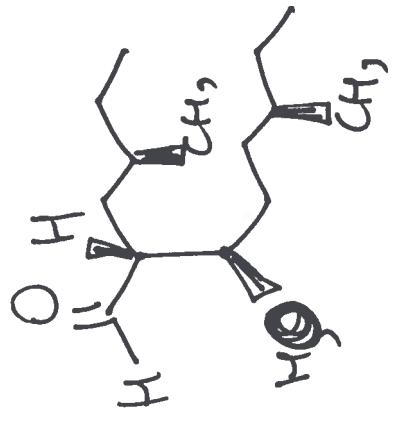
take home:



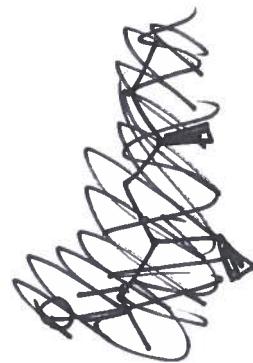
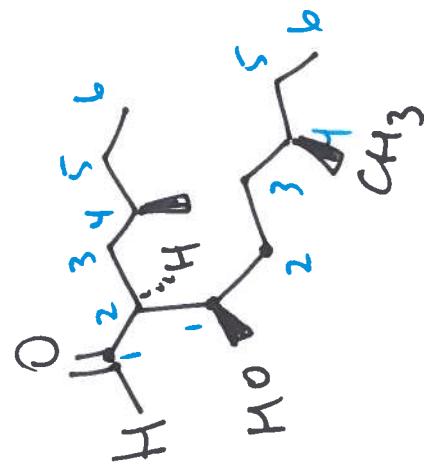
racemic
Mixture



①



fuller house



(8) Asymmetric catalysis:

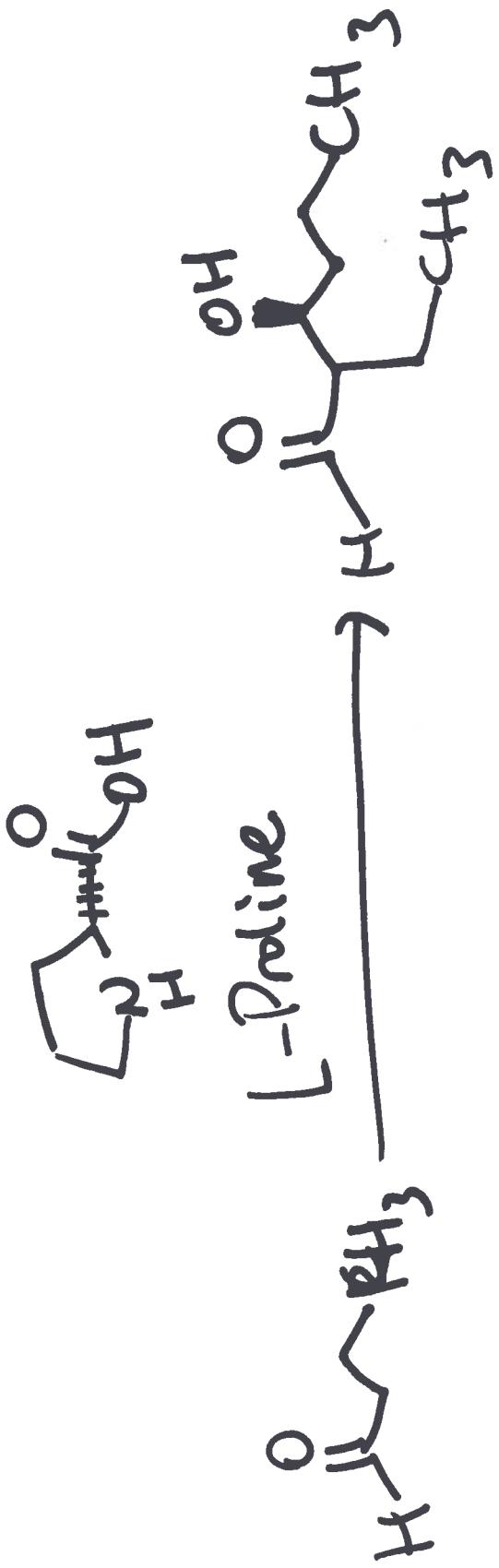
How can we get a single enantiomer of an aldol product???

use a chiral catalyst.

↳ Dave Evans.

1990's.

2001: List : amino acid catalyse

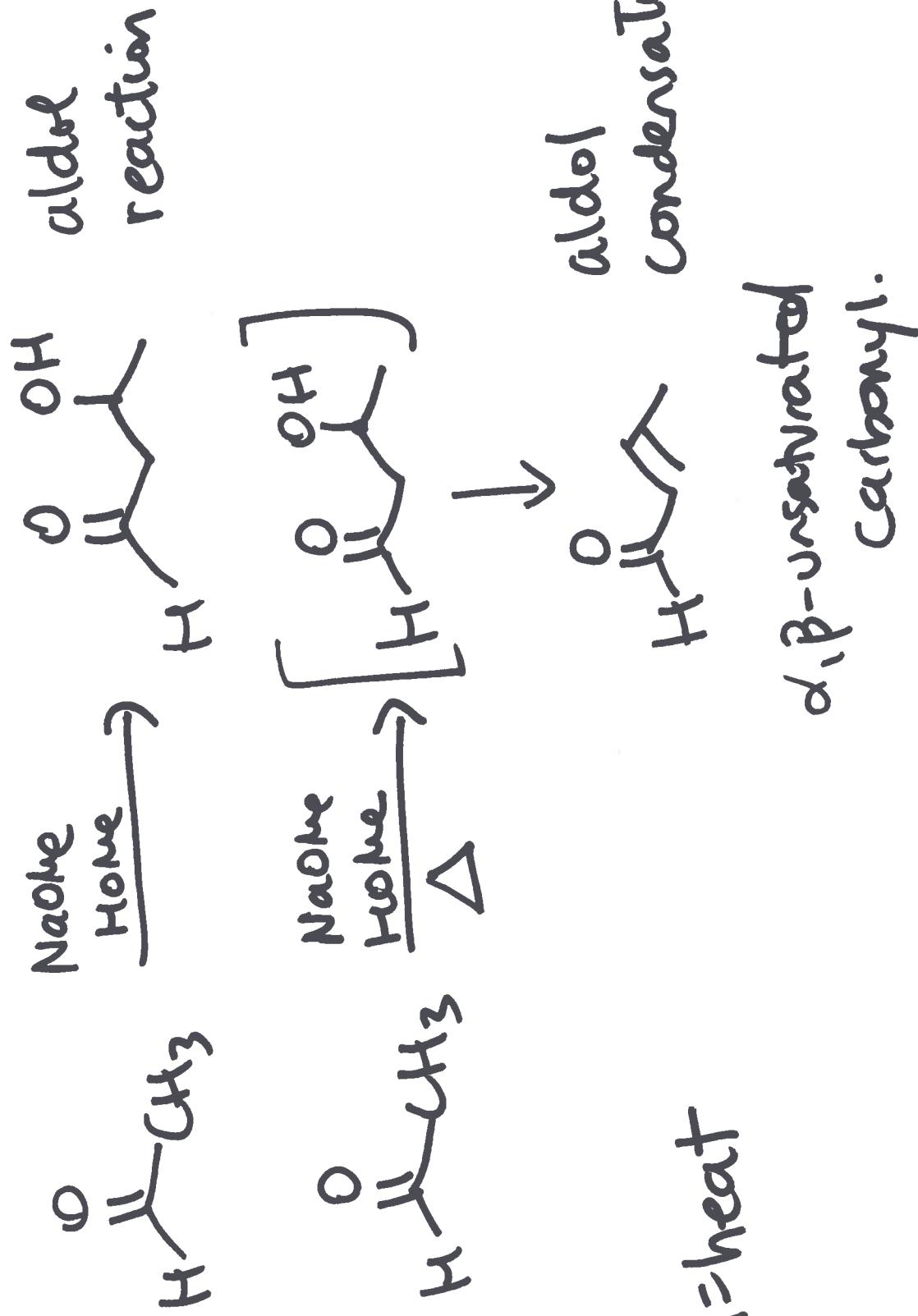


Single enantiomer
of
product.

Amines can catalyze
aldol reactions...
in active sites of enzymes.
Ubiquitous in biochemistry!

10

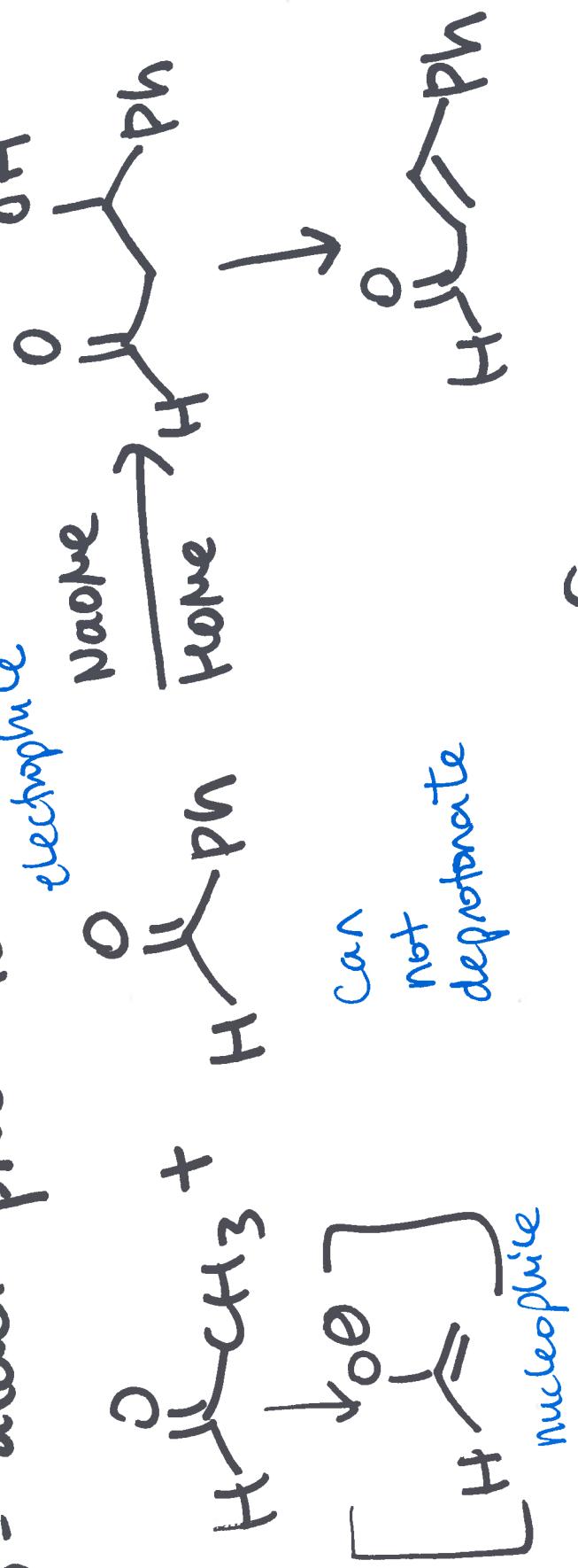
Aldol reactions vs aldol condensations



Δ = heat

α,β -unsaturated
carbonyl.

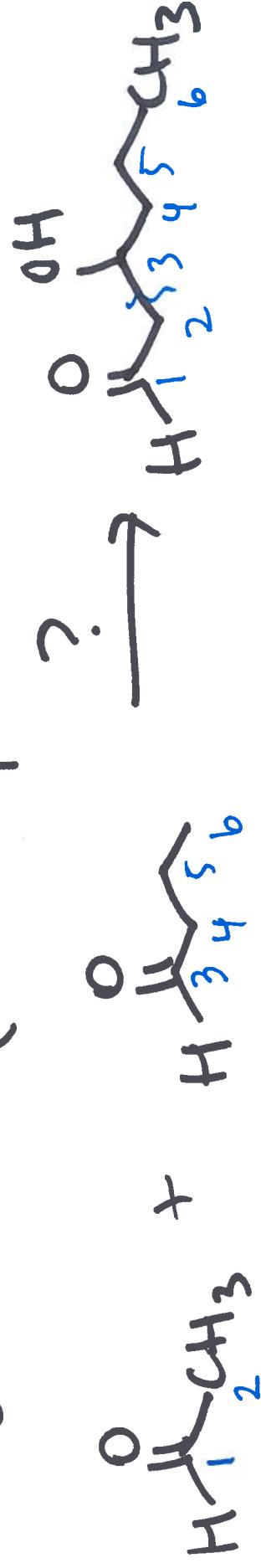
Cross - aldol products.



- only one aldehyde can form here!
- goes to condensation product because acetoacetic ring!
- epolata

⑫ What if both aldehydes can form enolates?

(= "enolizable")



Modern strategy: LDA
"Directed" aldol

PREFORM ENOLATE!



benefits :

- ① Cross product because control over which enolate formed
- ② Stop at aldol product
NO CONDENSATION!

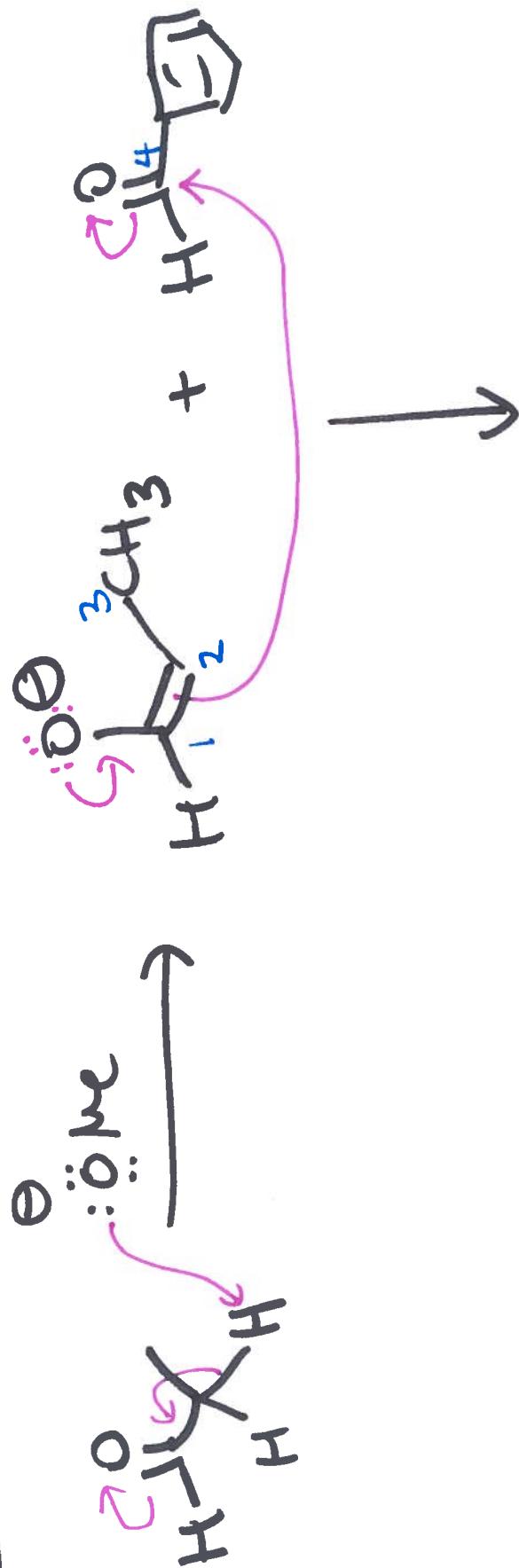
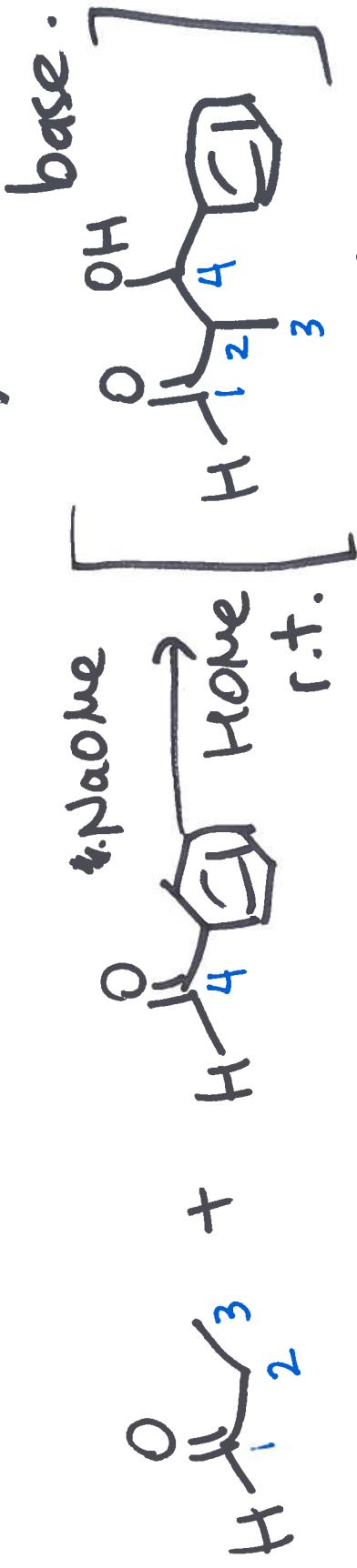
(13)

Aldol condensation : ONLY when excess base

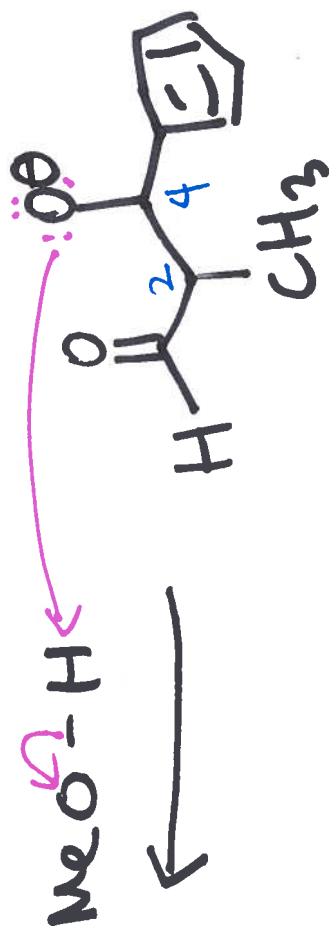
- $\text{LDA}, \text{THF}, -18^\circ\text{C} \rightarrow$ one equiv of base
- no extra no regenerat^g.

(H)

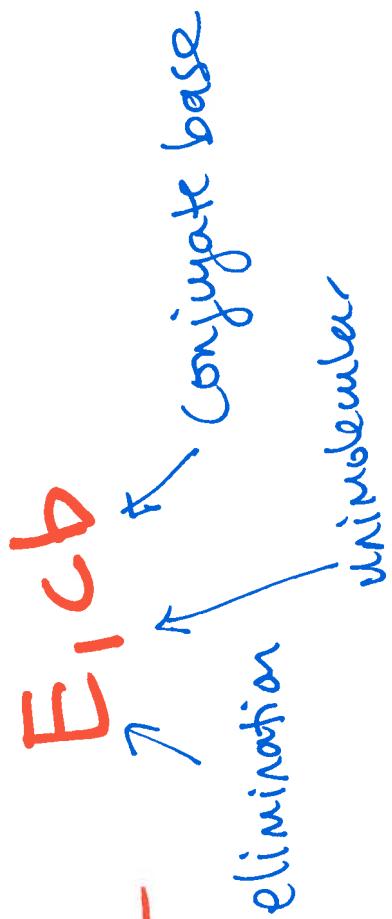
- NaOAc + Hone, r.t. \rightarrow regenerate the base.



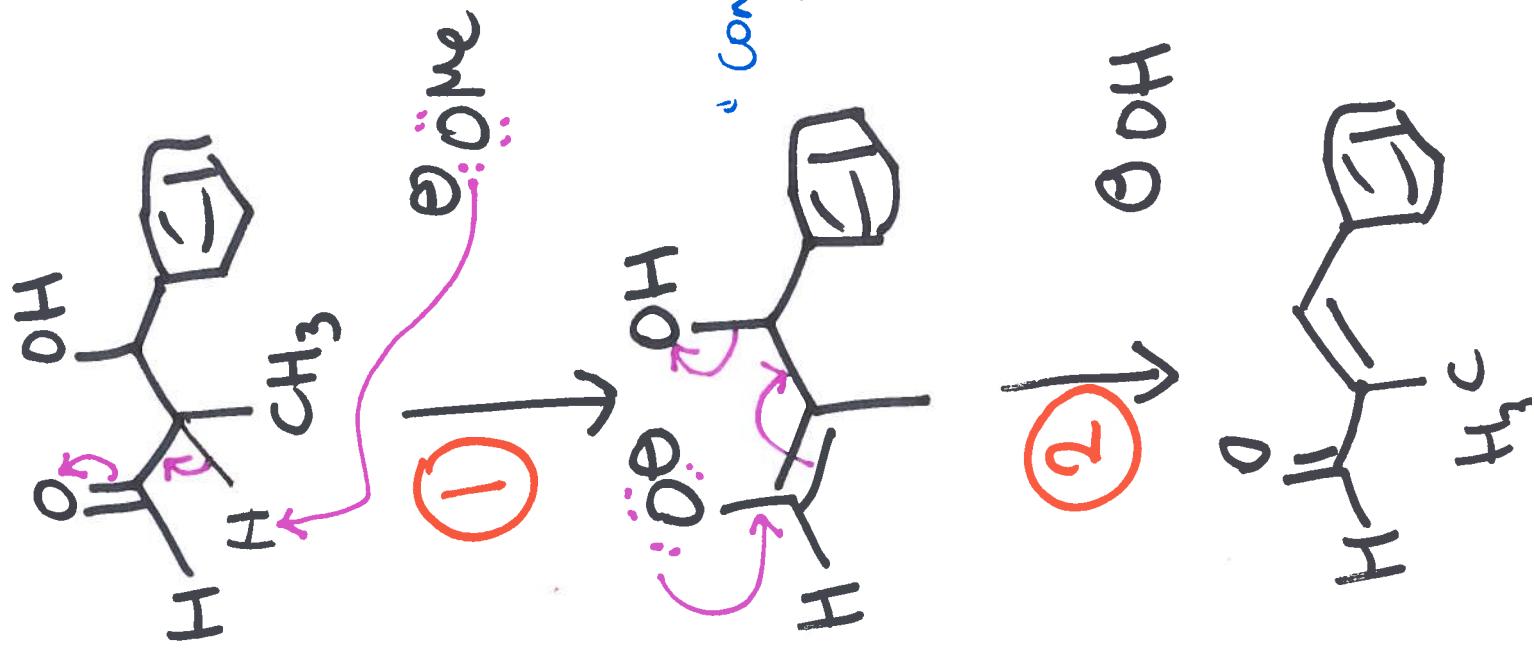
15



Mechanism of Elimination



2 steps = Eich.

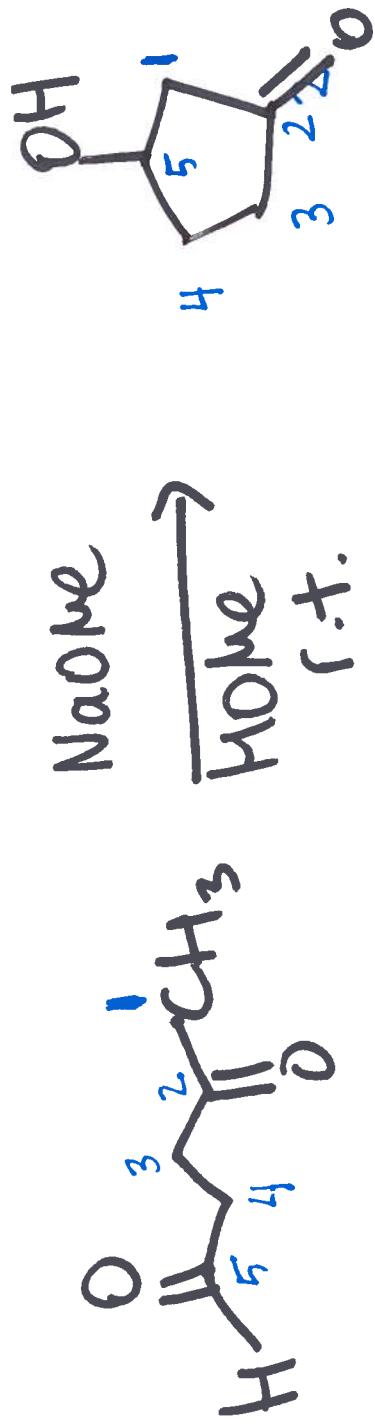


(16)

Intramolecular Aldol Reactions

- tethers aldehydes together!
- make 5 and 6-membered rings.

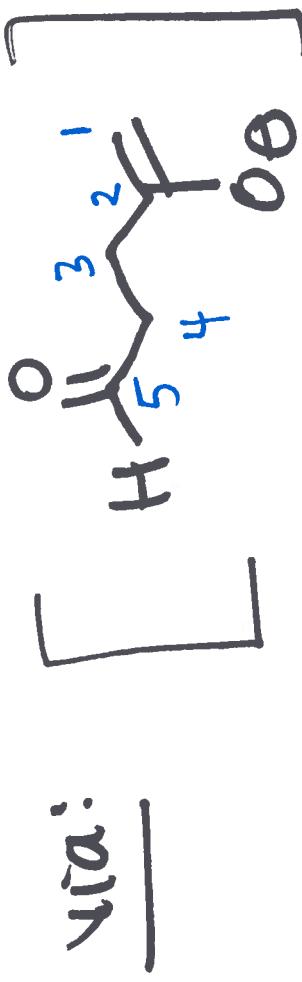
No 3 or 4 membered rings.



- Where can I form enolate???
- Is that nucleophilic α -carbon 5 or 6 carbon from a carbonyl?

5 or 6 carbons

(17)



another example:

