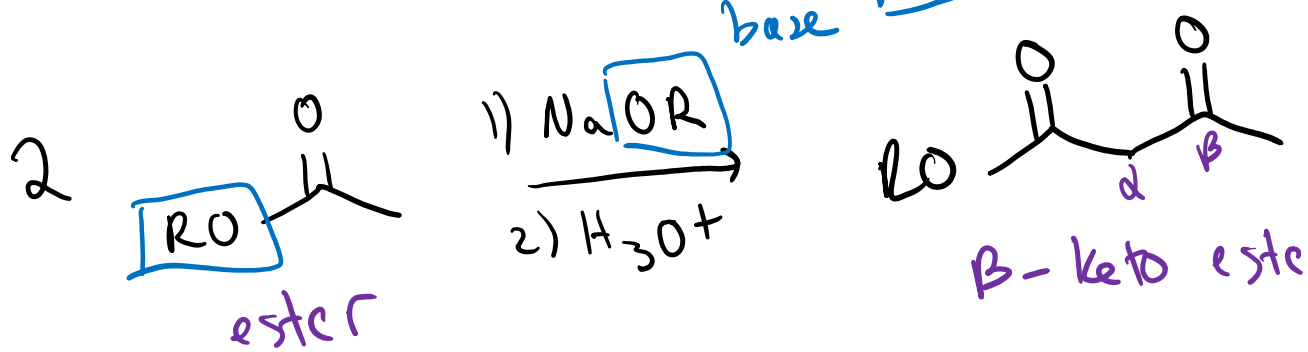
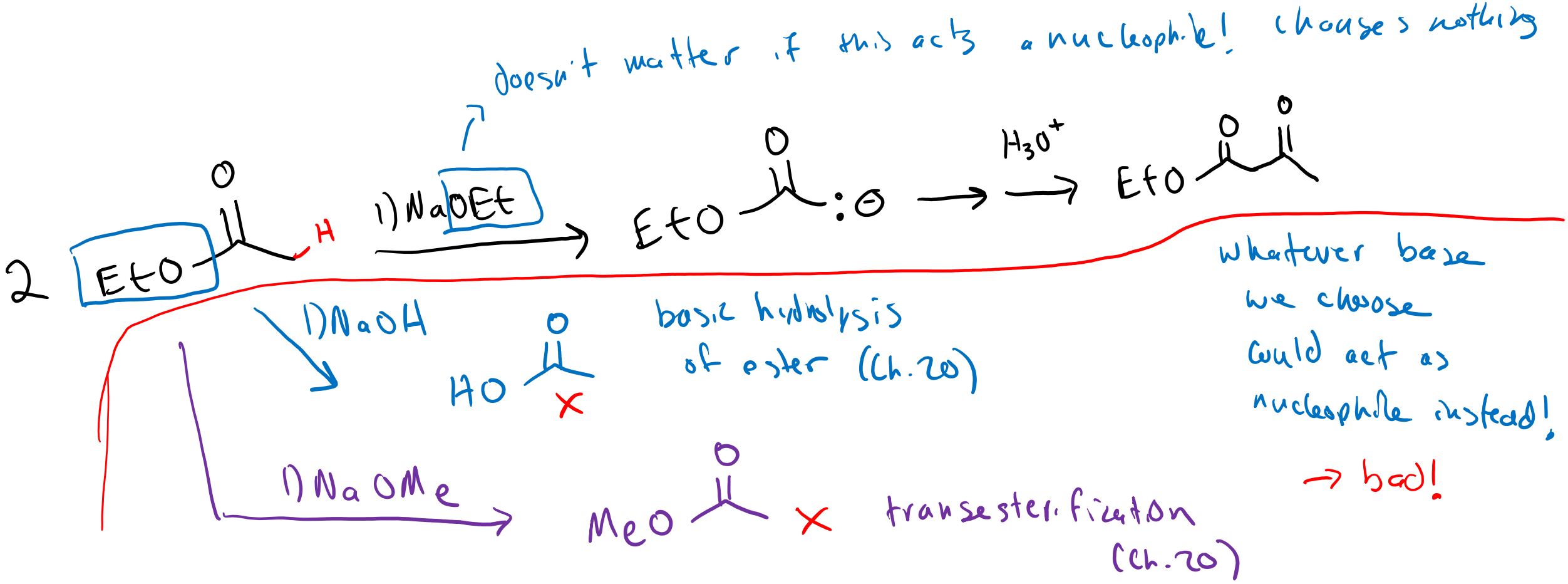
Aldol and Claisen Condensations

3/22/2022

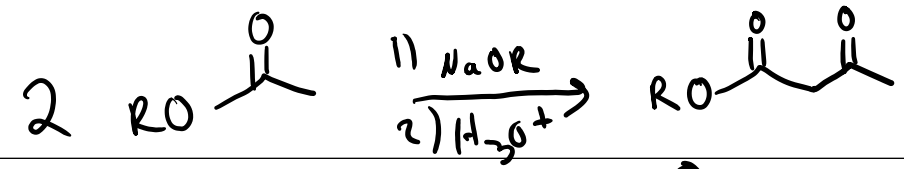
Claisen Condensation

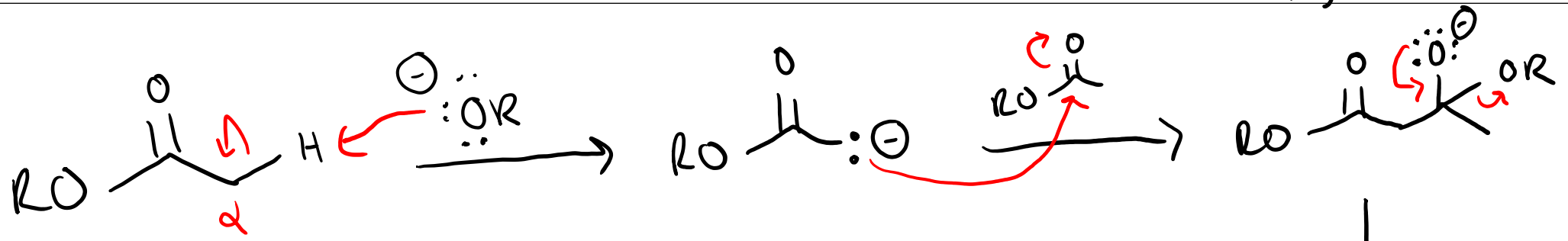
(21.4)



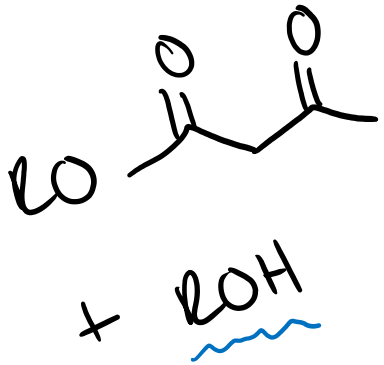


Claisen Condensation: Mechanism

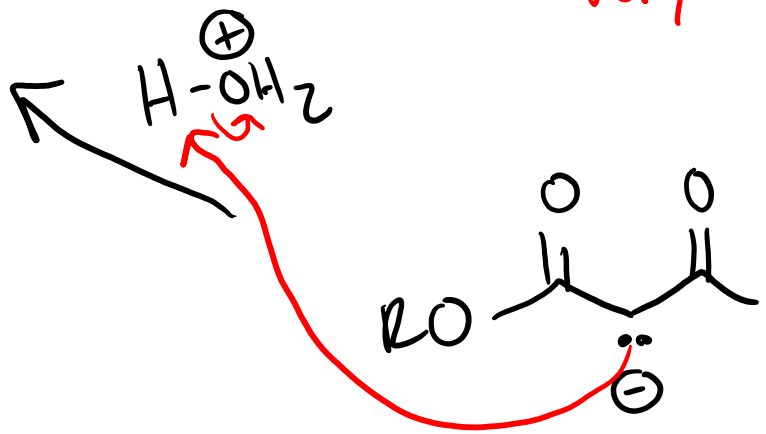


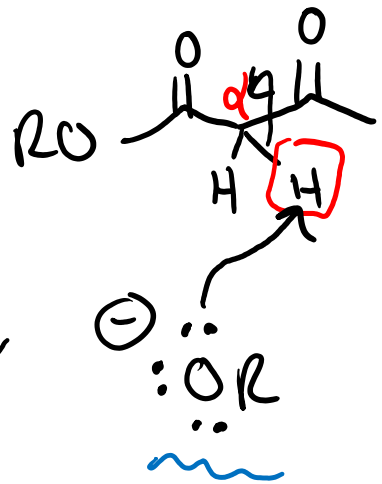


⊖OR acts as leaving group (Ch. 20)



"double-α" proton → very acidic



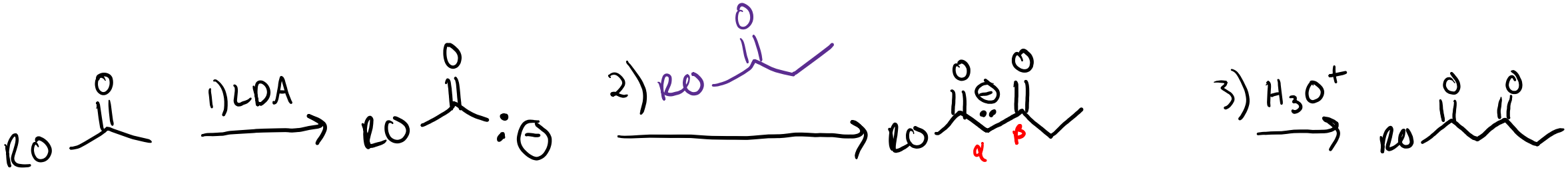


Crossed Claisen (or mixed Claisen)

Same problem as crossed aldol

- 4 different products

→ same strategy as crossed aldol (stepwise)



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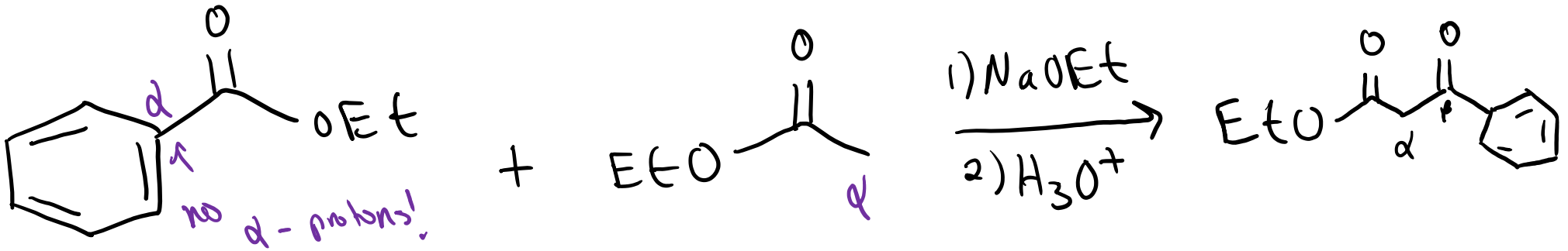
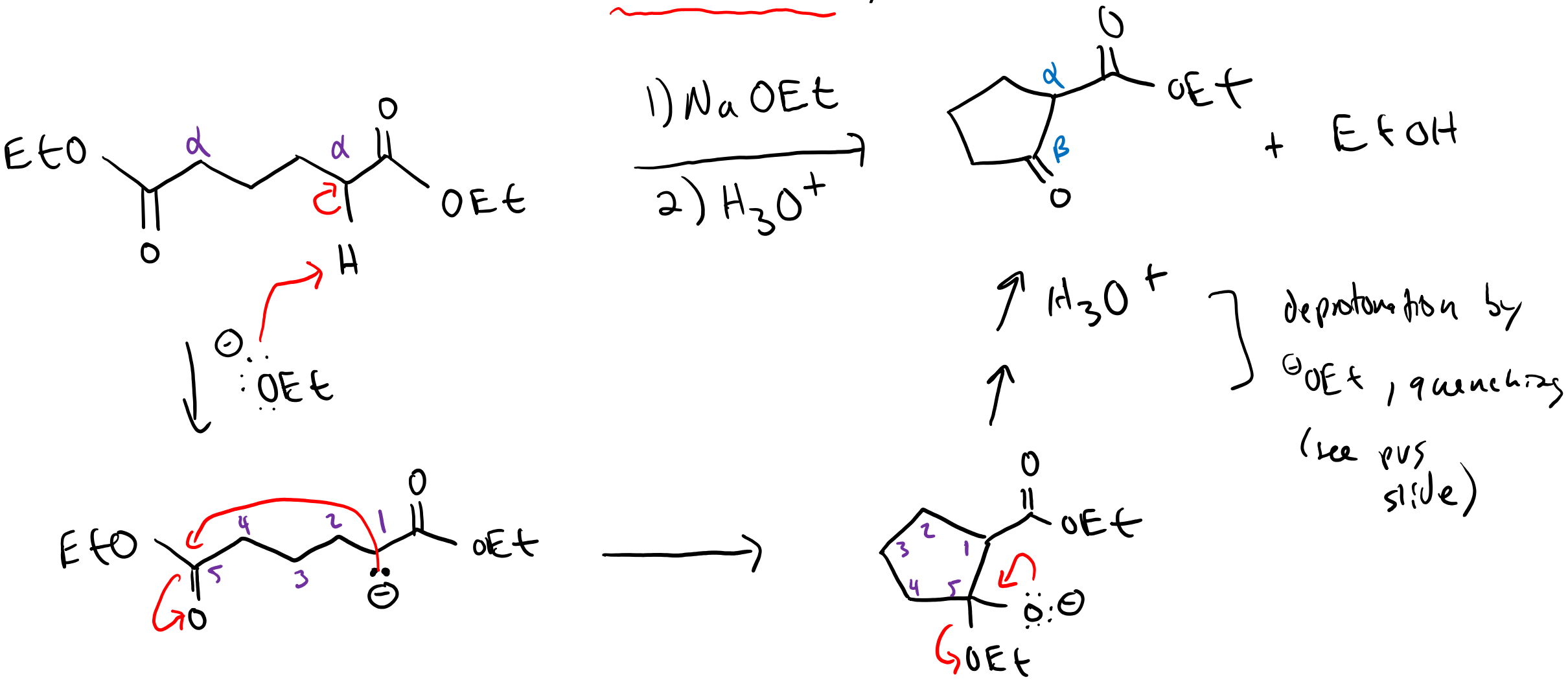
or, if one reactant has <u>no</u> α-protons



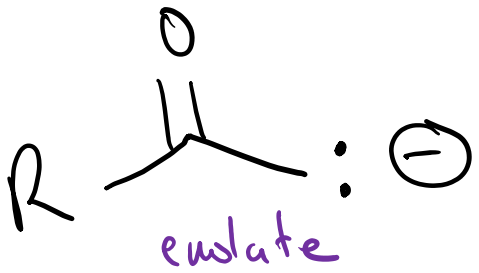
Intramolecular Claisen – "Dieckmann Cyclization"



Alpha-Alkylation of Enolates

(21.5)

Capable of S_N2 w/ alkyl halide.

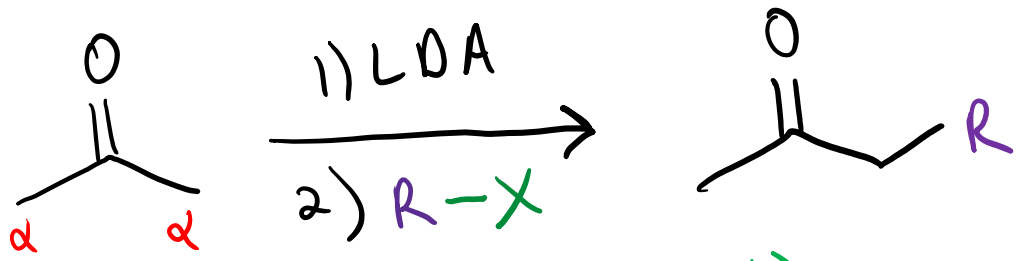


$pK_{aH} \cong 20$

strong base, good nucleophile

(we've seen this a lot)

overall:



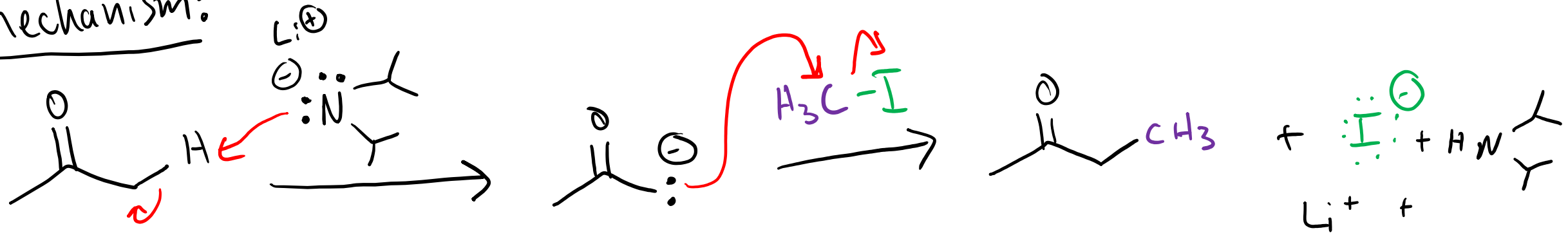
alkyl halide (or tosylate)

S_N2 w/ enolate!

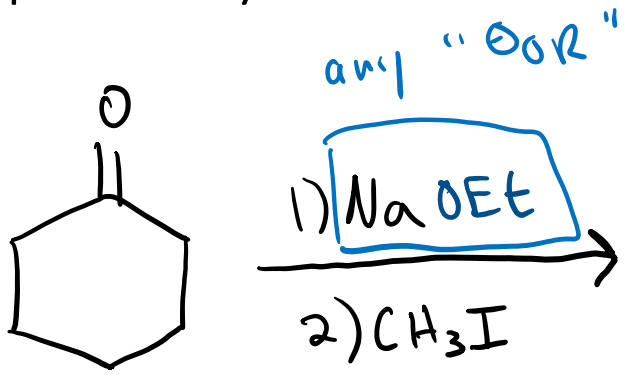
Normal S_N2 rules & restrictions apply

(no 3° R–X, 2° is also bad → favors E2)

mechanism:



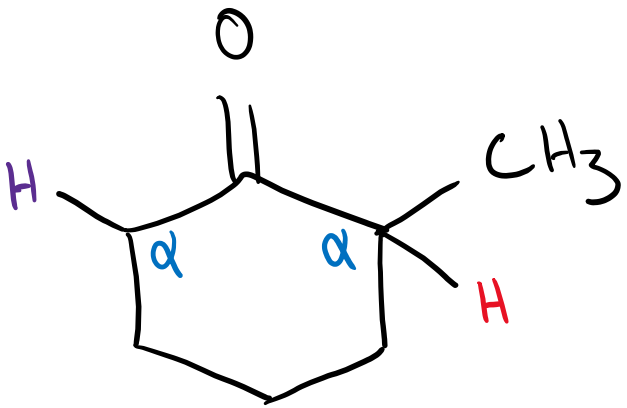
Alpha-Alkylation: Choosing a Base

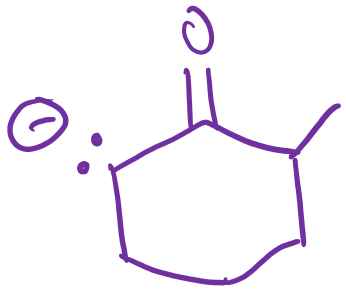


aryl "OR"

not strong enough base! lead to reversible deprotonation → aldol conditions!

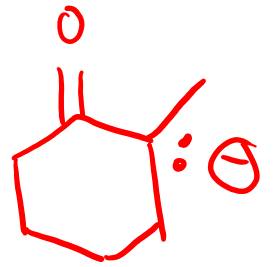
need full conversion to enolate! → use LDA or NaH





Base

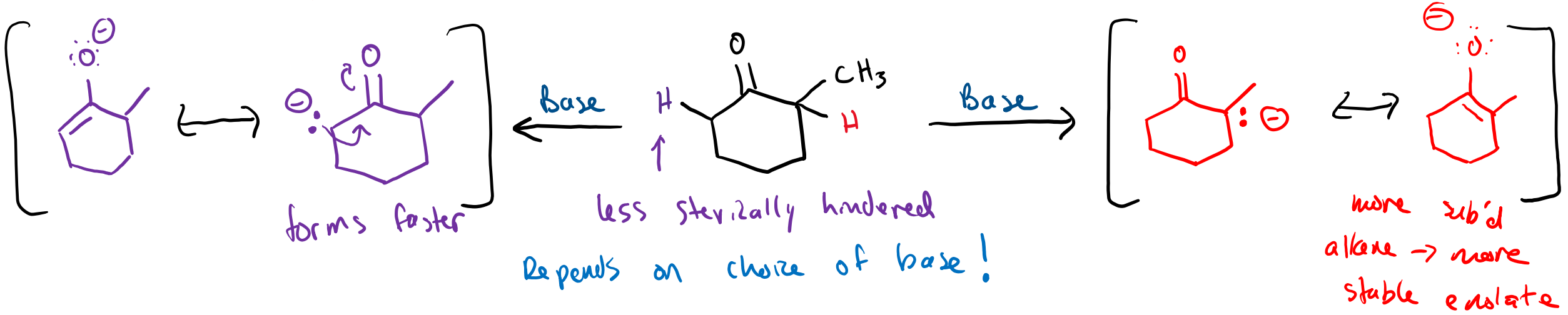
Base

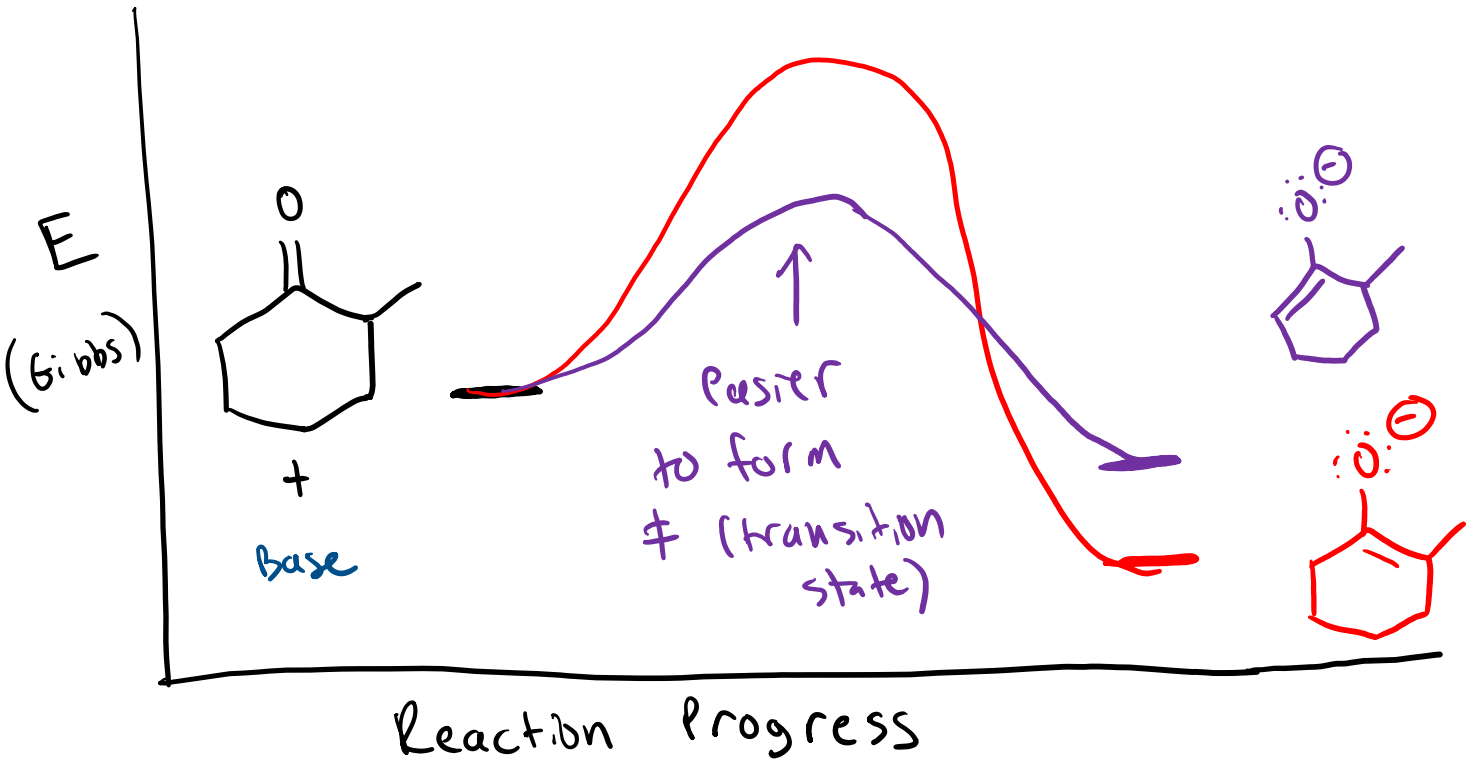


Which α-carbon gets deprotonated??

depends on base (LDA vs NaH)

Thermodynamic vs Kinetic Enolate: Choosing the right base





Kinetic (less hindered ‡) → Use a bulky base

LDA 

Thermodynamic (more stable) → Use a small, unhindered base

NaH

Thermodynamic vs Kinetic Enolate: Examples

less hindered α - carbon

more hindered α - carbon