

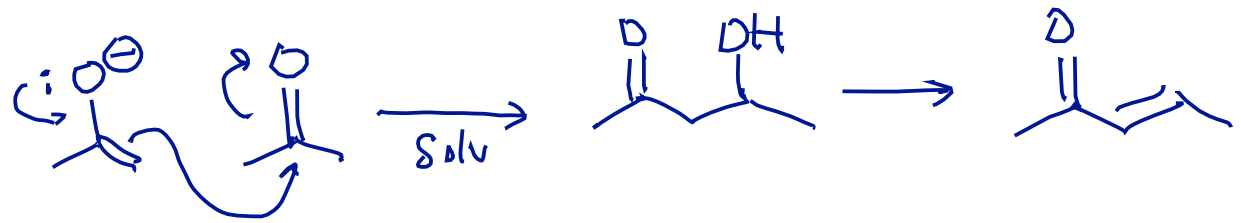
# Recap:

- Carbonyl compounds are acidic (slightly... pK<sub>a</sub>s!)
- β-dicarbonyl cpds can be completely deprotonated by <sup>-</sup>OH or <sup>-</sup>OR, but monocarbonyl cpds can't.
- Enols and enolates are nucleophilic at C

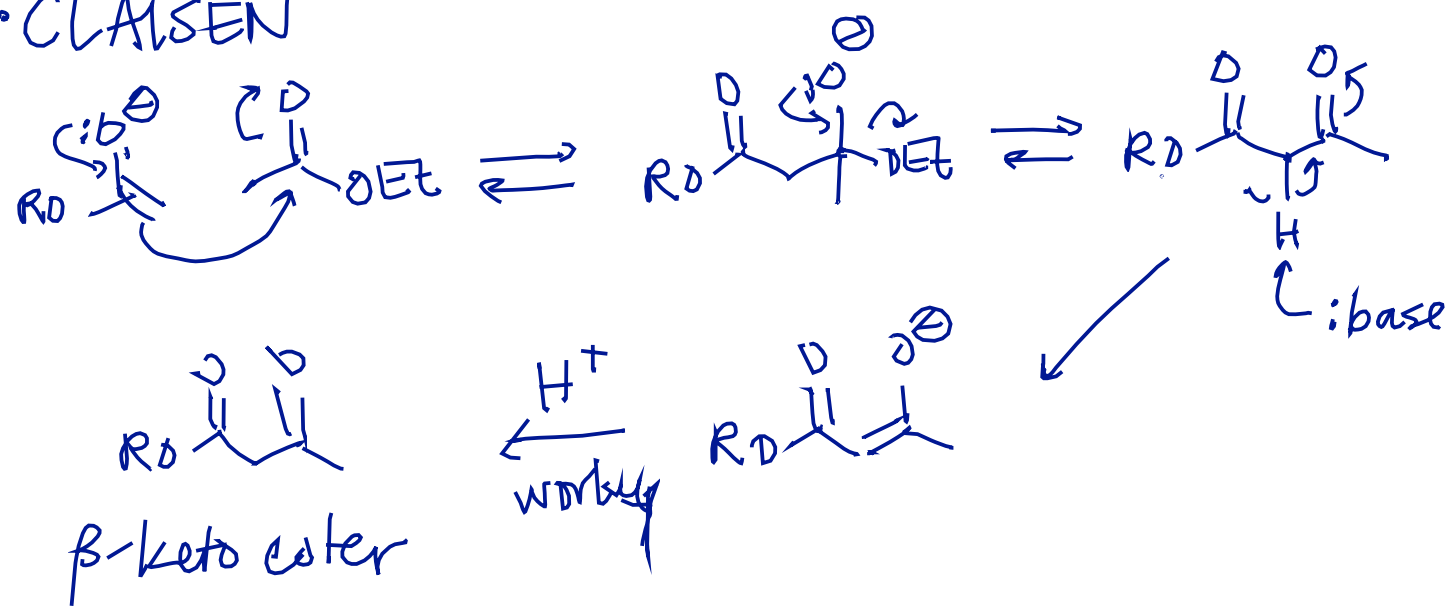


- Halogenation at α-carbons
  - ~ monohalogenation in H<sup>+</sup>
  - ~ complete halogenation in base

## • ALDOL

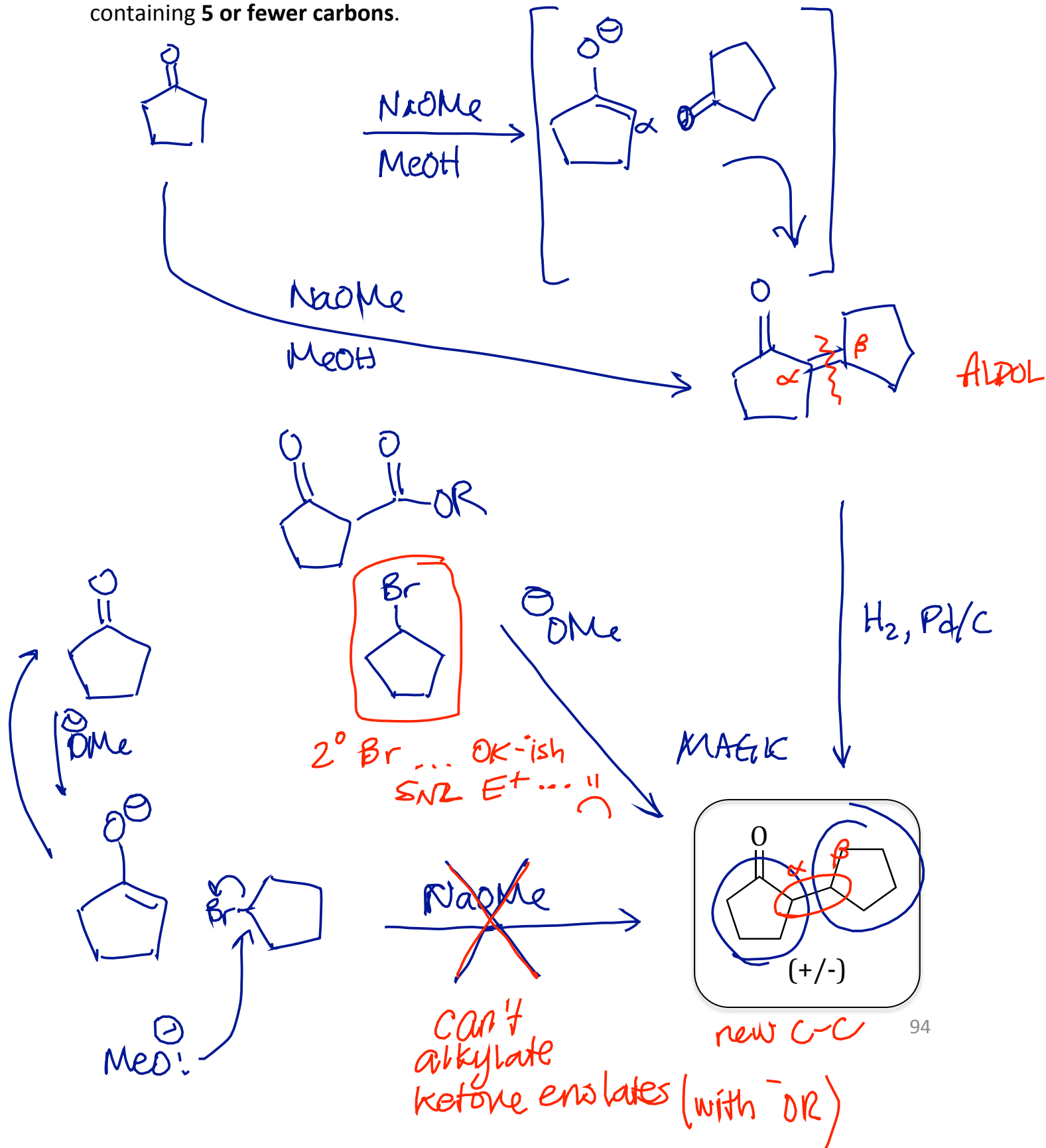


## • CLAUSEN



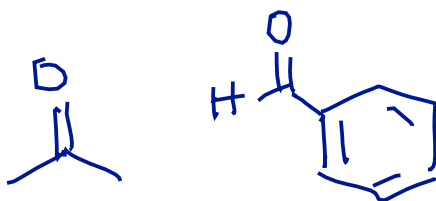
# Putting it Together: Synthesis Using Enolates

Provide a multi-step synthesis of the desired product from any organic reagents containing **5 or fewer carbons**.



## Putting it Together: Synthesis Using Enolates

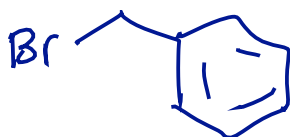
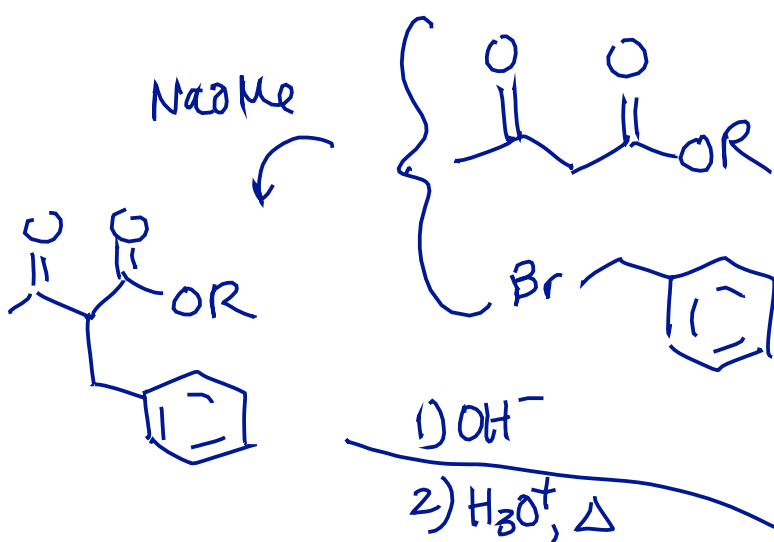
Provide a multi-step synthesis of the desired product from any organic reagents containing **7 or fewer carbons**.



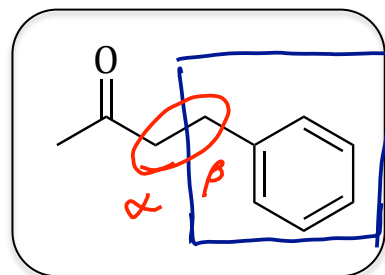
$\text{NaOMe}$   
 $\text{MeOH}$



$\text{H}_2$ ,  
 $\text{Pd/C}$



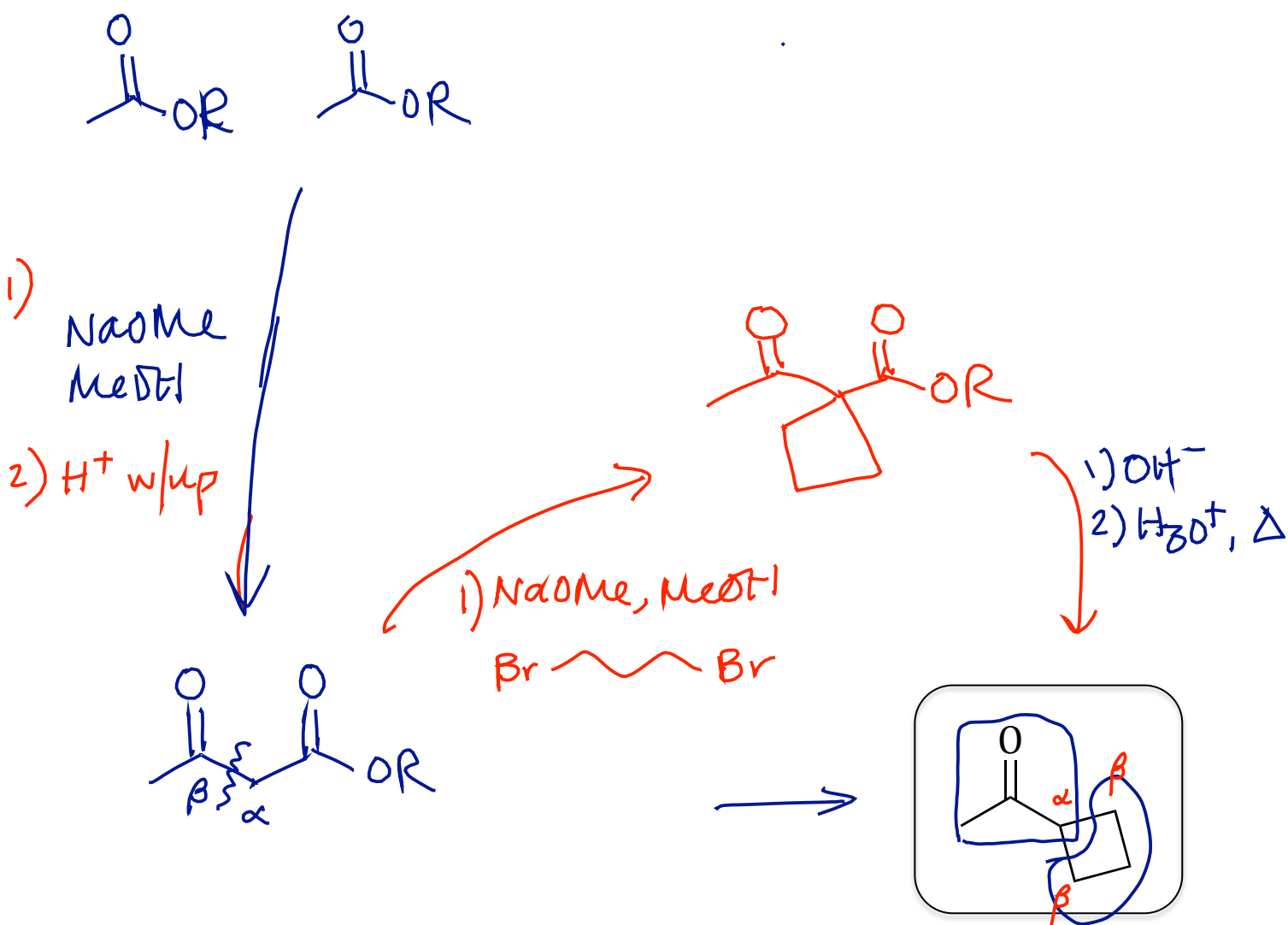
$\text{NaOMe}$   
 $\text{MeOH ?}$



CANNOT ALKYLATE KETONES DIRECTLY  
(w/  $\text{OR}^-$ ,  $\text{R-Br}$ )

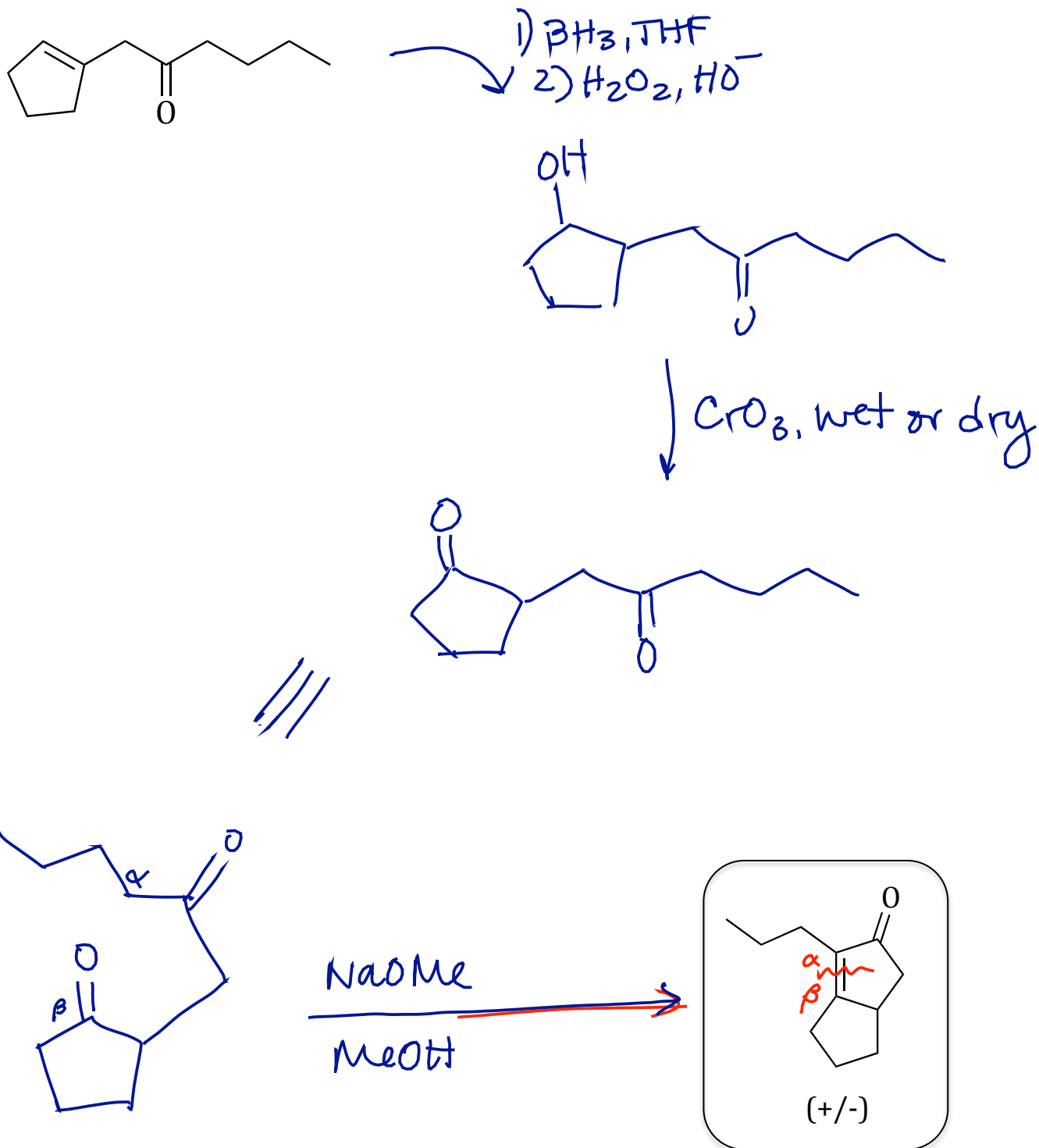
## Putting it Together: Synthesis Using Enolates

Provide a multi-step synthesis of the desired product from any organic reagents containing **3 or fewer carbons**.



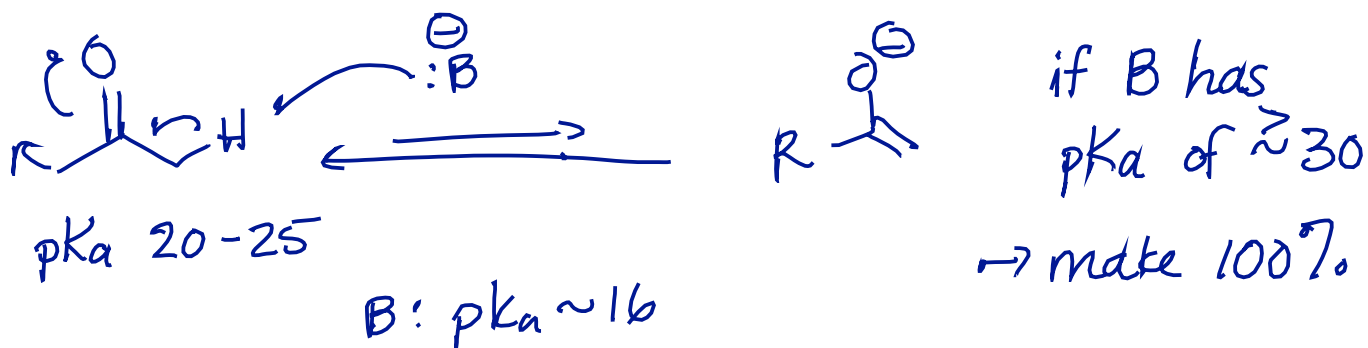
## Putting it Together: Synthesis Using Enolates

Provide a multi-step synthesis of the desired product from the indicated starting material; you may use any inorganic reagents you desire.



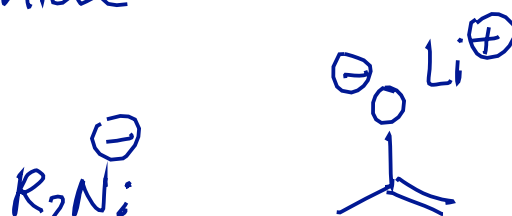
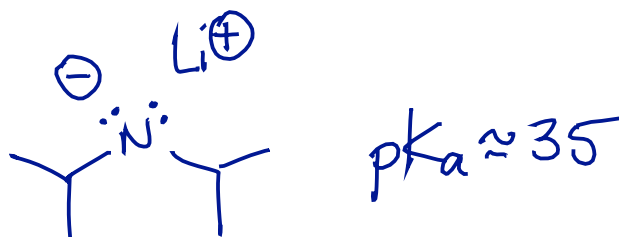
## Lithium Enolates

In our last lecture, we emphasized that enolates are generally present in only *small* concentrations at equilibrium. How might we be able to actually *make* an enolate?

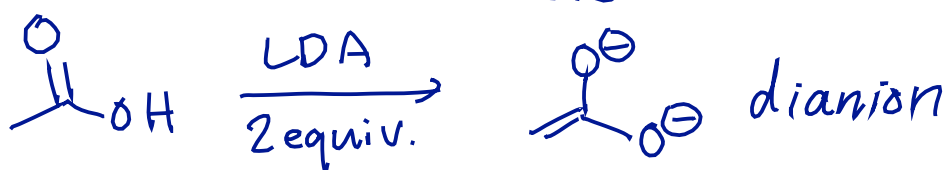
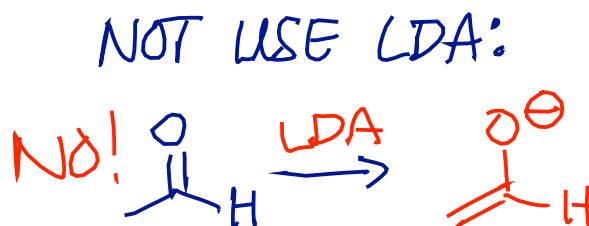


What base can we use to make a *lithium enolate*?

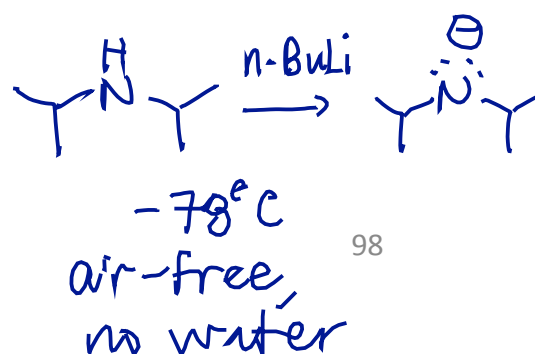
LDA – lithium diisopropyl amide



What types of enolates can we form using this technique?



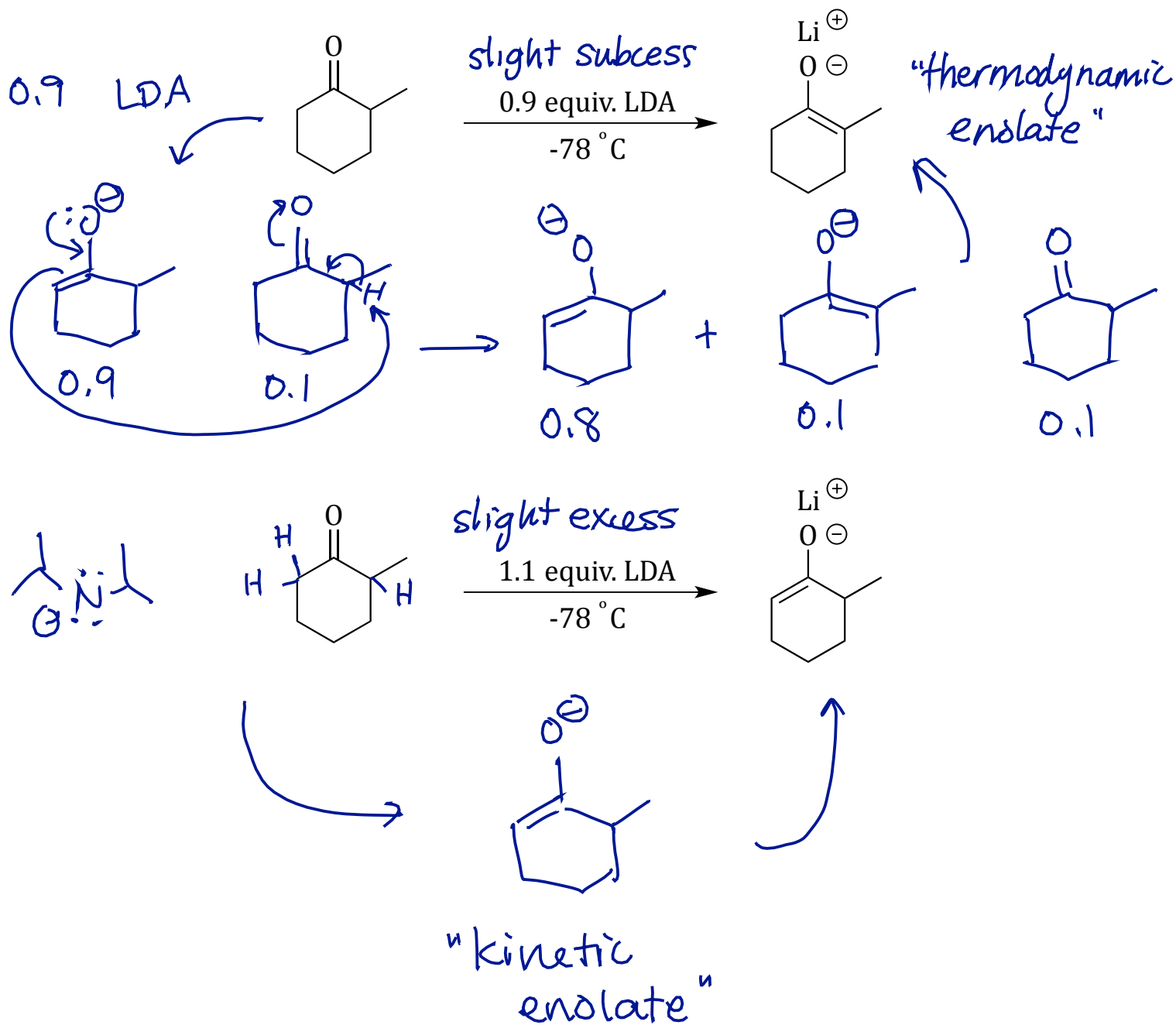
PROBLEM:



Reading: Section 22.7

## Lithium Enolates: Kinetic vs. Thermodynamic Enolates

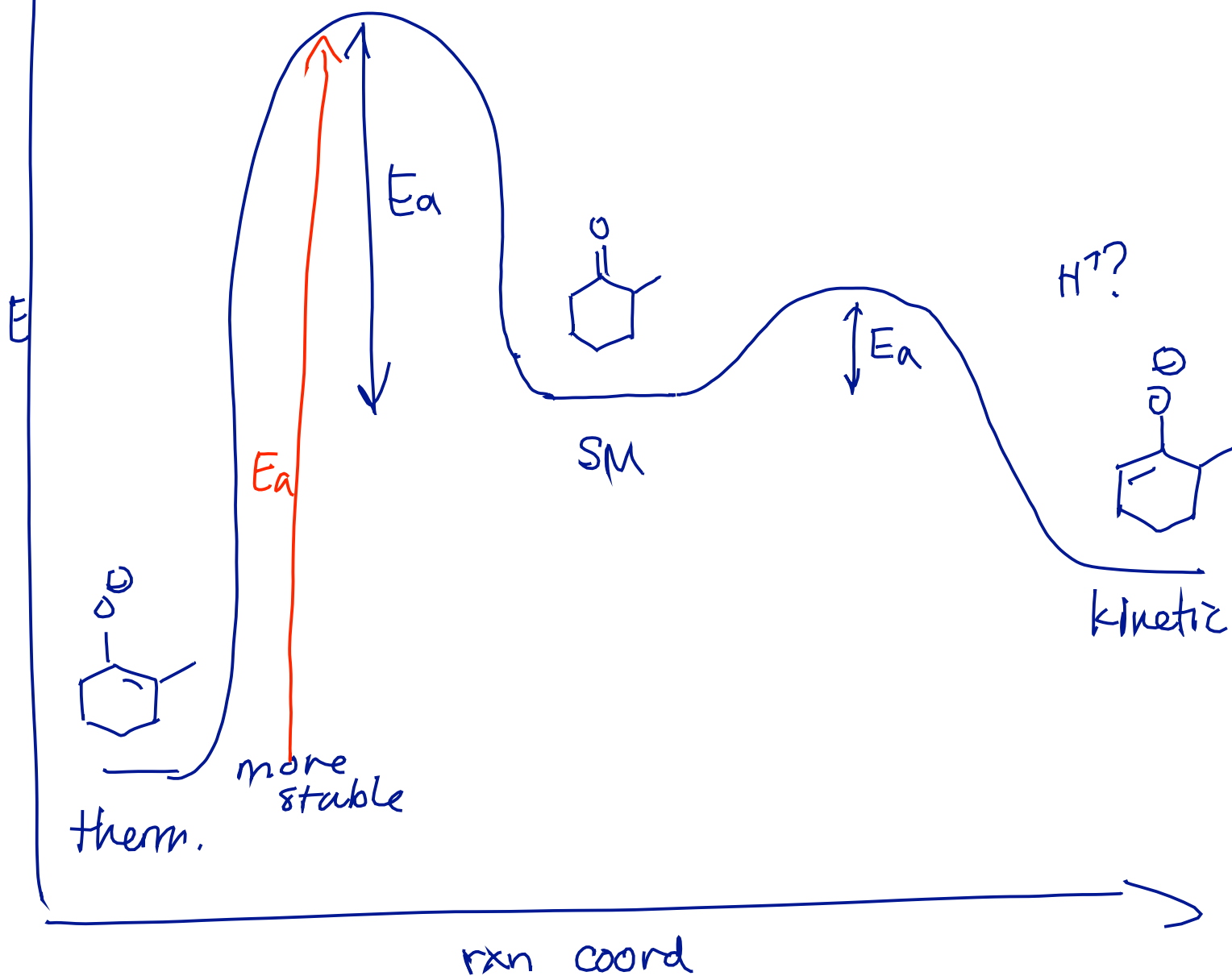
Explain why the following two reactions give *different* enolates:



# Kinetic vs. Thermodynamic Control Enolates

Thermodynamic — long rxn, allows equilibration  
higher temp

Kinetic — short rxn times, no equil., cold

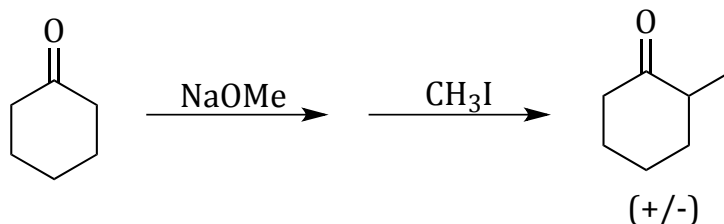


LDA: allowing equilibration [excess/subless]

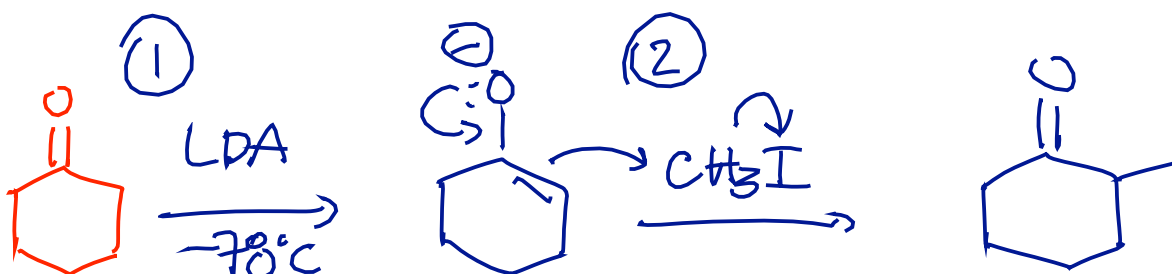


## Lithium Enolates: Alkylation

Last lecture, we said the following transformation couldn't be done *as written*. Why?

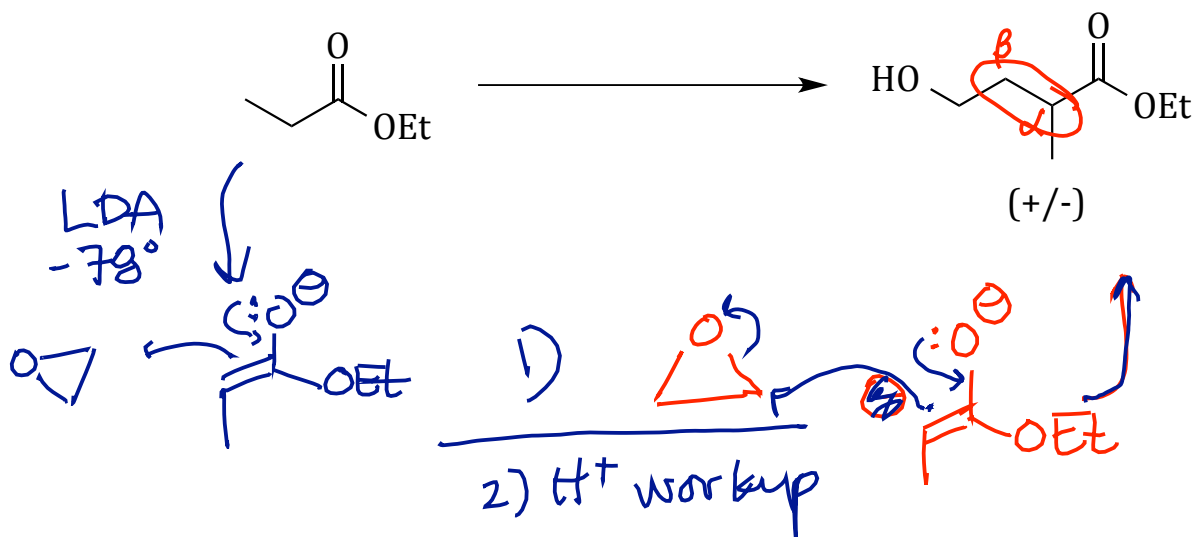


Now, can you figure out how to carry out the same transformation (without using a "phantom ester")?



alkylate ketone/~~aldehyde~~ enolates!

How could you carry out the following synthesis?

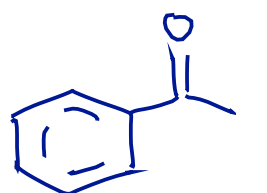


Reading: Section 22.7

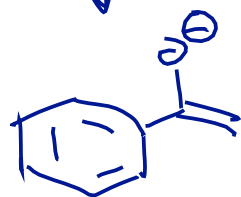
open epoxides w/ ester enolates (not ketone)

## Lithium Enolates: Application to "Crossed" Aldol & Claisen

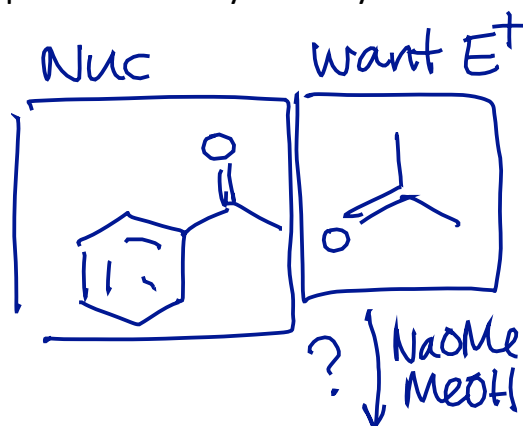
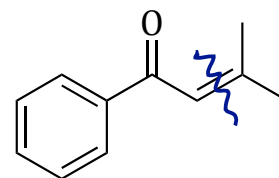
Last lecture, we hinted that "crossed" aldol and Claisen reactions are problematic; now you can do them! How could you synthesize the following products? Why would you have had trouble with these syntheses before?



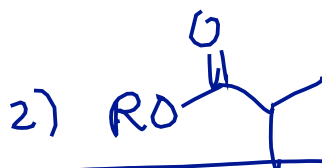
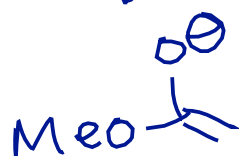
LDA,  $-78^{\circ}\text{C}$



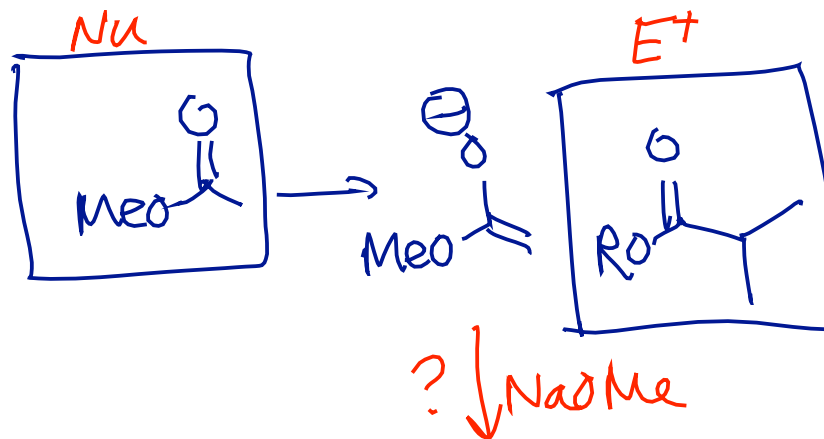
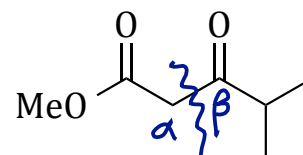
3)  $\text{H}^+$  w/ up



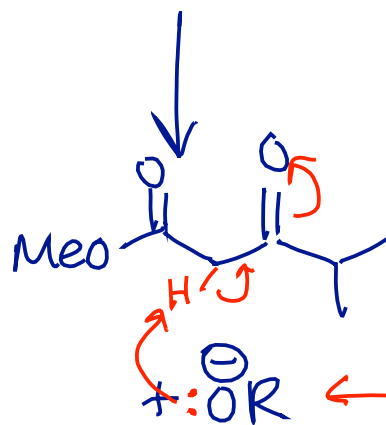
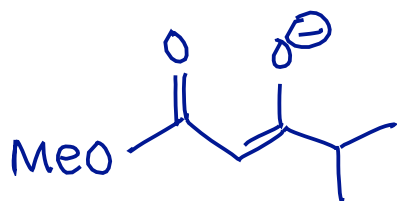
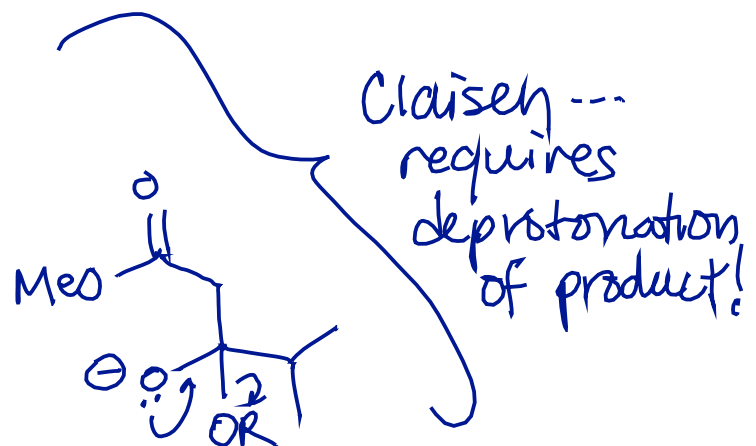
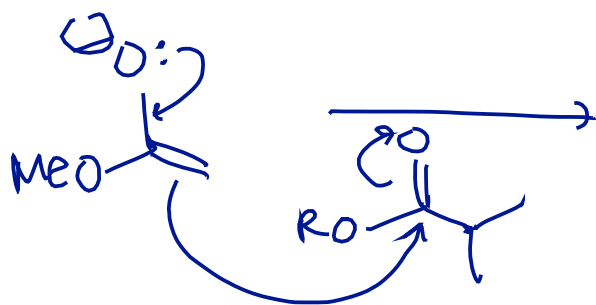
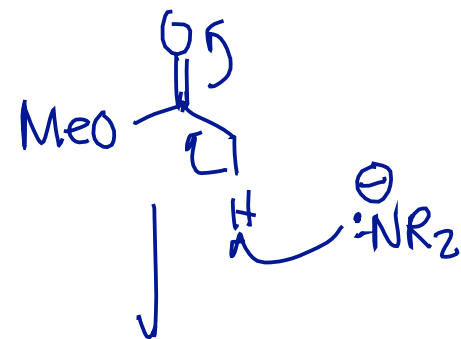
LDA  $\downarrow$   $-78^{\circ}$



3)  $\text{H}^+$  w/ up

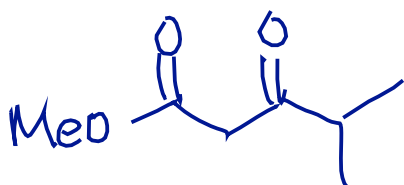


Why do we need  $H^+$  w/up after this reaction?



base is generated!

$H^+$  workup



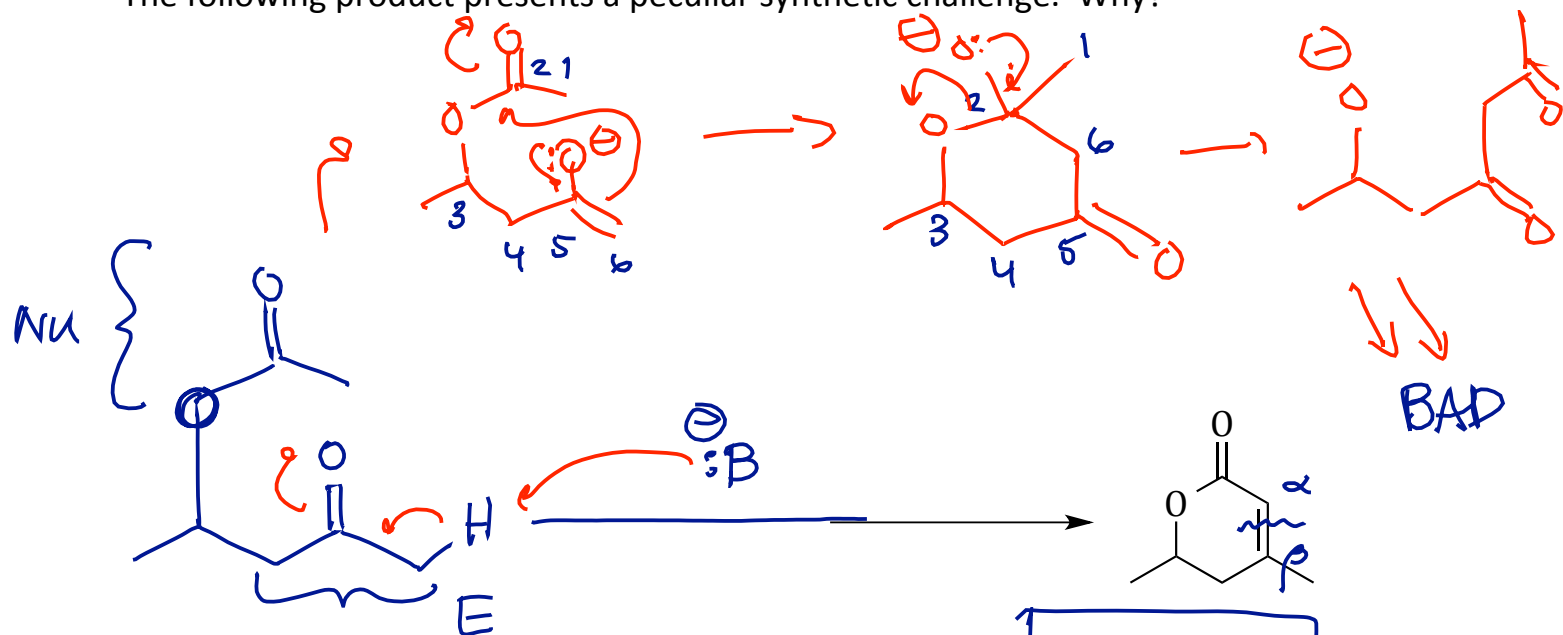
Obscure!

Week 5

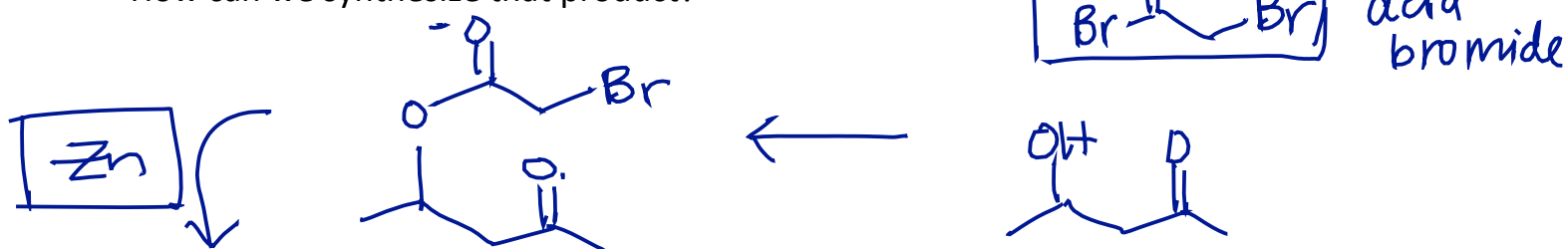
July 23, 2014

## Zinc Enolates: The Reformatsky Reaction

The following product presents a peculiar synthetic challenge. Why?



How can we synthesize that product?



Reformatsky:  
Umpolung

H<sup>+</sup> w/ op

