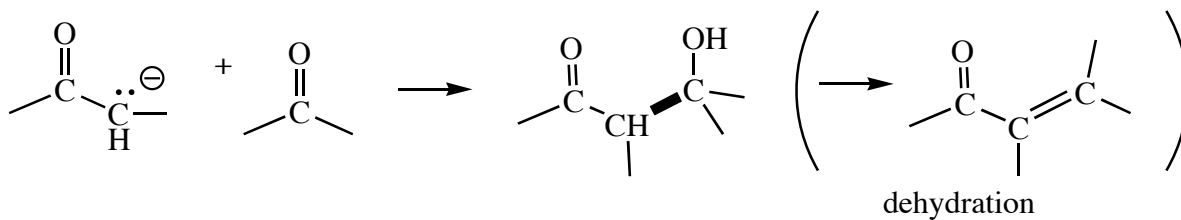


## Lecture outline

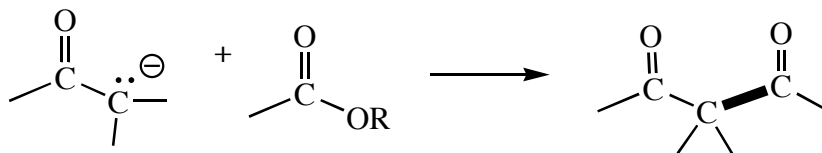
Carbonyl compounds undergo two main types of condensations —

**aldol condensation** —



Carbonyl *addition*

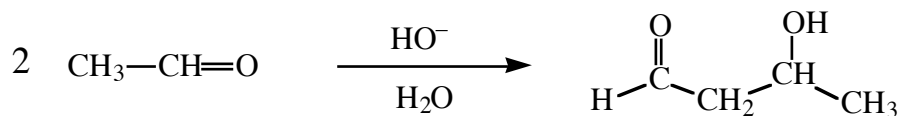
**Claisen condensation** —



Carbonyl *substitution*

## The aldol condensation

— usually accomplished with *base*-catalysis  
acid works also (enol attacks protonated carbonyl)



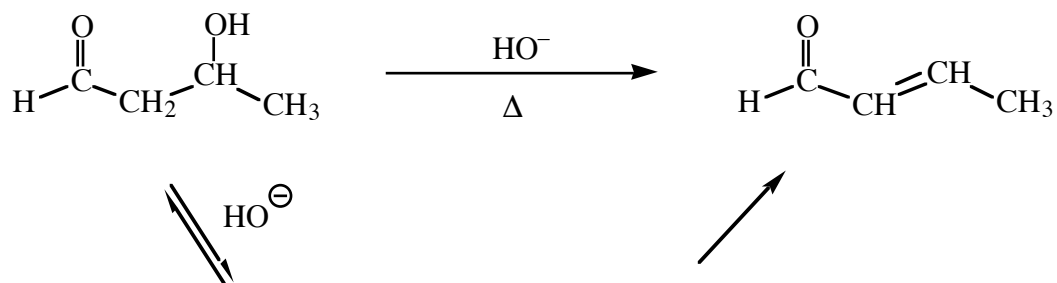
meh

— rxn is reversible

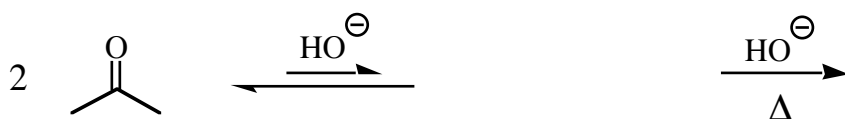
for addition to an aldehyde carbonyl, equilibrium favors condensation (addition) product

for addition to a ketone carbonyl, equilibrium favors reactants

— rxn can be driven to completion by dehydration of hydroxy-carbonyl  
cmpd initially formed — usually requires heat



— because the equilibrium for addition to most ketone carbonyls is unfavorable (i.e. lies toward reactants), this condensation will usually work *only* if the dehydration is induced with heat (or it if goes on its own).



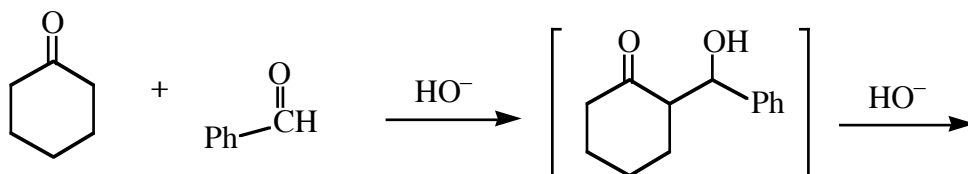
Variations —

a. "Crossed" or "mixed" aldol — rxn of 2 different carbonyl cmpds

— synthetically useful *only* if one product is formed. That normally means an enolate of a ketone with one type of  $\alpha$ -H adding to the carbonyl of an aldehyde with no  $\alpha$ -H.

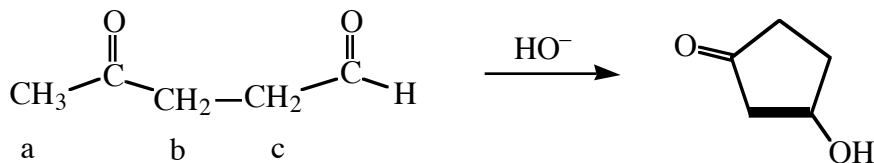
Why? Think about the nasty mixtures that could be formed if several different enolates were generated and each one could attack two different carbonyl groups. The restrictions above just mean that only *one enolate ion* is possible, and only *one carbonyl* gets attacked (more precisely, only one addition — to the aldehyde — has a favorable equilibrium).

e.g.,



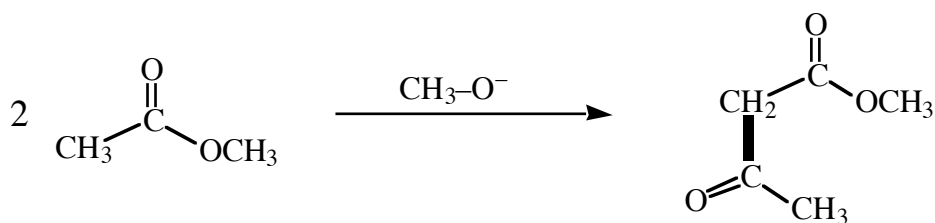
Dehydration can occur at room temp if new  $\pi$ -bond is conjugated at both ends

b. Intramolecular aldol — works best if 5- or 6-membered ring is formed



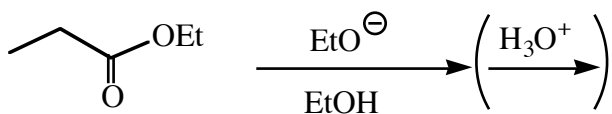
In this example, 3 different enolate ions can be formed.  
Why don't we get 3 different products?

## 2. The Claisen condensation



This condensation is catalyzed by base ( $\text{CH}_3\text{O}^-$ ), *however*, the base-catalyzed reaction is reversible, and the equilibrium favors the reactants. To make it go to completion, a full equivalent of base is used to completely deprotonate the condensation product. Now it can't go backward. Pretty clever, eh?

When acid is added at the end of the reaction, the stronger alkoxide base gets protonated first, then the product enolate ion. This way, when the final neutral product is formed there's no alkoxide around to reverse the process. (But if you take that product and add a little alkoxide catalyst in alcohol solvent, it falls apart — write the mechanism of that reaction — it's called a *retro*-Claisen)

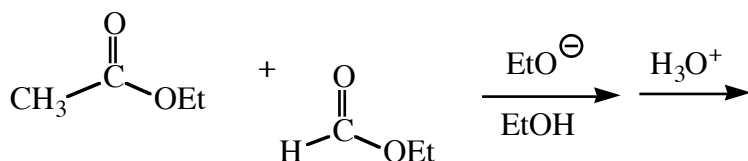


Variations —

a. "Crossed" or "mixed" Claisen

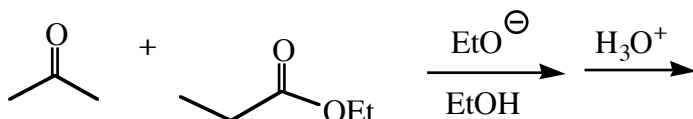
Again, with two different reactants, there is obviously the potential for creating a mess. These condensations are only synthetically useful *only* if they produce a single product. There are two main ways that can happen —

i. Only one ester has  $\alpha$ -Hs, and the other has a more reactive carbonyl

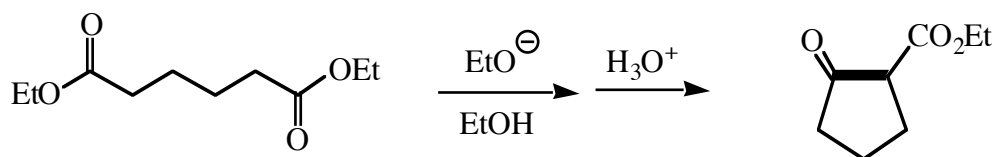


ii. Symmetrical ketone and ester.

*One enolate* is formed because ketones are a bit more acidic than esters ( $pK_a \approx 20$  vs 23). *Only the ester carbonyl is attacked* — well, both are attacked, but the equilibrium is unfavorable for addition to the ketone (aldol); addition to the ester (Claisen) can be driven to completion with a full equivalent of base.



b. Intramolecular Claisen ("Dieckmann" condensation)



mech:

