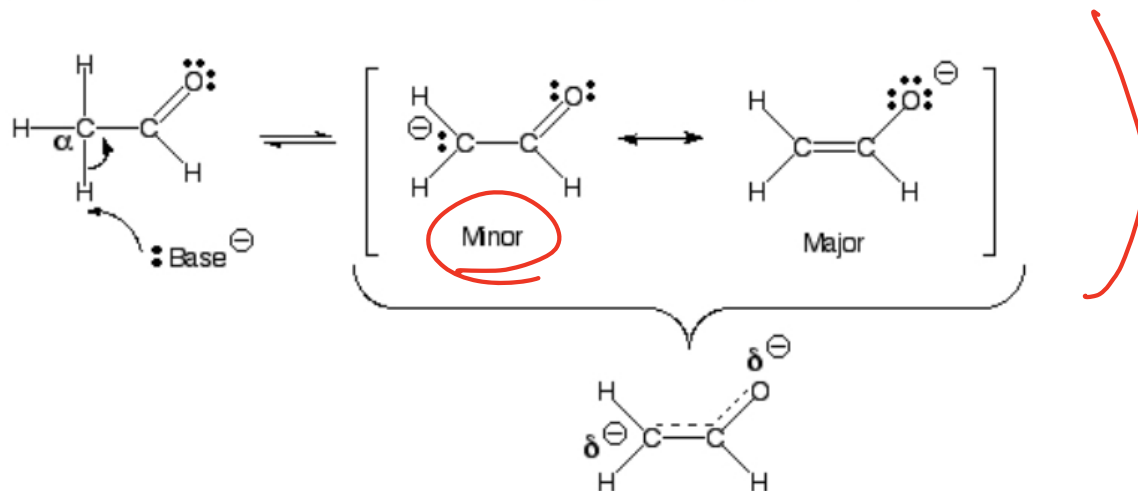
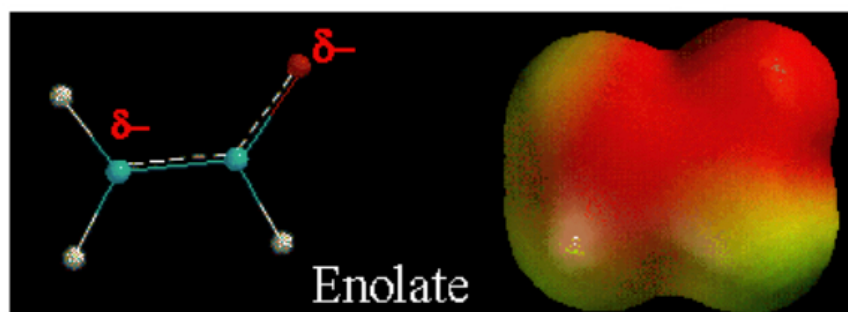




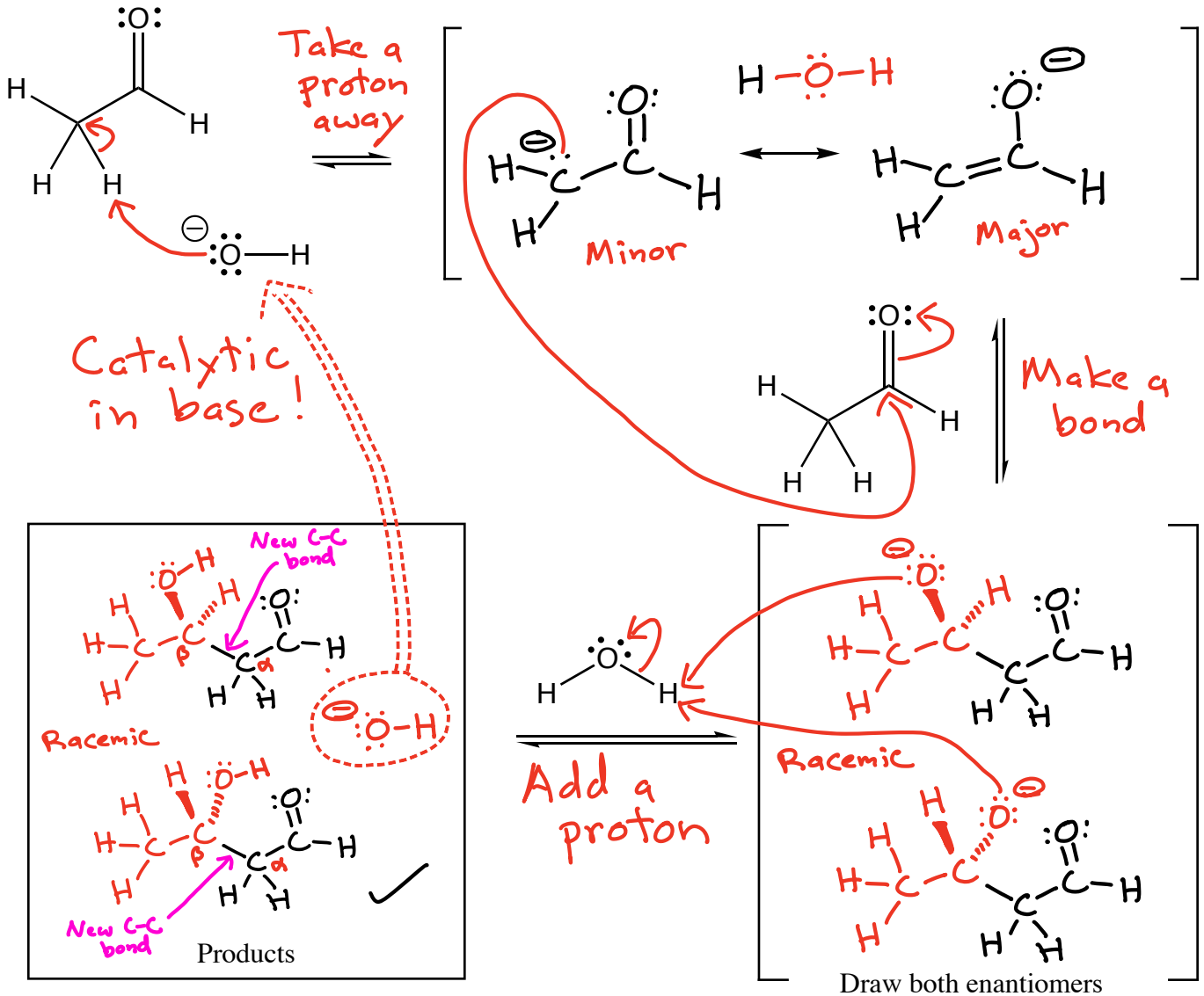
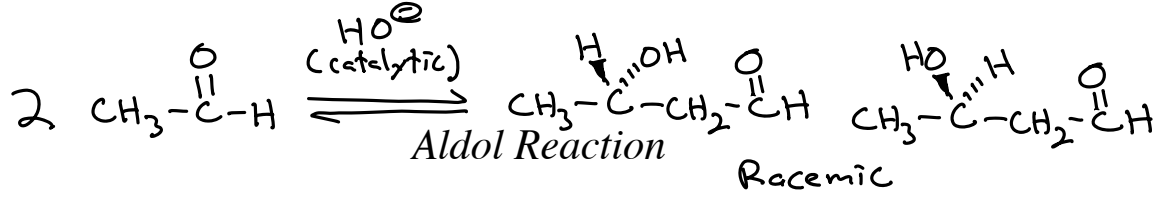
Enolates as nucleophiles



A) Enolates are resonance stabilized, with a partial negative charge on carbon and oxygen. ✓

B) Enolates are nucleophiles, so they could react at either the carbon atom or oxygen atom. The partial negative charges give them the **opportunity** to react at either the carbon or oxygen.

C) Reaction at the carbon atom gives the final product a C=O bond, while reaction at the oxygen atom gives the final product a C=C bond. However, C=O bonds are stronger than C=C bonds, **so the motive is to react at the carbon atom with most electrophiles.**

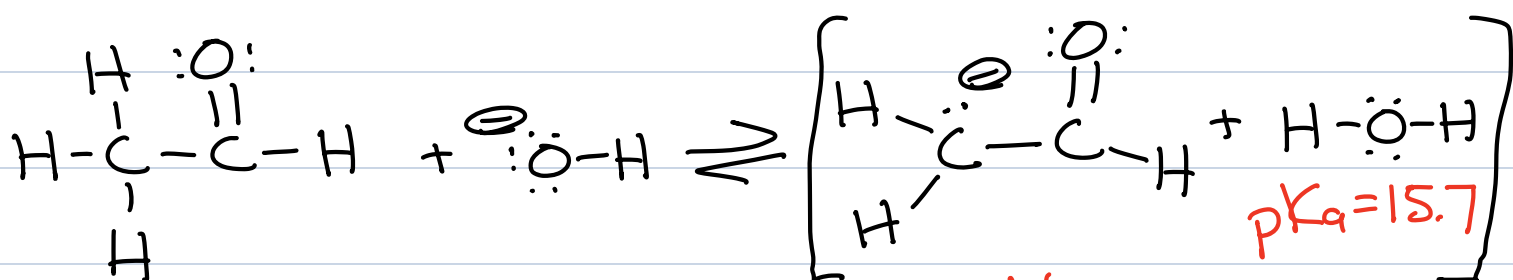


KRE \rightarrow β -hydroxy aldehyde
with a new C-C
bond between the
aldehyde α and β
carbons

Mechanism
A

Aldol Reaction Considerations

1) When HO^\ominus is used as the base, equilibrium of the first step favors the aldehyde



$pK_a = 18-20$
weaker base

This side favored at equilibrium

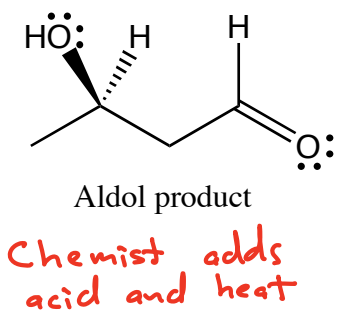
There will be excess aldehyde for the enolate to react with

2) Because there is HO^\ominus present at the beginning and end of the reaction there is little driving force (motive) for the aldol reaction \rightarrow the aldol reaction is reversible

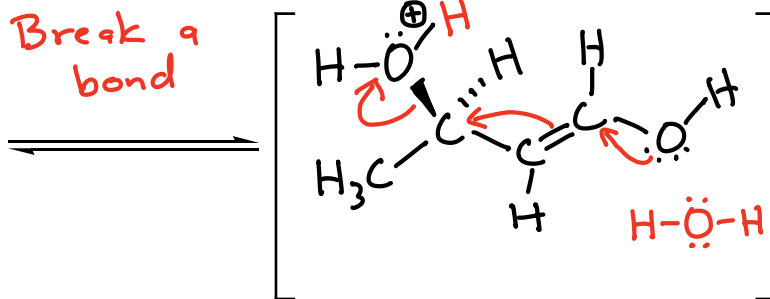
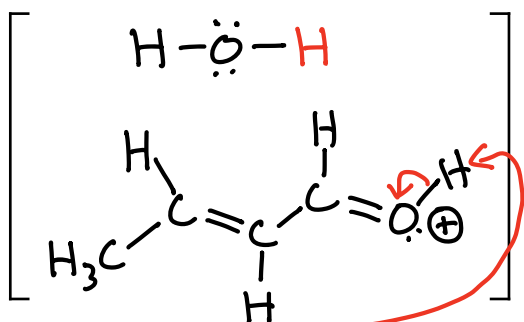
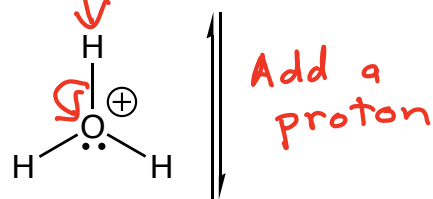
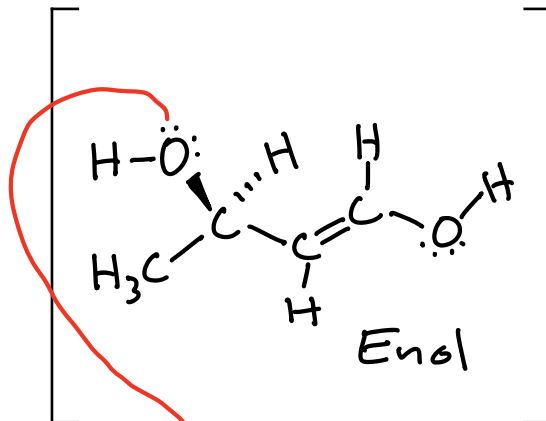
3) The aldol reaction is favorable for aldehydes but NOT for ketones

4) The reaction can make two new chiral centers

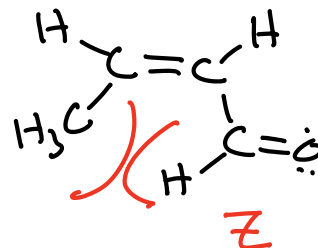
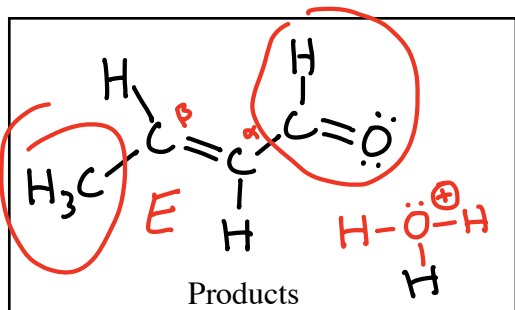
Acid catalyzed dehydration



tautomerization



KRE \rightarrow α,β -unsaturated aldehyde \rightarrow the C=C is where the new C-C bond is located



Not much of the Z product is formed because it has significantly more steric strain than E

THIS IS UNIQUE TO THIS EXAMPLE
 \Downarrow
 USUALLY BOTH E AND Z ARE FORMED



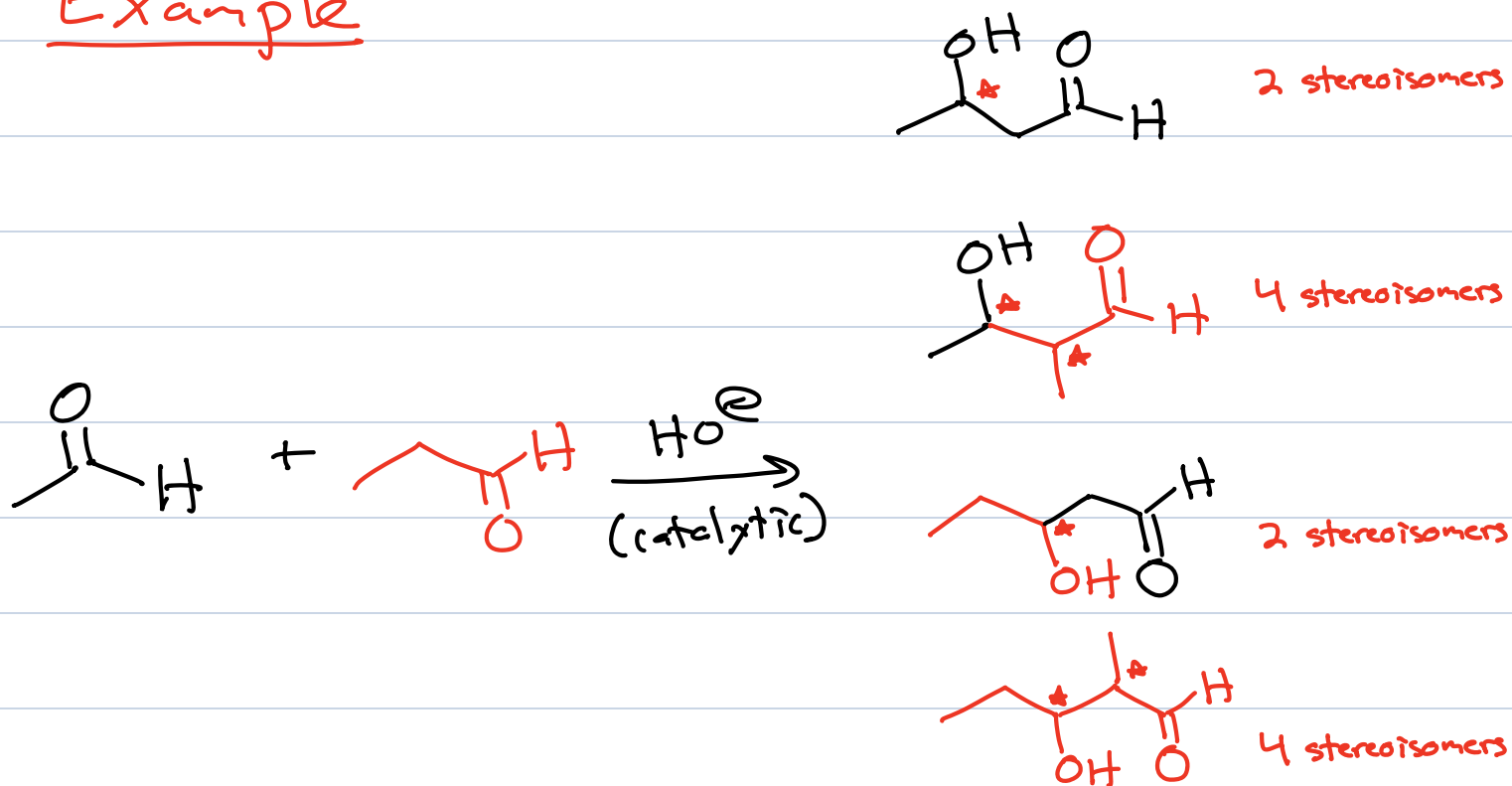
→ The dehydration product is conjugated and therefore stable.



→ The dehydration product can be used in a Michael reaction.

When you run a "mixed" aldol reaction, you generally get far too many reaction products to be useful.

Example



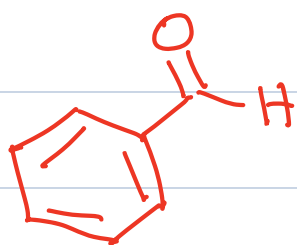
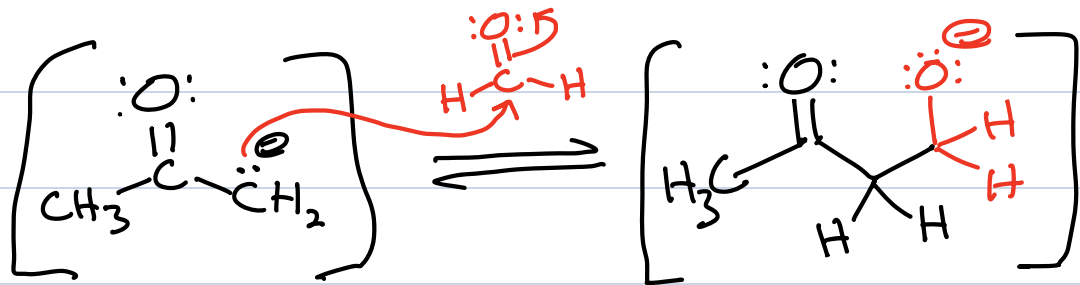
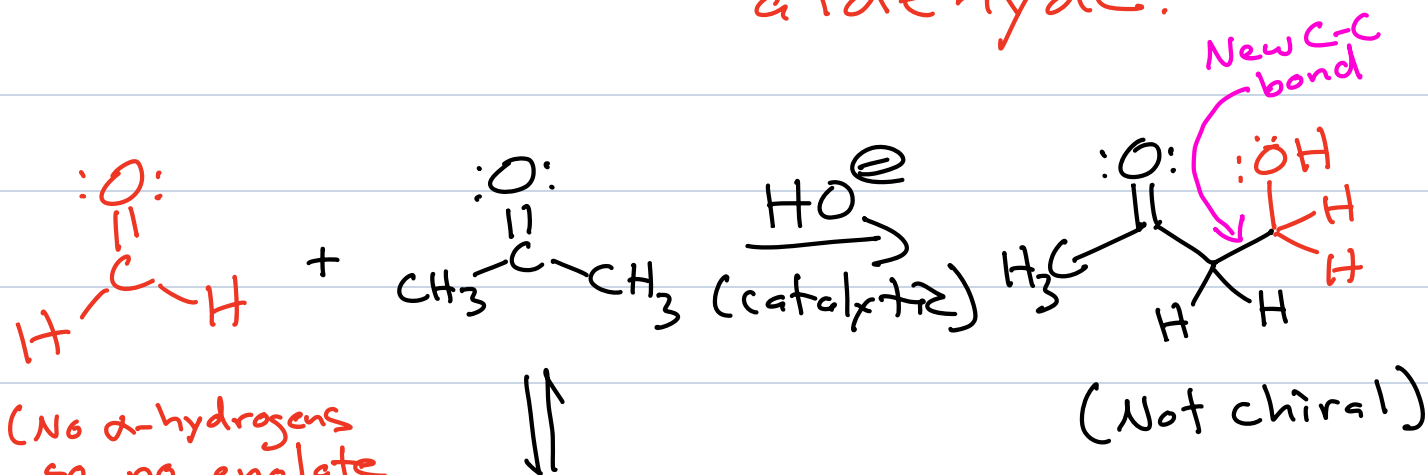
4 Different constitutional isomers!

12 Products including stereoisomers!

Key Idea \Rightarrow By understanding the reaction we can make this process productive!

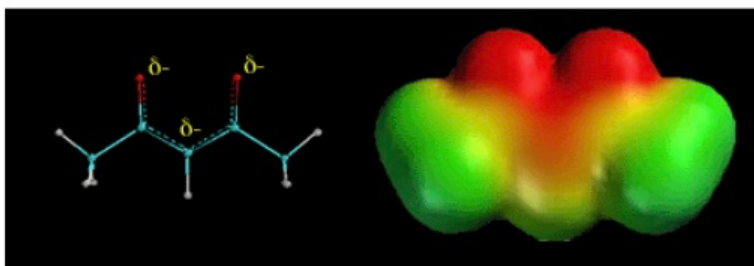
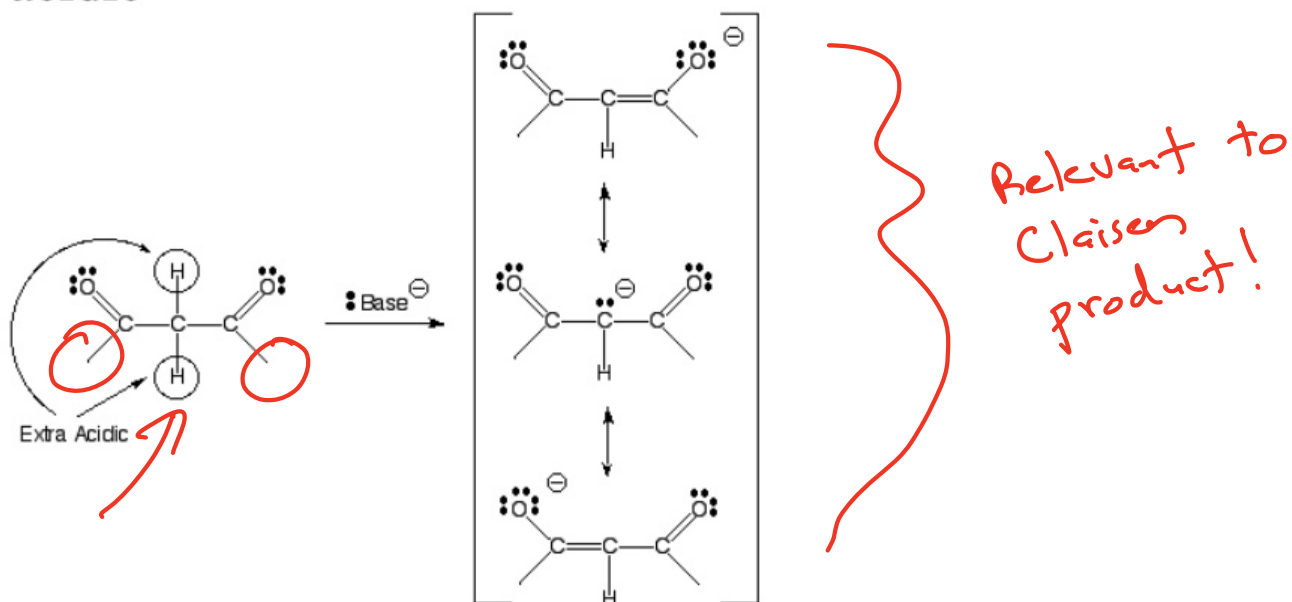
Strategic Workaround: Use an aldehyde with no α hydrogens and a ketone

The aldehyde cannot make an enolate, while the ketone can but that enolate can only make a stable product with the aldehyde.



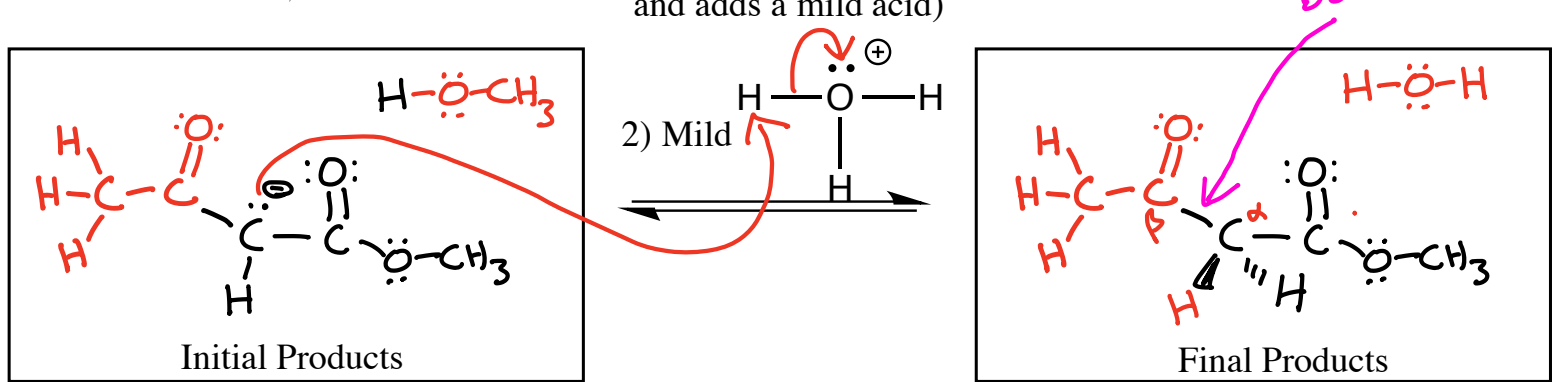
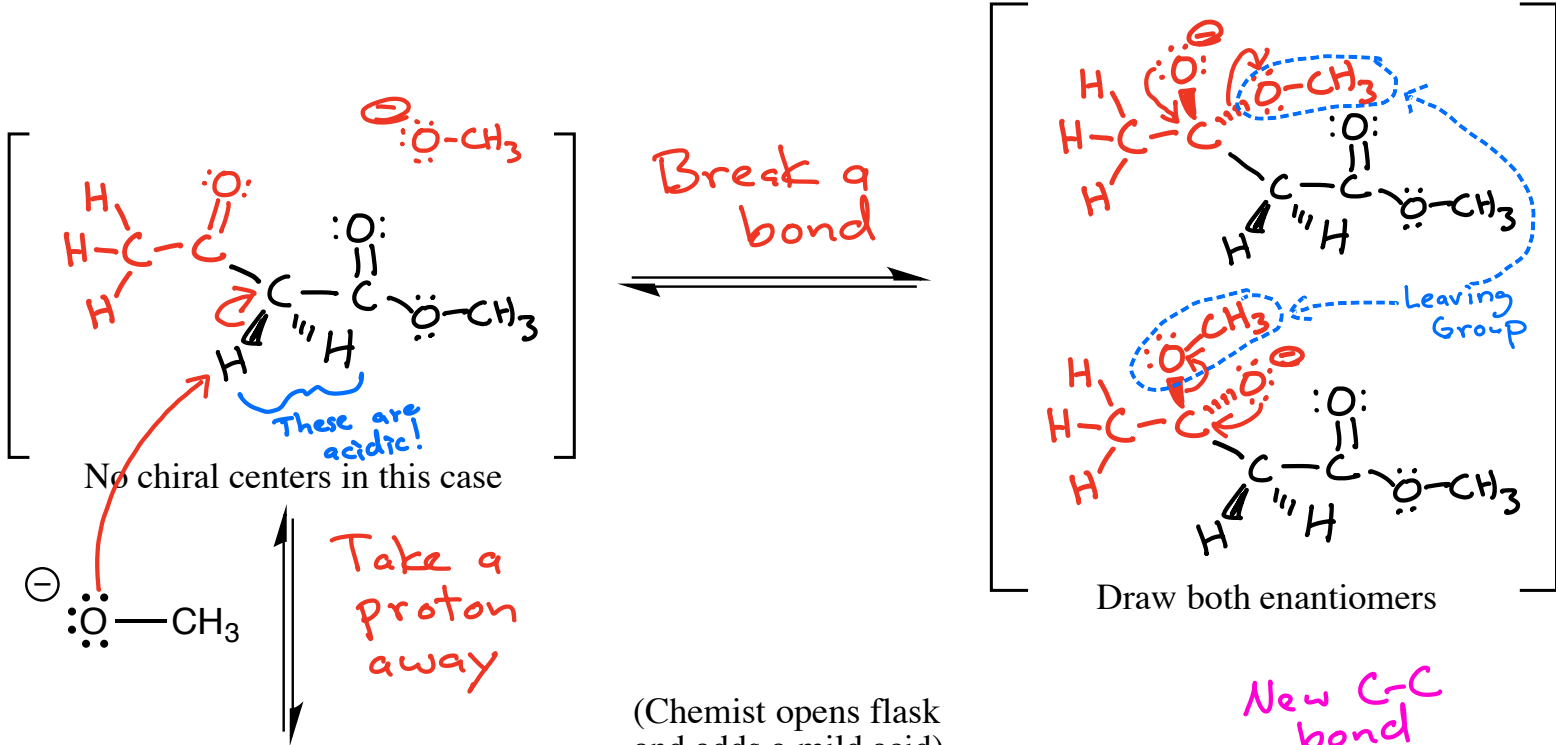
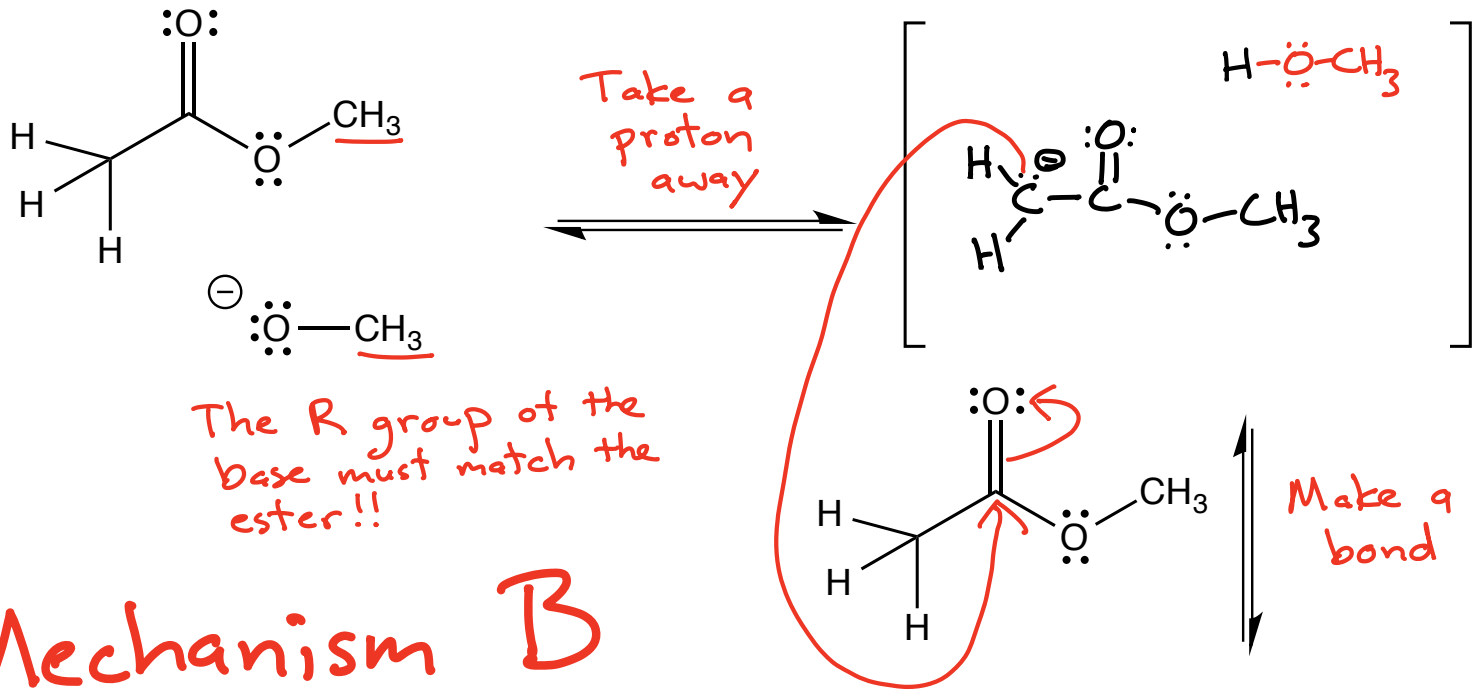
Another aldehyde that does NOT have any α -hydrogens

Beta-dicarbonyls have alpha-hydrogens that are extra acidic



The C-H hydrogen atoms between two carbonyl groups are even more acidic than normal hydrogens because the resulting anion is double resonance stabilized. The above electrostatic potential surface shows how the negative charge (red color) is spread over all three atoms as predicted by the three resonance contributing structures.

Claisen Condensation → "Aldol with Esters"



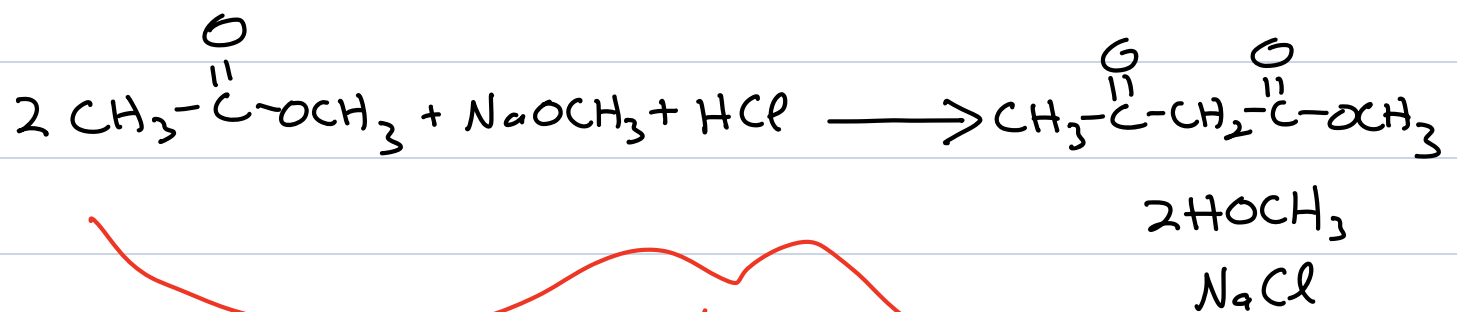
This is a much more stable anion compared to $\ominus \text{OCH}_3$, providing a strong driving force (motive) for the Claisen condensation reaction

KRE \rightarrow A β -keto ester with a new C-C bond between the α and β carbons

Before we add acid \rightarrow the last step drives the reaction because we make a relatively stable anion.

Note: The $^{\ominus}\text{OCH}_3$ is consumed during the reaction! (NOT catalytic in base like the aldol reaction)

Balanced Equation for the Overall Process



This is the balanced equation that is explained by the mechanism