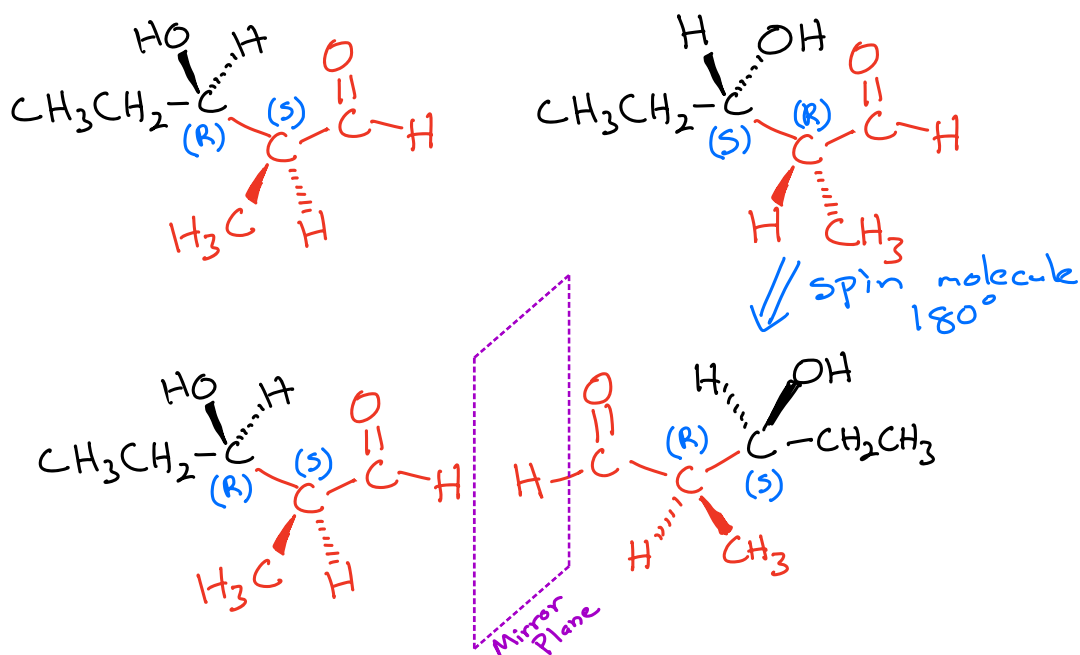
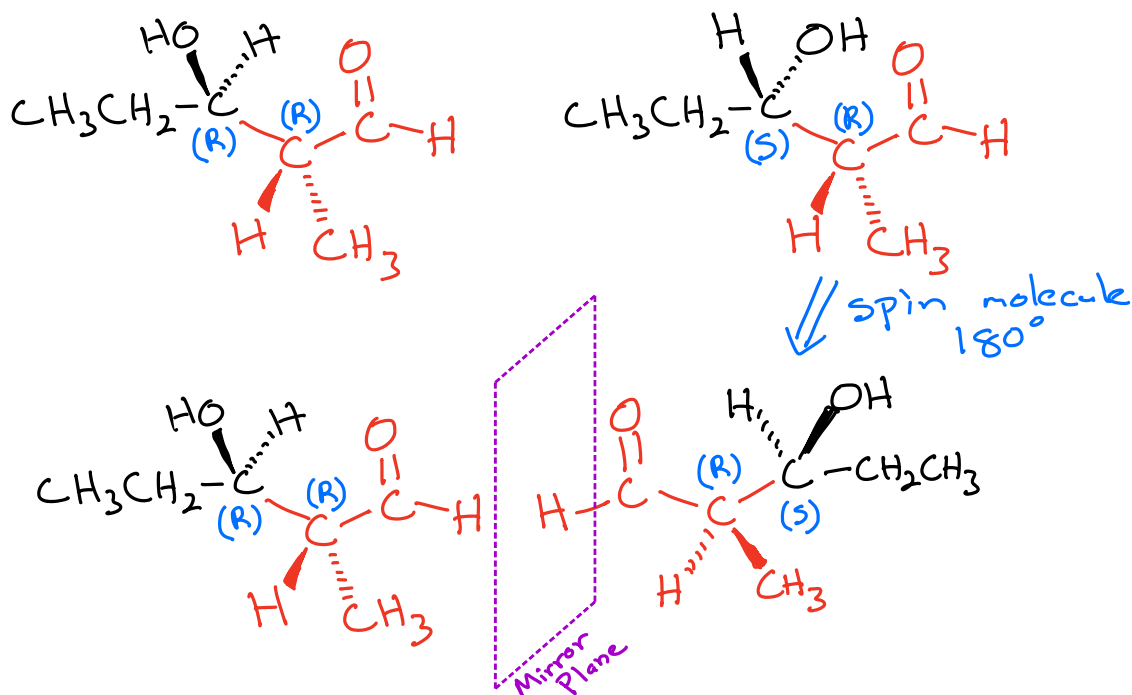




Enantiomers or Diastereomers?

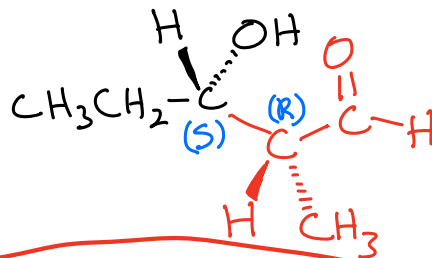
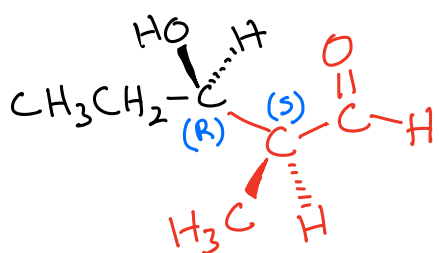


Enantiomers (Section 3.2) Stereoisomers that are nonsuperposable mirror images of each other; refers to a relationship between pairs of objects.

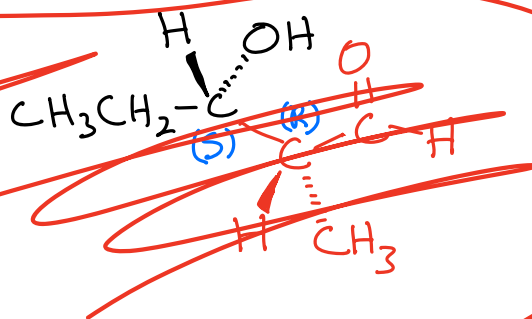
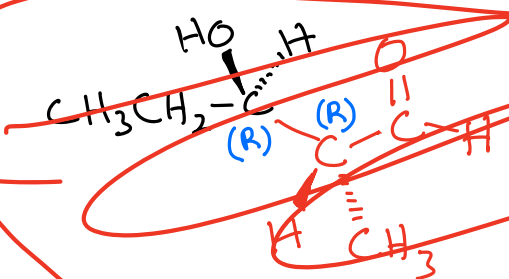


Diastereomers (Section 3.4A) Stereoisomers that are not mirror images of each other; refers to relationships among two or more objects.

Which pair of molecules could be a racemic mixture?



OR



Racemic mixture (Section 3.7C) A mixture of equal amounts of two enantiomers.

Weaker bases are favored at equilibrium

Compound	Chemical Structure	pK _a
	H-Cl	-7
Carboxylic acids*	$\text{R}-\text{C}(=\text{O})-\text{OH}$	3-5
β -Dicarbonyls*	$\text{RC}(=\text{O})-\text{CH}_2-\text{C}(=\text{O})\text{R}'$	10
β -Ketoesters*	$\text{RC}(=\text{O})-\text{CH}_2-\text{C}(=\text{O})\text{OR}'$	11
β -Diesters*	$\text{ROC}(=\text{O})-\text{CH}_2-\text{C}(=\text{O})\text{OR}'$	13
Water	HOH	15.7
Alcohols	RCH_2OH	15-19
Acid chlorides*	RCH_2-COCl	16
Aldehydes*	RCH_2-CHO	18-20
Ketones*	$\text{RCH}_2-\text{C}(=\text{O})\text{R}'$	18-20
Esters*	$\text{RCH}_2-\text{C}(=\text{O})\text{OR}'$	23-25
Terminal alkynes	$\text{RC}\equiv\text{C}-\text{H}$	25
LDA	$\text{H}-\text{N}(\text{i-C}_3\text{H}_7)_2$	40
Terminal alkenes	$\text{R}_2\text{C}=\text{C}-\text{H}$	44
Alkanes	$\text{CH}_3\text{CH}_2-\text{H}$	51

Strongest Acid
(Weakest conjugate base)



Weakest Acid
(Strongest conjugate base)

A) Reactions are favored (i.e. have a motive) if they lead to formation of a weaker acid and/or weaker base.

B) Checking pK_a values can predict if a reaction has a motive even if there are other steps besides a proton transfer.

C) Recall that the conjugate base of a stronger acid (lower pK_a) is a weaker base.

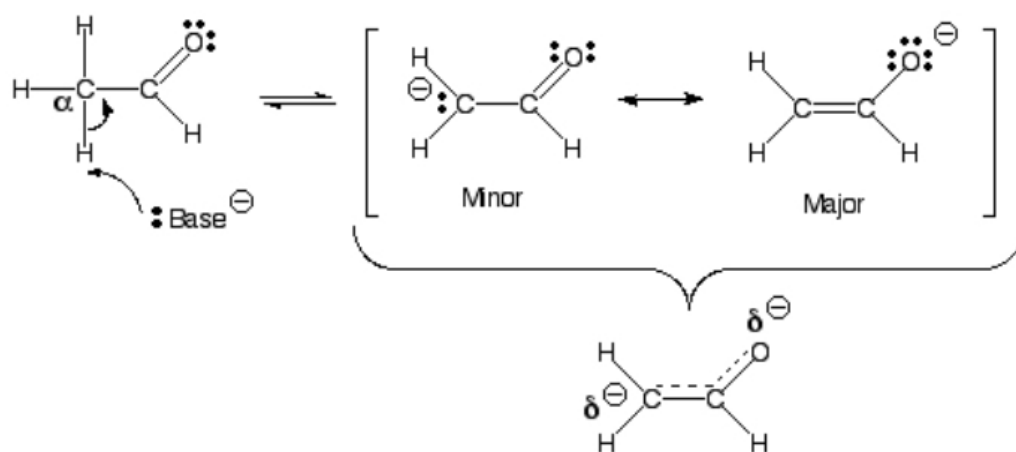
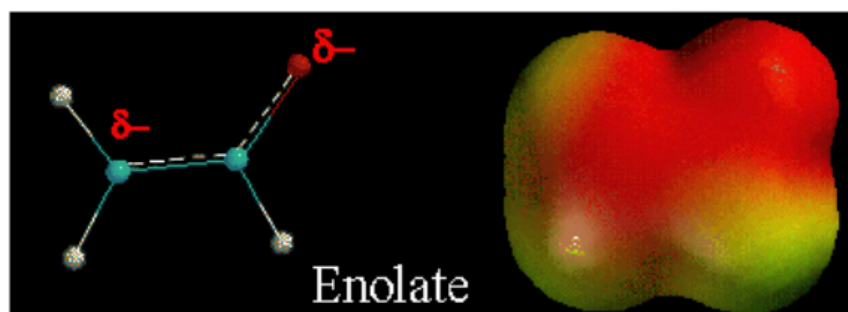
D) Check the pK's of the conjugate acid of the bases on either side of the equation. Lower pK_a value corresponds to stronger acid of the conjugate acid, and thus weaker conjugate base. The base with a stronger conjugate acid (lower pK_a value) will be the weaker base and will be favored at equilibrium.

E) Another way to look at it is that the base that is favored at equilibrium is the one that has the more stabilized anion, i.e. the one with the charge spread around more (electronegative) atoms.

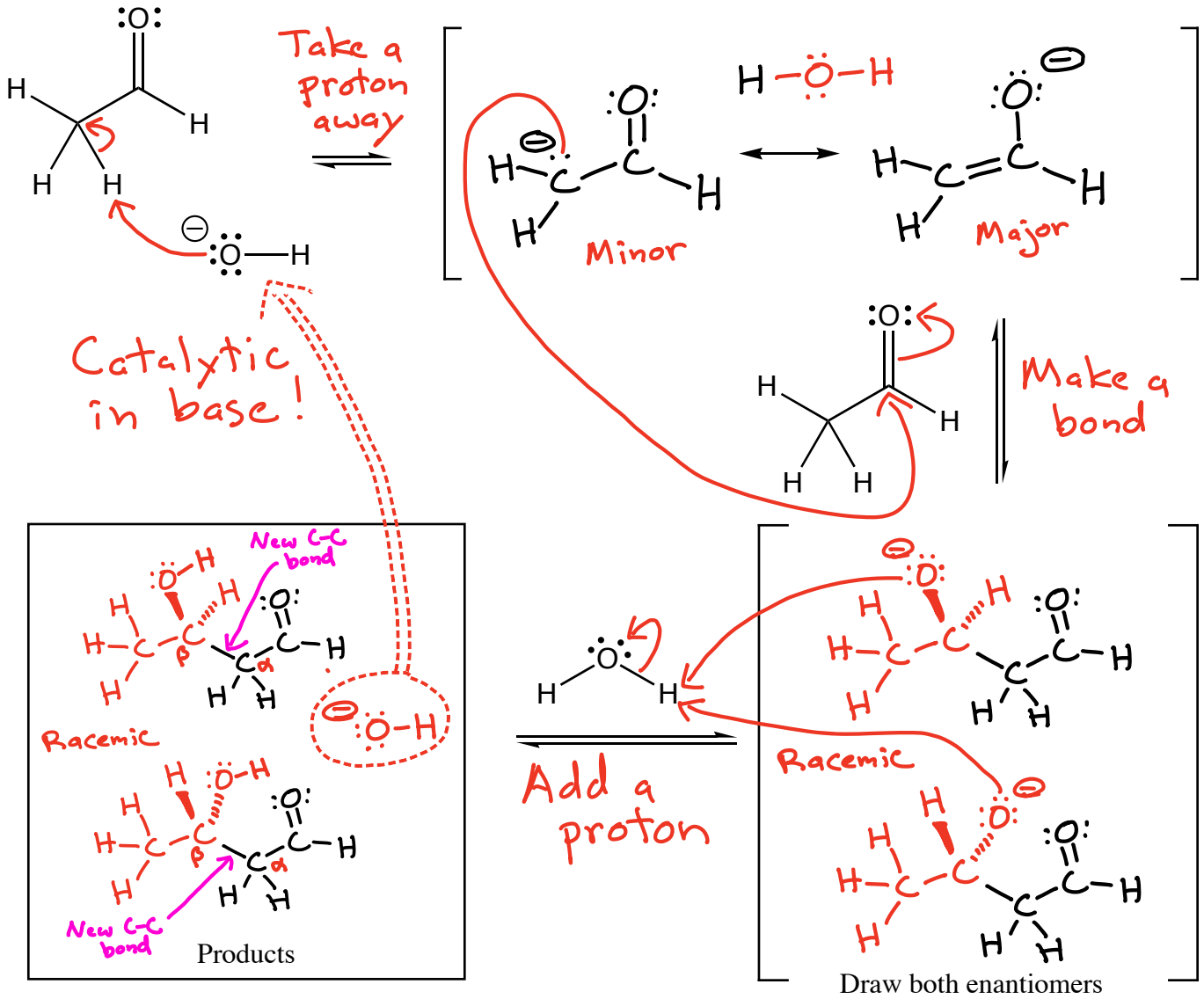
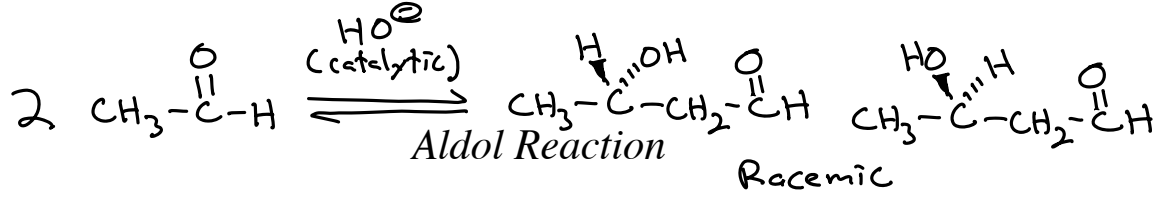
F) Above is a pK_a table that we will refer to often.

*These have resonance stabilized anions

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.**

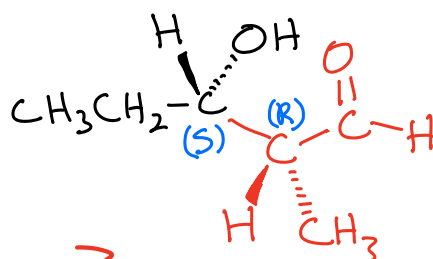
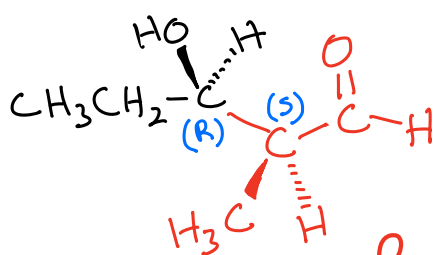
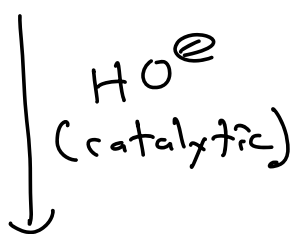
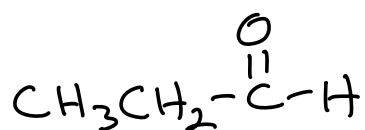


KRE \rightarrow β -hydroxy aldehyde
with a new C-C
bond between the
aldehyde α and β
carbons

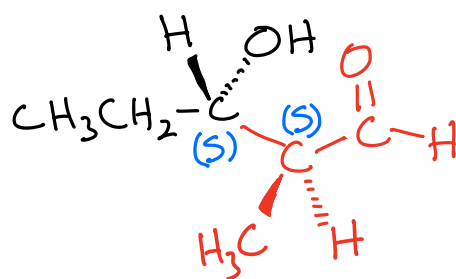
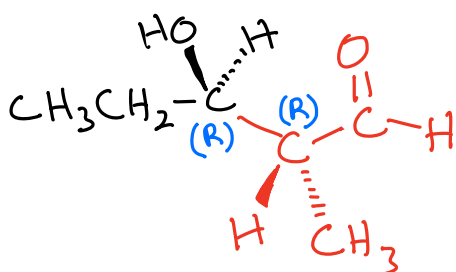
Mechanism
A

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

4) The reaction can make two new chiral centers

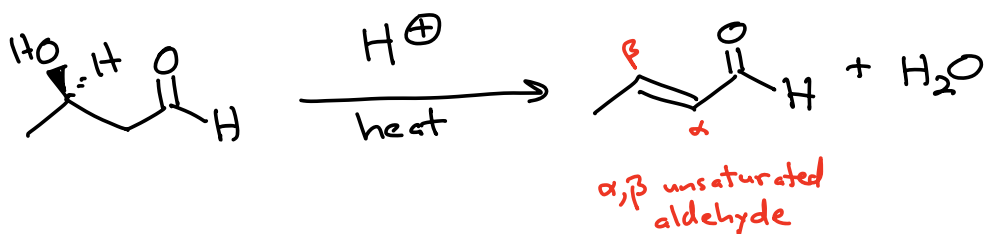


Racemic



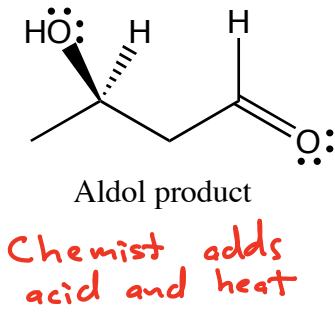
Racemic

In mild acid with some heating, the aldol product will dehydrate to give an α,β -unsaturated aldehyde.

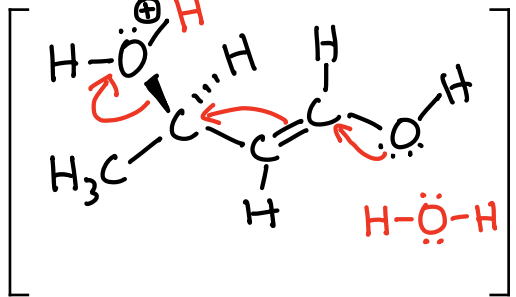
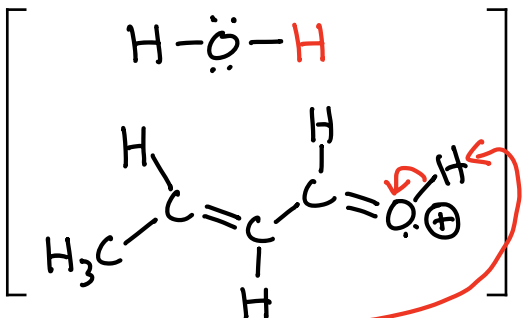
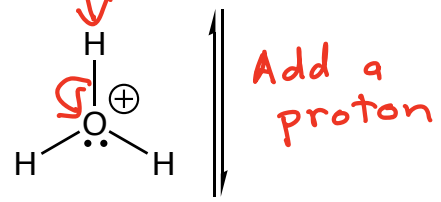
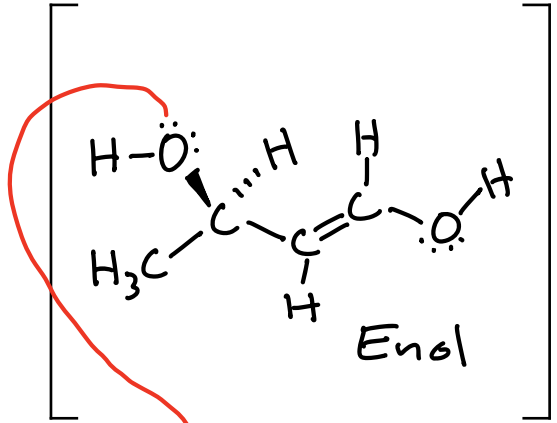


Note: The following mechanism is NOT the simplest you might think of, but it is the one with the lowest energy intermediates (no carbocations, etc.) so this is the correct mechanism

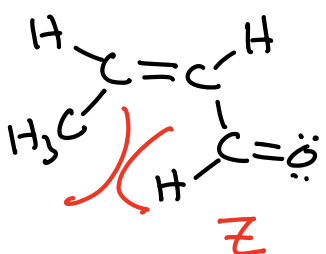
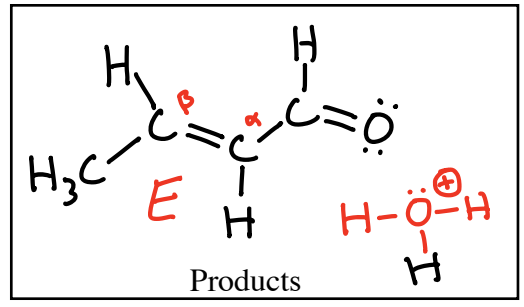
Acid catalyzed dehydration



tautomerization

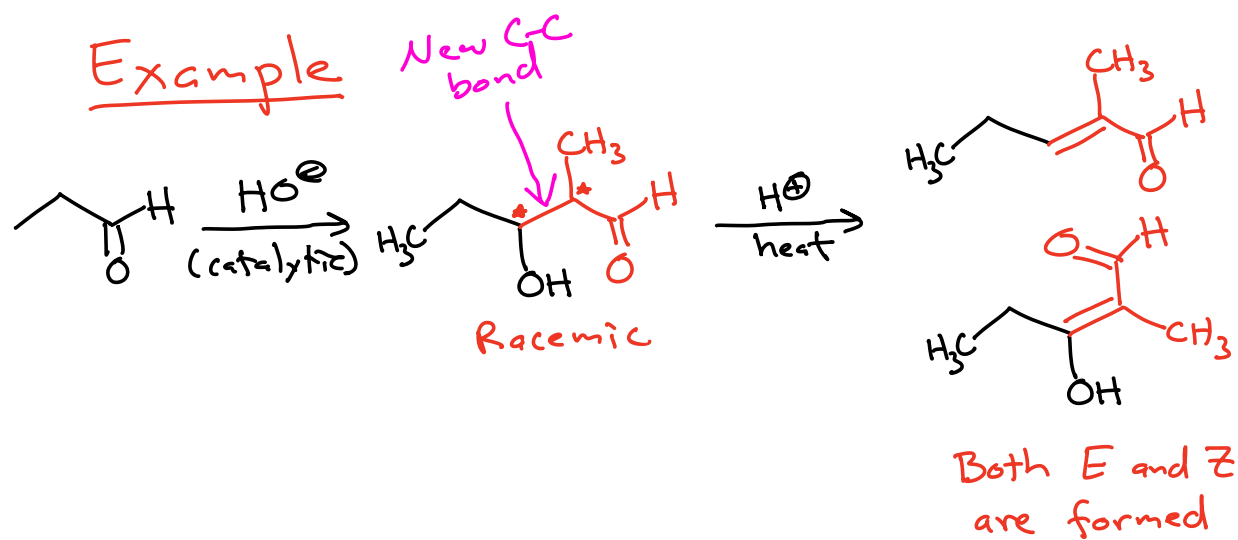


KRE \rightarrow α,β -unsaturated aldehyde \rightarrow the C=C is where the new C-C bond is located



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

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

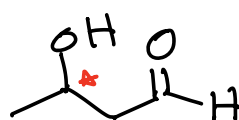
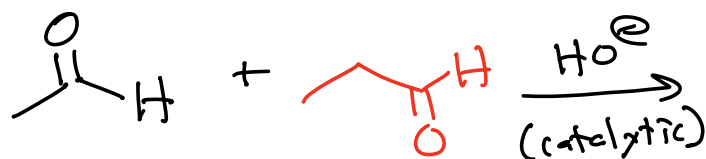


Time Capsule → The product is conjugated and therefore stable

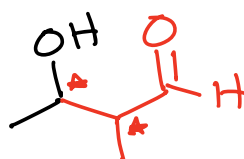
Time Capsule → The product can be used in a Diels-Alder reaction

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

Example



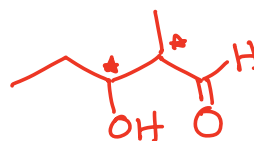
2 stereoisomers



4 stereoisomers



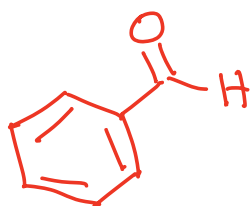
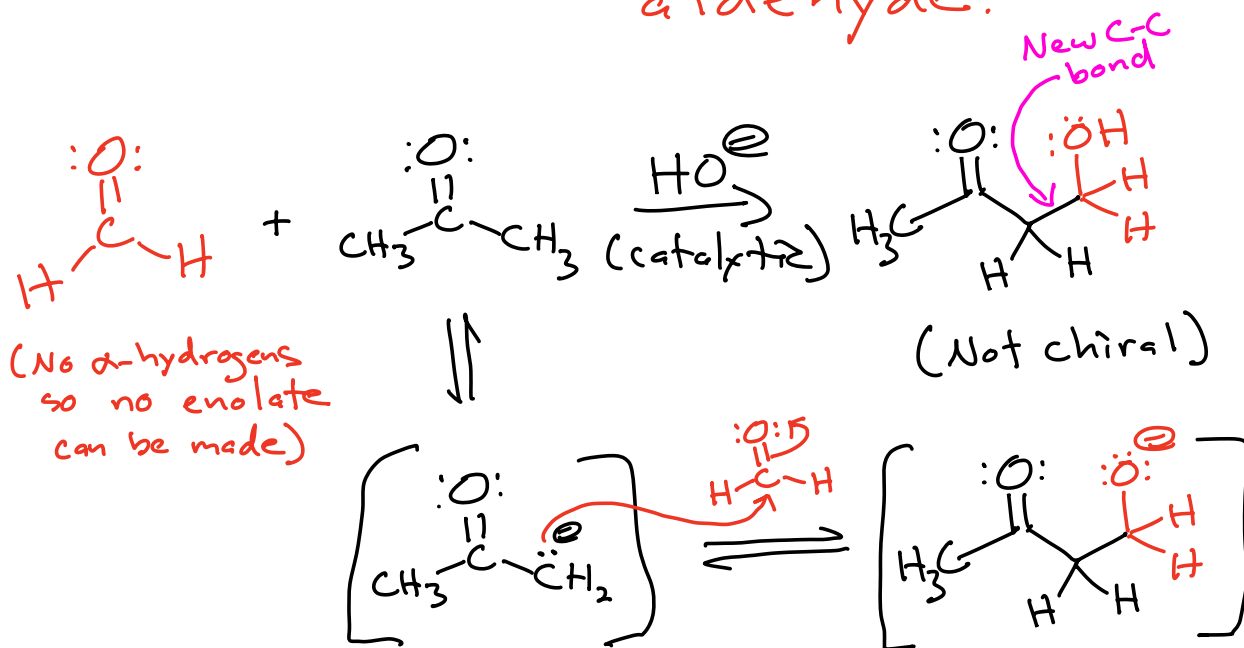
2 stereoisomers



4 stereoisomers

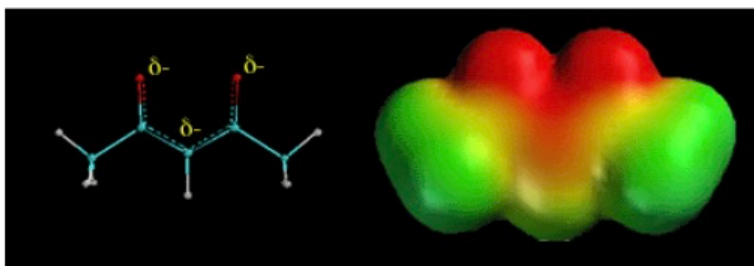
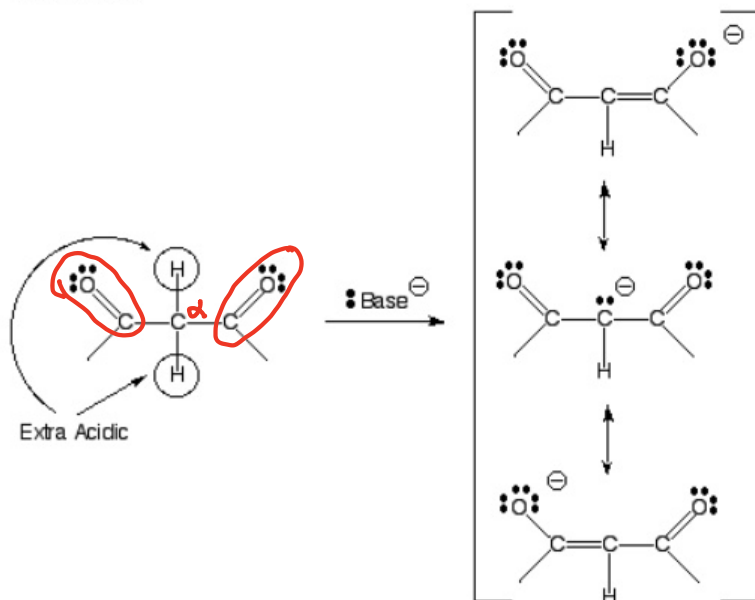
Strategic Workaround: Use an aldehyde with no α hydrogens and a ketone

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



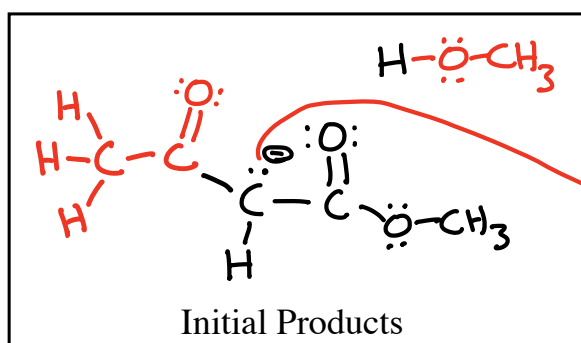
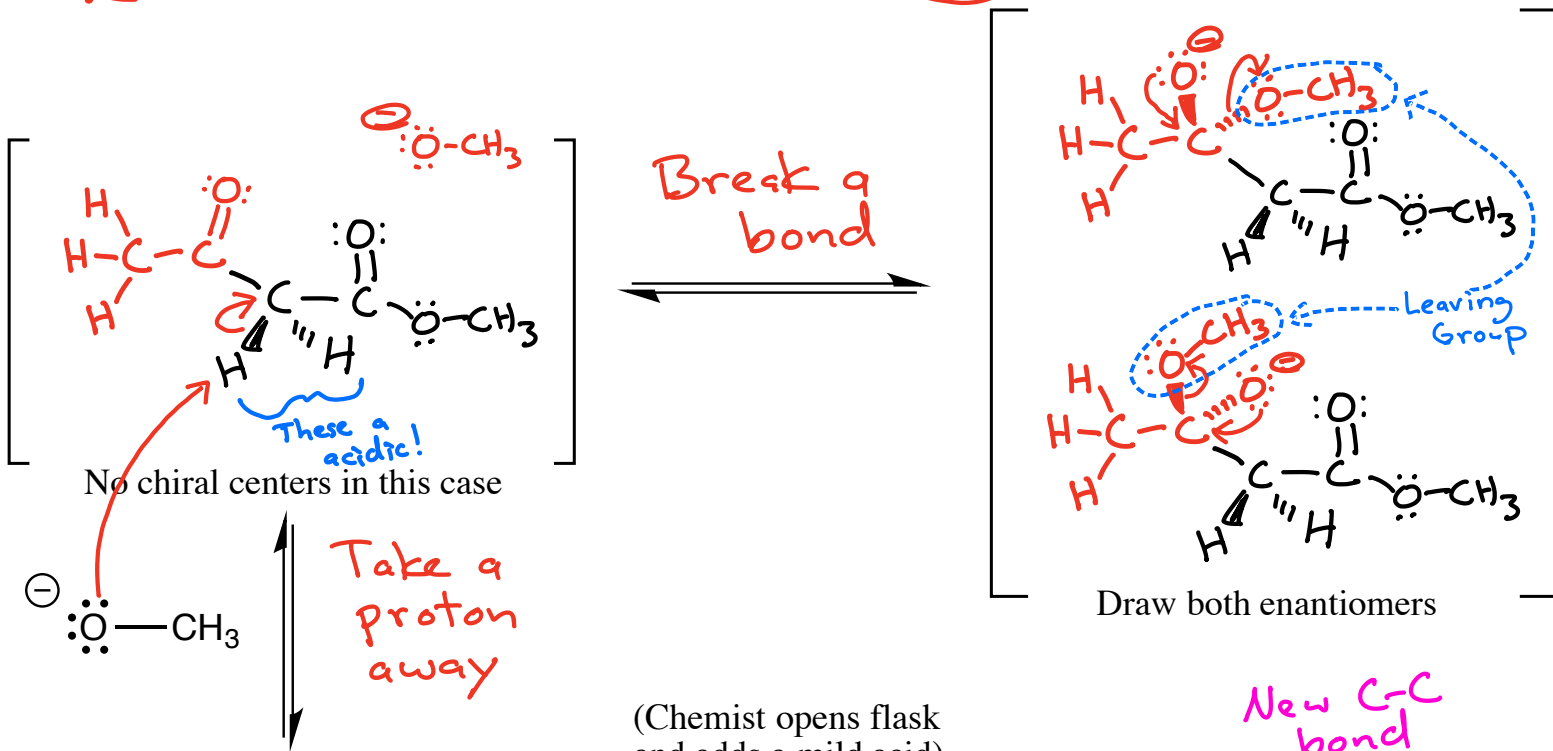
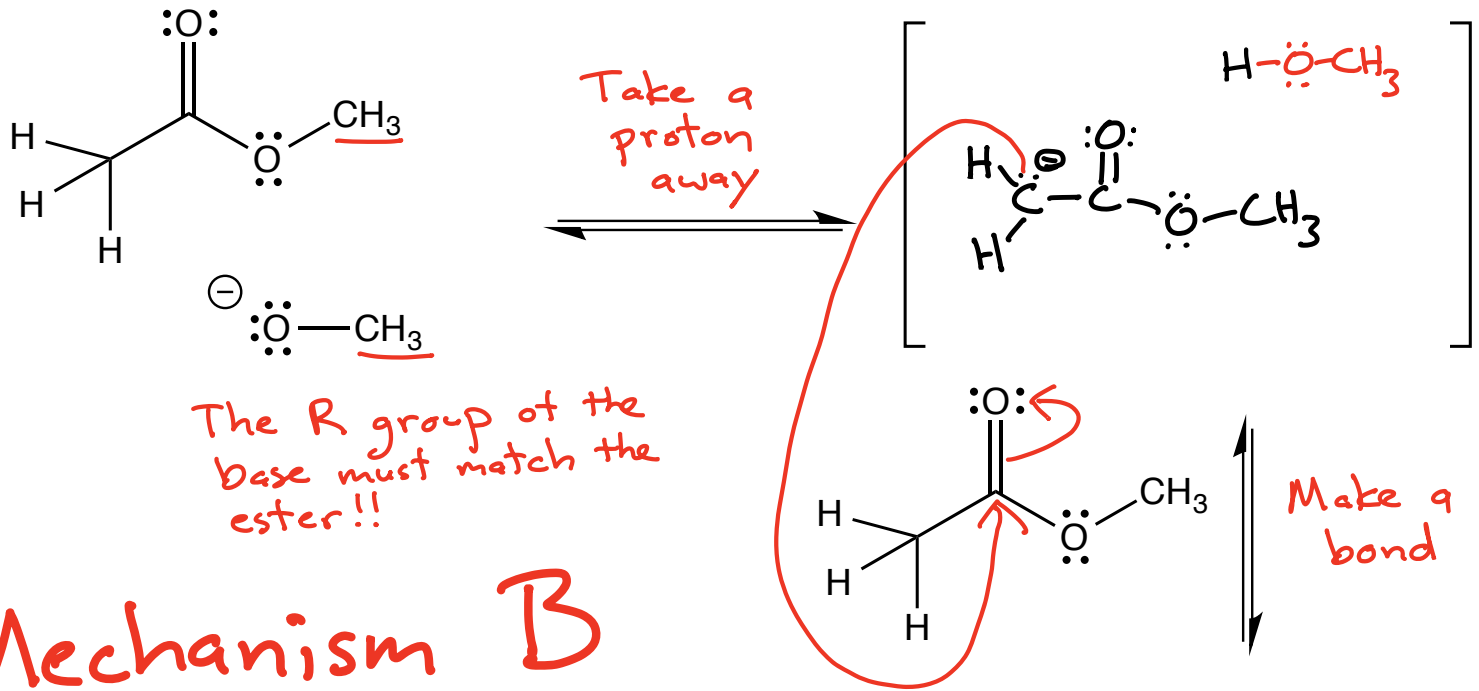
Another aldehyde that does NOT have any α -hydrogens

Beta-dicarbonyls have alpha-hydrogens that are extra acidic

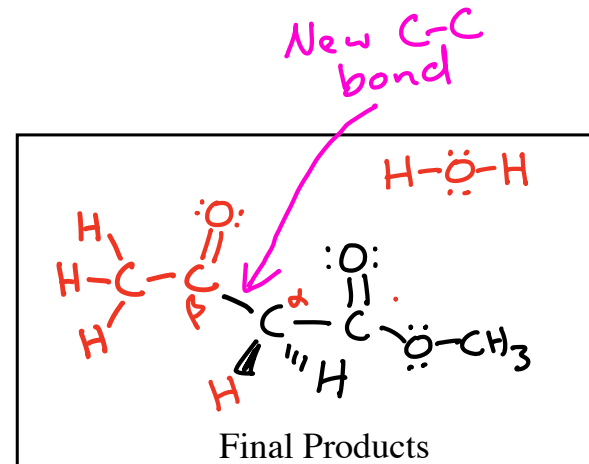
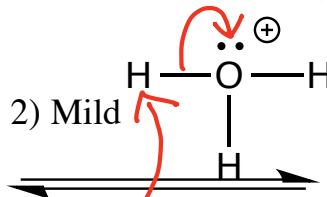


The C-H hydrogen atoms between two carbonyl groups are even more acidic than normal alpha hydrogens because the resulting anion is double resonance stabilized. The above electrostatic potential surface shows how the negative charge (red color) is spread over all three atoms as predicted by the three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

Claisen Condensation → "Aldol with Esters"



(Chemist opens flask and adds a mild acid)

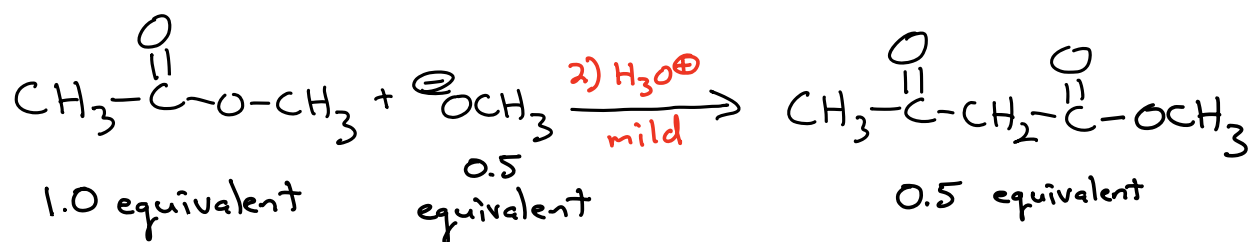


This is a much more stable anion compared to $\ominus\text{OCH}_3$, providing a strong driving force (motive) for the Claisen condensation reaction

KRE \rightarrow β -ketoester with a new C-C bond between the α and β carbon atoms.

Important point \rightarrow The $^{\ominus}\text{OCH}_3$ is consumed during the reaction!

The Claisen Condensation reaction is NOT catalytic in base like the aldol reaction!



Another way to say it:

