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ACT NOW

Brain cancer patient wins Gusher Marathon

By Avi Zaleon

Updated March 11, 2013 11:27 a.m.



Iram Leon and daughter Kiana Leon finish the Gusher Marathon in 3 hours 7 minutes and 35 seconds taking first place in the full marathon on Saturday, March 9, 2013. Photo taken: Randy Edwards/The Enterprise

A man racing against time crossed the finish line. His daughter, snugly sitting in a stroller he had been pushing for just over 26 miles, gained a memory that may live longer than her father.

"This is supposed to eat away at my memory in the end," Iram Leon said of the cancer in his left temporal lobe. "But I hope this memory is one of the last things to go and one she never loses."

Leon is 32 years old. He said his doctors have told him, "we're probably not going to beat this. We're just hoping to get you to 40."



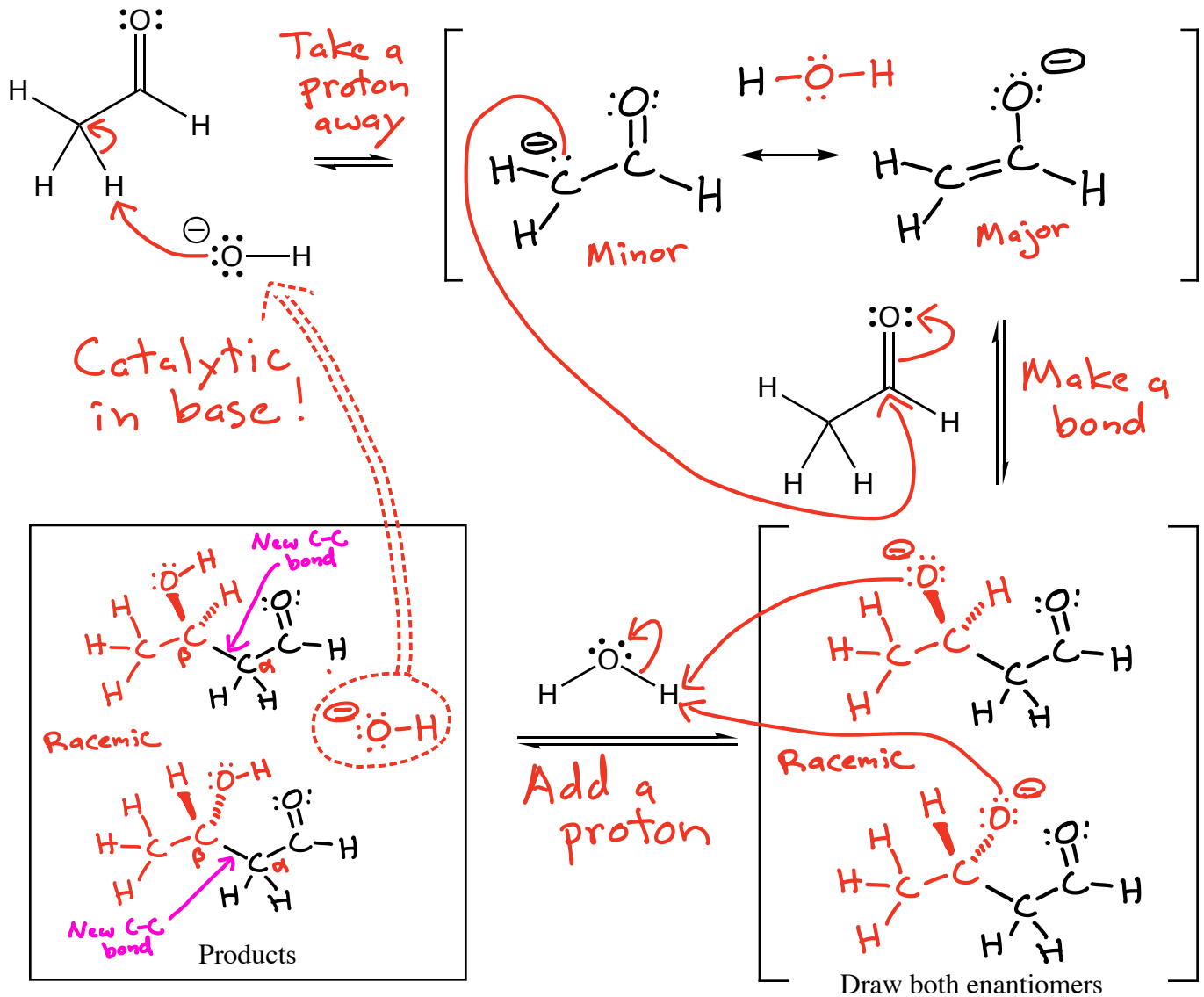
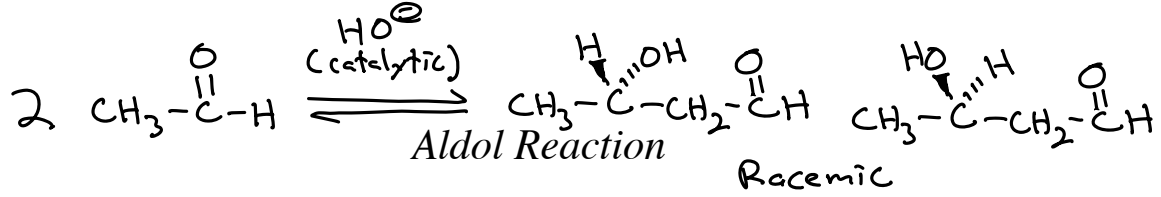
Hello Dr. Iverson,

You may not remember me, but I was in your organic chemistry class last semester.

This past summer I was diagnosed with lymphoma cancer. Initially I had lost all hope, I kept asking myself "why me?" and kept thinking of all things I hadn't accomplished in my lifetime. Nevertheless, I soon got over that fact and started my chemotherapy treatments. Each treatment got worse and worse as I experienced more and more of the side effects. At night I couldn't fall asleep from all psychological and financial stress, couldn't eat because of mouth sores, and when I did eat I would feel sick and nauseated. It wasn't until my third treatment that I remembered the many times you told the class that running could help quality of life. It took a couple of weeks for me to convince myself to start running but I eventually started slowly. I never thought how great of an affect physical activity could have. I was never obese so I never gave running or cardio any thought. As I started running on a regular basis I started seeing my symptoms disappear slowly. Soon when I would come back from running I suddenly had an appetite, regardless of the mouth sores I was hungry enough to eat. My sleeping schedule was started falling into place because I was so tired after running. My stress levels decreased enough that I could see the difference. Best of all it gave me something to do during my days at home, saving me from depression.

Running saved my life Dr. Iverson.

Thanks again,

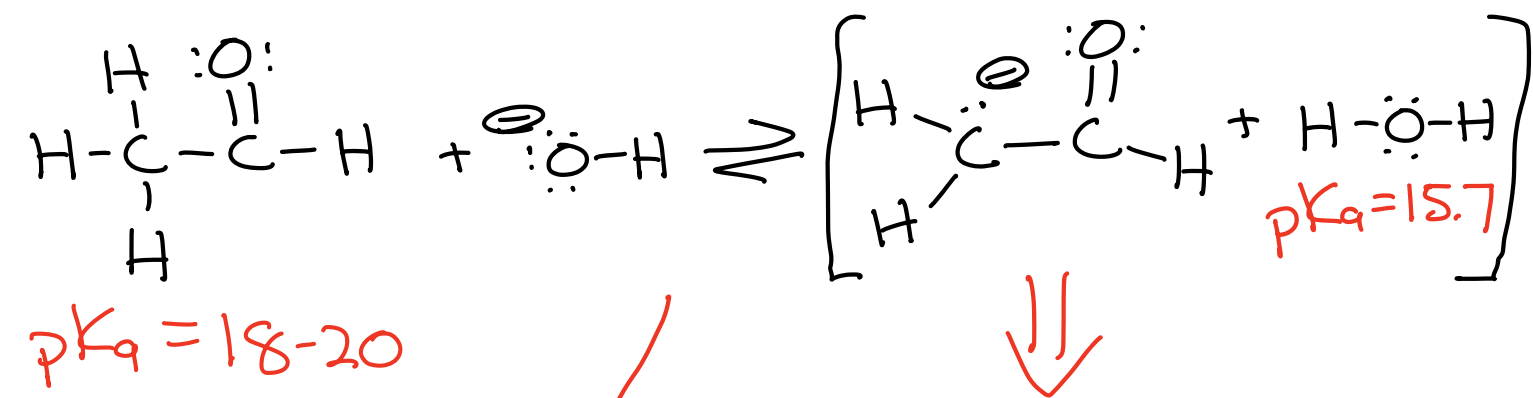


KRE → β -hydroxy aldehyde
with a new C-C
bond between the
aldehyde α and β
carbons

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

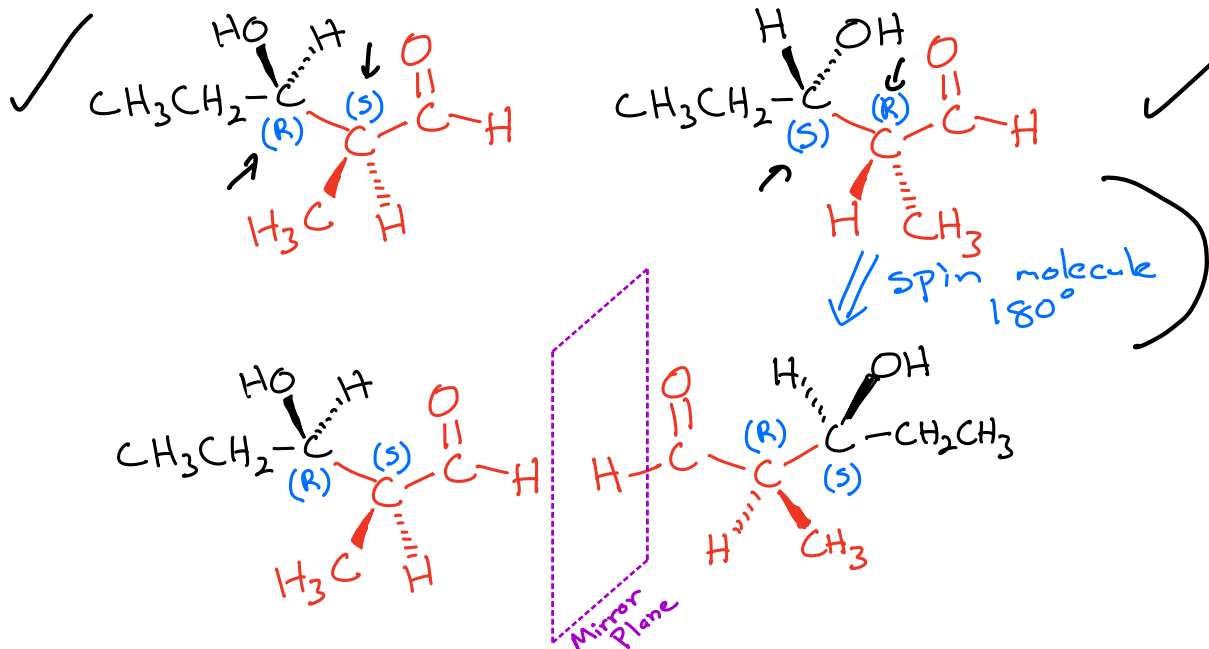
2) Because there is HO^\ominus present at the beginning and end of the reaction there is little driving force (motive) for the aldol reaction \rightarrow the aldol reaction is reversible

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

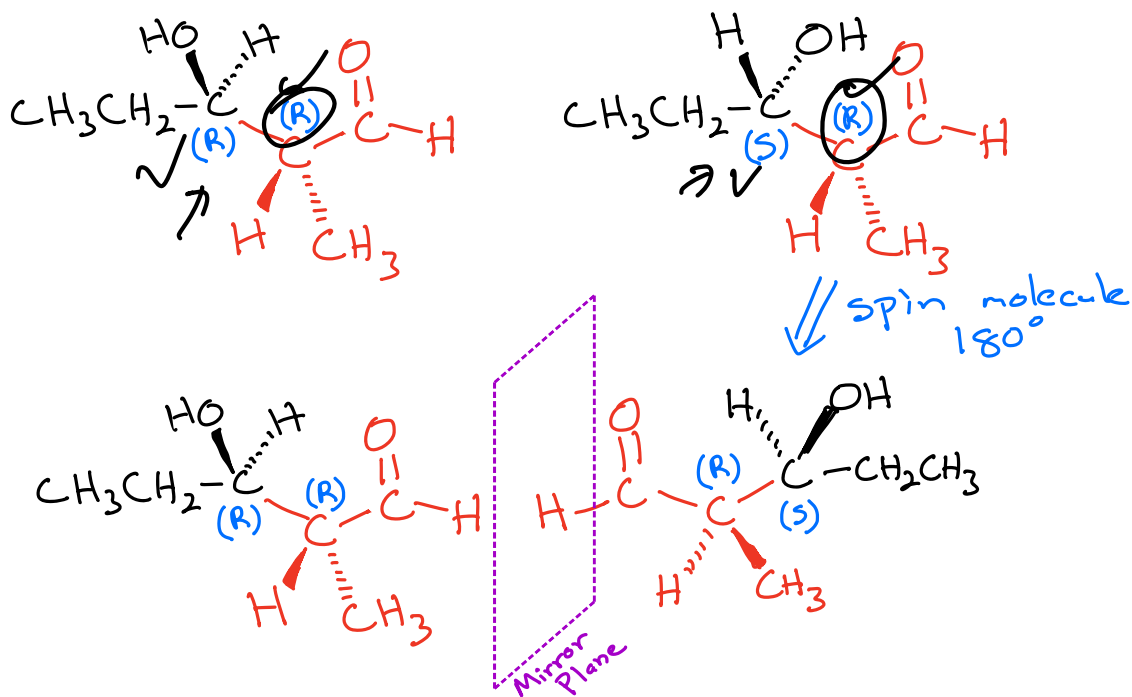
4) The reaction can make two new chiral centers



Enantiomers or Diastereomers?

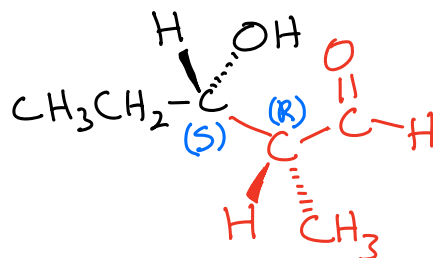
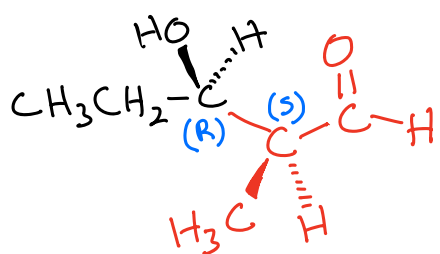


Enantiomers (Section 3.2) Stereoisomers that are nonsuperposable mirror images of each other; refers to a relationship between pairs of objects.

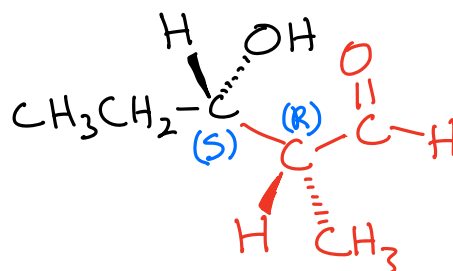
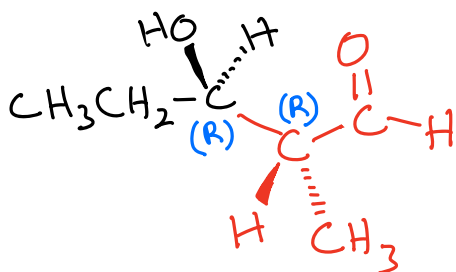


Diastereomers (Section 3.4A) Stereoisomers that are not mirror images of each other; refers to relationships among two or more objects.

Which pair of molecules could be a racemic mixture?

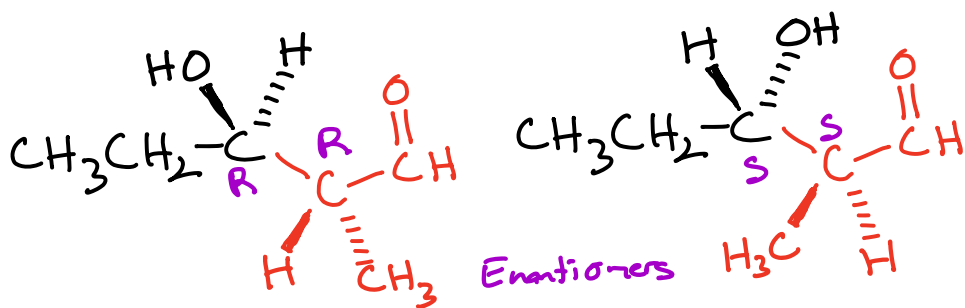
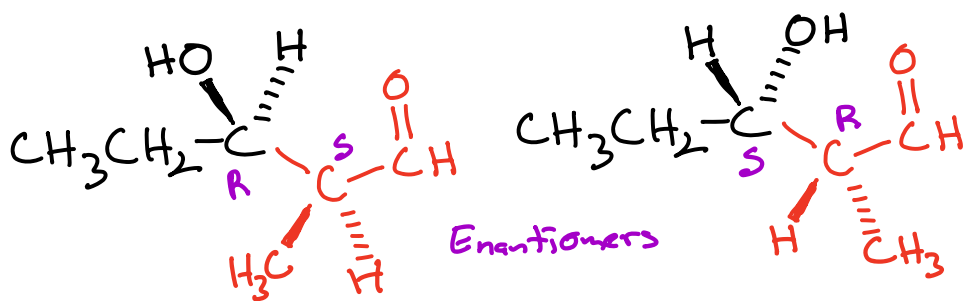
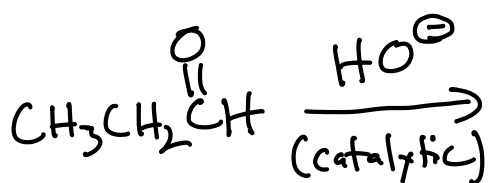


OR



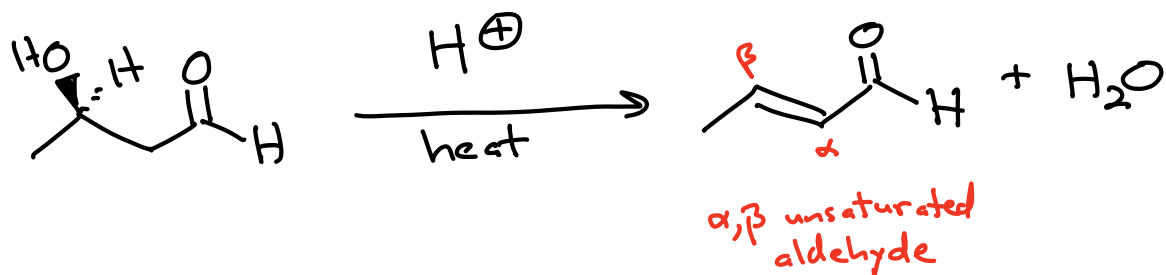
Racemic mixture (Section 3.7C) A mixture of equal amounts of two enantiomers.

Aldol Reaction: 2 new chiral centers



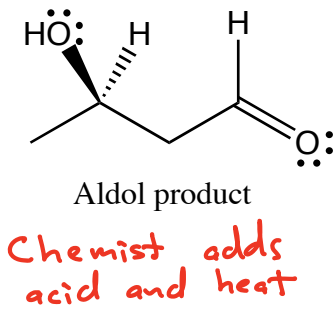
Racemic

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

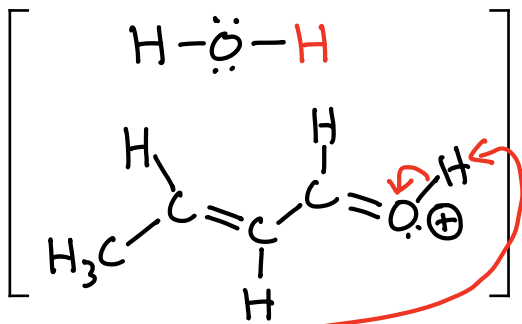
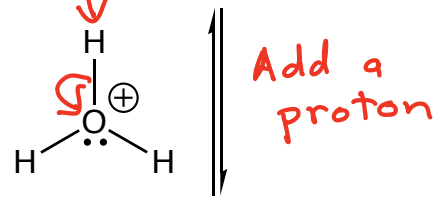
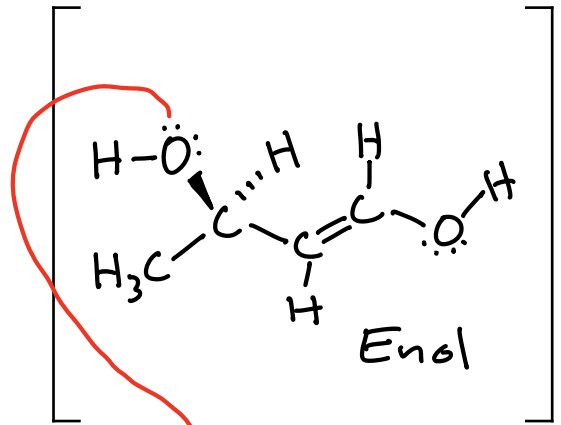


Note: The following mechanism is NOT the simplest you might think of, but it is the one with the lowest energy intermediates (no carbocations, etc.) so this is the correct mechanism

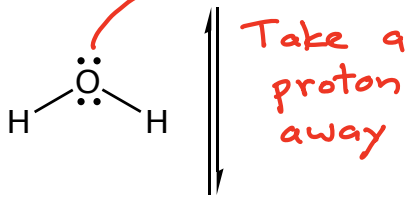
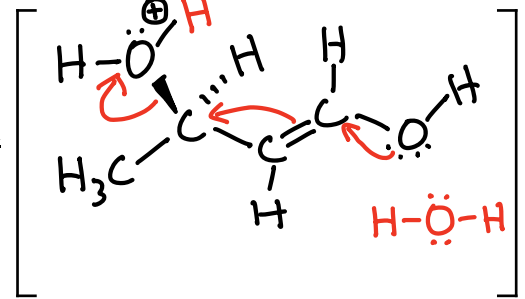
Acid catalyzed dehydration



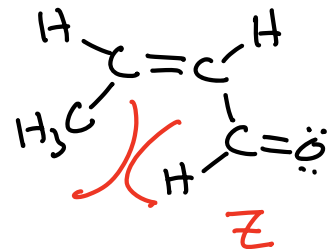
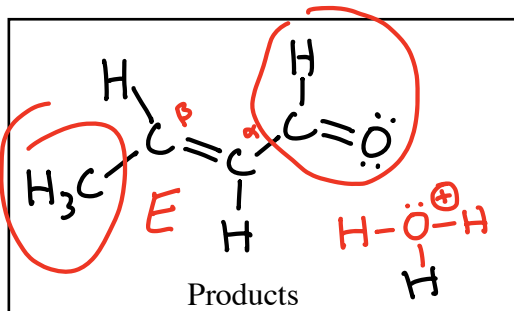
tautomerization



Break a bond

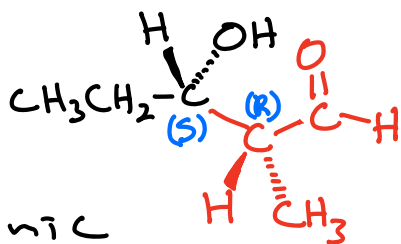
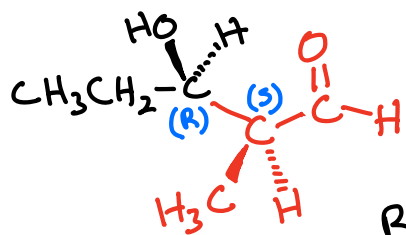
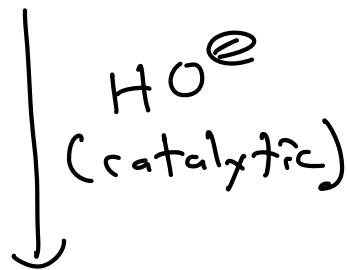
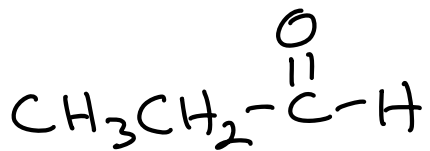


KRE → α,β-unsaturated aldehyde → the C=C is where the new C-C bond is located

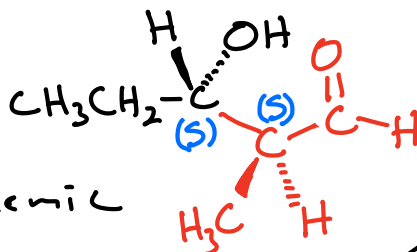
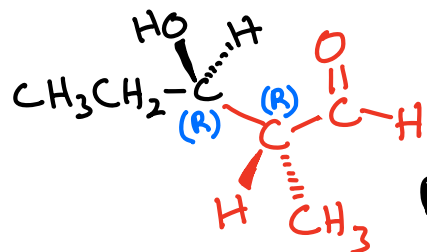


Not much of the Z product is formed because it has significantly more steric strain than E

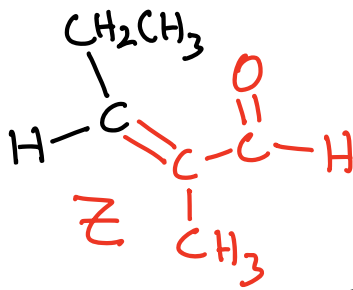
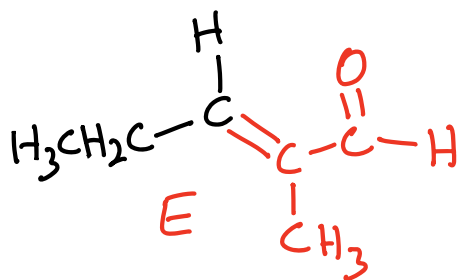
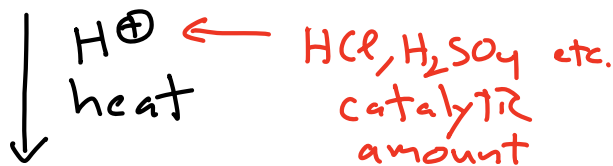
THIS IS UNIQUE TO THIS EXAMPLE
 ↓
 USUALLY BOTH E AND Z ARE FORMED



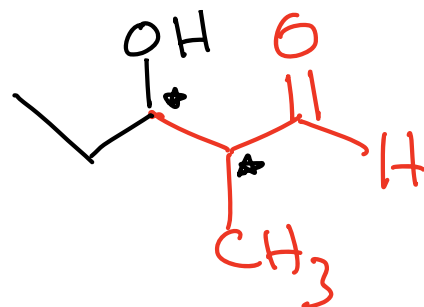
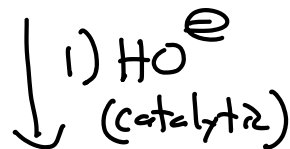
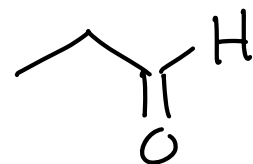
Racemic



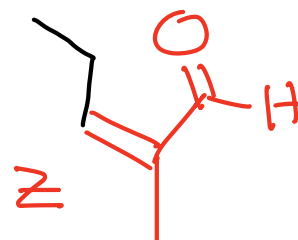
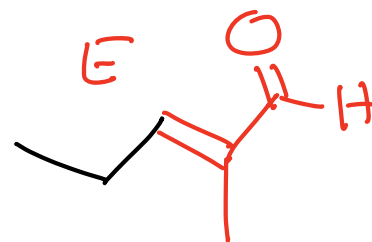
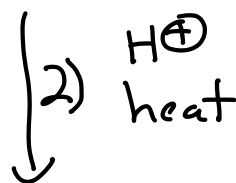
Racemic



(Need to draw both)



Racemic





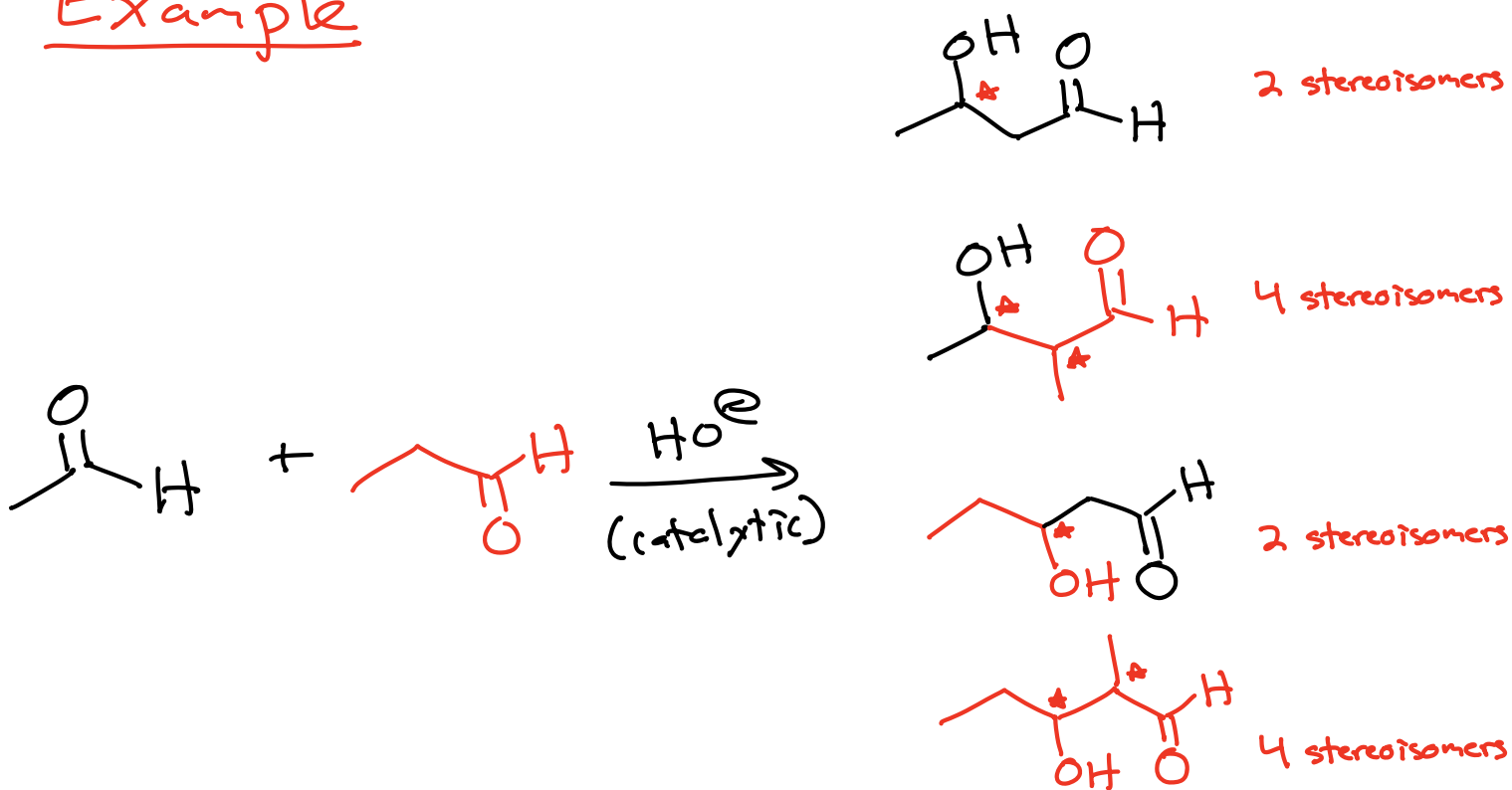
→ The dehydration product is conjugated and therefore stable.



→ 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



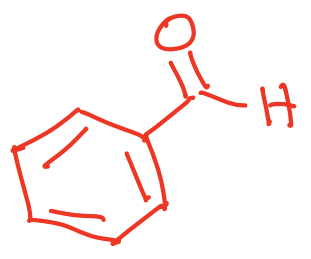
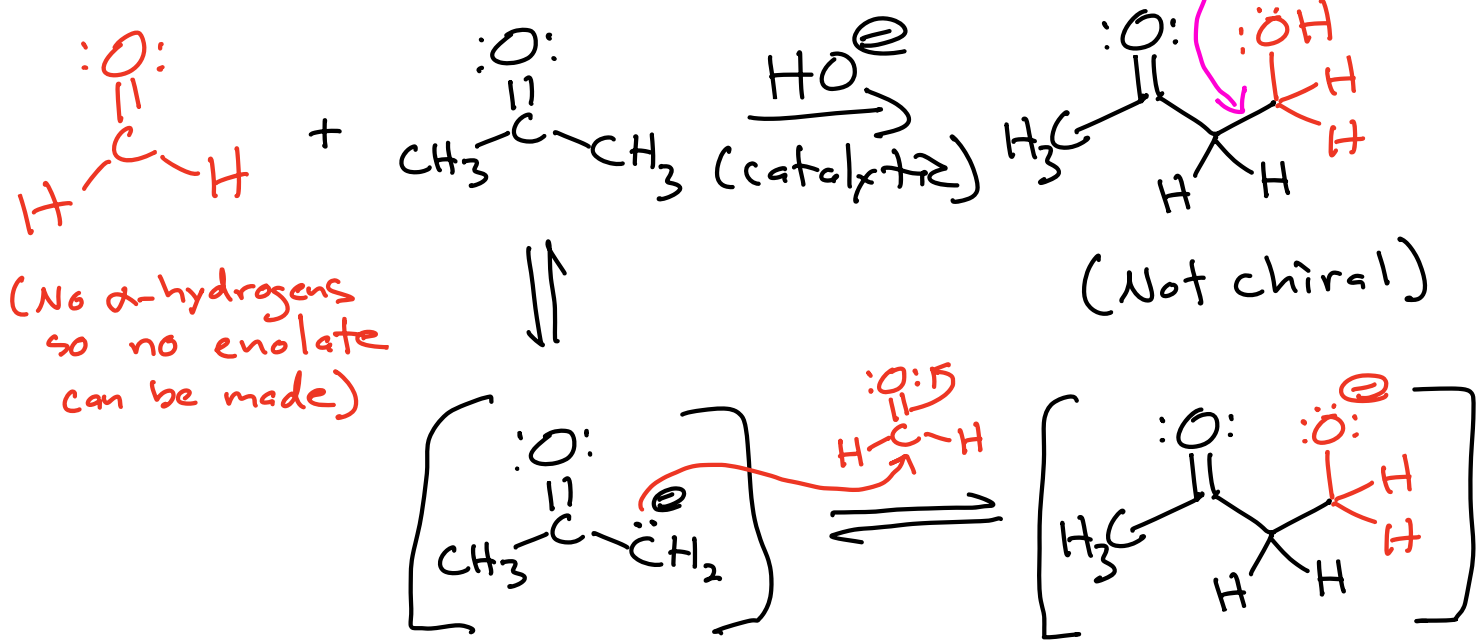
4 Different constitutional isomers!

12 Products including stereoisomers!

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

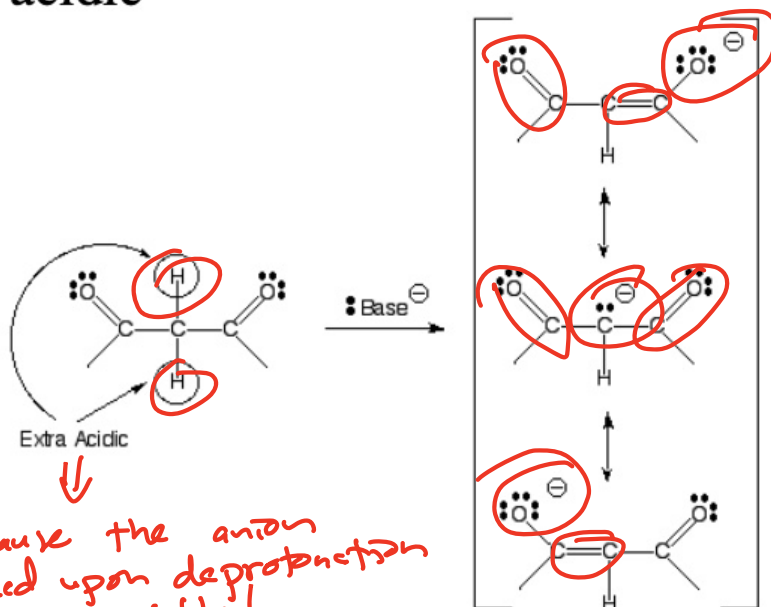
Strategic Workaround: Use an aldehyde with no α hydrogens and a ketone

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

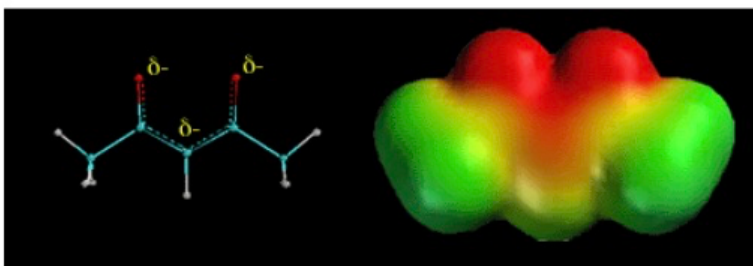
Beta-dicarbonyls have alpha-hydrogens that are extra acidic



Because the anion produced upon deprotonation is so stable!

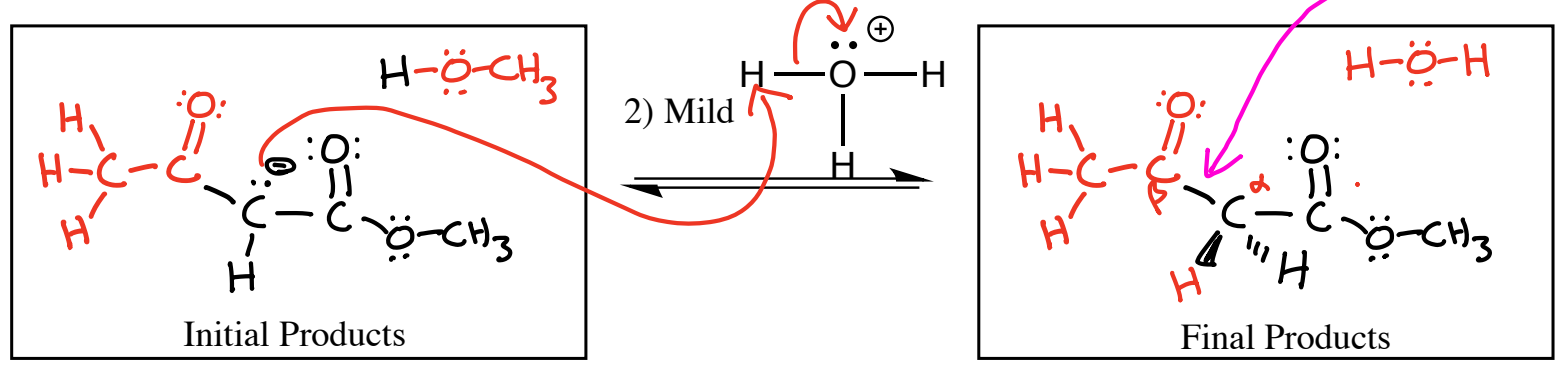
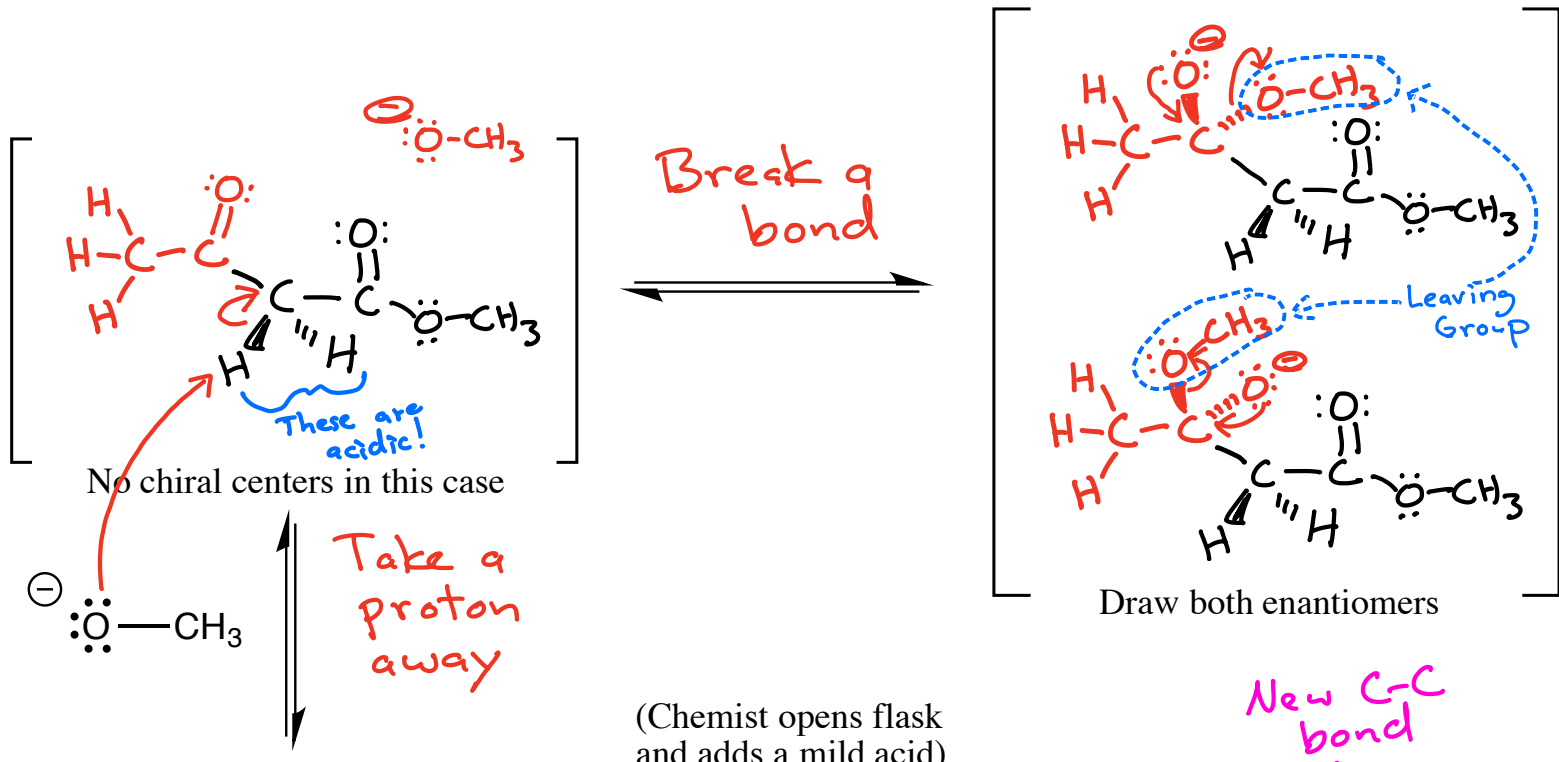
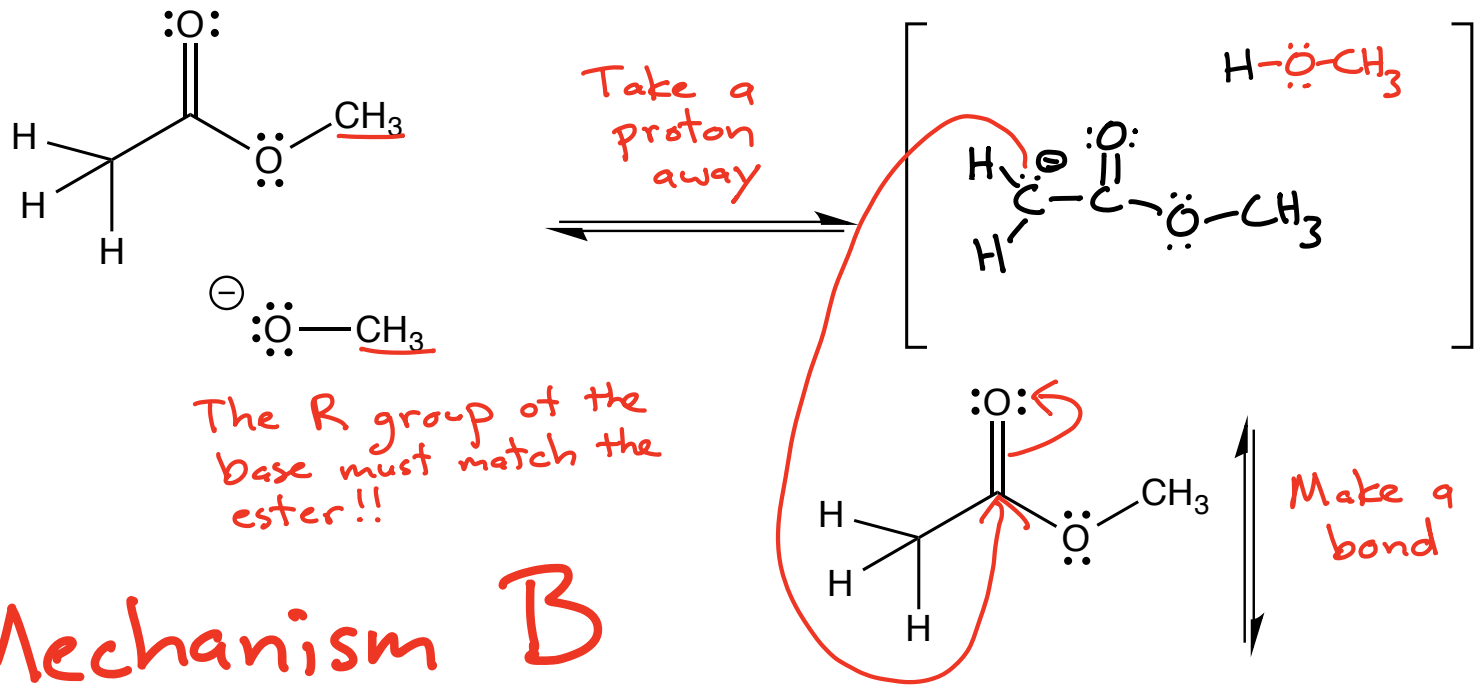
5 atom pi-way!
Charge delocalized over 3 atoms!

Super stable anion!



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.