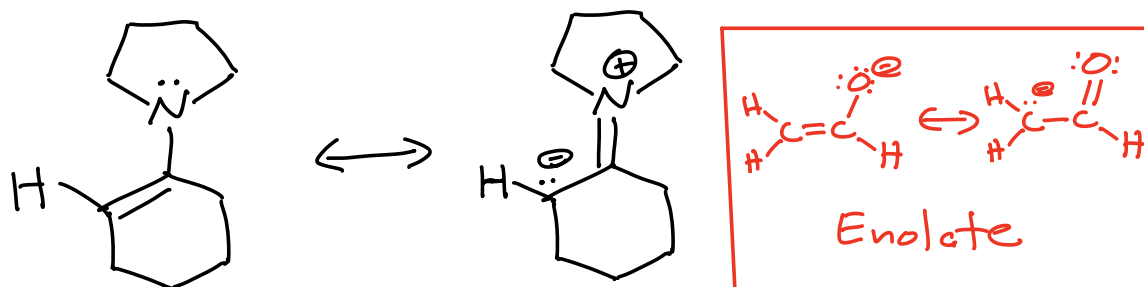


This process is reversible \rightarrow adding H_2O drives it to the left (ketone) and taking H_2O away drives it to the right (enamine)



Major Contributor

Minor Contributor (but still significant)

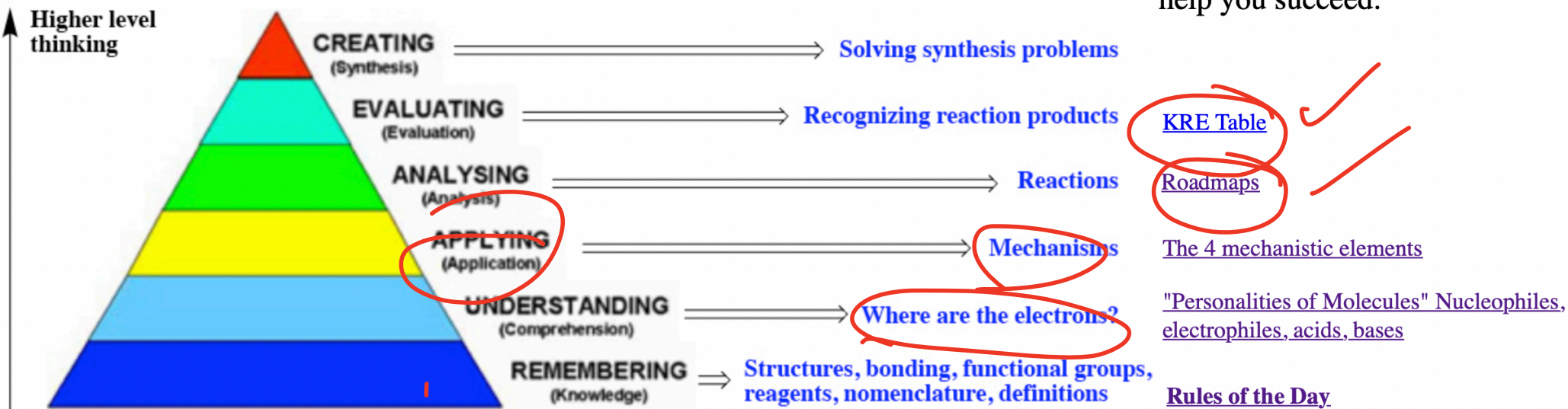
An enamine is a "minieme" of an enolate!! \Rightarrow

A "smaller" (i.e. less reactive) version of an enolate \Rightarrow α C is a nucleophile!!

Bloom's Taxonomy of Learning

Organic Chemistry Analog

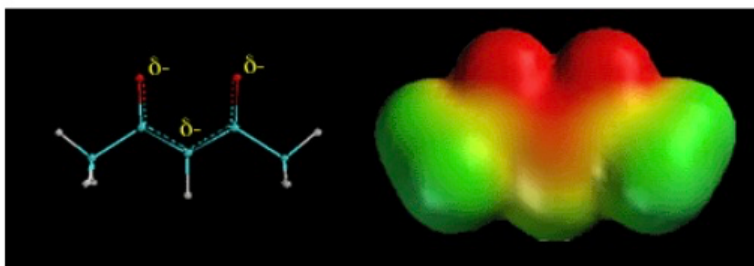
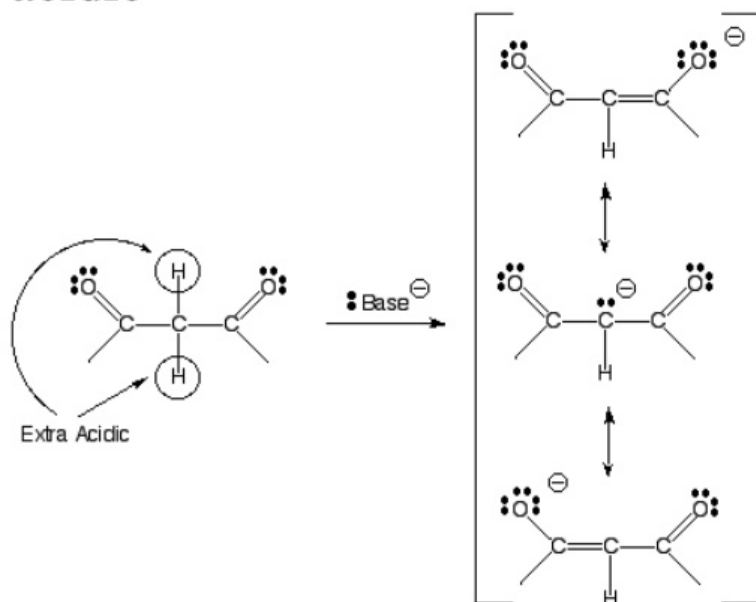
Tools we created to help you succeed:



Organic chemistry is difficult because it requires higher order thinking. According to Bloom's taxonomy of learning, the lowest level of learning involves pure memorization ("Remembering") As one moves up the pyramid to higher learning, understanding, applying, analysing, evaluating and creating are reached. I believe there are Organic chemistry analogs of all of these, culminating in synthesis which involves creativity along with all of the other levels of thinking. It is likely that many of you have never been challenged all the way to the top of the Bloom's taxonomy of learning pyramid before, explaining why this feels different and disorienting. **DO NOT GIVE UP.** As shown on the right, we have created tools to help you master each step up the ladder. On the above diagram you can click on the tools listed to go directly to them. Also, if you have any questions about how to study, [click here to read about the way I learned to study.](#) I never earned a grade lower than an A after I started using this method during my own college career.

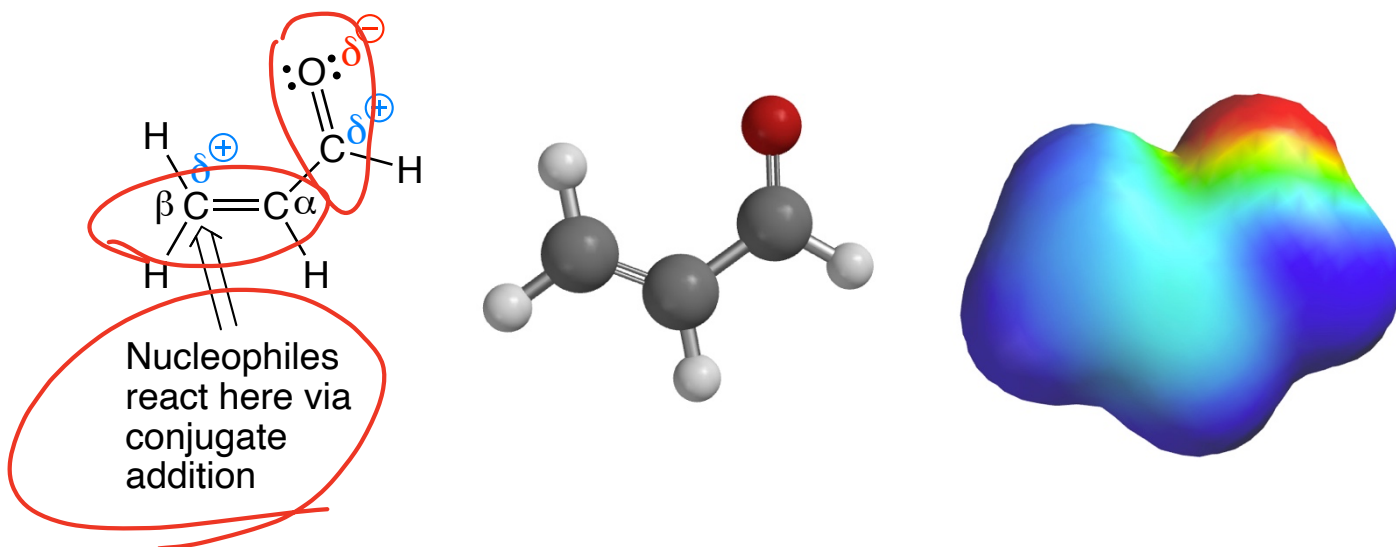
I understand that most of you are headed to the health professions, so you may be wondering if mastering synthesis problems will be important for you. I assert that it is. Solving a synthesis problem involves the detailed evaluation of a complex molecule while looking for KREs, then working backwards to the starting materials by analyzing possible reactions involved by thinking through your roadmaps, possibly applying your understanding of mechanism to make sure you predict the correct product for each reaction. This is the exact type of thinking you will need to diagnose a patient. A patient will present various complex combinations of symptoms, then you must evaluate which of these are important, then analyze, apply and understand how the patient got that way and how to get them back to their starting state (healthy) again. In other words, you will learn the "KREs of diagnosis" then work backwards to understand what happened to the originally healthy patient! Therefore, learning how to solve synthesis problems will teach you how to use higher level thinking skills, exactly the kind you will need to develop as a health care professional!

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.

Conjugate Addition



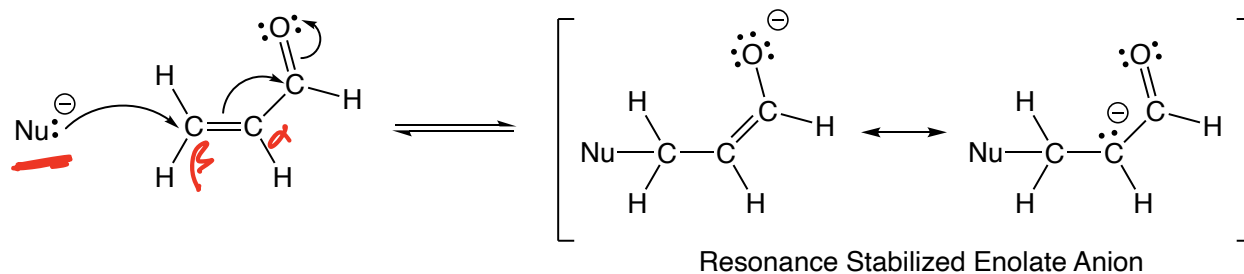
A) Alkenes adjacent to a carbonyl are conjugated and are therefore electrophilic.

B) These species are called α,β unsaturated carbonyl compounds. ✓

C) α,β unsaturated carbonyl compounds are conjugated, in that the pi electrons of the C=C and C=O bonds can delocalize over all four atoms. This lends some degree of extra stabilization to these species, because pi electrons prefer to delocalize.

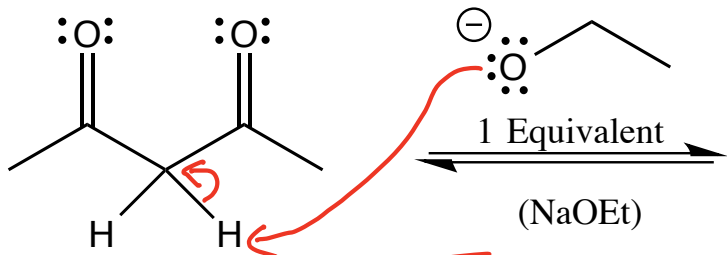
D) Nucleophiles can, however, react at the β carbon atom in a process called conjugate addition.

E) Conjugate addition is favorable because the intermediate formed is a resonance stabilized enolate, thus relatively low energy.

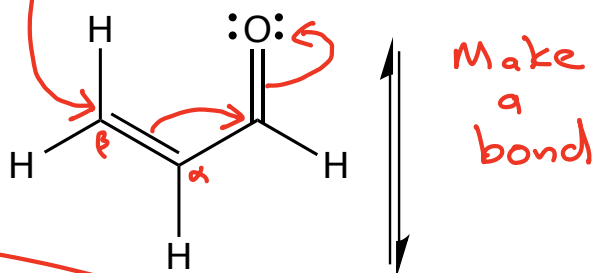
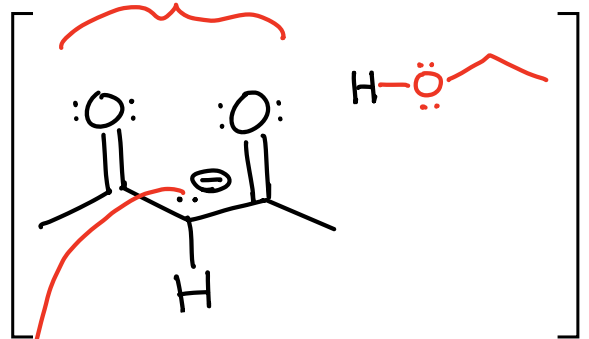


Michael Reaction

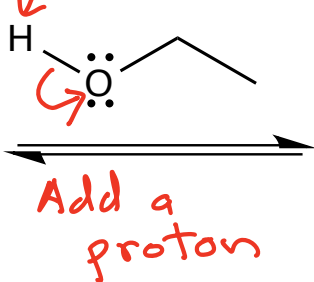
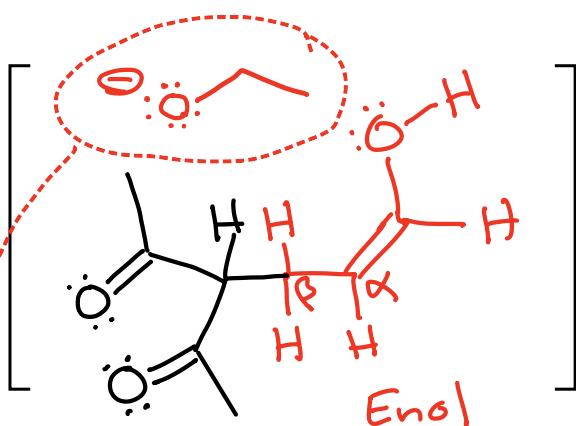
Nucleophile!



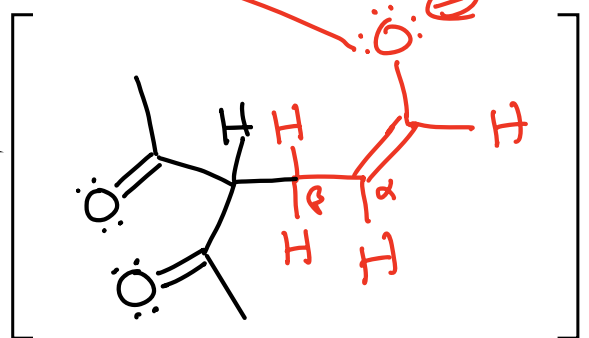
Take a proton away



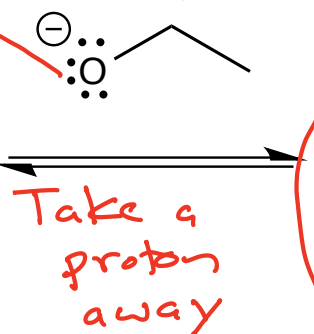
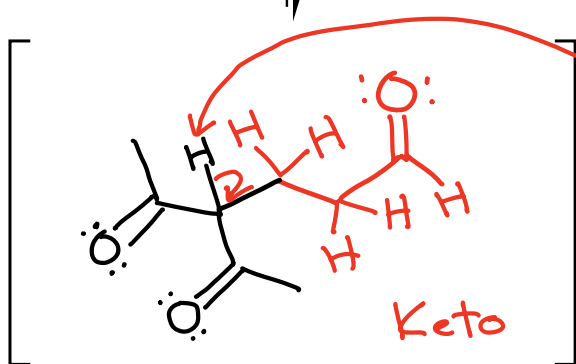
Make a bond



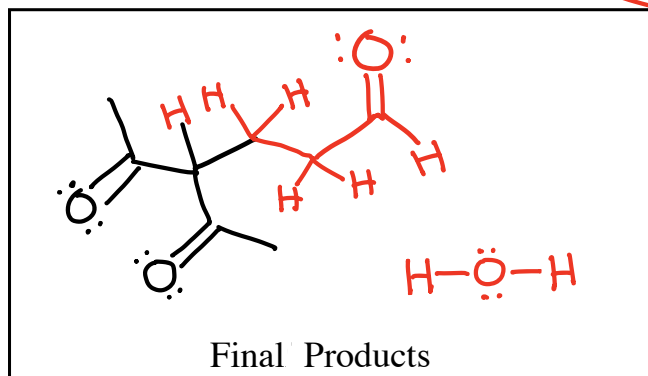
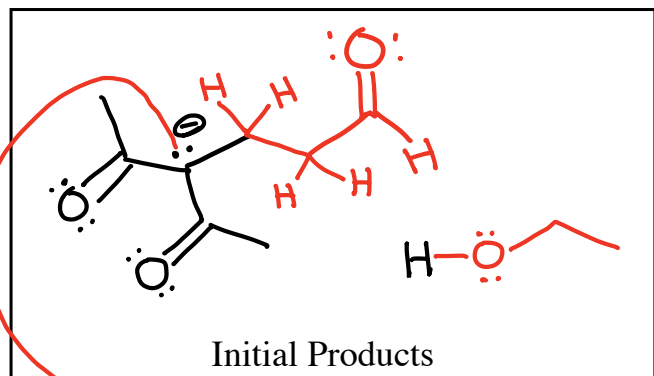
Add a proton



tautomerization



Take a proton away

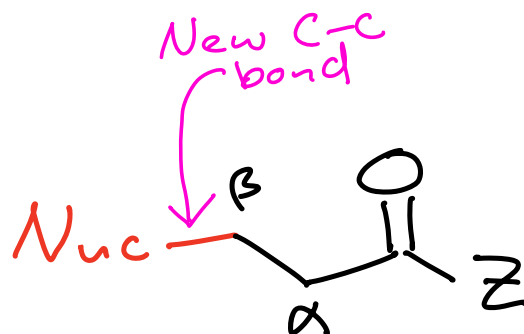
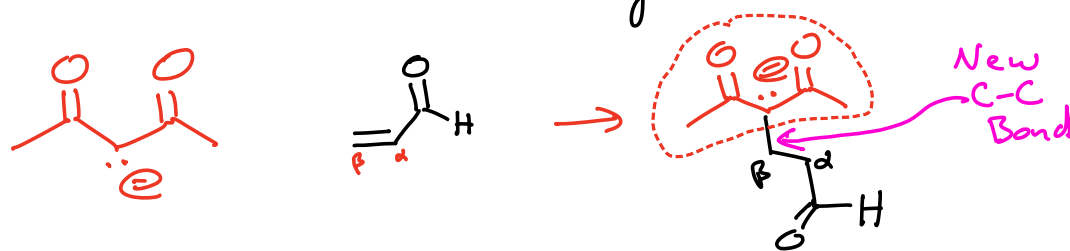


2) Mild

(Chemist opens flask and adds a mild acid)

Add a proton

Overall Balanced Equation



KRE \rightarrow A nucleophile (Nuc) makes a new C-C bond at the β carbon of a carbonyl

Nucleophiles \rightarrow β -dicarbonyl
enamine or amine

"Michael
Acceptor"

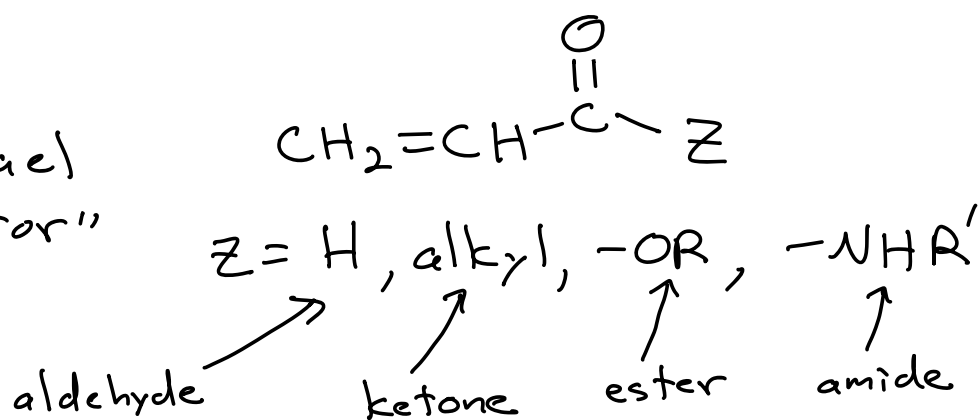
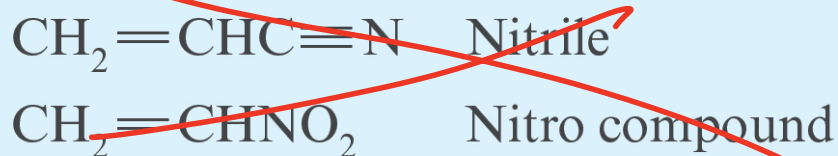
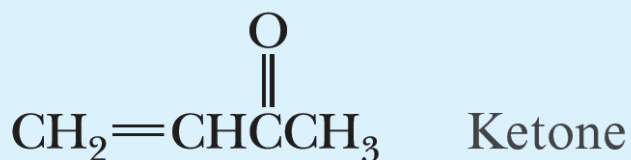
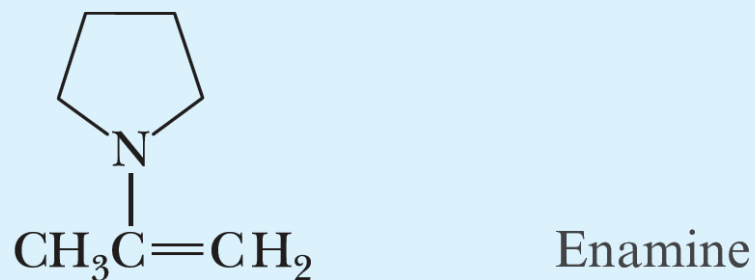
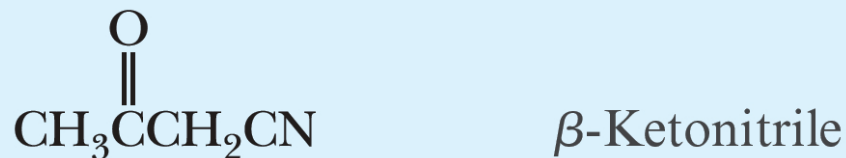
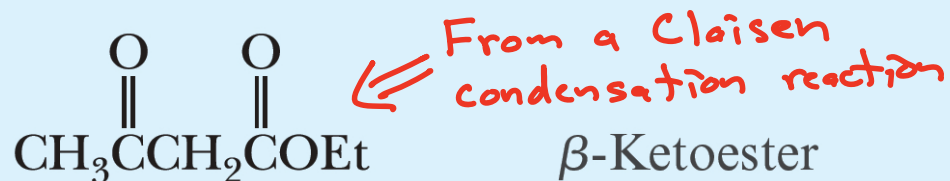
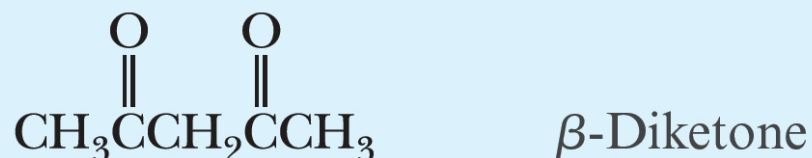


Table 19.1 Combinations of Reagents for Effective Michael Reactions

These Types of α,β -Unsaturated Compounds Are Nucleophile Acceptors in Michael Reactions

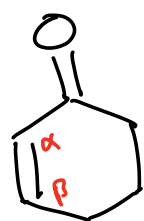
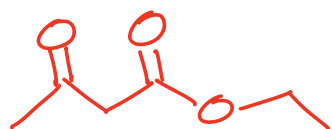


These Types of Compounds Provide Effective Nucleophiles for Michael Reactions



Example

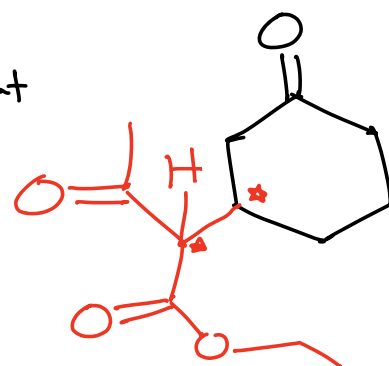
Nucleophile



Michael
Acceptor

1) 1.0 equivalent
 NaOEt

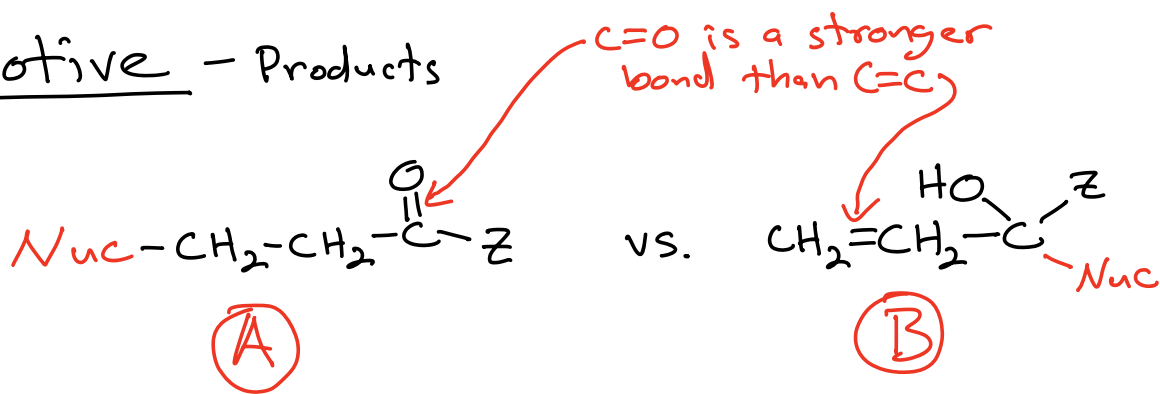
2) H_3O^+
Mild



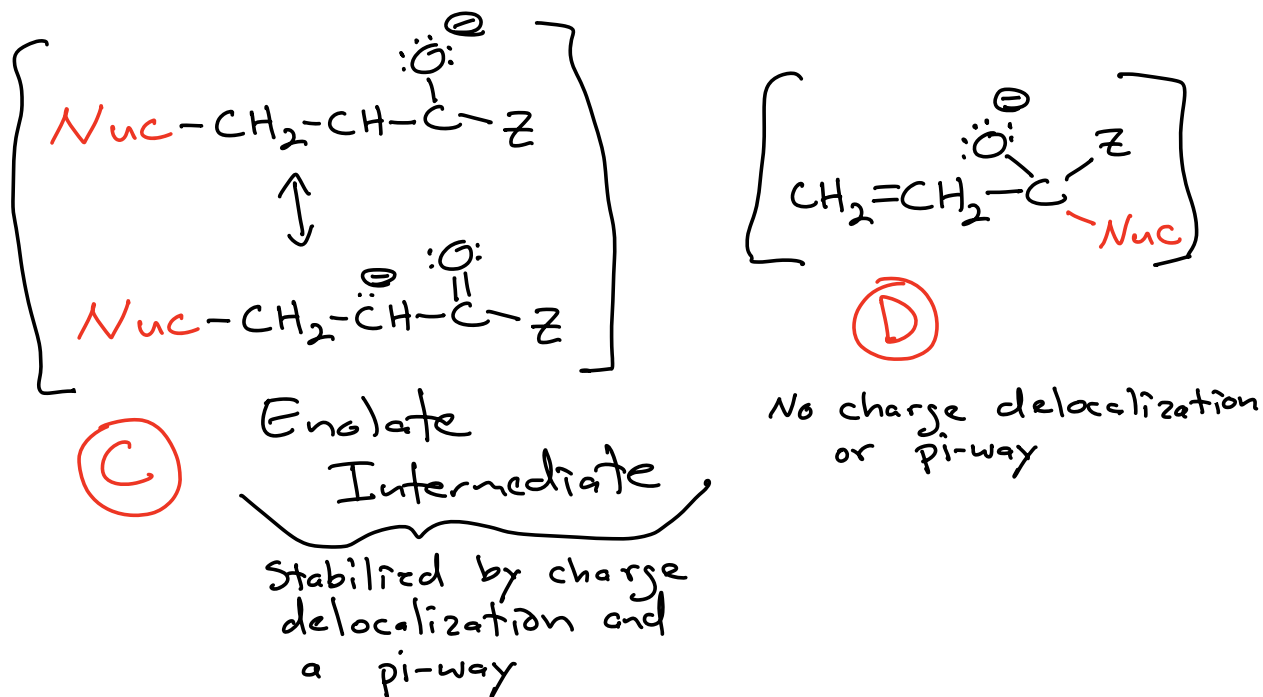
Racemic

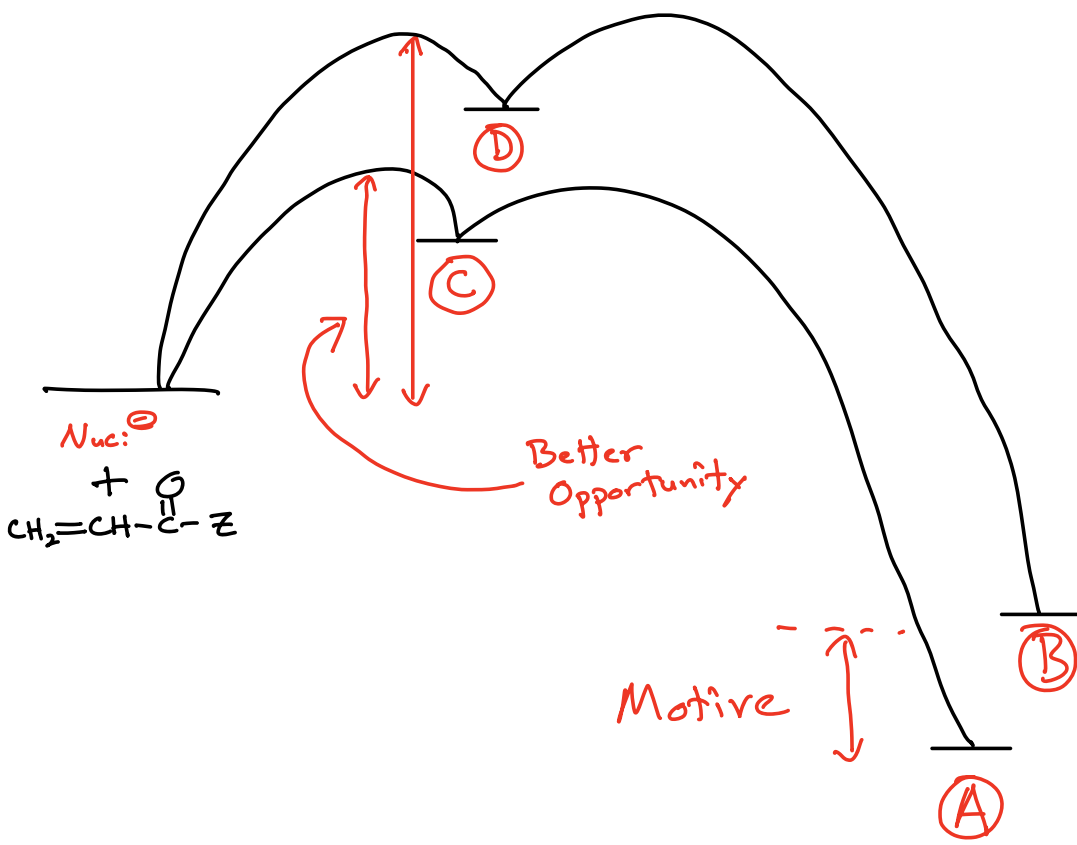
Why is conjugate addition
(reaction at C=C) favored
over reaction at the
carbonyl carbon?

Motive - Products

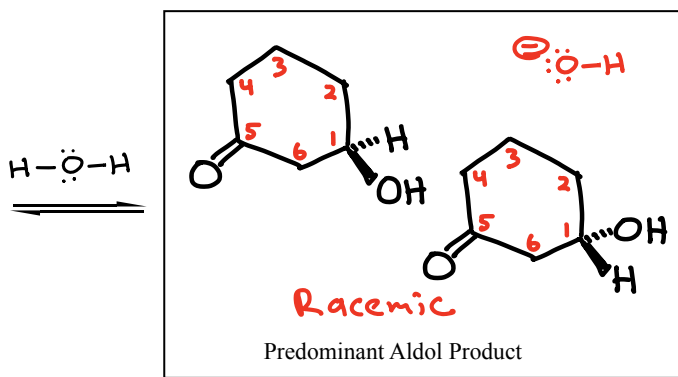
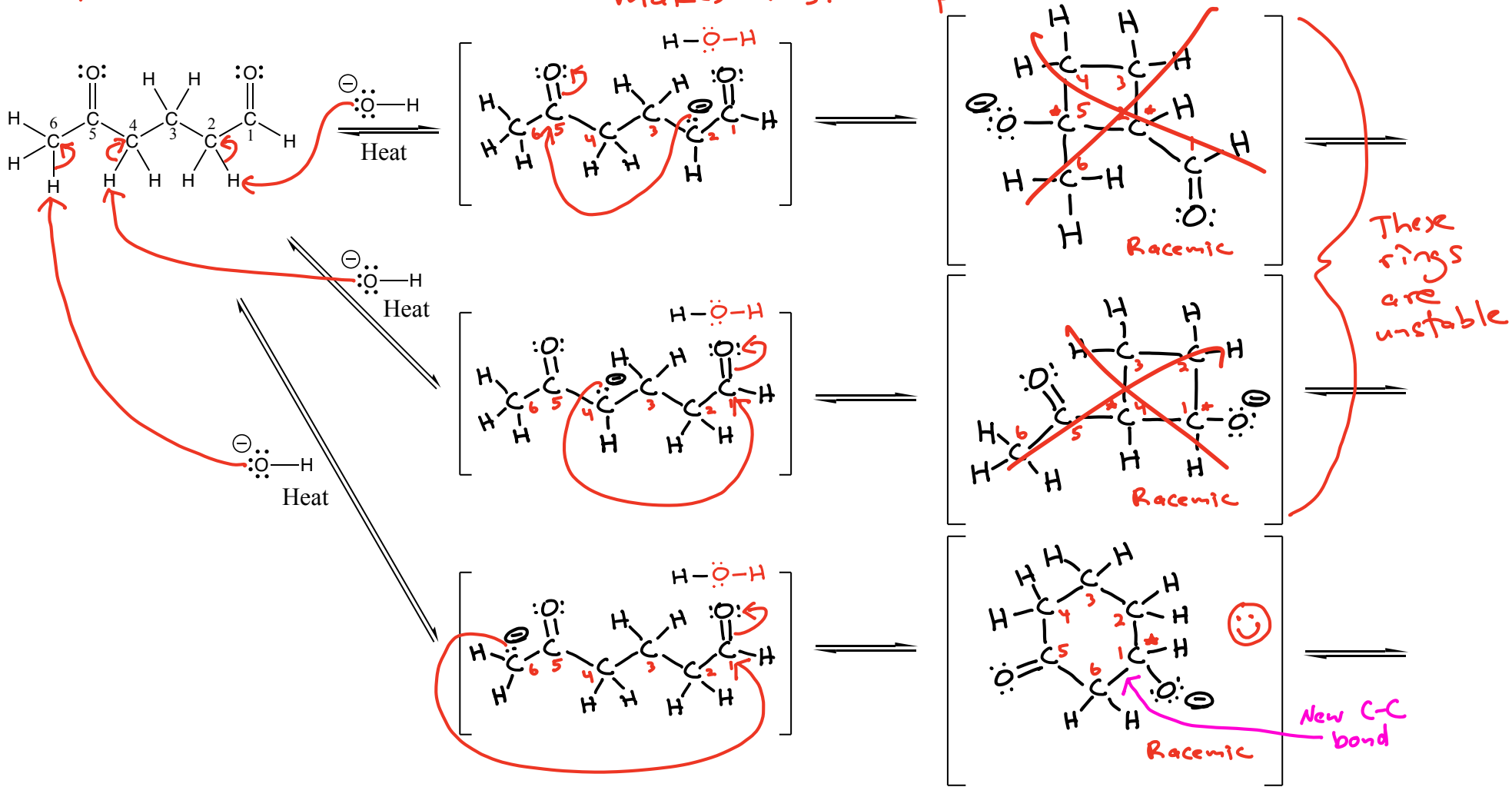


Opportunity - Intermediates





Cyclic Aldol Reaction → 3 different enolates are possible, but only one makes a stable product



Dehydration
Spontaneous dehydration - Multiple steps
You are not responsible for these

