

C. What's the difference between the acid-catalyzed reaction and base-catalyzed reaction?

1. Base: Nucleophile \Rightarrow enolate ion
electrophile \Rightarrow $C=O$ unchanged

2. Acid: Nucleophile \Rightarrow enol
electrophile \Rightarrow protonated carbonyl group

Example #1. Draw the mechanism of the base-catalyzed aldol reaction of each compound.

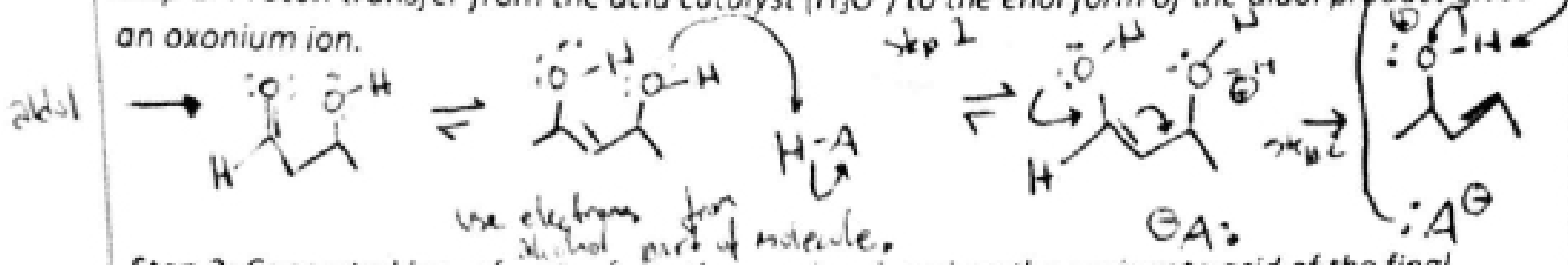
- a. Butanal (2 moles)
- b. Cyclohexanone (2 moles)
- c. Phenylacetaldehyde (2 moles)

D. It is possible to dehydrate a β -hydroxyaldehyde and/or β -hydroxyketone and usually the conditions that are necessary to bring this about are the same conditions that brings about the aldol reaction.

1. It's especially easy in the acid-catalyzed reaction; you can warm the aldol product in dilute acid
2. The major product of dehydration is where the $C=C$ bond is conjugated with the carbonyl group (α,β -unsaturated aldehyde or ketone)

Mechanism #3: Acid-Catalyzed Dehydration of an Aldol Product

Step 1: Proton transfer from the acid catalyst (H_3O^+) to the enol form of the aldol product gives an oxonium ion.

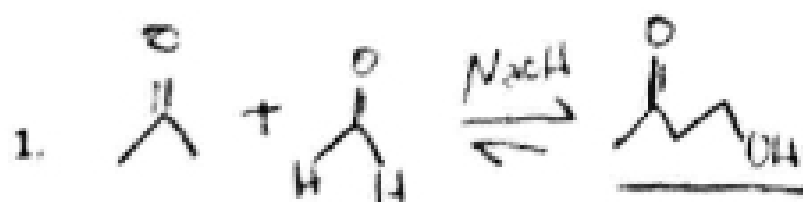


Step 2: Concerted loss of water from the oxonium ion gives the conjugate acid of the final product.



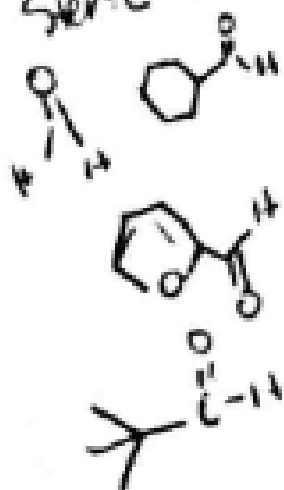
Step 3: Proton transfer from the conjugate acid of the final product to solvent completes the reaction and generates a new H_3O^+ .

- E. What happens if we use the enolate anion of one molecule and an enolate anion acceptor that's totally different from the enolate? When we switch it up, we call this a crossed aldol reaction.

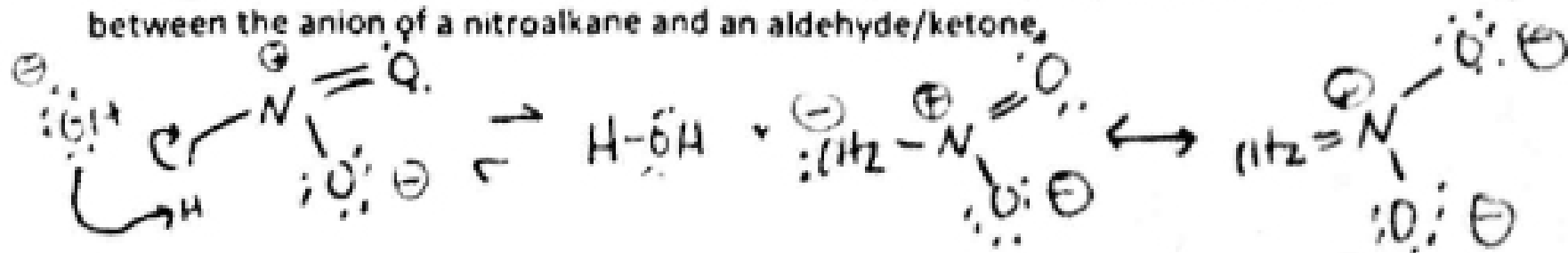


* For this to occur, one of the groups must have no α -hydrogens.

* Aldehydes react best because no steric hindrance.



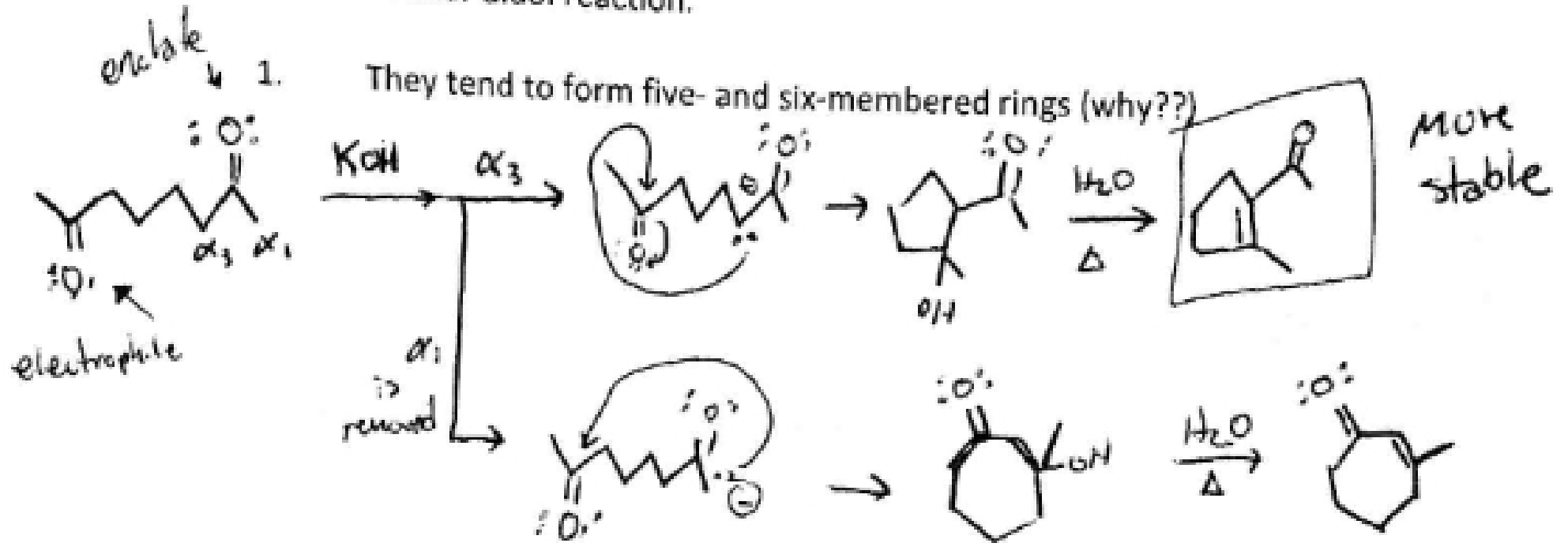
2. For a crossed aldol reaction to be successful, one of the reactants should have no α -hydrogens so an enolate won't form. It helps also if the compound w/ no α -hydrogens has the more reactive carbonyl. Nitro groups can be introduced into aliphatic compounds by way of a reaction between the anion of a nitroalkane and an aldehyde/ketone.



What is an enolate? and enolate ion.

- The α -hydrogens are sufficiently acidic that they are removed by bases (KOH or NaOH) and are stabilized by charge delocalization.

G. When both the enolate anion and the carbonyl group to which it adds are in the same molecule, aldol reaction results in the formation of a ring. This is called an intramolecular aldol reaction.

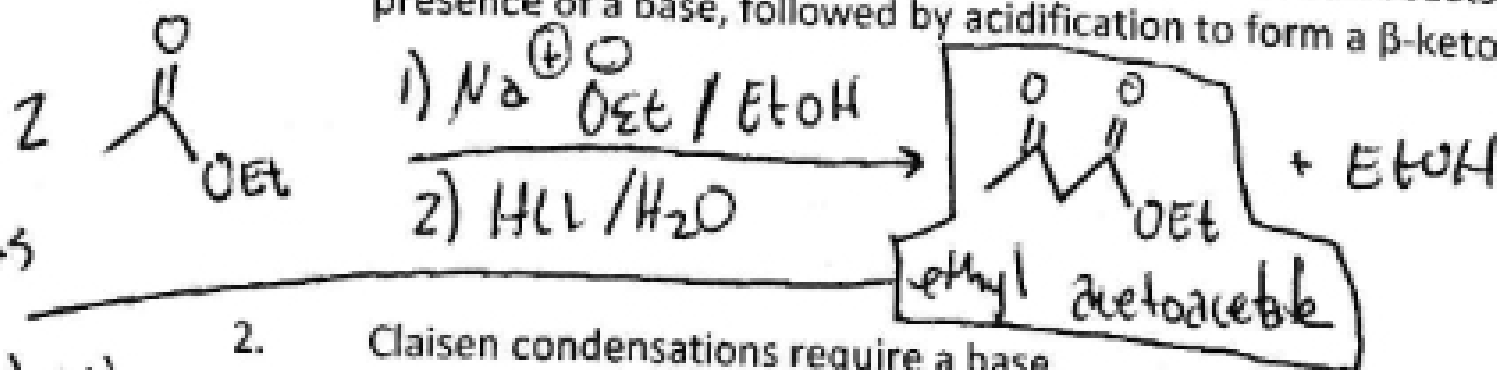


- In general, smaller rings form faster than larger rings because the reacting groups are closer together.

III. Claisen and Dieckmann Condensations

A. Esters can also be used to form an enolate ion and can participate in nucleophilic acyl substitution reactions. One of these reactions is the Claisen condensation reaction.

- The Claisen condensation takes two moles of ester and reacts it in the presence of a base, followed by acidification to form a β -ketoester



- Claisen condensations require a base.
 - Aqueous bases cannot be used because they would hydrolyze the ester.

KNOW THIS
structure.
Its name & how
to draw it.
Will be on 3/18/23
part of exam!