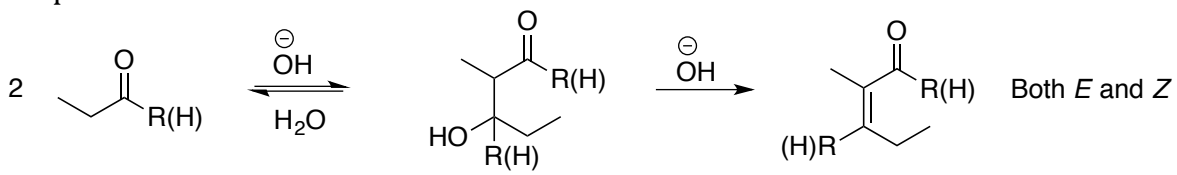
Chapter 23 Reaction Summary
Carbonyl Condensation Reactions

In all of the following reactions, one carbonyl compound (containing at least one acidic α-proton) will be the nucleophile (enolate) and the other carbonyl compound will be the electrophile. Some electrophilic carbonyl compounds do not contain a leaving group (aldehydes and ketones), while other contain a leaving group (esters and acid halides). In the case of no leaving group, an alcohol forms. This alcohol often gets dehydrated to an α,β-unsaturated carbonyl. When there is a leaving group, it will leave to reform the carbonyl functionality.

<u>The Aldol Condensation</u>

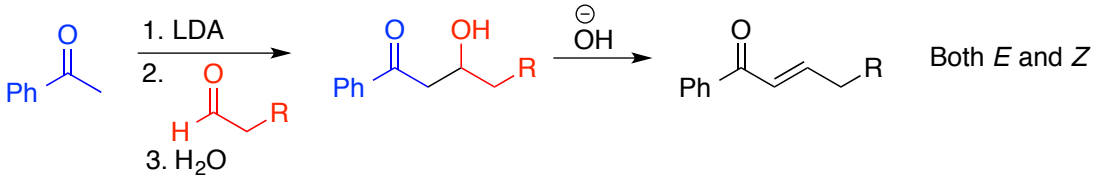
- Simple Aldol



β-hydroxycarbonyl α,β-unsaturated carbonyl

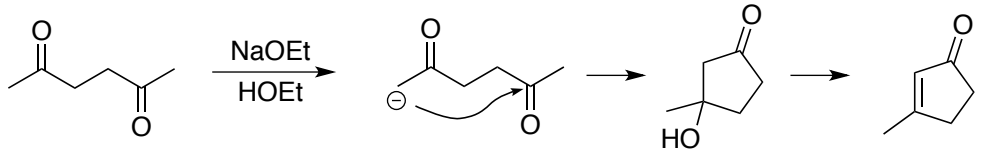
  - Two identical molecules of aldehyde or ketone in the presence of base provide a β-hydroxycarbonyl product.
  - The aldehyde/ketone <u>must</u> contain at least one alpha proton.
  - Under basic conditions, the β-hydroxycarbonyl is dehydrated to an α,β-unsaturated carbonyl compound.

- Directed Crossed Aldol



  - In a directed aldol two different ketones, two different aldehydes, or an aldehyde and a ketone are reacted together.
  - In this reaction, base is used to form the enolate of one carbonyl (nucleophile) and the second carbonyl compound (electrophile) is subsequently added.
  - This process is necessary when both carbonyl compounds have α-protons of similar acidities.

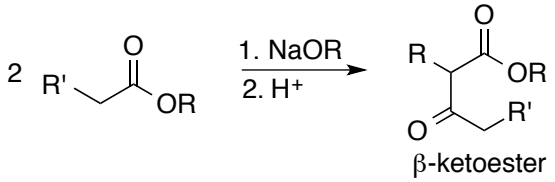
- Intramolecular Aldol



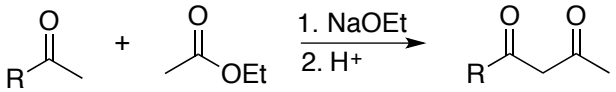
  - This reaction works with:
    - 1,4-dicarbonyl compounds (to form a 5 membered ring)
    - 1,5-dicarbonyl compounds (to form a 6 membered ring)
    - 1,6-dicarbonyl compounds (to form a 5 membered ring)
    - 1,7-dicarbonyl compounds (to form a 6 membered ring)
  - The negative charge that forms on one of the alpha-carbons will act as a nucleophile and cyclize to give a 5 or 6 membered ring.

The Claisen Condensation

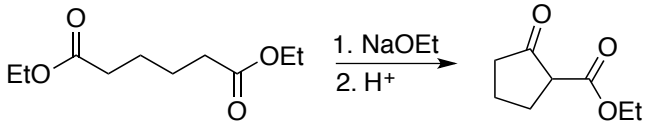
- Simple Claisen



  - A Claisen reaction occurs between two molecules of ester. One ester is the nucleophile and the other is the electrophile. Since the electrophile contains a leaving group, it is lost to reform the C=O.
  - The base used (NaOR) should have the same -OR group as the ester.
- Crossed Claisen

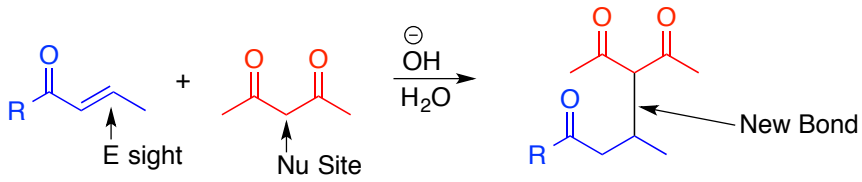


  - In a crossed Claisen, two different esters or a ketone and an ester are reacted in the presence of base.
  - When a ketone and ester are used, the ketone is the nucleophile and the ester is the electrophile. *The ketone is more acidic so its enolate is formed preferentially.*
- Intramolecular Claisen (Dieckmann Condensation)



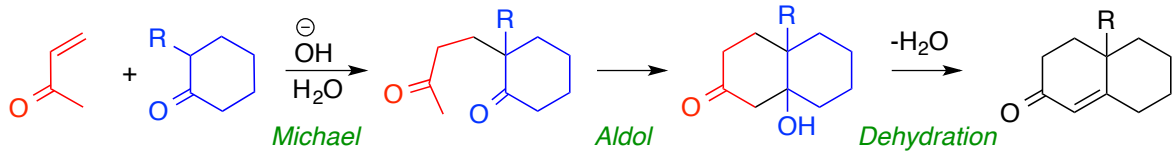
  - The Dieckmann Condensation occurs with 1,6 diesters to form 5-membered rings and 1,7-diesters to form 6-membered rings.

The Michael Reaction (Conjugate Addition)



- A Michael reaction occurs between an α,β-unsaturated carbonyl compound (Michael Acceptor, Electrophile) and a carbonyl compound (Nucleophile).
- The carbonyl compound that is the nucleophile is generally a 1,3-dicarbonyl compound.
- The electrophilic carbon in the Michael reaction is not the carbonyl carbon, but is the β-unsaturated carbon.
- The base can be either hydroxide (HO^-) or alkoxide (RO^-)

The Robinson Annulation



R = H or alkyl - reaction will work
R = $COCH_3$ or COOR - best yields

- The Robinson Annulation is a tandem Michael Reaction/Aldol Condensation that occurs between an α,β-unsaturated carbonyl compound and a second carbonyl compound.