

I. Condensation Reactions

A. Aldol condensation of aldehydes and ketones

Aldol condensations result from the combination of two molecules, usually with the loss of water.

Under basic conditions, the aldol reaction results from the nucleophilic addition of an enolate to another carbonyl group. The product is an "aldol", which may dehydrate to an α,β -unsaturated carbonyl compound. The reaction can be viewed as an alpha-substitution or a nucleophilic addition to a carbonyl:

The reaction is completely reversible, with aldehydes forming ~50% of the aldol under basic conditions and ketones forming ~1% of the aldol.

Acid-catalyzed self condensation proceeds via nucleophilic attack of an enol on an activated (protonated) carbonyl compound:

B. Dehydration of aldols

Aldols may undergo dehydration upon heating (in the presence of acid or base) to form α,β unsaturated aldehydes or ketones:

Dehydration is exothermic because it leads to a conjugated system, which is very stable thermodynamically. The exothermic dehydration step often drives the aldol equilibrium to the right, so that α,β -unsaturated ketones and aldehydes may be obtained in good yield despite an unfavorable equilibrium.

C. Crossed Aldol Condensations

Crossed aldol condensations result from the reaction of the enolate of one carbonyl compound with the C=O of another carbonyl compound. Mixtures of products may result unless the carbonyl is non-enolizable:

If a non-enolizable aldehyde or ketone (one containing no α -hydrogen atoms) is employed in large excess (so its carbonyl is more likely to be attacked by the enolate), reasonable yields of a single crossed aldol product result. The aldehyde to be enolized is added slowly to the basic solution containing a large excess of the non-enolizable aldehyde.

D. Intramolecular Aldol reactions. Cyclizations

Intramolecular aldol condensations involving diones, dialdehydes, or keto aldehydes produce 5- and 6-membered rings in good yield. Often the thermodynamic (more substituted enolate) leads to the observed product:

II. The Claisen Ester Condensation

Esters are less acidic than ketones because the ester carbonyl carbon is strongly stabilized by resonance, making it less electropositive. As a result, ester enolates are every strong nucleophiles.

The self condensation of esters involves nucleophilic acyl substitution of esters by ester enolates. The products are β -keto esters:

The driving force for the overall process is product deprotonation by the base present in the medium. Note that β -keto esters are more acidic than esters, aldehydes and ketones because the negative charge of the enolate is delocalized over both carbonyl groups:

Deprotonation of the β -keto ester provides a strong driving force for the Claisen condensation, making the overall reaction exothermic. Note that base is consumed in the deprotonation step:

B. The Dieckmann condensation

Intramolecular condensation of diesters leads to cyclic β -keto esters:

This process is useful for constructing 5- and 6-membered rings.

C. Crossed Claisen Condensations

The reaction of an ester enolate with another, non-enolizable ester leads to good yields of crossed Claisen products. The non-enolizable ester component may be a benzoate ester, a formate ester, a carbonate ester, or an oxalate ester.

E. Crossed Claisen Condensations between ketones and esters.
Since ketones are more acidic than esters, they are more likely to enolize than esters under basic conditions. Thus the ketone enolate condenses with the ester carbonyl to give substitution products: