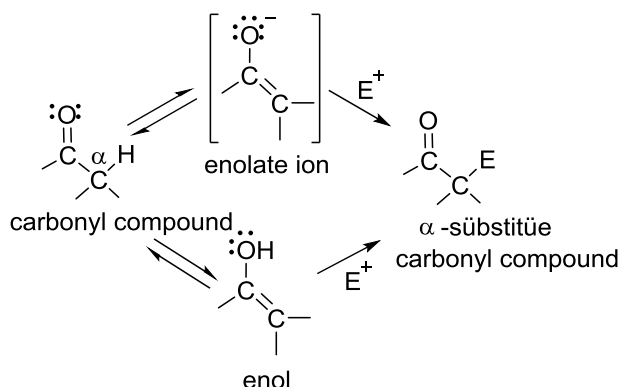


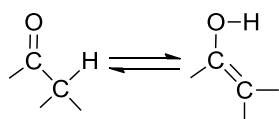
α -Substitution Reactions of Carbonyl Group

The α -substitution reactions occur when the mobile hydrogen atom (α -hydrogen) on carbon adjacent to the carbonyl group (α -position) is replaced by the electrophile (E). This reaction occurs via enol or enolate ions.



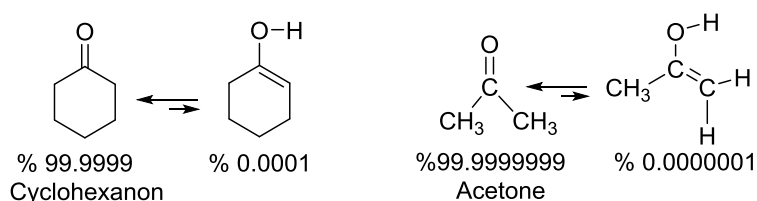
Keto-enol Tautomerism

Carbonyl compounds containing hydrogen atom in the α -carbon atom can be converted to the enol form by displacement of this hydrogen. This transformation between the two structures is an isomerism known as tautomerism. These isomers are called tautomers.



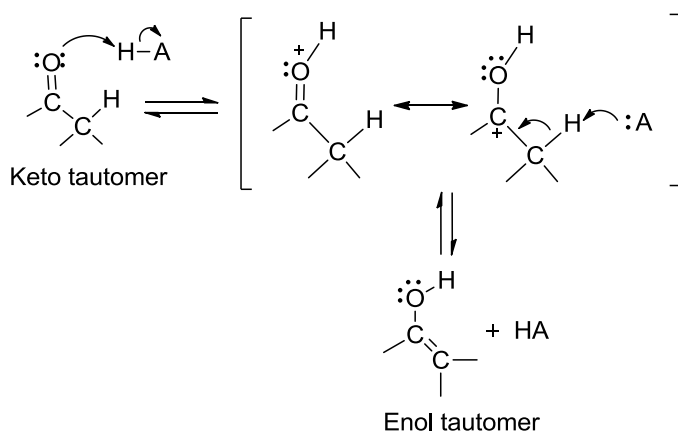
Many carbonyl compounds are present in keto form. It is often difficult to isolate the pure enol form.

Example:

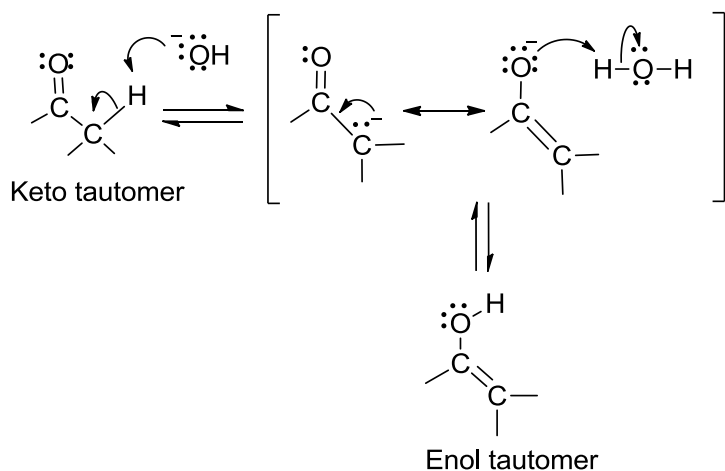


The keto-enol tautomerism of carbonyl compounds occurs by acid or base catalysis.

In acid-catalyzed keto-enol tautomerism; The protonation of the carbonyl oxygen atom (Lewis base) gives an intermediate cation, which then forms a neutral enol form with loss of H^+ in the α -carbon.

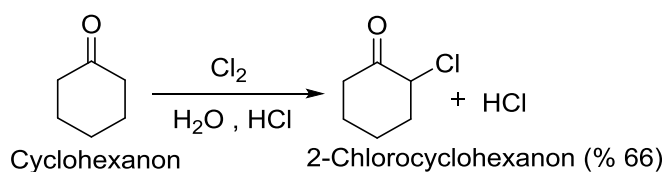
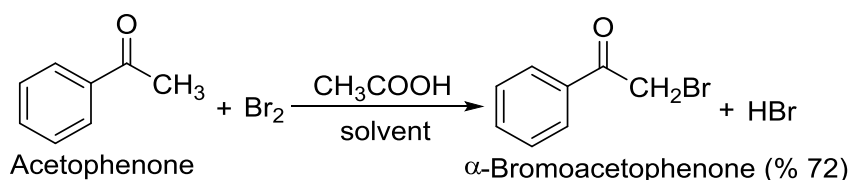


In the base-catalyzed enol formation, the enolate anion is formed primarily by the removal of the acidic hydrogen in the α -position of the carbonyl compound by the base, and the protonation of this anion forms the enol form.

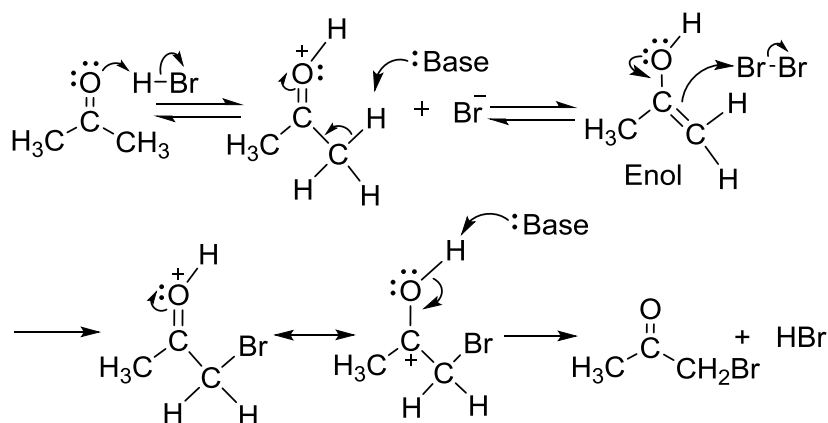


α -Halogenation of Aldehydes And Ketones

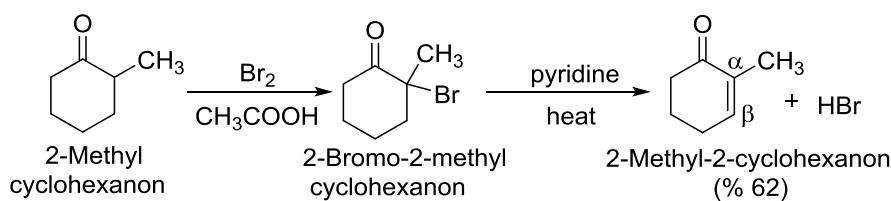
Aldehydes and ketones give halogen derivatives with Cl_2 , Br_2 , I_2 in α -positions in acidic solutions.



Acid-catalyzed bromination mechanism of acetone:



α -Bromoketones are suitable starting materials in organic synthesis. For this reason, dehydrobromination is used to obtain α, β -unsaturated ketone.



Note: Haloform Reaction (base catalysed)

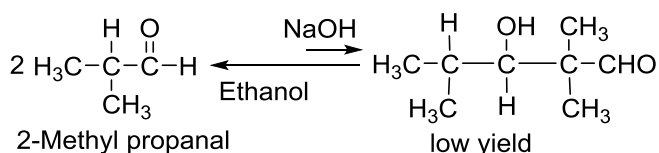
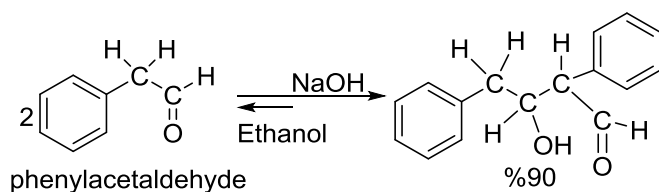
Carbonyl Condensation Reactions

Aldol Condensation of Ketones And Aldehydes

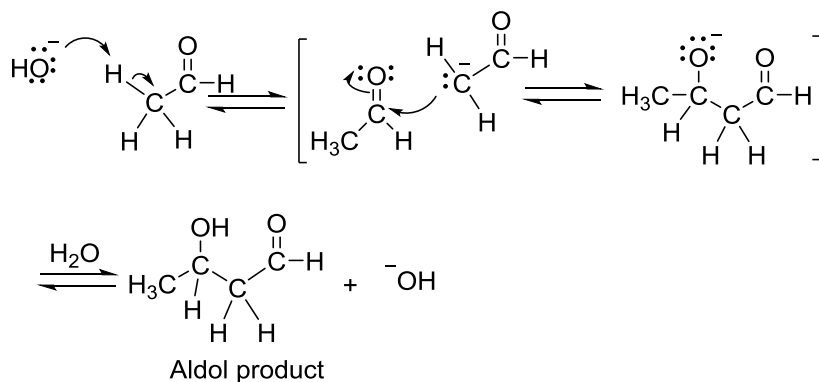
Condensations are very important enolate reactions of carbonyl compounds. Condensations are based on the combination of two or more molecules usually with the loss of small molecules such as water or alcohol.

Base-catalyzed aldol condensation can be described as the nucleophilic addition of one enolate ion to another carbonyl group. The β -hydroxy ketone or aldehyde formed after protonation is known as "**aldol**". This is because aldol molecules are derived from **al**dehyde and **al**cohol groups.

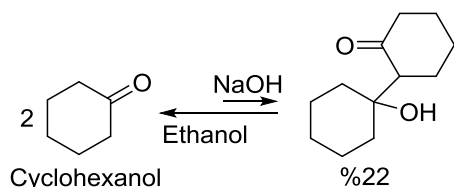
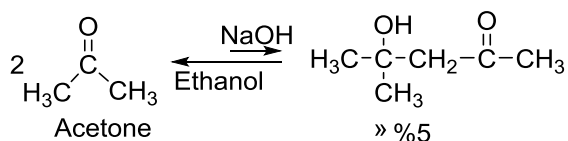
Example:



Mechanism of Aldol condensation:

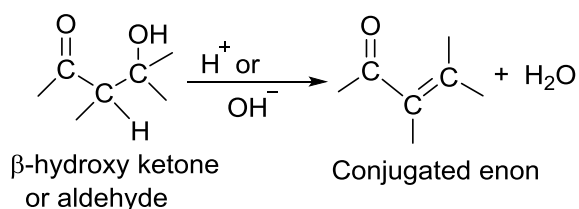


Aldol condensation is a reversible reaction. That is, the starting material is in equilibrium with the product, and the acetaldehyde aldol product is observed at 50%. Ketones give aldol condensation, but the product has a very low equilibrium concentration.

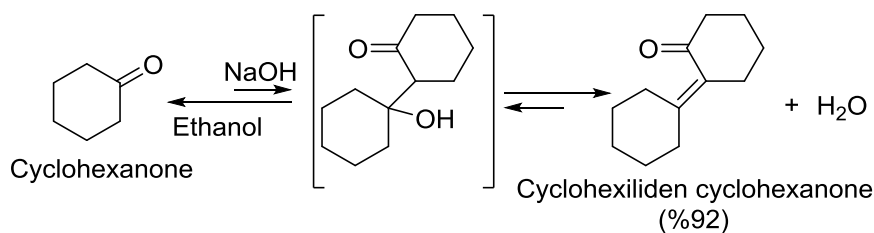
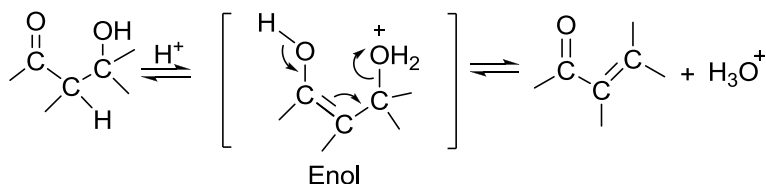
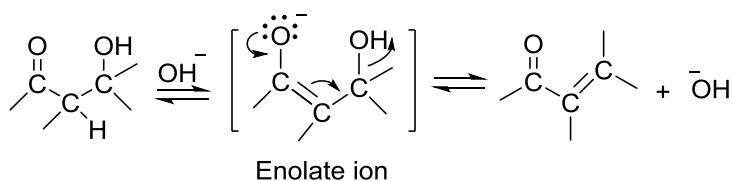


Dehydration of Aldol products

The β -hydroxy aldehydes and β -hydroxy ketones resulting from the aldol condensation are easily dehydrated to give conjugated enone structures.



In the basic environment, the enolate ion is formed as a result of acidic α -hydrogen separation, and the enone structure is obtained by separating the -OH group with the E_2 -like reaction. In the acidic environment, the enol structure is formed, and with the protonation and water elimination of the -OH group in this structure occurs enone structure.

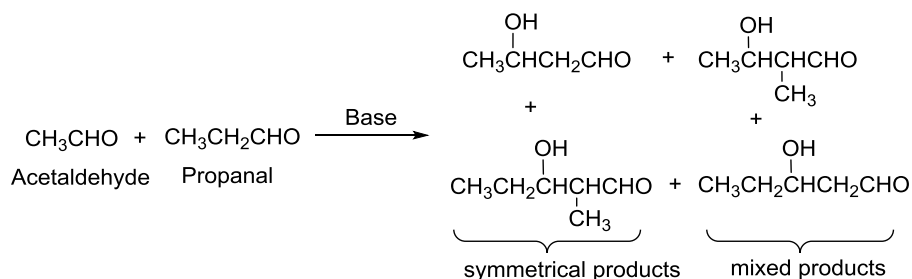


Mixed aldol reactions

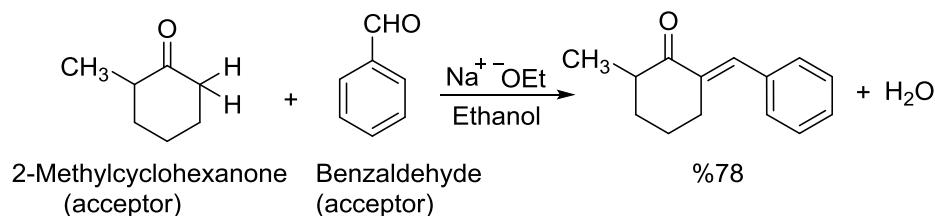
In the symmetric aldol reactions given up to now, both carbonyl compounds were the same.

Different aldehydes or ketones are used as starting materials in mixed aldol reactions.

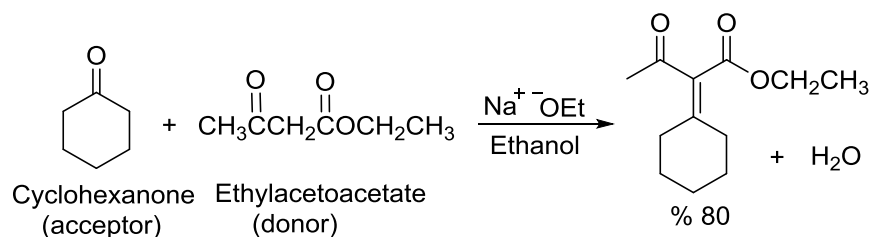
Example: Moving from acetaldehyde and propanal, 4 different products are reached. Two of them are symmetrical aldol products while two are mixed aldol products.



On the other hand, a single product can be reached with the mixed aldol reaction. If one of the carbonyl compounds does not carry α -hydrogen (this structure can not form an enolate ion), it acts as an acceptor for the nucleophiles.

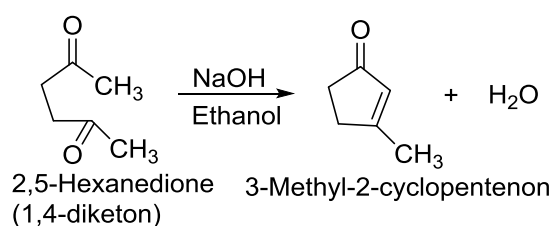


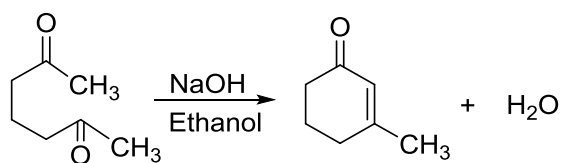
Furthermore, if one of the carbonyl compounds is more acidic, the enolate ion is formed more easily and the mixed aldol reaction occurs with high efficiency.



Intramolecular aldol reactions

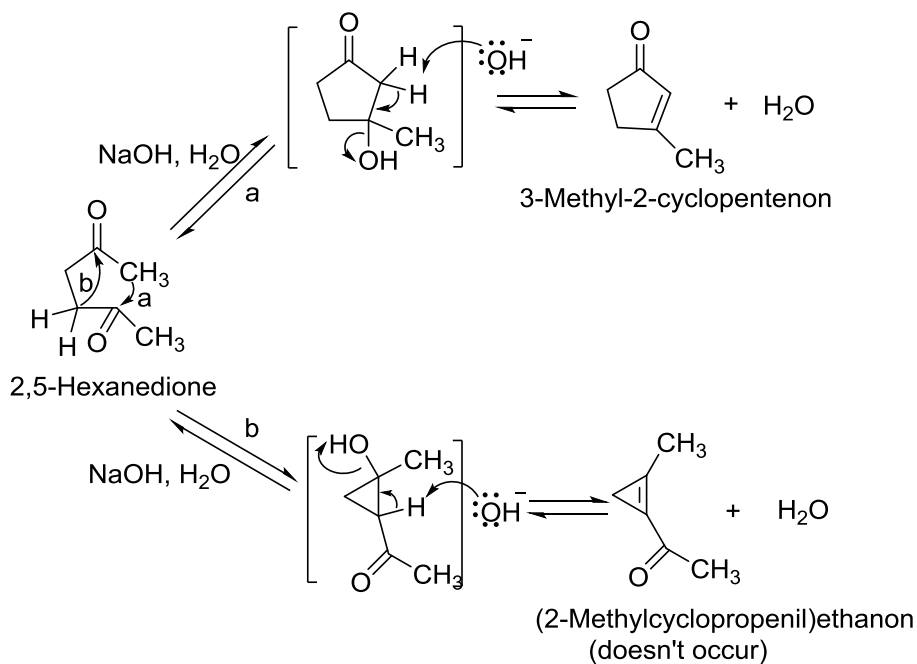
Intermolecular aldol reactions (between 2 molecules) as well as intramolecular aldol reactions are also found. Cyclic derivatives are obtained by intramolecular aldol reaction by moving from a structure carrying 2 carbonyl groups.





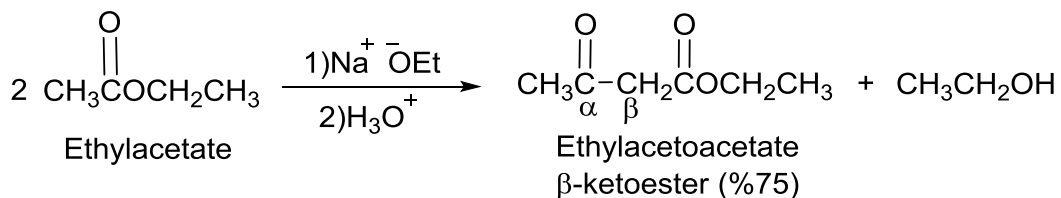
2,6-Heptanedione 3-Methyl-2-cyclohexanone
(1,5-diketone)

Mechanism of intramolecular aldol reaction:

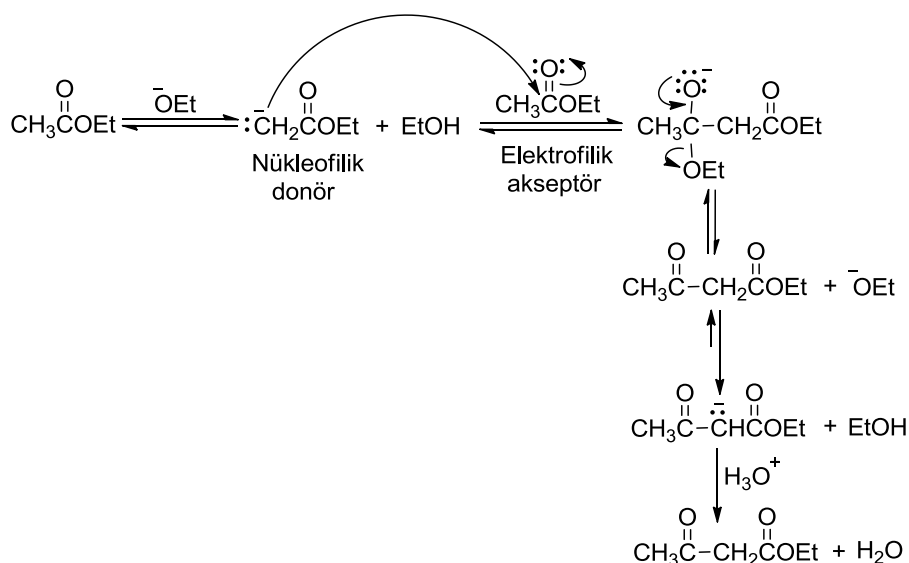


Claisen Condensation Reaction

Ester structures are weakly acidic, as aldehydes and ketones, and the α -hydrogen containing ester structure is treated with 1 mol base (NaOEt) to form the β -ketoester structure resulting in a condensation reaction. Ex. Ethylacetoacetate is obtained from ethylacetate in the presence of base. The reaction between these 2 ester molecules is called the Claisen condensation reaction.

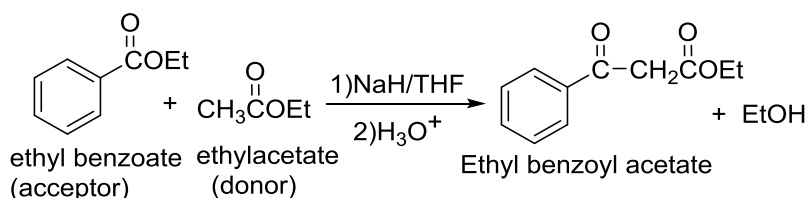


Mechanism of Claisen condensation reaction:

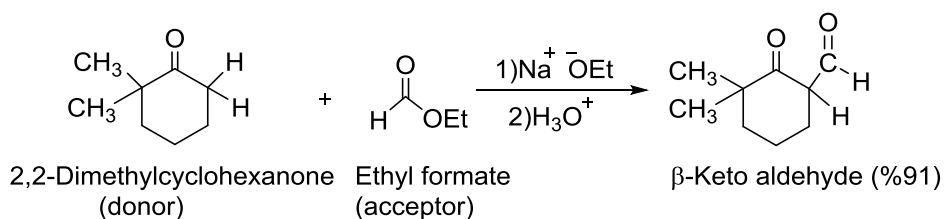


Mixed Claisen Condensation

Mixed Claisen condensation is done with two different ester derivatives. As previously mentioned, two different aldehyde or ketone compounds were used in the mixed aldol condensation. One of the ester components does not carry α -hydrogen, so the enolate ion can not form. For example, ethyl benzoate and ethyl formate can not form enolate ion and can not serve as donors, they act as electrophilic acceptors and give β -keto ester products with a very high yield.

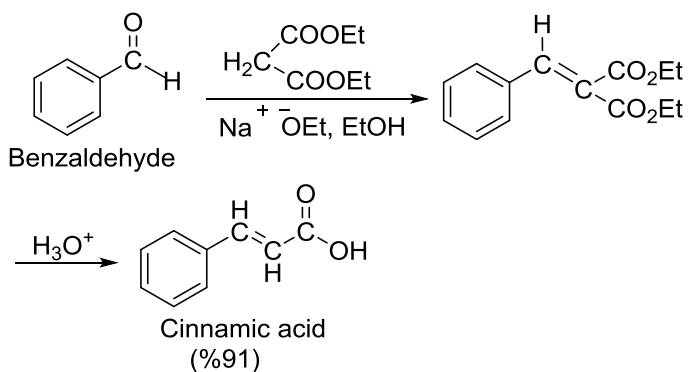


Mixed Claisen-like reactions can also occur between esters and ketones.



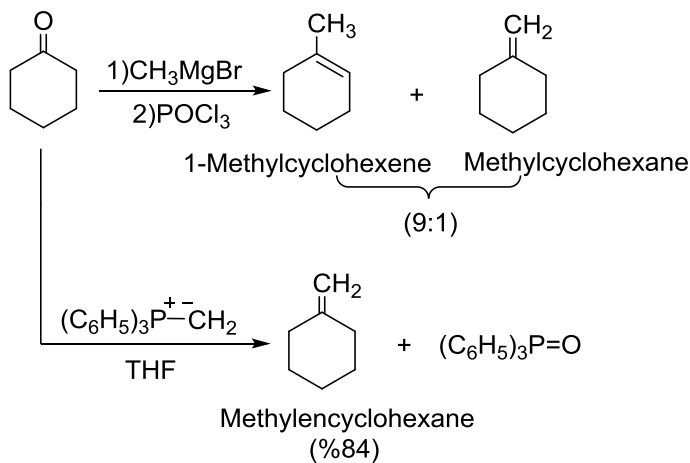
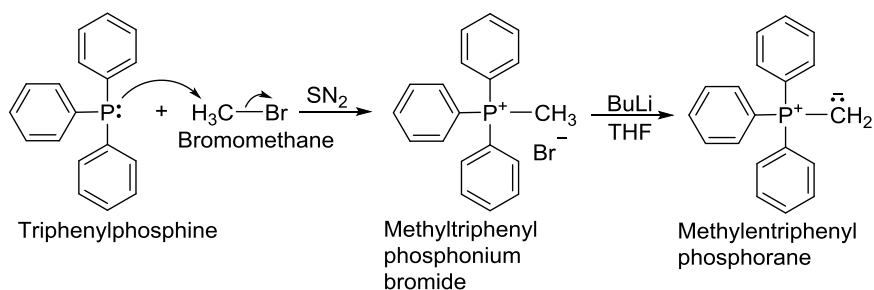
Malonic Ester Condensation

Malonic acid ethyl or methyl esters, which are also known as malonates, can be prepared by treatment malonic acid with ethyl or methyl alcohol. Since the α -hydrogens between the two carbonyl groups are highly active, the malono esters undergo base-catalysed condensation with aldehydes and ketones to form unsaturated acid or esters. The reaction is known as the **Knoevenagel reaction**.



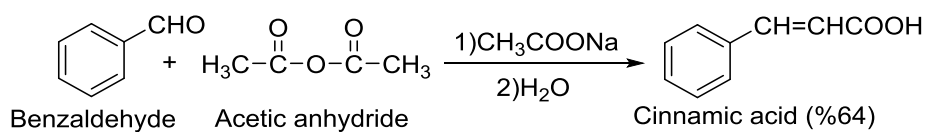
Wittig Reaction

It is the condensation reaction of the carbonyl compounds with the phosphates (Wittig reagents). Instead of the carbonyl group, double bonds are formed in the reaction to form alkenes. The Wittig reagent is obtained by a two-step reaction with a triphenylphosphine and alkyl halide.



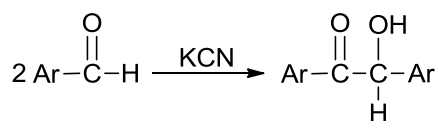
Perkin Reaction

Condensation of an aromatic aldehyde and an acid anhydride in the presence of Na or K salt of acid corresponding to anhydride is called the Perkin reaction.



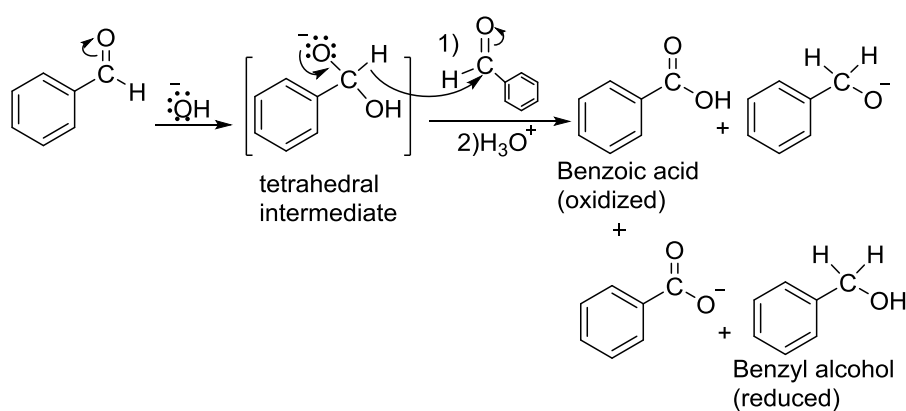
Acyloin Condensation

α -Hydrogen-free aldehydes give an addition reaction in the presence of alkali cyanide (KCN) and occur the acyloin, which is α -hydroxy ketone. (benzoin synthesis).



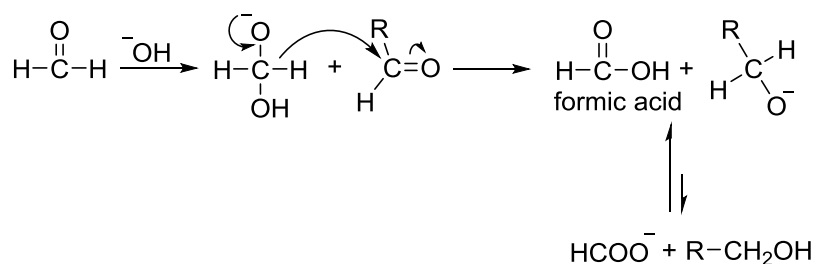
Cannizaro Reaction

α -Hydrogen-free aldehydes give cannizaro reaction in the base environment. One of the two aldehyde molecules is oxidized to carboxylic acid by giving two electrons to the other, while the other is reduced to alcohol by getting electrons. For example; The 2 molecule benzaldehyde interacts with one another to form benzoic acid by oxidation of a molecule and benzyl alcohol by reduction of the other molecule.

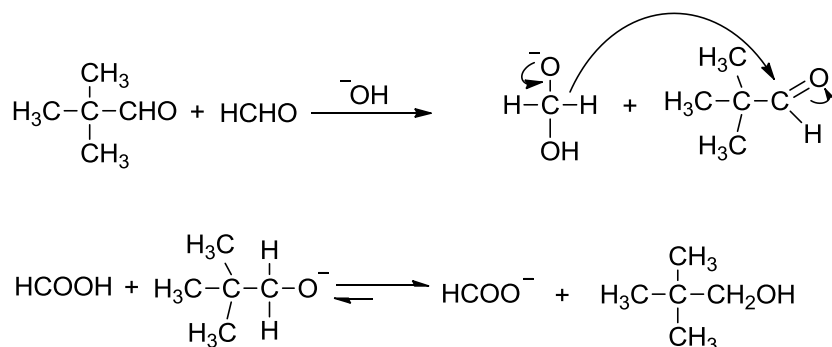


Mixed Cannizaro Reaction

When α -hydrogen-free aldehydes are treatment with formaldehyde, formaldehyde converted to formic acid and aldehyde structure converted to alcohol derivatives.

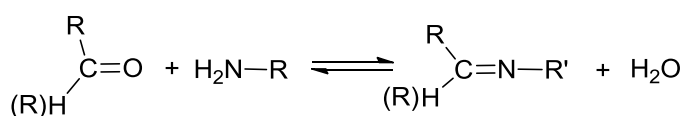
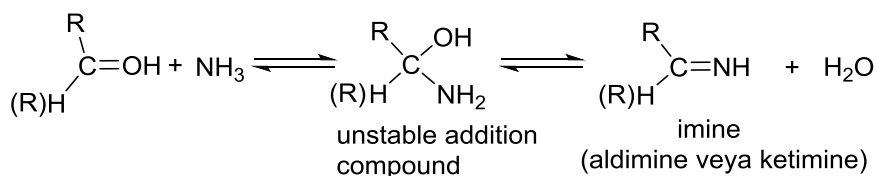


Example:



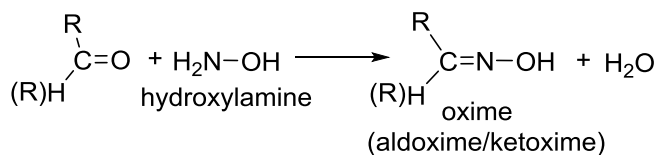
Condensation Reactions of Aldehydes and Ketones With Ammonia and Primary Amines, Formation of Imine

The aldehydes and ketones give an unstable addition product with NH_3 . The NH_3 may be separated from this product and re-introduced into the aldehyde and ketone, or the H_2O may be separated to form the imine compound. Imines are unstable and the reaction is recycled. Imines can be thought as nitrogen analogues of aldehydes and ketones. Imines, like amines, have alkali properties and substitution imines are called Schiff bases.

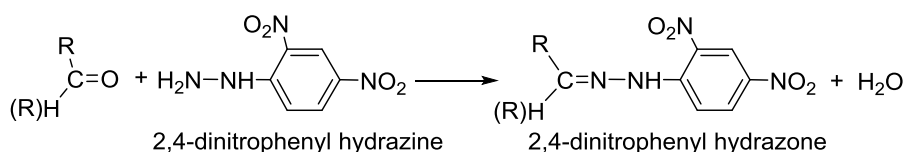
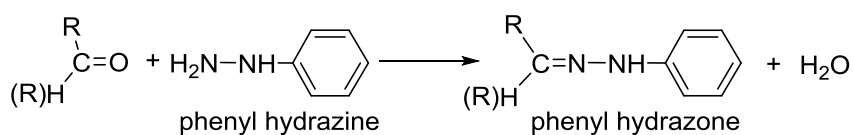
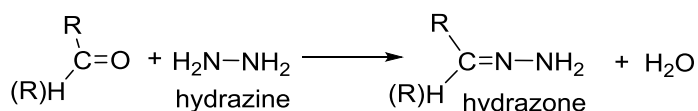


Condensation reactions with various amine derivatives

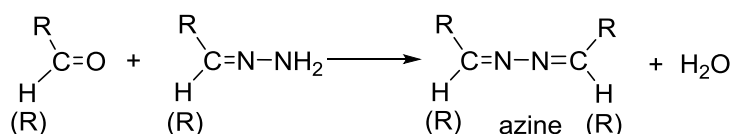
1) Carbonyl compounds with high activity are converted to the oxime by interaction with hydroxylamine hydrochloride in the presence of sodium hydroxide. Because oximes are stable and have definite melting point, they are used in the identification of aldehydes and ketones



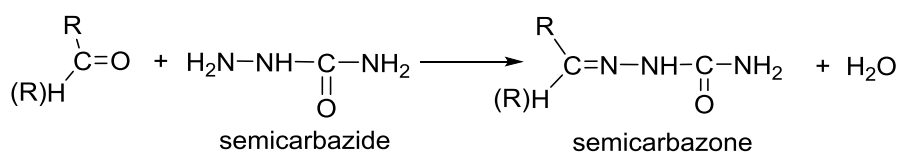
2) Hydrazine and 2,4-dinitrophenylhydrazine can also be used in the identification of carbonyl compounds, they form hydrazone.



Hidrodonlar özellikle aldehitlerle yoğunlaşma reaksiyonu verirler ve azinler oluşur.

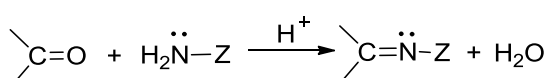


3) Another compound used in the identification of carbonyls is semicarbazide.



Thiosemicarbazone is obtained when thiosemicarbazide, which is a sulfuric derivative, is used instead of semicarbazide.

Condensation products of ketone and aldehyde with amine derivatives are summarized in the following table:



H ₂ N-Z	Reagent	Product	
-H	H ₂ ̈N-H	$\begin{array}{c} \diagup \\ \diagdown \end{array} \text{C}=\ddot{\text{N}}-\text{H}$	imine
-R	H ₂ ̈N-R	$\begin{array}{c} \diagup \\ \diagdown \end{array} \text{C}=\ddot{\text{N}}-\text{R}$	imine (schiff base)
-OH	H ₂ ̈N-OH	$\begin{array}{c} \diagup \\ \diagdown \end{array} \text{C}=\ddot{\text{N}}-\text{OH}$	oxime
-NH ₂	H ₂ ̈N-NH ₂	$\begin{array}{c} \diagup \\ \diagdown \end{array} \text{C}=\ddot{\text{N}}-\text{NH}_2$	hydrazone
-NHPh	H ₂ ̈N-NHPh	$\begin{array}{c} \diagup \\ \diagdown \end{array} \text{C}=\ddot{\text{N}}-\text{NHPh}$	phenylhydrazon
-NHCONH ₂	H ₂ ̈N-NH- $\overset{\text{O}}{\parallel}$ C-NH ₂	$\begin{array}{c} \diagup \\ \diagdown \end{array} \text{C}=\ddot{\text{N}}-\text{NH}-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}_2$	semicarbazone

Carbonyl condensation reactions are often carried out in weakly basic or weakly acidic environment.