

I. Enol and enolate formation

Enol formation is acid-catalyzed and **enolate** formation is base catalyzed, and both mechanism allow for reactions at the carbon α to the carbonyl. Under acid conditions the enol is normally present in very small concentration. Enolate formation can be made easier by increasing the acidity of the α -hydrogens e.g using a diketone such as 2,4-pentadione

Acid-catalyzed Reactions :

- (i) α -halogenation- involves reaction of the enol with the halogen, X_2 , to yield an α -halogenated ketone.
- (ii) Hell-Volhard-Zelinski- this involves a) reaction of a carboxylic acid with PBr_3 to form an acyl bromide b) formation of an enol and its bromination and c) hydrolysis of the acyl bromide back to the carboxylic acid to finally yield an α -brominated carboxylic acid. Base-catalyzed Reactions :

Base-catalyzed Reactions :

- (iii) α -halogenation- reaction of a carbonyl with a base such as ^-OMe and X_2 .
- (iv) alkylation- This involves reaction of the enolate anion with an alkyl halide, preferably an unhindered 1° halide, via an S_N2 reaction to give carbon-carbon bond formation at the α -carbon. One can a) either use a base such as ^-OMe and react the enolate as it forms or b) use a very strong base such as LDA (lithium diisopropylamide) or KH , completely form the enolate salt, and then react the enolate salt with the alkyl halide. With unsymmetrical ketones we can get the issue of **kinetic** versus **thermodynamic** control of the reaction.
- (v) Malonic ester synthesis - involves reaction of $CH_2(COOEt)_2$ in base with an alkyl halide :

$$R-X \rightarrow R-CH_2-COOH$$
- (vi) Acetoacetic ester synthesis - involves reaction of CH_3COCH_2COOEt in base with an alkyl halide :

$$R-X \rightarrow R-CH_2-COCH_3$$

II. Condensation Reactions

pages : 937-949, 955-958, 960-963

These reactions involve the nucleophilic addition of an enolate to a carbonyl, often followed by the loss of a water molecule to give the α,β -unsaturated ketone product.

- (i) Aldol Condensation- condensation reaction of aldehydes /ketones with following features:
 - a) reversible reaction yielding a β -hydroxy ketone (**Aldehyde+alcohol**)
 - b) can be catalyzed by either acid or base
 - c) can be **self** condensation or, if two reactants are available, **crossed**
 - d) often followed by loss of H_2O to give the stable, conjugated **enone**
 - e) **aldol cyclizations** can occur to yield 5 or 6 membered rings
- (ii) Michael Reaction- reaction of an enolate at the β -carbon of an α,β -unsaturated ketone.
- (iii) Robinson Annulation- involves a) the **michael** reaction of an enolate anion at the β -carbon of an enone followed by b) generation of a second enolate and **aldol** condensation with finally c) loss of water to give the formation of a **cyclic enone**.