

1. Aldol Reaction (Section 19.2) The aldol reaction involves nucleophilic addition of the enolate anion of one aldehyde or ketone to the carbonyl group of another aldehyde or ketone. The product of an aldol reaction is a β-hydroxyaldehyde or a β-hydroxyketone. An aldol reaction can be base catalyzed or acid catalyzed. If base is regenerated at the end of the reaction, it is base catalyzed, and if acid is regenerated, it is acid catalyzed. In both reactions, one or two new chiral centers are often created, leading to racemic products unless a starting aldehyde, ketone, or catalyst is chiral and present as a single enantiomer.

(a racemic mixture of four stereoisomers)

3. Claisen Condensation (Section 19.3A) The product of a Claisen condensation is a β -ketoester. Condensation occurs by nucleophilic acyl substitution in which the attacking nucleophile is the enolate anion of an ester. The Claisen condensation mechanism involves reaction of one ester molecule with base to form an enolate anion, which reacts as a nucleophile with another molecule of ester to give a tetrahedral carbonyl addition intermediate, in which the RO⁻ group is lost to give a β -ketoester, which is deprotonated at the α position by the RO⁻.

$$OEt \xrightarrow{1. EtO^-Na^+} OEt + EtOH$$
(racemic)

Acetoacetic Ester Synthesis (Section 19.6) This sequence is useful for the synthesis of monosubstituted and disubstituted acetones.

O
$$\begin{array}{c}
1. \text{ EtO}^{-}\text{Na}^{+} \\
2. \text{ CH}_{2} = \text{CHCH}_{2}\text{Br} \\
3. \text{ NaOH, H}_{2}\text{O} \\
\hline
4. \text{ HCl, H}_{2}\text{O} \\
5. \text{ heat}
\end{array}$$

Ethyl acetoacetate

A monosubstituted acetone

8. Malonic Ester Synthesis (Section 19.7) This sequence is useful for the synthesis of monosubstituted and disubstituted acetic acids.

COOEt
$$\begin{array}{c}
1. \text{ EtO}^{-}\text{Na}^{+} \\
2. \text{ CH}_{2} = \text{CHCH}_{2}\text{Br} \\
3. \text{ NaOH, H}_{2}\text{O} \\
\hline
4. \text{ HCl, H}_{2}\text{O} \\
5. \text{ heat}
\end{array}$$
COOH

Diethyl malonate

A monosubstituted acetic acid