A useful carbon-carbon bond-forming reaction known as the **Aldol Reaction** is yet another example of electrophilic substitution at the alpha carbon in enolate anions. The fundamental transformation in this reaction is a dimerization of an aldehyde (or ketone) to a beta-hydroxy aldehyde (or ketone) by alpha C–H addition of one reactant molecule to the carbonyl group of a second reactant molecule. Due to the carbanion like nature of enolates they can add to carbonyls in a similar manner as [Grignard reagents](https://en.wikipedia.org/wiki/Grignard_reagent). For this reaction to occur at least one of the reactants must have α hydrogens.

### General Aldol reaction

![General Aldol reaction](image)

### Going from reactants to products simply

![Going from reactants to products simply](image)

### Example 1: Aldol Reactions

1. \[
\begin{align*}
2 \text{H}_3\text{C}-&\text{C}=\text{O} \\
&\overset{\text{NaOH}}{\longrightarrow} \\
&\text{H}_3\text{C}-\text{C}(\text{H})\text{H}
\end{align*}
\]

2. \[
\begin{align*}
2 \text{H}_3\text{C}-\text{C}=\text{C}-\text{CH}_3 &\overset{\text{NaOH}}{\longrightarrow} \\
&\text{H}_3\text{C}-\text{C}(\text{H})\text{H}
\end{align*}
\]

### Aldol Reaction Mechanism

A three step mechanism:

**Step 1**: Enolate formation
Step 2: Nucleophilic attack by the enolate

Step 3: Protonation

Aldol Condensation: the dehydration of Aldol products to synthesize α, β unsaturated carbonyl (enones)

The products of aldol reactions often undergo a subsequent elimination of water, made up of an alpha-hydrogen and the beta-hydroxyl group. The product of this \(\beta\)-elimination reaction is an \(\alpha,\beta\)-unsaturated aldehyde or ketone. Base-catalyzed elimination occurs with heating. The additional stability provided by the conjugated carbonyl system of the product makes some aldol reactions thermodynamically and mixtures of stereoisomers (E & Z) are obtained from some reactions. Reactions in which a larger molecule is formed from smaller components, with the elimination of a very small by-product such as water, are termed Condensations. Hence, the following examples are properly referred to as aldol condensations. Overall the general reaction involves a dehydration of an aldol product to form an alkene:

**Figure:** General reaction for an aldol condensation

Going from reactants to products simply
Example 2: Aldol Condensation

Aldol Condensation Mechanism

1) Form enolate

2) Form enone

When performing both reactions together always consider the aldol product first then convert to the enone. Note! The double bond always forms in conjugation with the carbonyl.

Example 3

Intramolecular aldol reaction

Molecules which contain two carbonyl functionalities have the possibility of forming a ring through an intramolecular aldol
reaction. In most cases two sets of $\alpha$ hydrogens need to be considered. As with most ring forming reaction five and six membered rings are preferred.

![Reaction Diagram]

As with other aldol reaction the addition of heat causes an aldol condensation to occur.

![Condensation Diagram]

**Mixed Aldol Reaction and Condensations**

The previous examples of aldol reactions and condensations used a common reactant as both the enolic donor and the electrophilic acceptor. The product in such cases is always a dimer of the reactant carbonyl compound. Aldol condensations between different carbonyl reactants are called crossed or mixed reactions, and under certain conditions such crossed aldol condensations can be effective.

**Example 4: Mixed Aldol Reactions**

![Mixed Aldol Reaction]

The success of these mixed aldol reactions is due to two factors. First, aldehydes are more reactive acceptor electrophiles than ketones, and formaldehyde is more reactive than other aldehydes. Second, aldehydes lacking alpha-hydrogens can only function as acceptor reactants, and this reduces the number of possible products by half. Mixed aldols in which both reactants can serve as donors and acceptors generally give complex mixtures of both dimeric (homo) aldols and crossed
aldols. Because of this most mixed aldol reactions are usually not performed unless one reactant has no alpha hydrogens.

The following abbreviated formulas illustrate the possible products in such a case, red letters representing the acceptor component and blue the donor. If all the reactions occurred at the same rate, equal quantities of the four products would be obtained. Separation and purification of the components of such a mixture would be difficult.

\[
\text{A} \text{CH}_2\text{CHO} + \text{BCH}_2\text{CHO} + \text{NaOH} \rightarrow \text{A}–\text{A} + \text{B}–\text{B} + \text{A}–\text{B} + \text{B}–\text{A}
\]

The aldol condensation of ketones with aryl aldehydes to form \(\alpha,\beta\)-unsaturated derivatives is called the Claisen-Schmidt reaction.

Example 4: Claisen-Schmidt Reaction

![Claisen-Schmidt Reaction Diagram]

Contributors

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Further Reading

Khan Academy

The Aldol Reaction

Crossed Aldol Reactions

Wikipedia

The Aldol Reaction

Carey 5th Ed Online

The Aldol Reaction
Chemtube3D

Lithium Aldol Reaction