Aldol Condensation Notes

History and Application
Condensation reactions are molecular transformations that join together two molecules to produce a larger molecule and also a smaller molecule (usually water, hence the name condensation). Aldol reactions join two carbonyl containing molecules together forming a new carbon-carbon bond between the alpha carbon of one molecule and the carbon of the carbonyl of the second molecule. This forms a beta hydroxy carbonyl compound. If this product undergoes a subsequent dehydration, then an aldol condensation reaction has taken place.

\[
\begin{align*}
\text{A} & \quad \text{B} \\
\text{O} & \quad \text{O} \\
\text{OH} & \quad \text{O}
\end{align*}
\]

\[\rightarrow\]

\[
\begin{align*}
\text{A} & \quad \text{B} \\
\beta\text{-hydroxy carbonyl} & \quad \alpha,\beta\text{-unsaturated carbonyl} \\
\text{aldol reaction product} & \quad \text{aldol condensation product}
\end{align*}
\]

Condensation reactions are a convenient way to synthesize a functionalized larger molecule from smaller starting reagents. Condensation reactions are often utilized in the manufacture of pharmaceuticals, coatings and plastics. Plexiglass ® is polymerized methyl methacrylate. Methylmethacrylate is made via a crossed aldol reaction between propionaldehyde and formaldehyde.

Safety considerations for this experiment include:
Sodium hydroxide, the catalyst, is highly corrosive. If you notice that your hand or any other part of your exposed skin is slippery, wash thoroughly with water.
All of the organic compounds involved in this experiment are at least slightly toxic, and acetone, ethanol, and ethyl acetate are highly flammable. Handle them with the usual precautions. Have no open flames in the laboratory.
You will use a hot plate and a Mel-Temp apparatus during this experiment. As you know by now, portions of these become very hot during normal use. Handle these items with care, and don't touch the hot parts. They use electricity for heating; do not use water or other solvents carelessly around them. If the wires on any electrical apparatus are frayed, the shock and fire hazards are multiplied; do not use the apparatus.

Terminology relating to aldol reactions and condensations:
Condensation Reaction: Combination of two or more chemicals to produce a larger molecule and a small side product molecule. Often, but not always this small molecule is water.
Aldol Reaction: Two aldehydes or one aldehyde and one ketone reacting together via an enolate ion to form a larger \(\beta\)-hydroxy carbonyl molecule.
Aldol Condensation: When the \(\beta\)-hydroxy carbonyl product of an aldol reaction dehydrates and forms an \(\alpha\beta\)-unsaturated carbonyl molecule.
Conjugation: Alternating double and single bonds
Dehydration: Removing a proton from one carbon and a hydroxyl group from an adjacent atom, to form a water molecule and a double bond.

1. The reaction that is being carried out today combines two equivalents of a benzaldehyde with one equivalent of a ketone in the presence of a base to form a highly conjugated product. The sodium hydroxide base is a catalyst. Sodium hydroxide forms the enolate ion which acts as the nucleophile. Ethanol is the solvent.

2. Both starting materials, the ketone and the aldehyde, are clear colorless liquids. The product contains at least 17 carbons and is not soluble in water. All products are highly colored solid at room temperature. Look at the structure of the product. Why do you suppose it is colored? (Reread sections 16.11 & 16.12 of Klein for the answer.) Be sure to observe and document changes you see over the course of the reaction in your lab notebook.

3. The product will be isolated via vacuum filtration. A filter adapter must be inserted between Buchner funnel and filter flask or insufficient vacuum will result. Filter flasks (also called suction or vacuum flasks) tip easily. Always clamp flask. Remember to place filter paper in bottom of Buchner so that it covers all of the holes, wet paper with solvent being used (in this case ethanol or water), and turn on vacuum to seat filter paper. After vacuum has been engaged, you may pour in material to be filtered. To do this out of sequence will result in product being lost to bottom of suction flask. After material has been sufficiently dried, break suction either by removing Buchner or disconnecting hose, before turning vacuum off. Below is a diagram showing the suction filtration set-up.
4. A recrystallization of the product will be carried out. If you have forgotten the steps involved in recrystallization then reread the on-line notes from 2230L concerning recrystallization. The main purpose of a recrystallization is to purify solid compounds by removing impurities. This causes the mass and percent yield to decrease. Some desired compound is always lost when carrying out a recrystallization, hence percent yield will be further lowered. A successful recrystallization will have a narrower melting point range that is closer to the literature value than the starting material.

5. Choose the recrystallization solvent based on your aldehyde and ketone.

<table>
<thead>
<tr>
<th>Aldehyde</th>
<th>Ketone</th>
<th>Ketone</th>
<th>Ketone</th>
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<tbody>
<tr>
<td>I.</td>
<td>Ethyl Acetate</td>
<td>Ethyl Acetate</td>
<td>90% ethanol/10% Acetone</td>
</tr>
<tr>
<td>II.</td>
<td>Ethanol</td>
<td>Ethyl Acetate</td>
<td>90% ethanol/10% Acetone</td>
</tr>
<tr>
<td>III.</td>
<td>90% ethanol/10% Acetone</td>
<td>90% ethanol/10% Acetone</td>
<td>90% ethanol/10% Acetone</td>
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6. To carry out the recrystallization, place a 400 mL beaker with about 3 inches of water and a boiling stone on a hot plate. Add a clean test tube with a boiling chip and 1/2 to 2/3 full of recrystallization solvent in water to heat. Ensure the water temperature is below the boiling point of the solvent. (Ethyl Acetate b.p. = 77°C, Ethanol b.p. = 78°C, Acetone b.p. = 56°C, Toluene b.p. = 110°C) Place solid to be recrystallized in clean test tube along with a stir rod. The set up will look like the following.

With constant stirring, pipette hot solvent from test tube to test tube containing solid. Continue to add solvent with stirring until all solid is dissolved. Remove from test tube from water bath. Let sit undisturbed on counter top to form crystals. When at room temperature, place in ice/water slush. Recover the solids by vacuum filtration.
7. Literature melting points of possible products.

\[ \begin{align*}
X = \text{CH}_3, & \quad 170^\circ \text{C}, \quad X = \text{CH}_3\text{-O}^-, \quad 159^\circ \text{C} \quad X = \text{H}, \quad 118^\circ \text{C}, \\
X = \text{CH}_3, & \quad 235^\circ \text{C}, \quad X = \text{CH}_3\text{-O}^-, \quad 212^\circ \text{C}, \quad X = \text{H}, \quad 189^\circ \text{C}, \\
X = \text{CH}_3, & \quad 175^\circ \text{C}, \quad X = \text{CH}_3\text{-O}^-, \quad 129^\circ \text{C}, \quad X = \text{H}, \quad 113^\circ \text{C},
\end{align*} \]

8. The hydrogen attached to a carbon adjacent to a carbonyl (alpha position) has enhanced acidity with a pKa of about 20 or \(10^{30}\) times more acidic than a typical hydrocarbon having a pKa of \(~50\). The anion which forms on the carbon alpha to a carbonyl is called an enolate ion. The enolate ion is more stable than many other carbanions because it has two resonance forms. Remember ARIO from Klein 3.4-3.5. The hydrogen attached to a carbonyl of an aldehyde is not acidic. An aldehyde hydrogen has a pKa similar to that of a typical hydrocarbon.

\[ \begin{align*}
\text{pKa} & \approx 55 \\
\text{pKa} & \approx 45
\end{align*} \]

9. The reaction mechanism for the aldol condensation between acetone and benzaldehyde is below. The first step of the mechanism is the formation of an enolate ion by sodium hydroxide.
abstracting a hydrogen from a carbon in the alpha position to a carbonyl. Remember this hydrogen has an enhanced acidity.

\[
\text{H}_2\text{C} - \text{CH} + \text{Na}^+ \rightarrow \text{H}_2\text{C} - \text{CHO} + \text{Na}^+ \quad + \text{H}_2\text{O}
\]

The enolate ion then acts as a nucleophile and attacks the partially positive carbon of the carbonyl on the benzaldehyde. This anion then picks up a proton from a water and forms a beta-hydroxycarbonyl compound.

If the reaction stopped here it would be a single aldol reaction product. It does not stop, but instead undergoes a dehydration to form the stable conjugated \(\alpha\beta\)-unsaturated carbonyl product. The new double bond is in conjugated with the aromatic ring and imparts added stability. The resulting product, 4-phenyl-3-buten-2-one, is the result from a single aldol condensation reaction between benzaldehyde and acetone.

Our reaction today does not stop here, but instead carries out the whole reaction sequence again on the other carbon of the acetone. First the alpha carbon is deprotonated and an enolate ion anion forms.
Then the enolate nucleophile attacks the electrophilic carbon of the carbonyl, forming a new carbon carbon bond and a beta hydroxyl carbonyl. The hydroxide ion picks up a hydrogen from water.

In an identical fashion to earlier, the $\beta$-hydroxy carbonyl dehydrates and forms a double bond.
The product is highly conjugated, (Klein 16.12) and like many highly conjugated systems, it absorbs light in the visible range and is therefore colored.

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