Aldol Condensation Notes

History and Application

Many aldehydes have distinctive strong odors. Benzaldehyde smells like cherries and is found naturally in many fruits such as peaches, grapes, and cranberries. It is used as an artificial flavoring in many foods at low levels but is toxic at high levels. The lethal human dosage of benzaldehyde is estimated to be approximately 2 ounces (~ 50 g). Often chemicals that may be consumed safely at one concentration level have serious harmful side effects at another concentration.

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 hydroxyl carbonyl compound. If this product undergoes a subsequent dehydration, then an aldol condensation reaction has taken place.

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: A chemical reaction in which a small molecule is produced as a side product. 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 β-hydroxy carbonyl molecule.

Aldol Condensation: When the β-hydroxy carbonyl product of an aldol reaction dehydrates and forms an αβ-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 benzaldehyde with one equivalent of acetone in the presence of a base to form the product 1,5-diphenyl-1,4-pentadiene-3-one. The common name of this material is dibenzylactone.

2. This fairly complex reaction proceeds at a fast rate at room temperature. Both starting materials, acetone and benzaldehyde, are clear colorless liquids. The product is a highly colored solid at room temperature. Look at the structure of the product. Why do you suppose it is colored? (Reread sections 17.11-17.12 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. Suction (or vacuum or filter) 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 water), and turn on vacuum to seat filter paper. After this is done you may pour in material to be filtered. To do this out of sequence will frequently 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. Here is the apparatus for suction filtration using a Buchner funnel.
4. A recrystallization of the product will be carried out. The solvent that will be used is ethyl acetate. 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. When impurities are removed, the mass decreases and the percent yield will lower. Some desired compound is always lost when carrying out a recrystallization, hence percent yield will be further lowered. If a recrystallization was successful, the product will have a narrower melting point range that is closer to the literature value than the starting material.

5. To carry out the recrystallization, place a 400 mL beaker with about 2.5 inches of water on a hot plate. Add a clean test tube with a boiling chip and 2/3 full of ethyl acetate in water to heat. The ethyl acetate boils at 77°C, so be sure the water is not too hot. Place solid to be recrystallized in 50 mL E. flask and hold in hot water. With constant shaking, pipette ethyl acetate from test tube to E. flask until all of the solid in E. flask has dissolved. The set up will look like the following.

As soon as all of the solid has dissolved, remove small Erlenmeyer flask from water bath. Let sit undisturbed on counter top to form crystals. Placing in ice will further reduce the solubility of the solid and increase mass of solid recovered.

6. A percent yield for both the crude and the recrystallized product will have to be calculated. This reaction is the first time other than a 1 : 1 :1 stoichiometry has been encountered in this class. Pay close attention to the stoichiometry when calculating the theoretical maximum amount of product that can form from both
the benzaldehyde and the acetone. (The sodium hydroxide is a catalyst not a reactant.)

7. The hydrogen attached to a carbon in the alpha position (adjacent) to a carbonyl has enhanced acidity. The anion is called an enolate ion. The enolate ion is more stable than many other carbanions because it has two resonance forms.

8. 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.

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. This reaction does not stop here. It readily undergoes a dehydration to form the stable conjugated αβ-unsaturated carbonyl product. The new double bond in conjugated with the aromatic
ring and imparts added stability. The resulting product, 4-phenyl-3-butene-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.

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 above, the β-hydroxy carbonyl dehydrates and forms a double bond.

\[
\text{OH} \quad \text{H} \\
\text{OH} \quad \text{H} \\
\text{HO} \\
\text{O} \\
\text{OH} \\
\text{OH}
\]

The final product is called 1,5-diphenyl-2,4-pentadiene-3-one or dibenzalacetone.

9. Here are two sample problems. Answers, with hints, will be given later.

   a) Predict the product of the aldol **condensation** of acetophenone:

   \[
   \begin{array}{c}
   \text{CCH}_3 \\
   \text{O} \\
   \text{NaOH} \\
   \end{array}
   \]

   b) Predict the product of the aldol **reaction** shown. (Again, no water is produced).

   \[
   \begin{array}{c}
   \text{CH}_3\text{CH}_2\text{C-H} \\
   \text{O} \\
   \text{NaOH} \\
   \end{array}
   \]
Answers:

a) To predict the product of the aldol condensation of acetophenone, it helps to be able to figure out the mechanism. This is the reaction:

\[
2 \begin{array}{c} 
\text{CCH}_3 \\
\text{O} \\
\hline
\end{array} 
\xrightarrow{\text{NaOH}} 
\begin{array}{c} 
\text{CCH}_3 \\
\text{O} \\
\hline
\end{array} 
\]

The mechanism is predictable. First, make the enolate anion; then add the enolate anion to the unreacted acetophenone molecule; then perform an acid-base reaction to put a proton on the negatively charged oxygen, and finally eliminate a water molecule.

\[
\begin{array}{c} 
\text{CCH}_3 \\
\text{O} \\
\hline
\end{array} 
+ \text{OH} \rightarrow \begin{array}{c} 
\text{CCH}_2 \\
\text{O} \\
\hline
\end{array} 
+ \text{H}_2\text{O}
\]

\[
\begin{array}{c} 
\text{CCH}_2 \\
\text{O} \\
\hline
\end{array} 
+ \begin{array}{c} 
\text{CCH}_3 \\
\text{O} \\
\hline
\end{array} 
\rightarrow \begin{array}{c} 
\text{CCH}_2\text{C} \\
\text{O} \\
\hline
\end{array} 
+ \text{OH}
\]

Which means that the answer (the product) is:

\[
2 \begin{array}{c} 
\text{CCH}_3 \\
\text{O} \\
\hline
\end{array} 
\xrightarrow{\text{NaOH}} 
\begin{array}{c} 
\text{CCH}_3 \\
\text{O} \\
\hline
\end{array} 
\begin{array}{c} 
\text{CCH}_3 \\
\text{O} \\
\hline
\end{array} 
+ \text{H}_2\text{O}
\]

b) The key to predicting the product of this aldol reaction is a knowledge of the mechanism. Are you surprised to hear that?
The mechanism begins with an acid-base reaction to form the enolate anion. The anion with the negative charge on the end of the molecule opposite the carbonyl group has no resonance forms, is unstable, and therefore is not formed. The mechanism continues with nucleophilic addition to the carbonyl group, and finishes with another acid-base reaction. Since it's an aldol reaction and not a condensation, there is no elimination step.

The answer (you were asked to predict the product) is:

For more examples please see your lecture textbook.

---


