

Experiment 3. Condensation Reactions of Ketones and Aldehydes: The Aldol Condensation Reaction.

References: Brown & Foote, Chapters 16, 19, 23

INTRODUCTION:

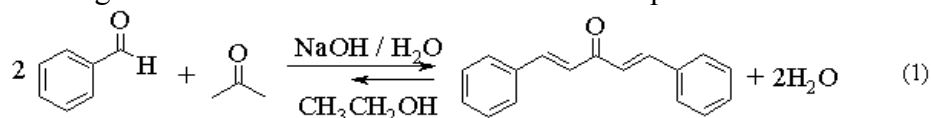
This experiment continues the saga of carbon-carbon bond formation. In terms of "real" chemistry as practiced in industry or by nature in biological systems, it is important to be able to change the molecular weight of a system by making and/or breaking carbon-carbon bonds. This experiment illustrates one general way this can be done using an **aldol reaction**. We will characterize the product by examining its UV/VIS properties.

BACKGROUND:

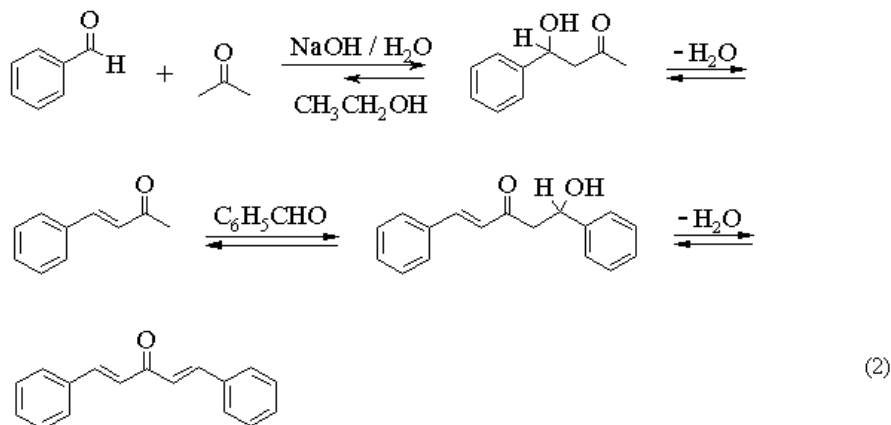
Aldol Condensation

The aldol reaction is a very general and mild method of making carbon-carbon bonds. It is an example of a *condensation* reaction, which always proceeds in two steps: nucleophilic addition followed by elimination. The aldol reaction involves condensation of two carbonyl compounds, one of which serves as the nucleophile (much like a Grignard reagent) and the other as the electrophile in the first step.

The overall transformation that you will carry out is shown in the following equation. Note that this involves making two carbon-carbon bonds and thus two separate aldol reactions.



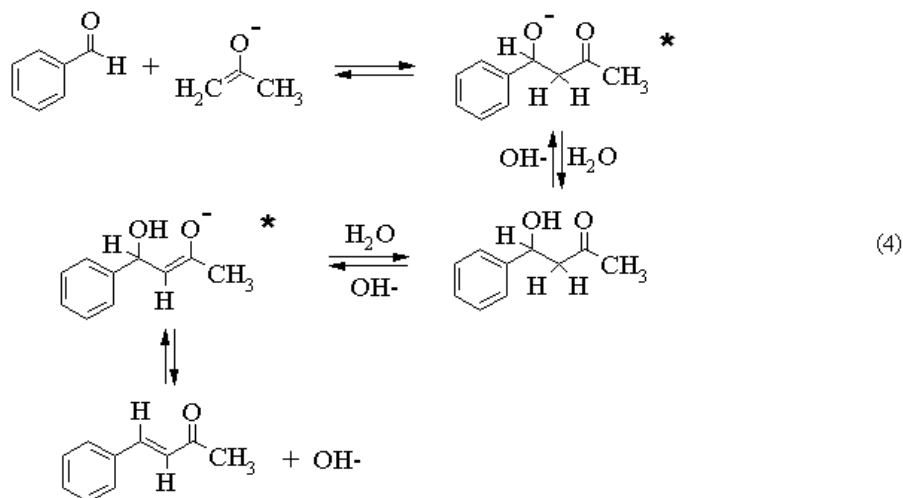
The above transformation involves some intermediates which are not shown in equation 1. These are the initially formed β -hydroxy-ketones shown in the scheme below (eq. 2). In some aldol reactions the β -hydroxy-carbonyl compounds are the major products. However, as you will see, all the reactions are reversible and, in the particular case you are studying, the equilibrium constant lies in favour of the unsaturated product, stabilized by conjugation. This conjugation is also what gives this ketone (and others) its colour.



The reaction scheme shown thus far simply records the neutral molecules involved in the transformation. In order to understand what is going on we need to examine some of the ionic intermediates. This is shown in the series of equilibria shown below (eqs. 3 & 4). Please note that resonance structures of the various ionic intermediates are not shown.



For this reaction to work, the one serving as the nucleophile must have hydrogens on the carbon adjacent to the carbonyl group. As you know, these " α -hydrogens" are rendered somewhat acidic by the C=O group. Removing one of these hydrogens by reaction with a base generates an *enolate* ion (product of eq. 3), which is a potent carbon nucleophile (reactant in eq. 4).



In order to simplify the mechanism only one half of the reaction is shown.

You should also be aware that there are a variety of other reactions occurring simultaneously with the ones shown above.

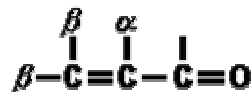
Purifying the product

Occasionally, a single suitable solvent for recrystallization can not be found. In this case, the use of *solvent pairs* is recommended. A useful solvent pair consists of two miscible solvents having different solvent powers (one has "good" solubility of the compound and the other has "poor" solubility). The compound is dissolved in just enough "good" solvent which has been heated until near the boiling point. Then the "poor" solvent is added drop wise until the solvent limit is reached (cloudiness is observed). A few drops of the "good" solvent is added to yield a clear solution (the solvent limit is just above the solubility of the compound in the hot solvent). As the solution cools and the solvent limit is lowered, crystals should start to form (the concept of different solubility at different temperatures is similar to the previous recrystallizations).

Woodward's Rules for Enones

The conjugation of a carbonyl group with a double bond leads to an intense absorption ($\epsilon = 8,000$ to $20,000$) corresponding to a $\pi \rightarrow \pi^*$ transition of the carbonyl group. Woodward examined the ultraviolet spectra of many enones and generated a set of empirical rules to predict the wavelength that the $\pi \rightarrow \pi^*$ transition occurs.

Values for Calculation of Enone Absorption



Base Value:

Six-membered ring or acyclic parent enone	= 215 nm
Five-membered ring parent enone	= 202 nm

Increments for:

Double-bond-extending conjugation	30
Alkyl group	α 10
	β 12

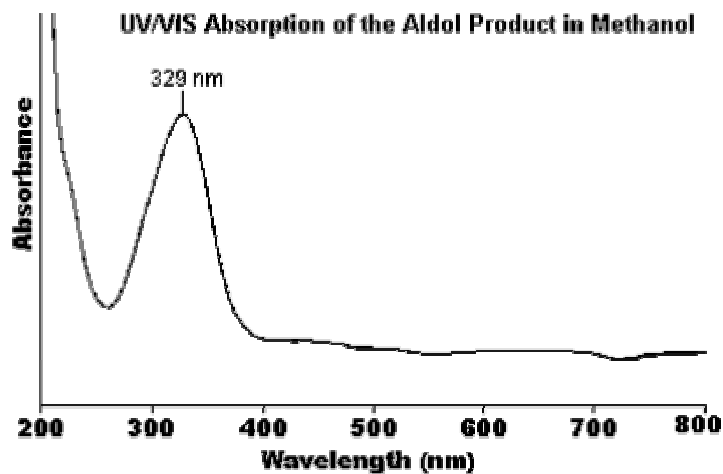
Polar Groups:

-OH	α 35
	β 30
-OCOCH ₃	α, β 6
-OCH ₃	α 35
	β 30
-Cl	α 15
	β 12
-Br	α 25
	β 30
-NR ₂	β 30
Exocyclic double bond	5
Homocyclic diene component	39
Solvent Correction	Variable

Applying these rules to our compound:

Acyclic parent enone	215 nm
Alkyl group (β)	12
Double-bond-extending conjugation (3 x 30)	90
Exocyclic double bond	<u>5</u>
	322 nm

The actual, observed absorption is 325 nm in hexane and 329 in Methanol, as seen in the following spectrum.



Beer-Lambert Law

The extent of absorption of UV/VIS radiation is proportional to the number of molecules undergoing absorption.

The relationship between absorbance (A), concentration, and the length of the sample path (l) is known as the *Beer-Lambert Law*.

$$\text{Beer-Lambert Law: } A = \epsilon [\text{cmpd}] l$$

where A is absorbance, ϵ is the *molar absorptivity* ($\text{M}^{-1}\text{cm}^{-1}$), $[\text{cmpd}]$ is the concentration of the compound being characterized, and l is the diameter of the sample cuvette (1.1 cm in our case). The molar absorptivity (ϵ) is a characteristic property of a compound and can range from 0 to $10^6\text{M}^{-1}\text{cm}^{-1}$.

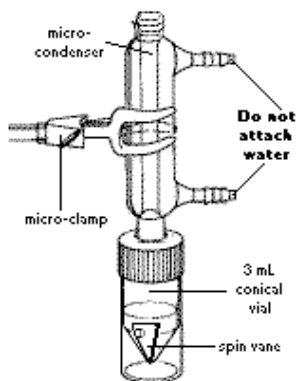
PRE-LAB PREPARATION:

1. What is the name of the product formed in equation 1?
2. Why might the unsaturated products be thermodynamically preferred over their precursor alcohols (see eq. 2)?
3. Review each ionic intermediate (marked with an * in eq. 4) and draw out the resonance structures where appropriate.

EXPERIMENTAL PROCEDURE:

Part A: Aldol Condensation

It is important in this reaction to follow precisely the instructions on the amount of materials used. Remember that acetone is a very volatile chemical. You should not let the vessel containing acetone sit around before you add the other reagents.



1. Reaction of Acetone with Benzaldehyde.

- a) Use a conical vial (3 mL size) fitted with a spin vane and a water condenser (without cooling water in the condenser). Use the magnetic stirrer in this experiment, not the heater-stirrer.
- b) Place in the vial benzaldehyde (294 mg; 280 μL), acetone (80.4 mg; 100 μL) and then the sodium hydroxide solution (1 mL). (The sodium hydroxide solution provided is made up using a mixture of water (57%) and ethanol (43%).)
- c) Stir the contents of the vial at room temperature for 30 minutes. You should observe the formation of a precipitate during this reaction period. Record the colour of the precipitate.

2. Isolating the Product

- a) Filter the product under vacuum using the Hirsch funnel. Make sure you transfer all of the solid into the funnel.
- b) Wash the product with water (several washes with 1 mL portions of distilled water) and check

that the filtrate from the final wash is near neutral using indicator paper. If the filtrate is still basic then continue to wash the product until all of the sodium hydroxide is removed.

- c) Dry the product by leaving it as a pressed down cake on the Hirsch funnel while you pull air through it using the aspirator.
- d) Dry the product as thoroughly as possible and weight it.
- e) Calculate the % yield of the crude product.

3. Purifying the Product

The product will be recrystallized using ethanol and water as *solvent pairs*.

- a) Put the unpurified product in a clean beaker (keep a small portion aside for the MP determination).
- b) Add a little more than enough hot ethanol ("good" solvent) to dissolve the product.
- c) Then water (the "poor" solvent) is added drop wise *just* until cloudiness is observed.
- d) Add a few drops of ethanol to yield a clear solution (solution must still be hot at this point) and then allow the solution to cool slowly.
- e) Collect the crystals by vacuum filtration using the Hirsch funnel.
- f) Dry the product as thoroughly as possible and re-weight it.
- g) Calculate the % yield of the purified product.

4. Characterization of the Product

- a) Obtain and label an IR spectrum of your recrystallized product.
- b) Determine and record the melting point of your crude and recrystallized products.
- c) Weight out approx. 0.01g (record to 3 decimals) of your final product and put into a 25 mL round bottom flask. Add 10.0 mL of absolute methanol. With a hollow stopper in the flask, swirl the solution to dissolve the solid. NOTE: If not all the solid dissolves, add more methanol, but record how much you add.
- d) Calculate the concentration of this solution.
- e) This concentration will give an absorption that is off the scale, so we will dilute it by a factor of 400 (divide your calculated concentration by 400). Take 10 μ L of your solution, using the syringe supplied by your TA, and expel it into a clean 5 mL conical vial. Add methanol up to the 4 mL mark.
- f) Dump the diluted solution into a cuvette and measure the absorption value at 329 nm using the Genesys 20 spectrophotometer.
- g) Calculate the molar absorptivity of your compound.
- h) Dispose your product in the SOLID WASTE jar provided.