

23. The Aldol Condensation: Synthesis of Dibenzalacetone

A. Introduction

In an aldol condensation, two molecules of aldehyde or ketone are joined together along with the loss of water. For example, in the aldol condensation shown in figure 1, two molecules of ethanal are reacted to produce an α,β -unsaturated aldehyde and water.



Figure 1. Aldol Condensation of Ethanal

To understand the aldol condensation, we must first understand the acidity of α -hydrogens, which are the hydrogen atoms directly attached to the α -carbon of a carbonyl compound. Depending on the particular carbonyl species, the pK_a of the α -hydrogen typically falls in the range of 17-25, which is quite acidic compared to a typical hydrocarbon. When a carbonyl compound containing α -hydrogen is subjected to a base, the compound will be deprotonated to give the conjugate base, which is called an enolate. Typical bases used to form an enolate are hydroxide (HO⁻) and ethoxide (EtO⁻). (Figure 2)

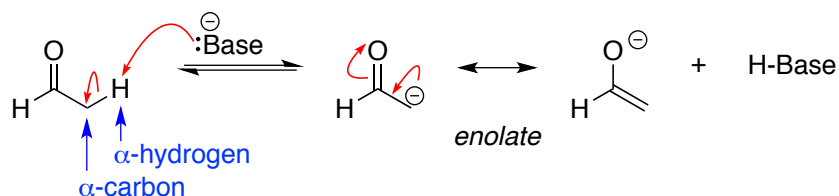


Figure 2. Enolate Formation

Once the enolate is formed, a carbon nucleophile is present in the reaction mixture. The next step parallels the addition of any nucleophile to a carbonyl compound (figure 3A). In the case of the ethanal enolate, once it is formed, it will react with a second molecule of ethanal present in the reaction mixture (figure 3B). The β -hydroxyaldehyde product contains an **aldehyde** and an **alcohol**, hence the name **aldol**.

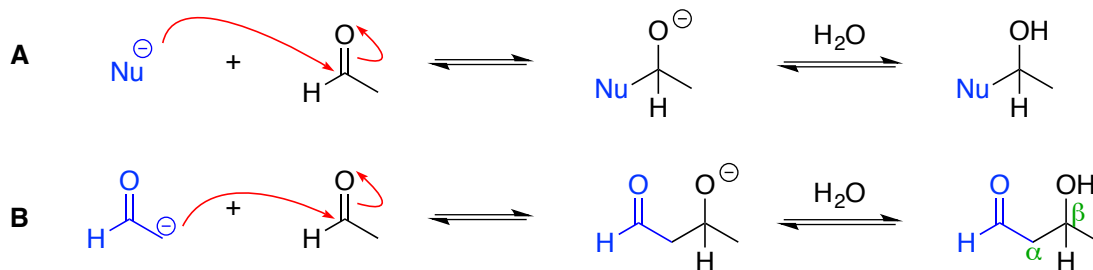


Figure 3. An Enolate as a Nucleophile

Under either acidic or basic conditions, the β -hydroxycarbonyl compound undergoes a **dehydration** to give an α,β -unsaturated carbonyl compound, the final product of the aldol

condensation. The driving force for this step is formation of a conjugated system. When a base is present, the base abstracts an α -proton to first form an enolate. Then, the hydroxyl group is eliminated to give the α,β -unsaturation as shown in figure 4. The net result of this step is the loss of water from the molecule, thus it is called a dehydration.

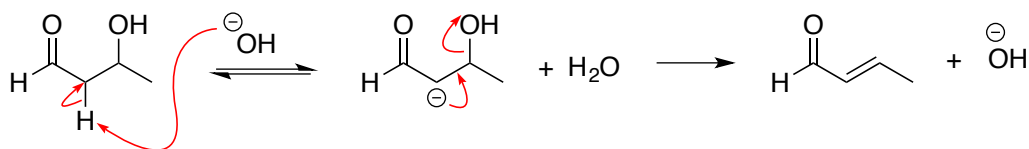


Figure 4. Dehydration Step of the Aldol Condensation

The aldol condensation is not limited to aldehydes. Ketones may also be used. In fact, it is possible to use two different carbonyl compounds to form a crossed aldol product. One limitation of the crossed aldol reaction is the fact that multiple products can form due to the presence of multiple different α -hydrogen. For example, as shown in figure 5, if a mixture of acetone and propanal is treated with base, two different nucleophilic enolates can form due to the presence of α -hydrogen on both acetone and propanal. Each of these nucleophilic enolates can react with both acetone and propanal to provide four different products. These products would be very difficult to separate making such a reaction synthetically useless.

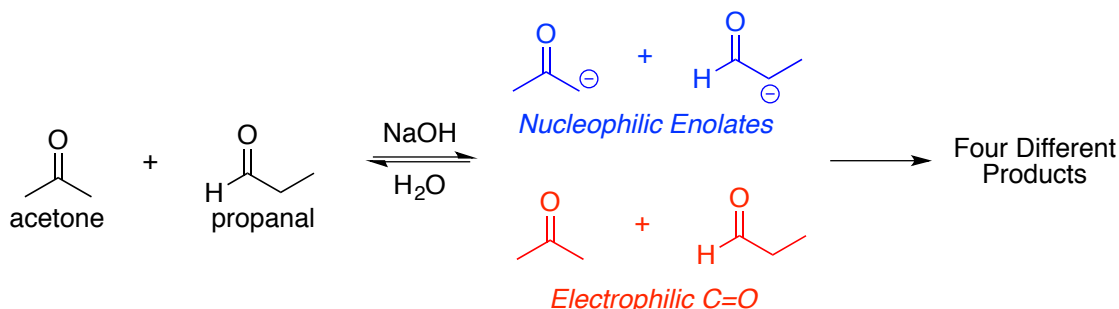


Figure 5. Limitation of the Crossed Aldol Condensation

There are a number of methods to work around the limitations of the crossed aldol condensation. One such method involves using one carbonyl compound that does not have any α -hydrogen, such as benzaldehyde and a second carbonyl compound, such as acetone, that has only one type of α -hydrogen. This limits the reaction to the formation of only one enolate. Additionally, since aldehydes are more reactive electrophiles than ketones, reaction of the enolate with benzaldehyde will occur more readily than self-condensation with another molecule of acetone. This specialized type of crossed aldol reaction is known as the **Claisen-Schmidt Reaction**.

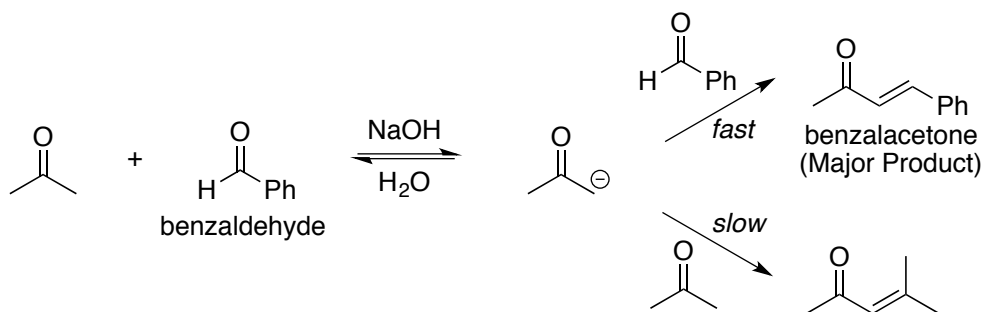


Figure 6. Claisen-Schmidt Reaction

The reaction shown in figure 6 involves the reaction of 1 equivalent of acetone with 1 equivalent of benzaldehyde to provide 1 equivalent of benzalacetone. If instead, two equivalents of benzaldehyde are used, a second aldol condensation can take place because benzalacetone contains acidic α -hydrogen. The final product of this reaction is dibenzalacetone as shown in figure 7.

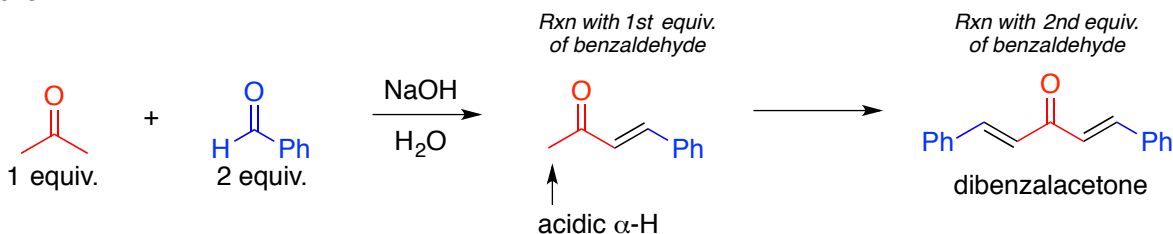


Figure 7. Claisen-Schmidt Reaction to Produce Dibenzalacetone

B. Experimental Procedure

In this experiment you will be performing the reaction shown in figure 7 to prepare dibenzalacetone. To prepare this product, it is critical that 2 equivalents of benzaldehyde be used in the reaction. A slight excess is okay, but you must not have a deficiency.

Reagent	Mol. Wt.	Density	Mass	Mmol	Equiv.
Benzaldehyde	106	1.04 g/mL			2
Acetone	58	0.791 g/mL			1
Aq. NaOH (10%)	40	--	0.5 mL*		-
Product					
Dibenzalacetone	234	--			

*Determination of an exact amount of NaOH is not necessary. 0.5 mL of a 10% aqueous solution should be sufficient.

Add 1 mL of ethanol to a small vial containing a screw cap and secure the cap. Weigh the vial and record this mass. Next, remove the cap and add seven drops of acetone to the vial. Replace the cap quickly and shake to affect mixing. Weigh the vial again and determine the mass of acetone added by subtraction. Record this mass in the reagent table above. Using this value, calculate the necessary mass of benzaldehyde.

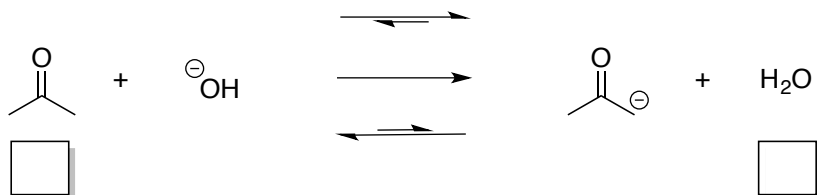
To a 3 mL conical vial containing a spin vane, add the calculated amount of benzaldehyde (a slight excess is okay). Transfer the acetone/ethanol solution to this vial via pipet. Place a septum and cap on the vial and commence stirring. Remove the cap and add 0.5 mL of 10% aqueous NaOH over a period of 5 min with stirring. Once NaOH addition is complete, cap the vial and allow it to stir rapidly for 25 min.

Dibenzalacetone will crash out of the solution as a solid during the course of the reaction. Collect this solid via Hirsch filtration and wash it several times with small portions of cold water. Allow the solid to air dry by continuing to apply the vacuum for 2-3 min. Recrystallize the solid by dissolving in 2 mL of hot ethanol. Allow the solution to cool slowly at room temperature and

then in an ice bath. Collect the crystals by Hirsch filtration. Calculate the yield, determine the melting point, and record an IR and $^1\text{H NMR}^a$ spectrum of the product.

C. Prelab Questions

- 1) The main mechanistic steps of the aldol condensation are shown in figures 2-4. Using this information, propose a complete electron pushing mechanism for the formation of dibenzalacetone from acetone and benzaldehyde.
- 2) Figure 5 describes the formation of 4 different aldol condensation products. Draw the structure for each of these products.
- 3) Is the enolate of ethanal or acetone formed more readily when reacted with ethoxide? *Hint: look up the pK_a 's for each molecule.*
- 4) Look up the pK_a for water and acetone and write these values in the boxes below each molecule in the provided reaction scheme. Considering this information, which of the three reaction arrows best describes enolate formation?



- 5) Considering the direction of the equilibrium from question 4, what do you think is the driving force for the aldol condensation?
- 6) Why is it necessary to measure out the acetone as a solution in ethanol? *Hint: look up the boiling point of acetone.*

D. Postlab Questions

- 1) Some aldol condensation reactions need to be heated to undergo the dehydration step. Explain why it was not necessary to heat the reaction that you performed in lab? *Think about what make the product especially stable.*
- 2) What important IR signals lead you to the conclusion that the reaction was successful? How would the IR spectrum be different if the reaction had stopped at benzalacetone?
- 3) Look up the literature melting point value for dibenzalacetone at www.sigmaaldrich.com. How does your experimental value compare?
- 4) Assign the $^1\text{H NMR}$ signals in the spectrum with each proton in dibenzalacetone. Which alkene proton is further downfield? Explain.

^a Your TA will obtain product from 1-2 students, record the $^1\text{H NMR}$ spectrum, and make enough copies to share with the entire class.