CHEM 322: CROSSED ALDOL CONDENSATION

Synthesis of Dibenzalacetone (1,5-Diphenyl-1,4-pentadien-3-one)

INTRODUCTION

In this experiment, you will perform a type of base-catalyzed crossed aldol condensation called the Claisen-Schmidt reaction. The aldol reaction is used extensively to synthesize new C-C bonds. In a crossed aldol synthesis, two different aldehydes or ketones (or one ketone and one aldehyde) react in the presence of dilute base to yield β-hydroxyaldehydes or β-hydroxyketones. In most base-catalyzed aldol reactions, the end product is an α,β-unsaturated aldehyde (or ketone) and a separate molecule of water. The initial product results from the attack of an α-carbon (in the form of an enolate ion) of aldehyde (or ketone) on an electropositive carbonyl of a second aldehyde (or ketone). A Claisen-Schmidt reaction product always has at least one double bond that is conjugated to both a carbonyl group and an aromatic ring. In this particular experiment, you will be preparing dibenzalacetone, a compound that once was used as an active ingredient in some sunscreen formulations because of its ability to absorb UV radiation. See the overall reaction below:

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\begin{align*}
2 \text{ benzaldehyde} + \text{ acetone} &\xrightarrow{\text{NaOH, Ethanol}} \text{ dibenzalacetone} \\
\end{align*}
\]

The two organic starting materials have many uses outside of chemistry. Benzaldehyde is found in almonds and almond paste which can be used in lots of cookie and nutritional bar recipes. Some uses of acetone are 1) a paint and varnish remover; 2) a solvent in many varnishes, rubber cements, lacquers, etc.; and 3) an indicator of metabolic disorders, like diabetes, if present at high concentrations in the bloodstream (acetone is a natural metabolic byproduct normally found in limited quantity in the body).

Normally, crossed aldol condensations produce 4 different products. However, several precautions have been taken to make this reaction successfully selective.

- 2.2 moles of benzaldehyde to 1 mole of acetone will be used instead of a 2.0 : 1 molar ratio of benzaldehyde to acetone as required by the stoichiometry. A slight excess is important because:
  1) The benzaldehyde may be contaminated from partial oxidation to benzoic acid;
  2) Enough benzaldehyde must be present to react with both methyl groups of acetone, preventing contamination by monobenzalacetone.
- Only one of the starting materials can undergo α-hydrogen abstraction to produce a carbanion which can be stabilized via keto-enol tautomerism.
- Conditions are right for a base-catalyzed dehydration of the β-dihydroxyketone formed as one of the intermediates in the reaction. This dehydration is very fast due to the stabilization gained by forming an extensive conjugated π-system.
In this experiment, a student tests one synthesis procedure (Route A) and compares it to a different synthesis procedure tested by another student (Route B). The two routes are similar because they use the same reagents and the same amounts of those reagents. The routes are different because in Route A, only half of the initial ketone-aldehyde mixture is able to react with the base in the beginning of the reaction. In Route B, a solution of acetone in water is slowly dripped into a mixture of the base and benzaldehyde. Once synthesis is complete, both routes use the same procedural steps for product isolation, purification, and characterization.

EXPERIMENTAL SECTION

Decide who will perform A vs. B below. One partner will do Synthesis Route A, and the other will do Synthesis Route B.

NaOH is hygroscopic so weigh this out quickly without spilling the pellets. If any pellets spill, clean them up immediately. This is an exothermic reaction, so do not turn the heat on. You may need to cool the beaker on ice to control the temperature as the NaOH pellets go into solution.

Synthesis Route A:

Add 20 mL of water to a 100 mL beaker. In another 100 mL beaker, weigh out 2.2 g of NaOH pellets. With good mixing on a stir plate, slowly add the NaOH pellets (a couple of pellets at a time over a couple minutes) to the 20 mL of water. **This is an exothermic reaction, so do not turn the heat on.** When the NaOH pellets are completely dissolved, bring the solution to room temperature, and then add 16 mL of 95% ethanol. Use a micropipetter to prepare a thoroughly mixed solution of 2.26 mL benzaldehyde and 0.73 mL reagent grade acetone in a small test tube equipped with a stopper.

Use a Pasteur pipette to transfer half the benzaldehyde/acetone mixture to the NaOH/ethanol/water solution. Re-stopper the test tube. Stir the reaction mixture at room temperature for 15 minutes. Transfer the remaining benzaldehyde/acetone mixture into the reaction mixture. Wash the small test tube with about 1 mL of 95% ethanol, and add this wash to the reaction mixture. Stir the reaction mixture at room temperature for an additional 15 minutes.

Synthesis Route B:

Add 18 mL of water to a 100 mL beaker. In another 100 mL beaker, weigh out 2.2 g of NaOH pellets. With good mixing on a stir plate, slowly add the NaOH pellets (a couple of pellets at a time over a couple minutes) to the 18 mL of water. **This is an exothermic reaction, so do not turn the heat on.** When the NaOH pellets are completely dissolved, bring the solution to room temperature and then add 17 mL of 95% ethanol. Continue stirring the mixture. Use a micropipetter to add 2.26 mL of benzaldehyde to the NaOH/ethanol/water solution. Into a small test tube equipped with a stopper, use a micropipetter to obtain 0.73 mL of reagent grade acetone, and another micropipetter to obtain 0.73 mL of DI water. Mix the solution thoroughly. Use a Pasteur pipette to add the acetone/water solution dropwise (about 4 -5 drops a minute – rate of addition is important!) to the mixture of benzaldehyde/NaOH/ethanol/water. Cap the solution of acetone and water in-between additions to minimize evaporation. Rinse the small test tube with approx. 1 mL of DI water, and add this to the reaction mixture. Stir the reaction mixture at room temperature for 30 min (begin timing at first sign of cloudiness).
Isolation, Purification, and Characterization of Product (Both Routes):

Collect the crude product using vacuum filtration on an appropriate size funnel. Wash the beaker out with about 20 mL of water, and add this to the funnel. The aqueous filtrate may be discarded.

Transfer the solid product to a clean beaker and add about 20 mL of cold 5% acetic acid in 95% ethanol. Stir the suspension, and vacuum filter again through an appropriate size funnel. Wash the solid, in the funnel, with a small amount (< 2 mL) of cold 95% ethanol.

Transfer the solid into a 50 mL beaker, and add a minimal amount of 95% ethanol. Cover with a watch glass and heat until all dissolves. Add more 95% ethanol if all the solid is not in solution as the solution begins to boil. Do NOT let this boil for more than a few seconds. (Make the decision whether more 95% ethanol is necessary as the solvent just starts to boil.) Once everything has dissolved, take the beaker off the heat and leave it covered. Let it cool slowly to room temperature; then (and only then) move it into an ice bath. Swirl occasionally. Scratch if crystals do not form. Prepare a clean vacuum filtration set up (choose proper funnel size). Remove the beaker from the ice bath and dry its outside, swirl, and dump everything into the funnel. Pull air through for at least 5 minutes, then spread the crystals onto a clean white paper towel (folded for safety!) so they can dry for at least a day. Measure yield, melting range, and obtain an IR spectrum (using the ATR accessory) of the product.

References:


WEEKS 5 & 6 ASSIGNMENT: Staple and turn in the following results stapled to your notebook pages.

1. Balanced chemical reactions to form each of the 4 Claisen-Schmidt products in this experiment specifically. Circle the major product.
2. Hard copy of IR spectrum, properly labeled
3. Melting range of product, listed
4. Mass of product, listed
5. Calculations for:
   a. Determination of limiting reagent (consider benzaldehyde and acetone)
   b. Theoretical yield (in grams) from the limiting reagent
   c. % yield
STUDY QUESTIONS for Discussion Quiz #5 or #6

1. Review the theory of the base-catalyzed crossed-aldol condensation
   a. Specific reaction and the transformations that occur
   b. Characteristics of a Claisen-Schmidt product
   c. Specific Claisen-Schmidt products in this reaction (di- and monobenzalacetone)
   d. How experimental conditions favored the major product over others

2. Synthesis Route A vs. Route B
   a. Procedural differences and similarities
   b. Differences in % yield and if/why procedural differences could have contributed to this
   c. Differences in purity (given characterization data and published data) and if/why procedural differences could have contributed to this

3. What is the order and purpose of major procedural steps in this experiment?
   a. What was the purpose of the acetic acid wash?

4. Aside from glassware transfers / spills / etc., during what steps may product have been lost due to chemistry reasons? Explain the chemistry of each.

5. Why would the presence of trace contamination in the final solid product cause melting point depression to occur?

6. What compounds would make strong IR comparisons with your experimental product, and what notable peak changes (presence/absence) would indicate the correct product had formed?

PRE-LAB QUESTIONS: (complete these in your notebook before coming to lab)

1. What is the name of your experiment?
2. What are some important safety considerations for this experiment?
3. How will this experiment help you practice / prepare for the Single and Double Unknown Analyses at the end of the semester?
4. What theory / concept from class will be demonstrated in this experiment?