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} \\
\rightarrow & \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 cookies and nutritional bars 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 because 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 successful.

- 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, students work as pairs to test two different procedures. In synthesis route A, only half of the initial ketone-aldehyde mixture will be able to react with the base in the beginning of the reaction. In synthesis route B, a solution of acetone in water will be slowly dripped into a mixture of the base and benzaldehyde.

Experimental Procedure:

****Decide with your partner which synthesis route each person will be doing. One student should do Synthesis Route A, and one student should do Synthesis Route B. ****

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, slowly add the NaOH pellets (a couple of pellets at a time over a couple minutes) to the 20 mL of water. Note: NaOH is hygroscopic so weigh this out as quickly as you can without spilling the pellets. If any pellets spill, clean them up immediately. Note: this is an exothermic reaction, so do not turn the heat on. You may need to cool the beaker to control the temperature as the NaOH pellets go into solution. When the NaOH pellets are completely dissolved, bring the solution to room temperature, if necessary, and then add 16 mL of 95% ethanol. Use a micropipetter to prepare a solution of 2.26 mL benzaldehyde and 0.73 mL reagent grade acetone. Thoroughly mix the components 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. Keep stirring 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, slowly add the NaOH pellets (a couple of pellets at a time over a couple minutes) to the 18 mL of water. Note: NaOH is hygroscopic so weigh this out as quickly as you can without spilling the pellets. If any pellets spill, clean them up immediately. Note: this is an exothermic reaction, so do not turn the heat on. You may need to cool the beaker to control the temperature as the NaOH pellets go into solution. When the NaOH pellets are completely dissolved, bring the solution to room temperature, if necessary, and then add 17 mL of 95% ethanol. Use a micropipetter to add 2.26 mL of benzaldehyde to the NaOH/ethanol/water solution. Use a micropipetter to obtain 0.73 mL of reagent grade acetone, and another micropipetter to obtain 0.73 mL of DI water. Combine these with good mixing into a small test tube equipped with a stopper. Use a Pasteur pipette to add the acetone/water solution to the mixture of benzaldehyde/NaOH/ethanol/water dropwise (about 4 -5 drops a minute. Rate of addition is important!). 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).
Purification and Isolation for Routes A and B:

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 in the sink.

Transfer the solid product to a clean beaker and add about 20 mL cold of 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 about 20 mL 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. 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.

Enrichment Questions:

1. Compare notes with the other student to compare and contrast the quality and purity of the products synthesized by two different routes.
2. What is the purpose of the 5% acetic acid in 95% ethanol wash? Hint: think about what is present in large excess at that time which could be contaminating the crude crystals.

References: (provided by a previous lab coordinator now employed elsewhere)


