Use of an Ionic Liquid for the Mannich Reaction

October 2\textsuperscript{nd} and 4\textsuperscript{th}


Background

The overall reaction that you will perform is the Mannich reaction shown below:

\[
\text{PhCHO} + \text{RCO} + \text{NH}_4\text{Ac} \rightarrow \text{PhN}^+ \text{C} = \text{C} \text{Ph} \]

In general, a Mannich reaction is the addition of an enol (or enolate) nucleophile to an imine electrophile. The imine electrophile is usually formed in situ from the reaction of a primary amine with an aldehyde:

\[
\text{R}-\text{N}^- + \text{R}^+ \text{CO} \rightarrow \text{R}-\text{N}^- \text{CO} \]

In this particular case, the reaction that occurs is actually a double Mannich reaction that leads to the formation of a six membered ring. The mechanism of the reaction is shown below:
In this experiment, half of the class will conduct the Mannich reaction in an ionic liquid, and half the class will conduct the reaction in a traditional organic solvent, ethanol. You will be responsible for comparing the yields obtained from the two different solvents and drawing conclusions about the wisdom of using ionic liquids for this Mannich reaction.

**Day 1 (October 2nd, 2012)**

1. You have already synthesized an ionic liquid during the last class. It should have been drying in your drawer over the weekend. Obtain a mass of your round-bottom flask + ionic liquid product and determine a yield for the ionic liquid product.

2. Obtain an IR spectrum of the ionic liquid by carefully using a pipette to place one drop on the IR machine. Look for key peaks in the IR spectrum that will indicate that you have formed your desired product. Note that you are not performing any other analysis for the first part of this reaction, so IR spectroscopy is your only option for product characterization.

3. Now you are ready to move on to the Mannich reaction. First step is to purify the benzaldehyde starting material. Measure 25 mL of benzaldehyde using a graduated cylinder, and transfer to a separatory funnel. Wash the benzaldehyde 3 times with approximately 20 mL of 10% aqueous Na2CO3 solution. After each washing, separate the layers and then put the benzaldehyde back into the separatory funnel for its subsequent washing. (Hint: Be sure you know which layer is benzaldehyde and which is the aqueous solution).

4. After the third washing, collect your benzaldehyde in an Erlenmeyer flask or beaker. Add a few scoops of MgSO4 and stir briefly with a stirring rod. Filter the anhydrous MgSO4 and keep the pure benzaldehyde filtrate.

5. Now that your benzaldehyde is pure, you are ready to set up the Mannich reaction. Follow ONE OF THE TWO PROCEDURES shown below:

**Procedure A (Ionic Liquid Group):**

To a 50-mL round-bottomed flask add freshly purified benzaldehyde (2.12 g, 20 mmol), 3-pentanone (0.861 g, 10 mmol), ammonium acetate (0.771 g, 10 mmol), and [bmim][BF4] (2.5 g).

Note: All of your reagents (except for ammonium acetate) are liquids. You are responsible for finding their densities and calculating the amounts of each that are required for this reaction to be run on this scale. Use either a graduate cylinder or a 1 mL syringe to measure out the liquid reagents.

Cap the round-bottom flask and store it in your drawers until the next class.

**Procedure B (Traditional Solvent Group):**

To a 50-mL round-bottomed flask add freshly purified benzaldehyde5 (2.12 g, 20 mmol), 3-pentanone (0.861 g, 10 mmol), ammonium acetate (0.771 g, 10 mmol), and ethanol (2.5 mL).

Note: All of your reagents (except for ammonium acetate) are liquids. You are responsible for finding their densities and calculating the amounts of each that are required for this reaction to be run on this scale. Use either a graduate cylinder or a 1 mL syringe to measure out the liquid reagents.

Stopper the flask and store in your drawer until the next class.

CLEAN UP EVERYTHING AS INSTRUCTED BY YOUR TA.

**Day 2 (October 4, 2012)**

**Procedure A (Ionic Liquid Group):**
1. Dilute the reaction mixture with 20 mL of deionized water and stir the suspension for 5 minutes. Collect the white precipitate by vacuum filtration. Save the filtrate for recovering the ionic liquid.

2. To purify the crude product, recrystallize it from approximately 15-20 mL of hot ethanol. To do this, transfer your crude precipitate to a beaker and add 15 mL of ethanol (measured via graduated cylinder). Heat the ethanol mixture until it starts to boil. At the same time, heat another beaker with pure ethanol. After both beakers are boiling, add enough ethanol to the first beaker so that the solid fully dissolves at boiling. Then slowly cool the beaker to room temperature. As the solution cools, your solid crystallize from the ethanol solution.

**Procedure B (Traditional Solvent Group):**

Add 20 mL of deionized water to your round-bottom flask and stir the suspension for 5 minutes. Collect the white precipitate by vacuum filtration and purify the crude product by recrystallization from hot ethanol (ca. 15-20 mL). Follow the instructions for group A for how to crystallize from hot ethanol.

Compare the reaction yield with that obtained from [bmim][BF4].

**Both Groups – Product Analysis**

1. Prepare a sample for 1H NMR analysis by dissolving 15-20 mg of the recrystallized product in approximately 1 mL of deuterated chloroform.

2. Obtain an IR of your recrystallized product.

3. Prepare a sample for GC analysis following instructions given to you by your tA.