Synthesis of Acetanilide

**Reaction**

\[
\text{Aniline} + \text{Acetic anhydride} \rightleftharpoons \text{Acetanilide} + \text{Acetic acid}
\]

**Purpose:**
Acetanilide is a useful precursor to many pharmaceuticals such as acetaminophen and penicillin.

**Experimental Procedure.** (Estimated time: 1.5 h.) Unless otherwise noted, all manipulations should be done in the chemical fume hood.

<table>
<thead>
<tr>
<th>Physical Properties of Reactants</th>
<th>MW</th>
<th>Amount</th>
<th>mmol</th>
<th>mp (°C)</th>
<th>bp (°C)</th>
<th>d</th>
<th>n_o</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aniline</td>
<td>93.13</td>
<td>100 µL</td>
<td>1.09</td>
<td>184</td>
<td>1.02</td>
<td>1.5863</td>
<td></td>
</tr>
<tr>
<td>Concd HCl</td>
<td></td>
<td>3 drops</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium acetate trihydrate</td>
<td>136.08</td>
<td>150 mg</td>
<td>1.10</td>
<td>58</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetic anhydride</td>
<td>102.09</td>
<td>150 µL</td>
<td>1.59</td>
<td></td>
<td>140</td>
<td>1.08</td>
<td>1.3901</td>
</tr>
</tbody>
</table>

Place 100 µL of aniline (in the hood) into a tared 10 X 75-mm test tube (standing in a small beaker or Erlenmeyer flask). Fit the test tube with a cork stopper. Now add 0.5-mL of distilled water; with swirling, followed by 3 drops of concentrated hydrochloric acid. (Hood) Add 10 mg of powdered decolorizing charcoal, or the pelletized form (Norit) to the resulting solution.

Gravity filter (flute the filter paper) this suspension (25-mm funnel fitted with fluted fast-grade filter paper (see instructor) into a 3.0-mL conical vial containing a magnetic spin vane. *Wet the filter paper in advance with distilled water and blot the excess water from the stem of the funnel.* Use an additional 0.5 mL of distilled water to rinse the test tube and the filtrate. Combine the rinses with the original filtrate. Your aniline hydrochloride solution is ready for reaction. Assemble the apparatus as shown below:

\[
\text{C}_6\text{H}_5\text{NH}_2, 100 \mu\text{L} + \text{H}_2\text{O}, 1.0 \text{mL} + \text{concd HCl}, 3 \text{drops} \\
+ \text{NaOAc} \cdot 3\text{H}_2\text{O}, 150 \text{mg} + (\text{CH}_3\text{CO})_2\text{O}, 150 \mu\text{L}
\]

CONICAL VIAL W/ MAGNETIC SPIN VANE AND AIR CONDENSER
Dissolve 150 mg (1.10 mmol) of sodium acetate trihydrate in 0.5 mL of distilled water in a 10 X 17-mm test tube. Cap the tube and set the solution aside for use in the next step.

Add, with stirring, 150 µL of acetic anhydride to the solution of aniline hydrochloride, followed quickly by addition (Pasteur pipet) of the previously prepared solution of sodium acetate.

Stir to thoroughly mix the reagents (~5 min.). You should see the formation of a white precipitate. Allow the reaction mixture to stand at room temperature for approximately 5 min and then place it in an ice bath for an additional 5-10 min to complete the crystallization process.

Collect the acetanilide product by filtration under reduced pressure using a Büchner funnel. Rinse the conical vial with two 0.5-mL portions of distilled water and use the rinse to wash the collected filter cake.

**Characterization.**
Weigh and determine the percent yield of the product. Take an IR (neat) of aniline. Obtain an IR spectrum of the product using the total internal reflectance attachment (or make a nujol mull). Draw the structure of the compound on the IR and label as many significant peaks as you can. Take the melting point of the product and compare it to the (Aldrich) literature data.

**Question (to be answered in your notebook):**

1. What do you expect the IR spectrum of the product to look like? i.e. what peaks will you expect to see? Interpret your IR spectrum and comment.