Lab #4: Crystallization

Objectives:
- Purify an impure sample of an antibiotic.
- Practice the crystallization technique.

Introduction:
The purpose of this experiment is to introduce the technique of crystallization, a very common procedure used to purify crude solids in the organic laboratory. The general technique involves dissolving the material to be crystallized in a hot solvent and cooling the solution slowly. The dissolved material has a decreased solubility at lower temperatures and will separate from the solution as it is cooled. This phenomenon is called crystallization if the crystal growth is relatively slow and selective or precipitation if the process is rapid and nonselective. Since the impurities are usually present in much smaller amounts than the compound being crystallized, most of the impurities will remain dissolved in the solvent even when it is cooled. The purified substance can then be separated from the solvent and impurities by filtration.

In this experiment, you will carry out a crystallization of impure sulfanilamide using 95% ethyl alcohol as the solvent. Sulfanilamide is one of the sulfa drugs, the first generation of antibiotics to be used in successfully treating many major diseases such as malaria, tuberculosis, and leprosy.

![Sulfanilamide](image)

The solubility of sulfanilamide in 95% ethyl alcohol is given in the following table:

<table>
<thead>
<tr>
<th>Temperature</th>
<th>Solubility (mg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0°C</td>
<td>14</td>
</tr>
<tr>
<td>20°C</td>
<td>24</td>
</tr>
<tr>
<td>40°C</td>
<td>46</td>
</tr>
<tr>
<td>60°C</td>
<td>88</td>
</tr>
<tr>
<td>78°C</td>
<td>210</td>
</tr>
</tbody>
</table>

Notice that the solubility increases significantly as the temperature increases. Therefore, 95% ethyl alcohol is an excellent solvent for crystallizing sulfanilamide. A graph of this is shown on the next page.

You will crystallize a sample of impure sulfanilamide by dissolving it in the minimum amount of boiling 95% ethyl alcohol (78 ºC) and then cooling the solution, first to room temperature, and then to 0 ºC in an ice-water bath.

The purity of the final material after crystallization will be determined by observing the color of your crystals and by performing a melting point on your sample. You will also weigh your sample and calculate the percent recovery. It is not likely that you will obtain a 100% recovery. This is true for several reasons: experimental loss, the original sample is not 100% sulfanilamide, and some sulfanilamide is soluble in the solvent even at 0 ºC. Because of this latter factor, some sulfanilamide will remain dissolved in the mother liquor (the liquid remaining after crystallization has taken place).
The melting point of a substance is often used to determine purity. The melting point of a sample is usually expressed as two numbers called the melting point range, such as 112 - 114°C. The first number is the temperature at which the substance begins to melt (when liquid is first observed) and the second number is the temperature at which the sample has completely melted (no solid left). A very pure sample will have a narrow melting point range that will be close to the literature value (supposedly determined on a very pure sample). An impure sample will have a lower melting point and the range will be bigger. The literature melting point of sulfanilamide is 164.5 - 166.5°C.

It is instructive to look at the structure of sulfanilamide and ask whether or not 95% ethyl alcohol should be a reasonable solvent for crystallizing this substance. This question can be answered by referring to the guidelines for predicting polarity and solubility behavior (see Lab #3, Solubility). There are several polar bonds in sulfanilamide, the NH and the SO bonds. Because of these bonds, sulfanilamide has some polar character. In addition, the NH2 groups and the oxygen atoms in sulfanilamide can form hydrogen bonds with ethyl alcohol. So even though, it is likely that sulfanilamide would be soluble in 95% the benzene ring part of sulfanilamide is quite nonpolar, sulfanilamide has an intermediate polarity because of the polar groups. Ethyl alcohol also has an intermediate polarity. Therefore ethyl alcohol since they have similar polarities. (Note that the other 5% in ethyl alcohol is usually a substance such as water or isopropyl alcohol that does not alter the overall polarity of the solvent.)

Although this kind of analysis is a good first step in determining an appropriate solvent for crystallization, without more information it is not possible to predict the shape of the solubility curve for the temperature vs. solubility data, as shown above. Therefore, knowing that sulfanilamide is soluble in 95% ethyl alcohol does not necessarily mean that this is a good solvent for crystallizing sulfanilamide. The shape of the solubility curve must also be known.

Pre Lab Questions: (Answers submitted at the beginning of lab)

1. Calculate how much 95% ethyl alcohol will be required to dissolve 0.8 g of sulfanilamide at 78 °C. Use the data from the introduction to this experiment to make this calculation. The reason for making this calculation is so that you will know ahead of time the approximate amount of hot solvent you will be adding. Be sure to keep a copy of these calculations for yourself!
2. What would happen if you failed to heat the ethanol to its boiling point during crystallization? How would this affect your results?

Procedure

In this experiment, the goal is to dissolve the sulfanilamide in the minimum of hot (boiling or almost boiling) solvent. Therefore, you must keep the mixture at (or near) the boiling point of 95% ethyl alcohol during the entire procedure. You will likely add considerably more solvent than the amount that you calculated (see Pre-Lab Calculations), since some solvent will evaporate. The amount of solvent is calculated only to indicate to you about how much solvent will be required: you should follow the procedure to determine the correct total amount of solvent needed.

1. Weigh 0.80 g of impure sulfanilamide and transfer this solid to a 25-mL Erlenmeyer flask. To a second Erlenmeyer flask, add about 15 mL of 95% ethyl alcohol and a boiling stone. The purpose of the boiling stone is to promote smooth boiling of the liquid. Be sure to add the boiling stone to the flask while the alcohol is at room temperature. Adding a boiling stone to a hot liquid may cause the liquid to erupt entirely out of the flask or to froth violently.

2. Heat the solvent beaker on a warm hotplate until it is almost boiling (you may need to turn up the hot plate to reach the boiling point of ethanol but turn it up slowly). Since 95% ethyl alcohol boils at a relatively low temperature (78°C), it evaporates quite rapidly. Setting the temperature of the hotplate too high will result in too much loss of solvent through evaporation. Do not heat the beaker of sulfanilamide yet.

3. Before heating the flask containing the sulfanilamide, add enough hot solvent with a Pasteur pipet or a plastic pipet to barely cover the crystals. Then heat the flask containing the sulfanilamide until the solvent is boiling. At first this may be difficult to see because so little solvent is present.

4. Add another small portion of solvent (about 0.5 mL), continue to heat the flask, and swirl the flask frequently. You may swirl the flask while it is on the hotplate or, for more vigorous swirling, remove it from the hot plate for a few seconds while you swirl it. Remember that the temperature of the solvent should be at or near the boiling point of 95% ethyl alcohol during this entire process. When you have swirled the flask for 10-15 seconds, check to see if the solid has dissolved. If it has not, add another portion of solvent. Heat the flask again with swirling until the solvent boils. Then swirl the flask for 10-15 seconds, frequently returning the flask to hotplate so that the temperature of the mixture does not drop.

5. Continue repeating the process of adding solvent, heating, and swirling until all of the solid has dissolved completely. Note that it is essential to add just enough solvent to dissolve the solid - neither too much nor too little. Because 95% ethyl alcohol is very volatile, you need to perform this entire procedure fairly rapidly. Otherwise, you may lose solvent nearly as rapidly as you are adding it and this procedure will take a very long time. The time from the first addition of solvent until the solid dissolves completely should not be longer than 15-20 minutes.

6. Remove the flask from the heat and place it on an insulating surface such as a notebook or a cork ring. The purpose of the insulating surface is to prevent the solution from cooling too rapidly. Cover the flask with a watch glass or inverted beaker to reduce the rate of cooling. Crystallization should begin by the time the flask has cooled to room temperature. If it has not, gently scratch the inside surface of the flask with a glass rod to induce crystallization. When it appears that no further crystallization is occurring at room temperature, place the flask in an ice-water bath using a beaker. Be sure that both water and ice are present and that the beaker is small enough to prevent the flask from tipping over.

7. When crystallization is complete, vacuum filter the crystals using a Buchner funnel (this will be demonstrated in the pre-lab lecture). Moisten the filter paper with a few drops of 95% ethyl alcohol and turn on the vacuum (or aspirator) to the fullest extent. Use a spatula to dislodge the crystals from the bottom of the flask before transferring the material to the funnel. Swirl the mixture in the flask and pour the mixture into the funnel, attempting to transfer both crystals and solvent. Therefore, you need to pour the mixture quickly, before the crystals have completely settled to the bottom of the flask. (You may need to do this in portions, depending on the size of your funnel and how skilled you are at this procedure.) When the liquid has passed through the filter,
repeat this procedure until you have transferred all the liquid to the Buchner funnel. At this point there will usually be some crystals remaining in the flask.

8. Using your spatula, scrape out as many of the crystals as possible from the flask. Add about 2 mL of ice-cold 95% ethyl alcohol (measured with a plastic pipet) to the flask. Swirl the liquid in the flask and then pour the remaining crystals and alcohol into the Hirsch funnel. Not only does this additional solvent help transfer the remaining crystals to the funnel, but the alcohol also rinses the crystals already on the funnel. This washing step should be done whether or not it is necessary to use the wash solvent for transferring all the crystals. If necessary, repeat with another 2-mL portion of ice-cold alcohol. You should wash the crystals with a total of about 4 mL of ice-cold solvent.

9. Continue drawing air through the crystals on the Buchner funnel by suction for about five minutes. Transfer the crystals onto a pre-weighed watch glass for air-drying. Separate the crystals as much as possible with a spatula. The crystals should be completely dried within 10-15 minutes and you may let them sit overnight. You can usually determine if the crystals are dry by observing whether or not they stick to a spatula or stay together in a clump. Weigh the dry crystals and calculate the percent recovery. Record the appearance of the crystals (color, shape, size of crystals). Your crystals will most likely look like needles or plates.

10. Determine the melting point of the pure sulfanilamide and the original impure material. Remember that the melting point of each sample should be reported as a range. Your instructor will show you how to prepare a sample for doing a melting point determination and how to use the melting point apparatus.
Lab #4 Report Sheet

Name___________________________

1. Weight of impure sulfanilamide (to three decimal points):

2. Appearance of pure sulfanilamide after crystallization (color, shape and approximate size of crystals):

3. Weight of purified sulfanilamide (to three decimal points):

4. Calculate the % recovery.

5. Melting point of impure sulfanilamide (should be a range):

   Melting point of pure sulfanilamide (should look this up):

Post-Lab Questions

1. Based on the appearance of the sulfanilamide before crystallization, do you think it is pure? Explain.

2. Give three reasons why the recovery was not 100%. Be specific.
3. In the crystallization procedure, the solution should be heated to the boiling point of 95% ethyl alcohol (78°C). If the solution is only heated to 40°C, how would this affect the results? Be specific.

4. In this problem, a solid is given with two possible solvents for crystallizing the impure solid. Which solvent would work best? Explain your choice. The solid is listed first.

a. ![Benzophenone](image)
   
   **Solid:** Benzophenone  
   **Possible Solvent:** Water or 95% Ethyl alcohol

b. ![Urea](image)
   
   **Solid:** Urea  
   **Possible Solvent:** Water or Hexane