This activity is an example of an organic preparation. You will be able to test the purity of your product using thin-layer chromatography.

### Requirements

#### Method 1
- access to a fume cupboard
- 100 cm³ conical flask
- 10 cm³ measuring cylinders (2)
- 100 cm³ beaker
- glass rod
- apparatus for vacuum filtration
- Hirsch funnel
- 2-hydroxybenzoic acid (salicylic acid) (2g)
- ethanoic anhydride (4 cm³)
- concentrated sulfuric(VI) acid (5 drops)
- glacial ethanoic acid (4 cm³)
- water bath containing crushed ice

#### Method 2
- access to a fume cupboard
- microwave oven
- thermometer (0–110 °C)
- 10 cm³ measuring cylinders
- 250 cm³ beakers (2)
- glass rod
- glass Petri dish
- apparatus for vacuum filtration
- Hirsch funnel
- 2-hydroxybenzoic acid (salicylic acid) (5 g)
- ethanoic anhydride (5 cm³)
- ice cubes
- water bath containing crushed ice

#### For testing the purity of aspirin samples
- access to a fume cupboard
- UV light source
- test tubes (3)
- watch glass
- dropping tubes or melting-point tubes (2)
- t.l.c. plates (silica-coated, fluorescent ones are ideal)
- small beaker to hold t.l.c. plate
- cover for the beaker
- ethanol (a few cm³)
- prepared aspirin sample (1 crystal)
- sample of pure aspirin
- sample of pure 2-hydroxybenzoic acid
- solvent for chromatography – cyclohexane, ethyl ethanoate, ethanoic acid (200:100:1)
- neutral iron(III) chloride solution, 0.1 mol dm⁻³ (1 cm³)
- iodine crystals
- aluminium foil or cling film

### Ethanoic anhydride should always be dispensed in a fume cupboard. Goggles and chemical-resistant gloves should be worn.

### Microwave ovens are sources of non-ionising radiation that produce local heating. Using a microwave oven can be hazardous. Superheating may occur, which can cause very hot liquid to be ejected from its container. Your teacher will provide you with up-to-date safety instructions.

### The chromatography solvent is harmful by inhalation (as are the vapours produced by this activity) and highly flammable. Work in a fume cupboard or in a well-ventilated laboratory as directed and avoid inhaling the fumes. Avoid naked flames. The chromatography solvent contains cyclohexane. Return residues containing cyclohexane to a residues bottle. Do not pour them down the sink.
Introduction

Aspirin (acetylsalicylic acid or 2-ethanoylhydroxybenzoic acid) can be made by a variety of methods, but they all start from 2-hydroxybenzoic acid (salicylic acid).

\[
\begin{align*}
\text{2-hydroxybenzoic acid} & \rightarrow \text{2-ethanoylhydroxybenzoic acid} \\
\text{ethanoic anhydride} & \rightarrow \text{H}_2\text{SO}_4
\end{align*}
\]

Two different methods are described below. One method uses concentrated sulfuric(VI) acid as a catalyst and glacial ethanoic acid as a solvent. In the other method, the reactants are heated in a microwave oven. This avoids the use of both concentrated sulfuric(VI) acid and glacial ethanoic acid. This second method is an example of a ‘green chemistry’ approach to manufacturing chemicals, in which reagents that are hazardous and dangerous for the environment are avoided as much as possible.

You will prepare a sample of aspirin by one of the methods described. If other students in your class use the other method to prepare aspirin, you can compare the methods and also compare the yield and purity of the aspirin that you make.

What you do

Method 1 – making aspirin using concentrated sulfuric(VI) acid as a catalyst

1. Working in a fume cupboard, swirl 2 g of 2-hydroxybenzoic acid (salicylic acid) with 4 cm\(^3\) of ethanoic anhydride (CARE Corrosive) in a 100 cm\(^3\) conical flask.
2. Add five drops of concentrated sulfuric(VI) acid (CARE Corrosive) and continue agitating the flask for about 10 minutes. Crystals of aspirin will appear and soon the whole solution will form a crystalline ‘mush’.
3. Stir in 4 cm\(^3\) of cold glacial ethanoic acid (CARE Corrosive) to dilute the mixture and cool by placing in a water bath containing crushed ice.
4. Filter off the crystals using a Hirsch funnel (a small funnel for vacuum filtration), washing once with ice-cold water.
5. Dry your purified sample on filter paper and weigh it.

Method 2 – making aspirin using a microwave oven

1. Weigh 5 g of 2-hydroxybenzoic acid (salicylic acid) into a 250 cm\(^3\) beaker.
2. Working in a fume cupboard, add 5 cm\(^3\) ethanoic anhydride (CARE Corrosive), using a small measuring cylinder, so as to wet the acid uniformly.
3. Cover the beaker with a glass Petri dish.
4. Place the beaker and Petri dish in a microwave oven (you will need to take turns with other students in your group). Also put a beaker containing 200 cm\(^3\) of water into the oven – this will absorb excess microwaves.
5. Irradiate the sample at full power for about 1 minute. Stop the oven and gently swirl the beaker. CARE The beaker will be hot. Check the temperature of the mixture.
6. The temperature should be in the range 120–130°C. If it is not, irradiate further to achieve this temperature. Do NOT overheat.
7. Carefully remove the hot beaker containing the reaction mixture from the oven. Allow the beaker to cool a little and then add about 50 cm\(^3\) of water that contains a few ice cubes. Stir the mixture.
8. Now cool the beaker by placing it in a water bath containing crushed ice. Continue to stir the mixture to prevent clumps of solid forming.
9. When the mixture is cold, filter off the crystals using a Hirsch funnel, washing once with ice-cold water.
10. Dry your purified sample on filter paper and weigh it.
**Testing the purity of your aspirin**

**CARE** The chromatography solvent used here is harmful by inhalation and highly flammable. Work in a fume cupboard or in a well-ventilated laboratory. Dispose of the chromatography solvent only as directed by your teacher. Ensure there are no sources of ignition.

1. Take three test tubes and add 2 cm$^3$ of distilled water to each.
2. To the first test tube add one crystal of the aspirin sample that you have made. Agitate gently.
   To the second test tube add one crystal of 2-hydroxybenzoic acid and agitate gently.
   To the third test tube add one crystal of known pure aspirin and agitate gently.
3. To each test tube in turn, add two drops of neutral iron(III) chloride solution and agitate to mix. Note down your observations.
4. Take, or cut, a pre-dried thin-layer chromatography plate that will fit into a small beaker (see Figure 1). Try to handle the t.l.c. plate by the edges only. Draw a fine pencil line about 1 cm from the bottom of the plate. This is the baseline.
5. Take a few crystals of the aspirin that you have prepared and dissolve them in a minimum volume of ethanol on a watch glass. Try a few drops, then add more ethanol if required.
6. On the baseline place a small spot of your aspirin sample. The spot is best made by using a very fine dropping pipette or a drawn-out melting-point tube. Apply a small quantity of the solution at a time; let it dry, and then add more. Try not to let the diameter of the spot exceed 5 mm.
7. Repeat steps 5 and 6 using pure salicylic acid and then pure aspirin. Ensure the three spots are well spaced out along the baseline but are not too close to the side edges of the t.l.c. plate. It is a good idea to label the top of the chromatography plate (in pencil) so that you know what each spot is.
8. Working in a fume cupboard or a well-ventilated laboratory, pour some of the chromatography solvent into the beaker to a depth of no more than 5 mm.
9. Place the chromatography plate in the beaker, making sure the solvent level is below the baseline.
10. Cover the beaker with cling film (or aluminium foil or a watch glass). Leave the solvent to rise up the t.l.c. plate. This will take about 15–25 minutes.
11. When the solvent has nearly reached the top of the plate, take the chromatogram out of the beaker. Place the plate in a fume cupboard and allow the solvent to evaporate. Dispose of the solvent from the beaker as directed by your teacher.
12. You can locate the positions of the substances on the plate by examining it under UV light. **(CARE** Do not look directly at the light source.) View the plate by reflected light.
13. Alternatively, place the sheet in another beaker which contains a few crystals of iodine. Do this in a fume cupboard. Cover the beaker with cling film (or aluminium foil). The spots, which were probably just visible before, should show up more clearly now.

**Questions**

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<td>1</td>
<td>On the basis of your observations in the tests with iron(III) chloride solution, do you think your product was pure aspirin? Explain your answer.</td>
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<td>2</td>
<td>What do the results from the thin-layer chromatography analysis tell you about the composition of your prepared aspirin sample?</td>
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<td>3</td>
<td>Write out the full, balanced equation for the preparation of aspirin from salicylic acid and ethanoic anhydride.</td>
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| 4 | Calculate the relative molecular masses of  
a salicylic acid  
b aspirin. |
| 5 | Calculate the percentage yield of aspirin that you obtained by your preparation method. Assume all of your sample is aspirin. |
| 6 | If possible, compare the yield and purity of aspirin obtained by the different preparation methods. |
| 7 | What are the benefits of using the microwave method (Method 2) rather than Method 1 to prepare aspirin? |