PAG 6.1

1.1 Aim

To complete a multi-stage process for the synthesis, purification, and identification of aspirin

1.2 Research

In PAG 6.1, students carry out the synthesis of aspirin, an organic solid, using a two-stage process starting from the oil of wintergreen. In the first stage, the oil of wintergreen, which contains methyl 2-hydroxybenzoate, is hydrolysed by heating under reflux with sodium hydroxide solution to produce 2-hydroxybenzoic acid (salicylic acid).

In the second stage, the 2-hydroxybenzoic acid is esterified using ethanoic anhydride to form aspirin (2-ethanoyloxybenzoic acid, or acetylsalicylic acid). The aspirin is recrystallised and analysed by thin layer chromatography and by melting temperature.

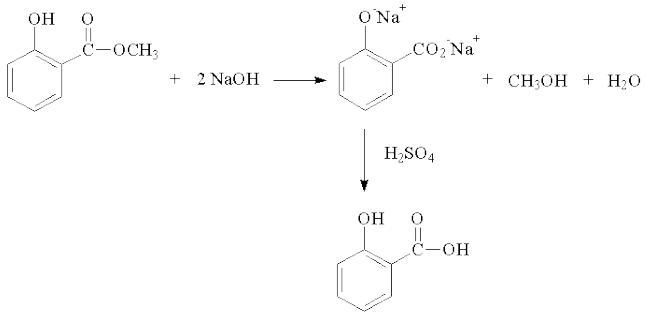

Figure 1.1: Production of Salicylic Acid (PubChem, 2022b)

The above reaction shows the production of Salicylic Acid from Oil of Wintergreen. It uses NaOH and H_2SO_4 to produce 2-hydroxybenzoic Acid.

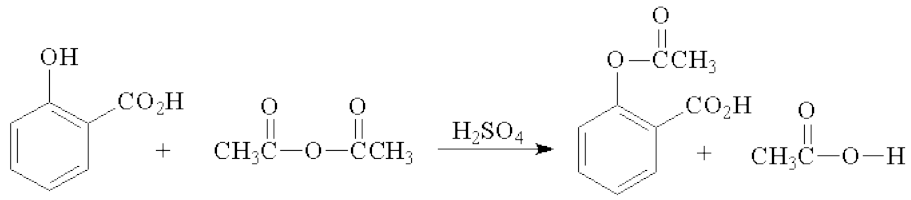

Figure 1.2: Production of Aspirin (PubChem, 2022a)

Figure 1.2 shows the production of Aspirin from Salicylic Acid.

1.3 Specification Point

Techniques and procedures:

- The synthesis and purification of a solid organic compound e.g. Aspirin
- The technique of thin layer chromatography (TLC), location of spots and interpretation
- Melting point determination
- Filtration and Recrystallisation

Prep of Salicylic Acid

2.1 Equipment

- Eye Protection
- Mass balance
- Measuring Cylinder ($10cm^3$)
- Measuring Cylinder ($50cm^3$)
- Quick-fit apparatus
- Pear-shaped flask ($50cm^3$)
- Liebig condenser and tubing
- Retort stand, boss and clamp
- Anti-bumping granules
- Water bath
- Beaker ($100cm^3$)
- Ice Bucket
- Distilled Water
- Dropping pipette
- Stirring rod
- Filtration apparatus
- Watch glass

2.2 Risk Assessment

Identity	**Hazard Info**	**Prevention**
2.0 mol/dm^3 NaOH(aq)	Danger to skin and eyes. Harmful if swallowed	Wear splashproof goggles. Avoid inhalation and take care when transferring NaOH

2.0 mol/dm^3 HCl(aq)	Danger to skin and eyes. Harmful if swallowed	Wear splashproof goggles.
Oil of Wintergreen	Can cause eye irritation and harmful if swallowed.	Keep lab well ventilated and wear eye protection

2.3 Method

1. Set up the apparatus for reflux using a 50cm^3 pear-shaped flask and Liebig condenser.
2. Add about 2.5 cm3 oil of wintergreen to a 10cm^3 measuring cylinder and record the mass.
3. Pour the oil of wintergreen into the pear-shaped flask.
4. Record the mass of the measuring cylinder again.
5. Using a 50cm^3 measuring cylinder, measure about 25cm^3 of 2.0 mol/dm^3 sodium hydroxide solution.
6. Add the sodium hydroxide solution to the pear-shaped flask. Add a few anti-bumping granules.
7. Heat the reaction mixture under reflux using a boiling water bath, sand bath or electric heater, for about 30 minutes.
8. Leave the mixture to cool, then pour into a 50cm^3 beaker which is being cooled in a larger beaker of ice and water.
9. Neutralise the reaction mixture by carefully add 2.0 mol/dm^3 hydrochloric acid to the mixture dropwise, stirring with a stirring rod. Keep adding acid until no more solid forms.
10. Filter the solid product from the reaction mixture using filtration under reduced pressure and wash with a small amount of cold distilled water.
11. Measure and record the mass of a watchglass, then transfer the solid product to the watchglass and leave to dry.
12. When the solid is dry, record the mass of the solid and the watchglass.
13. Store the product in a labelled, clean, dry sample tube for use in Part 2.

2.4 Results Table

Mass of Cylinder/g	Mass of Wintergreen/g	Mass of Salicylic Acid
35.54	7.52	

Prep of Aspirin

3.1 Equipment

- Splashproof goggles
- Mass Balance
- Distilled water
- Clean and dry sample tube with lid
- Conical flask ($100cm^3$)
- 2 x Measuring cylinders ($10cm^3$)
- Spatula
- Stirring rod
- Ice bucket
- Filtration Apparatus
- Watch Glass
- Sample tube and lid
- Glass marker pen

3.2 Risk Assessment

Identity	**Hazard Info**	**Prevention**
Ethanoic Anhydride $(CH_3CO)_2O)$	Danger to skin and eyes.	Store safely, maintain hygeine before, during and after use.
Concentrated H_2SO_4	Can cause severe skin burns and eye damage.	Wear eye protection and gloves.
Concentrated Ethanoic Acid (CH_3CO_2H)	Can cause severe skin and eye damage. Releases flammable vapours	Wear eye protection, gloves and avoid inhalation.

3.3 Method

1. Transfer about 2 g of the 2-hydroxybenzoic acid you made in Part 1 into the sample tube. Measure and record the mass of the sample tube and sample.
2. Transfer the 2-hydroxybenzoic acid into a 100cm^3 conical flask and measure the mass of the sample tube again.
3. Measure 4cm^3 ethanoic anhydride into a 10cm^3 dry measuring cylinder, and pour into the conical flask.
4. Add five drops of concentrated sulfuric(VI) acid to the flask and shake gently from side to side for about 10 minutes.
5. Cool the conical flask in a large beaker containing crushed ice to complete the crystallisation.
6. Using a clean measuring cylinder, measure 4cm^3 of cold glacial ethanoic acid and add this to the reaction mixture to dilute it.
7. Filter off the solid product using filtration under reduced pressure, washing once with ice-cold distilled water.
8. Measure and record the mass of a watchglass and then transfer the solid product to the watchglass and leave to dry.
9. When the solid is dry, record the mass of the solid and the watchglass.
10. Store the product in a labelled, clean, dry sample tube for recrystallisation in Part 3.

3.4 Results Table

Mass of Sample tube and Sample/g	Mass of sample/g	Mass of Solid/g

Recrystallisation

4.1 Equipment

- Eye Protection
- Mass Balance
- 2 x Conical Flask 100cm^3
- Dropping Pipette
- Spatula
- Stirring Rod
- Large Beaker
- Water Bath
- Filtration Apparatus
- Watchglass
- Sample tube and lid
- Glass marker pen

4.2 Risk Assessment

Identity	**Hazard Info**	**Prevention**
Ethanol C_2H_5OH	Highly flammable liquid.	Store safely, keep away from flames

4.3 Method

1. Transfer the majority of you impure aspirin to a 100cm^3 conical flask. Save a few crystals for analysis by chromatography in Part 4.

2. Warm approximately 30 cm3 of ethanol in another 100cm^3 conical flask, using an electric water bath/heating mantle/sand bath.
3. Add small amounts (0.5cm^3) of hot ethanol at a time to the impure aspirin until it has all just dissolved.
4. Quickly filter the hot solution using reduced pressure filtration, washing with a minimal small amount of hot ethanol.
5. Cool the filtrate slowly until needle-like crystals of aspirin form, then in an ice–water bath.
6. Filter the aspirin crystals, again using reduced pressure filtration and wash with ice-cold ethanol.
7. Measure and record the mass of a watchglass, then transfer the recrystallised aspirin to the watchglass and leave to dry.
8. When the solid is dry, measure and record the mass of the solid and the watchglass.
9. Transfer the aspirin into a labelled, clean, dry sample tube.

4.4 Results Table

Mass of Watchglass + Aspirin/g	Mass of Aspirin/g

Chromatography

5.1 Equipment

- Eye Protection
- UV Light
- 5 Watchglasses
- Dropping Pipette
- Thin layer chromatography plate
- Beaker 100cm^3
- Watchglass
- Pencil

5.2 Risk Assessment

Identity	**Hazard Info**	**Prevention**
Aspirin	Can cause skin irritation and respiratory problems	Store safely, avoid inhalation
Ethanol C_2H_5OH	Highly flammable liquid.	Store safely, keep away from flames.
Iodine Crystals (I_2)	Toxic, can cause respiratory problems	Store safely avoid inhalation
Salicylic Acid	Contact with skin can cause irritation	Avoid contact with skin

5.3 Method

1. Prepare your thin layer chromatography (TLC) plate by drawing a line in pencil about 1 cm from the bottom. Mark four crosses along the line. These crosses are where the samples will be placed.

2. Pour a 5mm depth of chromatography solvent into a 100 cm3 beaker and cover the beaker with a watchglass.

3. Place 2-3 crystals of the pure aspirin sample on a watchglass and dissolve in a drop of ethanol.

4. Place the capillary/pipette in the solution to draw up a small amount, then briefly touch to the first cross to apply the solution to the TLC plate. Alternatively, use a fine artist paint brush.

5. Allow the spot to dry, then repeat 3-4 more times, ensuring that the final diameter is no greater than 5mm.

6. Repeat steps 3-5 using clean apparatus for your aspirin samples from Part 2 and Part 3, and for a sample of salicylic acid (2-hydroxybenzoic acid).

7. Place the chromatography plate in the beaker and cover with the lid.

8. Allow the solvent to rise up the plate. This will take 15–20 minutes.

9. When the solvent has nearly reached the top of the plate, remove it from the beaker and mark the line of the solvent front with a pencil.

10. Place the plate in a fume cupboard until all of the solvent has evaporated.

11. Place the plate under a UV lamp and mark the locations of the substances using a pencil. **CARE: do not look directly into the UV light.** An alternative visualisation is to, in a fume hood, place the plate in a beaker containing a few crystals of iodine, and cover the beaker with cling film. Once the spots are visible, circle with pencil.

Melting Point

6.1 Equipment

- Capillary Tube
- Watchglass
- Spatula
- Melting point apparatus

6.2 Method

1. Seal the end of a melting point/capillary tube by rotating it in a Bunsen flame, then leave to cool.
2. Place a small amount of your recrystallised aspirin on a watchglass – carefully crush with a spatula if the crystals are large.
3. Fill the melting point tube with your recrystallised aspirin to a depth of about 5 mm, and tap the tube so that the solid is transferred to the sealed end.
4. Use the melting point apparatus to slowly heat the aspirin in the melting point tube until all the solid has melted.
5. Note the range over which the solid melts.
6. If you have time and some sample available, find the melting temperature of your impure aspirin from Part 2 to compare the difference in melting range of an impure and a pure sample.

References

PubChem. (2022a). Pubchem compound summary for cid 2244, aspirin. *https://pubchem.ncbi.nlm.nih.gov/compound/Aspirin.*.

PubChem. (2022b). Pubchem compound summary for cid 338, salicylic acid. *https://pubchem.ncbi.nlm.nih.gov/compound/Salicylic-acid.*.

Synthesis of Aspirin, Jun 29, 2020, James Chickos, David Garin, and Valerian D'Souza. University of Missouri–St. Louis; Chemistry

MaChemGuy, 2017, PAG6, Availible from:https://www.youtube.com/watch?v=YzXjgx7xrI