Aspirin – Practical work preparatory activity

Before completing practical task one you must answer these questions. You will need to read through the practical instructions carefully and be prepared to look up the information.

Structure of methyl 2-**hydroxybenzoate**	Functional groups in methyl 2-hydroxybenzoate	Structure of 2-hydroxybenzoic acid
Number of moles of methyl 2-hydroxybenzoate used in **practical one.**	Structure of product from **practical one**	**Maximum possible mass of** product in practical one.
Diagram of apparatus for heating under reflux	What is the connection between willow bark and aspirin? Make some **notes here.**	

Practical One- Hydrolysis of Methyl 2-hydroxybenzoate

The practical work completed in this term will allow you to prepare a pure sample of the common pharmaceutical aspirin from methyl 2-hydroxybenzoate. Your work in the next practical will be dependent on your work this week so work carefully in order to maximize your yield.

Introduction
In this week's activity you will take the ester methyl 2-hydroxybenzoate, hydrolyse it with aqueous sodium hydroxide and then separate the 2-hydroxybenzoic acid product.

Hydrolysis of the ester

a. Weigh out 3 g methyl 2-hydroxybenzoate into a 50 ml pear shaped flask.

b. Add 25 cm^3 of 2 mol dm^{-3} sodium hydroxide.

c. Add a couple of anti-bumping granules.

d. Set up for reflux.

e. Heat gently under reflux for 30 mins.

f. While refluxing, place a 100 cm^3 beaker containing 25 cm^3 of deionised water into an ice bath to cool.

g. After refluxing for 30 mins, allow the flask to cool for a couple of minutes and then pour the contents into a different 100 cm^3 beaker standing in an ice/water bath.

Separation of the 2-hydroxybenzoic acid
The reaction mixture in the beaker contains 2-hydroxybenzoate which is dissolved into solution with impurities and unwanted material. The addition of acid to the mixture causes the formation of 2-hydroxybenzoic acid which is insoluble in the solution and so appears as a precipitate.

h. Add conc. HCI(aq) dropwise, stirring continuously, until just acidic (test with UI paper) .

i. Filter using the vacuum pump, rinsing the beaker out with distilled water, and then the crystals with the ice cold water.

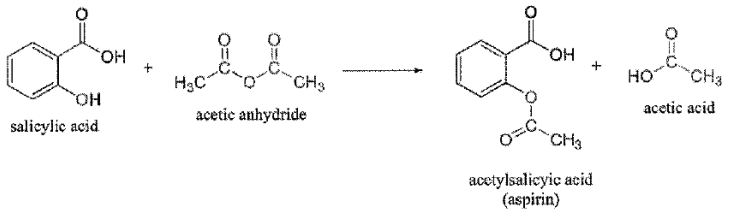
j. Place on a pre-weighed watch glass to dry.

Methyl 2-hydroxybenzoate	Harmful	WEAR EYE
2-hydroxybenzoic acid	Harmful	PROTECTION
2 $moldm^{-3}$ Sodium Hydroxide	Corrosive	AT ALL
Conc. Hydrochloric Acid	Corrosive	TIMES

Practical Two- Preparation of Aspirin

Introduction

In this week's activity you will take the 2-hydroxybenzoic acid (salicylic acid) you prepared last week and react it with ethanoic anhydride to produce aspirin. Ethanoic anhydride is a very reactive substance, you must wear gloves throughout this procedure.



Preparation

a) Pre-cool a 100 cm^3 beaker containing about 80 cm^3 of deionised water by standing it in an ice bath.

b) Weigh 2 g of the dry 2-hydroxybenzoic acid into a 100 cm^3 conical flask.

c) Add 4 cm^3 ethanoic anhydride and swirl to mix.

d) Carefully add 8 drops of conc. sulphuric acid

e) Place the flask into a hot water bath made from a large beaker containing water from the hot tap for 5-10 mins, swirling occasionally. The 2-hydroxybenzoic acid will dissolve.

f) Remove from the hot water bath.

g) Carefully add 10 cm^3 of the cooled water to the flask to remove excess anhydride.

h) Swirl the flask, let it cool until crystals start to appear then stand it in an ice/water bath for crystallisation to occur.

i) Leave it until no more crystals appear to be forming. (around 7-10 mins)

j) Filter using the vacuum pump, using the ice cold water to rinse out the flask and wash the crystals.

k) Place on a watch glass.

Purification by recrystallization

Your teacher will explain recrystallization to you while you wait for the crystals to form. There is space at the bottom of this page for you to make notes about this important technique.

a. Place the crude aspirin in a 100 cm^3 beaker.

b. Place the 100 cm^3 beaker containing the aspirin into a large beaker containing warm water from the hot tap. This is your water bath.

c. Add the minimum amount of ethanol needed to dissolve your crystals (approx. 20cm^3)

d. Remove from the water bath, Add 25 cm^3 deionised water (not ice cold) and leave the beaker to cool. Crystals will slowly begin to form. (This is quite slow and you will need to leave your beaker until your next lesson, make sure you label it).

2-hydroxybenzoic acid	Harmful
Aspirin	Harmful
Ethanoic Anhydride	Corrosive
Conc. Sulfuric acid	Corrosive
Ethanol	Flammable and Harmful

WEAR EYE PROTECTION AND GLOVES AT ALL TIMES.
AVOID NAKED FLAMES.
WIPE UP ALL SPILLAGES IMMEDIATELY.

Recrystallisation

Practical Three- Tests on aspirin

Obtaining a pure, dry sample

Take your beaker containing crystals from your last practical session, separate them from the solution by filtering them under reduced pressure.

Place your crystals onto a watch glass then carry out the tests below.

Test for phenol group

a. Put 2 cm^3 of deionised water into 2 test tubes.

b. Add a few crystals of aspirin to one and 2-hydroxybenzoic acid to the other.

c. Add 2 drops of neutral iron (III) chloride solution to each.

d. Note carefully your observations

Thin Layer Chromatography

a. Dissolve a few crystals of the aspirin and 2-hydroxybenzoic acid in a couple of drops of ethanol on a watch glass.
b. Carefully prepare your TLC plate by drawing a pencil line about 0.5cm up the plate.
c. Mark two crosses on the line.
d. On one of the crosses place a drop of your aspiring in solution.
e. Allow the drop to dry and then add another drop on top.
f. On the other cross place a drop of pure 2-hydroxybenzoic acid.
g. Allow the drop to dry and then add another drop on top.
h. The mobile phase is a mixture of cyclohexane, ethyl ethanoate and ethanoic acid. Use only a small amount to cover the bottom of the chromatography jar.
i. Place the TLC place in the jar and put the lid on.
j. After running the TLC and drying the plates in the fume cupboard, the plates will need to be placed in a covered beaker containing a few crystals of iodine to bring out the spots.
k. Sketch a diagram showing your chromatography plate after you have added the iodine.

Sketch of chromatography plate

Hazards and Precautions

Aspirin	Harmful
2-hydroxybenzoic acid	Harmful
Ethanol	Flammable and Harmful
Chromatography solvent (Cyclohexane, ethyl ethanoate, ethanoic acid 200:100:1)	Flammable, Harmful and Dangerous to the Environment.
Iodine	Harmful
Iron (III) Chloride	Low Hazard

WEAR EYE PROTECTION AT ALL TIMES.
AVOID NAKED FLAMES
ONLY USE CHROMATOGRAPHY SOLVENT IN FUME CUPBOARD.