Synthesis: Preparation of Salicylic Acid from Methyl Salicylate.

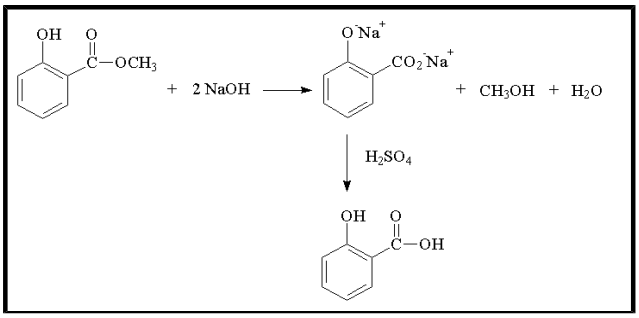
Introduction * ***Procedure***

(Adapted from Chickos, Garin and D'Souza, University of Missouri, St. Louis: http://www.umsl.edu/~orglab/

Introduction:

Many esters have "fruity" odors. Methyl salicylate, which is commonly referred to as oil of wintergreen and smells minty, is a compound having an ester function. It was first isolated in 1843 by extraction from a plant (*gaultheria spp*.) which is in the mint family. And, it was soon discovered that methyl salicylate has analgesic (eases pain) and antipyretic (lowers fever) properties that are almost identical to salicylic acid when taken orally. The similar medicinal effect probably results from hydroylsis to salicylic acid under the alkaline conditions found in the lower intestine. Methyl salicylate is lipophilic and can be absorbed through the skin. It is in a number of topically applied preparations. Methyl salicylate's pleasant odor results in it being used in flavoring foods and confections.

Under either acidic or basic aqueous conditions, esters can be hydrolyzed into their respective carboxylic acid and alcohol that they could have been prepared from. In this experiment, methyl salicylate, will be reacted with aqueous sodium hydroxide under reflux. Since this hydrolytic method results in a basic solution at the reaction's completion, the resulting carboxylic acid and phenolic (-OH) groups, which are acidic, are ionized at this stage and the compound exists as the sodium salt of salicylic acid, sodium salicylate, which is the conjugate base of salicylic acid. Therefore, the reaction mixture must be acidifed in order to recover the salicylic acid. The salicylic acid is then purified by crystallization from water.



Procedure: ***(Budget 1.5 lab periods)***

Complete the following table and place in your lab notebook under the ***Physical Constants Data*** section for this experiment.

	Structure	Molecular Formula	Molar mass(g/mol)	m.p oC.	b.p. oC	d g/mL	Safety
methyl salicylate				-8	223	1.17	
salicylic acid				159-161			
sodium hydroxide (6M)							
sulfuric acid (3M)							

Your synthetic target is to prepare 2.00g of pure salicylic acid. Calculate the amount of methyl salicylate in both **grams** and **mL** that you will need to start with as part of your prelab. Clearly show your calculation of how

many millimoles, grams, milliliters of methyl salicylate you plan to use to Dr. R. before going any farther. Then complete the calculations using the following experimental instructions, afterwards show your notebook again to Dr. R. for initialing.

Use 7 molar equivalents of base for each molar equivalent of methyl salicylate (MS). One molar equivalent is needed to neutralize the acidic phenolic hydrogen, another will neutralize the newly formed carboxylic acid. The rest of the base is in excess and must be neutralized with acid as well. The sodium hydroxide solution that is used is a 6M solution (6mol/L or 6mmol/mL).

Example calculation: If 1.52 g of MS were started with, which is 10 mmol of MS, 70 mmol of base (sodium hydroxide) is required. **? mL** 6M NaOH = 70mmol NaOH x mL/ 6mmol = **11.6mL, which can be rounded to 12mL**.

Add the aqueous sodium hydroxide to the methyl salicylate in an appropriate size single neck round bottom flask (rbf). [Specify the size in your prelab.] A white precipitate may form but it will dissolve upon heating. Add a boiling chip, and a very lightly greased condenser (to prevent the standard tapers from "freezing" together due to the base attacking the glass). Reflux for 30 minutes using a heating mantle. When the solution has cooled, transfer it to a 100 mL beaker. The disodium salt of salicylic acid is in the basic solution. Rinse the rbf with only a few mL of water and transfer this wash to the same beaker.

Neutralize the basic solution and acidify the disodium salt of the product by adding 3M sulfuric acid. Calculate how much sulfuric acid is needed to neutralize the amount of NaOH you actually used. [Specify the volume in your prelab.] A slight excess [2-3%] is needed so that the solution is definitely acidic in order to precipitate the product, salicylic acid. Check the acidity with pH indicator paper, add an additional 5-10% of the sulfuric acid to completely precipitate the SA.

Based on the example above 70 mmol of base that was used, which is 70 milliequivalents of base, you would need a minimum of 70 milliequivalents of acid, but remember sulfuric acid is diprotic and there are 2 equivalents per mole of acid.

Cool the solution to 0oC. Filter the crude salicylic acid using a Buchner funnel. Check the filtrate to be certain it is acidic. If not, add additional sulfuric acid to see if anymorel SA precipitates. The crude SA will contain water even after it is air dried for several minutes so weighing the crude product provides only an approximate, maximum yield.
Recrystallize the crude SA from very hot water (approx. 20 mL/g) using an Erlenmeyer flask. Use a minimum amount of boiling water by adding it slowly and observing how much compound goes into solution. Use a wooden stick to provide ebullation and prevent bumping. It may be necessary for you to gravity filter this solution. If so, this is one of the most difficult parts of the experiment since the solution and the glassware must be kept warm during the filtration otherwise the SA starts to precipitate too early. If necessary, gravity filter the hot solution using a piece of fluted filter paper in your powder funnel. Keep all solutions warm or else the SA will precipitate in the funnel rather than passing through into the receiver. If this occurs, it will be necessary to use a heat gun or heated filtrate to redissolve the solid.

The hot solution is cooled in an ice-water bath until precipitation appears to have ceased. The recrystallized salicylic acid is vacuum filtered, air dried for a few minutes, and then left in an open container to dry until the next lab period. At that time, you can weigh your dry sample and calculate your % yield. Record the melting point .

Post lab questions: Answer the following 3 questions plus the on-line questions (a-e).

1. What happened to the methanol produced in the reaction?
2. If you calculated that you needed 10 mL of 3M sulfuric acid but you discover that the only acid available is 6M hydrochloric acid, how many mL would you use?
3. If the entire salicylic acid sample that you obtained were reacted to produce a 100% yield of aspirin, how much aspirin (mg) would be produced.