

# Acetylsalicylic Acid (Aspirin) Synthesis

Johnson, Chad Philip; Thursday Lab, 1:00pm

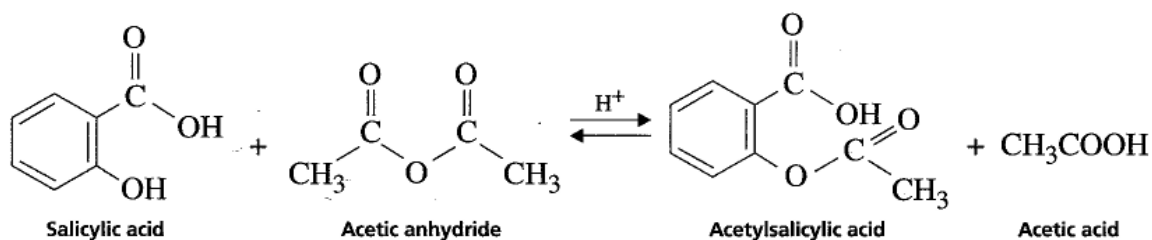
Submitted December 08<sup>th</sup>, 2011

## Introduction

Like many pharmaceuticals, the origin of aspirin comes from a biological chemical in nature. In the mid 18<sup>th</sup> century, a clergyman named Edward Stone discovered a new medicine within the bark of willow trees. This extract was used to treat many kinds of symptoms including fevers caused by malaria, acute rheumatism, general pain and discomfort, and swelling. Shortly thereafter, organic chemists were able to isolate and identify the active ingredient as salicylic acid. It was at this time when the compound would be produced for general consumption.

Improvements were necessary, as salicylic acid strongly irritated the stomach after ingested. A discovery in the late 19<sup>th</sup> century by the German chemist Felix Hofmann led to the synthesis of a new, similar compound called acetylsalicylic acid, which is what most people know to as aspirin. Its medicinal effects were the same as salicylic acid, but with muted levels of irritation, which made it much more convenient to use regularly as an analgesic.

Hofmann was able to produce acetylsalicylic acid by reacting salicylic acid with acetic anhydride in an acidic solution. The reactants undergo an esterification reaction, where the hydroxyl group (–OH) on the benzene ring of salicylic acid loses an H<sup>+</sup> and is replaced by an ester with an attached methyl group. In this experiment, I used Hofmann's methods to produce the same compound that is the primary ingredient in many of the "off the shelf" medicines that people take for everyday pain relief. The purity of my aspirin was measured by melting point temperature and infrared spectroscopy techniques.



**Figure 1.** Reaction scheme for the esterification of salicylic acid to form acetylsalicylic acid.

## Experimental Procedure

### *Reaction of salicylic acid with acetic anhydride*

To prepare the reaction, I added 2.005g of salicylic acid to a 125mL Erlenmeyer flask, along with 5.0mL of acetic anhydride and five drops of concentrated sulfuric acid. The contents of the flask were swirled until the solid dissolved completely. I then prepared a hot water bath at about 50°C and, using a hot plate and a thermometer attached to a ring stand, ensured that the temperature remained unchanged throughout the experiment.

Before submerging the 125mL flask within the hot water bath and beginning the experiment, I noticed that the mixture went through two changes: 1) complete dissolution of the solid after about five minutes to produce a clear and colorless liquid, and 2) reformation of the solid after about 15 minutes into a cloudy white and paste-like mixture. These new crystals dissolved once again and changed into a clear light-brown liquid after I secured the flask with a clamp to the ring stand and submerged it within the bath. The flask was removed after 15 minutes and then placed on the table so that it would return to room temperature. While cooling, the light-brown liquid began to return to the cloudy white, paste-like mixture from before.

After reaching room temperature, I mistakenly placed the flask into an ice water bath before the addition of 50mL of H<sub>2</sub>O. It remained this way for almost two minutes before I removed it, added the water as instructed by my lab manual and then returned it to the water bath. (I am noting this because I feel it had an adverse effect on the purity of my end product.) The flask was left to cool in the ice bath for an additional 10 minutes.

### *Retrieval of acetylsalicylic acid*

I prepared a filtration system by configuring a Büchner funnel lined with filter paper, a filter adapter and a filter flask attached directly to an aspirator, as detailed by the *Filtration* techniques section within our lab manual (Pavia 652). Using a spatula, I carefully added the contents of the 125mL Erlenmeyer flask to the funnel, washing out residual crystals with cold deionized water. After transferring all of the solid, the contents were left alone for about 10 minutes to remove any remaining liquids and impurities.

### *Tests for impurities*

A test for impurities using  $\text{Fe}^{3+}$  ions from ferric chloride was planned. Salicylic acid reacts with this ion to produce a red to violet color when it is present. Unfortunately, this resource was not available on the day of my experiment and had to be skipped.

I measured the melting point and compared it to the literature value. Also, IR spectroscopy was used to make additional observations about the products by using a KBr pellet. The pellet was created by mixing 0.155g of KBr into a very small amount of carefully ground product and inserting this into a die. Extreme pressure was applied to the die for two minutes within a Carver machine. This produced a clear pellet with white flecks that was about the size of a penny, which was then used to obtain an IR spectrum.

## **Results**

### *Yield, melting point and appearance*

**Table 1.** Data for the reaction of salicylic acid with acetic anhydride

Product	Yield (g)	Yield (%)	Experimental Melting Point	Literature Melting Point	Appearance
Acetylsalicylic Acid (Impure)	3.266g	163%	84°C - 86°C	135°C - 136°C <sup>†</sup>	White solid

<sup>†</sup> (Pavia 60)

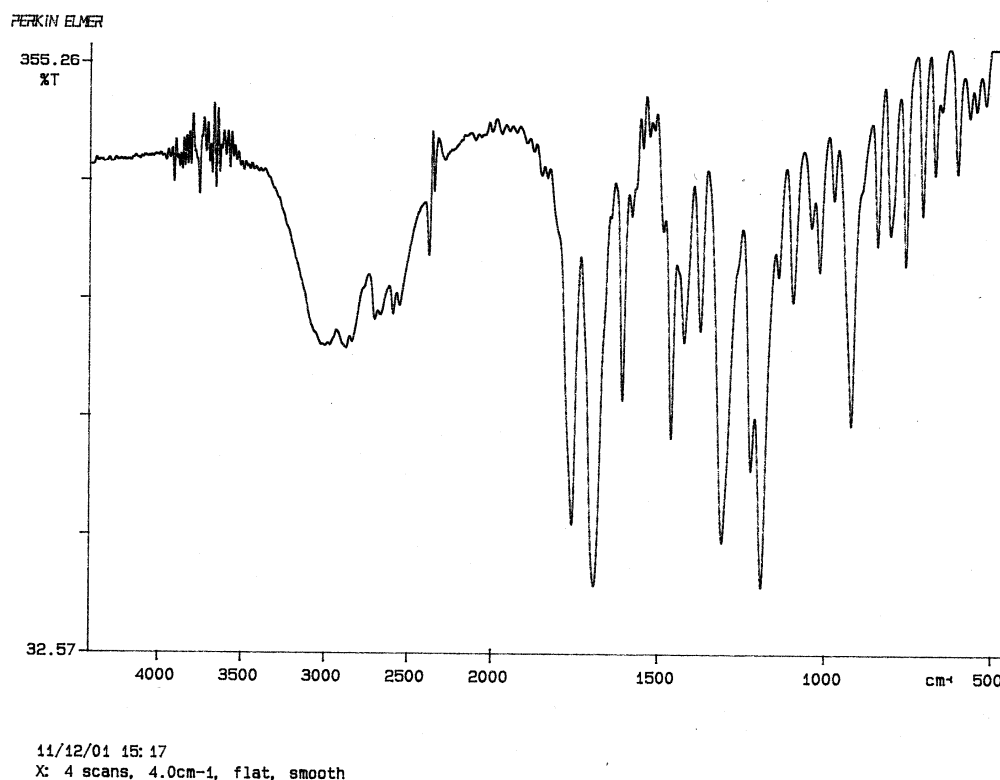
### *IR Data Summary*

The infrared spectrum did not help in determining exactly how many compounds remained in the final sample. However, one point of interest was that it appears as if the initial sample of salicylic acid reacted to completion. No traces of alcohol functional groups were observed in the 3400-3650  $\text{cm}^{-1}$  and 1050-1150  $\text{cm}^{-1}$  ranges (see Figure 2 on the next page), indicating that it was absent.

## **Discussion and Conclusion**

Many complications arose during this experiment that resulted in a very impure sample of acetylsalicylic acid. I believe that neglecting to add water to the mixture before submerging it into a cold water bath prevented many of the remaining impurities from being dissolved and subsequently removed.

Also, the lack of a ferric chloride test made reading the IR spectroscopy data more difficult and somewhat less certain. The very low melting point indicated that a high percentage of impurities remained in the product; these are likely to be acetic anhydride and acetic acid. I attempted to use IR spectroscopy data to distinguish whether only one of these two compounds was present, but found that this was not possible because both compounds have certain characteristics that are the same as acetylsalicylic acid (esters for acetic anhydride and carboxylic acid for acetic acid) and none that are unique.



**Figure 2.** IR spectrum for impure acetylsalicylic acid

## References

Pavia, D.L., Lampman, et al. *Introduction to Organic Laboratory Techniques, A Small Scale Approach*. 2<sup>nd</sup> ed. Belmont, CA: Brooks/Cole, 2005.