Microwave Assisted Green Synthesis of Aspirin From Over The Counter Pain Creams

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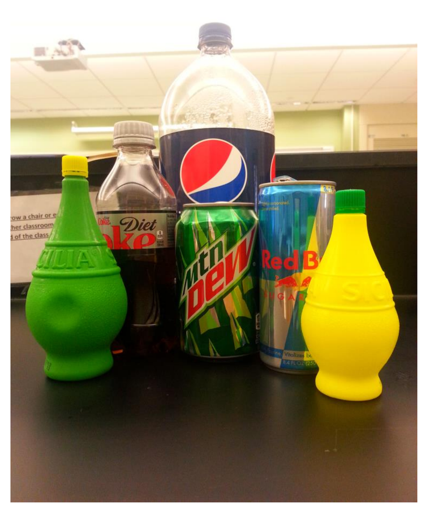
Abstract

Green chemistry, which has become a popular area of research, aims to devise processes that reduce or eliminate the production of harmful or hazardous substances (1). The isolation of methyl salicylate from over the counter pain creams, and its subsequent conversion to aspirin, while eliminating harmful reagents, was explored. Using microwave synthesis and green solvents (sodas and fruit juices) in place of sulfuric acid, salicylic acid (obtained via hydrolysis of methyl salicylate) was successfully converted to aspirin at an average researcher yield of 55% (individual yields were dependent on type of soda/juice). The successful synthesis was tested with first semester undergraduate organic chemistry students during the Fall 2013 semester, as a multi-week experiment. Student obtained results and yields were comparable, if not better.

Introduction

Previous research has shown that methyl salicylate (*MS*) from over-the-counter pain creams such as Tylenol Precise®, and Bengay® (2) could be used to make salicylic acid (*SA*); which can be hydrolyzed to aspirin (*As*) (3). Traditionally *As* synthesis is a reaction between *SA* an acetic anhydride catalyzed by a strong acid, in the presence of heat (4). The goal of this research was to combine the synthesis of *SA* from *MS* and the acid catalyzed conversion of *SA* to *As* via a greener, approach.



To convert the procedure to a green experiment beverages naturally containing acid were used in place of concentrated acid. In addition, a chemical microwave was used to improve reaction conditions. Microwave irradiation in synthesis reactions has become very common. It has offered many benefits such as improving yields of products, decreasing time needed, and also making experiments more efficient and less costly (5). Ideally, the new procedure will produce higher and purer yields of *As*, and will serve as a learning tool for undergraduate organic chemistry students.

Methods

Part 1: Extract active and inactive ingredients from over-the-counter pain cream and using methanol

Part 2: Extract *Methyl Salicylate* from menthol using MTBE

Part 3: Base catalyzed hydrolysis of *Methyl Salicylate* to form *Salicylic Acid*

Part 4: Place the *Salicylic Acid* in microwave tube with acetic anhydride and a few drops of pre-concentrated soda or juice as a catalyst. Microwave for 10 minutes, then add water and filter for *Aspirin* crystals.

Results/ Discussion

Figure 2. Average Percent Yield of Various Soda/ Juice Catalyst

Soda/Juice Catalyst	Average Research% Yield	Average Student* %Yield	pH
Pepsi	59.60%	68.89%	2.15
Lime	62.93%	70.43%	2.54
Lemon	55.81%	69.24%	2.56
Diet Coke*	58.23%	75.19%	3.41
Red Bull	59.00%	70.69%	3.43
Mountain Dew *	54.47%	55.53%	3.50
Grapefruit	50.53%	76.40%	3.54
Pineapple	41.00%	72.96%	4.06

- Hypothesized that a lower pH value would increase yields
- Obtained pH values of juices/sodas and determined there was no correlation between the pH and how well the catalyst worked
- Researcher yields were lower than student yields because students let crystals form over a week due to lab format, researcher let crystals form overnight
- Mountain Dew and Diet Coke only had one lab group of students to collect data
- The increased time, as the student data shows increases the yield, good for an undergraduate setting

- Products can be variously colored from different sodas and juices, this can be easily removed by recrystallization with hot ethyl acetate

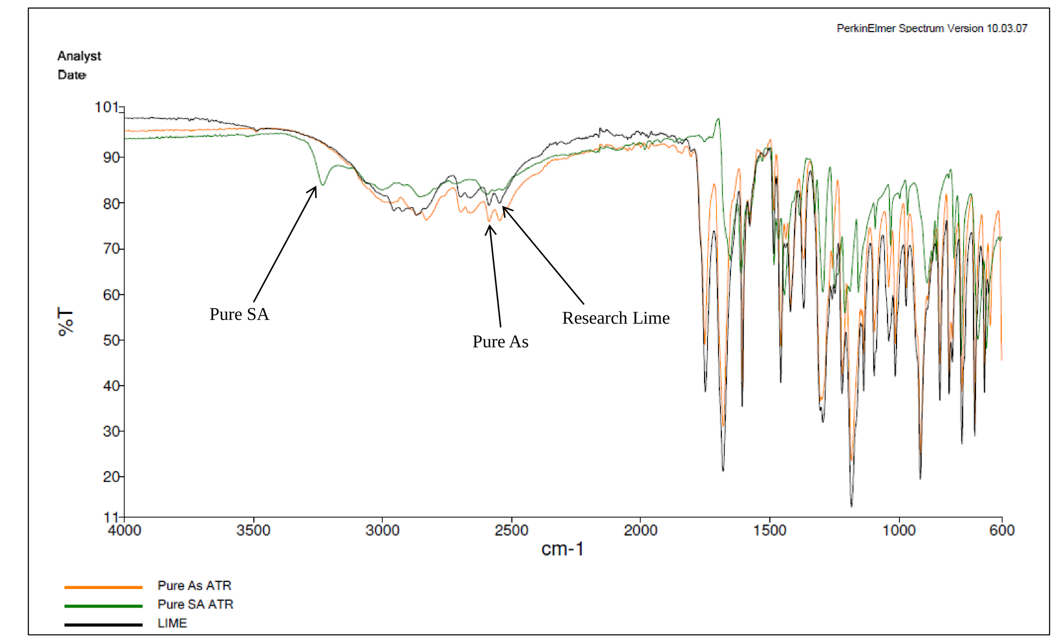
Figure 3. Average Melting Points of Various Soda/ Juice Catalyst

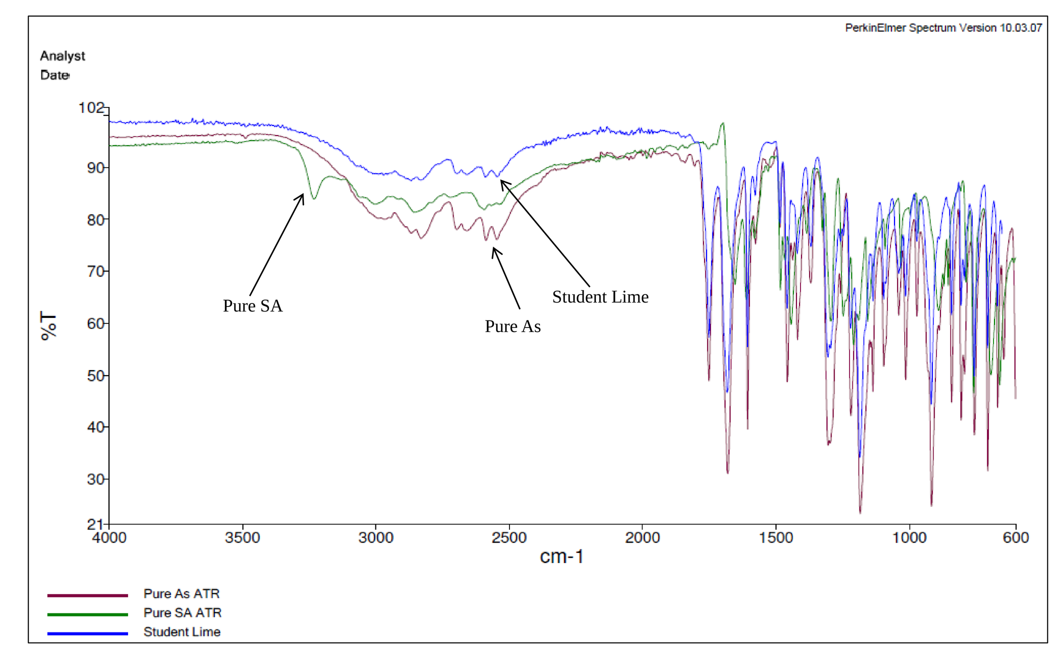
Product	Research Melt Point	Student Melt Point
Pure SA	158°C – 161°C	
Pure As	134°C – 136°C	
Diet Coke	129.05°C – 134.48°C	122.30°C – 125.95°C
Red Bull	123.25°C – 128.55°C	132.55°C – 135.33°C
Pepsi	122.45°C – 135.10°C	132.45°C – 135.60°C
Mountain Dew	122.05°C – 133.53°C	129.05°C – 133.35°C
Lemon	122.33°C – 130.18°C	124.65°C – 127.25°C
Lime	127.55°C – 132.13°C	125.65°C – 130.18°C
Pineapple	119.00°C – 126.50°C	125.93°C – 128.38°C
Grapefruit	128.10°C – 135.64°C	127.86°C – 130.60°C

- Melting points varied depending on the type of soda/juice used

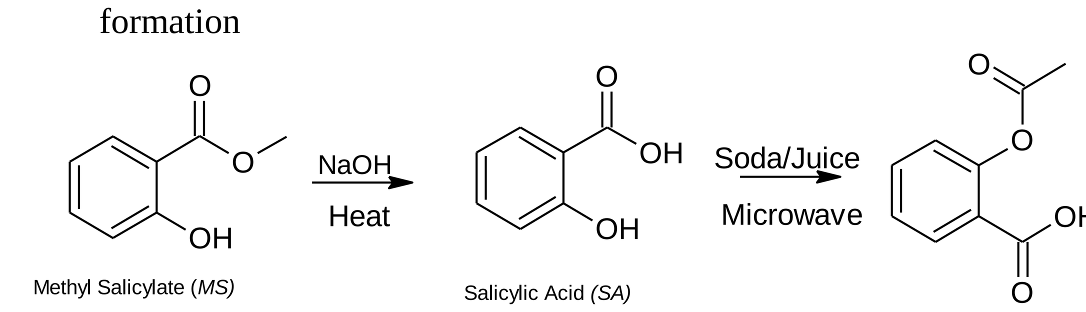
  Some tended to be a little lower than the melting point of pure As, indicating that there was still impurities in both the research and student samples

Results/ Discussion (cont'd)

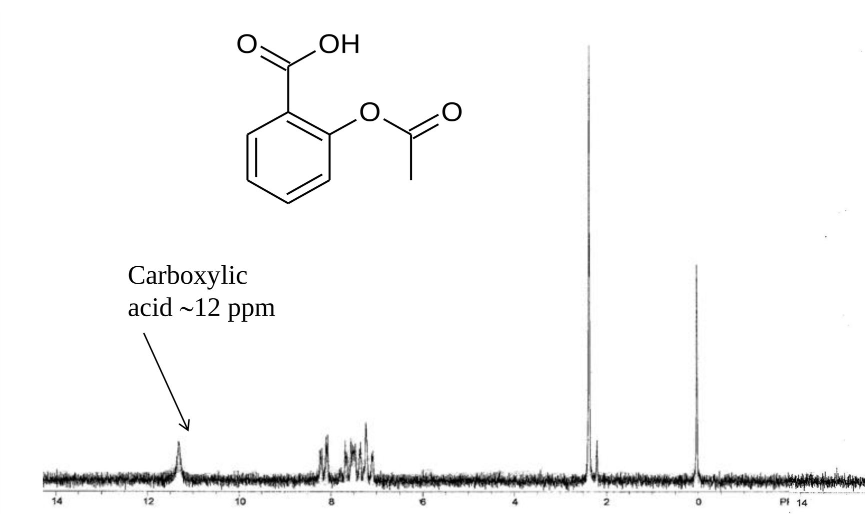




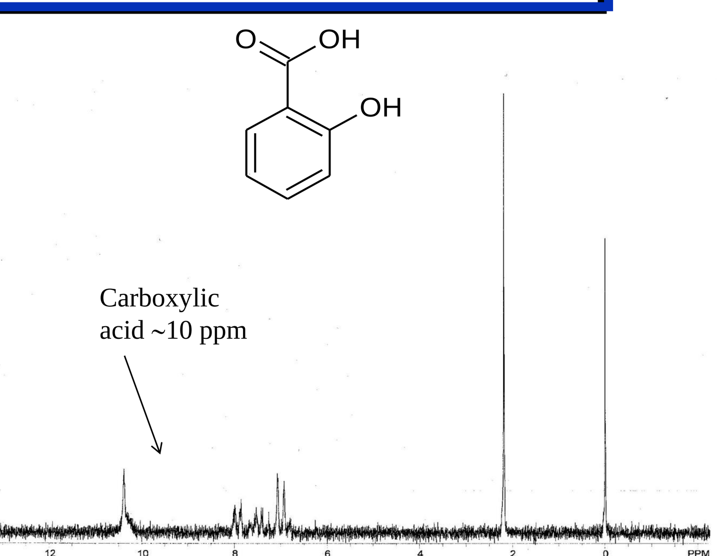
- Researched trials confirmed that pain cream conversion to SA was successful, and soda/juice catalyst were successful in microwave
- Student IRs are comparable to research IRs showing that As was successfully converted from SA in the Microwave
- This is seen on both IRs by the loss of a significant peak at approximately 3300 cm^{-1}
- As also has two different carbonyls (ester and acid) which shows up on the IR at about 1700 cm^{-1} this is also a significant indicator of product formation



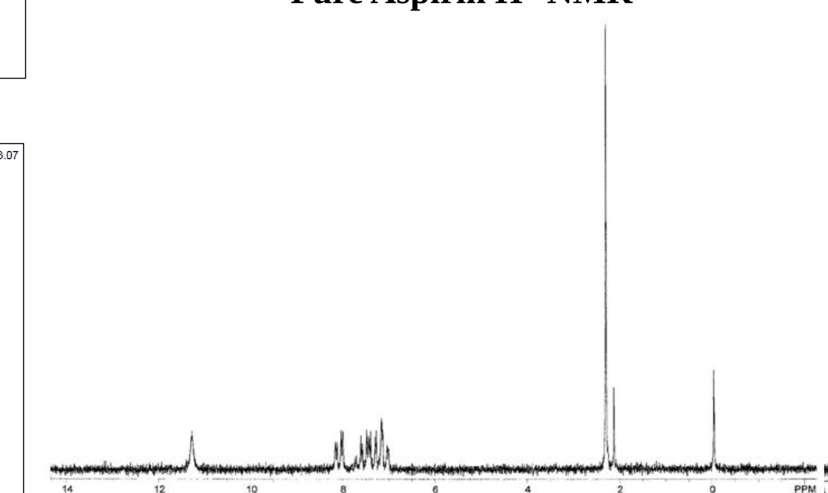
Results/ Discussion (cont'd)



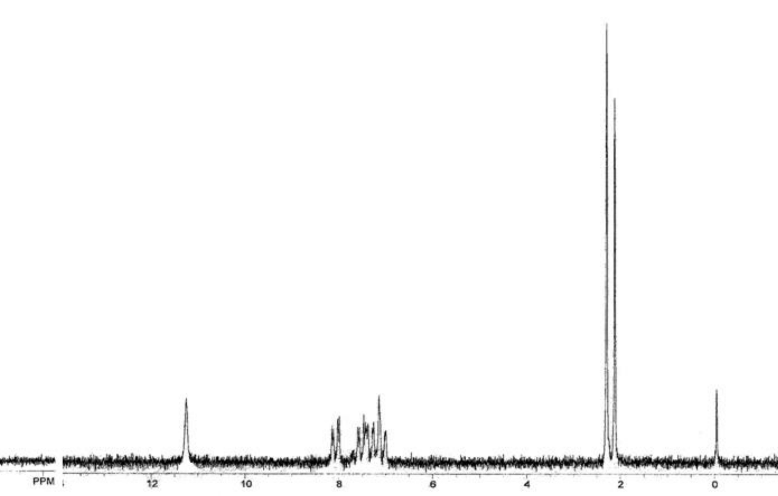
Pure Aspirin H^1-NMR



Pure Salicylic Acid H^1-NMR



Diet Coke H^1-NMR



Lime H^1-NMR

- H^1-NMR was also used to confirm product formation
- Key indicators on the H^1-NMR was the presence of two peaks at ~2 ppm for *As* (methyl and OH), and one peak at ~2 ppm for *SA* (OH); also the change in location of the carboxylic acid peak from ~10 ppm for *SA* to ~ 12 ppm for *As*

Conclusions

In conclusion, a greener aspirin synthesis using a microwave was successful in research, and as undergraduate organic chemistry lab experiment. The synthesis was produced a minimum Aspirin yield of 70% as a lab experiment .All data was supported by IR's , H-NMR's, and melting points .The procedure and method will be further tested to include more soda and juice catalyst and various pain creams.

Future Work

- Explore potential methods that will remove camphor
- Refine methods that will allow use of Icy Hot® pain cream

Acknowledgements

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