

# **The Synthesis of Aspirin from Wintergreen Oil**

A “Green” Two step synthesis of  
Aspirin

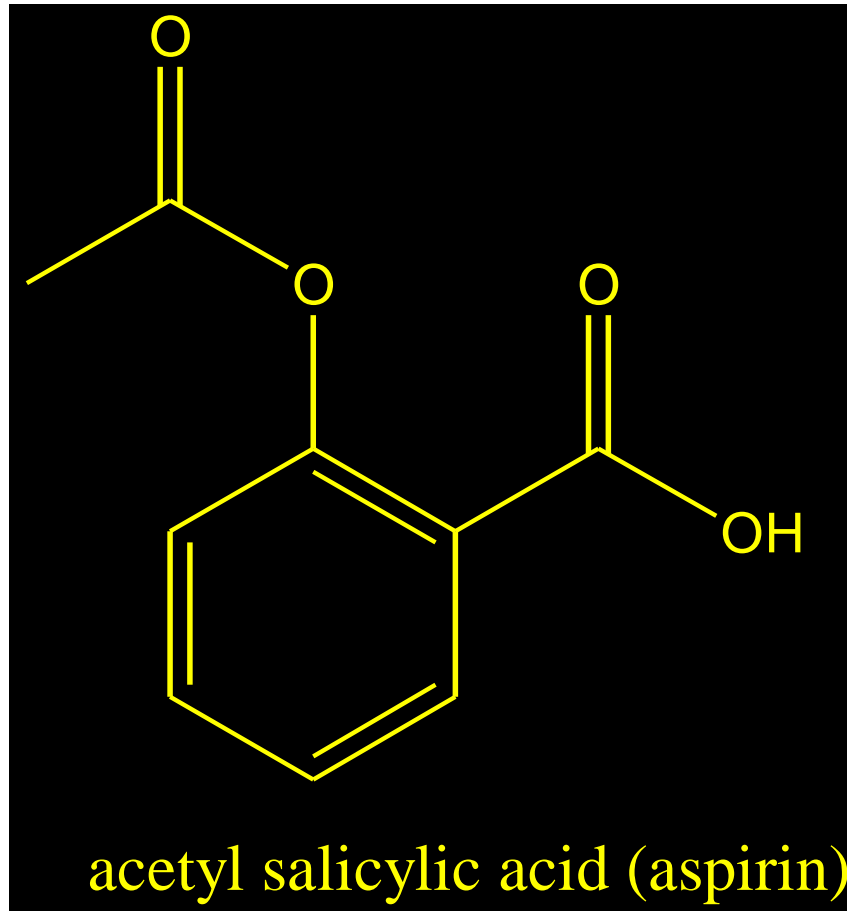
# Aspirin -Background

- also known as **acetylsalicylic acid** (abbreviated **ASA**), is a salicylate drug.
- Aspirin was first isolated by Felix Hoffmann, a chemist with the German company Bayer in 1897.
- Over \$1 Billion in annual sales
- World **production** of **aspirin** has been estimated at 45 thousand tons a year

# Aspirin –Biological Activity

- Analgesic (painkiller)
- Antipyretic (fever reducer)
- Anti-inflammatory (inhibition of the synthesis of prostaglandins)
- Side effects: gastric irritation, bleeding  
Inspiration for new analgesics, Tylenol & Advil

# Aspirin – Molecular Structure

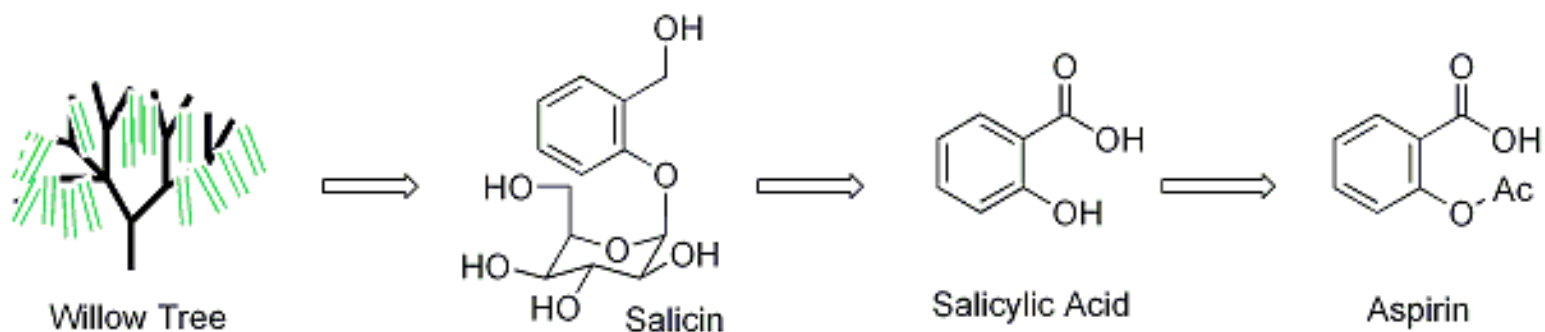


# The Problem

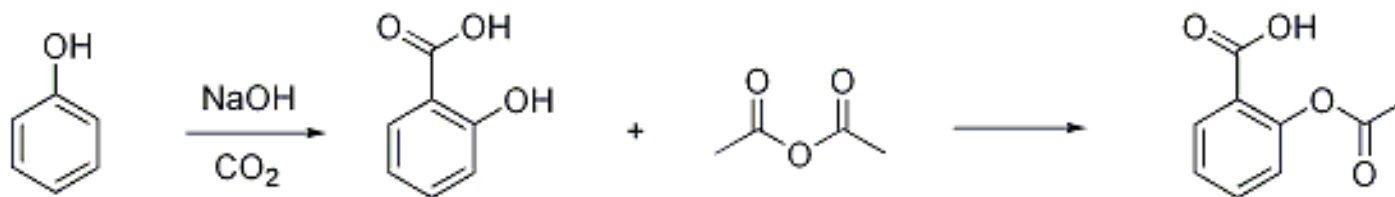
- Our new company is preparing to manufacture aspirin by a new synthetic route, a new “green” process from evergreen oil.
- The procedure is intended for manufacturing on a large scale (100 kg ).
- Testing for reproducibility as regards to yield and purity of Aspirin.



# Original Synthesis



First prepared by Gilm in 1859,  
introduced by Dreser into medicine in 1899.



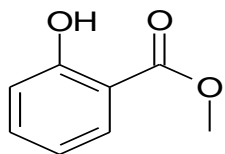
<http://www.ic.sunysb.edu/Class/che134/susb/susb028.pdf>

<http://www.sfu.ca/chemistry/students/courses/chem281/aspirin.htm>

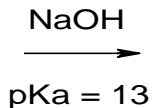
# Scheme 1: Synthesis of Aspirin

## STEP 1: Hydrolysis of methyl salicylate

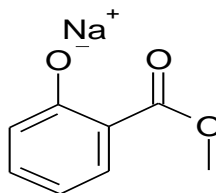
Wintergreen Oil  
Methyl Salicylate, MS



MW = 152.15  
MF = C<sub>8</sub>H<sub>8</sub>O<sub>3</sub>  
d = 1.18 g/ml  
pKa = 9.8

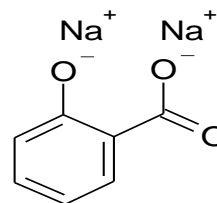


Sodium 2-(methoxy-carbonyl)phenolate



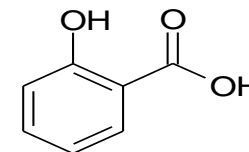
MW = 174.13  
MF = C<sub>8</sub>H<sub>7</sub>O<sub>3</sub>Na

Disodium salicylate



MW = 159.10  
MF = C<sub>7</sub>H<sub>4</sub>O<sub>3</sub>Na<sub>2</sub>

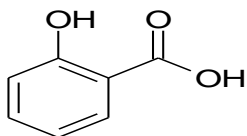
Salicylic Acid, SA



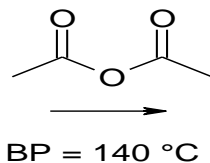
MW = 138.12  
MF = C<sub>7</sub>H<sub>6</sub>O<sub>3</sub>  
MP = 159 °C  
pKa = 2.9

## STEP 2: Acetylation of Salicylic Acid

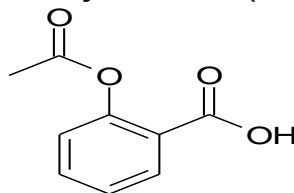
Salicylic Acid



MW = 138.12  
MF = C<sub>7</sub>H<sub>6</sub>O<sub>3</sub>  
MP = 159 °C



Acetylsalicylic Acid (Aspirin, ASA)



MW = 180.16  
MF = C<sub>9</sub>H<sub>8</sub>O<sub>4</sub>  
MP = 135 °C  
pKa = 3.5

# Experimental Procedure

- Perform Hydrolysis Reaction, Acetylation Reaction, Neutralization
- Perform typical organic synthesis chemistry laboratory techniques
  - Equipment setup, Refluxing, Crystallization, Filtration, Drying
- Perform identification and quantitative analyses using: IR, HPLC, MP
- Teams prepare final report comparing yield, purity, and identification of product using IR, MP, HPLC.



# Results & Calculations

**Table 1--Aspirin**

	<b>Product</b>	<b>Acetylsalicylic Acid</b>
	MW	180.16
1	Moles of Salicylic Acid	
2	Theoretical Yield (g)	
3	Dried/Isolated weight	
4	Wt % Purity (HPLC)	
5	Actual Yield (g)	
6	Moles of Aspirin	
7	Acetylation % Yield	

# Final Report

## Methyl salicylate identification ( yes or no)

Tests	Team 1	Team 2	Team 3	Team 4
MP				

## Step 1 Salicylic Acid Analyses

Tests	Team 1	Team 2	Team 3	Team 4
MP (135 lit)				
Spectrophotometric Weight % Assay				
Yield				

## Step 2 Acetylation: Salicylic Acid identification

Tests	Team 1	Team 2	Team 3	Team 4
IR conformity				

## Step 2 Aspirin Assays

Tests	Team 1	Team 2	Team 3	Team 4
MP-ID				
HPLC Area% Purity				
Yield				

# Final Report Questions

- What was the reproducibility of the reaction yield?
- How did the ID and quality of the methyl salicylate compare to the commercial grade?
- What other assays might be of value in determining the quality of the products?
- What recommendations does the synthesis team have to make?