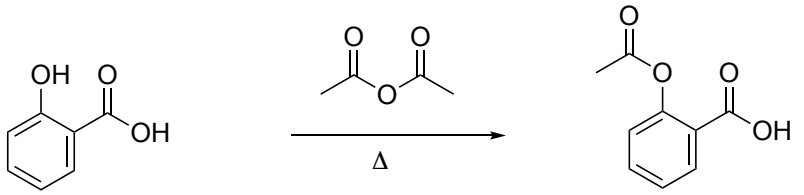
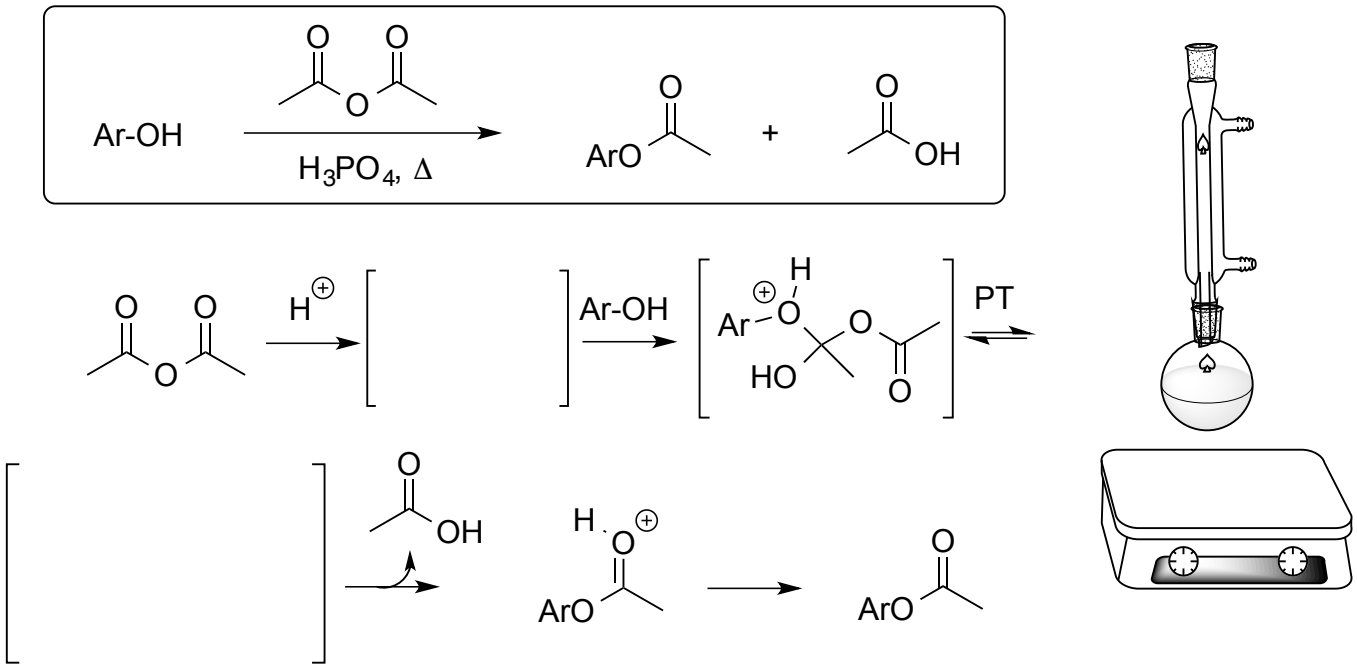
CHEM 8M, Experiment 5 – Synthesis of Aspirin

- Reaction Set Up, Work Up, Chemical Tests, IR,
- ^{1}H NMR Analysis and intro to ^{13}C NMR



Salicylic Acid **Acetylsalicylic Acid (Aspirin)**

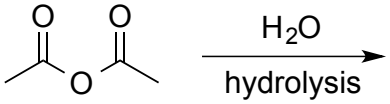
Reaction Mechanism & Set Up



Reaction Work Up

1. Cool for ~1 min

2. Add water to quench in warm water bath, 5 min



3. Crystallize

(a) Cool to RT, transfer to beaker

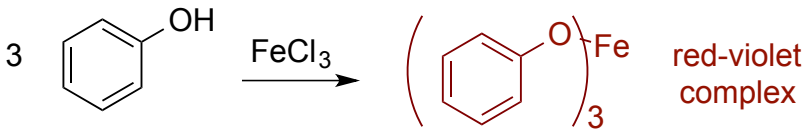
(b) Cool in ice bath, then scratch inside bottom of beaker, then wait!

(c) No crystals after ~5 min? Add seed crystal

- Wait at least 5 min *after* adding seed crystal to filter

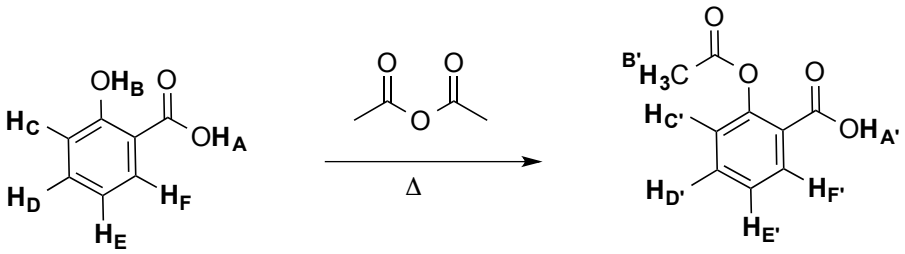
4. Vacuum Filtration

Ferric Chloride Test for Phenols



3 test tubes: (1) Salicylic Acid (2) Product (3) H_2O

IR Spectra of Salicylic Acid & Aspirin



Salicylic Acid

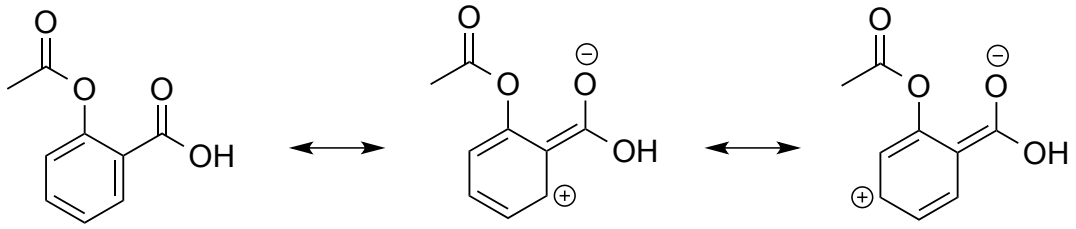
Acetylsalicylic Acid (Aspirin)

^{1}H NMR Analysis

Resonance effects in aromatic rings: *Predicting relative chemical shifts without calculations*

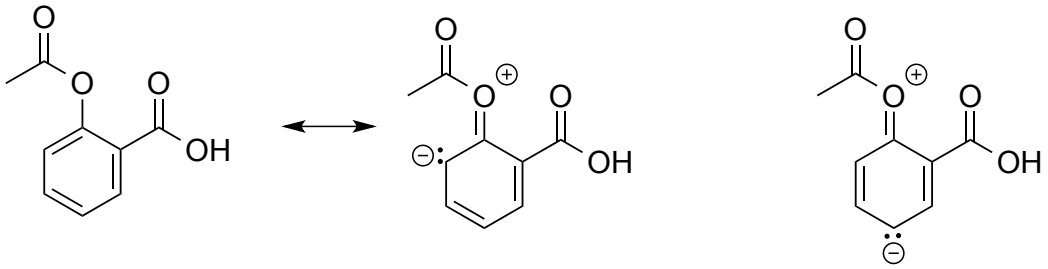
- Deshielding increases chemical shifts

EWG deshields the *ortho* & *para* H's

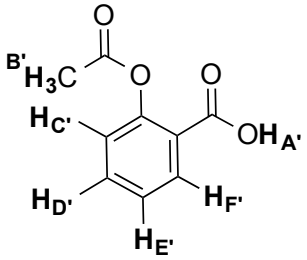


- Shielding decreases chemical shifts

EDG shields the *ortho* & *para* H's



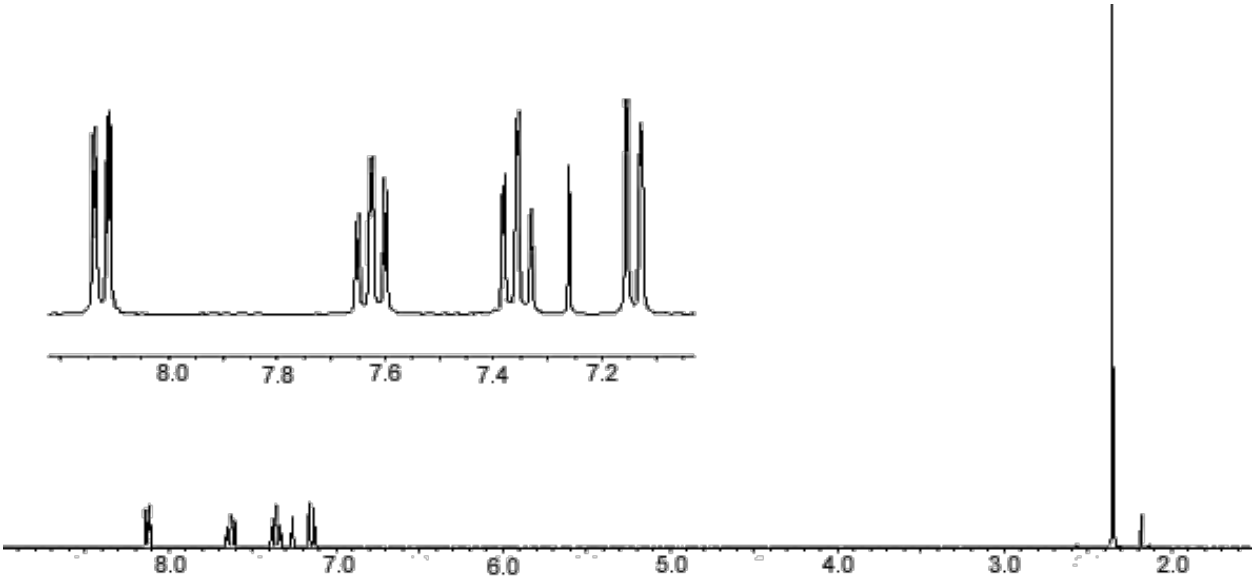
SUMMARIZE ^{1}H NMR of ASPIRIN



Acetylsalicylic Acid (Aspirin)

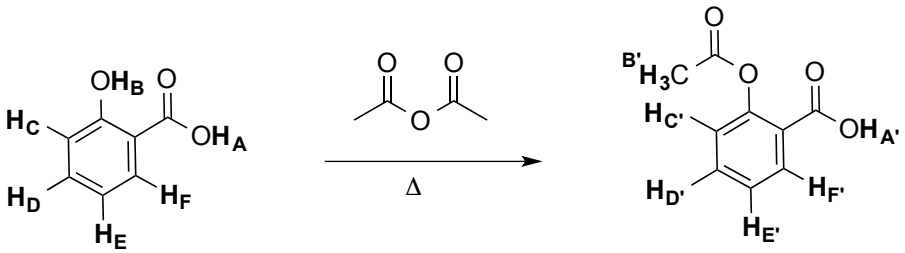
Most deshielded Ar-H (highest chem shift)

Most shielded Ar-H (lowest chem shift)



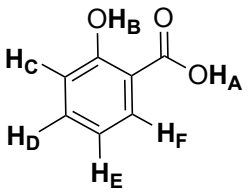
***11.5 ppm broad singlet** expected by not observed in this particular spectrum

What differences are expected / observed in the ^{1}H NMR of aspirin & its precursor?

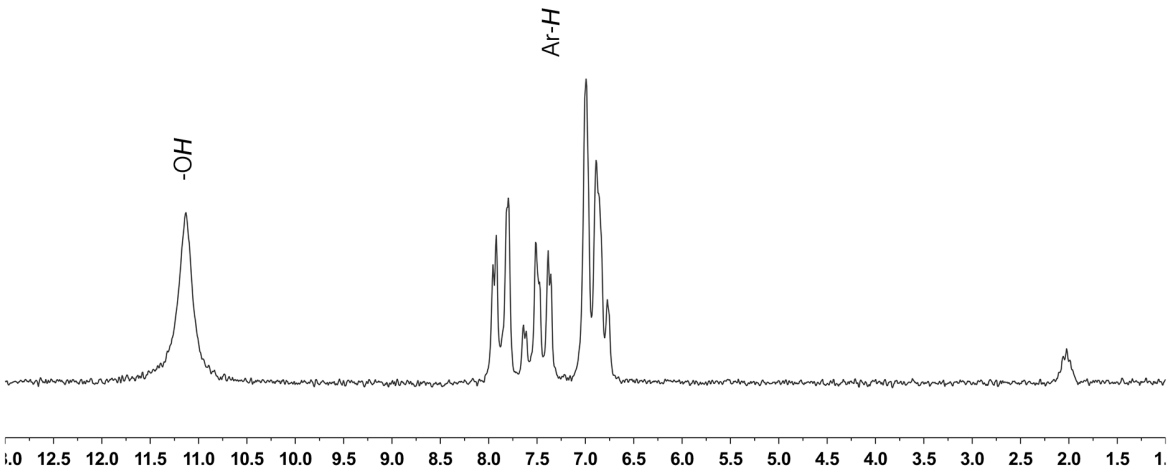


Salicylic Acid

Acetylsalicylic Acid (Aspirin)



Salicylic Acid



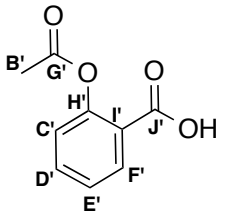
1H NMR Spectrum of Salicylic Acid

^{13}C NMR

- Exploring carbon nuclei of ^{13}C isotopes (< 1.1% abundance)
  - longer experiment, requires more sample

- ^{13}C nuclei resonate at higher chemical shifts (10-220ppm) than ^{1}H nuclei (0-12ppm)

- Similar deshielding effects to ^{1}H NMR



Acetylsalicylic Acid (Aspirin)

Deshielded **Shielded**

160 - 180 ppm	110 - 160	55 - 80	20 - 35
Carboxylic Acids, Esters O-**C**=O	Aromatic **Ar**	Alcohols, Esters O-**C**	Carboxylic Acids, Esters O=C-**C**

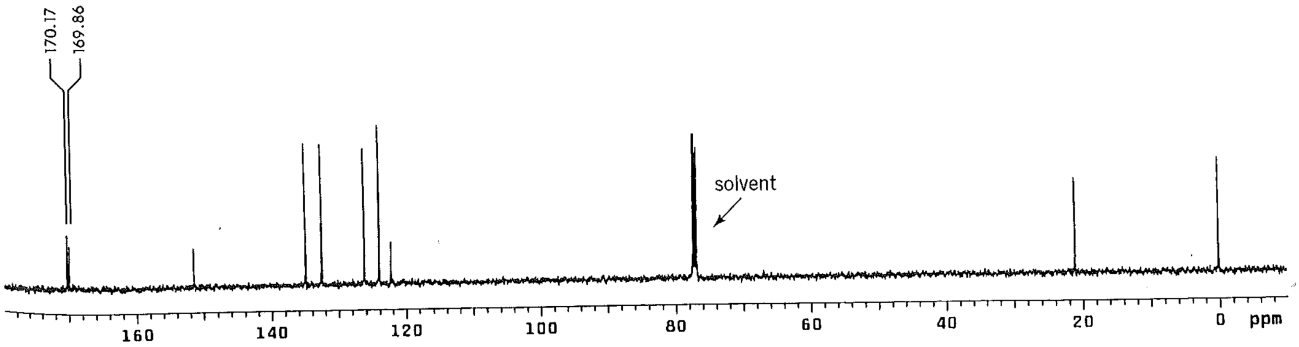
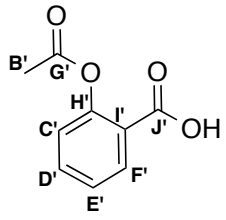


Figure 14.13 125.7-MHz ^{13}C-NMR spectrum of aspirin in $CDCl_3$.

 **Acetylsalicylic Acid (Aspirin)**	**Chemical Shift (Observed ppm)**	**Assignment(s) (A' – J')**	**Expected Chemical Shift Range (ppm)**
	169 & 170		
	152		
	125 – 135 (4 peaks)		
	122		
	20		