

Synthesis of Aspirin

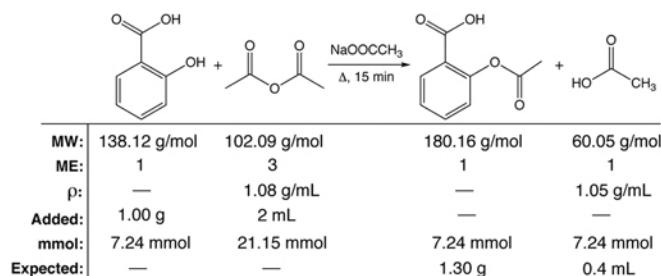
Incorporating instrumentation into undergraduate laboratories increases students' understanding of fundamental and practical characterization techniques.

The NMRReady™ benchtop spectrometer offers a portable and affordable option with a modern, network accessible, easy-to-use interface that can be easily incorporated into teaching laboratories.



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A Classic Undergraduate Experiment: O-Acylation of Salicylic Acid



Procedure:

Add anhydrous sodium acetate (0.2 g) to a suspension of salicylic acid in acetic anhydride & stir to combine. Heat the reaction mixture until the solids have fully dissolved (about 15 min). Remove from heat & add H₂O (11 mL) to ensure that excess acetic anhydride has been hydrolyzed. Place the flask in an ice bath to aid crystallization. After 20 min, collect the solid by vacuum filtration & wash with ice-water. Record the crude yield.

Transfer the crude product to an Erlenmeyer flask. Dissolve in minimal hot EtOH & add warm H₂O (10 mL). Once flask is sufficiently cooled, place in an ice bath until recrystallization is complete. Collect crystals by vacuum filtration, wash with minimal ice-cold H₂O. Dry & weigh the crystals, calculate percent yield & determine the melting point.

Key Concepts:

organic synthesis, O-acylations, base catalysis, stoichiometry, crystallization, vacuum filtration, percent yield, recrystallization, melting points

Students' Discussion:

From this data students are expected to discuss the reaction and assess the purity of their sample.

Although melting point can provide information about the sample purity, NMR data gives students greater insight into the amounts and types of impurities that may be present in their crude product. Additionally, this insight can be used to consider both the reaction and the possible byproducts that could form in side reactions.

Introducing a "hands-on" NMR component can illustrate these fundamental concepts while also training students in the most prevalent characterization method available to a chemist.

Enhance this Classic Experiment with the NMRReady:

Prepare a 0.25-0.5 M NMR sample of each of the following in *d*₆-acetone:

- 1) salicylic acid
- 2) acetic anhydride
- 3) crude aspirin
- 4) acetic acid
- 5) recrystallized aspirin

Additional time: ~1 min per sample = ~5 min

Measure a ¹H NMR spectrum for all five samples on the NMRReady™ benchtop spectrometer using the following parameters:

SW = 14 ppm ns = 16 scans
 time per scan = 4.6 sec total time = 1.2 min

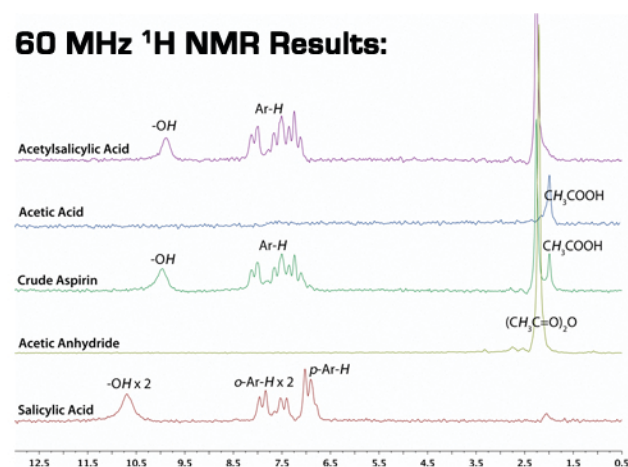
Additional time: ~1.2 min per sample = ~6 min

Work-up (*i.e.*, baseline correct, peak pick & integrate) the spectra & either print directly, save to USB drive and/or network folder & include copy in the report (*further details on back*).

Additional Concepts:

NMR sample preparation, NMR spectrometer operation, NMR characterization

60 MHz ¹H NMR Results:

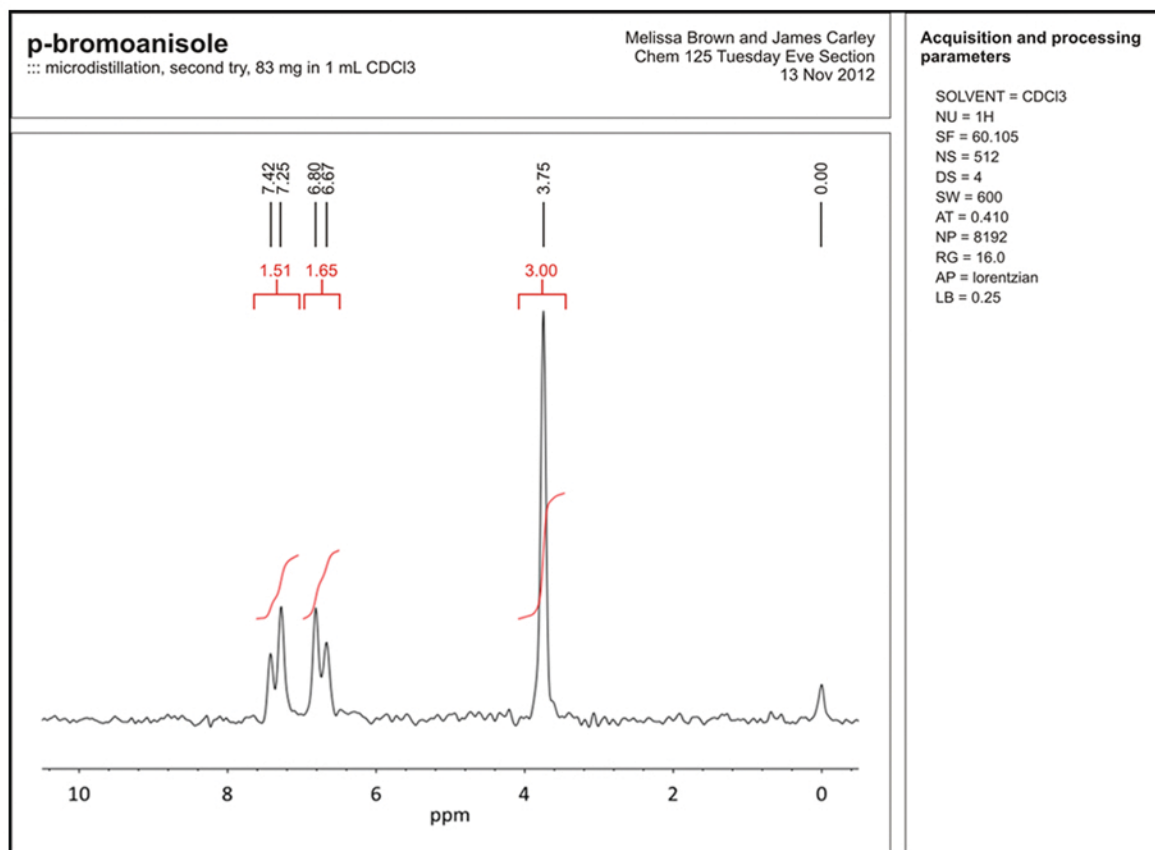


Extended Discussion:

- 1) Assign peaks in the ¹H NMR spectra.
- 2) What functional groups are absent/present in salicylic acid & aspirin? Use this information to explain the O-acylation reaction.
- 3) Assess purity of crude *versus* recrystallized aspirin.
- 4) What are the potential impurities in crude aspirin?
- 5) Can % purity be estimated from a peak integral?

Data Accessibility:

NMReady outputs to a networked drive and has a print option. Students can process and print in a third party software, like Mestrelab™, or use the NMReady directly. An example of data to be incorporated into a lab report processed and printed directly from the NMReady:



References:

- 1) Livengood, K. J., *Chem. Educ.* **2012**, *89*, 1001
- 2) Iler, H. D., *J. Chem. Educ.* **2012**, *89*, 1178
- 3) Olmsted, John III, *J. Chem. Educ.* **1998**, *75*, 1261

For additional ideas of how to incorporate the NMReady™ benchtop spectrometer into undergraduate laboratories please see:

- 1) S_N2 Reactions
- 2) Mixed Aldol Condensation
- 3) Biodiesel

available at:

www.nanalysis.com/experiments.html