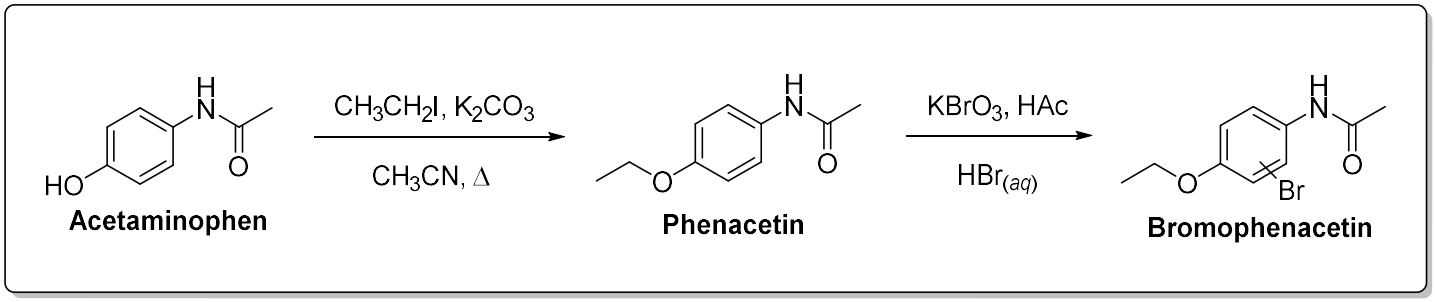
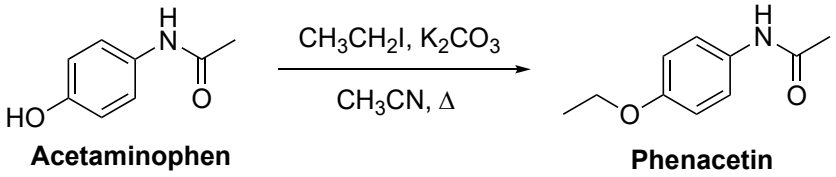
CHEM 110L, Experiment 3 – Synthesis & Bromination of Phenacetin



Part A. Synthesis of Phenacetin



Identify the **nucleophile**, **electrophile**, and **base** in the synthesis of phenacetin. Propose a **mechanism** for this transformation.

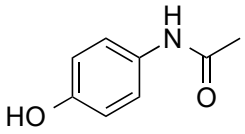
Draw a diagram of the **reaction setup**. What are the **safety concerns**? In which experiments have you used similar setups?

Draw a **flow chart with diagrams** of the **reaction work up** – label each layer with contents. In which experiments have you used similar reaction work ups?

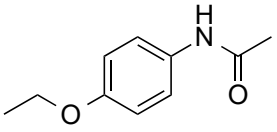
What are the **safety concerns** for the **reaction work up** and what can you get ready ahead of time to allow the work up run smoothly?

Phenacetin Analysis: What forms of analysis will you perform in Parts B? What are the **expected results** for each?

Predict the **^{1}H NMR spectra** for both compounds below – chemical shifts, integration, & splitting.



Acetaminophen



Phenacetin

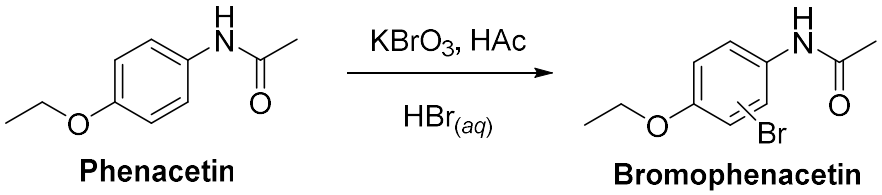
Describe each **coupling pattern**. Which of these are found in the spectra of acetaminophen and phenacetin?

Geminal **Vicinal** **Long-Range**

Part C. Bromination of Phenacetin: Substitution Puzzle

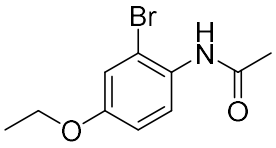
Electrophilic Aromatic Substitution (EArS) Reaction

- Identify both substituents as EDG or EWG. Is each weak or strong?
- To what position does each substituent direct the reaction?

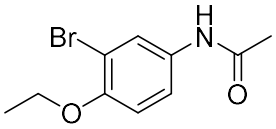


Phenacetin **Bromophenacetin**

Who's it gonna be?!

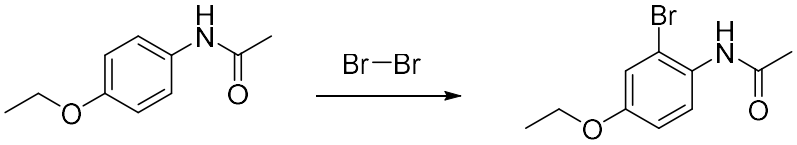


N-acetyl-2-bromo-4-ethoxyaniline
mp 96-97 °C

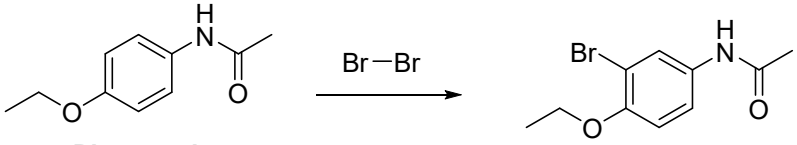


N-acetyl-3-bromo-4-ethoxyaniline
mp 112-114 °C

Potential Mechanisms



Phenacetin **"2-bromo"**



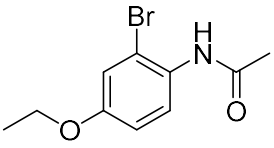
Phenacetin **"3-bromo"**

How will you know which product is made, based on only one ^{1}H NMR spectrum?

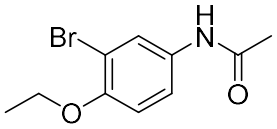
- Electron donating groups _____ chemical shifts in the _____ & _____ positions

- Electron withdrawing groups _____ chemical shifts in the _____ & _____ positions

- Predict the splitting patterns for the aromatic signals in each



N-acetyl-2-bromo-4-ethoxyaniline
mp 96-97 ^{o}C



N-acetyl-3-bromo-4-ethoxyaniline
mp 112-114 ^{o}C