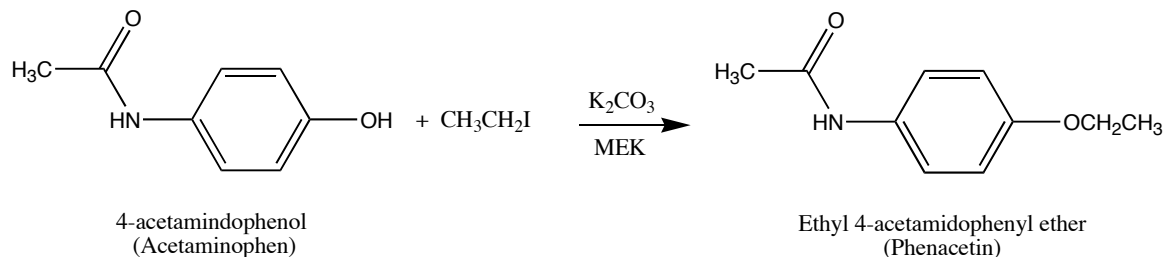


**ETHER SYNTHESIS: CONVERSION OF ACETAMINOPHEN INTO PHENACETIN**

**Required Pre-lab readings:** Ege, 5<sup>th</sup> Ed., sect 13.4, pp 498-501; Morhig, Chapter 19.

**Techniques you must be prepared to use:** reflux; extraction; rotary evaporation; recrystallization.

In the reaction today you will be converting 4-acetamidophenol (Acetaminophen) into ethyl 4-acetamidophenyl ether (Phenacetin). Both compounds are ingredients in many over-the-counter analgesics. This reaction is an example of the Williamson ether synthesis. For most ether syntheses strong bases such as amide ion are necessary to generate the nucleophile. In today's reaction the relatively weak base carbonate is used. Why does carbonate work?



In a 50 mL round-bottomed flask place 12 mmol of liquid ethyl iodide, 15 mL of methyl ethyl ketone (2-butanone; MEK) as solvent, Acetaminophen (1.5 g; ?? mmol.), and powdered anhydrous  $K_2CO_3$  (2.5 g; ?? mmol). Mechanically stir this mixture and reflux for 1 hour. After the reflux is complete cool the flask in an ice/water bath and gravity filter the contents into a separatory funnel. Use small amounts of ether to insure that you have quantitatively transferred all the organic material from the flask to the funnel. Wash the organic phase with 5% aq. NaOH (what is the purpose of this step?), then dry it ( $Na_2SO_4$ ) and decant into a flask and remove the solvents by rotary evaporation. The product is purified by recrystallization from water. Allow the purified product to air dry until next week when its weight and mp can be obtained.

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DATA SHEET****NAME:** \_\_\_\_\_**Section Number:** \_\_\_\_\_

Overall Reaction:

Mass of acetaminophen: \_\_\_\_\_

Theo moles phenacetin: \_\_\_\_\_

Moles of acetaminophen: \_\_\_\_\_

Theo mass phenacetin: \_\_\_\_\_

Volume of  $\text{CH}_3\text{I}$ : \_\_\_\_\_

Mass recovered phenacetin: \_\_\_\_\_

Moles of  $\text{CH}_3\text{I}$ : \_\_\_\_\_

Moles recovered phenacetin: \_\_\_\_\_

Mass of  $\text{K}_2\text{CO}_3$ : \_\_\_\_\_

% yield of phenacetin: \_\_\_\_\_

Moles of  $\text{K}_2\text{CO}_3$ : \_\_\_\_\_

Observed melting point of recovered phenacetin: \_\_\_\_\_

Literature melting point: \_\_\_\_\_

Literature source:

Calculations: (you may include these on a separate attached sheet)

Show the formal step-by-step "electron-pushing" mechanism for this reaction

Attach the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra for your starting material and product correctly identifying all of the peaks. All but the  $^1\text{H}$  NMR spectrum of your product will be distributed during class. To do this, draw the structure directly onto the spectrum and identify sets of equivalent nuclei on the structure using a, b, c... etc. Label the appropriate NMR signals in similar fashion. Fill in the table below using the  $^1\text{H}$  NMR spectrum of your product.

$^1\text{H}$  NMR Spectrum of Product:

$\delta$ (ppm)	Multiplicity	Number of H's	Identification

Draw the structure of your product below and include the labels (a,b,...) from the table above.