Synthesis of Ethyl n-Butyl Ether
Adapted by R. Minard and Todd Garber (Penn State Univ.) from Practical Organic Chemistry. Revised 3/26/99

Introduction:

The Williamson ether synthesis is an example of a nucleophilic substitution reaction. The nucleophile is an alkoxide anion which displaces a halide ion, typically chloride or bromide, from a primary haloalkane:

\[
\text{RO}^- \text{Na}^+ + \text{R}' - \text{X} \rightarrow \text{RO}^- \text{R'} + \text{Na}^+ \text{X}^-
\]

For this experiment, the specific reaction is:

\[
\begin{align*}
\text{O}^- \text{Na}^+ & \quad \text{n-bromobutane} & \quad \text{b.p. 104°C} \\
\text{Br} & \quad \text{Ethyl n-butyl ether} & \quad \text{b.p. 94°C}
\end{align*}
\]

The alkoxide can be generated by addition of metallic sodium to the corresponding alcohol. Alternatively, addition of concentrated sodium hydroxide to the alcohol sets up an equilibrium involving the alkoxide ion:

\[
\text{ROH} + \text{Na}^+ \text{OH}^- \rightleftharpoons \text{RO}^- \text{Na}^+ + \text{H}_2\text{O}
\]

Although the Williamson ether synthesis is a general method for the laboratory production of ethers, there are some limitations to its use. Since the alkoxide ion is a strong base, their use is limited to primary unhindered alkylating agents. Otherwise, elimination competes strongly with the nucleophilic substitution for the reactant molecules. Sometimes the reaction is run in a solvent which fosters the S_N2 process, such as DMSO or HMPA. The alcohol from which the alkoxide was derived provides an alternative solvent if it is inexpensive. FOR A MORE THOROUGH DISCUSSION OF WILLIAMSON ETHER SYNTHESIS, REFER TO YOUR ORGANIC CHEMISTRY TEXTBOOK.

The objectives of this experiment are: 1) to alkylate the ethoxide ion with 1-bromobutane; 2) to determine the product composition by gas chromatographic analysis; and 3) to confirm the structure of the product(s) by analysis with GC-mass spectroscopy.

Prelaboratory Exercise:

What would be the predominant products from the reaction of sec-butyl bromide with sodium ethoxide?

Cautions:

Ethanolic sodium hydroxide is extremely caustic! If you spill any on your skin, wash the affected area immediately with plenty of soap and water!

TLC

You are required to run a TLC to monitor the progress of the reaction. Plates should have three spots (or lanes) on the origin: one for the main organic starting material that is being transformed, one for a cospot (starting material and the reaction mixture), and one for the reaction mixture.

Synthesis:

Working rapidly, crush 3 average-sized, solid sodium hydroxide pellets into small particles using a mortar and pestle (obtained from the stockroom). Place the crushed sodium hydroxide in a reaction tube and then add 1 mL of 95% ethanol. Fit the reaction tube with the air condenser (distilling column). Heat the mixture using a sand bath, allowing it to reflux for 20 minutes.

After the 20 minutes, allow the hot solution to cool to room temperature. Add 0.8 mL (1 g) 1-bromobutane (n-butyl bromide) to the reaction mixture through the top of the air condenser. Once again, use the sand bath to
heat the mixture, allowing it to reflux for 1.5 hours. After the allotted time, allow the reaction mixture to cool to room temperature.

**Isolation and Purification:**
Remove the air condenser from the reaction tube and add 2 mL of water. Flick the tube to achieve good mixing and note which layer is the organic layer and which is the aqueous. After the layers have separated, use a Pasteur pipet to transfer the aqueous layer to a test tube. (Be sure to evaluate the layers to be sure which one is which!) Then add 1 mL of water to the organic layer, swirl, and after the layers separate, transfer the aqueous layer to the test tube. Repeat this extraction two more times with 1 mL of water. Save all of the aqueous washings temporarily, but when you are done with the experiment, discard the aqueous washings.
Next add 2 or 3 spatula tips of anhydrous magnesium sulfate to the organic layer, still in the original reaction tube, to absorb the traces of moisture. Agitate for 15 minutes to completely dry the organic layer. Filter out the magnesium sulfate using a Pasteur pipet. Transfer the dried product to a tared "shorty" vial and determine the weight of the isolated crude product.

**Cleaning-up:**
Allow the magnesium sulfate to dry in a fume hood before disposal in the trash bin. The aqueous washings from the purification of the product can be flushed down the drain.

**Product Analysis:**
In addition to TLC analysis, analyze your product by IR, UV-Vis, GC or NMR analysis as assigned on your Experiment Assignment sheet.
**GC:** Prepare your product for GC analysis according to your Lab Guide. This solution can be analyzed directly by gas chromatography using conditions described in the *Compendium of GC Conditions* to be found in room 206.
**NMR:** Run in CDCl₃. Integrate the spectrum so that you can determine the amount of starting material in your product.

**Final Report:**
Using the GC data, calculate roughly the percent conversion of 1-bromobutane to ethyl n-butyl ether. Make sure that you don't include solvent in the area calculation (area product / [area starting + area product]). Calculate the approximate yield by multiplying the percent conversion by the weight of the product.

**Postlab Questions:**
1. Draw the transition state structure for this reaction.
2. State which compound, ethyl n-butyl ether or 1-bromobutane, eluted from the gas chromatography column first (had the shorter retention time). Explain why the order of compound elution is reasonable in terms of molecular structure or boiling point. Experimentally, how could this have been confirmed by the chemist who prepared the data contained in the *Compendium of GC Data* in the Instrument Room?
3. Using the same experimental procedure as in this experiment (i.e. refluxing), explain why using bromoethane and sodium n-butoxide (which in principle, would give the same product) would not work as well. (Hint: look at boiling points of reactants.)