The S\textsubscript{N}2 Reaction: 1-Bromobutane
from K. L. Williamson, Macroscale and Microscale Organic Experiments, 2nd Ed. 1994, Houghton Mifflin, Boston. p247; revised 2/22/02

Prelab Exercise:
Review the mechanism of the S\textsubscript{N}2 reaction in the previous chapter. Prepare a detailed flow sheet for the isolation and purification of 1-bromobutane. Indicate how each reaction by-product is removed and which layer is expected to contain the product in each separation step.

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH} & \quad \rightarrow \quad \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Br} + \text{NaHSO}_4 + \text{H}_2\text{O} \\
1-\text{Butanol} & \quad \text{bp} 118^\circ\text{C} \quad \text{den} 0.810 \\
\text{MW} 74.12 & \quad \text{n} 1.399 \\
\text{NaBr, H}_2\text{SO}_4 & \\
1-\text{Bromobutane} & \quad \text{bp} 101.6^\circ\text{C} \quad \text{den} 1.275 \\
\text{MW} 137.03 & \quad \text{n} 1.439
\end{align*}
\]

Introduction:
In this experiment 1-butanol is converted to 1-bromobutane by an S\textsubscript{N}2 reaction. In general, a primary alkyl bromide can be prepared by heating the corresponding alcohol with

1. constant-boiling hydrobromic acid (47\% HBr),
2. an aqueous solution of sodium bromide and excess sulfuric acid, which is an equilibrium mixture containing hydrobromic acid, or
3. a solution of hydrobromic acid produced by bubbling sulfur dioxide into a suspension of bromine in water.

Reagents (2) and (3) contain sulfuric acid at a concentration high enough to dehydrate secondary and tertiary alcohols to undesirable by-products (alkenes and ethers), and hence the HBr method (1) is preferred for preparation of halides of the types R_2CHBr and R_3CBr. Primary alcohols are more resistant to dehydration and can be converted efficiently to the bromides by the more economical methods (2) and (3), unless they are of such high molecular weight as to lack adequate solubility in the aqueous mixtures. The NaBr-H\textsubscript{2}SO\textsubscript{4} method is preferred to the Br\textsubscript{2}-SO\textsubscript{2} method because of the unpleasant, choking property of sulfur dioxide. The overall equation is given above, along with key properties of the starting material and principal product.

The probable by-products are 1-butene, dibutyl ether, and the starting alcohol. The alkene is easily separable by distillation, but the other substances are in the same boiling-point range as the product. However, all three possible by-products can be eliminated by extraction with concentrated sulfuric acid, which does not dissolve the product.

Before undertaking a preparative experiment, you should analyze the procedure and calculate the molecular proportions of the reagents.
**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.

### Procedure: Synthesis of 1-Bromobutane

\[
\text{NaBr, H}_2\text{SO}_4 \quad \rightarrow \quad \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH} \quad \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Br} + \text{NaHSO}_4 + \text{H}_2\text{O}
\]

- In a 5-mL round-bottomed long-necked flask dissolve 1.33 g of sodium bromide in 1.5 mL of water and 0.80 g of 1-butanol. Cautiously, with constant swirling, add 1.1 mL (2.0 g) of concentrated sulfuric acid dropwise to the solution. The NaBr will dissolve during heating. Fit the flask with a distillation head and ice-cooled receiver (off the side arm), and reflux the reaction mixture on the sand bath for 45 minutes, taking care that none of the reactants distill during the reaction period.

- Wrap the upper end of the apparatus with damp cotton if escaping vapor is a problem. The upper layer that soon separates in the reaction flask is the alkyl bromide, because the aqueous solution of inorganic salts has the greater density. Remove the cotton, insulate the flask with cotton or glass wool, and distill the product into a collection vial until no more water-insoluble droplets come over, by which time the temperature of the distillate should have reached 115°C. If in doubt about whether all the product has distilled, collect some of the distillate in a small tube and examine it carefully. The sample collected in the receiver is an azeotrope of 1-bromobutane and water containing some sulfuric acid, 1-butene, unreacted 1-butanol, and di-n-butyl ether. To ease cleanup, wash the round-bottomed flask immediately. Rinse the distillation head with acetone so that it will be dry for use later in the experiment.

- Transfer the distillate to a reaction tube, rinsing the vial with about 1 mL of water, which is then mixed with the sample in the reaction tube. Note that the 1-bromobutane now forms the lower layer. Remove the 1-bromobutane with a Pasteur pipette, and place it in a dry reaction tube. Add 1 mL of concentrated sulfuric acid, and mix the contents well by flicking the tube. The acid removes many unreacted starting material as well as any alkenyl or ethereal by-products.

- Allow the two layers to separate completely, and then remove the sulfuric acid layer. The relative densities given above will help identify the two layers. An empirical method of distinguishing the layers is to remove a drop of the lower layer into a test tube of water to see
whether the material is soluble (H₂SO₄) or not (1-bromobutane). Separate the layers and wash
the 1-bromobutane layer with 1 mL of 3 M sodium hydroxide solution (density 1.11) to remove
traces of acid, separate, and be careful to save the proper layer. In experiments of this type, it is
good practice to save all layers until the product is hand.

Separate the layers and wash the 1-bromobutane layer with 1 mL of 3 M sodium hydroxide
solution (density 1.11) to remove traces of acid, separate, and be careful to save the proper layer.

- Dry a 5-mL round-bottomed flask by rinsing it with a milliliter of ethanol followed by a milliliter
  of acetone and then drawing air through it using the vacuum. Dry the cloudy 1-bromobutane by
  adding anhydrous calcium chloride pellets and mixing until the liquid clears and the calcium
  chloride no longer clumps together. After 5 min, decant the dried liquid into the dry 5-mL round-
  bottomed flask. It is very important when drying an apparatus of this type to remove all the wash
  solvent, acetone in this case; otherwise, it will contaminate the final product. Rinse the drying
  agent with two 1 mL portions of p-xylene (bp 137-138 °C), which is then transferred to the
  round-bottomed flask. The high-boiling xylene is a "chaser"; it chases all the bromobutane from
  the distilling flask. Otherwise, about 0.3 mL would remain behind.

- Add a boiling stone, pack the neck of the flask with a stainless steel sponge for fractional
distillation, and fit it with a dry distilling head and thermometer. Use the Viton (black) connector
  between the flask and the distilling head. Wrap the column with cotton or glass wool and distill,
collecting material boiling in the range 99 to 103 °C. Stop collecting the moment the temperature
  begins to rise above 103 °C. Most of the product will boil at 102 °C. A typical yield is in the range
  of 1 to 1.2 g.

Cleaning Up
Carefully dilute all nonorganic material with water (the pot residue, the sulfuric acid wash, the
sodium hydroxide wash), combine, and neutralize with sodium carbonate before flushing down
the drain. All organic material, because it is contaminated with small quantities of product, must
be placed in the halogenated organic waste container. The drying agent, wet with p-xylene,
goes in the hazardous waste container for solvent-contaminated drying agent.

Analysis
In addition to TLC analysis, you may be instructed to analyze your final product by NMR, GC, GC-
MS or RI. Analyze your sample according to your assignment sheet and the instructions on
Sample Preparation in the Lab Guide.
You may obtain a GC-MS after a suitable GC is obtained (all the peaks must be resolved in the
GC before you proceed to do a GC-MS with TA’s permission).

Post Lab Questions
1. Write reaction mechanisms showing how 1-butene and di-n-butyl ether are formed.
2. Why is it necessary to remove water before distilling the 1-bromobutane?
3. Interpret the ¹H NMR spectra of butanol given below.
$^{13}$C NMR spectrum of 1-butanol (22.6 MHz).

$^1$H NMR spectrum of 1-butanol (250 MHz).

$^{13}$C NMR spectrum of 1-bromobutane (22.6 MHz).