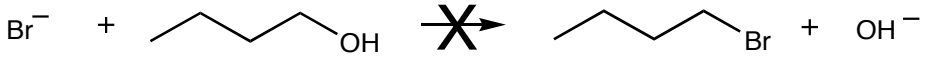
Nucleophilicity and Nucleophilic Substitution

Objective

To determine the relative nucleophilicity of Br^- and Cl^- ions and to compare the role of the nucleophile in S_N1 and S_N2 reactions.

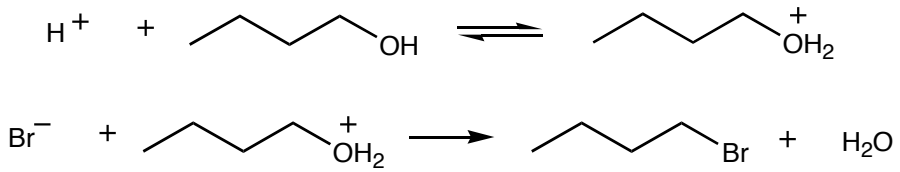
Background

Chloride and bromide are both nucleophiles. In this experiment, you will explore the nucleophilicity of Br^- and Cl^- ions and the importance of the nucleophile strength in S_N1 and S_N2 reactions. Typically, alcohols are not good leaving groups; OH^- ions too basic to be effective good leaving groups (see eq 1).



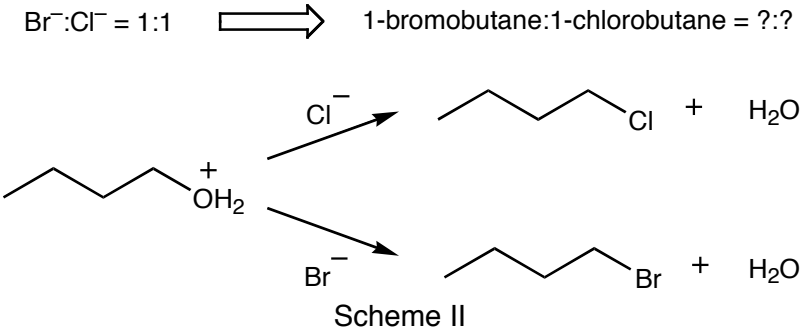
eq 1

However, in the presence of an acid, the alcohol is converted to a good leaving group. Once the alcohol has been converted to a good leaving group, it can be displaced by a nucleophile (see scheme I).



Scheme I

By reacting 1-butanol equimolar mixtures of Cl^- and Br^- and analyzing the product distribution we will determine which is the better nucleophile (see Scheme II). Further, comparing the product distributions for the reactions of 1-butanol and *t*-butanol (2-methyl-2-propanol) with our nucleophiles will provide us with information concerning the role of the nucleophile in S_N1 and S_N2 reactions.



Scheme II

The product mixtures will be analyzed by gas chromatography. Essentially, a small amount of the product mixture is injected into an instrument and the materials vaporize. A stream of helium gas pushes the vaporized products into a metal tube that has been packed with wax covered beads, the so-called "column". When the products reach beads, the products condense. However, the high temperatures inside the instrument cause the materials to vaporize and the stream of helium pushes the vaporized materials father into the column. The process of vaporization and condensation is repeated and the materials are moved down the column. Of course, the material that vaporizes more quickly moves down the column more quickly and, in this way, the components of the product mixture are separated. A detector registers the presence of the materials as they exit the column, and the output from the detector can be used to determine the relative yields of the components in the product mixture.

Procedure[1]

Reaction of 1-butanol with NH_4Cl and NH_4Br

Collect the pieces needed for a refluxing apparatus (an aluminum block with carve-outs for round-bottom flasks, a 25-mL round-bottom flask containing a magnetic spin bar, a water jacketed condenser, and a drying tube). Insert some glass wool into the drying tube and slightly moisten the glass wool (this will help trap any HCl and HBr that may be produced during the reaction). Using a warmed 10-mL graduated cylinder or a warmed 10-mL pipet, transfer 10 mL of the NH_4Br/NH_4Cl nucleophile solution to your 25-mL round-bottom flask. **CAUTION: the nucleophile solution contains concentrated sulfuric acid, and contact with your skin will cause a severe burn.** Assemble your refluxing apparatus. Remove the drying tube and using a long Pasteur pipet to reach though the condenser add 0.75 mL of 1-butanol directly to the acidic nucleophile solution. Turn on the cooling water, heat the solution to a gentle boil, and reflux the 1-butanol reaction for 75 minutes. Heating the aluminum block to 140 °C should be adequate to maintain a gentle boil.

While this reaction is refluxing, perform the reaction of the nucleophile solution with *t*-butanol.

Purification and drying of the product of the reaction of 1-butanol with NH_4Cl and NH_4Br

After refluxing, remove the apparatus from the aluminum block, allow the round-bottom flask to cool for five minutes. Further cool the round-bottom flask in cold tap water (not ice-water). Disassemble the apparatus and add 0.75 mL of pentane to the round-bottom flask. Remove most of the bottom, aqueous layer making certain not to remove any of the organic layer. Leaving any solids behind and starting from the top, carefully transfer the remaining organic and aqueous layers to a clean 3-mL conical vial. Allow these layers to separate and remove the lower aqueous layer. Working quickly but carefully, add 1.0 mL of water to the organic layer. Gently shake, and once the layers have separated, remove and discard the aqueous layer. Add 1 to 2 mL of an aqueous saturated sodium bicarbonate solution to the organic layer. Gently shake, and once the layers have separated, remove and discard the aqueous layer. Using a clean, dry Pasteur pipet transfer the organic layer to a 10x75 mm

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[1] Adapted from Pavia, Lampman, Kiz, and Engel, "Competitive Nucleophiles", *Introduction to Organic Laboratory Techniques: A Microscale Approach*. Saunders College Publishing, 1999.

test tube. Dry the organic layer with anhydrous sodium sulfate, and transfer the dry pentane–alkyl halide solution to a clean, dry 3-mL conical vial. Cap the vial until you are ready to analyze the mixture by gas chromatography..

Reaction of *t*-butanol with NH_4Cl and NH_4Br
Place 6.0 mL of the nucleophile solution in a 15-mL screw cap centrifuge tube. Cool the centrifuge tube in cold tap water. Once a few crystals have formed add 1.0 mL of *t*-butanol (2-methyl-2-propanol) to the centrifuge tube. Cap the tube, check for leaks, and shake for 5 minutes (wear gloves and vent occasionally) **CAUTION: the nucleophile solution is strongly acidic.** After shaking, allow the centrifuge tube to sit for 10 to 15 minutes. Slowly remove most of the water. After pausing briefly, to allow more water to settle out of the organic layer, remove the remaining water and if necessary, a bit of the organic layer (it is important to remove all of the water at this point even if it means losing a small amount of the organic layer). Transfer the organic layers to a 10x75 mm test tube that contains 0.05 g of solid sodium bicarbonate. Once the effervescence has stopped and a clear liquid is obtained, transfer the organic layer to a clean conical vial (or a clean screw-cap centrifuge tube) and cap the vial until you are ready to analyze the mixture by gas chromatography.

Experimental Report

1. Draw mechanisms for the reactions of 1-butanol with an acidic solution of Br^- ions and 2-methyl-2-propanol (*t*-butanol) with an acidic solution of Br^- ions. Label each mechanism as S_N1 or S_N2 so you can refer to them in part three.

2. Create a table and report your results and the results of two classmates. Remember to use the data collected from the gas chromatograph to express the yields of the products as relative yields (percent of a given product as compared to the total amount of products).

3. Using the relative yields tabulated in part 2, determine which halide ion is the better nucleophile.

4. Explain the product distributions (the relative yields of the alkyl halides) for the reactions. Remember to comment on the mechanism of the reaction, S_N1 vs S_N2, and the strength of the nucleophile when explaining the product distribution.

    a. Explain the product distribution for the reaction with 1-butanol.

    b. Explain the product distribution for the reaction with 2-methyl-2-propanol (t-butanol).