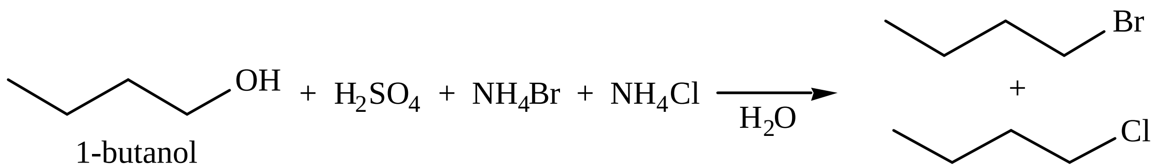
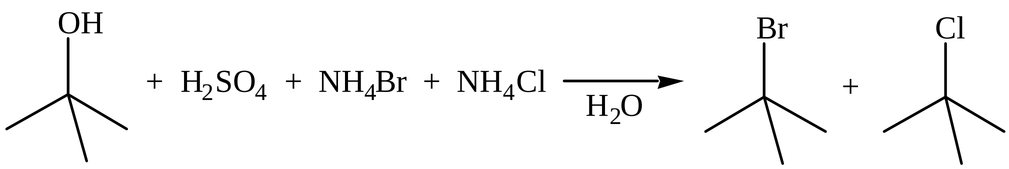
Competing Nucleophiles in Nucleophilic Substitution Reactions

Reactions:



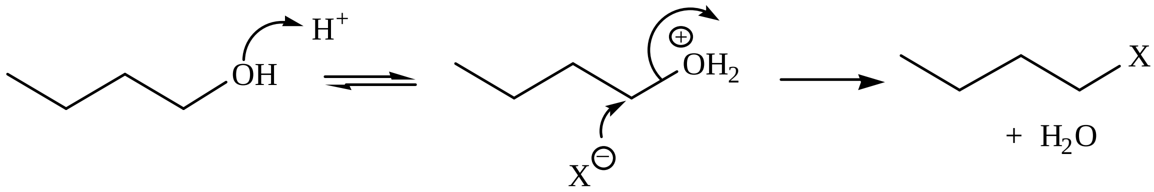


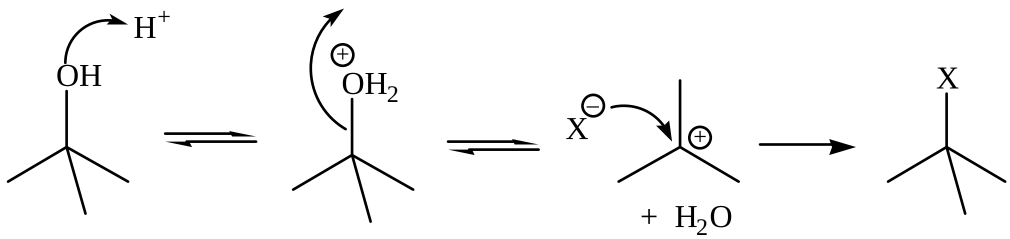
tert-butyl alcohol, or
2-methyl-2-propanol

Introduction:

The purpose of this experiment is to compare the relative nucleophilicities of chloride ions and bromide ions towards 1-butanol and 2-methyl-2-propanol. Equimolar amounts of the two nucleophiles will be present at the same time in each reaction, and they will be competing with each other as they react with the alcohols to form the alkyl halides. Therefore, you will get a mixture of alkyl bromide and alkyl chloride products for each of the reactions. The ratio of these two possible products will depend on several factors, including the strength of the nucleophile and the mechanism of the reaction. After performing these reactions, we will determine the ratio of products by GC analysis, and time permitting, by NMR analysis later in the term.

Alcohols do not react well in simple nucleophilic dislacement reactions because the hydroxide ion is not a good leaving group in these reactions. To avoid this problem, these reactions can be carried out in an acidic solution. In the rapid initial step of these mechanisms, the alcohol is protonated and the positively charged "-OH_2 group" is now a much better leaving group than the neutral "-OH" group. The displacement of this good leaving group is energetically favorable, and the reactions can proceed in high yield. The mechanisms for the reactions of the two different alcohols are shown below. "X" can represent either a chlorine or bromine atom.





The differences in these two mechanisms will affect the ratio of the alkyl bromide and alkyl chloride products for each reaction. After performing the lab, you will determine these ratios, and your lab report (in the discussion/conclusion section) should explain **why** you obtained these ratios. Factors to consider here are the type of reaction mechanism, the nature of the solvent, the nature of the nucleophiles, the structure of the alcohols, and the rate determining steps of the reactions.

Experimental Procedure for 1-butanol:

The sulfuric acid, ammonium bromide, and ammonium chloride will be provided to you as a solvent-nucleophile medium. One mL of this solution contains 0.42 mL of sulfuric acid, 0.1056 g of ammonium chloride, and 0.1944 g of ammonium bromide. From this information, you will be able to calculate the actual amounts of reagents in each reaction. **Note: this solvent-nucleophile medium contains a high concentration of sulfuric acid. Handle it with care!** Using a warm 25 mL graduated cylinder, obtain 20.0 mL of the solvent-nucleophile medium. The graduated cylinder must be warm in order to prevent precipitation of the salts. It can be heated by running hot water over the outside of the cylinder or by putting it in the oven for a few minutes. Immediately pour the mixture into a 50 mL round-bottom flask and clamp the flask above a sand bath. A small amount of the salts may precipitate as the solution cools in the flask. Don't worry! The salts will quickly redissolve during the reaction. Add a boiling chip to the reaction flask, and add 1.5 mL of 1-butanol to the flask with a pipette. Place a reflux condenser on this flask, and then allow the cooling water to slowly flow through the condenser. You will be provided with drying tubes. Loosely insert dry glass or cotton wool into the drying tube, add water dropwise onto the wool until it is partially moistened, and place the drying tube on top of the reflux condenser. This will trap the hydrogen chloride and hydrogen bromide gases produced during the reaction. An example of this set-up will be shown to you in the lab. Carefully lower this set-up so that the round-bottom flask is in the sand bath. The sand bath temperature should not exceed 150 ˚C, and the reflux ring should go no farther than 1/4 of the way up the condenser. In order to control the height of this reflux ring, you can increase or decrease the heating by moving the sand around your round-bottom flask. Heat the reaction mixture at reflux for 60 minutes.

When the 60 minutes of reflux has been completed, remove the sand bath and allow the reaction mixture to cool to room temperature. After the mixture has cooled for a few minutes, you can speed up this cooling process by immersing the reaction flask in a beaker of cold water. Do not remove the condenser until the flask is cool. At this point you should see an organic layer on top of the reaction mixture (The solvent-nucleophile medium has a large density). Add 1.5 mL of diethyl ether and gently swirl the flask. Using a disposable pipet, remove most of the aqueous (lower) layer. It is alright to leave a little of the aqueous layer in the flask; be sure that all of the organic layer is still in the flask. Now transfer all the liquids from the flask to a capped centrifuge tube (if any salts have precipitated, you should **not** transfer those to the centrifuge tube). Allow the phases to separate and remove the aqueous (lower) layer with a disposable pipet. Wash the organic layer with 1.0 mL of water, remove the water, and extract the organic layer with 1.0 mL of saturated sodium bicarbonate solution. Remove the sodium bicarbonate solution **and, using a dry pipet**, transfer the organic layer to a **clean, dry** centrifuge tube. Dry this organic layer with a small amount of granular sodium sulfate until the mixture turns clear. Transfer the dry organic layer to a small capped vial. Time permitting, you should then analyze your product by GC. Otherwise, line the cap with foil before storing your product overnight.

Experimental Procedure for 2-methyl-2-propanol:

Note: You should be able to do this procedure while your reaction with 1-butanol is refluxing.

Place 6.0 mL of the solvent-nucleophile medium into a capped centrifuge tube using a warm graduated cylinder. Allow the solution to cool to room temperature. A small amount of the salts may precipitate as the solution cools. The salts should redissolve during the reaction. Using a warm graduated pipet, add 1.0 mL of 2-methyl-2-propanol to the centrifuge tube. Cap the tube, and with occasional venting, shake the vial vigorously for two minutes. **Be careful here, the mixture is strongly acidic!** After shaking, allow the layers to separate while the tube is capped. Note: the products of this reaction are very volatile and should not be left in an open container. You should now have a distinct upper organic layer. Carefully remove most of the lower aqueous layer with a disposable pipet. Allow the material remaining in the centrifuge tube to separate further
(~1 minute), and remove all of the aqueous layer, including a **very small** amount of the upper organic layer. This is to ensure that the organic layer is not contaminated by any water. Using a **dry pipet**, transfer the remaining organic layer into a conical reaction vial containing about 0.1 g of solid sodium bicarbonate. As soon as the bubbling stops and a clear liquid is obtained (you may need to add a **small** amount of granular sodium sulfate to make the liquid clear), transfer the dry organic layer to a small capped vial. Time permitting, you should then analyze your product by GC. Line the cap with foil before storing your product overnight.

Analysis of the product:

You will analyze your products of both reactions by Gas Chromatography (GC). Water is very bad for a GC column. It is therefore essential that your sample be dry before injecting it into the GC column. If your product looks cloudy, it is most likely not dry. Check with your lab instructor before injecting any material on the GC column. Be sure to record the parameters for your GC trace. You should include: column temperature, injection temperature, helium gas flow rate, speed of the chart paper, the attenuation of the recorder, and the amount of material injected onto the GC column. By analyzing your GC trace, you will be able to get mole ratios of your alkyl bromide: alkyl chloride. You can convert these ratios to mole percentages. You should also record the retention times of your four different products.

Questions: (these answers can be included in your discussion)

1. Explain **why** you get the product ratios you observed in each reaction. Your explanation should include factors such as: the nature of the alcohols and how they affect the reaction mechanisms, the solvent and how it affects the relative nucleophilicities of the halides, and the rate determining steps of the reactions.

2. A careless organic chemistry student from Stanford was performing this experiment, and left his container of *tert*-butyl chloride and *tert*-butyl bromide open to the air for several hours. What happened to the composition of the halide mixture during this time?