EXPERIMENT #5

NUCLEOPHILIC SUBSTITUTION REACTIONS (S_N1 and S_N2)

Background
By the time you do this experiment we will have covered nucleophilic substitution reactions in class. Please review your class notes and chapter seven of your text before coming to lab. You should already be able to predict the results of these experiments based on your knowledge of the concepts. Many laboratory manuals include experiments designed to illustrate nucleophilic substitution reactions. This experiment was taken primarily from Introduction to Organic Laboratory Techniques, 3rd edition, by Donald L. Pavia, Gary M. Lampman, and George S. Kriz.

In this experiment you will determine the importance of the nucleophile under S_N1 and S_N2 conditions. You will allow an equimolar mixture of competing nucleophiles, Br^- and Cl^-, to react under S_N1 conditions with 2-methyl-2-propanol (tert-butyl alcohol) and under S_N2 conditions with 1-butanol. The alkyl halide products will be analyzed by gas chromatography to determine the relative amounts of the components in the product mixture.

Gas Chromatography (GC)
You are already familiar with thin-layer and column chromatography from Experiment #1; review your notes if you need to refresh yourself on the concept of chromatography. Then please read section 15.2 (p 749-752) in your textbook. Your text shows a picture of a typical chromatogram. The time it takes for a compound to elute from the column (and then for the signal to be detected as a “peak” on the chromatogram) is called the retention time, and can be used to qualitatively identify a compound. The chromatogram also gives quantitative information, since the area under a peak is proportional to the amount of the compound in the sample. You can therefore calculate the molar ratio of the components produced in the nucleophilic substitution reactions by comparing the peak areas that are tabulated by the instrument computer. Important Note: Quantitative comparison of chromatogram integrations assumes that the GC detector responds equally to each component of the mixture. This is not necessarily true. A rigorous quantitative estimation would require us to calibrate the instrument by estimating the response factor.

Experimental
You will be running the following reaction, where X^- is either Br^- or Cl^-:

\[
\text{ROH} + H^+ \quad \text{R} - \text{O}^- \text{H} \quad \text{R} - \text{O}^- \text{H} + X^- \rightarrow \text{RX} + H_2O
\]

You will need to prepare the equimolar mixture of Br^- and Cl^- in concentrated sulfuric acid, H_2SO_4. CAUTION: Sulfuric acid is a very strong, corrosive acid. Be very careful
handling it. Carefully add 38 mL of concentrated H₂SO₄ to 50 g of ice in a 250-mL Erlenmeyer flask. Set aside. Weigh 9.5 g of ammonium chloride and 17.5 g of ammonium bromide. Thoroughly crush any lumps, then transfer these salts to a 500-mL Erlenmeyer flask. Slowly add the sulfuric acid, a little at a time, and swirl to dissolve the salts. You may have to warm the mixture slightly and add as much as 5 mL of water to get the salts into solution. Allow the solution to cool slightly as you prepare the apparatus for the S₈1 and S₈2 reactions.

S₈2: Assemble an apparatus for reflux using a 500-mL round-bottomed three-necked flask, a condenser, and a gas trap. A demonstration set up will be available for you to see. Sketch the apparatus in your notebook.

S₈1: You will just need to set up a 125-mL separatory funnel.

Pour 35 mL of your acidic nucleophile mixture into the separatory funnel and replace the stopper. Pour the rest of the mixture into the 500-mL round-bottomed flask, add a boiling stone, and replace its stopper. Begin the S₈2 reaction first as directed below.

S₈2 reaction
Add 5 mL of 1-butanol (n-butyl alcohol) to the reflux apparatus by pouring it down the condenser. Replace the gas trap and heat at reflux gently for 75 minutes, making sure that the vapor ring does not rise more than a quarter of the way up the condenser. (While your reaction is under reflux, complete the S₈1 reaction as directed in the next section.) At the end of the reflux period, discontinue heating and lower the heating mantle to allow the flask to cool undisturbed (at this point, shaking the reaction flask may cause violent boiling and loss of product). Allow the flask to cool about 5 minutes in the air before putting it into an ice water bath. Cool in an ice-water bath for a few minutes, and then begin to swirl the mixture to facilitate more rapid cooling. Transfer the cooled solution to a 125-mL separatory funnel, leaving any solid material behind, and separate the layers. Be sure you know which is the organic layer and which is the aqueous layer. Wash the organic layer with 10 mL of water and then with 10 mL of saturated sodium bicarbonate solution. Again, make sure you know which layer is which, and remember to release the pressure build up in the separatory funnel. Dry the organic layer with anhydrous Na₂SO₄ and decant the clear solution into a small, dry vial. Cap the vial immediately to avoid loss of product. Analyze your products by gas chromatography.

S₈1 reaction
Add 5 mL of 2-methyl-2-propanol to the separatory funnel containing the nucleophile mixture. Since the melting point of 2-methyl-2-propanol is 25°C, use a warm graduated cylinder for measuring. Swirl the mixture gently, then release the pressure build up by venting the funnel. Keep swirling and venting the funnel until the pressures are equalized, and then shake the funnel vigorously, with occasional venting, for 2 minutes. Allow the layers to separate for about a minute, then drain the lower layer. Wait 10-15 seconds longer, then drain another small portion, this time including a bit of the upper, organic layer, just to be sure that the remaining organic layer is not contaminated with water. Pour the organic layer out of the top of the separatory funnel into a beaker containing 1 g of solid sodium bicarbonate. Stir, and as soon as the bubbling stops, decant the clear solution into a small, dry vial. Cap the vial immediately to avoid loss of product. Analyze your products by gas chromatography.
Prelab

1. Which is a better nucleophile in aqueous solution, Br\(^-\) or Cl\(^-\)? Why?
2. What products form in the S\(_{N}\)1 reaction in this experiment?
3. In what ratio (approximately) do you predict they will be formed?
4. What are the products of the S\(_{N}\)2 reaction in this experiment?
5. Do you expect the same ratio of products as in the S\(_{N}\)1 reaction? Explain why or why not.
6. Look up the boiling points and densities of all of the organic reactants and products. Densities will help you to determine which layer is the organic layer and which is the aqueous layer in your separatory funnel, and boiling points can help you to determine the order of elution of the products (and any unreacted starting material) from the gas chromatographic column.
7. Why is it necessary to perform the competing nucleophiles reactions under acidic conditions?
8. How many moles of Br\(^-\) and Cl\(^-\) are present in your prepared nucleophile mixture used the experiment?
9. This experiment will introduce you to a couple of new techniques. Most of you will be using a separatory funnel for the first time. Read an overview of the concept of extractions, the use of a separatory funnel and the use of drying agents found in one of the laboratory manuals in room 142 of the Science Library. In just a few sentences, summarize the use of the separatory funnel and explain how you can tell if your organic solvent is “dry.”

Report

A. Write mechanisms for the S\(_{N}\)1 and S\(_{N}\)2 reactions. Be sure to use arrows to show the movement of electrons. Discuss the results of your experiments run under both conditions. What was the molar ratio of your products? Explain how your results agree or disagree with your predictions. What other products (not H\(_2\)O) might you expect from the two reactions?

B. Answer the following questions.
1. A student completed the reactions, but left the products in an open Erlenmeyer flask until almost the end of the lab period before they were analyzed by gas chromatography. Would this affect the accuracy of the analysis? Clearly explain how the results might be affected.
2. What is the purpose of heating the S\(_{n}\)2 reaction mixture at reflux for 75 minutes? Why not simply boil the mixture in an Erlenmeyer flask?
3. Predict the major product(s) of the following reaction, including the correct stereochemistry. What is the function of AgNO\(_3\) in this reaction?