NUCLEOPHILIC SUBSTITUTION REACTIONS ($S_{N1}$ and $S_{N2}$)*

CH 241 EXPERIMENT #5; Week of November 9, 2015

Background
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 of the $S_{N1}$ and the $S_{N2}$ reactions will be analyzed by gas chromatography to determine the relative amounts of the components in the product mixtures.

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

$$ROH + H^+ \rightleftharpoons R \begin{array}{c} \Theta \end{array} O \begin{array}{c} H \end{array} + X^- \rightarrow RX + H_2O$$

First prepare the equimolar mixture of Br$^-$ and Cl$^-$ in concentrated sulfuric acid. **CAUTION:** Sulfuric acid is a very strong, corrosive acid. Be very careful handling it. Carefully add 38 mL of concentrated H$_2$SO$_4$ 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 into a 500-mL Erlenmeyer flask. Slowly add the sulfuric acid, a little at a time, and swirl to dissolve the salts. The mixture may have to be gently heated and/or as much as 5 mL of additional water may have to be added to get the salts into solution. Allow the solution to cool slightly while you prepare the apparatus for the $S_{N1}$ and $S_{N2}$ reactions.

$S_{N2}$: 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 and/or take a photograph of it with your electronic device.

$S_{N1}$: Pour 35 mL of your acidic nucleophile mixture into a 125-mL separatory funnel and replace the stopper.

$S_{N2}$ reaction (start first, then while your reaction is refluxing, complete the $S_{N1}$ reaction)

Pour the rest of the nucleophile mixture into the 500-mL round-bottomed flask, add a boiling stone, and replace its stopper. Add 5 mL of 1-butanol ($n$-butyl alcohol) to the reflux apparatus by pouring it down the condenser. Replace the gas trap and reflux gently for 75 minutes, making sure that the reflux ring does not rise more than a quarter of the way up the condenser.

* This experiment was adapted from *Introduction to Organic Laboratory Techniques*, 3rd edition, 1999 by Donald L. Pavia, Gary M. Lampman, and George S. Kriz.
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 at least 5 minutes in the air before putting it into an ice-water bath. Cool 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, then separate the layers. Be sure to check 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 aqueous sodium bicarbonate solution. The bicarbonate neutralizes any remaining acid to produce CO₂, so remember to release the pressure build-up in the separatory funnel often (vent…vent…vent). Dry the organic layer with anhydrous Na₂SO₄ and decant or pipet the clear solution into a small, dry vial. Cap the vial immediately to avoid loss of product. Analyze your products by gas chromatography.

**Sₙ₁ 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 to measure it. Swirl the mixture gently, then vent the separatory funnel. Keep swirling and “burping” the funnel until the pressures are equalized, 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 into the stopcock, 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.

All derived experimental data that are unique to your experiment, such as the gas chromatograms in this lab, should be carefully labeled immediately after you acquire them. The label minimally should include your names, the compound or reaction, and the date and time collected.

**PRELAB PREPARATIONS**

1. Which is a better nucleophile in aqueous solution, Br⁻ or Cl⁻? Why?
2. What are the products of the Sₙ₁ and Sₙ₂ reactions to be done in this experiment? Find the boiling points of the organic products.
3. Write mechanisms, with correct arrow formalism, for these Sₙ₁ and Sₙ₂ reactions.
4. What is the limiting reagent for each reaction? Show your calculations to support the answers.
WHAT SHOULD BE IN YOUR NOTEBOOK?

1. An entry of the title, date, and page number in your table of contents.
2. An entry of the title, date, and partner’s name on the first page of your experiment.
3. Masses and/or volumes of all materials that you used in this experiment.
4. A sketch of the reflux apparatus for the S_N2 reaction.
5. Brief description of the procedures you followed for S_N1 and S_N2 reactions.
6. Calculations showing the relative amounts (in mole percents) of the products in S_N1 and S_N2 reactions.

WHAT SHOULD BE IN YOUR LABORATORY REPORT?
(Do not exceed a total of two pages. Please type your report, and print double-sided.)

1. Title of the experiment with your name, your partner’s name, lab section, and date.
2. Introduction (1 paragraph): This should include the purpose of this experiment with an overview of S_N1 and S_N2 reactions but no data.
3. ChemBioDraw structures for S_N1 and S_N2 reactions. Only equations with proper structures are required, not mechanisms.
4. Results and Discussion: This should include the results of your experiments run under both conditions. What was the molar ratio of your products? Explain how the results agree or disagree with what you might have predicted. What byproducts (other than water) might you expect from the two reactions? Why is it necessary to perform the competing nucleophiles reactions under acidic conditions (Why doesn’t the reaction work with the halide anion and the unprotonated alcohol?)?
5. Conclusion (1 paragraph): Summarize any conclusions you can draw from the your data.
6. Attach gas chromatograms for both reactions (S_N1 and S_N2).