Experiment 5  \textit{S_N1 and S_N2 Reactions}

\textbf{Reading assignment:}  Review the mechanism of \textit{S_N1} and \textit{S_N2} reactions. See, for example, KPC Vollhardt and NE Schore, \textit{Organic Chemistry}, Chs 6, 7.

\textbf{Introduction:}

Nucleophilic substitution is one of the most useful and well studied class of organic reactions. These reactions can occur by a range of mechanisms. By now you have learned about the two limiting cases, \textit{S_N2} and \textit{S_N1}. However, many reactions go via mechanisms best described as intermediate between these two extremes.

The \textit{S_N2} reaction occurs in a single step. The nucleophile is attached as the leaving group — usually a halide ion — departs. The reaction displays second-order kinetics; its rate is proportional to the concentrations of the alkyl halide \textit{and the nucleophile}. The \textit{S_N1} reaction occurs in two separate steps. The first step is departure of the leaving group to form a carbocation which is the rate-determining step. In the second step the carbocation rapidly captures a nucleophile. The reaction rate depends only on the concentration of the alkyl halide and is thus first-order.

Which mechanism occurs for a given alkyl halide under a certain set of conditions and how fast it occurs depend on a variety of factors. The structure of the alkyl halide, the leaving group, the nucleophile, and the solvent can all play a role. The object of this experiment is to learn how variations in these parameters affect the rates of \textit{S_N1} and \textit{S_N2} reactions. You will have to decide what experiments to do to get the desired information.

Quantitatively measuring reaction rates involves monitoring the rate of change of the concentrations of reactant(s) and/or product(s) during a reaction. This is often a time consuming process. In this experiment we will determine reaction rates \textit{qualitatively} by measuring the time required for a visible change to occur — formation of a precipitate.

An assortment of alkyl, alkenyl, and aryl chlorides and bromides will be available in the lab. For the \textit{S_N2} reaction you will use a solution of sodium iodide in 2-butanoثن. Iodide is a good nucleophile, and if it displaces bromide or chloride, the NaBr or NaCl produced will precipitate. For the \textit{S_N1} reaction you will use a solution of silver nitrate in ethanol. Ethanol is a polar protic solvent and thus can promote ionization of certain organic halides. If such a reaction occurs, bromide or chloride ion is released, and a precipitate of AgCl or AgBr will form.

Keep in mind that in the REAL WORLD, experiments don't always work precisely the way you want, and sometimes you need to play around with the conditions a bit. And occasionally even one's best efforts give no results or results that are ambiguous. That's life in the "real" world as opposed to the world of perfectly (and often painstakingly) contrived undergraduate lab experiments that never ever fail.

For most of this experiment, you will work in groups of three. Each group member will prepare the prelab write-up and attach this and his/her results section to the discussion/conclusion section prepared by the entire group.

\textbf{Experimental procedure.} Each bench should set up one ice water bath and one water bath warmed to about 60 °C on a hot plate (try to keep the temperature stable). These will be useful if some of the reactions go too fast or too slow at room temperature.

\textit{Preliminary S_N2 reaction.} (Every group member should do this part.) In 3 clean, dry test tubes, place 1 drop each of \textit{n}-butyl bromide, \textit{sec}-butyl bromide, and \textit{tert}-butyl bromide (aka 1-bromobutane, 2-bromobutane, and 2-bromo-2-methylpropane). To each tube add 1 ml of 0.5-M NaI in 2-butanoثن. Note the time of the addition, and gently shake the tubes. Record the times required for precipitates to form. After 5 minutes place any tubes which do not contain precipitates in the warm water bath. (Make sure the bath temperature does not get above 70 °C or the solvent will evaporate.) Watch for formation of precipitates. After another 5 min allow the tubes to cool to room temperature and note whether any precipitates form. In your notebook, make a table of the times required for precipitates to form at each temperature.

\textit{Preliminary S_N1 reaction.} In 3 clean, dry test tubes, place 2 drops of each of the three alkyl bromides you used above. Repeat the procedure above with the 1% AgNO_3/EtOH solution (in place of the NaI/acetone solution) and record the results.

\textbf{Caution:} Silver nitrate is poisonous. It is caustic and irritating to skin and will turn it brown. Handle AgNO_3 solutions with gloves.
Compare your results with the other members of your group. How consistent are the data? What do the results imply about the relative rates of $S_{N}1$ and $S_{N}2$ reactions of primary, secondary, and tertiary alkyl halides? Are there any unexpected results?

Now each group should decide how to go about answering the following questions. Each group will need to decide who will do what experiments and which series of compounds each person should study to get the most clear-cut results. It may be necessary to adjust the conditions to get results, and it might be helpful to discuss how best to do this within the group as problems arise. Address as many of these issues as you can in the allotted time. The list of available halides is on the following page and will be posted in the lab. Check the list and note any deletions of compounds that are unavailable.

*For $S_{N}1$ and $S_{N}2$ reactions...

1. How does the reaction rate depend on branching at the $\alpha$-carbon (i.e., $1^\circ$ vs $2^\circ$ vs $3^\circ$ halides)?
2. What is the effect of branching at the $\beta$-carbon?
3. How does the leaving group affect the reaction rate?
4. What is the effect of a ring? Does ring size matter?
5. What effect does an aromatic ring have? Is its position important? What effect do electron-donating or -withdrawing substituents have? In particular, what does the $S_{N}2$ rate variation or lack thereof tell you about the nature of the transition state?
6. What effect does a double bond have? Is its position important? What about the number and positions of alkyl groups on the double bond? (Perhaps your answer to question 5 will give you some insight into the variation in the $S_{N}2$ reaction rate here.)

7. Does the Ag$^+$ affect the rate of the $S_{N}1$ reaction? How might you test for this?
8. For the $S_{N}1$ reaction, how does the solvent polarity affect the reaction rate? (try different alcohols or mixtures of alcohols and water.)
9. For the $S_{N}2$ reaction, how does the reaction rate depend on nucleophile concentration?
10. There may be other issues you would like to address if time permits. Be creative. *Any deviations from the standard conditions and procedures must be discussed with your TA or instructor first, just to be on the safe side.*

**Lab reports.** You should prepare the pre-lab material as usual. Look up the relevant data for $n$-butyl, sec-buty l, and tert-buty l bromides. You do not have to look up physical data for the other the compounds on the following page, but be prepared to identify them by name, since bottles often come labelled with only the name of the compound and not the structure.

Your data section should report the results for the experiments you did. Make sure your results are neatly tabulated. Each set of experiments should be labelled with a short heading that describes what was to be accomplished, e.g., "Effect of solvent polarity on $S_{N}1$ rxn rates". A large part of your grade on the report will depend on how many experiments you did, whether you did sensible things, and how careful you were in recording data and observations.

The group will collaborate on the discussion and conclusion sections. Collaborate means discuss the results and what they mean and reach a consensus if possible, then write the discussion section together — you'll find that you learn a lot this way. Collaborate does not mean each person chooses his/her third of the experiments, then goes home and writes one-third of the discussion, and then you all meet at the stapler. Turn in one copy of this part along with each individual pre-lab and data section. About one third of the grade will be assigned to each individual's work, and the score for the discussion section will be given to everyone in the group. (The graded discussion will be returned to the first author listed, and he/she can photocopy it to share with the other group members.)

There will be a lot of data to discuss, so the discussion section may require a few pages, but try to keep it as concise as possible. Be sure you critically analyze the data. What do the data tell you about the reactions? And what don't they tell you? Don't just summarize the results. Also, don't try to force the data to conform to your preconceptions about what should happen. If the data indicate that $3^\circ$ halides do faster $S_{N}2$ reactions than $1^\circ$, then that's the result. (Of course, you may have good reason to be suspicious of such a result and wish to reexamine the experimental data.) You should have time to discuss the results within your group during this lab period or the next, but you may need to get together outside of lab to work on the report. Please attach a cover page that lists the names of everyone in the group, and make sure that each individual's data contribution is clearly labelled.

The halides on the next page are expected to be available for this lab. You will be informed of any changes to this list in advance. Check the posted lists for any last-minute additions or deletions. Neopentyl bromide is rather expensive ($$$), so plan your experiments so that you use the smallest possible amount (no more than 2 drops per group).
Experiment adapted from the 1993 University of Chicago Chem 220 lab manual.

**Things to think about before lab —**

i. What are the products of the reactions? Write a balanced equation for R-Br reacting under S_N1 and S_N2 conditions.

ii. You want to look at the effect of β-branching by studying three closely related bromides. Would it be best to (a) run the three reactions side-by-side, (b) run them one-after-another, or (c) have each compound studied by a different group member? Explain.

iii. Why can these experiments be done in the solvents used? In other words, if you were looking for solvents to use, what properties would you look for? Keep in mind that you need to get a visible indication of reaction.

iv. After you answered iii, this one should be easy... Under our reaction conditions, we can study the S_N1 reaction of tBu-I, but not the S_N2 reaction of n-Bu-I. Why?

v. You are doing three parallel S_N2 reactions, and they all appear to go instantly at room temperature. What are two ways in which you might slow the reactions down?

vi. Answer question v for S_N1 reactions.

vii. Match the following names to the compounds in the list. You'd better be able to do this because the bottles are going to have names only, not structures.

- 3-bromopropene
- 2-bromobutane
- p-nitrobenzyl chloride
- bromodiphenylmethane
- chlorocyclohexane
- 2-halo-2-methylpropanes (3)
- 1-chlorobutane
- 3-bromopentane
- 3-bromocyclohexene
- p-methylbenzyl chloride
- benzyl bromide
- 2-methyl-3-bromopropene
- 1-bromo-2-methylpropane
- bromobenzene
- 1-bromo-2,2-dimethylpropane
- (Z)-1-bromopropene
- 2-bromopentane
- 1-bromoadamantane
- chlorobenzene
- bromocyclopentane
- p-methoxybenzyl chloride
- bromocyclohexane
- 1-bromobutane
- 1-bromo-3-methyl-2-butene