Experiment 7 —

Nucleophilic Substitution

Pre-lab preparation (1) Textbook Ch 8 covers the S_N2 and S_N1 mechanisms. Read/review as necessary. (2) Write the S_N2 reaction of 1-bromobutane with NaI. Illustrate the electron flow with curved arrows. Since this is a one-step reaction, you've just written the mechanism. (3) Write a balanced equation representing the S_N1 solvolysis of *tert*-butyl bromide in ethanol. The product is *t*-Bu–O–Et. Write the reaction mechanism. (Refer to the introduction below or the text if we haven't gotten to this mechanism in class before your lab.) (4) Draw the *structures* of all the organo-halides you will be using in this lab. Don't bother looking up physical properties of these. (5) You should, however, know the boiling points of the two solvents you'll be using. (6) We'll be using two different solutions — **NaI in acetone** for **S_N2** reactions, and **$AgNO_3$ in ethanol** for **S_N1** reactions. Briefly explain why (a) the S_N1 reaction pathway is *dis*favored with NaI/acetone, and (b) why the S_N2 pathway is *dis*favored with $AgNO_3$/EtOH.

Nucleophilic substitution is one of the most useful and well studied class of organic reactions. These reactions can occur by a range of mechanisms. S_N2 and S_N1 are the extremes.

The S_N2 reaction occurs in a single step. The nucleophile enters as the leaving group — usually a halide ion — departs. The reaction displays second-order kinetics; its rate is proportional to the concentration of the organo-halide *and the nucleophile*.

In the S_N1 reaction loss of the leaving group occurs first to generate a carbocation intermediate. The carbocation then captures a nucleophile, often the solvent (followed by proton transfer to produce the final neutral product). In this case the reaction is called a *solvolysis*. Because the first step is rate-determining, the S_N1 reaction displays first-order kinetics; its rate depends *only* on the concentration of the organo-halide. It will be easier to remember which label goes with which mechanism if you associate the "***1***" in S_N1 with ***carbocation*** rather than with the kinetic order of the reaction. (Perhaps this should be called S_NCarbocat or S_NC+.)

Which mechanism occurs under a certain set of conditions and how fast it occurs depend on a variety of factors. The structure of the organo-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 organo-halide structure affects the rates of S_N1 and S_N2 reactions.

Quantitatively measuring reaction rates involves monitoring the rate of change of the concentrations of reactant(s) and/or product(s) during a reaction. In this experiment we will determine reaction rates *qualitatively* by measuring the time required for a visible change to occur — formation of a precipitate.

An assortment of alkyl, alkenyl, and aromatic chlorides and bromides will be available. To encourage an S_N2 reaction mechanism you will use a solution of NaI in acetone. Iodide is a good nucleophile, and if it displaces bromide or chloride, NaBr or NaCl will precipitate (these are much less soluble in acetone than NaI). To encourage an S_N1 reaction mechanism you will use a solution of $AgNO_3$ in ethanol. Ethanol is a polar protic solvent and can promote ionization of certain organo-halides. If halide ion is released a precipitate of AgCl or AgBr will form.

Procedure. In the lab you will find 1-bromobutane, 2-bromobutane (aka *sec*-butyl bromide), *tert*-butyl bromide, allyl bromide, allyl chloride, benzyl chloride, and bromobenzene. ***Note that the allyl and benzyl halides are powerful lachrymators and should be tested in the hoods only.***

You will also find 1M NaI/acetone and 2% $AgNO_3$/EtOH. ***Note that silver nitrate is poisonous. It is caustic and irritating to skin and will turn it brown. Be sure to wear gloves when handling $AgNO_3$ solutions.***

The tests are performed by adding 2 drops of organo-halide to a small, *dry*, clean, *dry* test tube. Add about 1 ml of NaI/acetone or 1 ml $AgNO_3$/EtOH, and *record the time* required for precipitate to form. Keep in mind that our goal is to make semi-quantitative comparisons of rxn rates for a series of organo-halides, so running them all at the same time is not only more efficient, but will let you see the relative reactivities more clearly. *Cloudiness may be the onset of precipitation* (but a color change alone is not relevant). If no precipitate has formed after

about 3 minutes, warm the tube(s) to 40-50°C and record the time required for precipitation. If no reaction is visible after about 10 min, give up — we'll call that unreactive. On the other hand, if you want to compare reactions that appear to be instantaneous at room temperature, you'll need to slow these down to detect a difference in rates. Lowering the temperature is probably the first thing to try. (What else might you do to slow down an S_N2 reaction? What about an S_N1?)

S_N2 reactions. (1) Begin by examining the bromides under S_N2 conditions. *Make a table in your notebook* that shows the *structures* of the organo-bromides in the first column. In the next column, first *predict* the relative reactivities — which should react fastest, next fastest, etc. Don't mess around here, just do your best based on your current understanding and move on to the experiments. The third column of the table is for the observed time required for precipitate formation. Add the data from any higher temperature experiments you needed to do, and repeat at lower temp as necessary.

If there's a discrepancy between your predictions and your observations, discuss this with your partner and see if you can figure out the reason. If there's a glaring discrepancy, e.g. something that's the complete opposite what you learned in class, ask for help. Sometimes reagents or solutions get contaminated, bottles get mixed up, etc. Or you might be misunderstanding something. It's best to get things straightened out before going on.

(2) Now examine the organo-chlorides and allyl bromide, ***in the hood***. Adding allyl bromide will allow us to connect these relative rates to those in the previous set, and provides a direct comparison of leaving groups. Same as before — make a table, use *structures*, not compound names, make predictions first. Heat or cool as necessary.

(3) In your notebook, write a brief discussion of the results that addresses the following points — (a) What was the effect of substitution at the C undergoing nucleophilic attack, in particular, 1° vs 2° vs 3° alkyl. (b) Do the allylic and benzylic halides fit this pattern? If not, suggest an explanation. (c) Can the relative reactivity of bromobenzene be explained in terms of the principles established by the series of other compounds, or is some other factor important here? (d) What was the effect (if any) of changing the leaving group? How do you account for that?

S_N1 reactions. Test the same series of organo-halides with the $AgNO_3$/EtOH solution. Bromides first, then the allylic and benzylic compounds. Warm or cool if necessary. Write a brief discussion that addresses the same points that were raised in the context of the S_N2. Of course the key to S_N1 reactivity is very different.

Lucas test for alcohol (ROH) reactivity. Your final task for today is to determine whether the "Lucas reagent" promotes S_N1 or S_N2 reactions by examining how the reaction rate varies with the structure of the alcohol. The Lucas reagent is a solution of $ZnCl_2$ in concentrated HCl. Alcohols that react with the Lucas reagent are converted to the corresponding alkyl chlorides, RCl.

To perform a Lucas test, place 4-5 drops of ROH in a test tube, then add 2 ml of the Lucas reagent, stopper the tube, and shake. If a reaction occurs, the RCl will separate as a distinct liquid phase or form a cloudy emulsion.

Test the three alcohols provided — 1-butanol, 2-butanol, and *tert*-butyl alcohol — and determine whether the reactivity pattern is more consistent with an S_N2 or an S_N1 mechanism. Finally, write a mechanism for the reaction of your most reactive alcohol. Show each step clearly with curved arrows. To make this easier, ignore the presence of the Zn^{2+}, and just pretend that it works with aqueous HCl. (The reaction does, in fact, work with HCl alone in many cases; the Lewis-acidic Zn^{2+} speeds it up.)

Turn in your duplicate notebook pages with your data and observations, the brief discussions, and your Lucas test mechanism, and you're done. Thanks for coming and enjoy your evening.