EXPERIMENT 8
RELATIVE RATES OF NUCLEOPHILIC SUBSTITUTION REACTIONS

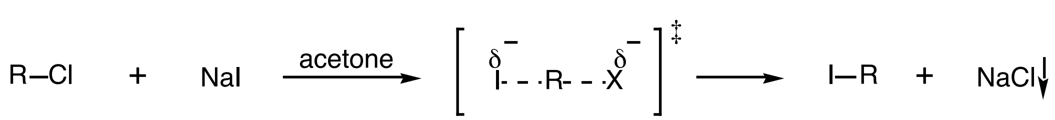
Reading Assignment: Smith, Chapter 7

Pre-lab Questions:

1) What determines whether 2-bromobutane undergoes an S_N1 or an S_N2 reaction? How would you favor S_N2 formation?
2) Benzyl bromide reacts rapidly with sodium iodide in acetone, and also reacts rapidly with ethanol and silver acetate. Bromobenzene doesn't react under either of these conditions. Explain.
3) Allyl bromide is a primary alkyl halide, yet it reacts rapidly with silver nitrate in ethanol. Explain.

There are two mechanisms for nucleophilic substitution. The S_N2 reaction involves a one step concerted displacement of the leaving group by a nucleophile with inversion of configuration. The S_N1 reaction is a 2-step reaction involving loss of the leaving group to form of a carbocation intermediate, followed by attack by a weak nucleophile with loss of stereochemistry.

In **Part 1** of this experiment, we will examine the factors that affect the relative rate of the S_N2 reaction for a series of alkyl chloride and alkyl bromides. We will see how alkyl halide structure and the nature of the leaving group effects the rate of an S_N2 reaction, and deduce the rate law by varying the initial concentrations of the nucleophile and alkyl halide, and observing the effect this has on the rate of the reaction. We will use reaction conditions that favor an S_N2 reaction: a solution of sodium iodide in acetone.



Iodide ion is an excellent nucleophile, and S_N2 reactions are favored in polar aprotic solvents such as acetone. Because acetone cannot sufficiently stabilize a carbocation intermediate, the competing S_N1 reaction is suppressed. Sodium iodide is soluble in acetone, but when bromide or chloride is the leaving group in this reaction, sodium bromide or sodium chloride precipitates as an insoluble salt. This precipitation drives the equilibrium to the right, and allows easy monitoring of the rate of the reaction.

In **Part 2** of this experiment, we will examine the factors that affect the relative rate of the S_N1 reaction for the same series of alkyl chloride and alkyl bromides. We will see how alkyl halide structure and the nature of the leaving group affects the rate of an S_N1 reaction, and deduce the rate law by varying the initial concentrations of the nucleophile and alkyl halide, and observing the effect this has on the rate of the reaction. We will use reaction conditions that favor an S_N1 reaction: a solution of silver nitrate in ethanol.

$$R{-}Cl \xrightarrow{AgNO_3} \left[\overset{\delta+}{R}\text{- -}\overset{\delta-}{Cl}\text{- -}\overset{\delta+}{Ag} \right]^{\ddagger} \longrightarrow R^+ + AgCl\downarrow + NO_3^-$$

$$R^+ + CH_3CH_2OH \longrightarrow ROCH_2CH_3$$

Ethanol is a polar protic solvent, and a poor nucleophile. The silver ion coordinates with the halide ion in the alkyl halide and enhances carbocation formation. The S_N2 reaction is suppressed because of the absence of a good nucleophile. When bromide or chloride is the leaving group in this reaction, silver bromide or silver chloride precipitates as an insoluble salt. This precipitation drives the equilibrium to the right, and allows easy monitoring of the rate of the reaction.

CAUTION

All alkyl halides are harmful if inhaled, ingested , or absorbed through the skin. Wear gloves, and do all work in an efficient fume hood.

Silver nitrate solutions are toxic and will discolor the skin.

Part 1. Factors that affect the Relative Rate of the S_N2 Reaction

Make sure all test tubes for Part 1 are clean and dry! Obtain 11 test tubes with stoppers (do not use rubber stoppers) for part 1.

Alkyl halide Structure: Measure 2 mL of 15% sodium iodide in acetone into each of three test tubes. Add 2 drops of 1-bromobutane (butyl bromide) to **tube 1**, 2 drops 2-bromobutane (*sec*-butyl bromide) to **tube 2**, and 2 drops 2-bromo-2-methylpropane (*tert*-butyl bromide) to **tube 3**, recording the time of each addition. Stopper and shake each. Note the time at which the first signs of cloudiness or precipitate appears. Closely observe for the first 15-20 minutes, and then at intervals throughout the lab period.

***Steric Effects**:* Measure 1 mL of 15% sodium iodide in acetone into each of two test tubes. Add 2 drops 1-bromobutane (butyl bromide) into **tube 1**, and 2 drops of 1-bromo-2,2-dimethylpropane (neopentyl bromide) into **tube 2**, recording the time of each addition. Stopper and shake each and observe closely. Note the time at which the first signs of cloudiness or precipitate appears.

***Leaving Group Effects**:* Measure 1 mL of 15% sodium iodide in acetone into each of two test tubes. Add 2 drops 1-bromobutane (butyl bromide) into **tube 1**, and 2 drops of 1-chlorobutane (butyl chloride) into **tube 2**, recording the time of each addition. Stopper and shake each and observe closely. Note the time at which the first signs of cloudiness or precipitate appears.

Rate Law: Measure 1.0 mL of 15% sodium iodide in acetone into each of two test tubes. At the same time, (or do one at a time and mark each time carefully), add 0.1 mL of 1.0 *M* 1-bromobutane in acetone to **tube 1**, and 0.1 mL of 2.0 *M* 1-bromobutane in acetone to **tube 2**. Record your observations.

Measure 1.0 mL of 1.0 *M* 1-bromobutane in acetone into each of two test tubes. At the same time, (or do one at a time and mark each time carefully), add 0.1 mL of 7.5% sodium iodide in acetone to **tube 1**, and 0.1 mL of 15% sodium iodide in acetone to **tube 2**. Record your observations.

Results and Conclusions for Part 1:

1. Which alkyl bromide reacts fastest with sodium iodide in acetone: butyl bromide, *sec*-butyl bromide, or *tert*-butyl bromide? Which reacts slowest? Explain how structure affects the rate in the S_N2 reaction.

2. Which alkyl bromide reacts fastest with sodium iodide in acetone: butyl bromide or neopentyl bromide? Both of these are primary alkyl bromides. Explain the difference in reactivity.

3. Which alkyl halide reacted fastest with sodium iodide in acetone: butyl bromide or butyl chloride? Explain how the nature of the leaving group affects the rate in the S_N2 reaction.

4. How did the following changes affect the rate of reaction of 1-bromobutane with NaI: doubling the concentration of 1-bromobutane? Doubling the concentration of NaI?

5. Write a generalized rate expression for an S_N2 reaction.

Part 2. Factors that affect the Relative Rate of the S_N1 Reaction

Make sure all test tubes for Part 2 are clean and dry! Obtain 11 test tubes with stoppers (do not use rubber stoppers) for part 2.

Alkyl halide Structure: Measure 2 mL of a 0.1 *M* solution of silver nitrate in absolute ethanol into each of three test tubes. Add 1 drop of 1-bromobutane (butyl bromide) to **tube 1**, 1 drop 2-bromobutane (*sec*-butyl bromide) to **tube 2**, and 1 drop 2-bromo-2-methylpropane (*tert*-butyl bromide) to **tube 3**, recording the time of each addition. Stopper and shake tubes ***continuously.*** Watch carefully for the first signs of cloudiness or precipitate formation.

***Leaving Group Effects**:* Measure 2 mL of a 0.1 *M* solution of silver nitrate in absolute ethanol into each of two test tubes. At the same time (or do one at a time and mark each time carefully), add 1 drop 2-bromo-2-methylpropane (*tert*-butyl bromide) into **tube 1**, and add 1 drop 2-chloro-2-methylpropane (*tert*-butyl chloride) into **tube 2**. Stopper and shake each and observe closely. Note the time at which the first signs of cloudiness or precipitate appears.

***Solvent Polarity Effects**:* Measure 2 mL of a 0.1 *M* solution of silver nitrate in absolute ethanol into one test tube. Into a second test tube, measure 2 mL of a 0.1 *M* solution of silver nitrate in 5% absolute ethanol/ 95% acetone. At the exact same time **(*get a partner to help*)**, add 1 drop 2-chloro-2-methylpropane (*tert*-butyl chloride) into each tube. Stopper and shake each and observe closely. Record observations.

Rate Law: Measure 0.5 mL of a 0.1 *M* 2-chloro-2-methylpropane (*tert*-butyl chloride) in absolute ethanol solution into one test tube. Into a second test tube, measure 0.5 mL of a 0.2 *M* 2-chloro-2-methylpropane (*tert*-butyl chloride) in abasolute ethanol solution. At the same time (or do one at a time and mark each time carefully), add 1.0 mL of of a 0.1 *M* solution of silver nitrate in absolute ethanol to each. Record your observations.

Measure 1.0 mL of a 0.1 *M* solution of silver nitrate in absolute ethanol into one test tube. Into a second test tube, measure 0.5 mL of of a 0.1 *M* solution of silver nitrate in absolute ethanol *AND* 0.5 mL absolute ethanol *(to ensure volumes are the same)*. At the same time (or do one at a time and mark each time carefully), add 1.0 mL of 0.1*M* 2-chloro-2-methylpropane (*tert*-butyl chloride) in absolute ethanol solution to each. Record your observations.

Results and Conclusions for Part 2:

1. Which alkyl bromide reacts fastest with silver nitrate in ethanol: butyl bromide, *sec*-butyl bromide, or *tert*-butyl bromide? Which reacts slowest? Explain how structure affects the rate in the S_N1 reaction.

2. Which alkyl halide reacted fastest with silver nitrate in ethanol: *tert*-butyl bromide or *tert*-butyl chloride? Explain how the nature of the leaving group affects the rate in the S_N1 reaction.

3. Which solvent gave the fastest reaction; ethanol, or the ethanol/acetone mixture? Explain how the solvent affects the rate in the S_N1 reaction.

4. How did changing the concentration of *tert*-butyl chloride affect the rate of the reaction? In part 1, we varied the concentration of the nucleophile in order to help determine the rate law. Why didn't we vary the concentration of nucleophile in Part 2?

5. Write a generalized rate expression for an S_N1 reaction.

Summarize your conclusions for Part 1 and Part 2 in your final lab report.

Post-lab Questions:

1) Secondary alkyl halides can undergo S_N2 and S_N1 reactions. Comparing results for Part 1 and Part 2, which is a faster reaction for secondary alkyl halides, an S_N2 or an S_N1 reaction? Explain.

2) 1-Bromoadamantane is a tertiary halide, yet it is 10,000 times slower than *tert*-butyl bromide when allowed to react with silver nitrate in ethanol. Explain.

3) Are alkyl fluorides good substrates in S_N2 and S_N1 reactions? Explain.

Reference:

1. This procedure is adapted from: A.M. Schoffstall, B.A. Gaddis, M. L. Druelinger, *Microscale and Miniscale Organic Chemistry Laboratory Experiments*, McGraw-Hill, 2000, p. 253, and J.R. Mohrig, C.N. Hammond, P.F. Schatz, T.C. Morrill, *Modern Projects and Experiments in Organic Chemistry: Miniscale & Standard Taper Microscale*, 2nd Ed., W.H. Freeman and Company, 2003, p. 67.