S$_N$2 REACTIONS OF ALKYL HALIDES

OBJECTIVE

To examine factors affecting the relative rates of the S$_N$2 reaction of alkyl halides such as:

alkyl halide structure
nature of the leaving group
properties of the nucleophile
steric hindrance

INTRODUCTION

The alkyl halides play an important role in organic synthesis. They can be easily prepared from alcohols or alkenes, among other starting materials. They in turn can be used in the synthesis of a large number of functional groups. These syntheses are often carried out by nucleophilic substitution reactions in which the halide is replaced by some nucleophile.

These substitution reactions can occur in one smooth step, or in two discrete steps, depending primarily on the structure of the alkyl group. These mechanisms are known as S$_N$2 and S$_N$1. In this laboratory period we will spend some time looking at S$_N$2 reactions.

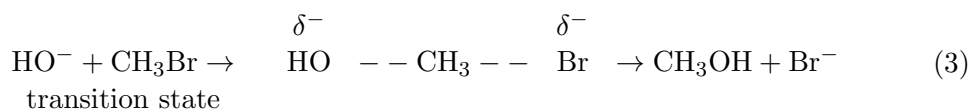To get started, let's propose a mechanism for the reaction:

$$CH_3Br + HO^- \rightarrow CH_3OH + Br^- \tag{1}$$

The rate of this reaction is directly proportional to the concentration of both methyl bromide and sodium hydroxide

$$\text{Rate} = k[CH_3Br][OH^-] \tag{2}$$

The reaction proceeds with inversion of configuration
Any ideas?

This mechanism was initially elucidated by Sir Christopher Ingold and Edward Hughes, in the 1930s. They interpreted the second-order kinetic behavior to mean that the rate-determining step is a bimolecular, concerted process

$$HO^- + CH_3Br \rightarrow \quad \overset{\delta^-}{HO} \; -- CH_3 -- \; \overset{\delta^-}{Br} \quad \rightarrow CH_3OH + Br^- \tag{3}$$
$$\text{transition state}$$

Therefore the following mechanism was proposed–the backside attack of the nucleophile, with the leaving group leaving in a concerted step. This backside attack causes the inversion of stereochemistry (known as Walden inversion).

PRE-LAB

1. Obtain reagent data for all stating materials (structure, formula, molecular weight, melting point, boiling point, density and applicable hazards.) Organize this information in a table.
2. Provide a brief outline of the experimental procedure.
3. Answer the following questions.

Questions

Question 1: Predict the product for the reaction of R-2-chlorobutane with NaI in acetone, indicating corect sterochemistry.

Question 2: Predict the outcome of each set of experiments. Justify your predictions.

Question 3: What is the difference between the S_N1 and S_N2 mechanisms. Is it possible for an alkyl halide to undergo S_N1 and also S_N2 reactions? Why?

Question 4: Is chlorine a better leaving group than bromine? Please explain.

Question 5: Table of physical constants

PROCEDURE

Waste disposal

The reaction mixtures from this experiment should be collected in the labeled waste container. Do not put them down the drain. Ask your teaching assistant if you have any questions concerning the proper procedures for waste disposal.

Part 1: Effect of Structure of the Alkyl Halide on the Relative Rates of S_N2 Reactions

Measure 2 mL of 15% sodium iodide in acetone into each of three clean, dry 10-cm test tubes. Add 2 drops of 1-bromobutane (butyl bromide) to the first test tube; add 2 drops of 2-bromobutane (sec-butyl bromide) to the second test tube; and add 2 drops of 2-methyl-2-bromopropane (t-butyl bromide) to the third test tube. Stopper the tubes with corks. (Do not use rubber stoppers.) Shake the tubes to mix. Observe closely during the first 15-20 minutes, then at intervals throughout the lab period. Look for any sign of cloudiness or precipitation. Record your observations and the time at which the initial cloudiness was observed for each reaction.

Part 2: Steric Effects and the Relative Rates of S_N2 Reactions

Measure 1 mL of 15% sodium iodide in acetone into each of two clean, dry 10-cm test tubes. Into one tube, add 2 drops of 1-bromobutane; into the other test tube, add 2 drops of 1-bromo-2,2-dimethylpropane (neopentyl bromide). Stopper the tubes and shake. Observe closely. Record your observations.

Part 3: Effect of the Leaving Group on the Relative Rates of SN2 Reactions

Measure 1 mL of 15% sodium iodide in acetone into each of two clean, dry 10-cm test tubes. Add 2 drops of 1-bromobutane into one test tube and add 2 drops of 1-chlorobutane into the other test tube. Stopper and shake the tubes. Observe closely. Record your observations.

IN-LAB QUESTIONS

Download and print the following worksheet. You will use this worksheet to record your answers to the In-Lab questions.

Questions

Question 1: Which alkyl bromide reacted fastest with sodium iodide in acetone: 1-bromobutane, 2-bromobutane or 2-bromo-2-methylpropane? Which alkyl bromide reacted slowest? Explain how the structure of the alkyl halide affects the rate of an S_N2 reaction.

Question 2: Which alkyl bromide reacted faster with sodium iodide in acetone: 1-bromobutane or 1-bromo-2,2-dimethylpropane (neopentyl bromide)? Both of these are primary halides. Why was there a difference in reactivity?

Question 3: Which halide reacted faster with sodium iodide in acetone: 1-bromobutane or 1-chlorobutane? Explain how the nature of the leaving group affects the rate of an S_N2 reaction. Would 1-iodobutane react faster or slower than the other halides? How would we know that the reaction took place? Explain.

Question 4: Write balanced equations for all substitution reactions that took place between the alkyl halides and NaI. Propose intermediates or transition states for each reaction.