

NMR Kinetics of the S_N2 Reaction between BuBr and I[−]: An Introductory Organic Chemistry Laboratory Exercise

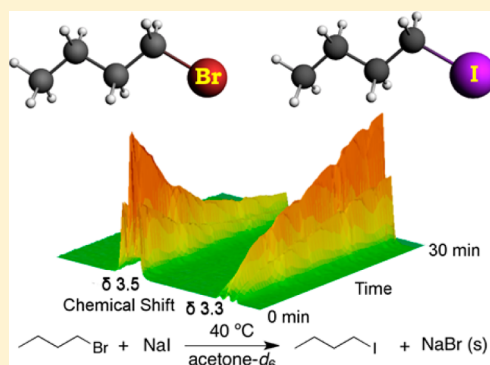
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S Supporting Information

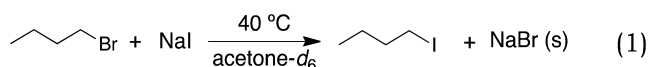
ABSTRACT: A simple organic chemistry experiment is described that investigates the kinetics of the reaction between 1-bromobutane (BuBr) and iodide (I[−]) as followed by observing the disappearance of BuBr and the appearance of 1-iodobutane (BuI) using ¹H NMR spectroscopy. In small groups of three to four, students acquire data to examine the concentration-dependence of both the organic substrate and the nucleophile under pseudo-first-order and second-order conditions. After data processing, students analyze three data sets (one second-order experiment, and two first-order experiments with different concentrations of iodide) using an electronic spreadsheet. Students discuss the experimentally determined rate law, comparing it to that predicted for this S_N2 reaction.

KEYWORDS: Second-Year Undergraduate, Hands-On Learning/Manipulatives, Laboratory Instruction, Organic Chemistry, Physical Chemistry, Kinetics, Rate Law, Mechanisms of Reactions, Nucleophilic Substitution, NMR Spectroscopy



For the last 10 years, an introduction to kinetics in the first term of second-year undergraduate organic chemistry has been taught with the experiment described herein; approximately 1000 students have completed the experiment.¹ The introductory organic chemistry course serves as an ideal setting for teaching kinetic theory, with this experiment coming two-thirds of the way through the first semester of a two-semester organic sequence. At this point, our students have a firm basis in structural concepts, are able to translate simple NMR spectra into chemical structures, and understand the concept of a reaction mechanism. Concurrent with this experiment, students are learning in the classroom the fundamentals of reaction kinetics and the mechanisms of bimolecular and unimolecular nucleophilic substitution at aliphatic carbons. While the kinetics topics include what are typically covered in introductory general chemistry courses, the organic context makes this material more accessible to students.

The experiment described follows the concentrations of 1-bromobutane (BuBr) and 1-iodobutane (BuI) in the reaction described in eq 1, relying on the fact that sodium bromide (NaBr) is essentially insoluble² in acetone (at 25 °C, $K_{sp} = 1.42 \times 10^{-6} \text{ M}^2$) to prevent the back reaction and, thus, simplify the kinetics observed. These organic compounds, while simple in structure, give NMR spectra that are readily recognizable to a beginning organic chemistry student, and the ¹H NMR experiment allows for the time-resolved evolution of their concentrations in a 30 min time-period when the reaction is carried out at 40 °C. Thus, a laboratory of 20 students, working in groups of 3 or 4 with guidance, can finish the collection of data in a 3 to 4 h time-period utilizing a single NMR instrument.



■ BACKGROUND

Kinetics experiments appropriate for organic chemistry students have been described in this *Journal*, as well as other chemistry education journals and secondary sources such as laboratory manuals. NMR spectroscopy has been utilized to illustrate kinetics in the organic^{3–5} and biochemistry curricula,^{6–8} including an excellent example⁹ that describes following the kinetics of the multistep acid-catalyzed esterification of trifluoroacetic acid under pseudo-first-order conditions. The kinetics¹⁰ of the so-called Finkelstein reaction¹¹ (eq 1) has also been presented as a kinetics experiment in which the concentration of sodium iodide (NaI) was followed under second-order conditions by conductivity.¹² This study by Pace was thorough, discussing the temperature dependence of the reaction, leaving group and substrate structure effects, as well as its dependence upon solution polarity. Each of these aspects of the reaction could in theory also be investigated using NMR spectroscopy, but the scope of the current article is limited to a simpler laboratory exercise by which students are introduced to second-order and pseudo-first-order kinetics. In particular, the utility of employing ¹H NMR spectroscopy is emphasized to aid students in visualizing this canonical one-step reaction. The simple spectra involved in this experiment allow students to “see” the reaction as it progresses, making it an ideal introduction to kinetics for organic students.

Table 1. Conditions 1, 2, and 3 for S_N2 Reaction between Bromobutane and Iodide^a

	Final concentrations	Soln A 0.70 M NaI	Soln B 0.30 M C ₄ H ₉ Br	Soln C 5.0 M C ₄ H ₉ Br
1	15:1 NaI/BuBr (0.60 M:0.040 M)	0.70 mL	0.10 mL	NONE
2	15:1 NaI/BuBr (0.30 M:0.020 M)	0.35 mL	0.050 mL + 0.40 mL acetone- <i>d</i> ₆	NONE
3	1:1 NaI/BuBr (0.60 M:0.60 M)	0.70 mL	NONE	0.10 mL

^aStock solutions A, B, and C are dissolved in acetone-*d*₆.

By the end of this two week experiment, students should understand the second-order kinetics of the S_N2 reaction under both second-order and pseudo-first-order conditions. They should be able to analyze the data from both sets of conditions, determining the experimental rate law and rate constants to support the bimolecular reaction mechanism.

EXPERIMENTAL METHODS

Two weeks are required to complete the experiment, 1 week for the experimental procedure and 1 week for the analysis.

Necessary Equipment

A Fourier-transform NMR spectrometer capable of timing control and temperature control for acquisition of data at 40 °C is required. This need not necessarily be a high-field instrument as the multiplets for the methylene groups proximal to the halides in 1-bromobutane and 1-iodobutane should be separated by 12 Hz on a 60 MHz instrument. The experiment could be run at ambient temperature; however, at a typical room temperature of 22 °C, the experiment would need substantially longer (approximately 2 h) to reach the same point of completion of the reaction. All of the data necessary to execute the analysis portion of the laboratory are included as the Supporting Information, so it is possible to “drylab” the acquisition portion of the experiment.

General Methods

Prior to the first run, the NMR spectrometer is warmed to 40 °C and tuned and shimmed utilizing a sample corresponding to Condition 1 (Table 1). Prior to each run, a starting shim file is read, and the automated shimming routine of the spectrometer is utilized throughout the run. Sixty individual free induction decays (FIDs) are collected following a single 90° pulse utilizing a two-dimensional experimental procedure. A detailed description of the parameters is in the Supporting Information. Alternatively, a series of 1D spectra can be acquired by incrementing the experiment number automatically.

Experiment

Each team of students mixes the components described for one of the conditions (Table 1) in a small disposable vial, adding sodium iodide last. The sample is transferred to an NMR tube, introduced into the magnet, and acquisition of NMR data is begun immediately. A stopwatch is used to measure the interval of time between the collection of each FID. Following data acquisition, the sample is removed, and observations about the state of the sample are recorded (NaBr precipitates during the course of the reaction). The data set is transferred to network storage for subsequent workup. The NMR data are worked up as described in the Supporting Information.

HAZARDS

While the amounts of reagents used in this experiment are rather small, appropriate protective gear including goggles should be worn during all manipulations. 1-Bromobutane and 1-iodobutane are both highly flammable halogenated hydrocarbons that are irritants to skin and eyes and toxic upon ingestion. Suitable precautions should be taken in the handling and disposal of these compounds and reaction solutions containing them. Sodium iodide and sodium bromide are both known as irritants. Chronic exposure to sodium iodide is reported to have effects on the fetus. Acetone-*d*₆ is highly flammable, an irritant to the skin and eyes, and toxic upon ingestion.

RESULTS

Representative spectra from early, middle, and late time points from Condition 1 are shown in Figure 1. A Quicktime movie illustrating the time resolution of the spectra is available (Supporting Information).

Analysis of Data

Each student group analyzed the data from all three conditions (Table 1). For each condition, the text file containing the integration data was imported into a spreadsheet program. The

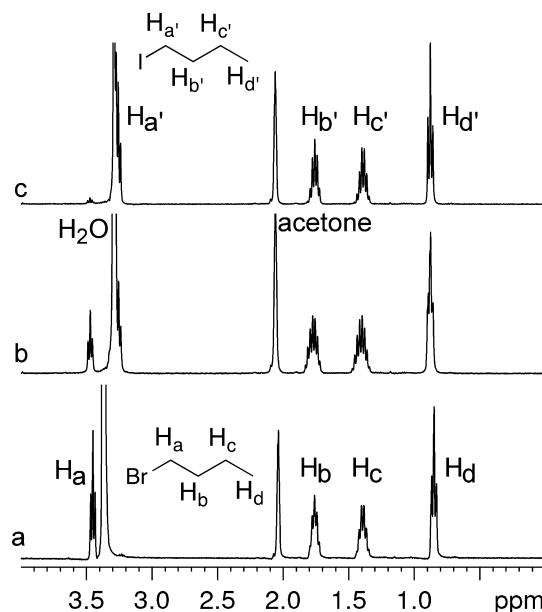


Figure 1. Representative spectra from student experiment under Condition 1: (a) First spectrum acquired, (b) 17th spectrum acquired, (c) last (60th) spectrum acquired. Adventitious H₂O and residual protons from acetone-*d*₆ indicated in (b).

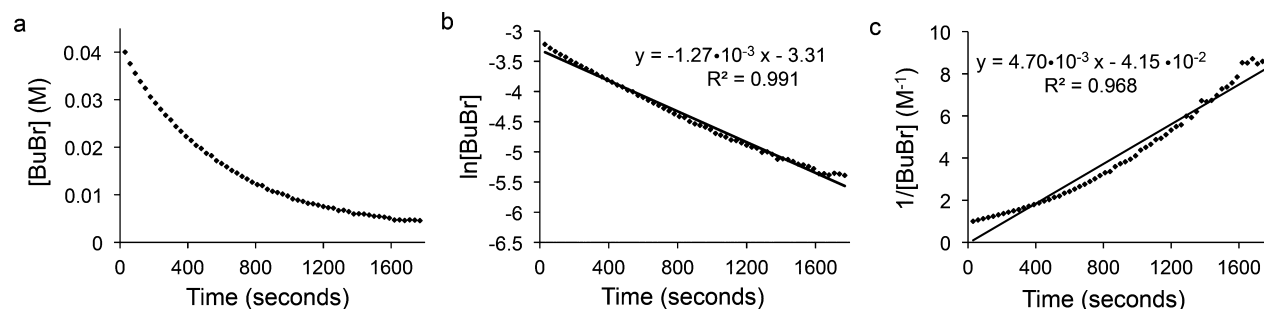


Figure 2. Representative plots from student acquisition of Conditions 1: (a) concentration of BuBr vs time, (b) natural log of concentration of BuBr vs time, (c) reciprocal concentration of BuBr vs time.

data were normalized and converted to concentration with the assumption that no side reactions occurred. Three plots were prepared for each of the conditions: [BuBr] vs time, $\ln$ [BuBr] vs time, and $1/[\text{BuBr}]$ vs time. From each of the conditions, the observed rate constant was calculated and converted into the “real” second-order rate constant for comparison purposes. Representative plots are in Figure 2 and the resulting rate constants are summarized in Table 2.

Table 2. Representative Results from Student Data from Kinetic Runs

	Conditions ^a	k_{pseudo} (s ⁻¹) ^b	k_{real} (M ⁻¹ s ⁻¹) ^b	k_{rev} (M ⁻¹ s ⁻¹) ^c
1	0.60 M NaI 0.040 M BuBr	1.3×10^{-3}	2.2×10^{-3}	2.8×10^{-3}
2	0.30 M NaI 0.020 M BuBr	8.8×10^{-4}	2.9×10^{-3}	4.0×10^{-3}
3	0.60 M NaI 0.60 M BuBr	-	2.0×10^{-3}	-

^aConcentrations of reagents in acetone-*d*₆. ^bRate constants determined with the assumption of $[\text{BuBr}]_{\infty} = 0$. ^cRate constants determined with non-zero $[\text{BuBr}]_{\infty}$.

DISCUSSION

The kinetics of this S_N2 reaction are particularly easy to follow and simple for students to understand because the reaction goes essentially to completion due to the insolubility of NaBr in acetone. Thus, if the reverse reaction is ignored, the differential rate law for the expected bimolecular substitution reaction is given by eq 2.

$$-\frac{d[\text{BuBr}]}{dt} = k_{\text{real}}[\text{BuBr}][\text{I}^-] \quad (2)$$

The conditions described in Table 1 resulted in pseudo-first-order conditions for both Conditions 1 and 2. Upon integration, eq 2 gives rise to an integrated rate equation (eq 3) where $k_{\text{pseudo}} = k_{\text{real}}[\text{I}^-]$.

$$-\frac{d[\text{BuBr}]}{dt} = k_{\text{pseudo}}[\text{BuBr}] \quad (3)$$

Conditions 3 also simplified the rate equation by virtue of the fact that the concentrations of the NaI and BuBr were equal. Assuming that there were no side reactions, the concentrations of the two reagents stayed equal throughout the reaction, and the integrated rate law coming from eq 2 (with the substitution of $[\text{BuBr}] = [\text{I}^-]$) can be expressed as eq 4.

$$-\frac{d[\text{BuBr}]}{dt} = k_{\text{real}}[\text{BuBr}]^2 \quad (4)$$

Figure 2b provides a representative example of the pseudo-first-order plot of the disappearance of BuBr. Figure 3 shows

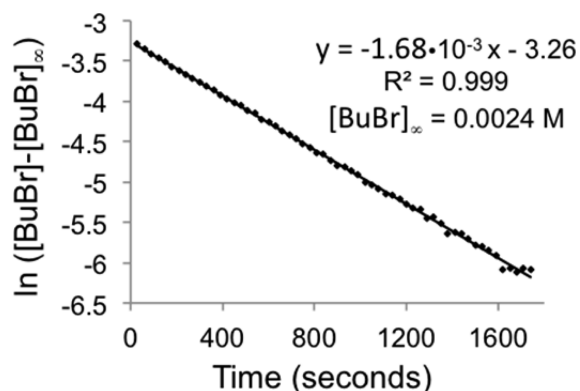


Figure 3. Natural log of concentration of BuBr vs time taking into account non-zero equilibrium concentration of BuBr.

the improvement in the fit if reversibility of the reaction was taken into account (a non-zero $[\text{BuBr}]_{\infty}$). Table 2 provides the numerical tabulation of the various rate constants taken on a single day for all three conditions, with the final column showing k_{rev} , the second-order rate constants¹³ obtained from conditions 1 and 2 by taking into account a non-zero $[\text{BuBr}]_{\infty}$. While there was some change upon allowing for reversibility, ignoring this detail still resulted in data that were sufficient to allow beginning kinetics students to ascertain the bimolecular nature of the reaction. In fact, the greater change appeared to be the change in the rate constant due to the difference in ionic strength between Condition 1 (0.60 M NaI) and Condition 2 (0.30 M NaI). This difference, readily detected by students and discussed more fully in Pace's article¹⁰ and the original literature,¹⁴ provided an excellent opportunity to discuss the depression of the rate of S_N2 reactions involving ionic substrates when highly polar reaction media are utilized.

As the students analyze the data, individual groups report their results on a blackboard in the classroom. The students are encouraged to compare their results with other groups, and students reporting outliers typically realize that a mistake has been made in the calculations. The students then complete a worksheet (available as Supporting Information) and provide sample plots to report their findings. In the past, other assessments have been utilized. In particular, this experiment was the basis of a lab report that the students wrote in the form

of a literature journal article. It serves exceptionally well in this capacity and provides a rather complete study that is not synthesis based.

The ability of the students to understand the basic kinetic concepts is additionally assessed with an exam question on the course final exam. Over a three year period in which the author taught one section of the class with a linked laboratory and class, on average three-quarters of the students performed on that exam question with an adequate to very good understanding of the material, while only 10% of the students showed little to no understanding of the material.

CONCLUSION

The reaction between 1-BuBr and NaI was readily followed by ^1H NMR spectroscopy in an experiment that emphasized the dynamic nature of the kinetic experiment by allowing beginning kinetic students to “see” the reaction as it progressed. It was, therefore, intended to be used as an introduction to kinetics, but it could be easily adapted to include or to be paired with the experiments described by Pace to increase the depth of the experimental data gathered and analyzed.

ASSOCIATED CONTENT

Supporting Information

Directions for the students suitable for a laboratory manual, notes for the instructor, raw data (JCAMP format), Excel workbooks with analyzed data, and a Quicktime movie of the time-resolved spectra. This material is available via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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