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Synthesis of 2,5-Dichloro-2,5-dimethylhexane by an S_N1 Reaction

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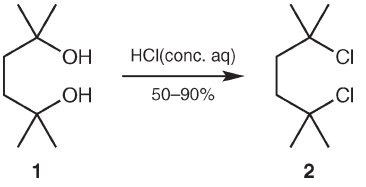
Using S_N1 reactions to instruct students in basic organic synthesis mechanisms and in isolation and characterization techniques is not novel, and these are the central reactions in many experiments described in this *Journal (1)* as well as commercial organic laboratory textbooks *(2)*. For example, in an experiment by Pavia et al. *(2)*, *tert*-amyl alcohol is converted to *tert*-pentyl chloride by an S_N1 reaction, is isolated by separatory funnel extraction, and is purified by drying over an absorbent followed by distillation. Herein we describe a safe, economical, and effective S_N1 experiment that we have implemented and assessed in our organic chemistry laboratory classes that focuses on the conversion of 2,5-dimethyl-2,5-hexanediol, **1**, to 2,5-dichloro-2,5-dimethylhexane, **2** (Scheme 1). This S_N1 experiment differs from the previous experiments by producing a solid product that can be filtered and on which tests such as solubility, melting point determination, and thin-layer chromatography (TLC) can be conveniently performed. With these isolation and characterization techniques, instructors can question students about the physical and reactive properties of their product. This lab is an effective approach to achieve student mastery of this central reaction type as demonstrated by the prelab and postlab assessment.

Scheme 1. Synthesis of 2,5-Dichloro-2,5-dimethylhexane, **2**



1 **2**

Experimental Details

There are three parts to this experiment: synthesis, solubility tests, and TLC analysis. In part I, students treat 2,5-dimethyl-2,5-hexanediol, **1**, with excess concentrated hydrochloric acid to synthesize 2,5-dichloro-2,5-dimethylhexane, **2**, using a modified literature procedure *(3)* (Scheme 1). Students weigh approximately 0.25 g of **1** and place it in a 25 mL Erlenmeyer flask. Next, students add approximately 2 mL of concentrated (35−37% by mass) hydrochloric acid to the flask containing **1** and gently swirl the contents of the flask for 5−10 min, taking care not to spill or splash any liquid outside of the container. Observant students may notice that a majority of the starting solid dissolves, and a different-textured white precipitate forms. Students collect the precipitated product by filtering the contents of the flask through a Buchner filter funnel and washing with a small volume of water. The solid is dried on the filter paper with air being drawn through it for 30−40 min. Students then weigh the recovered product and take a melting point to compare it with the melting point of the to the starting material. The lower melting point of **2** (lit. *(4)* mp 63−66.5 °C) compared to **1** (87 °C) provides an entry to ask students for an explanation in terms of intermolecular forces.

In part II, students perform solubility tests with **1** and **2** in different solvents. Students place a small quantity (∼3−5 mg) of **1** in each of three numbered test tubes and place a similar quantity of **2** into each of another set of three numbered test tubes. To the first test tube in both sets, students add 0.5 mL of methanol. To the second test tube in both sets, students add 0.50 mL of hexanes. To the third test tube in both sets, students add 0.50 mL of ethyl acetate. This part of the experiment familiarizes the students with the use of different types of solvents (polar protic, nonpolar, and polar aprotic) to assess solubility profiles of different types of organic compounds.

In part III, students spot a TLC plate with a small quantity of **1** and **2** dissolved in ethyl acetate and develop the TLC plate in a 95:5 hexanes/ethyl acetate solution in a TLC chamber. After the TLC plate is developed and the solvent has dried, students visualize the spots on the plate by staining the plate with a 5−20% by mass ethanol solution of phosphomolybdic acid (PMA). Three of the TLC slides developed in varying solvent systems and stained with PMA are shown in Figure 1. This part of the experiment allows students to practice TLC spotting skills and to learn about monitoring a reaction by TLC.

For the purposes of writing up their laboratory reports, students may also take the Fourier transform infrared (FTIR) spectra of **1** and **2**. The FTIR spectrum of **1** shows a clear hydroxyl group stretching frequency, whereas this frequency is absent in the FTIR spectrum of **2**. While spectroscopic analysis is not a necessary component of this laboratory experiment, departments with FTIR and NMR instruments may opt to incorporate the spectroscopic analysis of the reactants and products of this reaction. FTIR and NMR data of **1** are available from the Sigma-Aldrich Web site *(5)*. Spectra of **1** and **2** are included in the supporting material.

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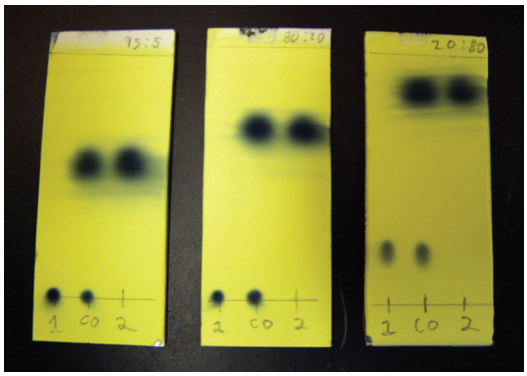

Figure 1. TLC slides spotted with **1**, a mixture of **1** and **2** (co), and **2**, stained with PMA and developed in 95:5, 80:20, and 20:80 hexanes/ethyl acetate (left to right).

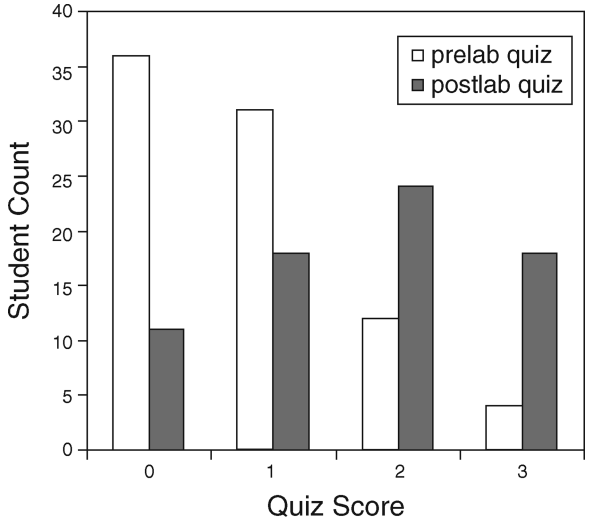

Figure 2. Comparison of student scores on prelab and postlab quizzes. The multiple-choice quizzes were graded numerically from zero to three (prelab quiz $n = 83$ and postlab quiz $n = 71$).

Hazards

Concentrated HCl and 5−20% phosphomolybdic acid staining solutions are corrosive if inhaled, ingested, or come into contact with skin. Methanol, hexanes, and ethyl acetate are volatile, flammable organic solvents. All students and the instructor should wear goggles, gloves, and lab coats or aprons. Compound **1** should be handled with care, since its properties are not fully known. The reactions should be carried out in a fume hood in well-ventilated room. The TLC plate should be handled with tweezers, not by hand. Finally, the product 2,5-dichloro-2,5-dimethylhexane should be handled with extreme care as its properties are unknown.

Assessment of Student Learning

This lab was assessed by two means: comparison of prelab and postlab scores on an in-class quiz and by a postlab anonymous student self-assessment. The prelab quiz was given directly before the lab, and the postlab quiz was administered one week after the lab. Both quizzes consisted of three questions, one of

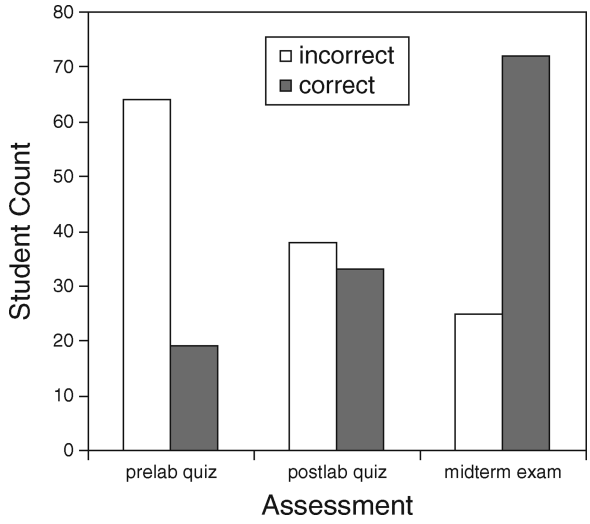

Figure 3. Comparison of student ability to correctly identify the S_N1 reaction mechanism on the prelab quiz, postlab quiz, and a midterm exam. The reaction mechanism question in the quizzes and exam was either correct or incorrect (prelab quiz $n = 83$, postlab quiz $n = 71$, and midterm exam $n = 97$).

which concerned the identification of an S_N1 mechanism, the central concept of the experiment. Additionally, a midterm exam was held two weeks after the lab with a question concerning the identification of an S_N1 mechanism. The average score on the three-point prelab quiz was 0.80 ± 0.86 and the average score on the postlab test was 1.69 ± 1.02. Statistical analysis reveals a statistically significant difference between prelab and postlab scores (using an unpaired homoscedastic t test, $P = 1.9 \times 10^{-8}$). Additional analysis shown in Figure 2 indicates that most students performed better on the postlab quiz than the prelab quiz as indicated by the overall increase in quiz scores.

Further analysis of the central concept question in the prelab quiz, postlab quiz, and midterm exam (Figure 3) indicates that the percentage of students who were able to correctly identify the S_N1 reaction mechanism increased from 22.9% to 46.5% from the prelab quiz to the postlab quiz, and further to

Table 1. Postlab Student Self-Assessment of the Laboratory

Comment	Student Response Mean ± SD
I enjoyed this lab.	3.39 ± 1.11
I would recommend that this lab exercise be kept in the chemistry lab curriculum.	3.56 ± 1.10
This lab exercise made me think.	3.93 ± 0.95
This lab exercise fit in well with the curriculum of the lecture.	3.89 ± 1.09
I hated this particular lab.	2.57 ± 1.03
This lab was an active process for me.	3.79 ± 0.87
I learned something from this lab.	4.01 ± 0.88
This lab made me ask questions, such as, "What happens to 2,5-dichloro-2,5-dimethylhexane when it dissolves in methanol?"	3.43 ± 1.21

74.2% on the midterm exam. While the increase in the ability to correctly identify the S_N1 reaction mechanism from the prelab quiz to postlab quiz reasonably may result from the exposure to the laboratory experiment, the increase observed on the midterm exam may also be attributable to factors such as instructor review and student study.

The students were also given the option to complete a postlab anonymous self-assessment. The assessment results are reported in Table 1. In the postlab survey, students reported that they learned something and indicated that they enjoyed the exercise. Thus, by all assessment measurements, students learned from this lab exercise.

Conclusion

We describe an easy and inexpensive S_N1 reaction in which the starting material and final product can be analyzed by melting point, FTIR spectroscopy, solubility analysis, and TLC. Prelab and postlab analysis indicates that this activity increased student understanding of this type of chemical reaction.

Acknowledgment

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Note

1. Exemption from human subjects approval was granted by the Arizona State University Institutional Review Board as pursuant to Federal regulations, 45 CFR Part 46.101(b)(1)(2).

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Supporting Information Available

FTIR, ^{13}C NMR, and ^{1}H NMR spectra of **1** and **2**.This material is available via the Internet at http://pubs.acs.org.

