The Cyclohexanol Cycle and Synthesis of Nylon 6,6: Green Chemistry in the Undergraduate Organic Laboratory

ARTICLE *in* JOURNAL OF CHEMICAL EDUCATION · DECEMBER 2011

Impact Factor: 1.11 · DOI: 10.1021/ed2000878

JOURNAL OF CHEMICAL EDUCATION

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The Cyclohexanol Cycle and Synthesis of Nylon 6,6: Green Chemistry in the Undergraduate Organic Laboratory

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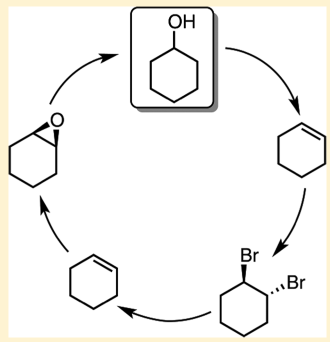
Supporting Information

ABSTRACT: A one-term synthesis project that incorporates many of the principles of green chemistry is presented for the undergraduate organic laboratory. In this multistep scheme of reactions, students react, recycle, and ultimately convert cyclohexanol to nylon 6,6. The individual reactions in the project employ environmentally friendly methodologies, and the scheme minimizes impact on the environment by reducing waste, using the product of one reaction as the starting material for the next.



KEYWORDS: *Second-Year Undergraduate, Curriculum, Laboratory Instruction, Organic Chemistry, Hands-On Learning/Manipulatives, Green Chemistry, Spectroscopy, Synthesis*

Green chemistry, which is based on the 12 guiding principles outlined in Table 1, is the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances.[1] Green chemistry is a topic of emerging importance and one that is well suited for incorporation into the modern undergraduate organic laboratory curriculum.[2] In recent years, a number of reports concerning green chemistry and education have appeared in this *Journal*,[3−6] and an ever-growing number of relevant laboratory experiments appropriate for the undergraduate chemistry curriculum have emerged.[7−22] In the words of *Chemical & Engineering News's* Editor-in-chief, Rudy Baum, "green" has indeed gone "mainstream",[23] and so it has become increasingly relevant that young chemists be exposed to alternative, environmentally friendlier methods for carrying out reactions of traditional importance.

Table 1. The 12 Principles of Green Chemistry

Number	Principle[a]
1	Prevention
2	Atom Economy
3	Less Hazardous Chemical Syntheses
4	Designing Safer Chemicals
5	Safer Solvents and Auxiliaries
6	Design for Energy Efficiency
7	Use of Renewable Feedstocks
8	Reduce Derivatives
9	Catalysis
10	Design for Degradation
11	Real-time analysis for Pollution Prevention
12	Inherenetly Safer Chemistry for Accident Prevention

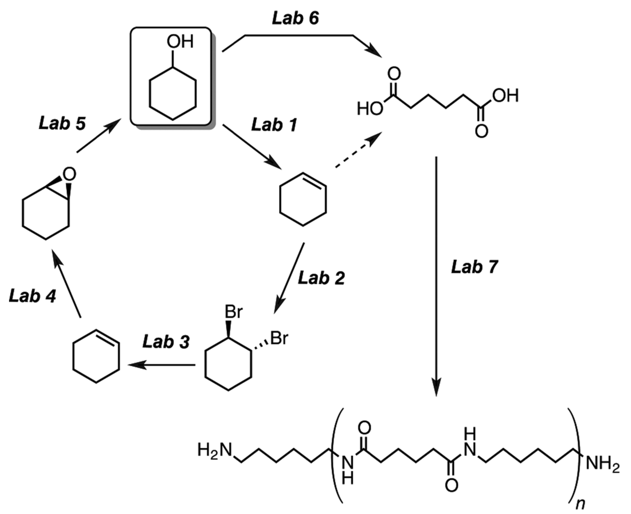
[a]The principles are from ref 1.

For many years, the laboratory curriculum contained traditional experiments from a published lab manual.[24] Although most of these experiments were very good and gave students hands-on experience with the reactions they were learning in the classroom, it was disappointing for students to spend 4 or 5 h in the lab synthesizing and characterizing a desired product, only to dump it into a waste container at the end of the period. Thus, a new project-based approach to the organic laboratory was developed in which the product of one reaction was used as the starting material for the next reaction, while also integrating reactions that were discussed in concurrent lectures. In addition, the laboratory curriculum was made more "green" by introducing newer, more environmentally friendly reaction methodologies and generating less waste. Although a few excellent green organic chemistry lab manuals are currently available,[25−27] a more comprehensive, integrated lab experience was sought with an emphasis on green chemistry. Thus, after several years of experimenting, a one-term project was developed called "The Cyclohexanol Cycle and Synthesis of Nylon 6,6" (Scheme 1), which is a multistep scheme of reactions in which students react, recycle, and ultimately convert cyclohexanol to nylon 6,6.

The reactions in the project make use of environmentally friendly methodologies, and the scheme is designed to minimize impact on the environment by reducing waste, using the product of one reaction as the starting material for the next. Although not intended to be an exercise in total synthesis,

Published: December 6, 2011

Scheme 1. The Cyclohexanol Cycle and Synthesis of Nylon 6,6



the scheme provides students with a unique opportunity to engage in a multistep synthesis project that employs many of the reactions they are learning about concurrently in lecture. In addition, the percent recovery of cyclohexanol allows for assessment of laboratory techniques and skills. This second-term project follows a techniques-based project carried out by our students during the first term,[28] and prepares them well for a research-based project that they complete in the third term.[29] The students find this project challenging and rewarding, and it seems to inspire in them a sense of ownership of and responsibility and accountability for their work. All laboratory experiments and related assignments are posted on a dedicated Web site and Zubrick's *The Organic Chem Lab Survival Manual* is used as a reference manual.[30]

■ EXPERIMENTAL OVERVIEW

Students begin the project with cyclohexanol (10 g on standard scale; 2 g on microscale), which they first convert to cyclohexene via Montmorillonite K10 clay-catalyzed dehydration in the first lab.[31] The cyclohexene is subsequently converted to racemic *trans*-1,2-dibromocyclohexane through an addition reaction in which molecular bromine is generated in situ under aqueous conditions in the second lab.[32] In the following reaction (lab 3), cyclohexene is recovered via zinc-mediated reduction in water,[33] and in the fourth lab, the cyclohexene is epoxidized with Oxone in aqueous acetone.[34] Reduction of the cyclohexene oxide with $LiBH_4$ in THF–methanol[35] regenerates the cyclohexanol in the fifth lab. The recovered cyclohexanol is then oxidized to adipic acid with H_2O_2 catalyzed by tungstic acid (H_2WO_4) in water in the sixth lab,[36] and the adipic acid is then used as a precursor for the synthesis of nylon 6,6 in the final lab period.[37] Students may also explore an alternate synthetic route to nylon 6,6 via the environmentally friendly tunstate-catalyzed oxidation of cyclohexene to adipic acid (dashed arrow, Scheme 1).[38] Each lab is approximately 4 h and students work individually. Students typically do not purify any of the intermediates, though this is certainly an option at the instructor's discretion. (On a 10-week quarter system, there is not time.) Percent yields are calculated for each reaction and percent recovery of cyclohexanol is calculated for the cycle. Reaction products may be analyzed and purity assessed by GC–MS or ^{1}H NMR spectroscopy at the instructor's discretion.

■ HAZARDS

General Laboratory safety procedures, including wearing safety goggles and gloves, must be followed at all times. All organic chemicals involved in this experiment are considered hazardous, and direct physical contact with them should be avoided. All wet-laboratory experiments must be performed in a fume hood, and wearing a laboratory coat or apron is advised. Detailed information about the hazards of the specific chemicals is available in the Supporting Information.

■ DISCUSSION

In 1933, E. C. Wagner published in this *Journal* a manuscript entitled "Some Student Experiments In and Out of the Cycloparaffin Series", in which a number of reactions of cyclohexanol and related compounds were presented to "give students some first-hand acquaintance with a series of compounds known in many instances only on the pages of their textbooks."[39] Although certainly innovative at the time, most of the experiments reported by Wagner do not comply with the "green standards" of present day. Wagner's report did, however, serve in part as our inspiration for the development of "The Cyclohexanol Cycle", as did the series of experiments, called "The Copper Cycle", which is part of the general chemistry laboratory curriculum at this university. In "The Copper Cycle" experiments, students carry out the series of reactions that converts a piece of copper metal via several different copper-containing compounds back into its original elemental form. The prospect of developing an analogously cyclic scheme of reactions for the organic lab was exciting, and so "The Cyclohexanol Cycle" was devised.

In "The Cyclohexanol Cycle", students carry out the series of reactions that begins and ends with cyclohexanol, an inexpensive and readily available organic compound (Scheme 1). Concurrently, students learn about these reactions in the classroom, including dehydration of alcohols, addition to alkenes, E2 elimination, epoxidation of alkenes, and hydride reduction. The recovered cyclohexanol is then oxidized to adipic acid, which is subsequently used for the synthesis of the polymer, nylon 6,6. All of the reactions in the scheme were adapted from the literature and many employ green methodology. For example, the dehydration of cyclohexanol (lab 1) is catalyzed by Montmorillonite K10 clay, a naturally benign aluminosilicate mineral that is inexpensive, safe to use, and easy to handle (green chemistry principles 3, 5, 7, 9, and 12).[40] The bromination of cyclohexene (lab 2) is effected via in situ generation of bromine from HBr and H_2O_2 (green chemistry principles 3, 4, and 5). Laboratories 3, 4, and 6 are all conducted in water (green chemistry principle 5) and produce minimal waste or byproducts. Further, the cycle is designed to minimize impact on the environment by reducing waste, using the product of one reaction as the starting material for the next. Indeed, minimal waste is generated throughout the project, and the cost per student (for reagents, solvents, and supplies) is less than \$60 on standard scale or less than \$12 on microscale. The cost per student is kept low by employing simple, inexpensive reagents from Sigma–Aldrich such as cyclohexanol (\$0.03/mL), Montmorillonite K10 clay (\$0.05/g), zinc metal (\$0.07/g), Oxone (\$0.03/g), and tungstic acid (\$0.36/g).

dx.doi.org/10.1021/ed2000878 | J. Chem. Educ. 2012, 89, 262–264

■ CONCLUSIONS

"The Cyclohexanol Cycle and Synthesis of Nylon 6,6" represents a one-term, integrated project for the undergraduate organic laboratory that provides students with a contextual basis for learning about the principles of doing green chemistry, while also gaining hands-on experience with the reactions that they are concurrently learning in the classroom. Students develop a sense of accomplishment upon shepherding a batch of cyclohexanol through a series of functional group transformations and using their recovered material to synthesize nylon 6,6, a product with which they are all quite familiar.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Detailed instructions for the students; notes for instructors; detailed information about the hazards of the specific chemicals. This material is available via the Internet at http://pubs.acs.org.

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■ ACKNOWLEDGMENTS

We thank the National Science Foundation CCLI A&I program (Grant No. DUE-0310624) for support in purchasing our Bruker Avance 300 MHz NMR spectrometer and DePaul University's College of Liberal Arts & Sciences for funding and support of this work. The following DePaul undergraduate students are acknowledged for their participation and contributions: Stephanie Reeve, Barrett Unger, and Mark Aparece.

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