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Laboratory Experiment

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Visualizing Molecular Chirality in the Organic Chemistry Laboratory Using Cholesteric Liquid Crystals

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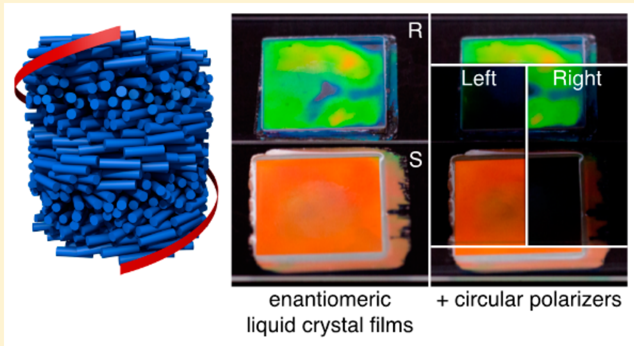
S *Supporting Information*

ABSTRACT: Although stereochemistry is an important topic in second-year undergraduate organic chemistry, there are limited options for laboratory activities that allow direct visualization of macroscopic chiral phenomena. A novel, guided-inquiry experiment was developed that allows students to explore chirality in the context of cholesteric liquid crystals. As part of the experiment, which requires no specialized equipment, students visually distinguish two enantiomers. A chiral imine is synthesized in one step from an assigned (but unknown to students) enantiomer of 1-phenylethylamine and then dissolved in a nematic liquid crystal host, inducing a helical structure. The resulting cholesteric liquid crystalline material selectively reflects circularly polarized light with a handedness that depends on the absolute configuration of the starting amine, easily detected using circularly polarizing filters from disposable 3D glasses. Working in teams, students examine the behavior of both dopant enantiomers and the racemic mixture. Analysis of our students' responses to post-lab questions indicates comprehension of most of the ideas introduced in lab.



KEYWORDS: *Second-Year Undergraduate, Laboratory Instruction, Organic Chemistry, Hands-On Learning/Manipulatives, Inquiry-Based/Discovery Learning, Chirality/Optical Activity, Enantiomers, Materials Science, Stereochemistry, Synthesis*

INTRODUCTION

Stereochemistry plays a critical role in all disciplines of chemistry.[1,2] The topic can be especially challenging to learn because it requires students to be able to visualize three-dimensional molecular structures.[3] For this reason, multiple teaching activities have been designed for use during lectures in order to help students build mental models of chiral molecular structures.[3−5] However, there are not as many laboratory experiments that teach students about the concept of chirality.[6] Typically, students carry out experiments involving resolution,[1,7−10] polarimetry,[2,11,12] or the synthesis of chiral compounds.[13−15] Even when not the focus of an experiment, specific rotation values are typically used as evidence that an optically active compound was synthesized. None of these experiments, however, allow students to observe a palpable, visual display of chirality.

The experiment presented here provides students with an opportunity to connect the abstract concept of molecular chirality to observable behavior by using liquid crystals to provide an obvious, macroscopic distinction between enantiomers. Toward this goal:

1. The students synthesize an imine.
2. They examine liquid crystals and their phase behavior.
3. They determine the absolute stereochemistry of a product mixture.
4. They identify a structure−property relationship between chiral dopants and liquid crystals.

This experiment is designed as a student-centered, guided-inquiry investigation.[16−20] Unlike traditional verification experiments, guided-inquiry laboratories are carefully structured to offer students an opportunity to "discover" structure−property relationships by examining trends or patterns in their data. Guided inquiry experiments provide students with a tested procedure to reach a predetermined, but unspecified, outcome. Students share their observations and data with each other, collaborate to generate explanations, and draw reasonable conclusions for the observed phenomena. As a result, they achieve a more robust understanding of the concepts targeted in the experiment, resulting in increased retention of knowledge.[16] The implementation of inquiry helps students to develop thinking, communication, and problem-solving skills.[17,21]

Background

The experiment is based on the use of liquid crystals for the high-throughput determination of enantiomeric excess.[22−25] This method relies on the dissolution of an enantioenriched dopant in a nematic liquid crystal host. In the achiral (undoped) nematic phase, there is a slight orientational order of individual rod-like molecules, which, on average, are parallel

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to each other (Figure 1, left). When a chiral solute is dissolved in a nematic host, the structure twists, resulting in a helical

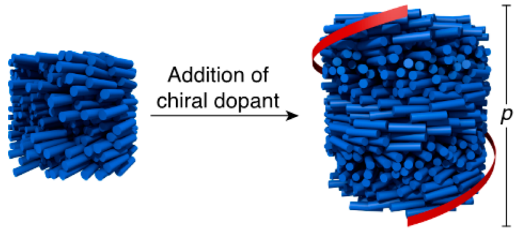


Figure 1. Cholesteric liquid crystal obtained by addition of a chiral solute to an achiral nematic host. *p* is the pitch of the helix.

chiral nematic, or cholesteric, phase (Figure 1, right). Opposite enantiomers of the dopant yield opposite twist senses of the induced helix. Helices with short pitches (*p*) are obtained from high concentrations of dopants with high helical twisting powers; in general, this requires that the chiral dopant and achiral host structurally resemble each other and possess a high compatibility.[22,23]

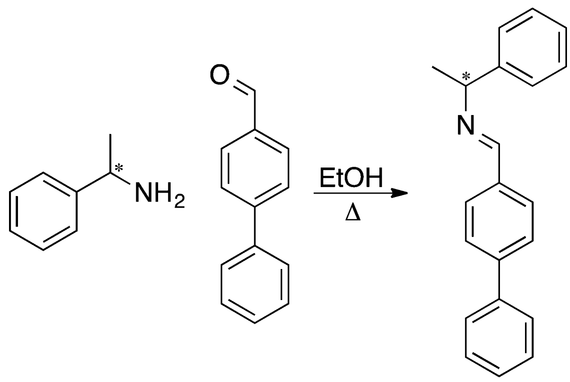
A useful property of cholesteric phases is the selective reflection of light. Incident light with a wavelength similar to the pitch of the helix is reflected when it strikes a film of a cholesteric liquid crystal with the proper molecular alignment. The reflected light is circularly polarized, with the handedness depending on the twist sense of the cholesteric helix.[24,26] In other words, a left-handed helix will selectively reflect left-handed circularly polarized light, and vice versa. Therefore, the absolute configuration of the constituent molecules can be distinguished based on the polarization of light reflected from the film.

This laboratory experiment can be integrated into existing experiments on polarimetry, and especially the resolution of racemic 1-phenylethylamine by crystallization with tartaric acid.[8,10] The experiment was carried out by chemistry and biochemistry majors in a second-semester undergraduate organic chemistry laboratory course, but it could also be carefully implemented in a first semester of organic chemistry laboratory and used with nonmajors. A related experiment has been developed by Van Hecke, in which students synthesize a particular enantiomer of a cholesteric liquid crystal and then examine its properties.[27] This previous experiment focuses on measurement of the physical properties of the liquid crystal itself, including determinations of the temperature-dependence of the helical pitch and the handedness of the reflected circularly polarized light. In contrast, the experiment described here is structured around contrasting the macroscopic behavior of different enantiomers.

■ EXPERIMENTAL PROCEDURES

The lab consists of two parts. In Part I, students individually synthesize the chiral dopant *N*-(4-phenylbenzylidene)-1-phenylethanamine (PBPEA) through imine condensation of 1-phenylethylamine and biphenyl-4-carboxaldehyde (Scheme 1). This dopant lacks the methoxy group found in the original work on ee quantification using liquid crystals.[23] Biphenyl-4-carboxaldehyde is substantially less expensive than 4-(4-methoxyphenyl)benzaldehyde and the resulting dopant gives functionally similar results; PBPEA has been used previously as a chiral dopant in nematic liquid crystals.[28,29] The synthetic procedure can be conveniently carried out in about 30 min.

Scheme 1. Synthesis of the Chiral Dopant *N*-(4-Phenylbenzylidene)-1-phenylethanamine from 1-Phenylethylamine and Biphenyl-4-carboxaldehyde



Students are not told the absolute configuration of their sample of 1-phenylethylamine; some are given the (*R*)-amine and some the (*S*)-amine. They determine the absolute configuration at the end of the experiment. Following reflux, product of good purity is obtained by simple filtration. The dopant is easily characterized by its melting point (88−90 °C) and the peak associated with the imine group (1645 cm^{-1}) in its IR spectrum (see the Supporting Information).

In Part II of the experiment, students, in groups of three, observe the properties of a mixture of the chiral dopant PBPEA from Part I and nematic liquid crystals *N*-(4-methoxybenzylidene)-4-butylaniline (MBBA) and 4-(ethoxybenzylidene)-4-butylaniline (EBBA). MBBA is a liquid crystal between 21 and 46 °C, while EBBA is a liquid crystal between 35 and 79 °C. Students determine the melting and clearing temperatures of EBBA in order to observe that liquid crystals are an intermediate state of matter between the crystalline solid and the isotropic liquid state.

A mixture of both MBBA and EBBA is used because it is liquid crystalline at room temperature even with a large amount of dissolved chiral dopant.[30] Each student prepares the mixture in a mortar, places a drop on a glass slide, and covers it with a coverslip. In most cases, nothing remarkable is observed at this point. However, shearing of the coverslip promotes a planar alignment of the molecules with the long molecular axes oriented in the plane of the glass slide.[31] As a result, a multicolored shimmering/sparkling of the mixture is observed (Figure 2).

Any circular polarizers can be used to determine the absolute configuration of the PBPEA dopant compounds. Standard, disposable 3D movie glasses with polarized filters as their lenses are convenient, and may inspire a special interest in students;

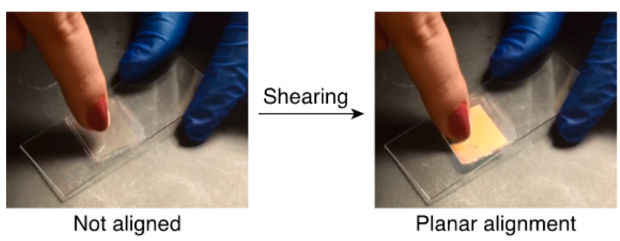


Figure 2. Observation of the chiral doped liquid crystal mixture with shearing: mixture before touching (left), same mixture during shearing (right).

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further, the shape of the glasses ensures that the students look through the polarizers from the correct side. The light reflected by the (*R*)-mixture has the same handedness as the right circular filter in the 3D glasses. Conversely, the light reflected by the (*S*)-mixture has the same handedness as the left circular filter in the 3D glasses.

Students heat the glass slides so that the mixtures transition from the liquid crystalline state to the isotropic liquid and become transparent. Shearing a drop of the melted mixture does not generate the reflective colors as before. After cooling and reshearing the mixture, in some cases students may obtain a permanent color for their mixtures without subsequent shearing. The permanently colored mixtures obtained may vary in color from red-orange to green (Figure 3). Some students also see a combination of colors.

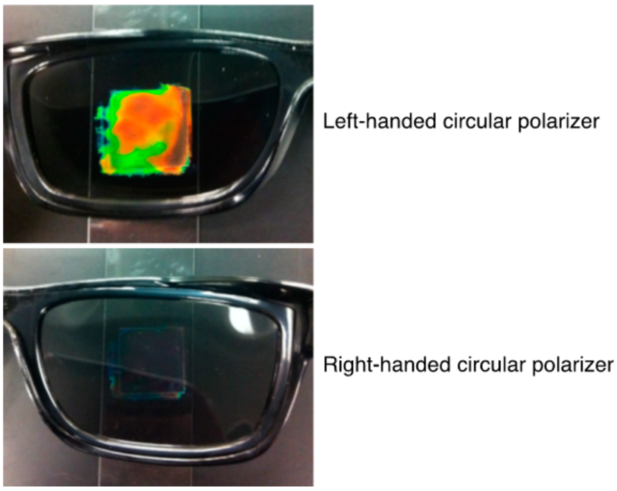

Figure 3. Observation of a student's (*S*)-dopant mixture through different lenses of 3D glasses after heating and cooling, which generated permanent coloration of the film.

Finally, students prepare a racemic mixture and compare their observations to glass slides containing (*R*)- and (*S*)-enantiomers, alternating between different lenses of 3D glasses while shearing the coverslip. No color is generated by the racemic mixture. The reflection of visible light is sufficiently sensitive to enantiomeric excess that students should not observe it even if they do not prepare an exact 1:1 racemate; no reflection is observed even for mixtures of 20% ee.

HAZARDS

1-Phenylethylamine is corrosive. The toxicity of the synthesized chiral imine PBPEA is unknown. Imines are often carcinogenic. Biphenyl-4-carboxaldehyde, ethanol, MBBA, and EBBA are irritants to the skin, eyes, and respiratory system. All chemicals in the experiment should be handled with goggles and protective gloves. The synthesis should be conducted in a fume hood.

RESULTS AND DISCUSSION

The experiment was performed in spring, 2015, by 84 chemistry and biochemistry majors enrolled in an introductory organic chemistry laboratory II course. Typical student yields of PBPEA are 50−70%; however, care must be taken to fully dry the material as about 15% of the students reported yields in excess of 100%. In general, this error does not affect the later results on the liquid crystal mixtures. The values for the melting ranges of PBPEA obtained by the students vary from 64 to 90 °C. More than 90% of students were able to identify the configuration of the assigned (unknown) reactant used for dopant synthesis correctly.

Student Learning Outcomes

Analysis of students' responses to 11 post-lab questions (see Supporting Information) indicated comprehension of most of the ideas introduced in the experiment. Students were able to identify and reasonably explain the color present in their product mixtures versus the absence of color in prepared racemic mixtures. This experiment also introduced them to the liquid crystalline state of matter. After measuring EBBA's melting and clearing temperatures, students understood that liquid crystals are states of matter between crystalline solids and isotropic liquids.

Some challenges faced by the students included offering an explanation for the color formation effect. Most students confused the concept of selective reflection of circularly polarized light with the more familiar optical rotation of linearly polarized light taught in lecture. For example, one student responded:

> *...a chiral compound has a specific rotation that is equal in magnitude but opposite in direction from its enantiomer, so this is what explains why my chiral dopant showed color under the right 3D lens, and my partners' under the left—my partners had the same enantiomer, and I had the other enantiomer.*

Care must, therefore, be taken in pre-laboratory remarks and during the laboratory experiment itself to ensure that these two concepts are not conflated; the student guide provides information about cholesteric liquid crystals' selective reflection of light (Supporting Information). Another incorrect idea found in some students' responses was the idea that the color disappeared when the glass slide was heated because a racemic mixture was produced. These students did not understand that the color disappeared because a phase transition occurred from liquid crystal to an isotropic liquid, and as a result, the bulk structure was no longer helical and did not selectively reflect light. While racemization at elevated temperature is arguably not unreasonable, it is inconsistent with the reappearance of chiral phenomena once the film cooled back into the liquid crystal phase.

SUMMARY

A guided-inquiry experiment to distinguish enantiomers and identify their absolute stereochemistry using liquid crystals was designed and successfully implemented in an undergraduate organic chemistry course. Students were able to construct content knowledge about chirality and observe the macroscopic manifestation of chirality with the naked eye. With the use of circular polarizers in 3D glasses, more than 90% of students correctly determined the absolute stereochemistry of the assigned (unknown) reactant used for chiral dopant synthesis. The students were also introduced to liquid crystals and examined their phase behavior.

ASSOCIATED CONTENT

Supporting Information

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Student laboratory guide, a facilitation guide for the instructor, report grading rubric, CAS registry numbers of chemicals, NMR and IR spectra collected by the author (PDF, DOCX)

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Notes

The authors declare no competing financial interest.

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