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A Guided Inquiry Liquid/Liquid Extractions Laboratory for Introductory Organic Chemistry

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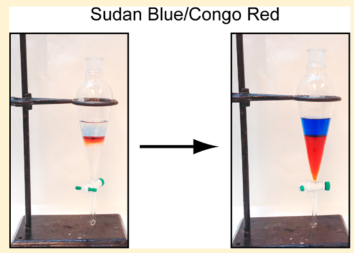
Supporting Information

ABSTRACT: A guided inquiry laboratory experiment for teaching liquid/liquid extractions to first semester undergraduate organic chemistry students is described. This laboratory is particularly useful for introductory students as the analytes that are separated are highly colored dye molecules. This allows students to track into which phase each analyte partitions and allows them to determine if they have successfully separated a mixture of two dyes. During the first part of this experiment, students determine how the partitioning of the various analytes changes as a function of the pH of the aqueous layer. They use these data to determine appropriate solvents for separating mixtures of dyes. After students have learned about the theory and practice of liquid/liquid extractions using dyes, they then separate and identify an unknown simulated cutting agent from a simulated drug. This experiment provides students with a better understanding of the theory and practice of liquid/liquid extractions, and introduces them to a real-world application of this technique.



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One of the primary skills that is taught in an introductory undergraduate organic chemistry laboratory course is the ability to purify single components from complex mixtures using liquid/liquid extraction. In addition to being a key skill in organic chemistry, this technique is also an excellent opportunity for students to apply their knowledge of a range of topics, including molecular polarity, intermolecular forces, and acid/base reactions. Although there are several existing laboratories that teach this technique,[1−8] students often fail to make the necessary connections between concepts and practice because many of them have difficulty analyzing their results and determining which compounds have partitioned into a given layer. Herein, a new, guided inquiry laboratory is presented that teaches students about the principles involved in liquid/liquid extraction using colored dyes for quick and vivid analysis, and provides an opportunity for them to apply their new knowledge to develop a liquid/liquid separation method for a "real-world" application.

The use of colored analytes has been a mainstay in teaching chromatographic separations.[9−16] However, there have been very few applications in liquid/liquid extractions.[7,8] The experiment described provides a substantial improvement over these examples in that it uses dyes with pH-sensitive solubilities (Figure 1). This feature not only allows students to track the location of their analytes (aqueous vs organic layer) but also allows students to design solvent combinations that will separate molecules based on their predominant structures at a certain pH. The immediacy of the results and the pH sensitivities of the dye are what make this experiment especially valuable. The goals are (1) to provide experience in predicting the solubility of compounds in various solvents based on the structures of the compounds and (2) to learn how to use liquid/liquid extractions to separate compounds based on differences in their solubilities. Using colored analytes, students can make and test predictions about solubility, allowing them the freedom to explore factors that affect molecular solubility and whether a molecule is more likely to partition into an aqueous vs an organic phase. These predictions are then applied to separating mixtures of dye molecules using liquid/liquid extraction. As these molecules contain a mixture of basic and acidic groups, students must consider the pH of the aqueous layer in devising the separations. Students are able to see instantly if their separation is successful and can quickly determine how to separate mixtures of molecules. Understanding of the principles behind liquid/liquid extraction is ultimately tested as students must apply their knowledge to separate and to identify a simulated cutting agent (an agent used to dilute a pure illicit drug before sale) from a simulated "drug" mixture as an example of a real-world use for this technique.[17,18]

This experiment is a valuable addition to an Organic I laboratory curriculum as it introduces students to many important laboratory skills. By participating in this laboratory, students increase their understanding of the factors that influence solubility and gain experience performing liquid/liquid extractions.

MATERIALS AND METHODS

Before the lab, an instructor makes the dye solutions (2% w/v in ethanol) and 1 M solutions of HCl (aq) and NaOH (aq) for

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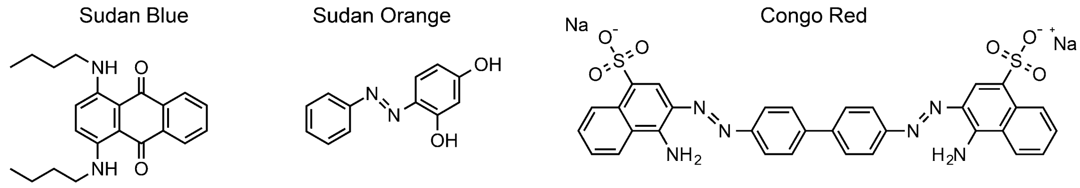

Figure 1. Structures of the dye molecules examined in the first two parts of this experiment.

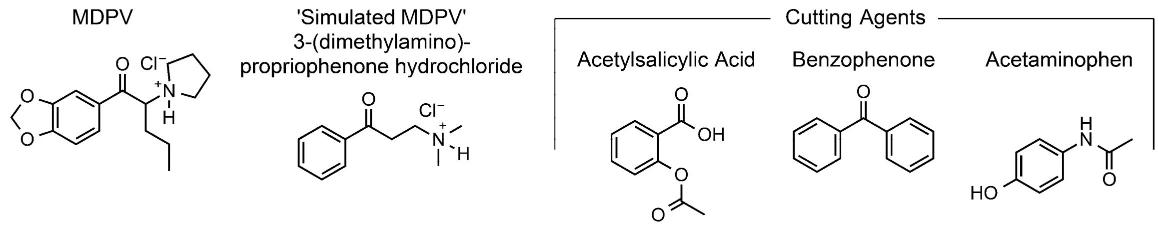

Figure 2. Structures of the compounds used in Part III of this experiment.

use during this lab. Also, vials containing 100 mg of simulated drug samples (10% w/w of a particular cutting agent) are prepared. Cutting agents are chosen such that students should be able to separate them from the simulated "drug" and identify them by their functional groups using IR spectroscopy. Acetylsalicylic acid, benzophenone, and acetaminophen are used as cutting agents in this experiment; however compounds with similar functionalities and physical properties could be used as well. 3-(Dimethylamino)propiophenone hydrochloride is used to simulate methylenedioxypyrovalerone (MDPV) hydrochloride (an active component of "bath salts"), a designer drug that has hallucinogenic effects. This drug is chosen as it reached national attention due to several crimes committed by people under its influence.[19] 3-(Dimethylamino)-propiophenone hydrochloride is used as a substitute because it is a relatively inert molecule that poses few safety risks while having the same functionality and predicted solubilities as MDPV. The hydrochloride salt is used to better mimic the appearance and behavior of MDPV·HCl.

■ EXPERIMENTAL DETAILS

Students work either alone or in groups of two to complete this experiment. The experiment is divided into three parts, and is done in two, 3 h laboratory periods. Parts I and II are done in the first week, and Part III is done in the second week. Students must complete each part and answer a set of associated questions before moving on to the next section.

Part I: Testing Compound Solubility

As part of the prelab for week one, students answer a series of questions about the effects of pH on the structure of the dyes and the effects of formal charge on solubility in aqueous vs organic solvents. Students are assigned this experiment concurrent with their lecture discussion of pK_a values and the Henderson−Hasselbalch equation.

Students start the lab by running small-scale solubility tests to verify the predictions they make in the prelabs. Students determine the relative solubilities of the three dyes in hexanes, and aqueous solutions of pH 2, 7, and 10. Students must reach a hypothesis that explains all of their data from Part I before moving on to Part II.

Part II: Using Liquid/Liquid Extractions To Separate Compounds Based on Solubility

Students are given two solutions, one containing equal parts Sudan Blue and Congo Red, and a second containing equal parts Sudan Blue and Sudan Orange. Based on the results from Part I, students develop and test separation methods using liquid/liquid extractions with hexanes and the appropriate aqueous solution in a separatory funnel. Because the dyes are highly colored, students can readily determine if their separations are successful. Students document and rationalize their results, making changes to their hypotheses about the factors that govern relative solubility as needed.

Part III: Simulated Analysis of Illicit Drug Samples

Students are given a vial that contains simulated MDPV spiked with one of the unknown cutting agents (Figure 2). Students then consider a scenario in which they work for the Drug Enforcement Agency (DEA) and, by identifying the cutting agent used, they will help to determine who is making and distributing the drug. This application helps draw student interest and allows them to see the relevance of this technique.

Students devise a method for separating the "MDPV" and the cutting agent. Students are provided a list of potential cutting agents that includes the three agents used, as well as several distractor chemicals included to make the experiment more challenging. Students take a crude IR spectrum or run a TLC plate to determine the likely identity of their cutting agent.[20] Students are not given TLC conditions but must determine them on their own. They compare the functionalities present in the cutting agent and the "MDPV" to develop a method to separate the two compounds. After the separation, students use IR spectroscopy and TLC to identify and to show the purity of the cutting agent.

■ HAZARDS

HCl and NaOH are both hazardous to the skin and eyes. They should be handled with caution. Congo Red may cause cancer and is a severe eye irritant, as is Sudan Orange. Hexanes are highly flammable and volatile and may be harmful if inhaled; *n*-hexane is a neurotoxin. Ethyl acetate is highly flammable, causes serious eye irritation, and may cause dizziness or drowsiness. Acetylsalicylic acid and acetaminophen are both harmful if swallowed, cause skin irritation, and cause severe eye irritation. Acetaminophen is toxic to aquatic life. Benzophenone may be harmful in contact with skin, is suspected of causing cancer, and is very toxic to aquatic life. Students are required to wear safety goggles and gloves and to work in fume hoods at all times during this experiment.

■ DISCUSSION

Prior to performing this experiment, students had a difficult time grasping the effect that changing the pH of a solution could have on the structure and properties of a molecule in that solution. Indeed, many students struggled with their prelab questions, despite having recently learned about pH effects in the lecture portion of the course. By completing this experiment, most students increased their understanding of pH-dependent solubility. After completing parts I and II of the experiment, students had a good grasp of the principles behind liquid/liquid extractions, and were able to draw generalizable conclusions about how molecular structure could influence compound solubility. By the end of the first, 3 h lab period, all of the students had successfully separated both the mixture of Sudan Blue and Congo Red and the mixture of Sudan Orange and Sudan Blue.

Students were able to draw on these conclusions to determine an effective strategy to purify the cutting agent away from the "MDPV" during the second week of the experiment. By the end of the second, 3 h lab period, all students were able to separate and identify their cutting agent. By comparing student responses to the pre- and postlab questions, it was evident that most students had increased their understanding of the factors that influence solubility and what was needed to carry out a successful liquid/liquid extraction (see Supporting Information for questions).

■ CONCLUSIONS

This experiment has been run as a part of an Organic Chemistry I laboratory course for two years (110 total students completed this experiment). This experiment was a valuable addition to the curriculum as it was an effective means to introduce liquid/liquid extractions, and to give students practice determining how pH can affect solubility. To assess student learning, scores on the week one prelab assignment were compared to those on the postlab assignment (see Supporting Information for assignments). The average student score on the prelab was 64% compared with an average postlab score of 84%. This indicated that students increased their understanding of liquid/liquid extractions, and how solubility changes as a function of pH.

This laboratory had many benefits from a student perspective. First, by learning this technique using dye molecules, students immediately and easily determined into which layer their molecule partitioned (aqueous or organic). They also quickly determined how this partitioning changed as a function of the pH of the aqueous layer. Additionally, they were able to determine if they had separated a mixture of two dyes, or if further extraction was required to separate their compounds. This instantaneous readout allowed students to make and test hypotheses regarding solubility and pH.

Finally, students were given the opportunity to apply their knowledge by using a liquid/liquid extraction to separate a simulated drug and cutting agent. Students used the conclusions they drew regarding dye solubility in a new context, thus demonstrating how liquid/liquid extractions could be applied to a variety of circumstances. By framing the final part of this experiment in the context of a narcotics investigation, student interest was heightened and it was demonstrated to students how the techniques that they learned in organic chemistry lab could help them in their future careers.

■ ASSOCIATED CONTENT

Supporting Information

A list of chemicals and hazards, a copy of the student handout and instructor notes for the lab, solubility data for the three dyes, solvent systems for separating the dye mixtures and for separating "MDPV" from each of the cutting agents, and notes about troubleshooting the lab. 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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(20) Depending on where in the laboratory sequence this experiment falls, students may not have learned about TLC or IR spectroscopy. See the Supporting Information for suggestions for alternate scenarios that do not require this knowledge.