MULTI-OUTCOME EXPERIMENT DEVELOPMENT FOR UNDERGRADUATE ORGANIC CHEMISTRY INSTRUCTIONAL LABORATORIES

by

KASEY LEIGH YEARTY

(Under the Direction of Richard Morrison)

ABSTRACT

Undergraduate organic chemistry laboratory courses across the United States complete similar experiments at various institutions. These experiments follow "cookbook"-style procedures and use known starting materials to synthesize known products. Students completing these experiments have little to no variation in their observations, results, data analysis, or reports, limiting opportunities for critical thinking. The use of multi-outcome experiments (MOEs) in organic chemistry requires critical thinking from students to identify the starting material and/or product for an experiment using spectroscopic analyses. The number of options for unknown starting materials generates student results that differ from student to student, providing more unique learning experiences and individualized lab reports. Herein are described a variety of MOEs for the undergraduate organic chemistry laboratory: a modified separation of a three-component mixture via acid-base extraction, an oxidation of secondary alcohols, a Williamson ether synthesis, a Fischer esterification, and a synthesis of azo dyes. MOEs such as these steer undergraduate organic chemistry laboratory courses away from "cookbook" reactions and more strongly reinforce lecture-learned concepts such as spectroscopic analyses.

INDEX WORDS: Second-Year Undergraduate, Laboratory Instruction, Organic Chemistry**,** Inquiry-Based / Discovery Learning, NMR Spectroscopy

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DEDICATION

To my husband Cam and our four-legged son BoBo. Mama and Daddy, I made it!

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LIST OF ABBREVIATIONS

DCM	dichloromethane
FTIR	Fourier-transform infrared
g	gram
H_2SO_4	sulfuric acid
HCl	hydrochloric acid
L	liter
mg	milligram
mL	milliliter
MOE	multi-outcome experiment
MP	melting point
NaCl	sodium chloride
NaOCl	sodium hypochlorite
NaOH	sodium hydroxide
NMR	nuclear magnetic resonance
POGIL	process oriented guided inquiry learning
PBL	problem-based learning
SOE	single-outcome experiment
TA	teaching assistant
TBAB	tetrabutylammonium bromide
TMS	tetramethylsilane
TLC	thin layer chromatography

CHAPTER 1

INTRODUCTION AND LITERATURE REVIEW

Kasey L. Yearty, Caroline E. Glessner, and Richard W. Morrison. Submitted to the *Journal of Chemical Education*, March 11, 2019.

ABSTRACT

Undergraduate organic chemistry laboratory courses at US universities and colleges commonly require students to perform laboratory experiments that are selected from a limited set of similar experiments. These experiments have traditionally followed cookbook-style procedures that use known starting materials to synthesize known products. An alternative is the multi-outcome experiment (MOE). MOEs provide opportunities to reinforce lecture-learned concepts, increase the individualization of the student laboratory experience, and facilitate active student engagement with modern analytical techniques. The use of MOEs in organic chemistry promotes critical thinking by requiring students to identify the experiment's starting material and/or product using spectroscopic analyses. This chapter outlines the structure and development of MOE procedures, providing the framework for the experiments outlined in this manuscript-style dissertation.

EXPERIMENT DESIGN IN THE UNDERGRADUATE LABORATORY

There is a wide range of current experiment designs in science education. Dr. Molly Wilker from Luther College recently described experiment design methods in higher education, stating "A broad range of approaches to upper-level, undergraduate laboratory instruction exist including expository, inquiry, discovery, problem-based, and authentic research activities."[1] Instructors can evaluate the merits of each type of design, considering strengths and weaknesses based upon the student population in which the methods will implemented. To understand and design curricula that meet the needs of the students, one must first understand the benefits and shortcomings of each design.

Expository instruction includes the traditional single-outcome ("cookbook-style") experiment, where students reinforce topics by completing procedures that have known outcomes.[2-3] These experiments reliably produce the same results and are commonly found in the undergraduate laboratory curriculum. Dr. Wilker further noted that "with these traditional methods, the typical undergraduate student is focused on collecting the required data, but demonstrates little ownership of the work and a lack of interest in deeper understanding."

The incorporation of inquiry-based instruction has also been well documented in the literature.[4-18] It is generally categorized as structured, open and guided. Dr. Suzanne Perin succinctly described the divisions as follows:

> "In structured inquiry, students investigate a teacher-presented question through a prescribed procedure leading to a predetermined discovery. Guided inquiry involves teachers providing the questions but students investigating and coming to their own conclusions about the questions. The most complex and autonomous level is the open inquiry, where the teacher defines a framework and assists students in making choices throughout, but students not only formulate their own questions but also the means to answering them."[19]

One popular example of the integration of guided inquiry learning into the undergraduate laboratory curriculum is through process oriented guided inquiry learning (POGIL). POGIL is another pedagogy used to create "inquiry-driven rather than verification based" experiments for the undergraduate laboratory.[20] Dr. Sally Hunnicutt and coworkers described the POGIL model for physical chemistry laboratories as centering on "'data-think cycles' in which students answer preparatory questions, make a prediction, follow a standard protocol (procedure) to test the prediction, and then analyze the data". As students work through each cycle, they probe concepts more deeply.[20] Dr. Laura Bruck and Dr. Marcy Towns have also provided guidelines and suggestions for preparing students to benefit from inquiry-based activities.[21] These authors suggested that foundational knowledge, appropriate laboratory skills, and student independence are key areas to develop prior to implementing new activities. They suggested that sharing clear expectations and guiding students through a facilitative approach are the most beneficial methods for faculty preparation.[21] Dr. Towns has also worked with other colleagues to develop rubrics for assessing the level of inquiry included in the undergraduate laboratory.[22]

A third method of instruction in the physical and life science laboratories includes discovery-based learning.[23-28] First introduced in 1961 by Jerome Bruner, an American psychologist, discovery-based learning gives students hands-on experience through interactions with objects or exploring environments. These interactions provide students with the ability to determine what information is necessary to solve a problem, rather than being provided the information by an instructor. Discovery-based learning is an active learning strategy, where learners participate in self-guided exploration. By determining what factors are relevant and proposing solutions to problems on their own, students can hone their skills of proposing innovative solutions to problems.[29]

Problem-based learning (PBL) has also played an important role in undergraduate laboratory instruction.[30-31] This method has been succinctly summarized by Dr. Preetha Ram from

Emory University by stating “a PBL classroom is organized around collaborative problem-solving activities that provide a context for learning and discovery”.[32] While many of the aforementioned methods of instruction can incorporate active-learning strategies, an example of how active learning can be intertwined with PBL was recently described by Dr. Anna Cavinato from Eastern Oregon University. Dr. Cavinato illustrated the challenges and successes for implementing problem-based active learning experiments in analytical coursework for undergraduates.[33] In these active learning activities, students began with a problem and used the literature as support to develop hypotheses. Students then designed and executed their experiments, determining what measurements to take along the way. The information collected was then processed by students to inform their hypotheses and to draw conclusions.[34]

Finally, authentic research activities or research-based coursework rounds out the review of major experiment typologies in undergraduate laboratory instruction.[4, 35-48] Through this instruction method, students engage in carefully studying original sources of information in the literature, use evidence to design experiments, and practice communicating science to members of professional communities. Authentic research activities may be incorporated into the classroom for shorter-term assignments or when semester-long activities may not be desired. Undergraduate students can also participate in semester-long research-based coursework, where they are provided with some parameters for a problem and engage in investigating the problem for several months. By providing opportunities for semester-long projects, students can dedicate more of their own individuality and creativity to the project and get experience with research-based career pathways.

ORGANIC CHEMISTRY AND MULTI-OUTCOME EXPERIMENTS

While there are a variety of instructional methods incorporated in the undergraduate laboratory experience, this dissertation focuses on meeting the needs of organic chemistry students. Organic chemistry is a course traditionally taken during the sophomore year at undergraduate institutions. The curriculum covered includes topics such as “synthesis, characterization, physical

properties of small organic molecules and macromolecules, and the mechanisms of common organic reactions."[49] Organic chemistry students are commonly enrolled in a co-requisite undergraduate organic chemistry instructional laboratory. The American Chemical Society's supplement for organic chemistry instructional laboratories lists practical topics for the laboratory curriculum. Such topics include the "spectroscopic analysis of starting materials and products; deducing structures by interpretation of modern spectroscopic and computational data, and its use to answer the formulated hypothesis".[50-51] The supplement also states that "[s]ince this may be the only course in organic chemistry a student may see, the lecture and laboratory must reinforce each other. It is appropriate for the primary treatment of spectroscopy, including NMR and IR spectroscopy, to be done in the laboratory setting."[50] Organic chemistry ultimately provides students with the building blocks for upper level coursework in their fields of study. A survey of practices, procedures, and techniques that the associated laboratory course encompasses across the nation was first reported by researchers at Lamar University in 2011.[52]

Although problem-based or process-oriented guided-inquiry methodologies appear in upper level chemistry (physical, analytical, etc.) laboratory coursework, the organic chemistry laboratory curriculum commonly includes cookbook-style verification experiments, which are noted herein as single-outcome experiments (SOEs). In the expository SOE model, students begin an experiment with known reagents and complete the same procedure as their peers. The students experience little to no variation from their peers in their observations, their data analyses, and their reports. Although students may successfully complete the experiment, a limitation of SOEs is the minimal application of student critical thinking skills.[1] Because the experiment model does not provide inquiry-driven opportunities and the outcomes are consistently uniform with their classmates, students can go through the motions of the experiment without critically engaging in the material. This unintended student complacency then limits the opportunities for instructors to reinforce important fundamentals of organic concepts, such as the characterization of small organic

compounds. However, the SOE provides a consistent process for students to learn and become proficient in standard laboratory techniques, as indicated by its traditional inclusion in the undergraduate teaching laboratory.

One alternative to SOEs is the multi-outcome experiment (MOE). The multi-outcome experiment, which is described herein, can best be described as using expository instruction as its foundation; therefore, it is necessarily built upon the same outcomes of reinforcing foundational topics and increasing student "ownership" of their laboratory experience. MOEs are hands-on learning activities involving modern analytical techniques. In an MOE, students begin the experiment with one unknown reagent. A typical MOE is designed to allow for at least three possible identities for the unknown reagents. The inclusion of an unknown component also allows for active student participation in the laboratory experience by carefully noting how their observations vary from their classmates. While the students still complete a similar procedure as their classmates, the students will experience variations in their observations, their data analyses, and their reports. By characterizing the product of the transformation using analytical techniques specified in the MOE procedures, students must recall what information each analytical technique provides to them. Once the students have elucidated the structure of the product, students then retroactively determine the identity of their unknown. Students gain hands-on experience with the synthetic transformation and analytical tools, recognize the applicability of the analytical tools, and recall information learned in the associated lecture course to solve the problem of their mystery reagent. The outcomes of a well-designed MOE are as follows:

- To reinforce lecture-learned concepts
- To increase individualization of the laboratory experience
- To facilitate active engagement with modern analytical techniques

Organic chemistry laboratory experiments are intended to be synchronized with the associated lecture course. Because of this synchronization, the laboratory is the ideal place to

reinforce the concepts learned in the lecture through hands-on learning experiences. MOEs are useful to showcase synthetic transformations and/or highlight the utility of modern analytical techniques. In a typical MOE, students perform reactions that they have just learned in their associated lecture course.

Completion of MOEs leads to increased individualization of the laboratory experience. Typically, in cookbook-style experiments, all of the students receive a uniform sample set of computer-generated spectra; in MOEs described in this dissertation, however, students collect or receive raw data from their own products. By generating the data from their own products, students have a final lab report and an overall laboratory experience that is unique from that of their peers, even those within the same class and laboratory section.

MOEs allow students to actively engage with modern analytical techniques. In MOEs described herein, students in sophomore organic chemistry courses utilize NMR technology to analyze the products that they have produced in the classroom. Commonly, access to NMR spectrometers is reserved for upper level or advanced courses due to the cost of maintenance, expensive deuterated solvents, and limited free instrument time. This limited access is one key reason why instructors often opt to provide idealized or computer-generated spectra to sophomore organic chemistry students to gain experience interpreting spectra. However, the advent of benchtop NMR technology has made this analytical technique available to more students, even the typically high-enrollment sophomore organic chemistry courses. With supervision from their teaching assistant (TA), students collect spectra of the products that they have produced before they leave the classroom each day. This hands-on student engagement with NMR spectroscopy, and, potentially, additional modern analytical techniques, is invaluable to undergraduate students.

THE STRUCTURE OF AN MOE

An MOE has several key components: an unknown starting material, a common synthetic transformation and/or laboratory technique, and an appropriate analytical technique for product

elucidation. The data collected from the analytical technique informs the students about the identity of the product. From this, students can apply lecture-learned concepts to determine the identity of their unknown starting material.

During the experiment, students work in pairs. The students select one of the possibilities for the unknown starting material and record the code associated with that unknown option in their laboratory notebook. The students then complete the experiment by following the provided procedures. Once the product has been obtained, standard information, such as the mass, color, and any other potentially relevant observations, are recorded. The students then characterize the product using the analytical techniques specified in the procedures. Students are given one week to interpret their data and write individual post-lab reports culminating in the identification of their unknown starting material.

THE DEVELOPMENT OF AN MOE

There are several considerations associated with the development of MOEs. When considering the overall structure of the experiment, at least one component must be able to be modified with interchangeable options. The reagents, both known and unknown, used in the experiment must be appropriate for undergraduate use. Proper personal protective equipment must be worn by all individuals in the laboratory and work must be done in a fume hood or under local ventilation systems, such as a snorkel.

Once an experiment has met the above criteria, the instructor must determine which analytical techniques is most appropriate for identifying the product produced, thereby enabling the students to determine the identity of the unknown component used in the experiment. While the verification or determination of physical properties (boiling point or melting point) is used in research settings, MOEs take advantage of student engagement with analytical instrumentation. The instrumentation incorporated must correspond to the unambiguous identification of one of the possible products produced in the MOE.

Finally, each of the potential known and unknown reagent combinations must produce similar products within a standard lab period, typically three-hours. The researcher has found this particular challenge to be the most difficult to overcome because the developer must consider the varying stoichiometric ratios of the known versus unknown reagent combinations. One way to overcome this challenge is to include unknown possibilities that are constitutional isomers. Another method is to utilize purification techniques, such as an extraction or column chromatography, to remove any excess of other reagents used during the experiments. Once this step has been completed, the MOE is ready for implementation.

Outside of the challenges associated with developing the experimental procedures, there are also challenges associated with the implementation of novel experiments with graduate-level TAs in large-enrollment courses. While this is not a universal challenge, as instructors at smaller colleges may prepare for implementation themselves or work one-on-one with the TA for the course, it is still a challenge that must be addressed. At the University of Georgia, the TAs may be from a wide variety of backgrounds, including being from departments other than Chemistry. Moreover, some TAs may have matriculated into graduate school directly following their undergraduate work, while others may have returned to graduate work after spending several years working. With these variances in mind, the researcher works with each TA to prepare them for MOE implementation. In the week prior to implementation, TAs are provided with the procedure and a general overview of the experiment. The TAs are instructed to refrain from describing the information gleaned from either of the spectroscopic techniques to the students over the course of the lab period, instead directing the students to further investigate these questions for themselves. The TAs also review the benchtop ^{1}H NMR spectra of the anticipated products. Students are provided with the procedure via a course management website. Immediately before performing the experiment, students attend a pre-laboratory lecture delivered by their TA. This lecture highlights

the purpose of the experiment, pertinent safety information, the reaction mechanism, and an overview of the procedure.

During this lecture, TAs also inform students of an extra credit opportunity associated with the experiment: a postlab survey. This survey is administered via Google Forms and provides the students with an outlet to electronically document their results. By completing the survey, which is to be completed in addition to the standard postlab report, students receive five bonus points. In the survey, students are asked to identify their unknown component, to report the mass of their product, and to rank the identification tools available to them in decreasing order of their usefulness in identifying the unknown component. Students are also asked to indicate their confidence levels for identifying their unknown component *without* the benchtop NMR spectra and *with only* the benchtop NMR spectra. Finally, students are provided opportunities to elaborate on their responses and leave additional feedback about their experience. The example MOEs included in Chapters 2-6 of this manuscript-style dissertation provide a framework for the development of future MOEs and support for their incorporation into the undergraduate instructional laboratory curriculum. In the culminating chapter (Chapter 7), the researcher ties together the major results by offering perspectives on MOEs and future directions of exploration.

CHAPTER 2

THE INCLUSION OF BENCHTOP NMR TECHNOLOGY IN THE ANALYSIS OF PRODUCTS FROM THE SEPARATION OF A THREE-COMPONENT MIXTURE VIA ACID-BASE EXTRACTION

Kasey L. Yearty, Caroline E. Glessner, Christina N. Cortes, Shaen M. Deimling, and Richard W. Morrison. To be submitted to the *Journal of Chemical Education*.

ABSTRACT

Until recently, liquid-liquid extraction was introduced in the organic chemistry instructional laboratory by separation of a three-component mixture via acid-base extraction. The experiment included the separation of known acidic, basic, and neutral components: benzoic acid, benzocaine, and 9-fluorenone, respectively. Following separation of the components, melting points were determined to confirm their identities. One limitation of this experiment design included students' general association of the yellow color of 9-fluorenone with the organic layer, a generalization that persisted throughout the semester. The liquid-liquid extraction experiment was redesigned to incorporate an unknown component and the inclusion of FTIR and ^{1}H NMR spectral analyses of experimental results. The modified experimental protocol provided students with the identities of two components, the neutral component (diphenylmethanol) and the basic component (benzocaine), for example. Following extraction and crystallization of each, the identities and functionalities of the two known components were confirmed using melting point data and instructor-provided spectra. Students determined the melting point and acquired spectral analyses to identify their unknown acidic component, either o-toluic acid, benzoic acid, or 2-methoxybenzoic acid. The modified procedure was uniquely designed to allow the instructor to select as the experimental unknown either the acidic, basic, or neutral component of the three-component mixture.

BACKGROUND

The separation of a mixture of components is a common experiment performed in introductory organic chemistry laboratories. The single-outcome version of this experiment includes the separation of known acidic, basic, and neutral components such as benzoic acid, benzocaine, and 9-fluorenone, respectively. Students complete this separation through the liquid-liquid extraction technique, specifically through an acid-base extraction. Following separation of the components by single proton transfers, melting points are determined to confirm their identities. An unfortunate consequence of the experimental design is the misperception by students that the yellow color of 9-fluorenone is common to all organic layers. Therefore, the experiment was redesigned to incorporate an unknown component and the inclusion of FTIR and ^{1}H NMR spectral analyses of experimental results to include applications of these analytical techniques. The modified experimental protocol provides students with the identities of two components, the neutral component (diphenylmethanol) and the basic component (benzocaine). Following extraction, crystallization, and characterization of each component, the identities of the two known components are confirmed. Students determine the melting point and perform spectral analyses to identify their unknown acidic component, either benzoic acid, 2-methoxybenzoic acid, or *o*-toluic acid (see Figure 2.1). Because the components are all white powders, this also addresses the issue of color conflation. This procedure is unique because it allows for potential manipulation of the basic neutral component of the mixture to increase the number of outcomes and hands-on experience in ^{1}H NMR spectroscopy.

This experiment is one of a series of MOEs developed and implemented in the undergraduate organic chemistry teaching laboratories at the University of Georgia. Of all MOEs in the series, the separation of a three-component mixture experiment is the first to which students are exposed in the curriculum. This experiment also represents the first practical experience that students have with both FTIR and NMR instruments.

METHODS

In total, 1,462 students were evaluated across four semesters: 370 students in Fall 2017, 367 students in Spring 2018, 166 students in Summer 2018, and 559 students in Fall 2018. Early iterations of the protocol included 100 milligrams (mg) of each of the components. This amount was scaled up to 500 mg of each component to ensure an adequate quantity of product for student characterization. During the iterations including the melting point, the researcher posed that students were heavily reliant on the melting point for the identification of the unknown component. This hypothesis stemmed from verbal cues provided by students during implementation and by students' previous experience with melting point. Therefore, the melting point determination was included during the Fall 2017 and Spring 2018 semesters, but it was removed from the Summer 2018 and Fall 2018 semesters. TAs monitored the sample injection process by students and assisted with the processing of the resulting spectra in MestreNova. All spectra collected in the section were sent to students for comparison purposes during analyses. Students also completed a post-lab survey to electronically document their results.

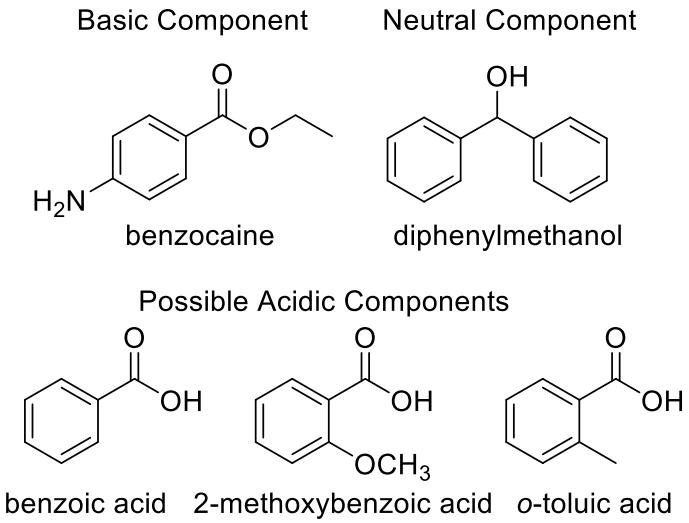


Figure 2.1. Component Key Provided to Students

HAZARDS

Safety glasses, lab coats, and lab gloves must always be worn. Please review online SDS sheets of all chemicals including products. Sodium hydroxide is a strong base and hydrochloric acid is a strong acid. Both chemicals are caustic and will cause severe burns if they come in contact with your eyes or skin. In addition, hydrochloric acid solutions can evolve harmful vapors depending on their concentration. Make sure that your localized ventilation system (snorkel) is properly positioned to avoid inhaling any hazardous fumes. Make sure that your snorkels are turned on and functioning properly before dispensing any liquids. Methylene chloride is volatile. Chronic exposure is possibly carcinogenic, and care must be taken to avoid breathing any fumes or allowing any liquid to contact your skin. Any vapor or liquid exposure should be reported to your TA immediately. Dispose of all liquid waste in the appropriately labeled bottle in the lab hood.

RESULTS

In total, 1,026 out of 1,462 students (70.18%) correctly identified the unknown acidic component across the between the Fall 2017 – Fall 2018 semesters. A full table of student responses is included (see Table 2.1) along with a breakdown of responses for each acidic component (see Table 2.2).

Table 2.1. Student Identifications of Unknown Acidic Components

Unknown Acidic Components	*# Correct*	*# Students*	*Percent*
Benzoic Acid			
Fall 2017	112	127	88.19%
Spring 2018	130	137	94.89%
Summer 2018	38	64	59.38%
Fall 2018	117	176	66.48%
Total	397	504	78.77%
2-Methoxybenzoic Acid			
Fall 2017	83	116	71.55%
Spring 2018	77	111	69.37%
Summer 2018	36	50	72.00%
Fall 2018	146	191	76.44%
Total	342	468	73.08%
o-Toluic Acid			
Fall 2017	94	127	74.02%
Spring 2018	94	119	78.99%
Summer 2018	25	52	48.08%
Fall 2018	74	192	38.54%
Total	287	490	58.57%
Combined Totals for all Acidic Components			
Fall 2017	289	370	78.12%
Spring 2018	301	367	82.02%
Total with Melting Point	590	737	80.05%
Summer 2018	99	166	59.64%
Fall 2018	337	559	60.29%
Total without Melting Point	436	725	60.14%
Overall	1026	1462	70.18%

Table 2.2. Complete Listing of Student Identifications of Unknown Acidic Components

Unknown Acidic Component	*Benzoic Acid*	*2-Methoxybenzoic Acid*	*o-Toluic Acid*
Benzoic Acid			
Fall 2017 (n = 127)	112 (88.19%)	11 (8.66%)	4 (3.15%)
Spring 2018 (n = 137)	130 (94.89%)	5 (3.65%)	2 (1.46%)
Summer 2018 (n = 64)	38 (59.38%)	19 (29.69%)	7 (10.94%)
Fall 2018 (n = 176)	117 (66.48%)	33 (18.75%)	26 (14.77%)
2-Methoxybenzoic Acid			
Fall 2017 (n = 116)	13 (11.21%)	83 (71.55%)	20 (17.24%)
Spring 2018 (n = 111)	5 (4.50%)	77 (69.37%)	29 (26.13%)
Summer 2018 (n = 50)	9 (18.00%)	36 (72.00%)	5 (10.00%)
Fall 2018 (n = 191)	25 (13.09%)	146 (76.44%)	20 (10.47%)
o-Toluic Acid			
Fall 2017 (n = 127)	8 (6.30%)	25 (19.69%)	94 (74.02%)
Spring 2018 (n = 119)	2 (1.68%)	23 (19.33%)	94 (78.99%)
Summer 2018 (n = 52)	15 (28.85%)	12 (23.08%)	25 (48.08%)
Fall 2018 (n = 192)	45 (23.44%)	73 (38.02%)	74 (38.54%)

The ^{1}H NMR spectra collected by students of their acidic components are shown in Figures 2.2-2.4. When examining the ^{1}H NMR spectrum from Figure 2.2, students, may begin by assessing the number of aromatic protons present, which is 5H. Students then notice that there are no additional signals present, effectively eliminating o-toluic acid and 2-methoxybenzoic acid as options for this spectrum. As students move on to Figures 2.3 and 2.4, they notice that while the aromatic proton signals differ slightly, they still add up to 4H. This leaves the 3H singlet farther upfield as an identifier of the spectrum's respective acidic component. In Figure 2.3, this singlet is at ~2.5 ppm, whereas in Figure 2.4, the singlet is farther downfield at ~4.0 ppm. The difference in the chemical shifts of these two protons provide clues about the proximity of the protons to electronegative elements such as any halogens, oxygen, and nitrogen. The students then note that difference between the structures of o-toluic acid and the 2-methoxybenzoic acid is that one has an ether substituent and one has an alkyl substituent; therefore, the spectrum that has the 3H singlet at

~2.5 ppm (Figure 2.3) must be the spectrum of o-toluic acid and the remaining spectrum with the 3H singlet at ~4.0 ppm (Figure 2.4) must be the spectrum of 2-methoxybenzoic acid.

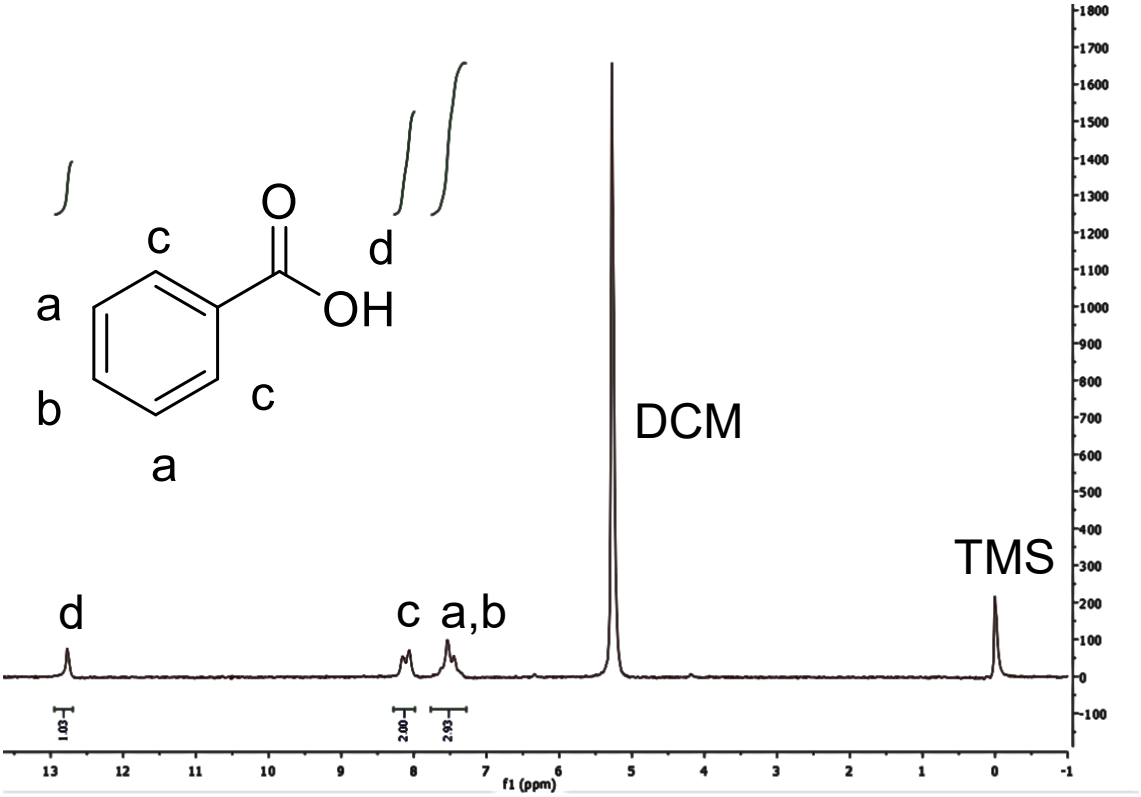


Figure 2.2. Student ^{1}H NMR spectrum of benzoic acid from the 82 MHz picoSpin benchtop ^{1}H NMR. The structure and assignments are provided for clarity. Two drops of tetramethylsilane (TMS) were included to mark 0 ppm. The presence of dichloromethane (DCM) indicates the solvent for the sample.

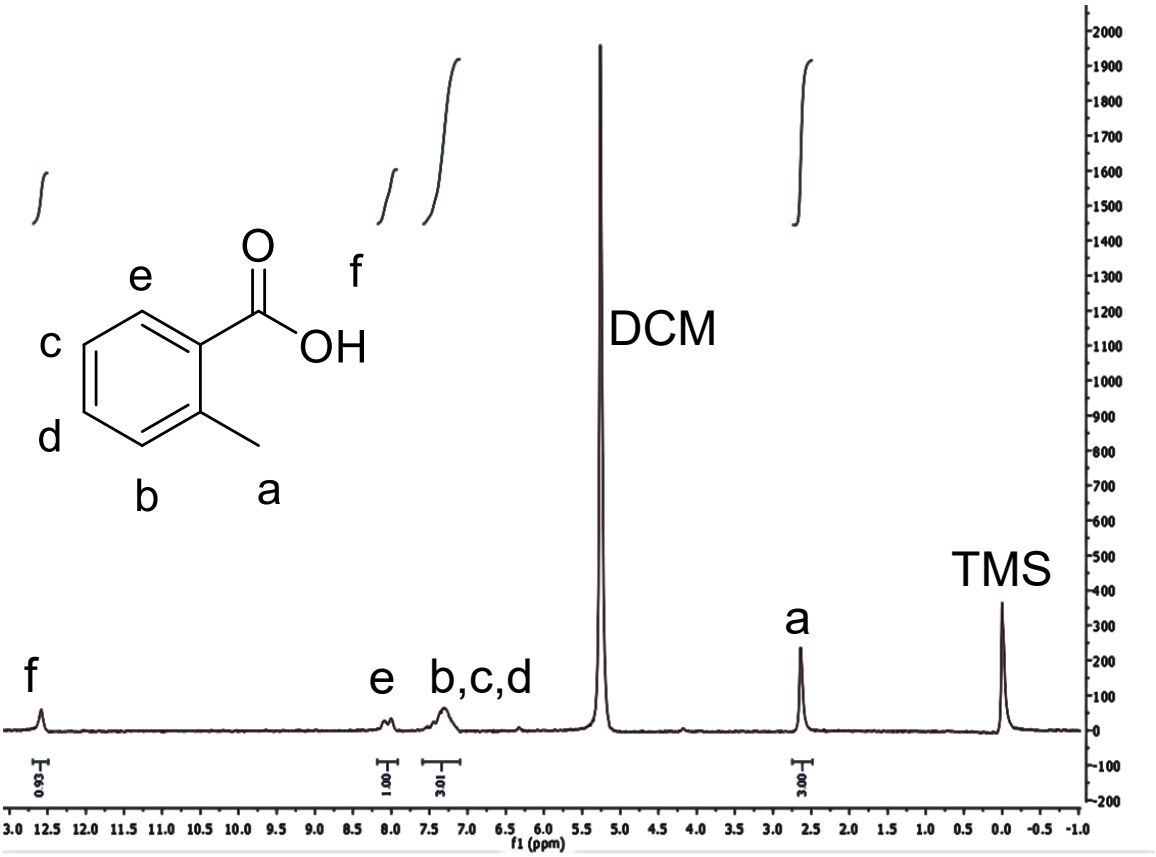


Figure 2.3. Student ^{1}H NMR spectrum of *o*-toluic acid from the 82 MHz picoSpin benchtop ^{1}H NMR. The structure and assignments are provided for clarity. Two drops of tetramethylsilane (TMS) were included to mark 0 ppm. The presence of dichloromethane (DCM) indicates the solvent for the sample.

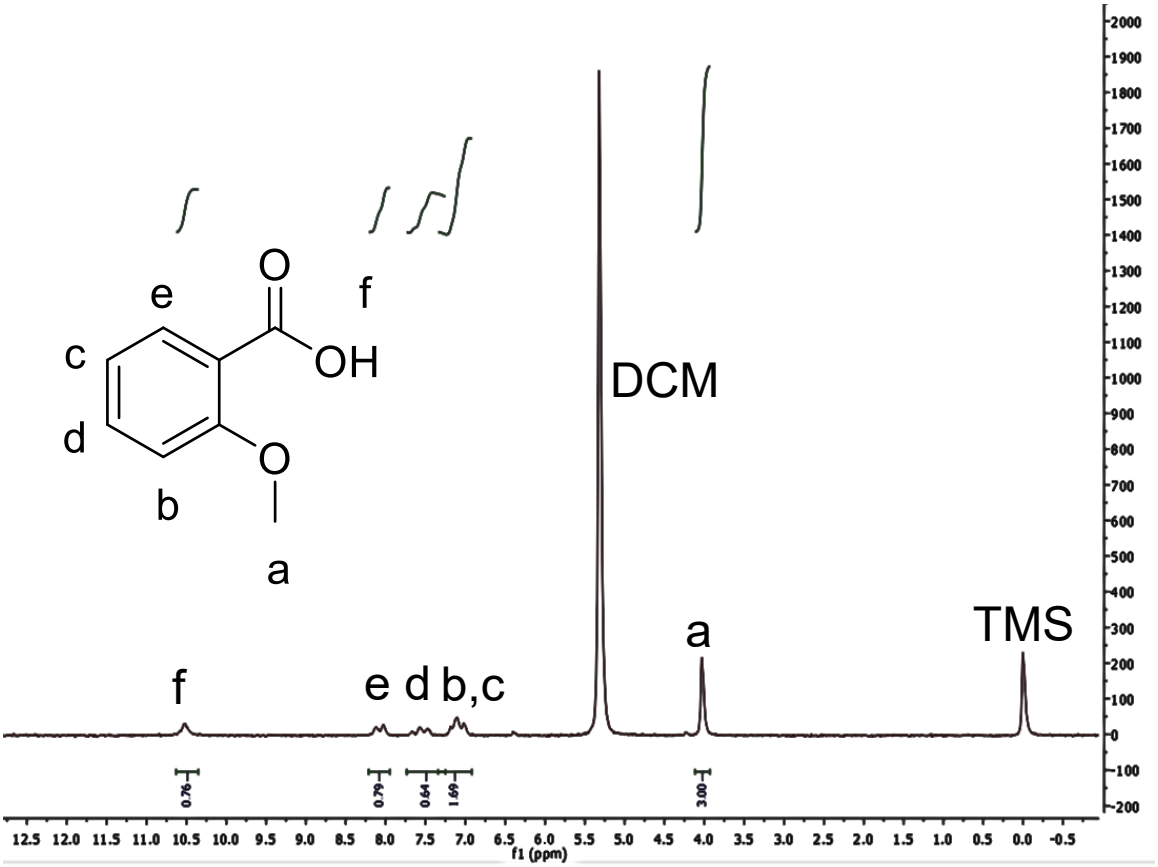


Figure 2.4. Student ^{1}H NMR spectrum of 2-methoxybenzoic acid from the 82 MHz picoSpin benchtop ^{1}H NMR. The structure and assignments are provided for clarity. Two drops of tetramethylsilane (TMS) were included to mark 0 ppm. The presence of dichloromethane (DCM) indicates the solvent for the sample.

DISCUSSION

This experiment allowed students to utilize bench top NMR technology in the laboratory setting. Obtaining product spectra of student-recovered products is important because it allowed students to gain experience studying actual, rather than idealized, spectra of their recovered products. The 1,462 students who completed a survey reported an average percent recovery rate of 67.94% for their basic component, 78.03% for the acidic component, and 84.29% for the neutral component. These percent recoveries are insightful because they illustrate the students' first three series of liquid-liquid extractions. The lowest percent recovery rate is the basic component, which was isolated first, followed by the acidic component, which was isolated second. The neutral component was the last component to the isolated and had the highest percent recovery. Recovering

the neutral component required students to carefully remove the methylene chloride. If too much heat was applied during this process, students could potentially melt the recovered product. It is also important to note that if students did not adequately remove the solvent, the recovered product may still be wet, impacting the resulting percent recovery.

In the University of Georgia curriculum, first-semester organic chemistry students completed two experiments in which the melting point was utilized for product confirmation prior to this experiment. This was the first experiment in which students were exposed to both IR spectroscopy and ^{1}H NMR spectroscopy. Moreover, ^{1}H NMR was the last of the two spectroscopic techniques presented to students. The students' heavy reliance on melting point determination was evident by the student rankings of the usefulness of each identification tool (see Figure 2.5). During the Fall 2017 and Spring 2018 iterations, the melting point was reported as the most useful analytical technique for correctly identifying the unknown acidic component by 73.24% and 63.49% of students. FTIR and ^{1}H NMR were reported by students as the second most useful and least useful analytical technique, respectively, for correctly identifying the unknown acidic component during these same semesters. This data highlights that students had not yet gained an appreciation for the utility of FTIR and ^{1}H NMR spectroscopies. While FTIR provides opportunities for functional group confirmation and ^{1}H NMR provides opportunities for structure elucidation, students appear to be more comfortable with melting point determination. The students look up the literature values of melting points on a weekly basis, but they may not yet be familiar with databases or literature sources of FTIR and ^{1}H NMR spectra, further contributing to their reliance on the melting point. Because this experiment was an elaboration of a single-outcome experiment, the melting point determination remained in the experiment with the two new spectroscopic techniques in addition. Students generally completed the experiment in the order of their familiarity with the techniques, which matched their ranking of the usefulness of the identification tools. In other words, students determined the melting point and then used the FTIR

spectrum to confirm the presence of the functional groups in their proposed component. The ^{1}H NMR spectra were generally the last points of data to be collected by students. In these same semesters where melting point was included, 47.03% and 56.13% of students selected ^{1}H NMR as the least useful tool for identifying the unknown acidic component (see Figure 2.6).

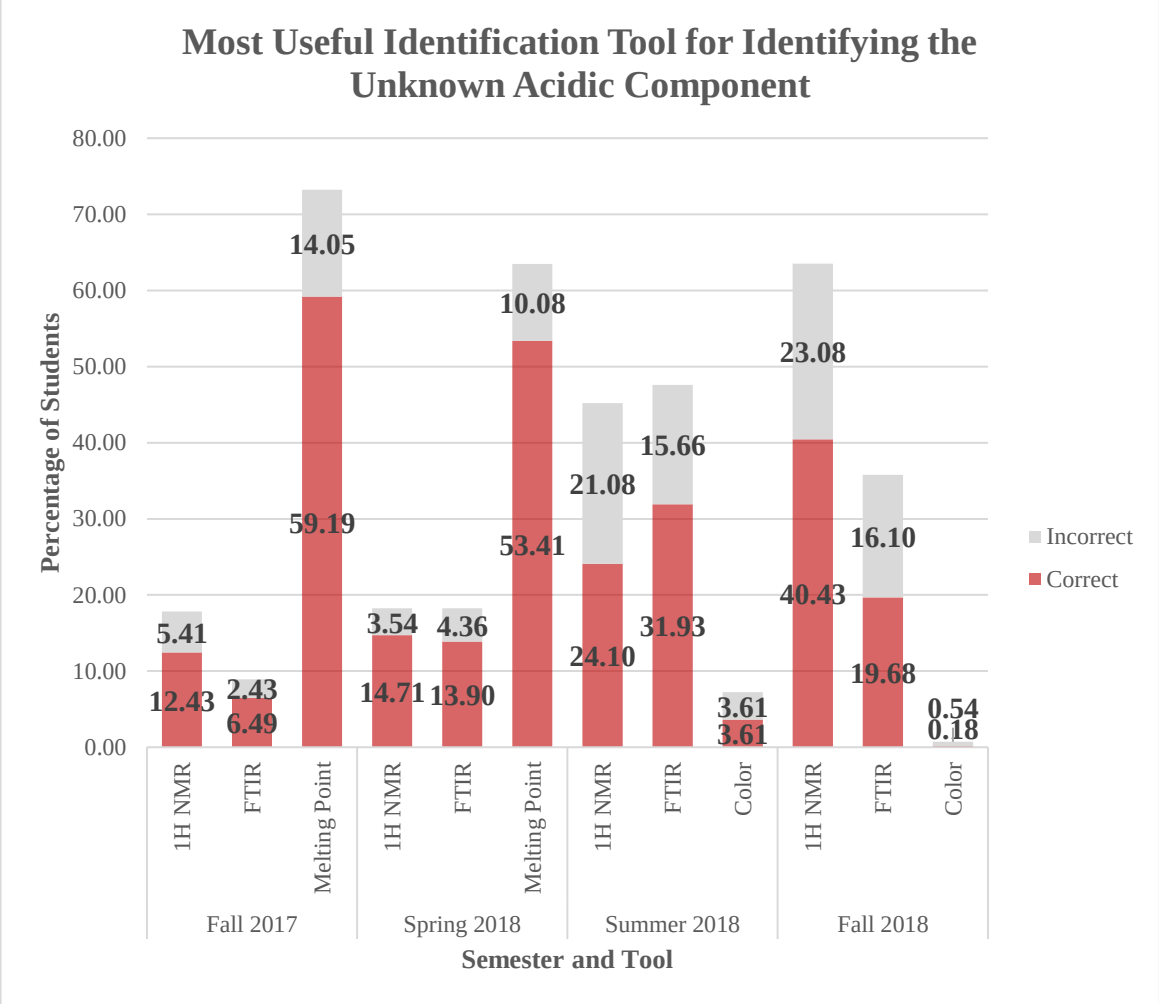


Figure 2.5. Postlab survey responses indicating which analytical tool was most useful for identifying the unknown acidic component. The melting point was removed during the Summer 2018 and Fall 2018 iterations.

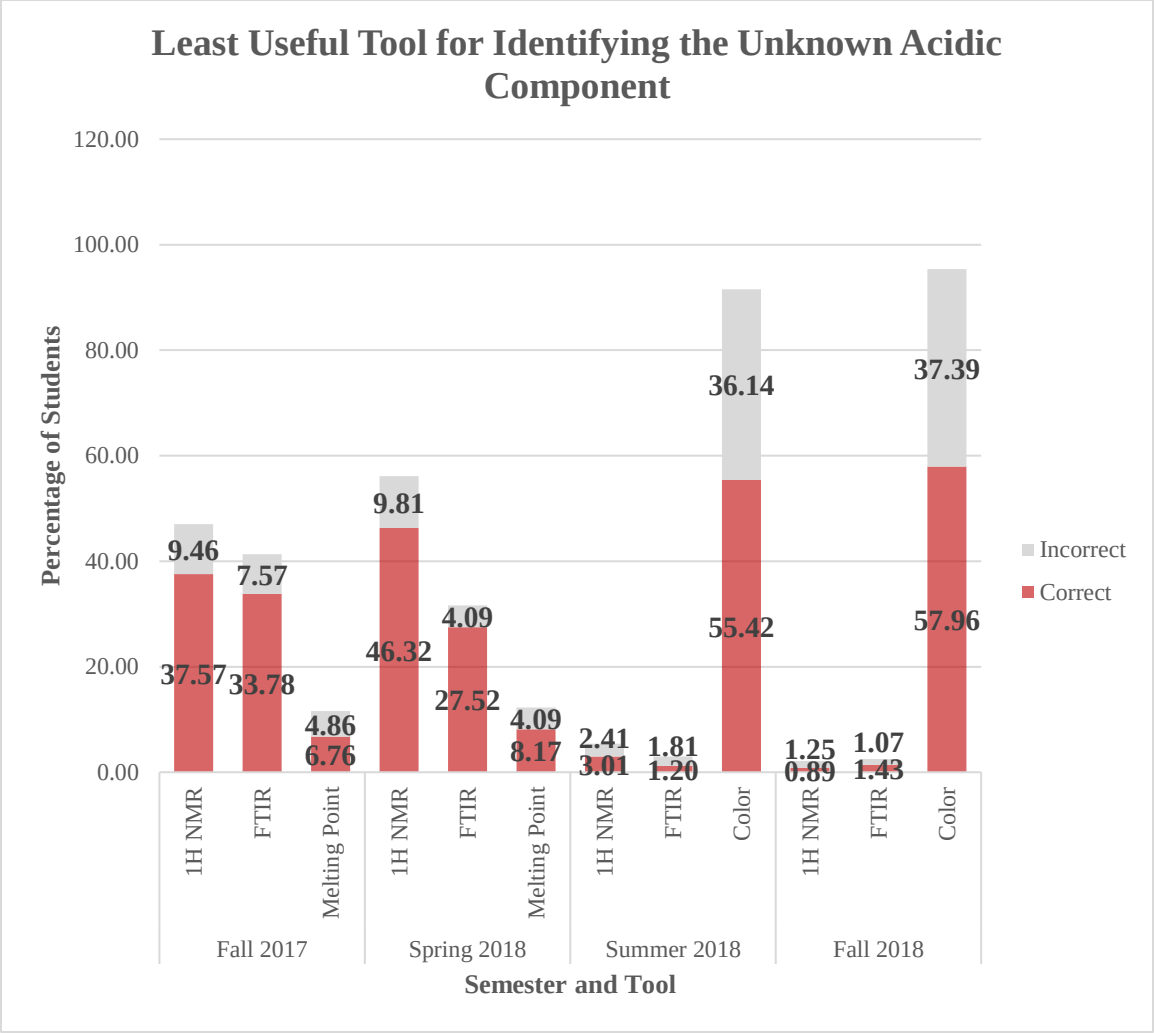


Figure 2.6. Postlab survey responses indicating which analytical tool was least useful for identifying the unknown acidic component. The melting point was removed during the Summer 2018 and Fall 2018 iterations.

Students reported their confidence levels for correctly identifying the unknown acidic component with *only* the benchtop ^{1}H NMR spectrum (see Figure 2.7). Interestingly, for the semesters in which melting point was included (Fall 2017 and Spring 2018), the majority of students selected "somewhat confident" or "least confident", with 11.08%-14.44% of students selecting "most confident". However, once the melting point was removed from the experiment, students became more reliant on the benchtop NMR spectra, as evidenced by the doubling of the "most confident" responses to 28.31%-32.56%. The overall number of "least confident" responses

also dropped by half, from 45.95%-50.95% with the melting point included to 20.75%-27.71% without the melting point included. This provides further evidence of the students' dependence on the melting point, meaning that they did not use the spectroscopic analyses originally as intended. By removing the melting point determination, the application of lecture-learned materials became more essential as students incorporated FTIR and ^{1}H NMR into their analyses to identify their unknown acidic component. Therefore, the researcher's goal of reinforcing lecture-learned concepts was better realized when the melting point was removed from the experiment. After the melting point was removed, the most popular response of students (43.98%-46.69%) was that they were "somewhat confident" in their responses *with only* the benchtop ^{1}H NMR spectra.

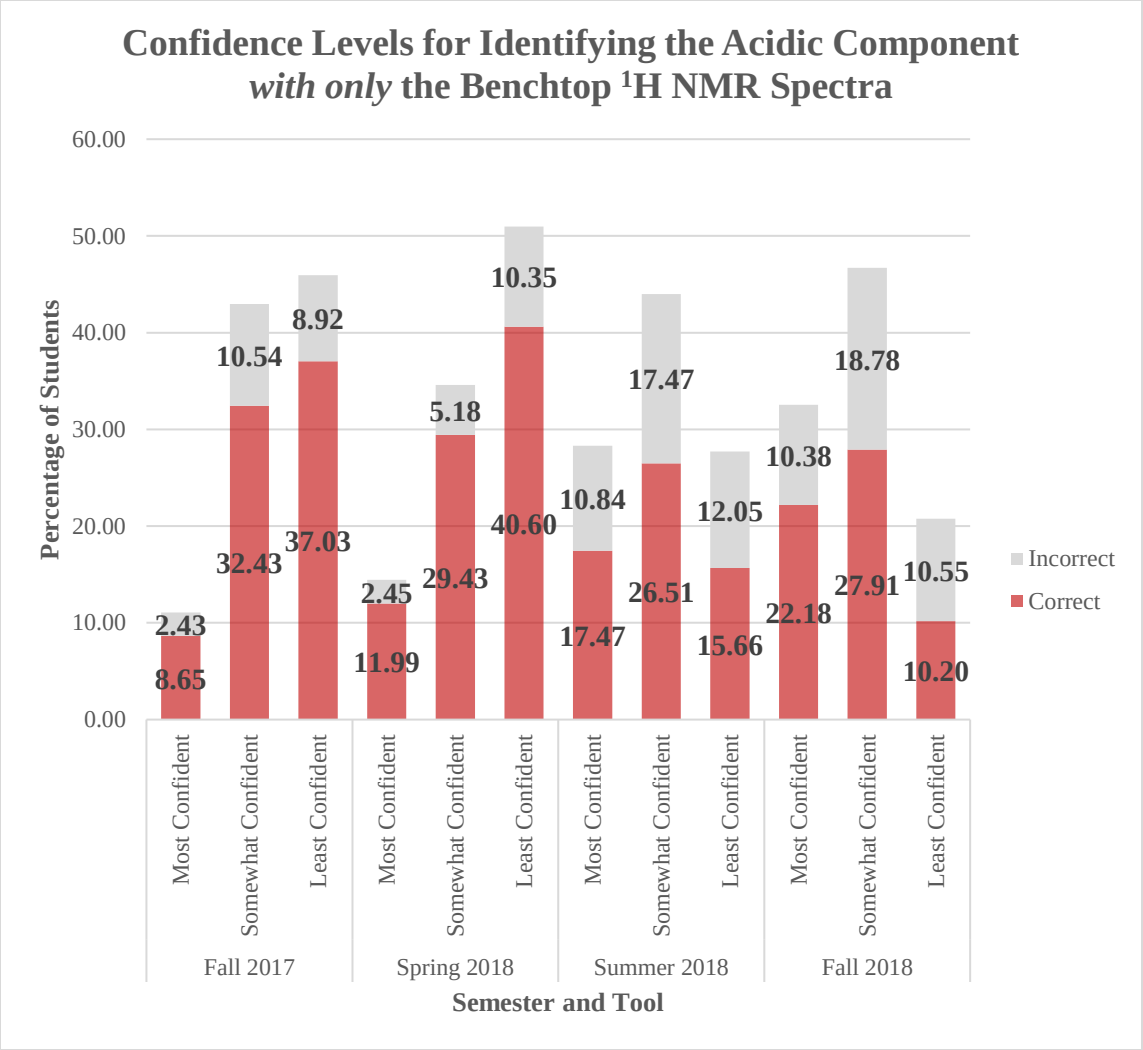


Figure 2.7. Postlab survey responses indicating student confidence levels for correctly identifying their unknown acidic component with only benchtop NMR spectra. The melting point was removed during the Summer 2018 and Fall 2018 iterations.

Students also reported their confidence levels for correctly identifying the unknown acidic component *without* the benchtop ^{1}H NMR spectrum (see Figure 2.8). For the semesters in which melting point were included (Fall 2017 and Spring 2018), the majority of students selected "most confident" (35.69%-38.11%) or "somewhat confident" (43.87%-48.92%), with 12.97-20.44% of students selecting "least confident". However, as soon as the melting point was removed from the experiment, students were driven to rely more heavily on the benchtop NMR spectra, which they were not as familiar with because they had learned it in tandem with performing this experiment.

This shift was indicated by the decrease of the "most confident" responses from 38.11%-35.69% to 5.90%-7.83%. Simultaneously, the overall number of "least confident" responses more than quadrupled to 51.20%-55.81% of student responses. This further illustrates the students' previous dependence on the melting point, meaning that they did yet feel confident in their ability to use the spectroscopic analyses for structure elucidation. By removing the melting point determination, students were guided to use their collected spectra for structure elucidation. In summary, the goal of the MOE to reinforce lecture-learned concepts became more essential as students used solely FTIR and ^{1}H NMR analyses to identify their unknown acidic component.

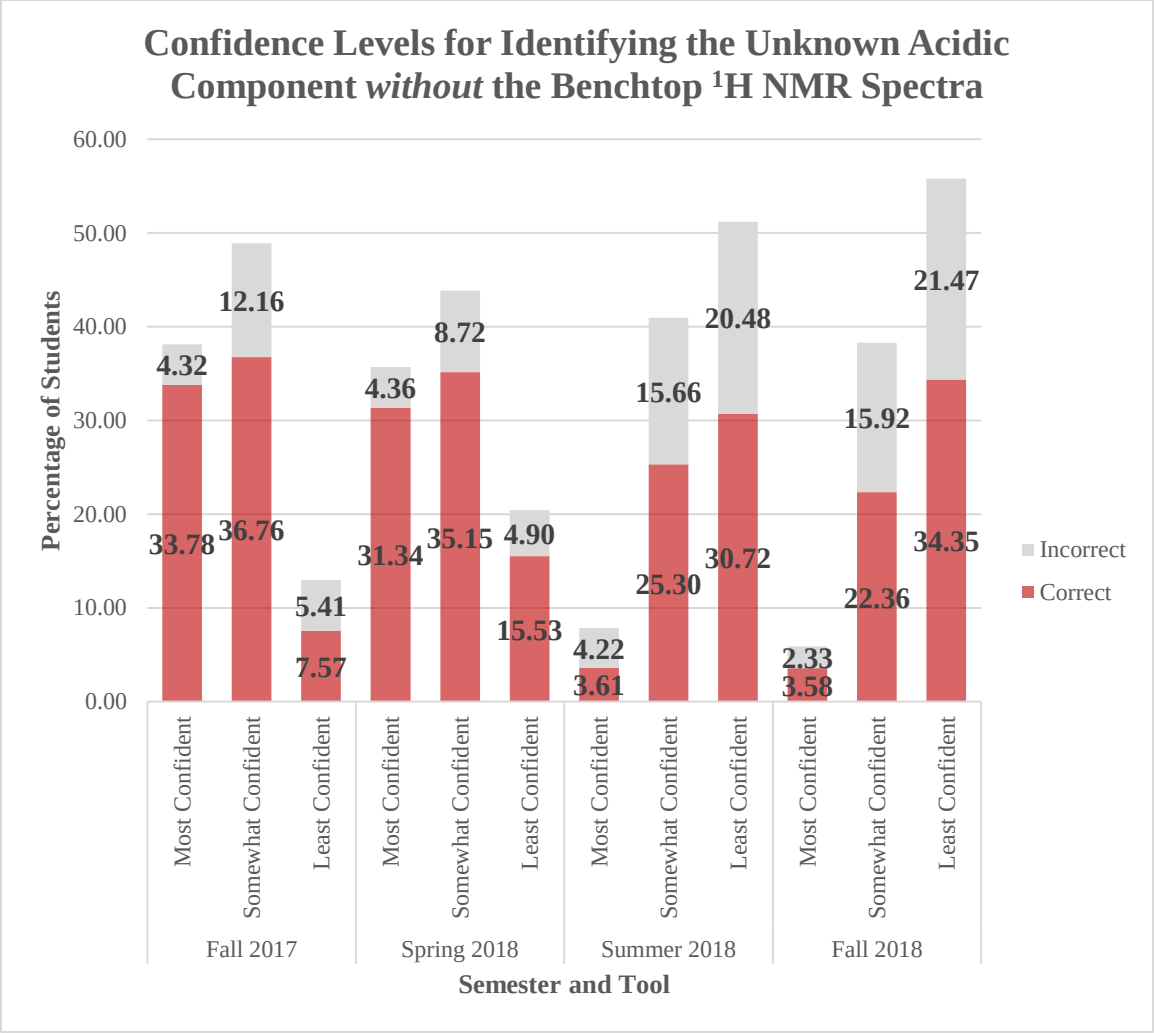


Figure 2.8. Postlab survey responses indicating student confidence levels for correctly identifying their unknown acidic component without benchtop NMR spectra. The melting point was removed during the Summer 2018 and Fall 2018 iterations.

One limitation of this experiment is that students may be introduced to FTIR and ^{1}H NMR spectroscopy in the lecture after the first of the week's sections have completed the experiment. This is because these techniques are taught in tandem with the experiment in the lecture course. If taught in tandem, the full benefits of utilizing the two techniques in class may not be realized by students until they complete their analyses. During the described iterations, all students were taught these techniques in their associated lecture courses by the end of the week of the experiment, with

instructors using this experiment as a benchmark in the semester's curriculum. Students then had one week to apply this new knowledge to their collected data.

Although the inclusion of FTIR and ^{1}H NMR spectroscopy are advantages of this experimental design, their incorporation can be limited by the three-hour time frame for the course. For example, rather than having students collect FTIR and ^{1}H NMR spectra of each of their recovered products (36 FTIR and 36 ^{1}H NMR spectra for a 24-student section), representative spectra of the basic and neutral components can be collected during the class period and distributed to that particular section of students by the graduate teaching assistant. Students can then solely focus on obtaining the FTIR and ^{1}H NMR spectra of their unknown acidic component, allowing for more effective use of time on the instrument.

Because the benchtop NMR instrument uses a capillary tube rather than expensive NMR tubes to house a sample during a scan, care must also be taken to carefully inject the solid samples from this experiment because NMR capillary tube may become clogged if samples are not adequately solvated. Graduate teaching assistants must be properly trained on how to use the instrument, how to prepare NMR samples from solid products, and on quick instrument maintenance to ensure that the experiment is successful in each lab section. The resulting spectra of the recovered solids dissolved in methylene chloride will contain a large solvent signal which can also be surprising to new instrument users.

This experiment provides a glimpse into the mindset of the first-semester organic chemistry students immediately after learning FTIR and ^{1}H NMR spectroscopies. While the researcher has seen students later in their organic chemistry coursework (and in this body of work) indicate a heavier reliance on benchtop NMR spectroscopy, the data from this experiment show that the first-semester organic chemistry students are not yet indicating a higher level of reliance. However, the student feedback gathered from these iterations clearly shows that the MOE goal of reinforcing lecture-learned concepts was met. One student noted that the experience "…taught me the

practicality of using IR and H NMR." A second student reported "…enjoy[ing] the experiment, especially after spending weeks learning how to study H-NMR and IR." The student continued stating that "…it was fun and rewarding to use these techniques in a way that actually helped us figure something real out." A third student also commented on the correlation between the laboratory experiment and the correlated lecture experience. The student described the experience of his or her pair, stating that he or she "…liked how we used different techniques, all of which we've learned about in lecture, in our experiment to determine the identity of the unknown."

CONCLUSIONS

An MOE for the Separation of a Three-Component Mixture via Acid-Base Extraction was developed and successfully implemented at the University of Georgia. A total of 1,026 out of 1,462 students (70.18%) correctly identified the unknown acidic component across the Fall 2017 – Fall 2018 semesters. This experiment provided a glimpse into the mindset of students immediately after learning two new spectroscopic techniques: FTIR and ^{1}H NMR spectroscopies. Overall, the design created more individualized student learning experiences and reinforced lecture-learned concepts.

EXPERIMENT NOTES

This work was classified as "not human research" by the Institutional Review Board at the University of Georgia (STUDY00004276). Undergraduates Shaen Deimling and Caroline Glessner assisted with the development and implementation of this experiment. The researcher would like to acknowledge Dr. Douglas M. Jackson for participating in discussions about the original design of the project. Special thanks are also extended to Ryan Maynard, Christina Cortes, Dr. Richard Hubbard, Fabian Tejedor Rojas, the CHEM 2211L TAs, and the CHEM 2211L students for assisting with or participating in the implementation in the organic chemistry main sequence laboratory course.

CHAPTER 3

THE OXIDATION OF AN UNKNOWN SECONDARY ALCOHOL

Kasey L. Yearty, Caroline E. Glessner, and Richard W. Morrison. Submitted to the *Journal of Chemical Education*, March 11, 2019.

ABSTRACT

Single-outcome experiments are used in the undergraduate instructional laboratory, particularly for large lectures associated with multiple sections of instructional laboratories, due in large part to efficiencies associated with chemical purchases, experiment preparations and assessments. Despite the practical advantages, single-outcome experiments are not effective in encouraging students to critically analyze and interpret their acquired individual results. Instead, students are satisfied if their results are the same as or similar to all of their classmates' results, limiting the opportunity for engagement with the laboratory content. In contrast, multi-outcome experiments require students to explore the same chemical reaction or transformation but obtain individual results. Individualization of results is accomplished by using a set of starting materials or reagents, one of which is assigned to each student. Students do not know the identity of the assigned component, but may be given possible options for its identity. Students elucidate the identity of their individualized products using modern analytical techniques such as gas chromatography, Fourier-transform infrared (FTIR) spectroscopy, and nuclear magnetic resonance (NMR) spectroscopy, and deduce the unknown component of their experiment. Multi-outcome experiments are highly effective tools for teaching and reinforcing chemistry content and application.

An example multi-outcome experiment for the oxidation of alcohols is described herein. A traditional single-outcome experiment was modified to utilize a common household oxidizing agent (hypochlorite bleach), rather than a heavy metal-containing alternative. For the multi-outcome experiment (MOE) modification, one unknown secondary alcohol (2-pentanol, 3-pentanol, or 3-methyl-2-butanol) was oxidized using bleach. Each student pair was assigned one of three possible unknown alcohols, all of which were constitutional isomers of secondary alcohols. Students knew the identities of the three possible alcohols. Analysis of their oxidation products was accomplished using FTIR and benchtop ^{1}H NMR spectroscopies. Students interpreted their spectra

and deduced the identity of the unknown alcohol they were assigned. This experiment provides a tangible framework to understand the applicability of the oxidation reaction and the utility of ^{1}H NMR spectroscopy.

BACKGROUND

The oxidation of alcohols using household bleach is well described in the literature.[53-60] Single-outcome, or "cookbook", versions of this experiment culminate with identical observations, data analyses, and results across the classroom. At the University of Georgia, the *Honors/Majors Advanced Organic Chemistry* laboratory course has previously oxidized an unknown alcohol using household bleach.[61-62] This unknown alcohol was traditionally isoborneol, which was subsequently oxidized to camphor. Camphor's structure was then elucidated by students using 2D NMR techniques. When completing the previously mentioned single-outcome oxidation experiment, student experiences and results were uniform with respect to their observations, data analyses, and the resulting white powdery product. In this new MOE, adapted from a procedure described by Mohrig and coworkers, students were provided with one of three unknown secondary alcohols (Figure 3.1).[63] One important aspect of the three unknowns in this experiment is that 2-pentanol, 3-pentanol, and 3-methyl-2-butanol are all constitutional isomers and, therefore, have the same molecular weight. This benefit made the purification process easier to streamline because it was not necessary to consider stoichiometric excess for any of the unknown alcohols. Utilizing a low-cost, household oxidizing reagent (hypochlorite bleach), these unknown alcohols were oxidized to the respective ketones and analyzed using FTIR and benchtop ^{1}H NMR spectroscopy. In addition to the reinforcement of spectroscopic techniques, the use of an environmentally-friendly reagent (household bleach) as the oxidizing agent rather than toxic chromic acid, the exothermic nature of the oxidation reaction itself, and the effects of this process on stereochemistry are also highlighted in this experiment.

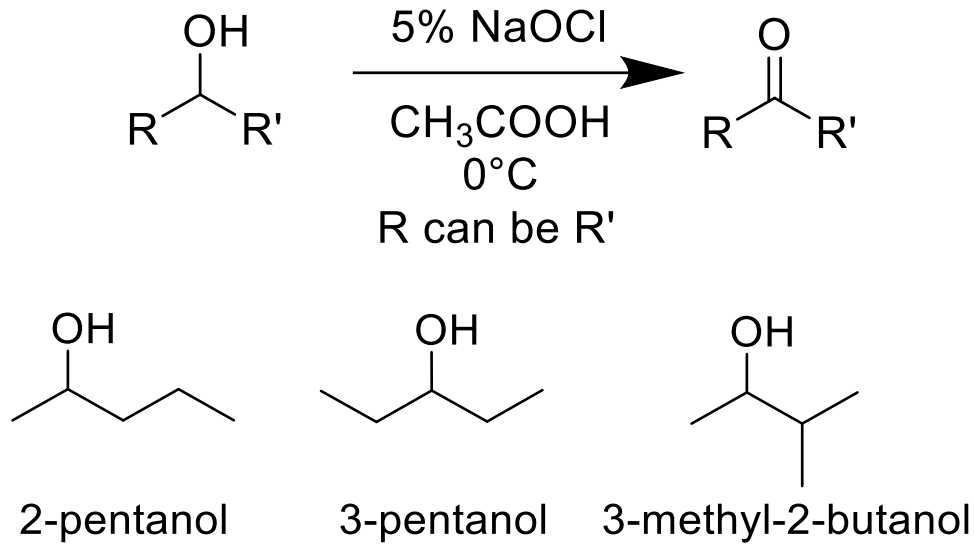


Figure 3.1. General reaction scheme and the constitutional isomer options provided to students for the unknown secondary alcohol.

METHODS

In total, 336 students were evaluated across two semesters: 90 students in Summer 2018 and 246 students in Fall 2018. A 2.1 gram (g) scale for the unknown alcohol was used for this MOE in order to prepare sufficient quantities for a subsequent MOE studying the reduction of aldehydes and ketones. Initially, the oxidation MOE was implemented in the Spring 2018 sophomore Advanced Organic Chemistry II laboratory course, a course comprised of 50 Honors students and chemistry majors. After Spring 2018, two additional trials of the experiment were performed in the sophomore Organic Chemistry II laboratory course, which typically has a higher enrollment than the advanced section. It is of note that the Spring 2018 iteration of the experiment included double the volume of dichloromethane (ten milliliters per portion) during the extraction segment of the procedure. This volume was reduced by half (five milliliters per portion) during the subsequent iterations to minimize solvent use. Trials were also conducted to change methylene chloride to diethyl ether, but extraction with diethyl ether did not yield sufficient isolated product for student analysis. Students collected FTIR spectra and benchtop ^{1}H NMR spectra of their products. The ^{1}H NMR neat samples were spiked with two drops of tetramethylsilane (TMS) to mark 0 ppm. The

samples were injected into the benchtop NMR instrument by the students, and the spectra were collected. The resulting spectra were processed by the TA using MestreNova. All spectra collected in the section were sent to the students for comparison purposes during analyses. The students also completed a post-lab survey to electronically document their results.

HAZARDS

Safety glasses, lab coats, and lab gloves must always be worn. Please review online SDS sheets of all chemicals including products. Sodium hypochlorite (NaOCl) is the active ingredient in household bleach and will bleach colored clothing. Acetic acid and NaOCl are irritants and should be washed away immediately if in contact with skin or eyes. Use caution when working with 6M sodium hydroxide (NaOH) as it is caustic and may cause burns. Make sure that your localized ventilation system (snorkel) is properly positioned to avoid inhaling any hazardous fumes. Make sure that your snorkels are turned on and functioning properly before dispensing any liquids. Methylene chloride is volatile. Chronic exposure is possibly carcinogenic, and care must be taken to avoid breathing any fumes or allowing any liquid to contact your skin. Take care when dispensing and evaporating methylene chloride. Any vapor or liquid exposure should be reported to your TA immediately. Dispose of all liquid waste in the appropriately labeled bottle in the lab hood.

RESULTS

For the 336 survey respondents, 81 out of 90 students (90.00%) correctly identified their unknown alcohol in Summer 2018 and 203 out of 246 students (82.52%) correctly identified their unknown alcohol during Fall 2018. The student identifications of their unknown alcohols are summarized in Tables 3.1-3.2. During the two iterations, students reported mass of their final product as being an average of 0.8553 g (41%) of 2-pentanone, 1.2639 g (60%) of 3-pentanone, and 0.9436 g (45%) of 3-methyl-2-butanone.

Table 3.1. Student Identifications of Unknown Secondary Alcohols

Unknown Secondary Alcohol	*# Correct*	*# Students*	*Percent*
2-Pentanol			
Summer 2018	22	26	84.62%
Fall 2018	68	84	80.95%
Total	90	110	81.82%
3-Pentanol			
Summer 2018	25	26	96.15%
Fall 2018	68	78	81.18%
Total	93	105	88.57%
3-Methyl-2-Butanol			
Summer 2018	34	38	89.47%
Fall 2018	67	84	79.76%
Total	101	121	83.47%
Combined Totals for all Secondary Alcohols			
Summer 2018	81	90	90.00%
Fall 2018	203	246	82.52%
Overall	284	336	84.52%

Table 3.2. Complete Listing of Student Identifications of Unknown Secondary Alcohols

Unknown Secondary Alcohol	*2-Pentanol*	*3-Pentanol*	*3-Methyl-2-Butanol*
2-Pentanol			
Summer 2018 (n = 26)	22 (84.62%)	2 (7.69%)	2 (7.69%)
Fall 2018 (n = 84)	68 (80.95%)	7 (8.33%)	9 (10.71%)
3-Pentanol			
Summer 2018 (n = 26)	1 (3.85%)	25 (96.15%)	0 (0.00%)
Fall 2018 (n = 78)	0 (0.00%)	68 (87.18%)	10 (12.82%)
3-Methyl-2-Butanol			
Summer 2018 (n = 38)	1 (2.63%)	3 (7.89%)	34 (89.47%)
Fall 2018 (n = 84)	9 (10.71%)	7 (8.33%)	67 (79.76%)

The ^{1}H NMR spectra collected by students of their product ketones are shown in Figures 3.2-3.4. When examining the ^{1}H NMR spectrum from Figure 3.2, students may begin with the 6H doublet farthest upfield. This upfield signal represents the protons that are the farthest away from the ketone present in each potential product. By understanding that these 6H have one neighboring

proton, the students may immediately rule out 2-pentanone and 3-pentanone products. This leaves 3-methyl-2-butanone as the only option for this product. Upon further analysis, students recognize that the remaining 3H singlet and 1H septet are farther downfield, hence closer to the ketone functional group. By piecing all this information together, students can confirm that the product obtained in Figure 3.2 is 3-methyl-2-butanone, and the starting alcohol must have been 3-methyl-2-butanol. Similar processes can be applied to the products depicted in Figures 3.3 and 3.4.

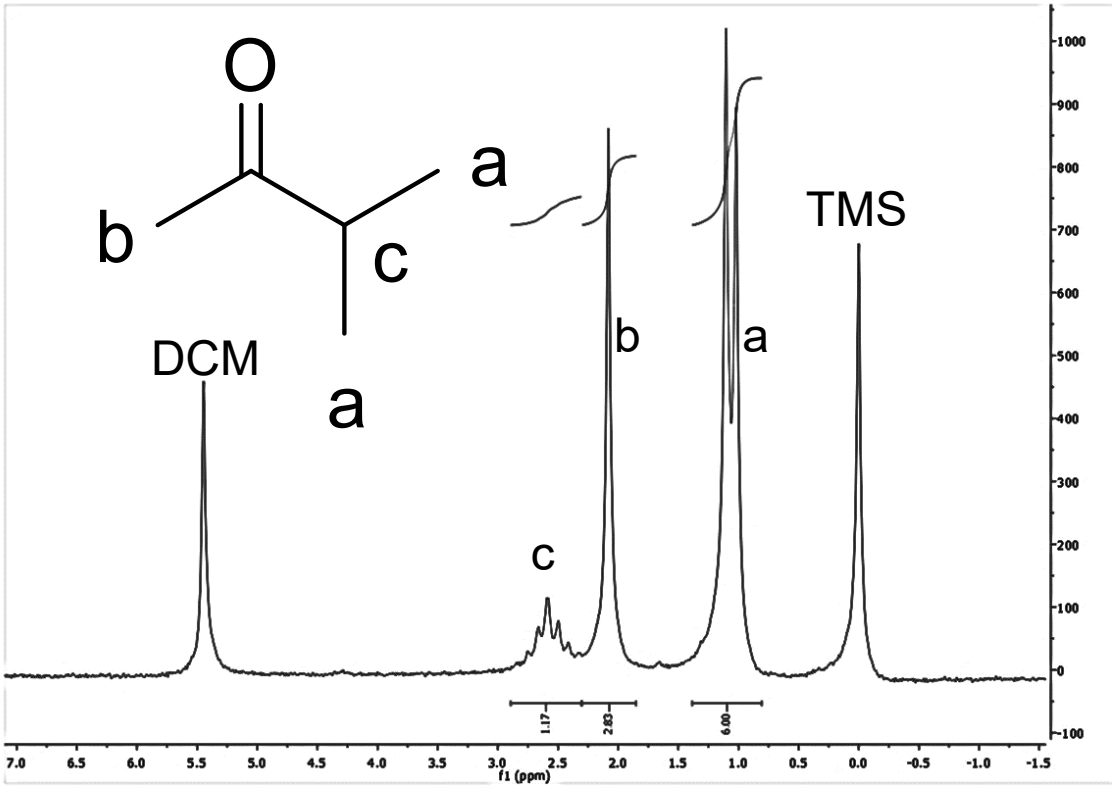


Figure 3.2. Student ^{1}H NMR spectrum of 3-methyl-2-butanone from the 82 MHz picoSpin benchtop ^{1}H NMR. The structure and assignments are provided for clarity. Two drops of tetramethylsilane (TMS) were included to mark 0 ppm. The presence of dichloromethane (DCM) indicates residual solvent used during the extraction.

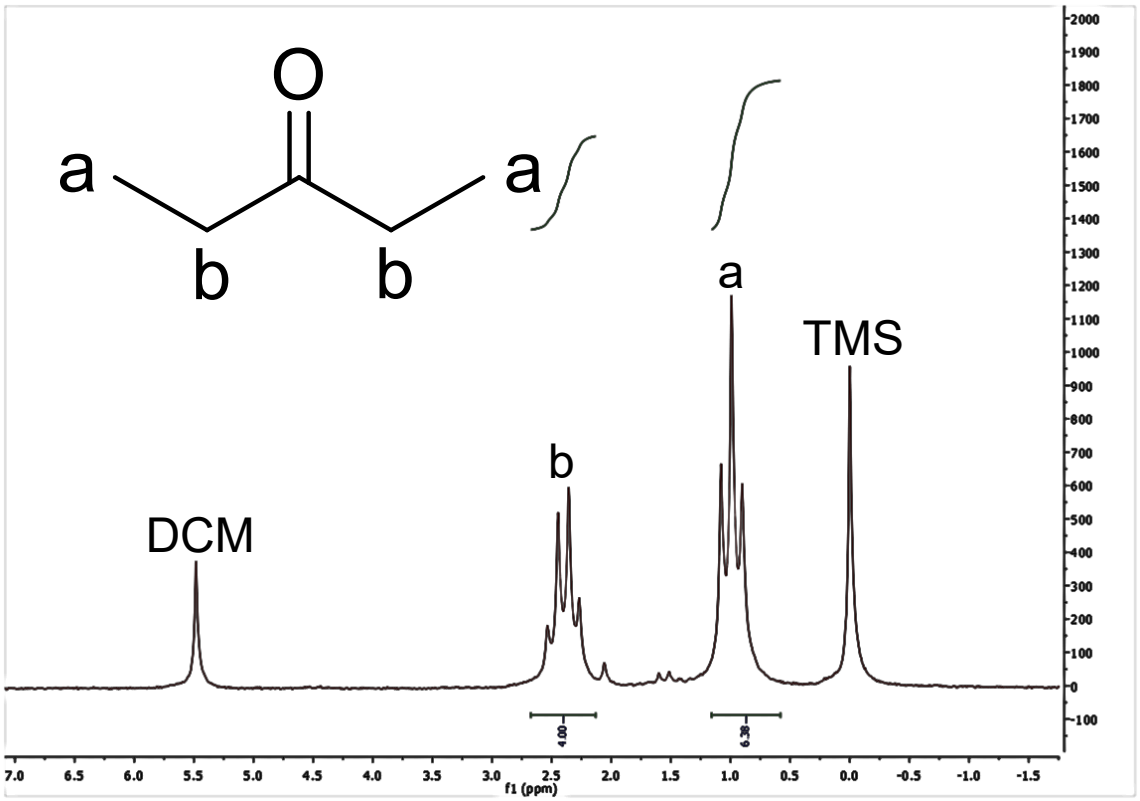


Figure 3.3. Student ^{1}H NMR spectrum of 3-pentanone from the 82 MHz picoSpin benchtop ^{1}H NMR. The students were provided with the integration values listed on the spectrum. The structure and assignments are provided for clarity. Two drops of tetramethylsilane (TMS) were included to mark 0 ppm. The presence of dichloromethane (DCM) indicates residual solvent used during the extraction.

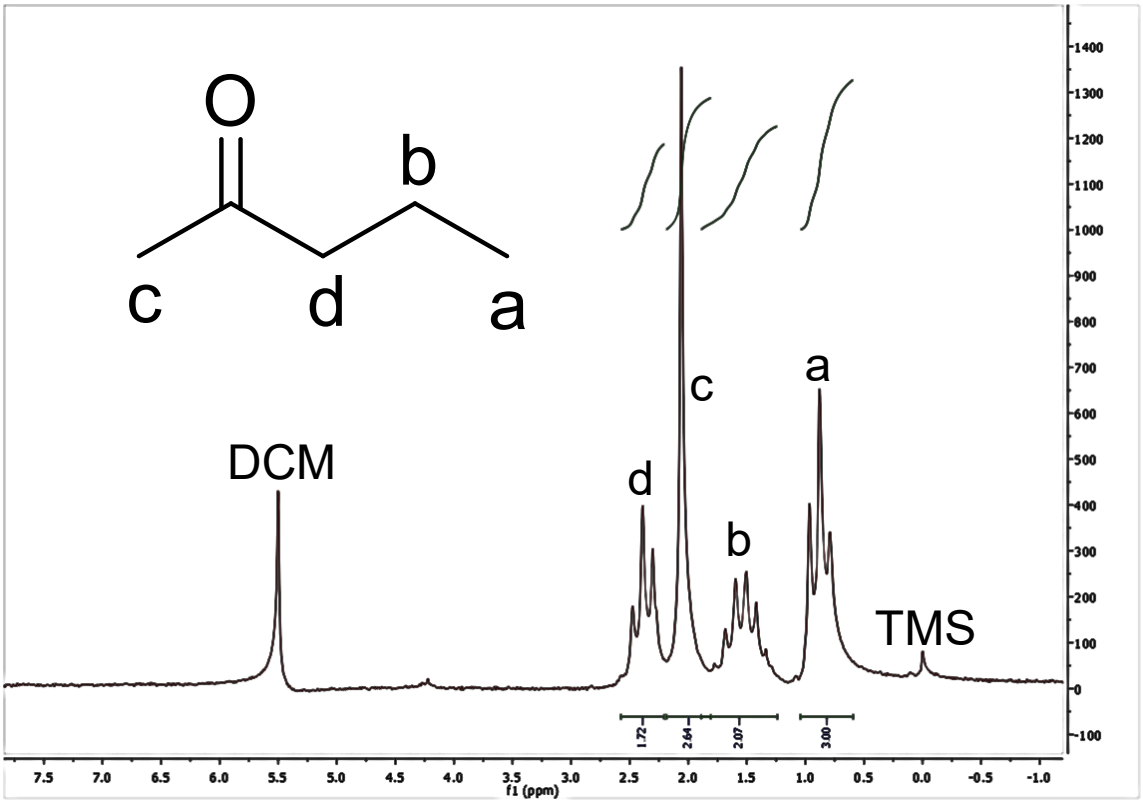


Figure 3.4. Student ^{1}H NMR spectrum of 2-pentanone from the 82 MHz picoSpin benchtop ^{1}H NMR. The students were provided with the integration values listed on the spectrum. The structure and assignments are provided for clarity. Two drops of tetramethylsilane (TMS) were included to mark 0 ppm. The presence of dichloromethane (DCM) indicates residual solvent used during the extraction.

DISCUSSION

In this experiment, students successfully oxidized secondary alcohols into ketones using household bleach and analyzed their products using FTIR and ^{1}H NMR. Students were thus provided with the opportunity to apply what they had learned in the associated lecture course to a product that they made in the laboratory. For both iterations, the most useful, second most useful, and least useful identification tools were reported as ^{1}H NMR spectroscopy, FTIR spectroscopy, and color, respectively (see Figures 3.5 and 3.6). While the ketones were all the same color, the "color" option has been traditionally incorporated into the postlab survey so that the survey is standardized with postlab surveys for other MOEs which have been developed by the researcher.

The researcher also asked students to elaborate on their responses, thus encouraging them to critically analyze their spectra in comparison to the spectra of their peers. One student stated, “The specific integration numbers in addition to the chemical shifts and the splitting patterns that were displayed on the ^{1}H NMR spectrum really helped me tell the difference between the ketone products and, therefore, they allowed me to better identify the starting alcohols that were oxidized to make the product.” Another student recognized the utility of FTIR spectroscopy in this experiment, by stating, “The only feature of the IR spectroscopy useful was the absence or presence of certain functional groups, but this was only helpful in determining if the reaction went to completion.” The students generally indicated that the products formed were all clear, colorless liquids, recognizing that color was not a helpful indicator for determining the identity of the unknown alcohol.

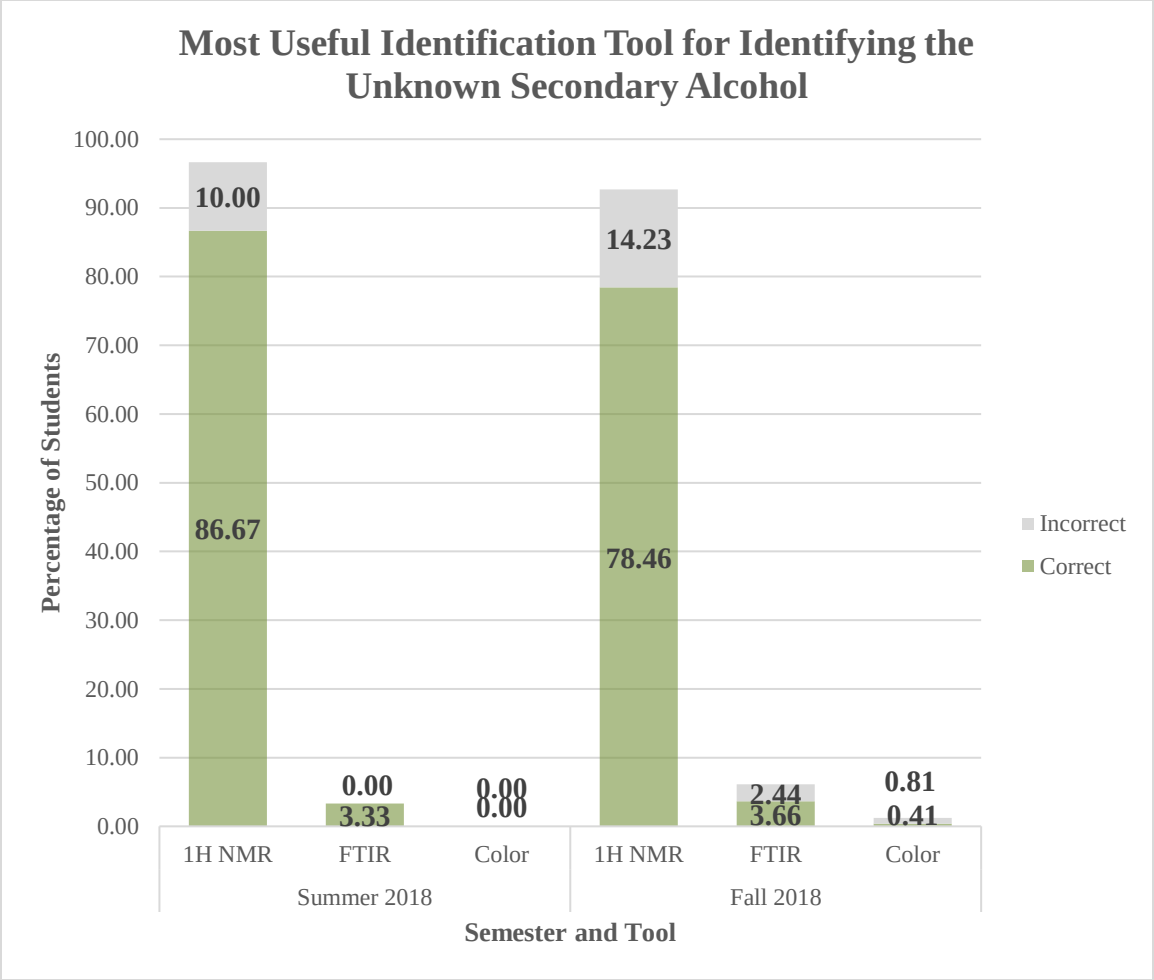


Figure 3.5. Postlab survey responses indicating which analytical tool was most useful for identifying the unknown secondary alcohol.

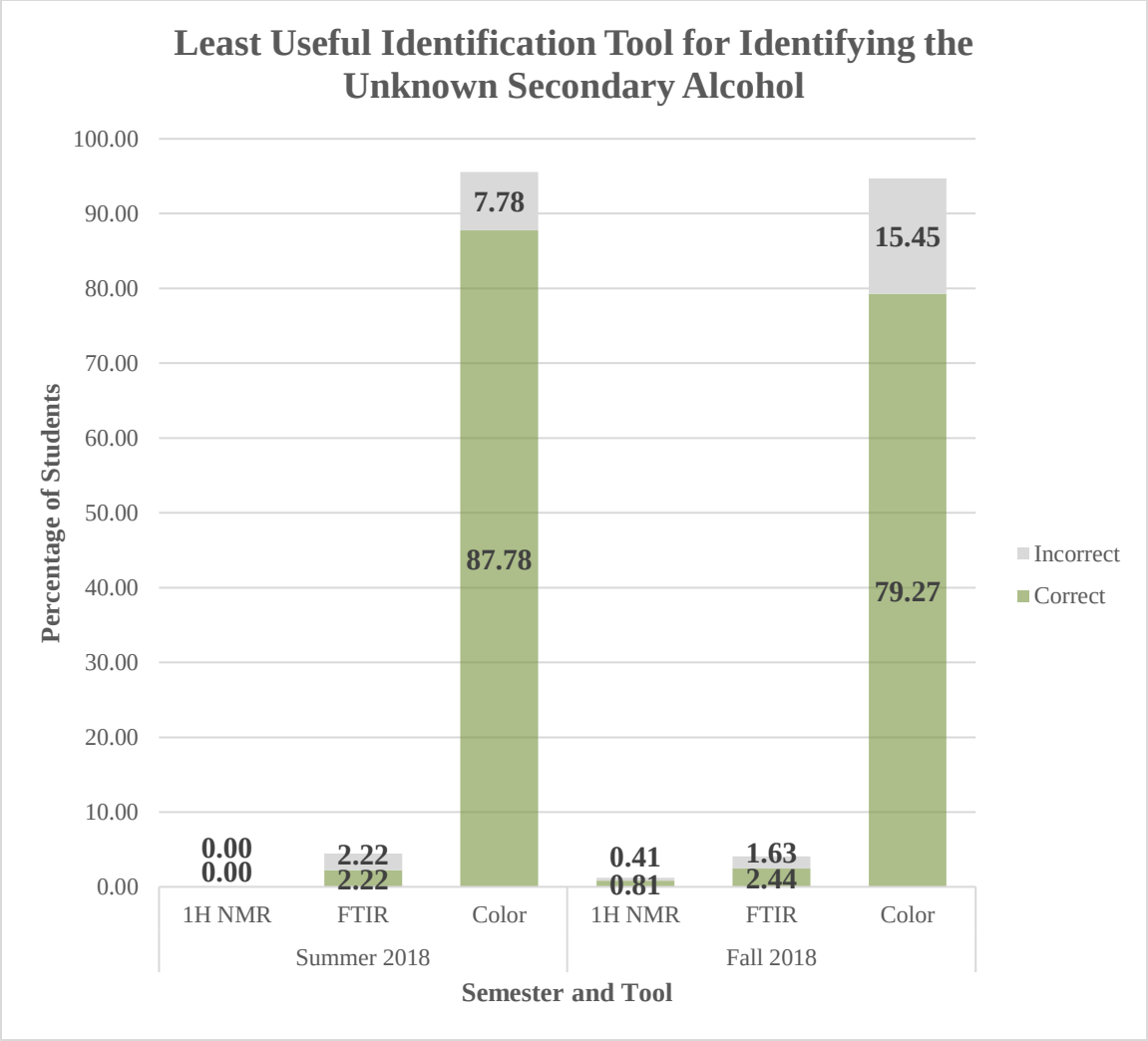


Figure 3.6. Postlab survey responses indicating which analytical tool was least useful for identifying the unknown secondary alcohol.

In addition to these rankings, students also self-reported their confidence levels in their ability to identify correctly the unknown alcohol *with only* the benchtop ^{1}H NMR spectra of their products. Figure 3.7 illustrates a downward trend in student confidence levels, with most students indicating that they would feel "most confident". Furthermore, students self-reported their confidence levels in their ability to identify correctly their unknown alcohol *without* the benchtop ^{1}H NMR spectra of their products. In Figure 3.8, an upward trend is noted for student confidence levels, with the greatest population of students selecting "not confident".

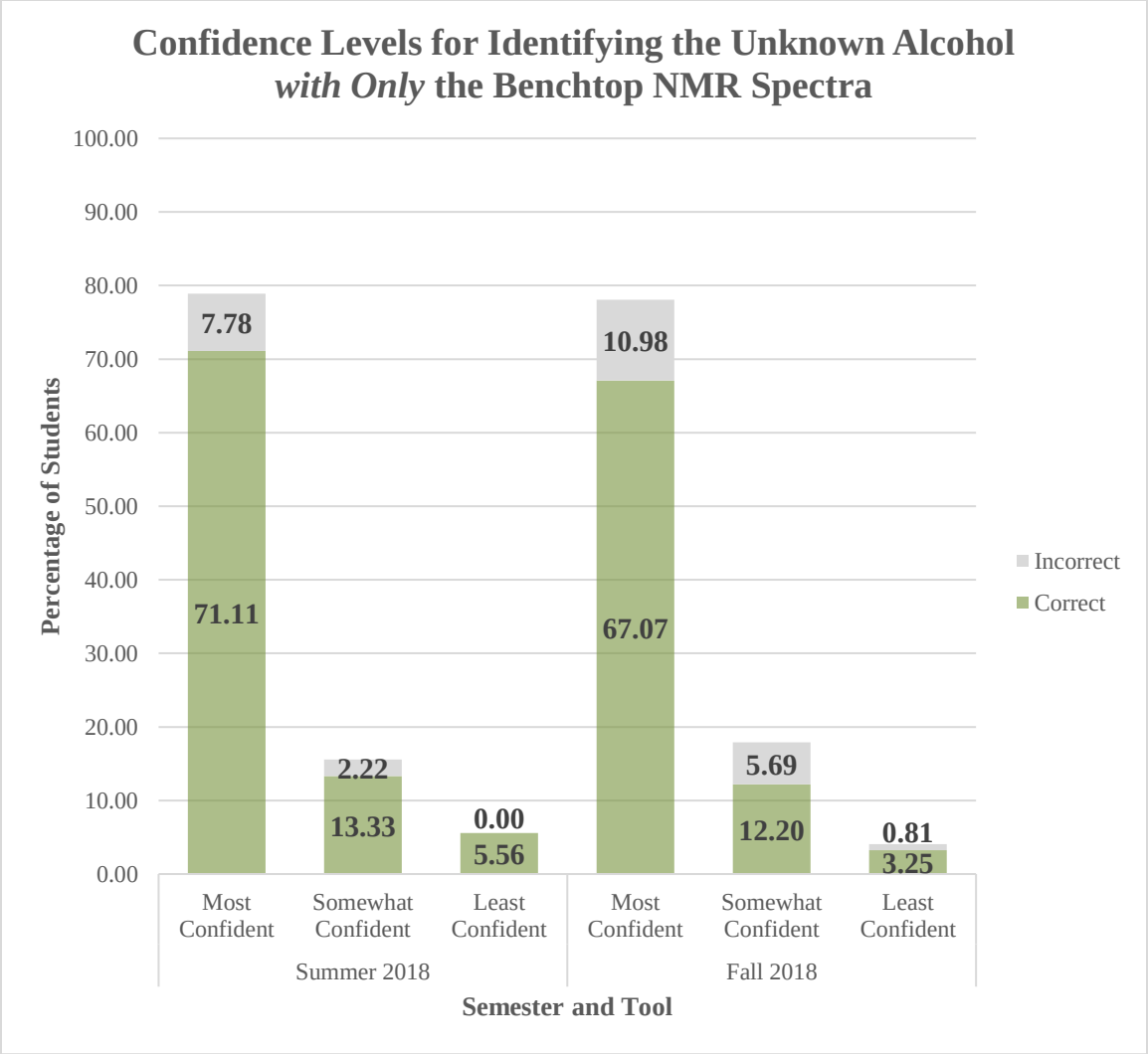


Figure 3.7. Postlab survey responses indicating confidence levels for correctly identifying the unknown secondary alcohol *with only* the benchtop ^{1}H NMR spectra

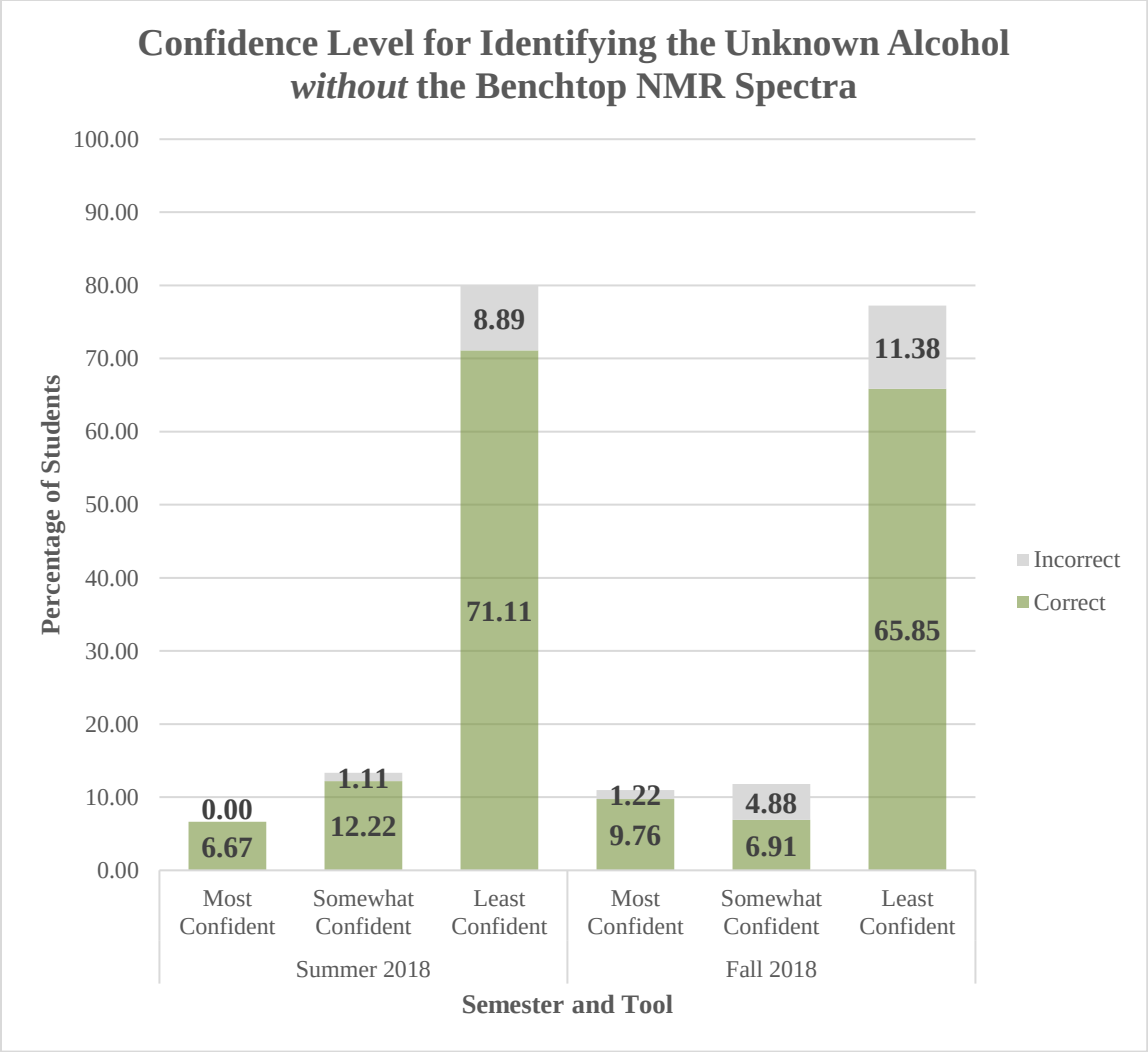


Figure 3.8. Postlab survey responses indicating confidence levels for correctly identifying the unknown secondary alcohol *without* the benchtop ^{1}H NMR spectra

Several lecture-learned concepts were reinforced with the students through this MOE, including the oxidation of alcohols and spectral analyses using ^{1}H NMR and FTIR spectroscopies. Students collected NMR spectra of their products that they created with their assigned unknown secondary alcohols. They then used the chemical shifts, splitting patterns, and integrations along with their products' molecular formula to piece together the structure represented in their product spectra. This allowed the students to identify the ketone product. One student described this experience as follows:

> "The specific peaks on the spectra were different for each starting alcohol, making it easy to determine which alcohol corresponded to each ^{1}H NMR spectra. The triplet at approximately 1 ppm indicates that the 6 hydrogens with that specific splitting pattern are adjacent to a carbon with two hydrogens. Those 6 hydrogens indicate that the ketone has two methyl groups present on the carbon chain, eliminating 3-methyl-butan-2-ol as a possible starting material, as that alcohol contains 3 CH_3 groups. The quartet at approximately 2.25 ppm indicates that 4 hydrogens on the molecule have 3 neighbors. This narrows the possible starting material down to 3-pentanol, as the two secondary carbons in this molecule are each adjacent to a carbon with three hydrogens."

This student's representative response illustrates that while the students could look at the number of signals in the spectrum to determine their product, other factors were taken into consideration, such as splitting patterns and integration values. The repetition of this type of analysis and structural elucidation of self-made products is an integral component of MOEs. The structure was then matched to one of the three potential secondary alcohol options provided to students. Another student noted the correlation of this experiment with the lecture course, stating the following: "This was an easy introductory lab that actually lined up with the material we have been studying in lecture. It's short and to the point…".

The students who participated in the MOE had a more individualized laboratory experience because they collected and analyzed their own unique data. Their laboratory experience was not uniform across the section or class, unlike the experience in the single-outcome version of the experiment. Student experiences during this MOE became more individualized once students were assigned an unknown at the beginning of the laboratory period and culminated with the ^{1}H NMR spectra of the resulting ketones, which varied by chemical shift, splitting patterns, integrations, and number of signals.

Finally, this MOE actively engaged students with two modern analytical techniques: FTIR and ^{1}H NMR spectroscopies. With TA supervision, students collected spectra of their products and interpreted these data to determine the identity of their products. Many students described their spectral analyses in the postlab survey as previously illustrated. A student noted the following: "Using the ^{1}H NMR data was incredibly useful for aiding in the identification of the product as it provided information on the splitting of the [protons] which helped with figuring out how the [protons] were bonded and how many were bonded to each carbon, and how many different unique bonds there were in the compound." While other standard measurements and observations (i.e., product mass and color) were recorded throughout the experiment, the data collected from the postlab survey discussed above clearly shows that these spectroscopic analyses, primarily ^{1}H NMR spectroscopy, were key to student identification of the product and the unknown starting material. Additionally, the commentary provided in the student feedback demonstrates an understanding and an appreciation of the utility of the ^{1}H NMR spectroscopy. Overall, MOEs accompanied by benchtop NMR greatly increased student familiarity and confidence with data analysis and their mastery of concepts introduced in the associated lecture.

CONCLUSIONS

The inclusion of the Oxidation of Unknown Secondary Alcohols in the undergraduate instructional laboratory curriculum provided opportunities for the reinforcement of lecture-learned concepts, increased individualization of the student laboratory experience, and the facilitation of active student engagement with modern analytical techniques. In this MOE, students successfully oxidized unknown secondary alcohols to ketones in second-semester sophomore organic chemistry laboratory courses. Students utilized the analytical techniques available to them to characterize and identify their product ketones, then determining the identity of their unknown secondary alcohol.

EXPERIMENT NOTES

This work was classified as “not human research” by the Institutional Review Board at the University of Georgia (STUDY00005731). Undergraduate Caroline Glessner assisted with the development and implementation of this experiment. Special thanks are extended to Dr. Richard Hubbard, Fabian Tejedor Rojas, the CHEM 2212L TAs, and the CHEM 2212L students for assisting with or participating in the implementation in the organic chemistry main sequence laboratory course.

CHAPTER 4

REINFORCING NMR SPECTROSCOPY: A MULTI-OUTCOME EXPERIMENT FOR THE WILLIAMSON ETHER SYNTHESIS

Kasey L. Yearty, Ryan K. Maynard, Christina N. Cortes, and Richard W. Morrison. Submitted to the *Journal of Chemical Education,* April 6, 2018.

ABSTRACT

Williamson Ether experiments are commonly performed in undergraduate organic chemistry instructional laboratory courses. In this MOE, students were provided 4-bromophenol and one of three alkyl halides: 1-bromopentane, 1-bromobutane, and 1-bromo-3-methylbutane. The alkyl halides served as the unknown component of the experiment, and students were provided with a trio of potential identities. The 4-bromophenol was deprotonated using 25% KOH, forming the phenoxide conjugate base, which was subsequently reacted with one of the unknown alkyl halides. After purifying the reaction mixture, students analyzed their products using FTIR and ^{1}H NMR spectroscopies. The experimental results herein summarize the inclusion of this experiment in our large enrollment second-semester organic chemistry laboratory courses during the Fall 2017 and Spring 2018 semesters.

BACKGROUND

Experiments involving the Williamson ether synthesis, a reaction first discovered by Alexander Williamson in 1850, are commonly performed in undergraduate organic chemistry teaching laboratories.[64-74] While this reaction is a standard experiment across the United States, the use of unknown alkyl halides in tandem with the use of benchtop NMR technology for product characterization has yet to be reported. The multi-outcome version of this classic experiment includes outfitting the procedure with multiple unknown alkyl halide starting materials and the benchtop NMR analysis of products. This MOE involves the formation of the conjugate base of 4-bromophenol. Once the phenoxide ion is formed, it serves as the nucleophile in the S_N2 attack on the primary alkyl halide. The primary alkyl halide used in this experiment is unknown to students, and they are provided with a component key listing possible identities for the unknown alkyl halide. This procedural adaptation allows students to practice ^{1}H NMR analysis of larger molecules and apply their knowledge of solubility, particularly because the original version of the experiment did not highlight solubility. The unknown primary alkyl halides are not water-soluble; hence, a phase-transfer catalyst must be used to assist in this reaction. The alkyl halides used in this experiment include 1-bromopentane, 1-bromo-3-methylbutane, and 1-bromobutane (Figure 4.1). To purify the products, a flash chromatography column is incorporated using silica gel as the stationary phase and methylene chloride as the mobile phase. Thin layer chromatography is included to monitor the purified product solution for any remaining starting materials. Although the prepared products are simpler in structure, the new design incorporates holistic concepts while simultaneously reinforcing NMR spectroscopy. The reaction scheme for this experiment is shown in Figure 4.2.

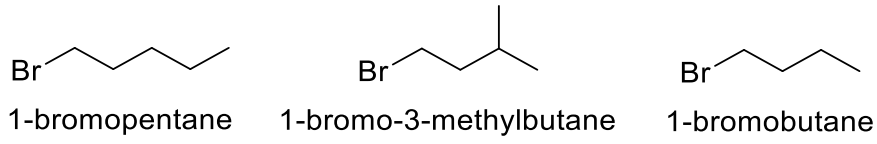


Figure 4.1. Component Key Provided to Students

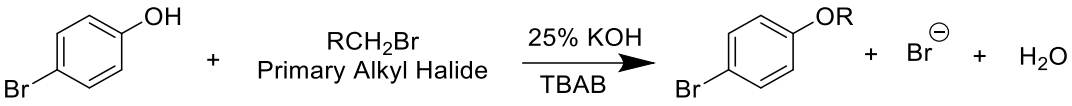


Figure 4.2. Example Reaction Scheme for the Williamson ether synthesis

METHODS

Previously at the University of Georgia, the Williamson ether synthesis was a multi-week experiment. The experimental design built upon an existing multi-week synthesis in which students first isomerized (R)-(-)-Carvone to Carvacrol. Then, the conjugate base of Carvacrol was subsequently utilized in a Williamson ether synthesis. Recent modifications to simplify the ^{1}H NMR spectrum of the product included replacing the phenoxide conjugate base of Carvacrol with the phenoxide conjugate base of 4-bromophenol. 4-Bromophenol is a symmetrical phenol derivative (pK_a 9.17). This modification removed alkyl groups to declutter the upfield region of the ^{1}H NMR spectrum, facilitating student identification. A procedure by Black et. al. was modified to incorporate 4-bromophenol and adapted to include multiple primary alkyl halides.[75] In total, three primary alkyl halides were included in the procedure: 1-bromobutane, 1-bromo-3-methylbutane, and 1-bromopentane. Students were provided with a trio of potential alkyl halides that may serve as their specific unknown in the experiment. After the product ethers were isolated and the mass recorded, standard observations were noted (color, etc.). TLC, FTIR, and ^{1}H NMR were performed for the purified products.

This experiment was implemented over the course of four semesters, with some procedural variations between the Fall 2017 and subsequent iterations. For the Fall 2017 semester, 150 students were evaluated, and the experiment was completed on a microscale version. The reflux occurred

via conventional heating for one hour, and the column was run using a Pasteur pipette. Teaching assistants (TAs) assisted with the injection of samples and the subsequent spectral processing during this first iteration. During the Spring 2018, Summer 2018, and Fall 2018 iterations, 304, 76, and 184 students were evaluated, respectively. The conjugate base of 4-bromophenol was prepared as a class demonstration by the TA. The procedure was streamlined to include a larger volume of material so that a microwave-promoted reflux could be utilized. The flexiWAVE microwave from Milestone was used for this promotion that shortened the reflux period from one hour to approximately 25 minutes. Small columns with tapered ends were prepared by the Scientific Glassblowing Shop at the University of Georgia using 24/40 tubing. These columns were employed in the laboratory with air adapters from the air lines in the hoods to provide positive pressure for the columns. Students injected their own samples into the NMR instrument during this second iteration of the experiment. TAs monitored the injection process and assisted with the processing of the resulting spectra in MestreNova. All spectra collected in the section were sent to the students for comparison purposes during analyses.

In total, 714 students were evaluated across four semesters. A post-lab survey was administered to monitor the students' identifications of their unknown alkyl halides and recovery rates for each component. The survey also tasked the students with ranking the usefulness of each analytical technique utilized in this experiment. Students self-reported confidence levels for correctly identifying their unknown alkyl halide with and without each analytical technique or observation.

HAZARDS

Safety glasses, lab coats, and lab gloves must always be worn. Please review online SDS sheets of all chemicals including products. Never seal a reflux apparatus airtight. Use caution to avoid inhalation when using silica gel; it is a severe respiratory irritant. Sodium hydroxide is a strong base and will cause severe burns if it comes in contact with your eyes or skin. Make sure

that your snorkel is properly positioned to avoid inhaling any hazardous fumes. Methylene chloride is volatile. Chronic exposure is possibly carcinogenic, and care must be taken to avoid breathing any fumes or allowing any liquid to contact your skin. Take care when dispensing and evaporating it. Make sure that your snorkels are turned on and functioning properly before dispensing any liquids. Any vapor or liquid exposure should be reported a TA immediately. Dispose of all liquid waste in the appropriately labeled bottle in the lab hood.

RESULTS

In total, 523 out of 714 students (73.25%) correctly identified the unknown alkyl halide across the between the Fall 2017 – Fall 2018 semesters. A full table of student responses is included (see Table 4.1) along with a breakdown of responses for each alkyl halide (see Table 4.2).

Table 4.1. Student Identifications of Unknown Alkyl Halides

Unknown Alkyl Halide	***# Correct***	***# Students***	***Percent***
1-bromo-3-methylbutane			
Fall 2017	51	57	89.47%
Spring 2018	100	110	90.91%
Summer 2018	25	33	75.76%
Fall 2018	47	55	85.45%
Total	223	255	87.45%
1-bromobutane			
Fall 2017	24	36	66.67%
Spring 2018	70	108	64.81%
Summer 2018	13	18	72.22%
Fall 2018	45	68	66.18%
Total	152	230	66.09%
1-bromopentane			
Fall 2017	35	57	61.40%
Spring 2018	45	86	52.33%
Summer 2018	17	25	68.00%
Fall 2018	51	61	83.61%
Total	148	229	64.63%
Combined Totals for all Alkyl Halides			
Fall 2017	110	150	73.33%
Spring 2018	215	304	70.72%
Summer 2018	55	76	72.37%
Fall 2018	143	184	77.71%
Overall	523	714	73.25%

Table 4.2. Complete Listing of Student Identifications of Unknown Alkyl Halides

Unknown Alkyl Halide	*1-bromo-3-methylbutane*	*1-bromobutane*	*1-bromopentane*
1-bromo-3-methylbutane			
Fall 2017 (n = 57)	51 (89.47%)	1 (1.75%)	5 (8.77%)
Spring 2018 (n = 110)	100 (90.90%)	6 (5.45%)	4 (3.64%)
Summer 2018 (n = 33)	25 (75.76%)	6 (18.18%)	2 (6.06%)
Fall 2018 (n = 55)	47 (85.45%)	5 (9.09%)	3 (5.45%)
1-bromobutane			
Fall 2017 (n = 36)	12 (33.33%)	24 (66.66%)	0 (0%)
Spring 2018 (n = 108)	25 (23.15%)	70 (64.81%)	13 (12.04%)
Summer 2018 (n = 18)	4 (2.22%)	13 (72.22%)	1 (5.56%)
Fall 2018 (n = 68)	17 (25.00%)	45 (66.17%)	6 (8.82%)
1-bromopentane			
Fall 2017 (n = 57)	14 (24.56%)	8 (14.04%)	35 (61.40%)
Spring 2018 (n = 86)	19 (22.09%)	22 (25.58%)	45 (52.33%)
Summer 2018 (n = 25)	5 (20.00%)	3 (12.00%)	17 (68.00%)
Fall 2018 (n = 61)	2 (3.28%)	8 (13.11%)	51 (83.60%)

The ^{1}H NMR spectra collected by students of their product ethers are shown in Figures 4.3-4.5. Three signals appear in all of the spectra: the two 2H doublets in the aromatic region of the spectrum and the 2H triplet at 3.6 ppm. The two 2H doublets represent the four protons on the aromatic ring, and the 2H triplet represents the methylene unit closest to the oxygen of the ether. When examining the ^{1}H NMR spectrum from Figure 4.3, students may begin with the 6H doublet farthest upfield. This upfield signal represents the protons that are the farthest away from the oxygen of the ether and the halogenated aromatic ring present in each potential product. By understanding that these six protons have one neighboring proton, the students may immediately rule out the 1-bromo-4-butoxybenzene and 1-bromo-4-pentoxybenzene products. This leaves 1-bromo-4-(isopentyloxy)benzene as the only option for this product. Upon further analysis, students recognize that the remaining 3Hs are represented by the overlapping signal that appears at ~1.6 ppm. By piecing all this information together, students can confirm that the product obtained in

Figure 4.3 is 1-bromo-4-(isopentyloxy)benzene, and the starting alkyl halide must have been 1-bromo-3-methylbutane. Similar processes can be applied to the products depicted in Figure 4.4 and 4.5. It is of note that the dispersion of signals on the 82 MHz NMR does not allow for unambiguous identification of methylene groups for the ethers. However, students readily identified 1-bromo-4-(isopentyloxy)benzene by the 6H doublet. The identification of 1-bromo-4-butoxybenzene improved when laboratory assistants instructed students to consider the integration value for the complex signal at 1.5 ppm. The identification of 1-bromo-4-pentoxybenzene improved when laboratory assistants instructed students to consider the integration value for the complex signals at 1.25 ppm and 1.5 ppm.

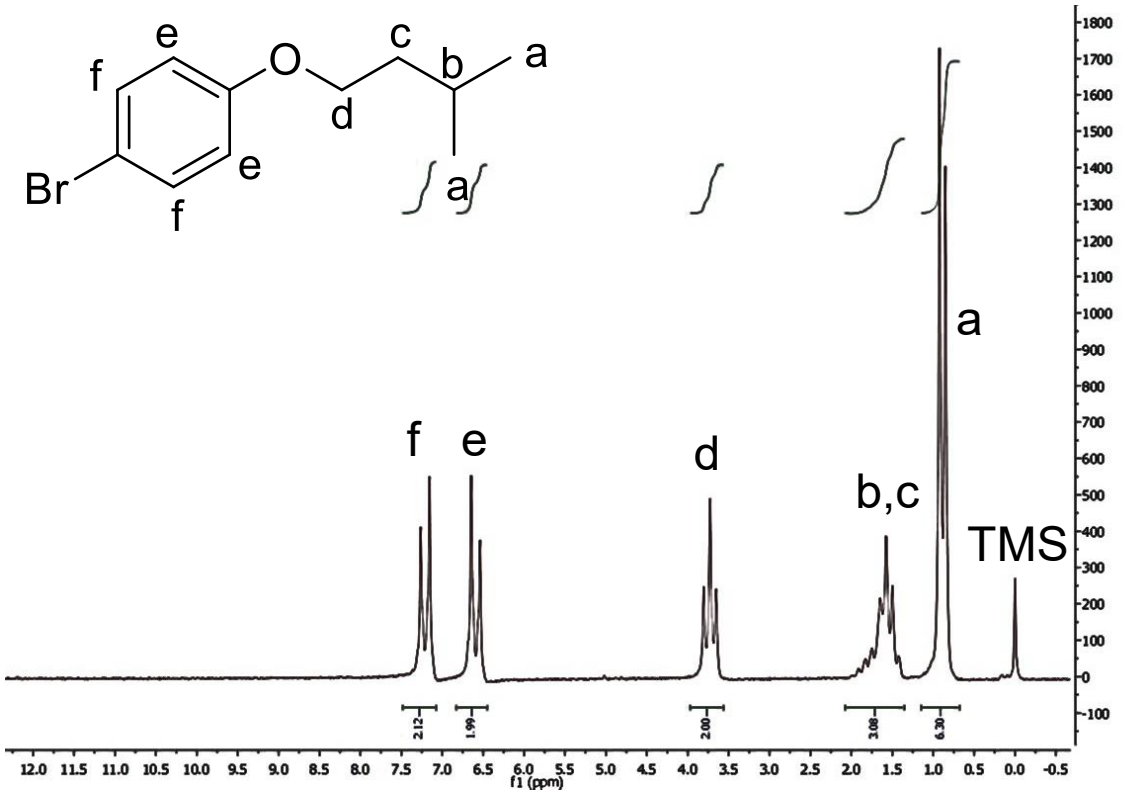


Figure 4.3. Student ^{1}H NMR spectrum of 1-bromo-4-(isopentyloxy)benzene from the 82 MHz picoSpin benchtop NMR. The students were provided with the integration values listed on the spectrum. The structure and assignments are provided for clarity. Two drops of tetramethylsilane (TMS) were included to mark 0 ppm.

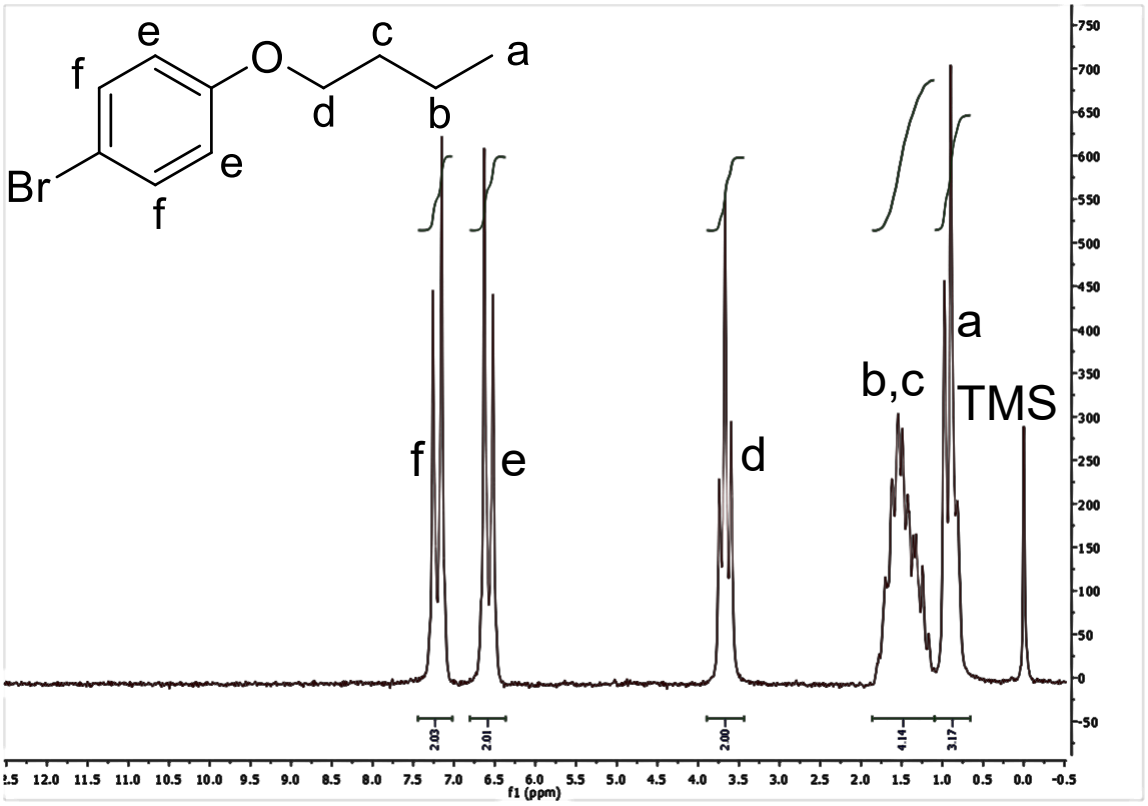


Figure 4.4. Student ^{1}H NMR spectrum of 1-bromo-4-butoxybenzene from the 82 MHz picoSpin benchtop ^{1}H NMR. The students were provided with the integration values listed on the spectrum. The structure and assignments are provided for clarity. Two drops of tetramethylsilane (TMS) were included to mark 0 ppm.

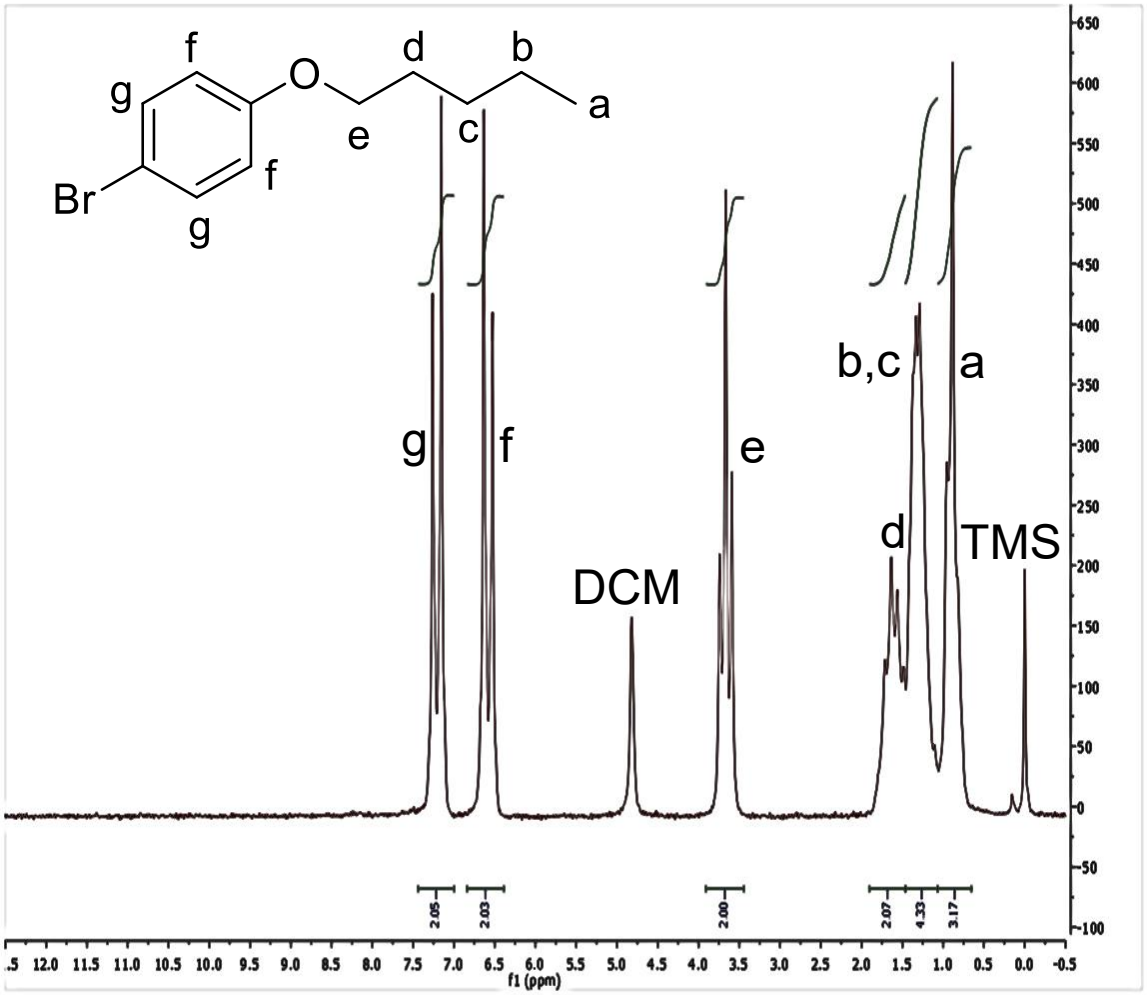


Figure 4.5. Student ^{1}H NMR spectrum of 1-bromo-4-pentoxybenzene from the 82 MHz picoSpin benchtop ^{1}H NMR. The students were provided with the integration values listed on the spectrum. The structure and assignments are provided for clarity. Two drops of tetramethylsilane (TMS) were included to mark 0 ppm.

DISCUSSION

In this experiment, students successfully prepared ethers through a Williamson ether synthesis using the conjugate base of 4-bromophenol and an unknown primary alkyl halide. This experiment provided students with access to MW-promoted reflux (beginning with the Spring 2018 iteration) and the characterization of student-synthesized products using benchtop NMR technology. The use of benchtop NMR technology in the undergraduate organic chemistry instructional laboratories is important because it provides an opportunity for students to prepare

their product and immediately collect spectra of their unique product. The characterization of these products reinforces the utility of this spectroscopic technique and gives the students real spectra, rather than idealized or computer-generated spectra. Prior to the Summer 2018 semester, this was the first MOE that students performed in the second semester organic chemistry course and it was the first experiment of the semester that included NMR spectroscopy. Therefore, in their analyses, students had to recall and apply their knowledge of spectral analyses. During the Summer 2018 and Fall 2018 iterations, the experiment was the second MOE that students performed in the second-semester organic chemistry course.

Benchtop ^{1}H NMR was reported as the most useful analytical technique for correctly deducing the identity of the unknown alkyl halide by 84.70%-93.48% of students from Fall 2017-Fall 2018 (see Figure 4.6). Of these students, 59.56%-75.00% of students correctly identified their alkyl halide. FTIR and TLC were generally reported as the second and third most useful analytical technique for correctly identifying the unknown alkyl halide. Conversely, 68.67%-86.84% of students reported color as the least useful analytical technique for correctly deducing the identity of the unknown alkyl halide (see Figure 4.7).

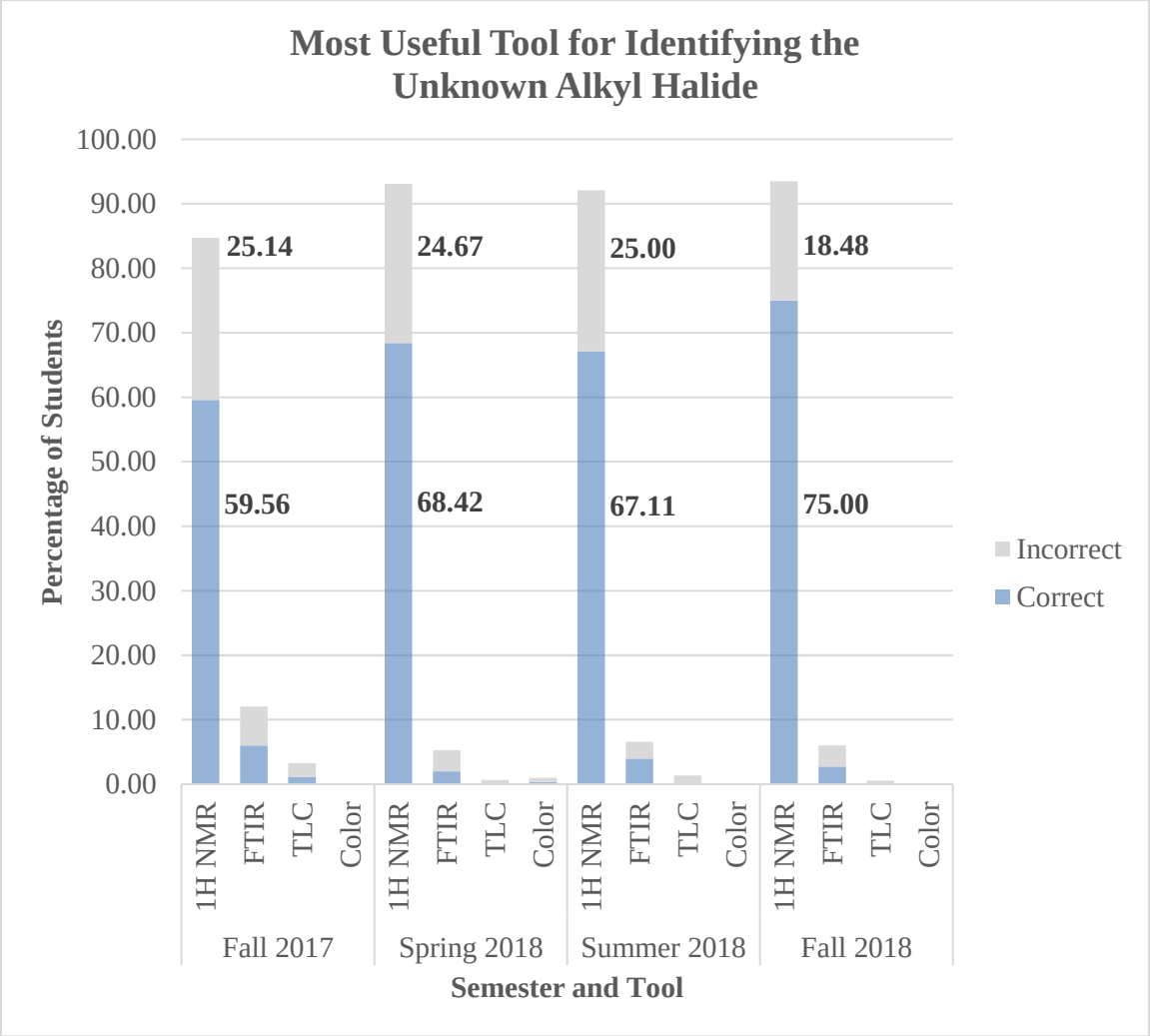


Figure 4.6. Postlab survey responses indicating which analytical tool was most useful for identifying the unknown alkyl halide. N = 150 students (Fall 2017), 304 students (Spring 2018), 76 students (Summer 2018), and 184 students (Fall 2018).

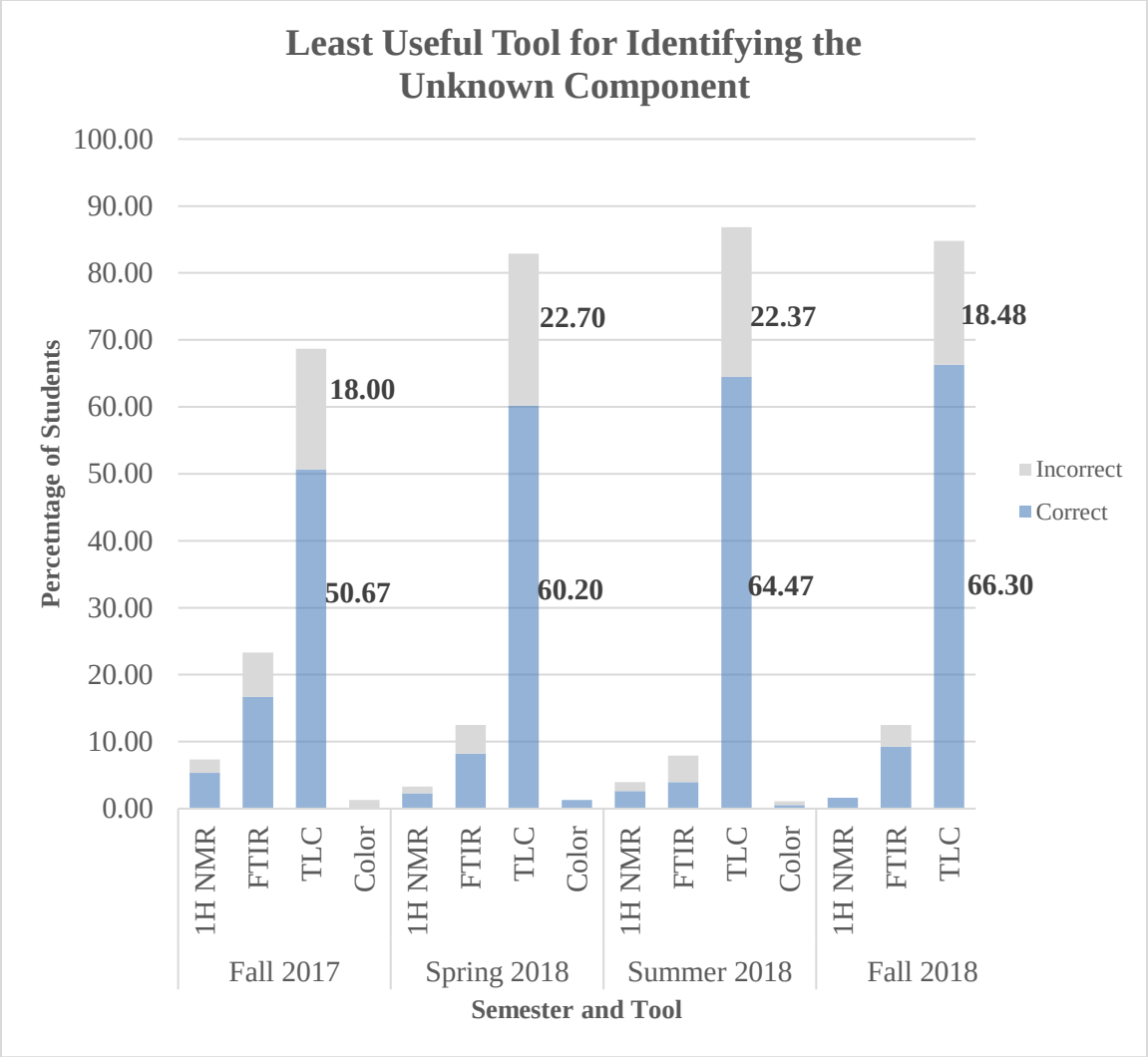


Figure 4.7. Postlab survey responses indicating which analytical tool was least useful for identifying the unknown alkyl halide. N = 150 students (Fall 2017), 304 students (Spring 2018), 76 students (Summer 2018), and 184 students (Fall 2018).

Students also reported their confidence levels for correctly identifying the unknown alkyl halide with *only* the benchtop ^{1}H NMR spectrum (see Figure 4.8). 38% of students in the Fall 2017 cohort reported being "most confident". Of these 57 students, 52 (91.23%) correctly identified their unknown alkyl halide. In subsequent iterations, 72.04% of Spring 2018 students, 86.84% of Summer 2018 students, and 75.54% of Fall 2018 students reported being "most confident". For the Fall 2017 semester, this was the first time that the students had seen an ^{1}H NMR spectrum of their products. The large increase in "most confident" responses is indicative of these later groups of

students having previously completed the Separation of a Three-Component Mixture MOE during their first-semester organic chemistry experience in Fall 2017. For the Summer 2018 and Fall 2018 cohorts, this experiment was the third MOE developed by the researcher that the students had encountered in all of their organic chemistry curriculum.

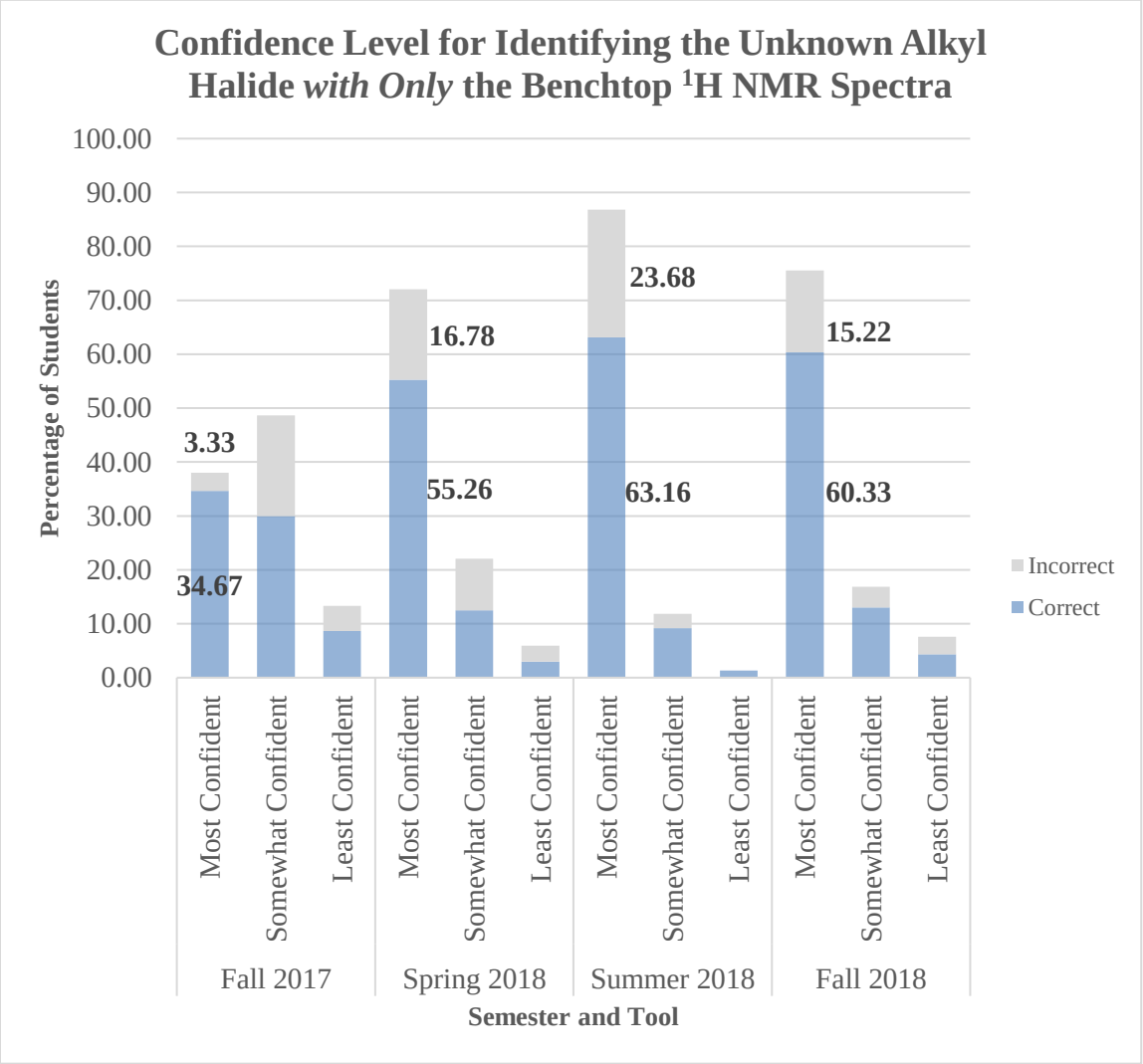


Figure 4.8. Postlab survey responses indicating student confidence levels for correctly identifying their unknown alkyl halide with only benchtop NMR spectra. N = 150 students (Fall 2017), 304 students (Spring 2018), 76 students (Summer 2018), and 184 students (Fall 2018).

Students also reported confidence levels for correctly identifying the unknown alkyl halide *without* the ^{1}H NMR spectrum (see Figure 4.9). Throughout the iterations, 71.33%-86.96% of

students reported being "not confident". In comparison to the responses with *only* NMR spectra, these responses for confidence *without* the NMR spectra offer similar insight. This may be attributed to the variety of time intervals for the Fall 2017 cohort for when NMR spectroscopy was introduced in their first-semester course and its appearance now in the laboratory associated with the second-semester course. It may also be attributed to the students' familiarity with the technique.

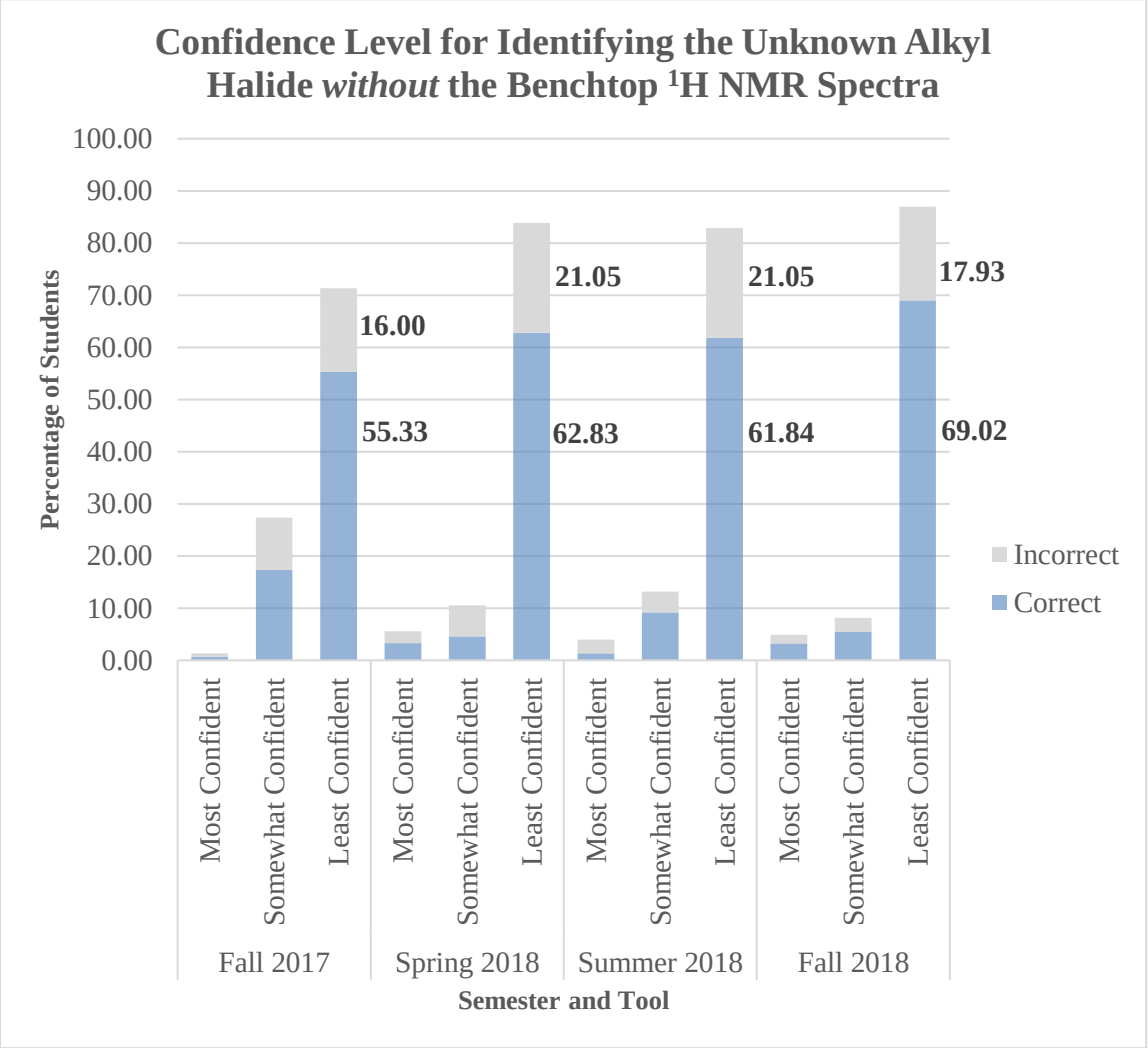


Figure 4.9. Postlab survey responses indicating student confidence levels for correctly identifying their unknown alkyl halide without benchtop NMR spectra. N = 150 students (Fall 2017), 304 students (Spring 2018), 76 students (Summer 2018), and 184 students (Fall 2018).

One limitation of this experiment is the removal of the solvent at the end of the procedure. If the solvent is not sufficiently removed via rotary evaporation, namely if the diethyl ether is not

fully removed, it can hinder the visibility of product signals upfield in the ^{1}H NMR spectrum. Therefore, it is crucial that students recognize when solvent is remaining in the sample and how to appropriately remove it. This can be managed through TA instruction when the students collect their ^{1}H NMR spectra. Secondly, because this experiment is employed at the beginning of the second semester curriculum in which NMR spectroscopy is employed, students must refresh their knowledge of this tool prior to attending class.

In the postlab the survey, students were provided opportunities to elaborate on their responses or give additional feedback. Students noted the ^{1}H NMR spectrum as being "crucial" in product analysis or the "primary factor" in being able deduce the starting material. Another student noted "it would take someone very experience with FTIR to differentiate [1-bromobutane and 1-bromopentane] using that technique alone", recognizing the utility of ^{1}H NMR in his or her analyses. Throughout the implementations, several students have elaborated on their survey responses. One student stated "^{1}H NMR was the most useful in determining the identity of the unknown alkyl halide. The splitting patterns and the chemical shifts of various groups helped a lot to determine the proper carbon chain attached to the bromine." Another student "…liked combining all the techniques to solve a problem." A third student commented on his or her use of comparison to identify the product: "The ^{1}H NMR spectrum was different for each potential product, so identifying both the number of distinct shifts and the splitting patterns made us fairly confident in ruling out possible compounds and confirming that our product was what we thought it was." This evidence highlights the critical analyses the students performed when deducing the identity of their specific unknown alkyl halide and the reinforcement of lecture-learned concepts in the undergraduate laboratory.

CONCLUSIONS

A multi-outcome experiment for the Williamson ether synthesis was developed and successfully implemented at the University of Georgia. A total of 523 of 714 students (73.25%)

correctly identified the unknown alkyl halide across the Fall 2017 – Fall 2018 semesters. This experiment created more individualized student learning experiences and reinforced lecture-learned concepts.

EXPERIMENT NOTES

This work was classified as "not human research" by the Institutional Review Board at the University of Georgia (STUDY00004291). Undergraduate Ryan Maynard assisted with the development and implementation of this experiment. Special thanks are extended to Caroline Glessner, Christina Cortes, Dr. Richard Hubbard, Fabian Tejedor Rojas, the CHEM 2212L TAs, and the CHEM 2212L students for assisting with or participating in the implementation in the organic chemistry main sequence laboratory course.

CHAPTER 5

IMPLEMENTATION OF BENCHTOP NMRS INTO ORGANIC CHEMISTRY TEACHING LABORATORIES THROUGH SPECTRAL ANALYSIS OF FISCHER ESTERIFICATION PRODUCTS

Kasey L. Yearty, Joseph T. Sharp, Emma K. Meehan, Doyle R. Wallace, Douglas M. Jackson, and Richard W. Morrison. Accepted by the *Journal of Chemical Education*. Reprinted here with permission of publisher.

ABSTRACT

^{1}H NMR analysis is an important analytical technique presented in introductory organic chemistry courses. NMR instrument access is limited for undergraduate organic chemistry students due to the size of the instrument, price of NMR solvents, and the maintenance level required for instrument upkeep. The University of Georgia Chemistry Department acquired three benchtop ^{1}H NMRs for the undergraduate organic laboratories. These instruments can sit on a standard lab bench, can analyze samples without NMR solvents, and are easily maintained. In this Fischer esterification experiment, students used unknown starting alcohols to synthesize esters through Fischer esterification. Upon completion of the reaction, students identified the unknown starting alcohol via spectral analyses of the products. Over the course of four semesters, 704 out of 940 students (75%) correctly identified the starting alcohol and 71% of students surveyed indicated that ^{1}H NMR spectrum was the most helpful identification tool in their analyses. This experiment established for students the utility of NMR spectral analysis and provided them with the opportunity to employ technology commonly used in academic research facilities.

BACKGROUND

The Fischer esterification reaction and its application in multi-outcome experiments has been studied for many years and is commonly included in organic chemistry laboratory curricula across the country.[62, 76-82] The reaction produces an ester and water from a carboxylic acid and an alcohol as shown in Figure 5.1. Because this reaction is reversible, Le Châtlier's principle can be utilized to drive the reaction towards the desired product esters. In practice, removal of the ester product through distillation drives the reaction to completion. The removal of water can accomplish the same goal if the product ester has a higher boiling point than water. In this experimental procedure, students were provided with a known carboxylic acid and an unknown alcohol for esterification. Students were then asked to identify the unknown alcohol via analysis of the ester product synthesized.

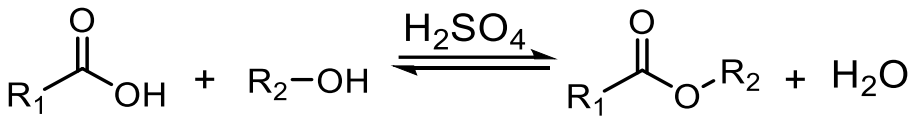


Figure 5.1. Generic Fischer esterification scheme

METHODS

Prior to ^{1}H NMR analysis, students performed a standard Fischer esterification experiment using acetic acid and an unknown alcohol (either 1-propanol, 1-butanol, or isopentyl alcohol) as shown in SI Procedure 5.1.[61] The product was transferred into a pre-labeled vial for ^{1}H NMR analysis. Students were provided with a tutorial for analyzing product spectra (see SI Handout 5.1), including a sample spectrum of ethyl acetate shown in Figure 5.2. A total of 940 students were evaluated. Our data includes the students' identification of their starting material from Spring 2014, Spring 2015, Fall 2015, and Spring 2016. In Fall 2015 and Spring 2016, a post-survey was also employed where the usefulness of ^{1}H NMR in the study was measured quantitatively in three ways: 1) by the correct identification of the starting alcohol; 2) by the student responses in the usefulness of the analytical tool; and 3) by student confidence levels in their response using only the ^{1}H NMR

spectrum. This survey data has been summarized in the discussion section of this chapter and in the Supporting Information.

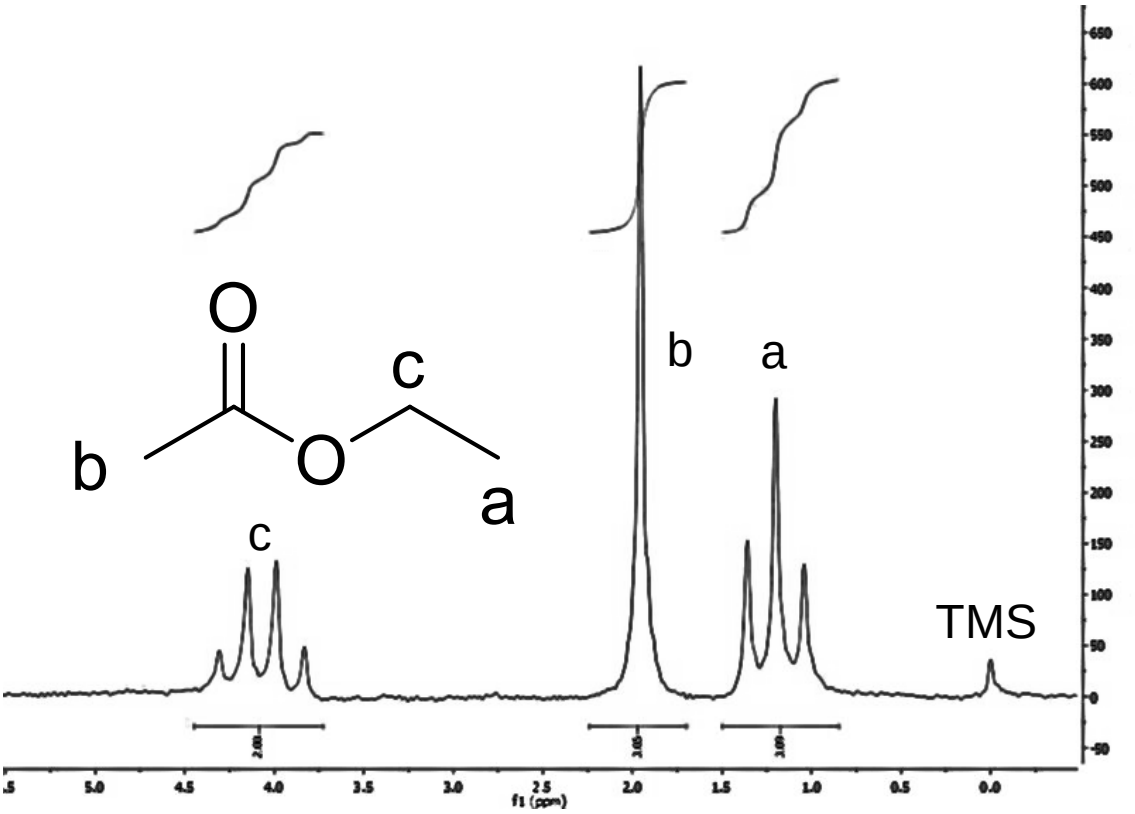


Figure 5.2. Sample ^{1}H NMR spectrum of ethyl acetate from the 45 MHz PicoSpin benchtop NMR. Two drops of tetramethylsilane (TMS) were included to mark 0 ppm.

HAZARDS

Safety glasses, lab coats, and lab gloves must always be worn. Please review online SDS sheets of all chemicals including products. Alcohols and esters are flammable. Acetic acid and sulfuric acid cause severe burns and should be treated with care. Pressure may build up when neutralizing with sodium bicarbonate due to the release of carbon dioxide gas. Perform the experiment in a well-ventilated room or hood away from sources of ignition.

RESULTS

For all four semesters studied, 704 students out of 940 (75%) students successfully identified the starting alcohol (see Table 5.1). After an initial correct identification rate of 90% in

Spring 2014, the subsequent semesters' correct identification rates were closer in value with an average of 68.3% ± 4.2%. Specific data listed by semester is depicted in the Supporting Information along with data listed by the unknown alcohol used for the reaction.

Table 5.1. Combined Semester Data by Alcohol for Spring 2014, Spring 2015, Fall 2015 and Spring 2016

Unknown	*Students*	*Correct*	*Percent*
1-Propanol	408	336	82.35%
1-Butanol	282	160	56.74%
Isopentyl alcohol	250	208	83.20%
Total Semester Responses	*Students*	*Correct*	*Percent*
Spring 2014	260	233	89.62%
Spring 2015	164	110	67.07%
Fall 2015	214	140	65.42%
Spring 2016	302	221	73.18%
Total Combined Student Responses			
Combined Spring Semesters	726	564	77.69%
Fall Semester	214	140	65.42%
All Semesters	940	704	74.89%

The ^{1}H NMR spectra collected by students of their product esters are shown in Figures 5.3-5.5. There are two signals that appear in all three product spectra. First, the students will see a triplet located near 4.1 ppm, which represents the 2H on the methylene unit closest to the singly bound oxygen of the ester. A 3H singlet near 1.0 ppm represents the 3H on the terminal carbon of the ethanoate parent chain. The other signals represent the remaining protons on the products and can be used to distinguish the products. The splitting patterns on Figure 5.3 are the most well-resolved. The students can see a 3H triplet and a 2H multiplet. This represents the only structure with two unique sets of protons left: propyl acetate. The dispersion of signals on the 45 MHz NMR does not allow for unambiguous identification of methylene groups for the butyl and isopentyl acetate esters. However, students can readily identify isopentyl acetate by the 6H doublet (see Figure 5.5).

Identification of butyl acetate improved when laboratory assistants instructed students to consider the integration value for the complex signal at δ 1.5 (see Figure 5.4).

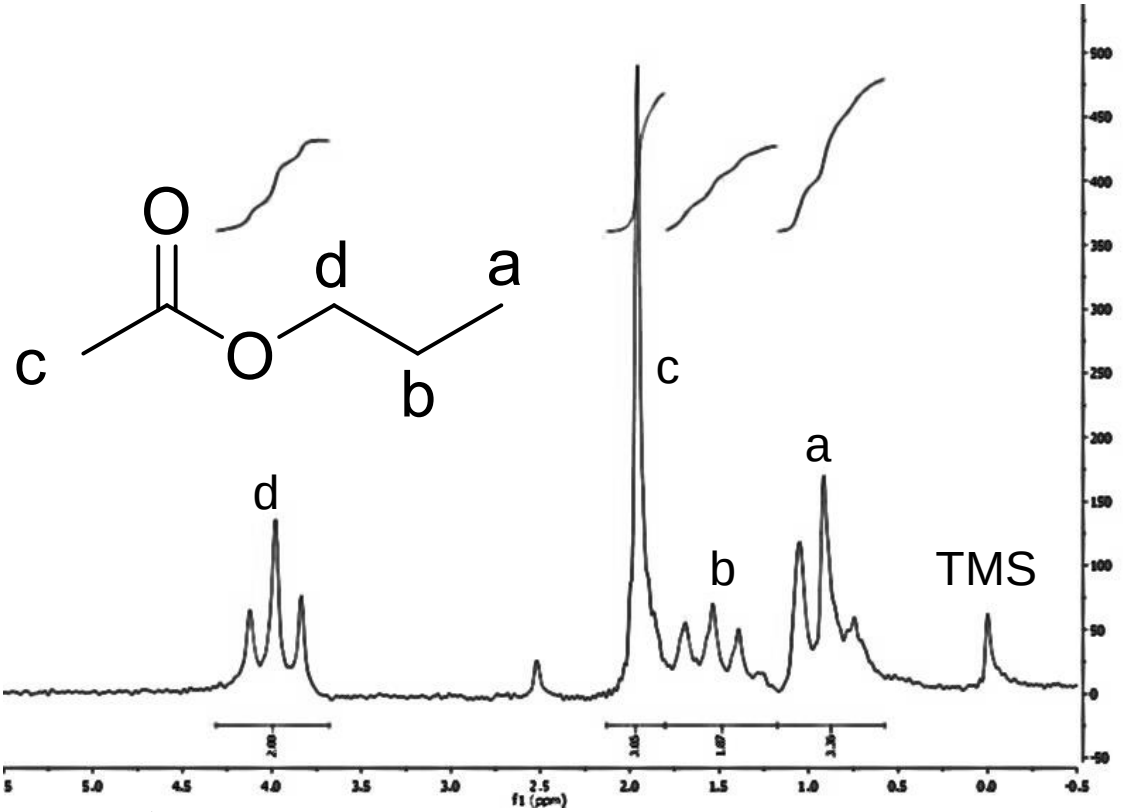


Figure 5.3. [1]H NMR spectrum from the 45 MHz PicoSpin NMR for Unknown Q31641A (Propyl Acetate) provided to students. The students were provided with the integration values listed on the spectrum. The integration values, structure, and assignments are provided for clarity. Two drops of tetramethylsilane (TMS) were included to mark 0 ppm.

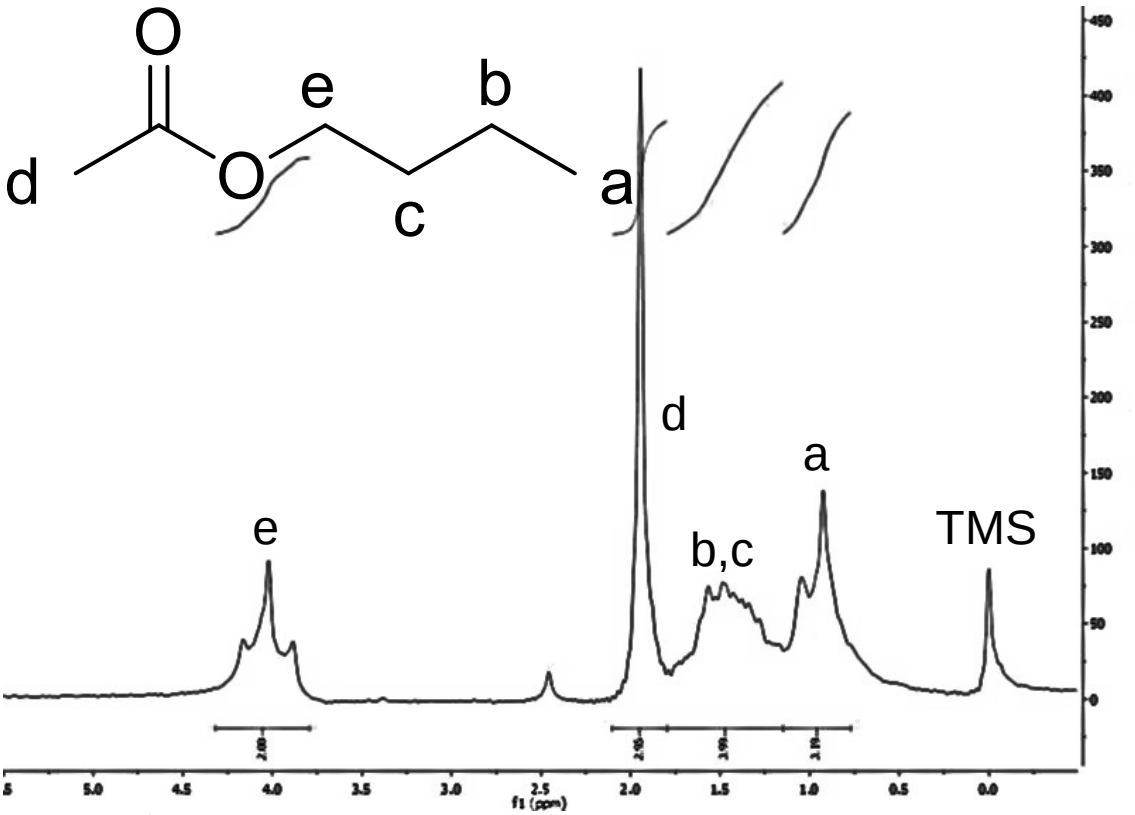


Figure 5.4. ^{1}H NMR spectrum for Unknown 552743B (Butyl Acetate) from the 45 MHz PicoSpin NMR provided to students. The students were provided with the integration values listed on the spectrum. The integration values, structure, and assignments are provided for clarity. Two drops of tetramethylsilane (TMS) were included to mark 0 ppm. Note: The 4H complex signal at δ 1.5 corresponds to methylene protons C and D. The integration value for this complex signal uniquely identified butyl acetate.

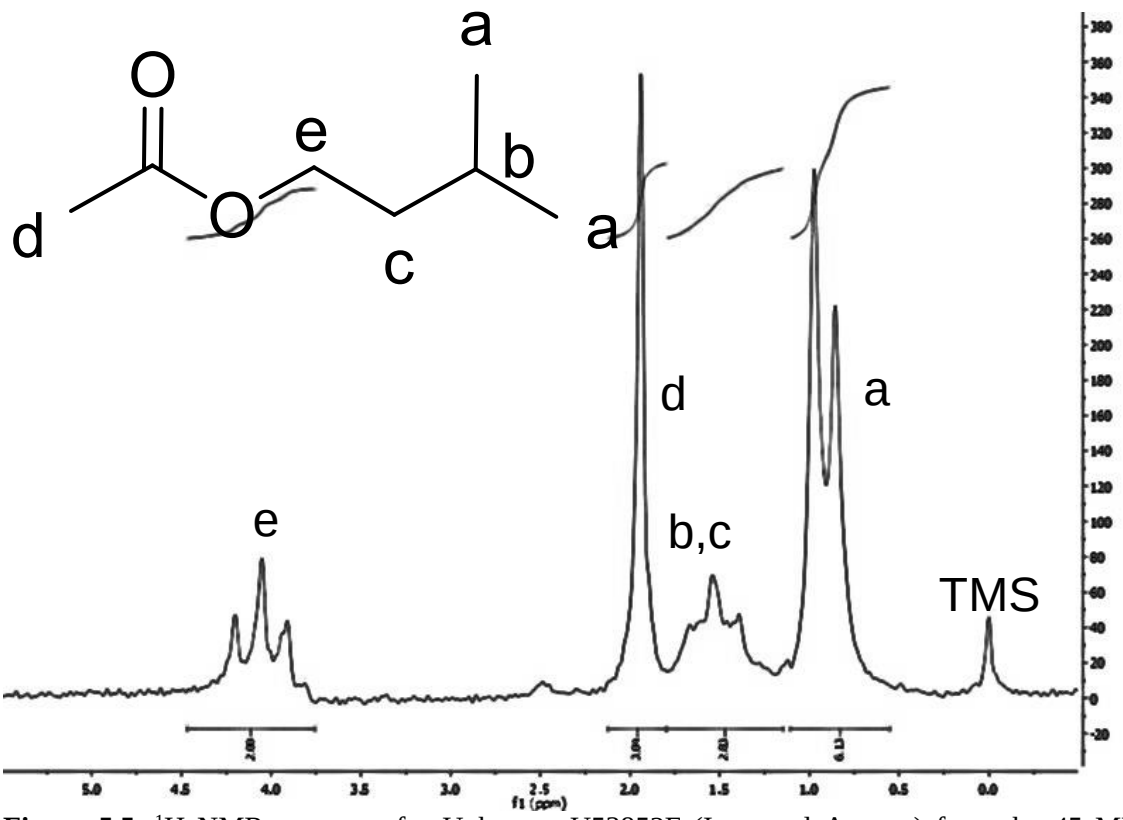


Figure 5.5. ^{1}H NMR spectrum for Unknown U53852F (Isopentyl Acetate) from the 45 MHz PicoSpin NMR provided to students. The students were provided with the integration values listed on the spectrum. The integration values, structure, and assignments are provided for clarity. Two drops of tetramethylsilane (TMS) were included to mark 0 ppm.

DISCUSSION

Each analytical technique used to characterize the ester product provided a piece of the puzzle to identify the starting alcohol. The FTIR spectra indicated that an ester was present but did not indicate which specific ester was formed. However, collecting FTIR spectra of the starting materials and product was beneficial for students because it allowed them to monitor the reaction for completion, observing the disappearance of the alcohol stretch and the appearance of the carbonyl stretch. It was also instrumental in reinforcing the purpose of FTIR; i.e. to determine the functional groups of a molecule. The boiling point determination proved inconsistent, as students sometimes recorded boiling points that were several tens of degrees lower than the literature value of the product ester. Some groups had trouble obtaining enough volume of the product to successfully distill the ester, which was remedied by grouping students that were assigned the same

unknown into larger groups and combining their samples in order to obtain the boiling point using a Hickman still. Students also noted the fruity aroma of the volatile product, which some claimed helpful. The ^{1}H NMR spectra provided the most clues about the individual connectivity of atoms as described in the earlier results section of this chapter.

As a part of the postlab report, students were asked a series of questions to rank the identification tools that they felt were most useful in successfully identifying the unknown starting alcohol. Figure 5.6 shows that 75.70% of students surveyed in Fall 2015 and 67.22% of students surveyed in Fall 2016 indicated that ^{1}H NMR was the most helpful tool. This ranking of tool utility was followed by FTIR spectroscopy, scent, and boiling point in Fall 2015. In Spring 2016, the ranking was, in order of most useful to least, ^{1}H NMR, boiling point, scent, and FTIR spectroscopy. The color was reported as the least useful tool in both semesters (see Figure 5.7).

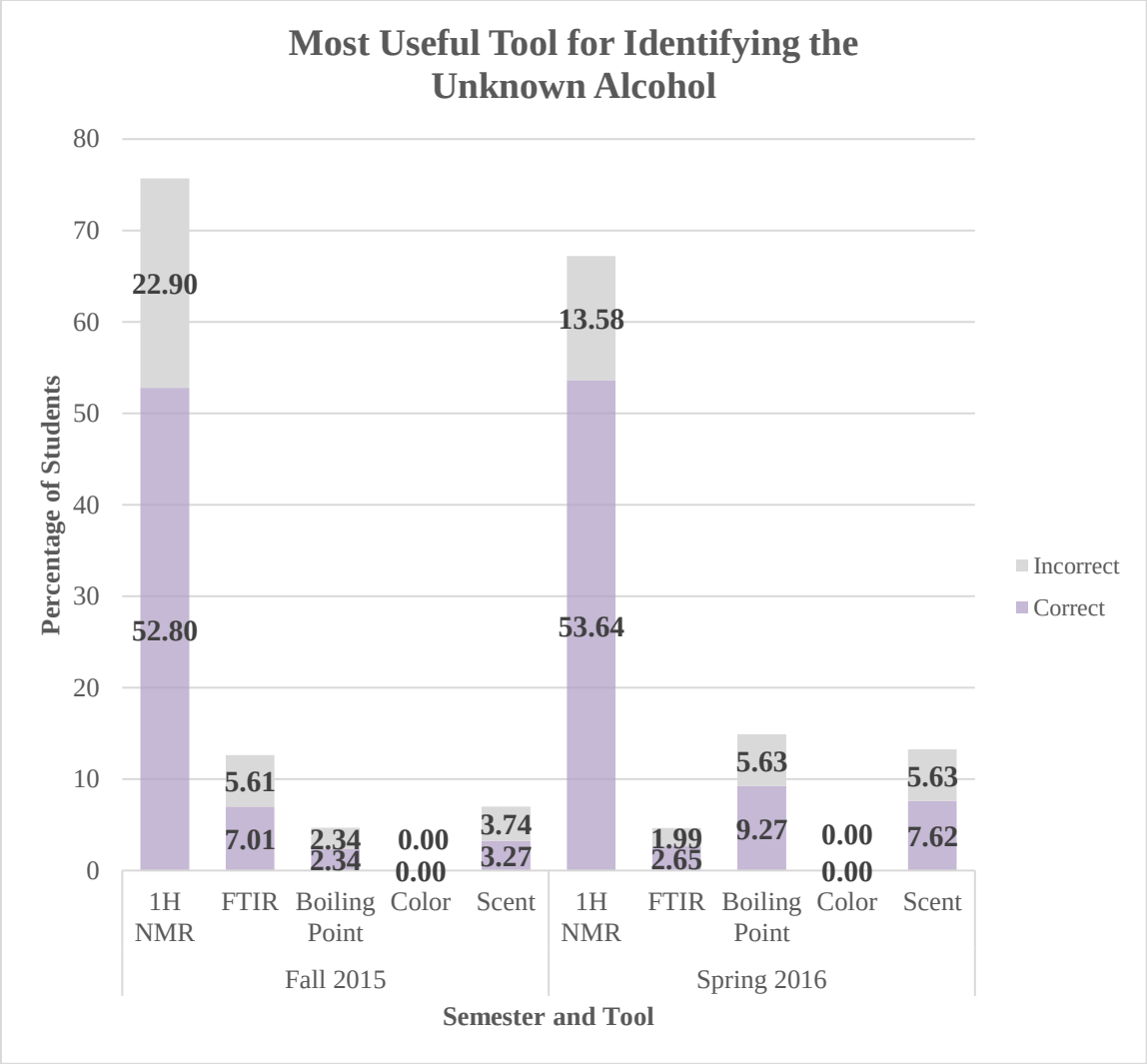


Figure 5.6. Postlab survey responses indicating which analytical tool was most useful for identifying the unknown alcohol. N = 214 students (Fall 2015) and 302 students (Spring 2016). This survey question was not administered during the Spring 2014 and Spring 2015 iterations of the experiment.

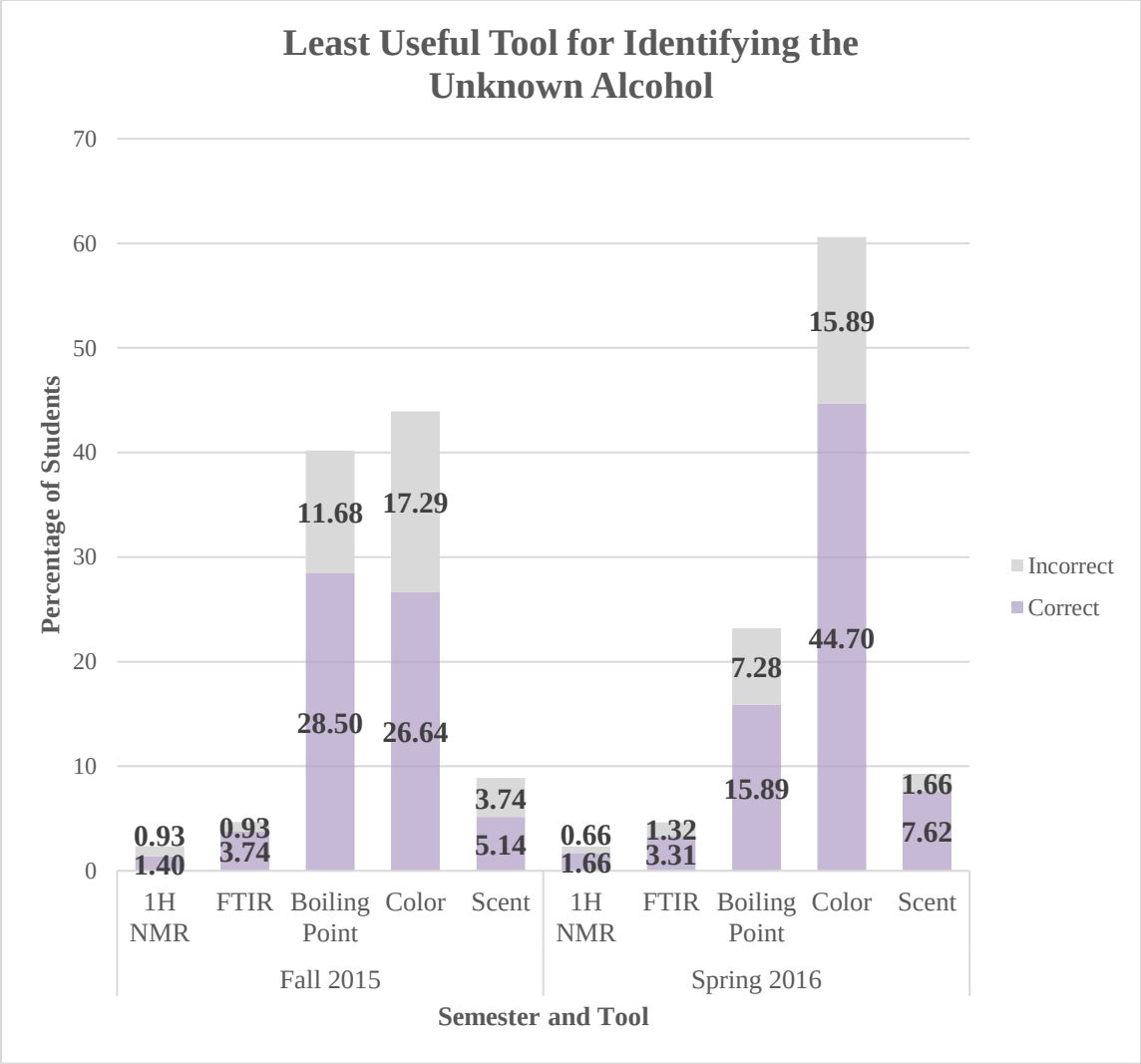


Figure 5.7. Postlab survey responses indicating which analytical tool was least useful for identifying the unknown alcohol. N = 214 students (Fall 2015) and 302 students (Spring 2016). This survey question was not administered during the Spring 2014 and Spring 2015 iterations of the experiment.

Surveyed students indicated feeling "most confident" (32.71% in Fall 2015 and 36.42% in Spring 2016) or "somewhat confident" (49.51% in Fall 2015 and 43.38% in Spring 2016) in correctly identifying the unknown alcohol with only the benchtop ^{1}H NMR data (Figure 5.8). Recall that this is the very first MOE that students encountered, meaning that this is the first time that the students collected a spectrum of their own products and analyzed them. The level of uncertainty illustrated students' previous reliance on other identification techniques and inexperience with non-

idealized spectra. It is also of note that the majority of students who selected “somewhat confident” still identified their unknown alcohol correctly.

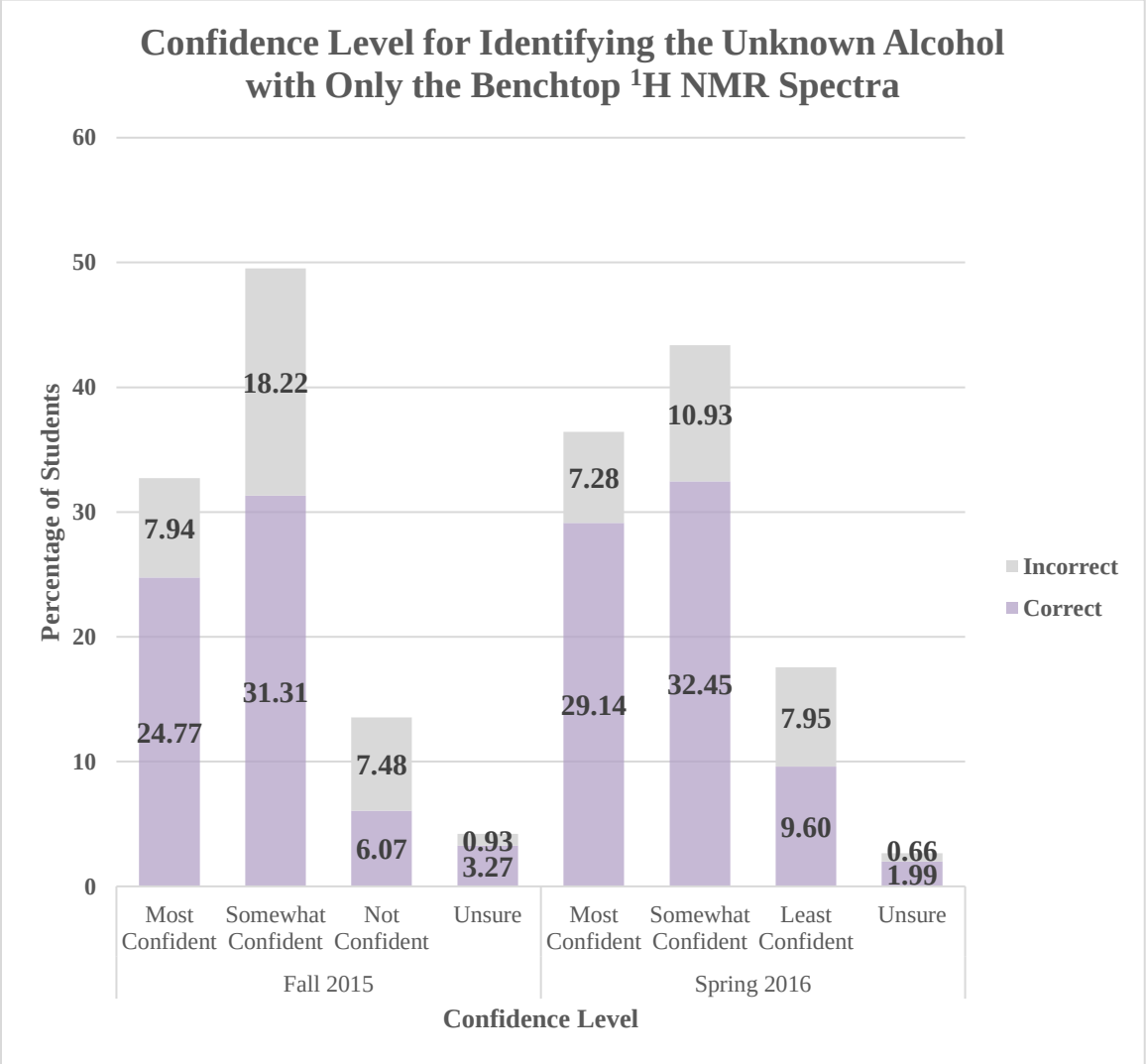


Figure 5.8. Postlab survey responses indicating student confidence levels for correctly identifying their unknown alcohol with only benchtop NMR spectra. N = 214 students (Fall 2015) and 302 students (Spring 2016). “Unsure” was included as a response option in the earliest MOE surveys, but was removed in later surveys because of its similarity in connotation to the “not confident” response. This survey question was not administered during the Spring 2014 and Spring 2015 iterations of the experiment.

On the other hand, students indicated feeling “not confident” (45.79% in Fall 2015 and 45.36% in Spring 2016) or only “somewhat confident” (34.58% in Fall 2015 and 40.40% in Spring 2016) in correctly identifying the unknown starting alcohol without the inclusion of the benchtop

^{1}H NMR data (Figure 5.9). This demonstrated students' understanding that the other tools for identification were less beneficial for structure elucidation than the ^{1}H NMR data. It is also of note that while the students understood this, the students' reported confidence levels illustrate that they are not yet comfortable analyzing non-idealized spectra. At this point in the main sequence (high-enrollment) sophomore organic chemistry curriculum, students have only encountered idealized or simulated spectra in their lecture coursework, not in the laboratory setting.

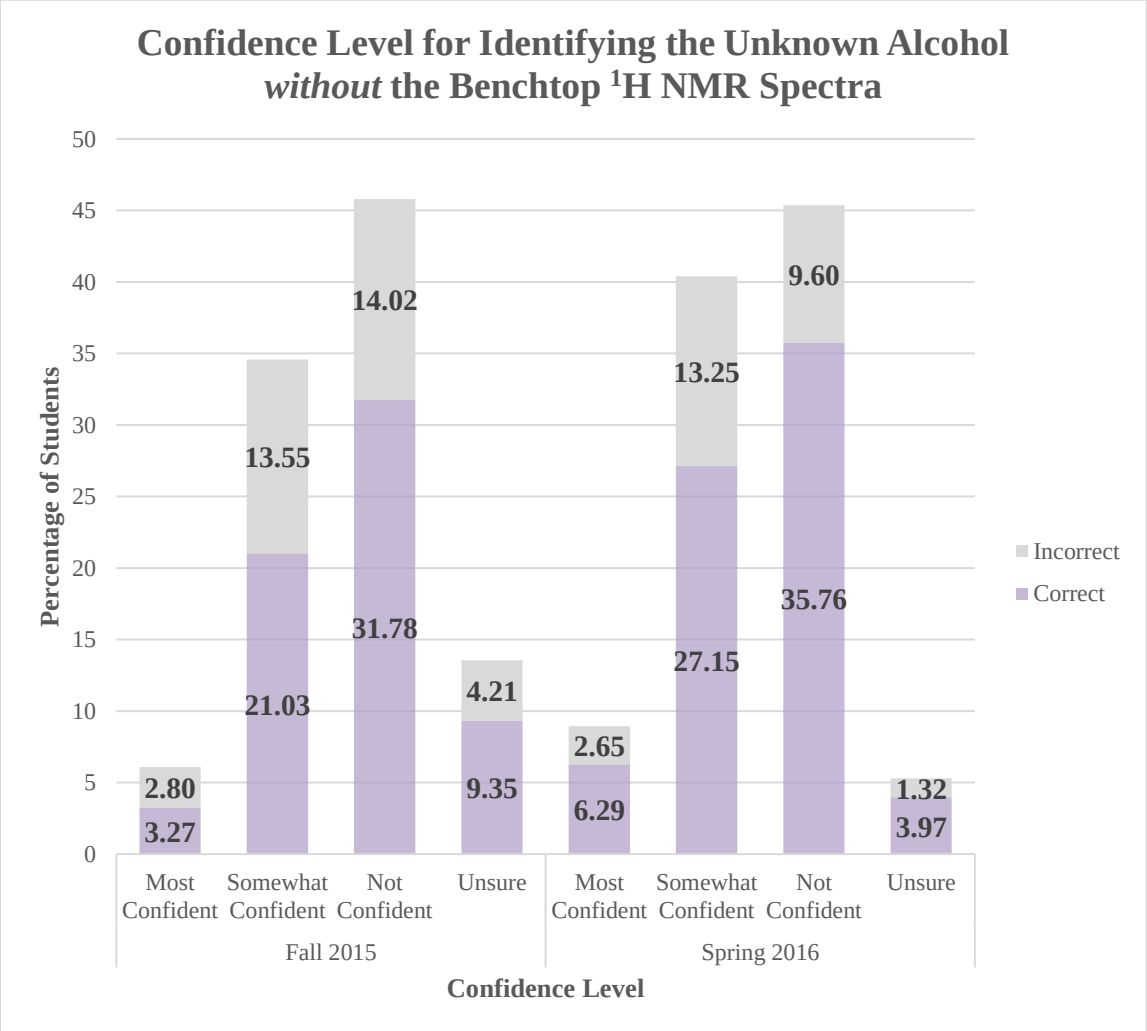


Figure 5.9. Postlab survey responses indicating student confidence levels for correctly identifying their unknown alcohol without benchtop NMR spectra. N = 214 students (Fall 2015) and 302 students (Spring 2016). "Unsure" was included as a response option in the earliest MOE surveys, but was removed in later surveys because of its similarity in connotation to the "not confident" response. This survey question was not administered during the Spring 2014 and Spring 2015 iterations of the experiment.

Overall, both students and teaching assistants surveyed provided positive feedback when asked about the incorporation of the benchtop ^{1}H NMR instrument into the Fischer esterification experiment. One student stated that "^{1}H NMR was the easiest and most efficient method of identification of the unknown alcohol." Another student stated that "it is important for the students to actually see a ^{1}H NMR spectrum that is not straight out of the textbook. It helps give a little clarity between lab and lecture." Students also stated that without the ^{1}H NMR data, "it would have been very hard for me to identify my unknown" and that the incorporation of the benchtop ^{1}H NMR data "should continue to be used for this experiment in the future."

The teaching assistants (TAs) for the students participating in the survey indicated that the benchtop ^{1}H NMR data was the most useful tool for students to correctly identify the unknown. Most indicated that students would not be able to correctly identify the unknown alcohol without the benchtop ^{1}H NMR data and indicated confidence that the students would be able to correctly identify the unknown alcohols with only the benchtop ^{1}H NMR data for the product ester.

CONCLUSIONS

This experiment allowed students to gain hands-on experience with ^{1}H NMR spectroscopy and analysis of actual student experimental results, as opposed to computer generated or idealized spectra. Overall, 75% of students over four semesters correctly identified their unknown starting alcohol from experimental results, with 71% of surveyed students indicating that the ^{1}H NMR spectrum was most helpful in identifying the ester product.

EXPERIMENT NOTES

All data prior to Spring 2016 was collected on the 45 MHz benchtop NMR instrument. This project was financially supported by the UGA Office of STEM Education as a part of the Board of Regents' STEM Initiative. The work presented in this chapter was published by the author and colleagues in the *Journal of Chemical Education*.[83] Changes have been made to streamline this chapter of the dissertation with the entire body of this dissertation (i.e. the description of MOEs

from the abstract and background section was removed because it is in Chapter 1, tables and figures were moved to the chapter rather than in the supporting information). This work was classified as "not human research" by the Institutional Review Board at the University of Georgia (STUDY00004198). Undergraduate Joseph (Joey) Sharp assisted with the development of this experiment. Undergraduates Emma Kate Meehan and Doyle Wallace assisted with the implementation of this experiment. Special thanks are extended to Dr. Richard Hubbard, Fabian Tejedor Rojas, the CHEM 2212L TAs, and the CHEM 2212L students for assisting with or participating in the implementation in the organic chemistry main sequence laboratory course.

CHAPTER 6

CHEMISTRY IN THE ARTS: AN INTERDISCIPLINARY LOOK AT STUDENT-SYNTHESIZED AZO DYES

Kasey L. Yearty, Christina N. Cortes, Margaret W. Morrison, and Richard W. Morrison. To be submitted to the *Journal of Chemical Education*.

ABSTRACT

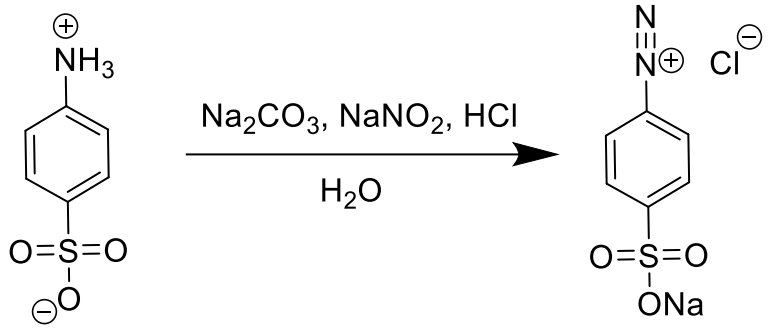
Multi-outcome experiments (MOEs) are used in organic chemistry labs to provide an alternative to traditional "cookbook" experiments; these MOEs require students to utilize critical thinking skills, thereby providing a unique and productive learning experience for students. Herein, *Organic Chemistry II* laboratory students prepared an azo dye by reacting two starting materials, only one of which was known to the students. The students were given three possible options for the identity of the unknown starting material. Upon completion of the reaction, the students recorded standard measurements, such as mass and color, and used FTIR and benchtop ^{1}H NMR spectroscopies to identify the structure of the resulting molecule. The students then employed their critical thinking skills to retroactively identify the unknown starting material. The multi-outcome method demonstrates the specific utility of NMR spectroscopy, which gave the students insight into the connectivity of atoms in their product. In addition to the experiment's utility for enrollees in the *Organic Chemistry II* laboratory course, *Chemistry in the Arts* students studied the dyes produced by the *Organic Chemistry II* students to learn how light interacts with these dyes and applied them to various media, creating unique colors and works of art. Both courses engaged with the same materials in vastly different ways, helping each to better understand their field's role in the process and how it is complimented by the other.

BACKGROUND

The Azo Dye experiment is unique among the six included in this document. Whereas the other five consisted solely of MOE development for existing experiment types, the Azo Dye also includes a portion where the product of the MOE experiment was taken to the UGA campus in Cortona, Italy. There, students enrolled in the *Chemistry in the Arts* course analyzed the products with UV-Vis spectroscopy, mixed egg tempura with the dyes, and created paintings. These two phases of the experiment development and implementation are labeled Phase I (the MOE) and Phase II (pigment application) in the remainder of this chapter. The reaction scheme for Phase I along with the unknown coupling reagents used are described in Figures 6.1 and 6.2.

In addition to the experiment's utility for enrollees in the *Honors/Majors Advanced Organic Chemistry II* course *(referred to as Honors/Majors)*, the *Chemistry in the Arts* students used the product azo dyes to learn how light interacts with these dyes and apply them to various media, creating unique works of art. Since the *Chemistry in the Arts* students did not taken part in the synthesis of the azo dyes, they began their analyses of the dyes by taking a series of UV-Vis spectra. This analysis allowed them to determine the precise colorizing pigment that corresponded with the dyes. Both courses engaged with the same materials in vastly different ways, helping each to understand better their field's role in the process and how it is complimented by other. In addition to developing greater technical proficiency in their own field, students garnered a greater appreciation for the interdisciplinary nature of these processes. Similar experiments involving azo dyes have been documented in the literature, with some including service or outreach efforts to showcase the application of azo dyes.[84-92]

Part 1: Formation of the Diazonium Salt



Part 2: Formation of the Azo Dye

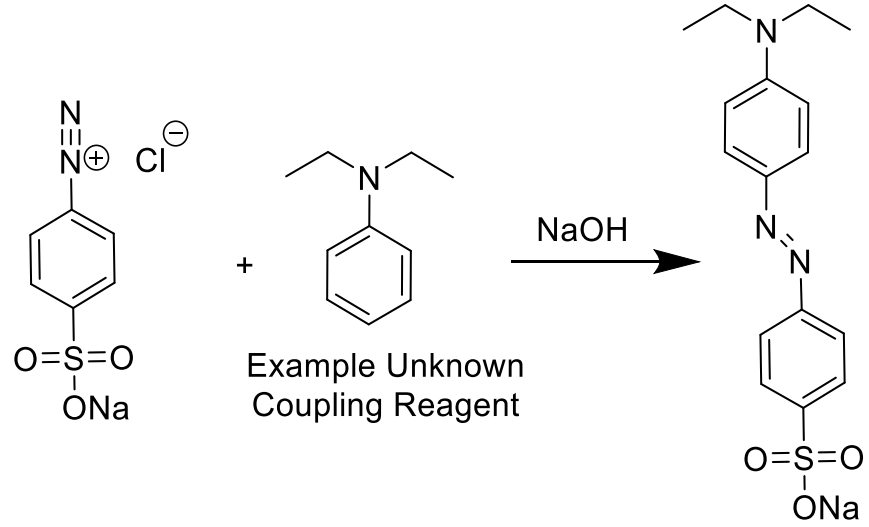


Figure 6.1. Example Reaction Scheme for the Synthesis of Azo Dyes.

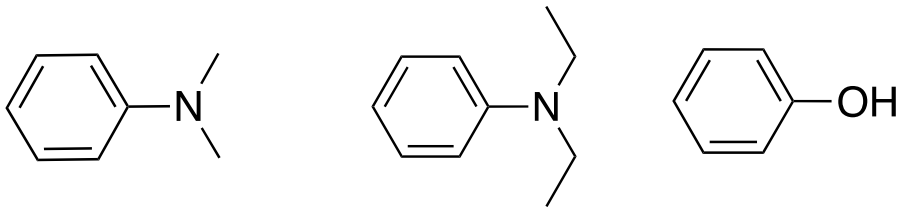


Figure 6.2. Coupling reagent options provided to students (left to right: N,N-dimethylaniline, N,N-diethylaniline, phenol).

The University of Georgia Cortona, Italy campus offers a *Chemistry in the Arts* course (CHEM 1110) (see Figure 6.3). This course is designed for non-science majors and fulfills the Area

II Core Requirement as well as the Franklin College requirement for a science course with accompanying laboratory. In the *Chemistry in the Arts* course, students discuss the colors of the visible light spectrum and learn about UV-Vis spectroscopy. The Phase II portion of this experiment is designed to provide *Chemistry in the Arts* students with samples synthesized by *Honors/Majors* laboratory students in order to perform UV-Vis spectroscopic analyses.

Abbreviations have been used to describe the dyes with a shorter moniker. In the *Honors/Majors* segment, the dyes are described by their common names, where applicable. For example, Methyl Orange represents sodium 4-{[4-(dimethylamino)phenyl]diazenyl}benzene-1-sulfonate. Ethyl Orange represents sodium 4-((4-(diethylamino)phenyl)diazenyl)benzenesulfonate. The dye prepared with phenol does not have a common name, so it is referred to as simply Phenol. The Phenol dye represents sodium 4-((hydroxyphenyl)diazendyl)benzenesulfonate. Because of the art students' familiarity with color in the Chemistry in the Arts course, the dyes were provided different monikers for this phase of the project. While in Cortona, ethyl orange was referred to as the red-orange dye, methyl orange was referred to as the orange dye, and the dye produced with phenol was referred to as the yellow dye. These abbreviations can be found throughout Chapter 6 and the corresponding segment of the SI.

Figure 6.3. Map of Italy with a flag indicating the location of Cortona

PHASE I – DEVELOPMENT OF THE AZO DYE MOE

METHODS

During Phase I, the procedures for the multi-outcome experiment were developed and implemented. The resulting procedure (modified from a procedure by Dr. Jeff Altig) involved the combination of an aminobenzenesulfonic acid and an aromatic coupling reagent, resulting in the synthesis of various azo dyes.[93] In total, three coupling reagents were included in the procedure: N,N-dimethylaniline, N,N-diethylaniline, and phenol. Students were provided with three potential coupling reagents that served as their specific unknown in the experiment. The research goal of Phase I was to create a viable set of procedures to produce and analyze pigments that the *Honors/Majors* students classify by their different colors and spectroscopic characteristics.

In total, 54 *Honors/Majors* students were evaluated during the Spring 2018 semester. Students collected FTIR spectra and were provided with the 400 MHz NMR spectra of their individual products. The ^{1}H NMR samples were prepared with D_2O. The resulting spectra were processed by the researcher using MestreNova. Because the students were provided with the individual 400 MHz NMR spectra of their products, further directions were provided to students about the location of remaining water and the deuterated NMR solvent signals in the spectra. All spectra collected in the section were sent to the students for comparison purposes during analyses. The students also completed the standard MOE post-lab survey to electronically document their results.

HAZARDS

Safety glasses, lab gloves, and lab coats must always be worn. Please review online SDS sheets of all chemicals including products. The diazotized sulfanilic acid must remain cooled in an ice bath until it is to be used. Take care when working with sodium nitrite, which is toxic to aquatic life. Use caution when working with sodium hydroxide (NaOH) as it is caustic and may cause burns. Make sure that your localized ventilation system (snorkel) is properly positioned to avoid inhaling any hazardous fumes. Make sure that your snorkels are turned on and functioning properly before dispensing any liquids. Report any spills or accidents immediately to your TA. All generated waste must be collected in the appropriately labeled hazardous waste container.

RESULTS

For the 54 survey respondents, 51 out of 54 *Honors/Majors* students (94.44%) correctly identified their unknown coupling reagent in the Spring 2018 semester. The student identifications of their unknown alcohols are summarized in Tables 6.1-6.2. During the iteration, students reported the mass of their final product as being an average of 3.031 g (90%) of methyl orange, 1.974 g (68%) of ethyl orange, and 1.840 g (45%) of the phenol dye. Figure 6.4 showcases all the dyes collected by the students during this iteration.

Table 6.1. Student Identifications of Unknown Coupling Reagents

Unknown Coupling Reagent	*# Correct*	*# Students*	*Percent*
N,N-dimethylaniline	16	18	88.89%
N,N-diethylaniline	19	19	100.00%
Phenol	16	17	94.12%
Total	51	54	94.44%

Table 6.2. Complete Listing of Student Identifications of Unknown Coupling Reagents

Unknown Coupling Reagent	*N,N-dimethylaniline*	*N,N-diethylaniline*	*Phenol*
N,N-dimethylaniline			
Spring 2018 (n = 18)	16 (88.89%)	2 (11.11%)	0 (0%)
N,N-diethylaniline			
Spring 2018 (n = 19)	0 (0%)	19 (100%)	0 (0%)
Phenol			
Spring 2018 (n = 17)	0 (0%)	1 (5.88%)	16 (94.12%)

Figure 6.4. Compilation of the dyes produced by the Spring 2018 *Honors/Majors* students.

DISCUSSION

As previously stated, this experiment was implemented in the Spring 2018 *Honors/Majors* course. The implementation served as the beta-test of the developed experimental procedure with the researcher being present during all trials to observe TAs and students throughout the course of the MOE. This beta-testing process is consistent with how other MOEs described in this dissertation

were developed and provides opportunities for the researcher to further streamline or incorporate small revisions as needed. After the observation period, the researcher noted that no further modifications for TAs or students were needed in the described experiment. The discussion below incorporates the observations taken during the beta-testing.

One issue encountered during this procedure was that students rushed through the recrystallization process or hastily left product in the Büchner funnel during isolation. One group also recrystallized their product at too high a temperature, essentially burning the product. This produced a markedly darker color than other samples collected using the same reagents. This can be seen in the second vial from the left in Figure 6.4. This vial should be the same color and consistency as the vial to its immediate right. The darker color and chunkier consistency were immediate results of this user error. The NMR spectrum for the burnt sample also depicted greater concentrations of trace solvents and impurities. The TAs of the sections in which this occurred immediately addressed this with students as it was occurring and followed up with a section-wide announcement to prevent these actions from continuing in the section.

Due to solubility issues, the benchtop NMR instrument is not a suitable instrument for product characterization. Figures 6.5-6.7 showcase example spectra collected by TAs in the NMR facility for the UGA Chemistry Department. The students were provided with locations for potential trace solvents, such as ethanol, water, and DMSO. Students then used the remaining signals to identify the structure of their product and deduce the unknown coupling reagent used. For example, when considering Figure 6.5, students recognize that there are 8H in the aromatic region. These protons are present in each product dyes, so the remaining signals will provide more distinguishing clues about the remainder of the structure. The 6H singlet located near 3.0 ppm is indicative of the two methyls of the amine, indicating that the unknown coupling reagent used was N,N-dimethylamine. Similar processes can be applied to the products depicted in Figures 6.6 and 6.7.

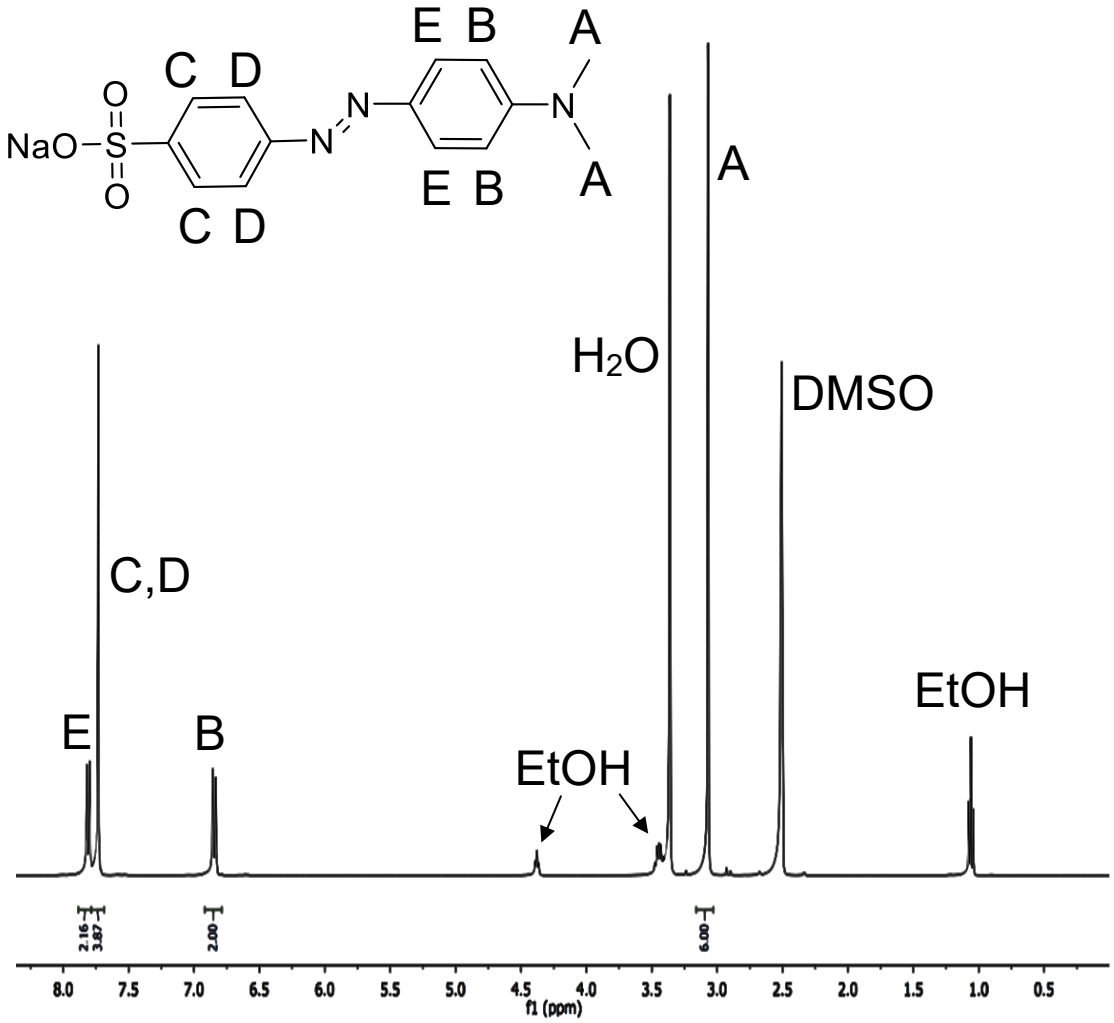


Figure 6.5. Sample ^{1}H NMR spectrum of methyl orange from the 400 MHz ^{1}H NMR. The structure and assignments are provided for clarity. DMSO was used as the NMR solvent. Residual water and traces of ethanol are present from the recrystallization process.

When considering Figure 6.6, students recognized again that there are 8H in the aromatic region. The 6H triplet located near 1.2 ppm and the 4H quartet located near 3.5 ppm were representative of the two ethyls of the amine, indicating that the unknown coupling reagent used was N,N-diethylamine.

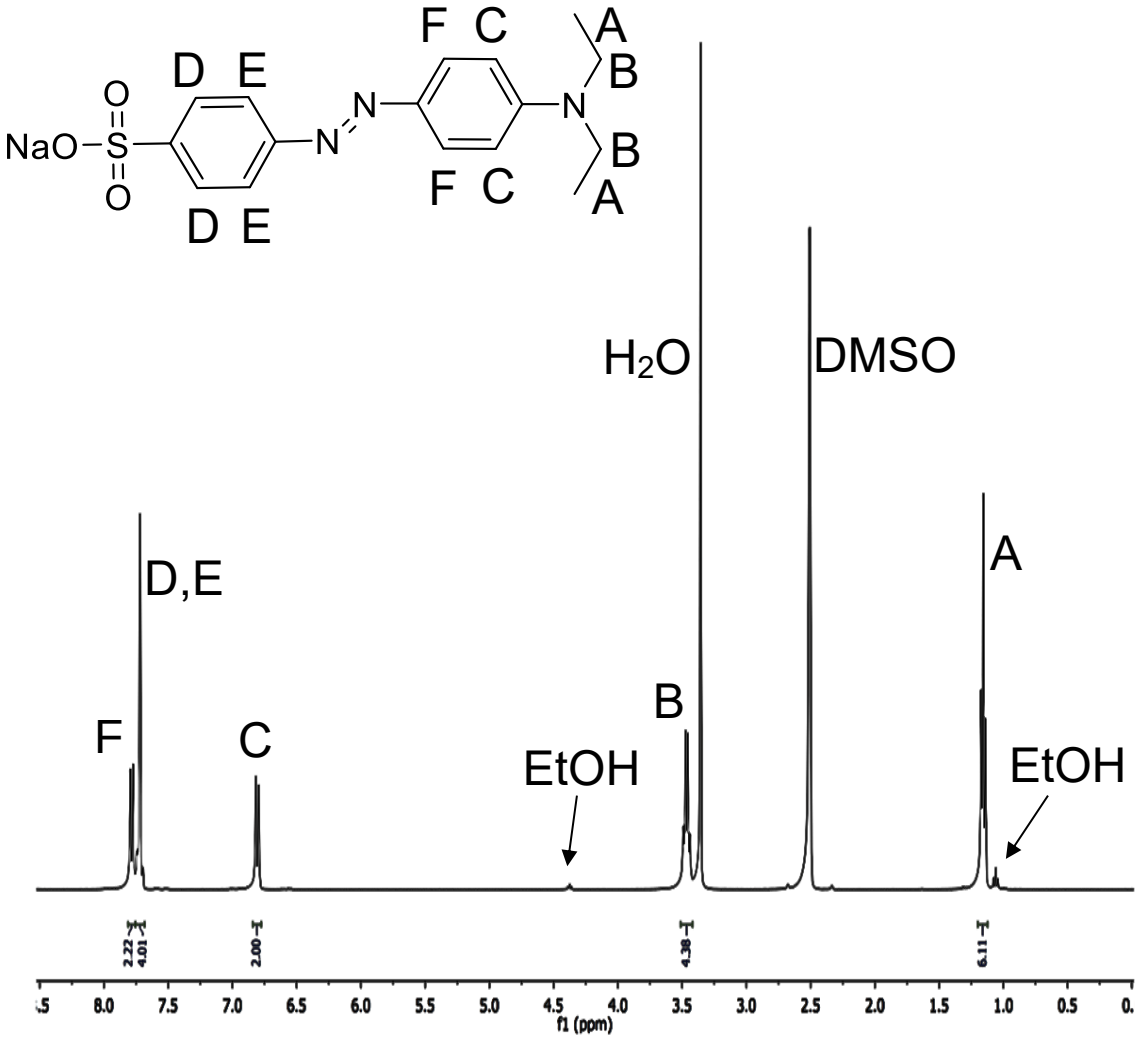


Figure 6.6. Sample ^{1}H NMR spectrum of ethyl orange from the 400 MHz ^{1}H NMR. The structure and assignments are provided for clarity. DMSO was used as the NMR solvent. Residual water and traces of ethanol are present from the recrystallization process.

Finally, when considering Figure 6.7, students recognized again that the remaining signals reflect the deuterated DMSO and a broad singlet that represents the hydroxyl proton labeled as A. Therefore, the presence of this broad signal and the lack of the 6H singlet or the 6H triplet and 4H doublet indicated that the unknown coupling reagent used must be phenol.

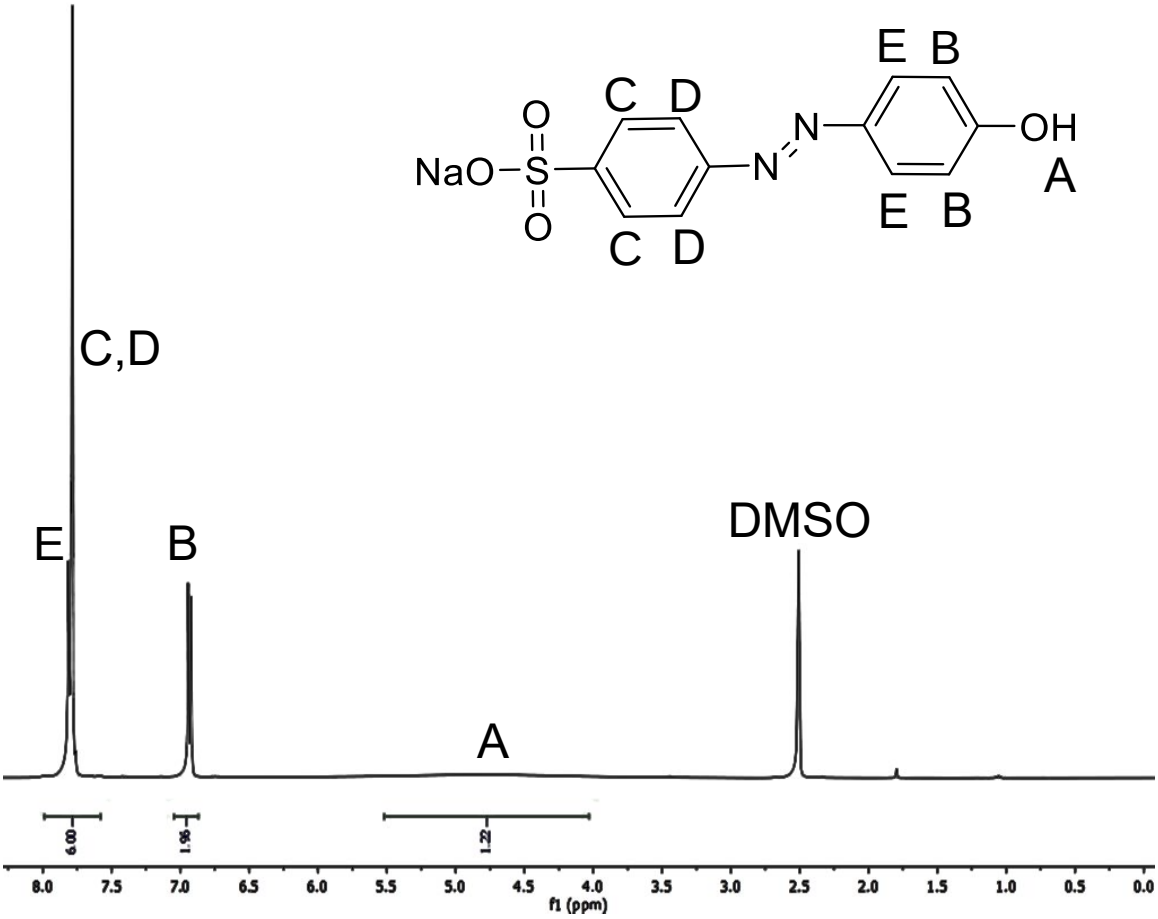


Figure 6.7. Sample ^{1}H NMR spectrum of phenol dye from the 400 MHz ^{1}H NMR. The structure and assignments are provided for clarity. DMSO was used as the NMR solvent. Residual water and traces of ethanol are present from the recrystallization process.

During the iteration, the most useful identification tool was reported as ^{1}H NMR spectroscopy by 88.89% of students (see Figure 6.8). Color was indicated as the least useful identification tool by 77.78% of students (see Figure 6.9). This was intriguing because a quick Google search of both methyl orange and ethyl orange, the common names of two of the dyes, resulted in images of the visibly distinctive colored dyes. One student who selected color as the most useful identification tool specifically commented on this, stating "The color was the most useful identification technique for deducing the identity of the unknown coupling reagent. This was because during the prelab, I found the azo dyes that were options for the unknowns". However, if

the students solely used the systematic names of the dyes in a Google search, images of the dyes were not shown as results. Using the photographs produced from the Google search would allow for a process of elimination to determine which dye resulted from the phenol coupling reagent. Because there are a limited number of experiments in organic chemistry that deviate from the "white powder" product, the researcher's initial concern was that the bright and distinguishable colors of the product would indicate to the students what product they made; however, this was not demonstrated as the case by the Spring 2018 students. FTIR was reported as the least useful analytical technique by 18.52% of students.

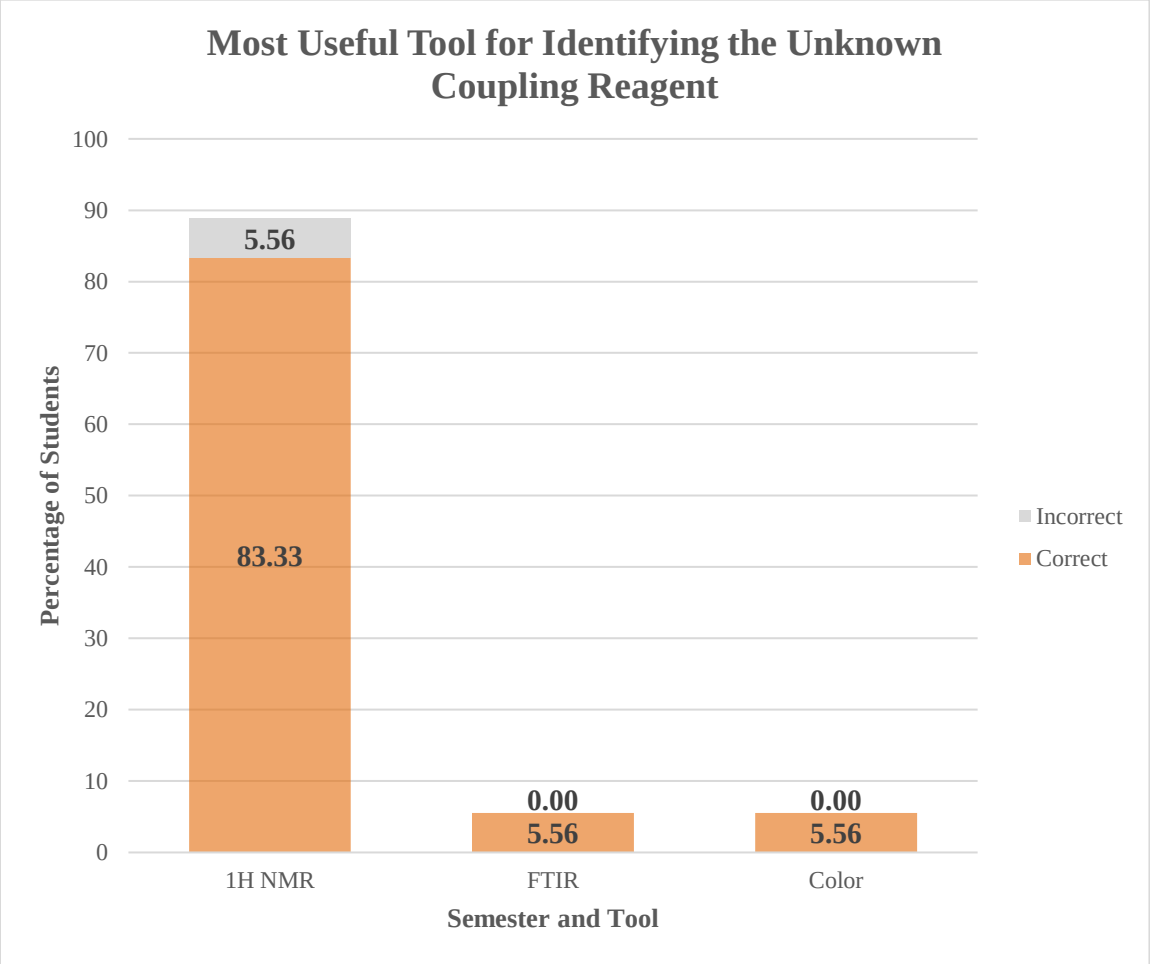


Figure 6.8. Spring 2018 *Honors/Majors* student survey responses to indicate what the most useful tool for identifying the unknown coupling reagent. N = 54 students.

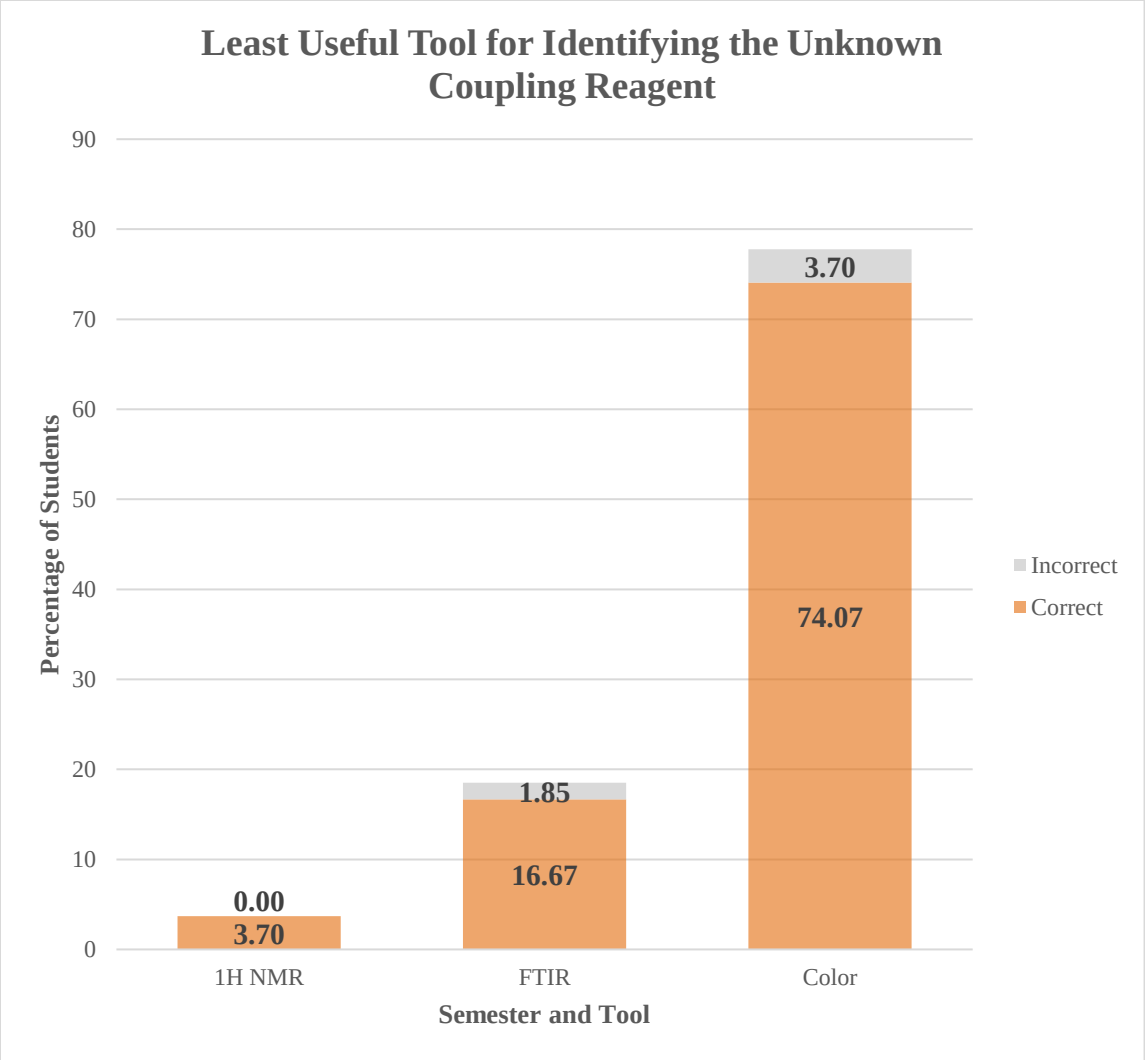


Figure 6.9. Spring 2018 *Honors/Majors* student survey responses to indicate what the least useful tool for identifying the unknown coupling reagent. N = 54 students.

In addition to these rankings, students also self-reported their confidence levels in their ability to identify correctly the unknown coupling reagent *with only* the ^{1}H NMR spectra of their products. Figure 6.10 illustrates a downward trend in student confidence levels, with most students indicating that they would feel "most confident". Furthermore, students self-reported their confidence levels in their ability to identify correctly their unknown alcohol *without* the ^{1}H NMR spectra of their products. In Figure 6.11, an upward trend is noted for student confidence levels, with the greatest population of students selecting "not confident".

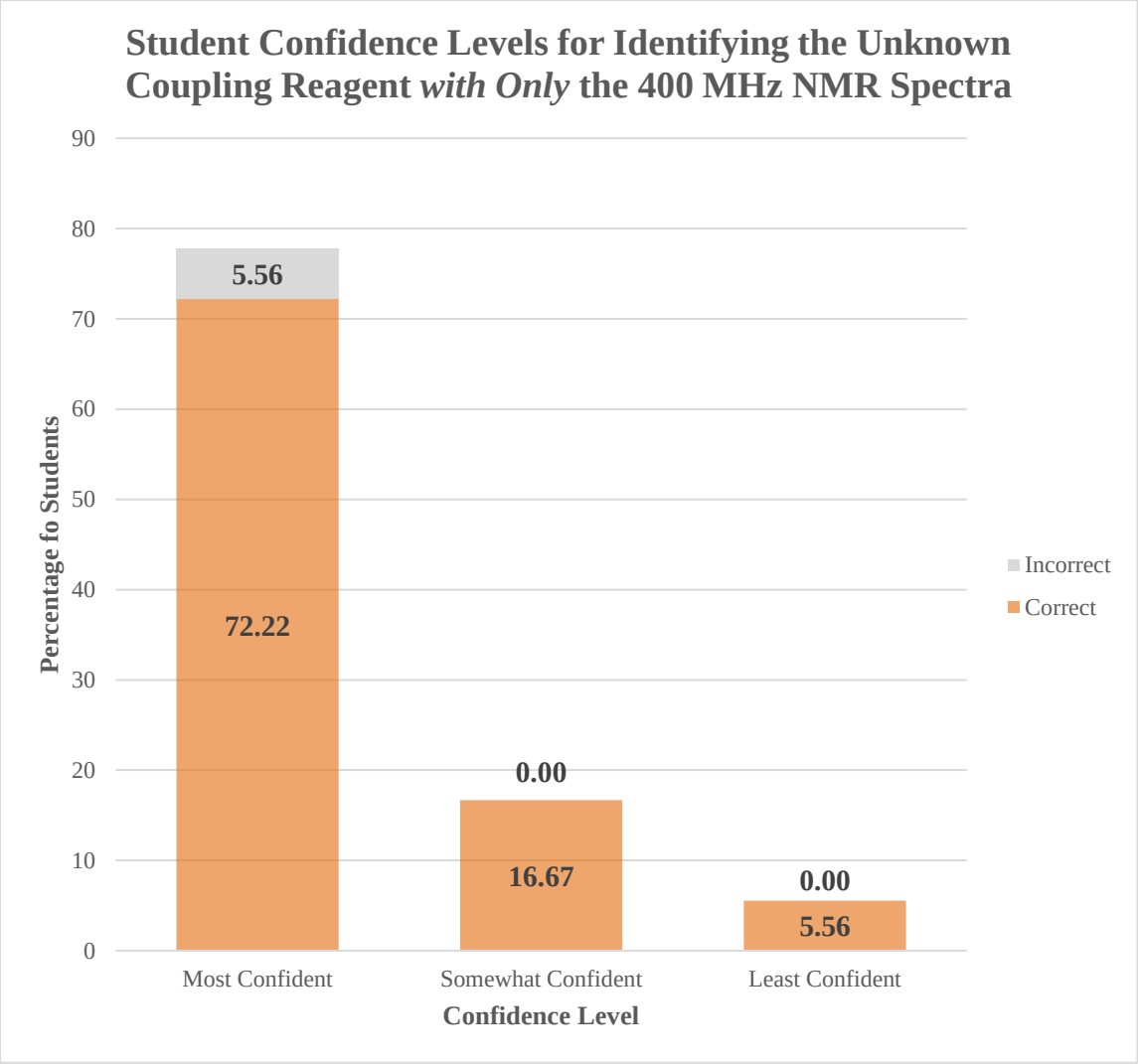


Figure 6.10. Spring 2018 *Honors/Majors* student confidence levels for identifying the unknown coupling reagent *with only* the 400 MHz NMR spectra. N = 54 students.

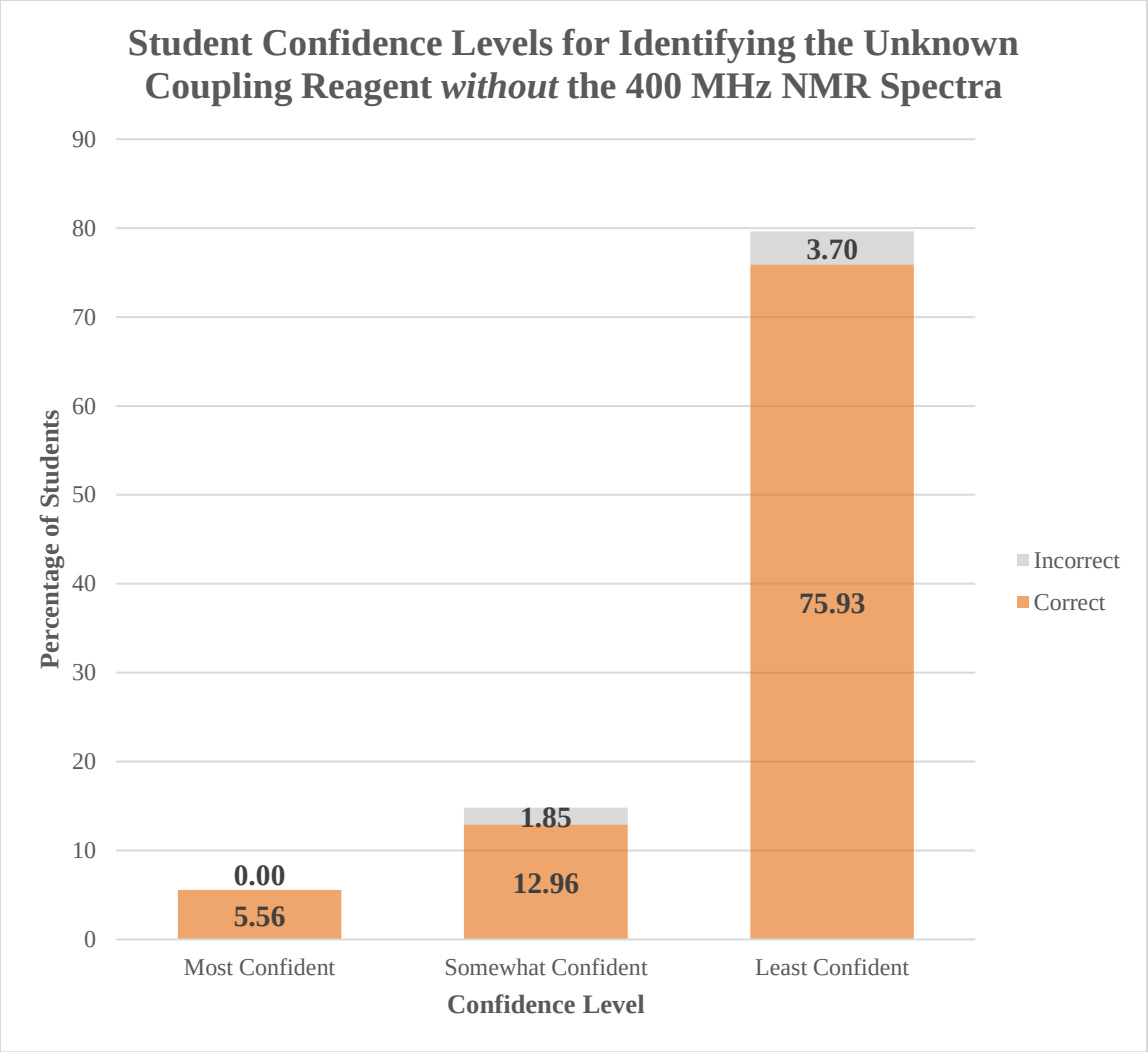


Figure 6.11. Spring 2018 *Honors/Majors* student confidence levels for identifying the unknown coupling reagent *without* the 400 MHz NMR spectra. N = 54 students.

The students also had an opportunity to provide additional feedback about their experience. One student noted, "^{1}H NMR is useful with its integrations showing relative number of protons, as well as showing the types of protons present and their environments." Another student reported that NMR was a "[v]ery useful, very holistic process to get an idea and pin down the identity of most to many organic chemical compounds." A third student described NMR as "truly an innovation". Before beginning the experiment, the students were directed to retain their final products in vials for use in the *Chemistry in the Arts* study abroad course. This piece of information

resonated with several students. “I think we should have more labs like this one where the products we make are actually put to use” one student noted. Another student commented on their appreciation for product conservation, stating “I really enjoyed this lab, and I'm glad we're not just throwing away the chemicals we spent hours making.”

PHASE II – STUDY OF AZO DYES IN THE *CHEMISTRY IN THE ARTS* COURSE

METHODS

In preparation for Phase II (Summer 2018), the researcher worked with Professor Margaret Morrison from the UGA Lamar Dodd School of Art. Professor Morrison used azo dyes created by the research team to see what binder may serve best during the summer implementation. Walnut oil was used first and renderings using the dye using this binder are shown in Figure 6.12. Professor Morrison added commercially available white and blue paints that were on hand to see the range of colors that could be produced from mixtures of the dyes with the each other and with the purchased paints.

Figure 6.12. Example renderings of the dyes mixed with various binders (walnut oil, pine oil, etc.)

Egg tempera was also explored as a viable binder for the dyes. To prepare the egg tempera, egg yolks were carefully separated from the egg whites. The yolk membranes were then pierced with a sharp object (such as the handle end of a paint brush as shown in Figure 6.13) to collect the inside of the yolk. The membrane of the yolk was then discarded. The dyes were then mixed into the emulsion and applied to various media. When the researcher and Professor Morrison initially explored this method for use with the dyes, it was noted that an initial sketch was still visible underneath several layers of the egg tempera paint (see Figure 6.14). This is promising for artists, and especially artists-in-training, because it allows for the artist to see the rendering underneath, which may help the overall work take shape. Additionally, eggs would be a readily available resource in the town of Cortona, Italy, where the UGA campus is located, while walnut oil would be a more difficult product to procure. For these two reasons, it was determined that the egg tempera would be used for the implementation of Phase II.

Figure 6.13. The researcher recreating the puncturing of the egg yolk which was used to make the egg tempera binder.

Figure 6.14. Example renderings of the dyes mixed with egg to create egg tempera. Note that the sketch of the sunflower (center of work with three yellow petals) is visible underneath the applied layers of paint.

During June 2018, the dyes were transported to the UGA Study Abroad campus in Cortona, Italy. Once on campus, the researcher facilitated the interaction of the *Chemistry in the Arts* students with the azo dyes. In total, seven students participated during the Summer 2018 implementation of Phase II. These students were provided with directions for serial dilutions and performed the dilutions using equipment on hand. Because the portable UV-Vis spectrophotometer can send data over a wireless internet connection to individual users' email addresses, the students collected their spectra in a nearby computer lab that had a stronger wireless connection. The spectra were then processed using Excel with additional instructor assistance. The process that the students completed was then related to the process that art conservators use during restoration processes. This supplemental instruction was tailored to match the students' experience in Italy with the study abroad program to date.

RESULTS

During Phase II, the *Chemistry in the Arts* students used Excel to plot the spectra resulting from their serial dilutions. The students then used the spectra and tabular data to determine the λ_{max} of the dye. The absorbances at these λ_{max} values were then used to create a standard calibration curve (Beer-Lambert plot) and analyses of linearity were performed. Figures of these curves are included in the Discussion section.

DISCUSSION

Figure 6.15. The Chemistry Shack located at the UGA Study Abroad campus in Cortona, Italy

In Phase II of this MOE, students had a quaint laboratory experience in the "Chemistry Shack" at the UGA campus in Cortona, Italy (see Figure 6.15). The seven students enrolled were divided into three groups, with each group working directly with one of the three dyes (see Figure 6.16). The students were first introduced to the dyes through a lecture discussing the preparation of the dyes by the *Honors/Majors* students. The *Chemistry in the Arts* students then studied the dyes as indicators. The researcher dissolved a small amount of each individual dye in water in a small

flask. Student volunteers then slowly added a drop of 1M hydrochloric acid to the solution, noting the changes in color as the pH of the solution changed. Another student volunteer then added a drop of 1M potassium hydroxide at a time to the acidic solution, noting the changes in color as the pH increased.

Figure 6.16. Azo dyes in Cortona, Italy. From top to bottom: ethyl orange, phenol dye, and methyl orange.

Next, the students were introduced to UV-Vis spectrophotometry. It is important to note that the students enrolled in the *Chemistry in the Arts* course were art or art-related majors, meaning that the introduction was completed in more general terms than it would have been for more chemistry-focused students. Serial dilutions and the color wheel were also described for the students before the hands-on activities began. The students followed step-by-step directions for completing the serial dilutions of the dyes. These dilutions were then stored in cuvettes for analyses with the UV-Vis spectrophotometer in the computer lab (Figures 6.17 and 6.18).

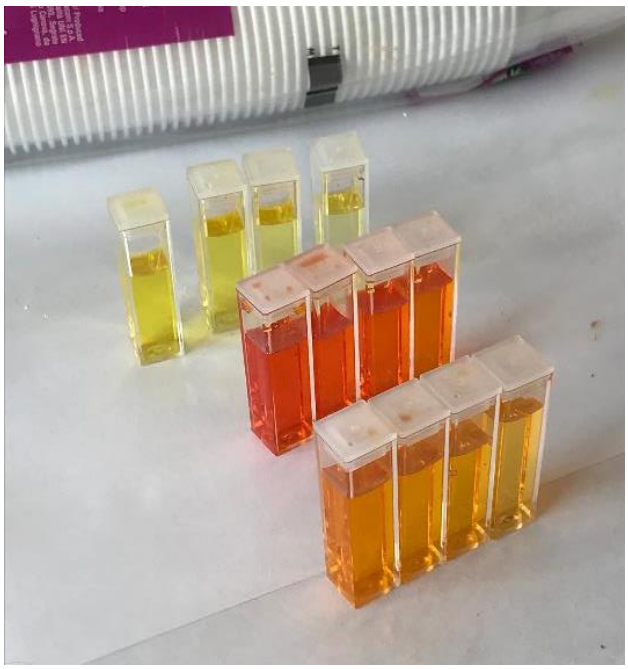


Figure 6.17. Serial dilutions prepared by *Chemistry in the Arts* students using the azo dyes in Cortona, Italy. From top to bottom: phenol dye, ethyl orange, and methyl orange. The cuvettes are arranged in order of most concentrated (least) to least concentrated (right) in each row.

Figure 6.18. A *Chemistry in the Arts* student using the portable UV-Vis spectrophotometer in the computer lab at the UGA campus in Cortona, Italy.

Once the UV-Vis spectra were plotted, the researcher worked with the students to plot the overlain spectra, determine the λ_{max} from the spectra, and construct a standard calibration curve. The student collected and processed data are depicted in Figures 6.19-6.24. It is of note that some absorbances collected were greater than 1.0. The process used by these art students was illustrative of the general process used for collecting UV-Vis data. After comparing the results from all students, the class discussed the inaccuracies that can occur with high absorbance values and how to prepare samples with lower absorbances.

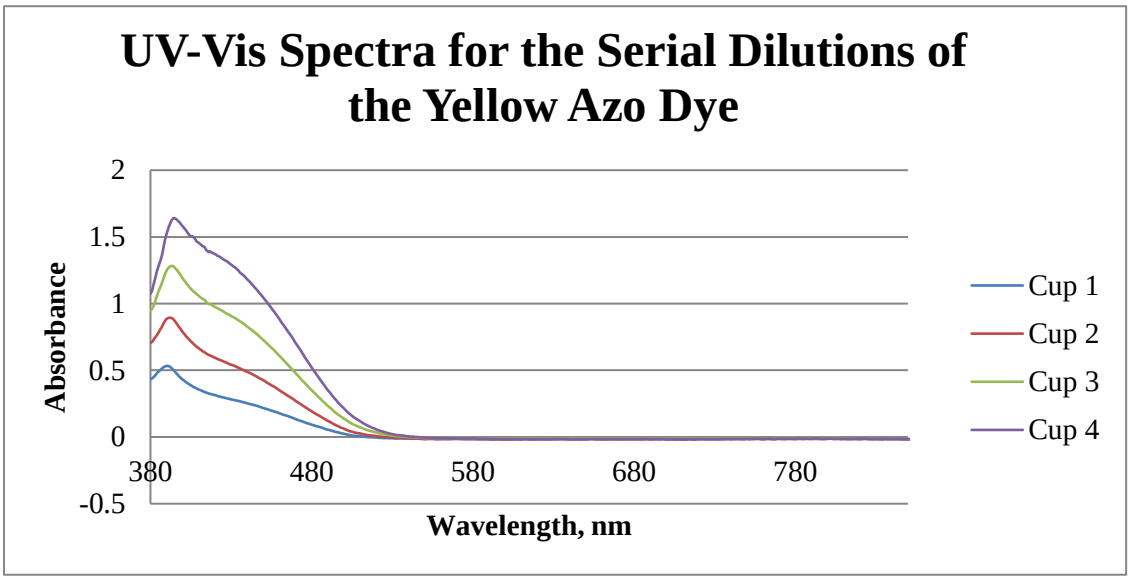


Figure 6.19. Absorption spectra for a serial dilution of the phenol azo dye collected by *Chemistry in the Arts* students.

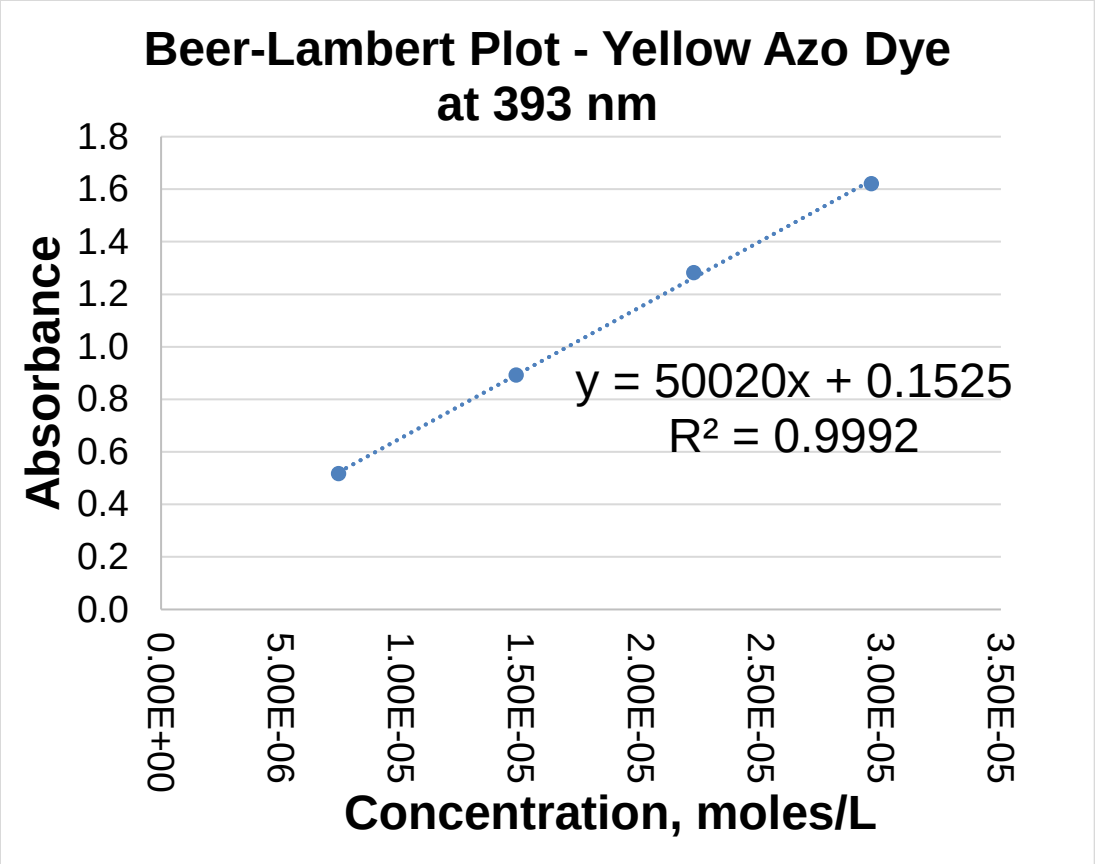


Figure 6.20. A Beer-Lambert plot (standard calibration curve) produced using the λ_{max} from the absorption spectra of the phenol azo dye collected by *Chemistry in the Arts* students.

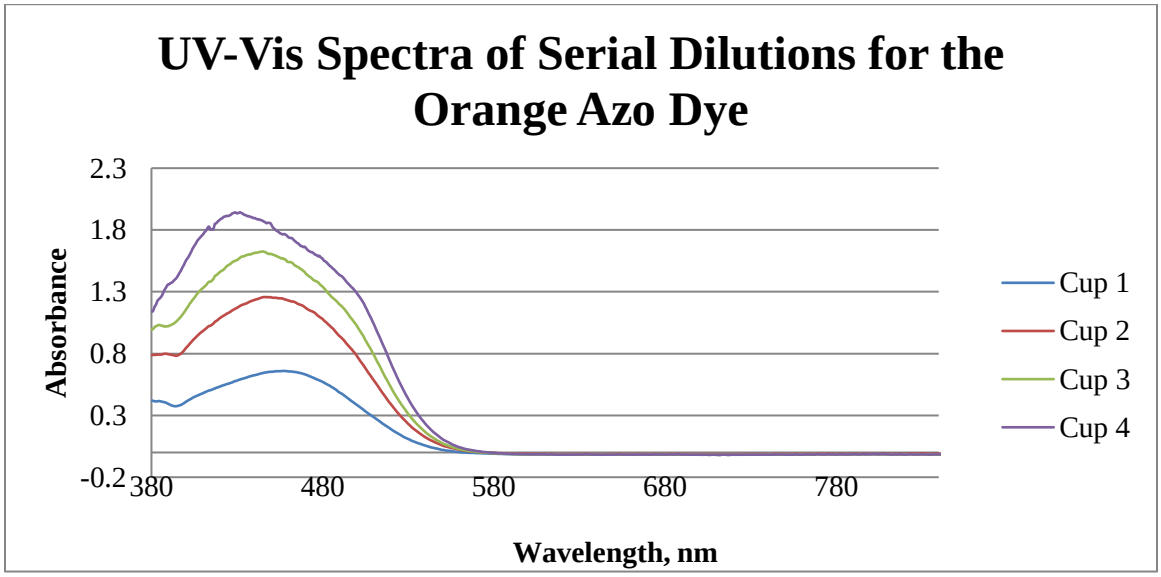


Figure 6.21. Absorption spectra for a serial dilution of the methyl orange azo dye collected by *Chemistry in the Arts* students.

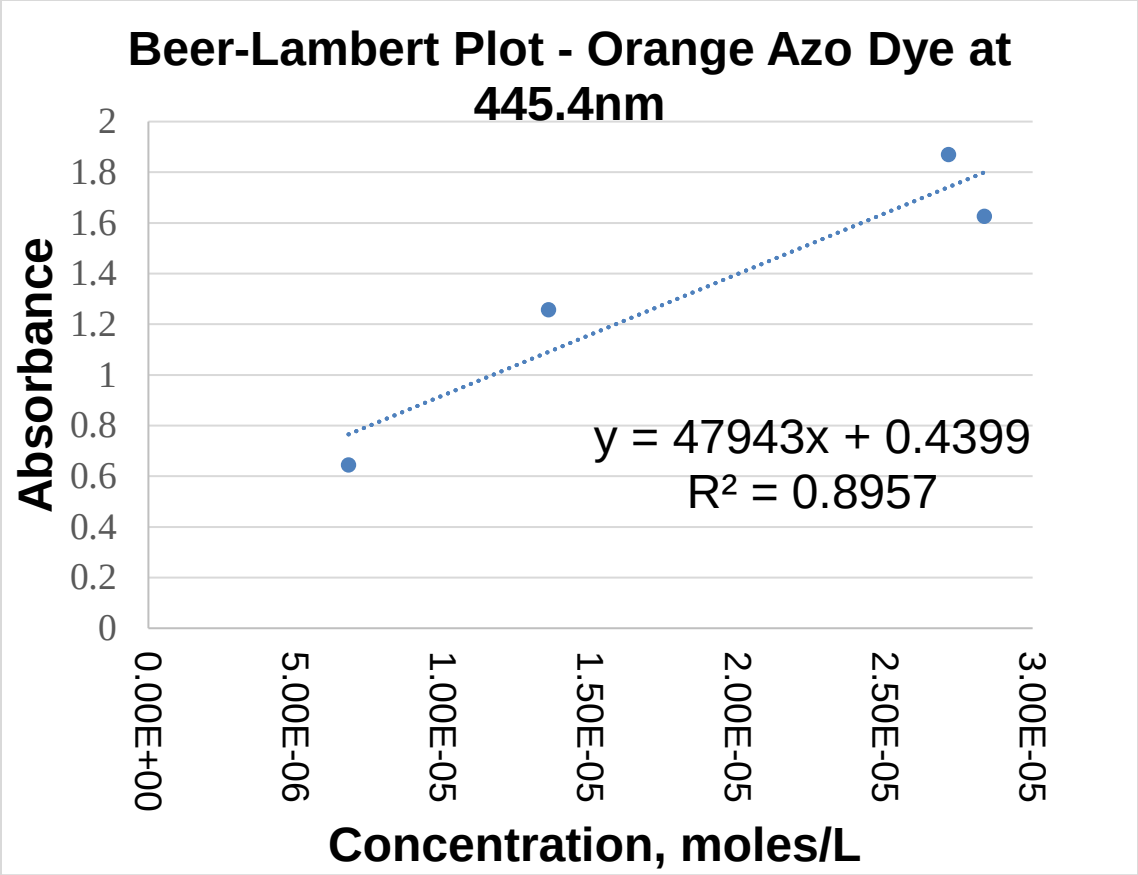


Figure 6.22. A Beer-Lambert plot (standard calibration curve) produced using the λ_{max} from the absorption spectra of the methyl orange azo dye collected by *Chemistry in the Arts* students.

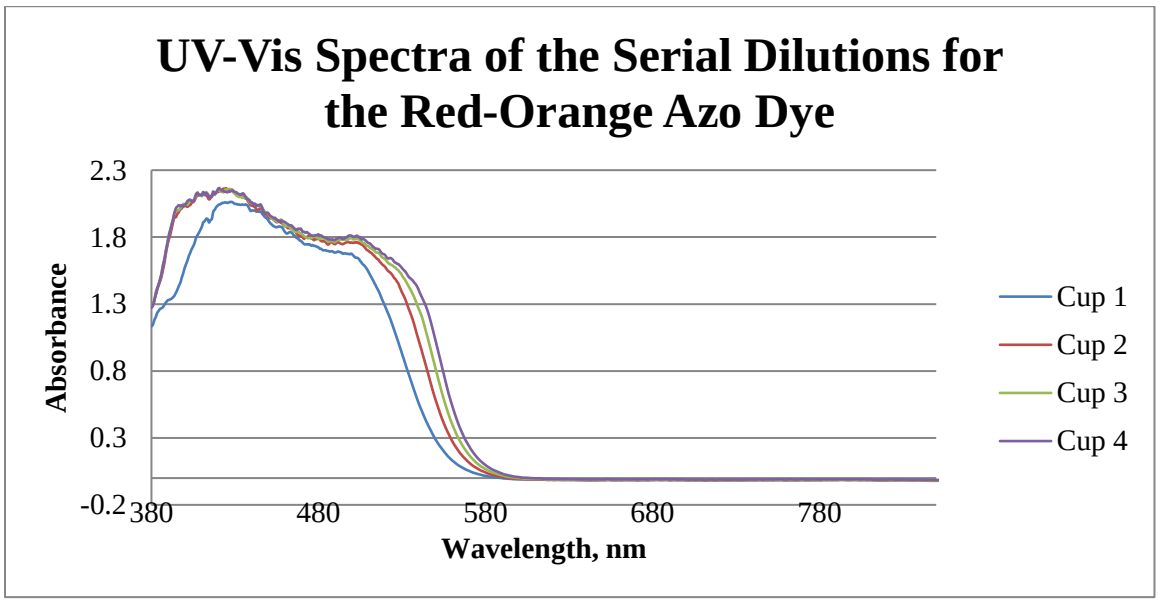


Figure 6.23. Absorption spectra for a serial dilution of the ethyl orange azo dye collected by *Chemistry in the Arts* students.

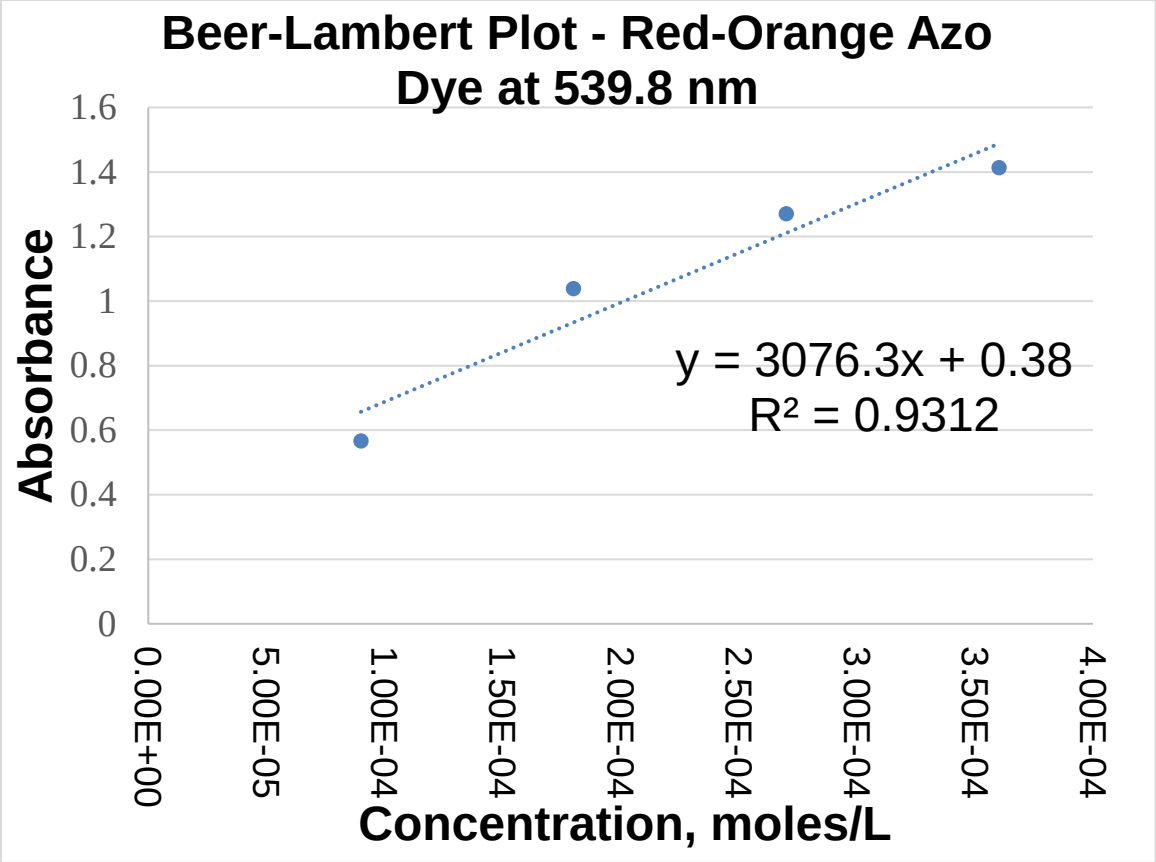


Figure 6.24. A Beer-Lambert plot (standard calibration curve) produced using the λ_{max} from the absorption spectra of the ethyl orange azo dye collected by *Chemistry in the Arts* students.

After these curves were prepared, the researcher related the λ_{max} back to the color wheel and the overall process that the students completed back to the restoration activities during art restoration endeavors. The researcher discussed the importance of the linearity of serial dilution data, with the students analyzing the linearity of their own data through their computated R^2 values. The students also calculated the concentration of samples of their dye using given absorbances. The students then created works of art, which were similar to those rendered by the research team on the wooden discs shown in Figure 6.25.

Figure 6.25. Works of art created by the research team using egg tempera paint made with the dyes. Acrylic paint was also included to widen the color palette.

CONCLUSIONS

In this experiment, students' interactions with azo dyes were very vastly different, with one population synthesizing the dyes and a second population studying the application of the dyes. In Phase I, *Honors/Majors Advanced Organic Chemistry II* students successfully synthesized dyes using an unknown coupling reagent. 51 of 54 students (94.44%) correctly identified their unknown coupling reagent using spectroscopic analyses of their product. In Phase II, *Chemistry in the Arts* students collected UV-Vis spectra to determine each dye's precise colorizing pigment and used the dyes to create works of art. Both groups of students indicated an appreciation of the work that the other class was doing with the dyes, gaining insight into disciplines outside of their own.

EXPERIMENT NOTES

This work was classified as "not human research" by the Institutional Review Board at the University of Georgia (STUDY00005120). Undergraduate Christina Cortes assisted with the development and implementation of this experiment. Special thanks are extended to the CHEM

2312HL/2412L TAs and students for assisting with or participating in the implementation in the *Honors/Majors* course. This work was financially supported by the generosity of the UGA Graduate School through a Summer Research Travel Grant. Financial support was also provided through a Scholarship of Teaching and Learning Mini-Grant through the UGA Graduate School and the UGA Center for Integrated Research, Teaching, and Learning.

CHAPTER 7

PERSPECTIVES ON MULTI-OUTCOME EXPERIMENTS

REVIEW OF MOEs

This dissertation describes the development and implementation of five MOEs. The first MOE (the Separation of a Three-Component Mixture via Acid-Base Extraction – Chapter 2) may be implemented once first-semester undergraduate organic chemistry students have been introduced to both FTIR and ^{1}H NMR spectroscopies. The four remaining MOEs are designed for inclusion in the second-semester undergraduate organic chemistry instructional laboratory course. This dissertation serves as a starting point for the development of this type of experiment. As previously outlined in Chapter 1, the outcomes of a well-designed MOE are as follows:

- To reinforce lecture-learned concepts
- To increase individualization of the laboratory experience
- To facilitate active engagement with modern analytical techniques

Because organic chemistry provides students with the building blocks for upper level coursework in their fields of study, the concepts and/or analytical instruments incorporated can be altered to meet the needs of any student population. The example MOEs included reinforce the concept of ^{1}H NMR spectroscopy through the direct analyses of individual spectra of student products. However, NMR spectroscopy was not the only lecture-learned concept reinforced by these MOEs. FTIR spectroscopy, acid-base reactions, the oxidation of alcohols using bleach, the Williamson ether synthesis, the Fischer esterification, and the preparation of a diazonium salt with subsequent preparation of an azo dye are concepts that are also consistent with lecture instruction. The experiments typically aligned with the coverage of the same material in the lecture course,

allowing students to draw comparisons between content from both lecture and laboratory settings. Additionally, students increased their proficiencies with various laboratory skills or techniques, such as liquid-liquid extraction, using drying agents, purification using column chromatography, and microwave heating.

The incorporation of MOEs into the undergraduate organic chemistry curriculum at the University of Georgia provided opportunities to increase the individualization of the laboratory experience. Previously, SOEs provided students with exactly the same experience, from the in-class observations to data analyses to results. MOEs provided students with opportunities to determine the identity of their mystery starting material, involving the students in their laboratory experience and critically engaging the students with course materials. The work products produced by students were also more diverse, with unique observations or analyses intertwined into each postlab report. These differences allow students to individually experience the scientific process by considering their own findings, discussing the findings of their classmates, and providing thorough explanation for why they have selected their specific option as the identity of the unknown component. The researcher has oftentimes seen students not only discuss why they have chosen their selection, but also why they have not selected the other options. Students have also described in detail the same process illustrated by the researcher in each of the chapters found in this dissertation for identifying the unknown component from the collected spectra.

Throughout the implementation of these experiments, the students frequently expressed their excitement to work with modern or new technology. In four of the five MOEs, benchtop NMR instruments were specifically employed. NMR technology was first "miniaturized" in the early 2000s, and benchtop NMR instruments were first used in the UGA undergraduate instructional laboratory setting in Spring 2014. In summary, this dissertation documents 3,505 instances of student interactions with ^{1}H NMR spectra, a number that only accounts for students that have completed a postlab survey. Although the students' engagement with the technology also included

careful supervision from their teaching assistant (TA) to monitor sample injections and for the processing of spectra, the researcher aims to continue increasing the level of student independence on the benchtop NMR instruments. This can be accomplished by including instrument training for students prior to the inclusion of these experiments in the semester or the use of online training videos.

COMMON QUESTIONS

Over the course of developing the laboratory experiments included within this dissertation, the author has had the opportunity to present preliminary findings at numerous conferences across the country. While sharing these findings and the development experiences with the broader scientific community, a number of questions have consistently been posed to the author. Generally, these questions concern the initial stages of the laboratory development process, the training of personnel, and the reception of this type of experiment by the students. The frequency with which these broad themes consistently arise warrant a short discussion about the topics.

Concerning the initial stages of laboratory development, the first step of MOE data collection involves fully developing the multi-outcome experiment for a beta-test group. For the experiments included in this dissertation, SOEs in the existing curriculum were first assessed to determine the skills and components that should be carried over from the starting experiment into the MOE. If there was not an existing experiment in the curriculum for the desired chemical transformation, experiments from other institutions were considered. Each component of the selected experiment was carefully reviewed to find an appropriate place to include a minimum of three options for an unknown component. The Azo Dye MOE provides an ideal example to illustrate this process. This experiment was modified from an existing SOE included in the curriculum at New Mexico Tech. Initially, the safety of each potential reagent in the experiment was assessed and their reactivities were compared. Once an aminobenzenesulfonic acid derivative was selected for use, a list of potential aromatic coupling reagents was created. This list was

shortened upon considering differences in price and molecular structure. The aromatic coupling reagent must have a low cost so that it can be used throughout the *Honors/Majors* course, a course with a 50-100 student enrollment. Second, the reagent must provide distinguishable product features in the FTIR and/or ^{1}H NMR spectrum so that students can determine the unknown starting material. Because the products were also used with art students, it was preferable for the dyes to also have visibly different colors to the naked eye and result in a distinguishable UV-Vis product spectrum. After the appropriate reagents were selected, the researcher developed a detailed, step-by-step procedure for synthesizing and purifying the product dyes. By purifying the product, the resulting spectra allowed students to clearly identify the unknown. In order to arrive at a procedure which accomplishes this, each combination of the aminobenzenesulfonic acid and unknown coupling reagent was vetted accordingly. For example, if each reagent coupled as intended and was easily purified as confirmed via spectral analyses, the process was repeated to verify the result at least three times. The dyes were then mixed with binders and applied in various media for painting to ensure that the dyes resulted in visibly different pigments upon final use.

After a prototype experiment is developed and beta-tested in small laboratory sections, successful mass implementation of the MOE is dependent upon the developer's ability to train the personnel who are working directly with the students as they undertake the experiment. When considering the implementation of MOEs, an increase in TA training items for any needed instrument or technique proficiencies and overall lab management practices must be employed.[94-98] While the initial training curve may be steep for new instrument managers, benchtop NMR instrument users typically find the process user-friendly in terms of running spectra. Challenges may arise if the instrument's capillary tube becomes clogged or if the frequency at which the instrument is operating shifts as it adapts to its environment. However, these challenges are mostly associated with the inclusion of solid samples that must be dissolved before being injected or with viscous liquid samples. Because the MOEs incorporate new technology, more instrumentation is

being utilized during the class period compared to previous curriculum. This naturally is associated with more classroom circulation and careful guidance for each laboratory section. Additional hands-on assistance may be required by the TA for tasks such as instrument management and the demonstration of new purification methods for students.

The researcher has commonly met with the TAs prior to experiment implementation, offering suggestions for increasing time efficiencies and how to keep the experiment moving. For example, the researcher has encouraged the TAs to walk students through the extraction and column chromatography segments of the experiments while executing the microwave procedure for the Williamson ether synthesis. By capitalizing on the available down time during the experiment, the students are better prepared for the next steps, mitigating some of the demand for hands-on assistance from the TA. The researcher has also encouraged TAs to announce the time that it should take to complete a task (i.e. 5-10 minutes maximum for the extraction procedure or reminding students when the halfway point has been reached in the laboratory period) to keep students focused on the tasks at hand. Afterall, the students should be building experience and skills as chemists. These skills include the timely completion of procedures and product characterization. Outside of these classroom management strategies, the researcher has also worked directly with TAs to build their own experiences. For example, all TAs regularly complete benchtop NMR training to refresh their skill set, learn to troubleshoot, and review any technology changes in the NMR processing software. The researcher was also on-call for all implementations to provide additional instrument support as needed.

When analyzing the student responses to the postlab surveys, the researcher has often been asked about student reception of the experiments, including student appreciation of analysis techniques and information retention across the iterations. Specifically, this researcher has been asked what evidence is available to indicate that students are not simply selecting NMR as the most useful identification tool out of habit. The researcher designed the survey to not only provide

students a space to rank the identification tools or indicate confidence levels, but also to provide an elaboration of their previous response. Oftentimes, it is evident that the elaborations reflect a level of detail similar to what is found in the students' discussion section of their postlab report. In other words, the students commonly describe the chemical shifts, integrations, splitting patterns, the number of unique protons, and more in their elaboration. This is not solely evident for the elaboration of why ^{1}H NMR was selected, but also evident for other identification tools. The researcher has included example responses to this effect throughout this dissertation.

Another question involves the increase in the percentage of students who have correctly identified their unknown component between semesters where withdrawal and re-enrollment may be common. For example, there is an increase in the correct identification percentage for the Williamson ether synthesis between the Spring and Summer semesters. The Spring semester section is the standard matriculation semester in which students enroll in Organic Chemistry II, while the Summer semester may include students who withdrew from the course during the previous Spring semester. Although the students in summer semester may have completed the experiment before in the previous Spring semester and withdrawn from the course, the researcher's colleague has developed and implemented additional experiments in the undergraduate organic chemistry laboratory that fall after the mid-term withdrawal deadline. Therefore, these experiments have not been seen by the students who may have withdrawn from the course in a previous semester.

FUTURE DIRECTIONS

Although the initial concepts of the MOE have been described herein, an assessment of the correlation between MOE deployment and lecture concept retention has yet to be employed. This may be accomplished by studying the performance in the associated lecture course for students who have participated in MOEs and for students who have participated in SOEs for the same material. Perspectives about the need for this type of work or preliminary reports for similarly

developed work are available in the literature.[99-105] The goal of such a research project would be to understand the extent to which new laboratory curriculum reinforces concepts in the associated lecture course. Additionally, a study to monitor the engagement of students in MOE versus SOE content may provide important information about how to best further experiment design. Similar studies have been completed in the literature and provide a framework to begin this elaboration of current work.[106-112]

The five experiments described in this dissertation represent a starting point for MOE development; however, much potential remains for the continuation of this work. Additional SOEs within the UGA curriculum are primed to be replaced with MOEs, and existing MOEs can continue to be optimized and increased levels of variation added in each MOE. This can be facilitated through increasing the number of options for unknown components so that students have a wider set of options to choose from. Alternatively, the students can complete the experiment without potential identities for the unknown components included, creating a true test of the students' structural elucidation skills. Moreover, multiple unknown components may be incorporated into the experiment, such as having both an unknown carboxylic acid and an unknown alcohol in the Fischer esterification experiment. This increased level of variation allows for more potential combinations of reagents (i.e. three unknown carboxylic acids possibilities and three unknown alcohols possibilities would give rise to obtaining nine possible esters).

Although the MOEs described in this dissertation are employed in the undergraduate organic chemistry laboratory courses, this experiment design could also be applied to other fields. For example, in a high school or general chemistry course, the UV-Vis spectroscopic analyses of dyes used to prepare the candy coatings of various candies could easily be rendered into a MOE format.[113] This experiment would reinforce UV-Vis spectrophotometry, serial dilutions, and Beer-Lambert plots which are included in the associated lecture curriculum. Each student pair would receive a different color of candy, increasing the level of individualization. Finally, the students

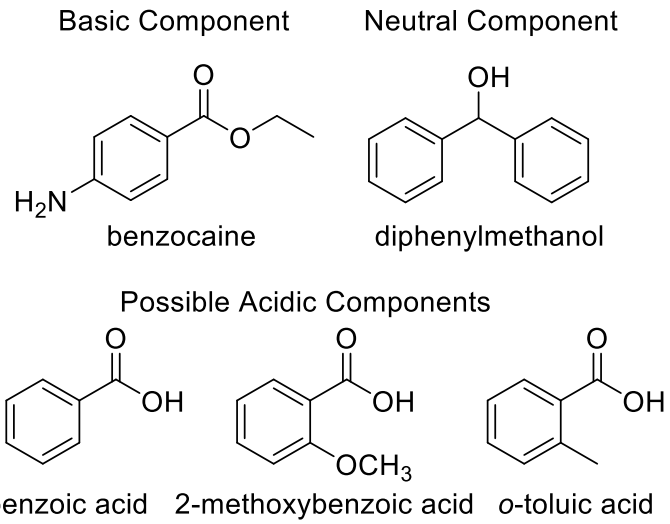
might use portable UV-Vis spectrophotometers, if available, to actively engage in the use of modern analytical techniques. An example MOE for a physical chemistry course could include the speed of sounds in gases, where students are provided with an unknown gas (such as air, carbon dioxide, or nitrogen) and use an Nd:YAG laser coupled with an oscilloscope to study the speed of sound.[114-116] This experiment would require students to recall the factors that impact the speed of sound, the use of lasers to create sound, and how oscilloscopes can be used. Finally, an upper level environmental chemistry course might complete an MOE involving the removal of toxic pollutants from water by student synthesized metal-organic frameworks.[117] In this MOE, students might reinforce concepts such as oligosaccharides, common water pollutants, and X-ray crystallography.

This dissertation has outlined the framework for the development of multi-outcome experiments. MOEs represent another level of diversity in the realm of laboratory design. Herein have been described five experiments to support the undergraduate organic chemistry laboratory curriculum. These five experiments depict the initial exploration of student learning supported by MOEs and offer a foundation for future curriculum expansion.

SUPPORTING INFORMATION – CHAPTER 2

Procedure 2.1. Separation of a Three-Component Mixture via Acid/Base Extraction

Extraction is a routine technique used to separate mixtures of compounds. Recently, you used solid/liquid extraction to isolate trimyristin from ground nutmeg seeds. This week you will be separating a three-component mixture containing an acidic, basic, and neutral component. This will be accomplished using a technique known as acid/base extraction, a specific type of liquid/liquid extraction. Each compound's inherent acid/base properties will be exploited to move the components between immiscible aqueous and organic layers throughout the experiment. As each component is isolated from the primary solution, it will be collected and analyzed. The individual acid/base reactions that take place during the course of this experiment are simple proton transfers that lead to significant shifts in compound solubility. These solubility shifts will allow for the sequential isolation of each compound and successful overall separation. You will learn how even the simplest of chemical properties can be utilized for effective component separation. You will also learn how to utilize infrared (IR) spectroscopy and hydrogen-1 nuclear magnetic resonance (^{1}H NMR) spectroscopy to identify and verify the molecular structure of various compounds. These techniques are used frequently by chemists and will be very useful tools for you throughout the semester. This early introduction to IR and ^{1}H NMR will help familiarize you with each technique.



New Techniques: Acid/Base Extraction (liquid/liquid), Separatory Funnel Extraction, IR Spectroscopy, ^{1}H NMR Spectroscopy

Old Techniques: Suction Filtration and Melting Point Determination

Table of Reagents:

Gather all relevant physical data for the following compounds.

Benzoic Acid (structure, MW, MP, solubility in water)

2-methoxybenzoic Acid (structure, MW, MP, solubility in water)

o-toluic Acid (structure, MW, MP, solubility in water)

Benzocaine (structure, MW, MP, solubility in water)

Diphenylmethanol (structure, MW, MP, solubility in water)

Sodium Hydroxide (structure, MW, pKa, solubility in water)

Hydrochloric Acid (structure, MW, pKa, solubility in water)

Methylene Chloride/Dichloromethane (structure, MW, BP, density, solubility in water)

Water (structure, MW, BP, density)

Sodium Sulfate (structure, MW, MP, solubility in water)

Sodium Chloride (structure, MW, MP, solubility in water)

In today's experiment you will be using this data to confirm the identity and calculate the percent recovery of your separated components.

Safety:

Safety glasses and lab gloves must always be worn. Sodium hydroxide is a strong base and hydrochloric acid is a strong acid. Both chemicals are caustic and will cause severe burns if they come in contact with your eyes or skin. In addition, hydrochloric acid solutions can evolve harmful vapors depending on their concentration. Make sure that your snorkel is properly positioned to avoid inhaling any hazardous fumes. Methylene chloride is volatile. Chronic exposure is possibly carcinogenic, and care must be taken to avoid breathing any fumes or allowing any liquid to contact

your skin. Take care when dispensing and evaporating it this week. Make sure that your snorkels are turned on and functioning properly before dispensing any liquids. Any vapor or liquid exposure should be reported to your TA immediately. Dispose of all liquid waste in the appropriately labeled bottle in the lab hood.

Experimental Procedure: Component Isolation via Acid/Base Extraction

Weigh out 500 mg of the acidic, basic, and neutral components respectively. Dissolve the mixture in 20 mL of methylene chloride. Add the resulting solution to your separatory funnel.

- Make sure that the stopcock of the separatory funnel is properly fitted and in the closed position prior to adding the organic solution. If it is not, you will pour your solution straight through the funnel and onto the bench top. It is strongly recommended to practice opening and closing the stopcock of the separatory funnel with water inside prior to beginning the experiment.
- Keep track of your layers as you isolate them so that you do not mix up your organic/aqueous phases and the components dissolved within them. Do not discard any of the layers obtained until the experiment is finished. More than one group has inadvertently discarded their final product after mixing up their isolated layers. Adding a few drops of distilled water can assist in the identification of a layer should you mix up your layers. What will happen when you add water to an aqueous or an organic layer?

Isolating the Basic Component: Benzocaine

Add 10 mL of 2M HCl to the solution in the separatory funnel. Seal the funnel with a stopper and shake it vigorously for 30-60 seconds to ensure that the contents mixed thoroughly.

- Make sure that your separatory funnel is pointed down and away from anyone in close proximity as you shake it. Vent the funnel regularly during the mixing process to ensure that excess pressure does not build up. The organic solvent is volatile and gas pressure will build up if not properly vented.

Once you have finished shaking, allow the funnel to stand undisturbed as the immiscible liquids separate to form distinct layers. Once the layers have stabilized, drain the lower, organic layer into a 100 mL beaker and set it aside. Be sure to remove the stopper while the funnel is standing undisturbed and during draining. Drain the remaining, aqueous layer into a separate 100 mL beaker and carefully label it. Now, add the organic layer back into the separatory funnel and repeat the extraction with an additional 10 mL aliquot of 2M HCl. Again, drain the organic layer into a 100 mL beaker and set it aside briefly. Next, combine the remaining aqueous layer with the original aqueous layer that you isolated during the first extraction. Add approximately 5 mL of 6M NaOH dropwise (slowly) to the beaker containing the combined aqueous layers. This will neutralize the acidic solution and regenerate the neutral amine. Is the neutral species soluble in water? Take note of any crystal formation that occurs. Cool the resulting mixture in an ice-water bath for 10 minutes. (Note: if crystals do not form, add an additional 5 mL of 6 M NaOH drop wise to the beaker in the ice bath.) Once crystal formation has finished, isolate the solid product using suction filtration. Rinse the 100 mL beaker and the Buchner funnel with 5 mL of ice-cold water to help ensure that all your crystals have been recovered. Pull air through your filtration apparatus for 10-15 minutes to dry the product. Additional drying time under a heat lamp may be necessary. Collect a ^{1}H NMR spectrum of your product with assistance from your TA. After this spectrum has been collected, determine the experimental melting point and obtain a FTIR spectrum of this known compound.

Isolating the Unknown Acidic Component: A Carboxylic Acid

Pour the organic layer that you set aside earlier back into your separatory funnel. Extract this layer twice with two 10 mL aliquots of 1 M NaOH. Set the organic layer to the side again and concentrate your attention on the combined aqueous layers. Add approximately 5 mL of 6M HCl dropwise (slowly) to the beaker containing the combined aqueous layers. This will neutralize the basic solution and regenerate the neutral carboxylic acid. Is the neutral species soluble in water? Take note of any crystal formation that occurs. Cool the resulting mixture in an ice-water bath for

10 minutes. (Note: if crystals do not form, add an additional 5 mL of 6 M HCl drop wise to the beaker in the ice bath.) Once crystal formation has finished, isolate the solid product using suction filtration. Rinse the 100 mL beaker and the Buchner funnel with 5 mL of ice-cold water to help ensure that all your crystals have been recovered. Pull air through your filtration apparatus for 10-15 minutes to dry the product. Additional drying time under a heat lamp may be necessary. Weigh the recovered crystals. Collect a ^{1}H NMR spectrum of your product with assistance from your TA. After this spectrum has been collected, determine the experimental melting point and obtain a FTIR spectrum of this unknown compound.

Isolating the Neutral Component: Diphenylmethanol

The acidic and basic components of our starting mixture have been properly isolated. Now it is time to isolate the neutral component. Add the organic layer back into the separatory funnel. Extract the organic layer with a 10 mL portion of distilled water and separate it. Add the organic layer back into the empty funnel and wash it with a 10 mL portion of brine (saturated salt water). Drain the organic layer into a dry 100 mL beaker and add approximately 500-750 mg of anhydrous sodium sulfate (drying agent). Once the solid has been added, swirl the flask briskly in order to distribute the sodium sulfate throughout the solution as thoroughly as possible. Sodium sulfate crystals will aggregate with any water remaining in solution and isolate it from the methylene chloride thereby "drying" your organic layer. Now decant the liquid from the sodium sulfate into a clean, pre-weighed round bottom flask. Make sure that only the organic liquid is transferred at this stage. No solid should be poured into the final round bottom flask. Carefully remove the dichloromethane via rotary evaporation. Note that your product is also a solid and should crystallize on the side of your flask, meaning heating the water bath too high may melt your product. *If you have a small amount of liquid volume left that is not reducing in volume, you may have potentially melted your crystals If this occurs, consider placing the flask (once sufficiently cooled) into an ice bath and scratch the glass with your stirring rod to induce crystallization.* Collect a ^{1}H NMR

spectrum of your product with assistance from your TA. After this spectrum has been collected, determine the experimental melting point and obtain a FTIR spectrum of this known compound.

Results/Discussion/Conclusion:

In your post-lab write-up, make sure that your percent recovery calculations are presented in a clear and accurate manner. Was this percent recovery reasonable? Why or why not? This isn't always a simple question to answer. Compare and contrast the melting point ranges of your isolated components and the literature values for each. Which compound's melting point is closest to the measured melting point? If there is a significant difference from the possible values, what could account for it? What can you determine about each product from its respective FTIR and ^{1}H NMR spectra? Can you identify the compound due to the presence of FTIR absorption bands particular to a specific functional group (or the lack thereof)? Can you identify the compound by the hydrogen splitting patterns or the integrations? Remember: restating the procedure is discouraged unless it is used to explain an error in data collection. Be sure to include a detailed mechanism for each of the acid/base conversions that take place during this experiment. In addition, provide a detailed flowchart that shows how each component was isolated during the reaction. Use the flowchart provided in the techniques section as inspiration.

Acid-Base Extraction Data Sheet

Unknown acidic component: _____ (letter/code)

Initial weight of basic component: _____

Final weight of basic component recovered: _____

Melting point of recovered basic component (range): _____

Initial weight of acidic component: _____

Final weight of acidic component recovered: _____

Melting point of recovered acidic component (range): _____

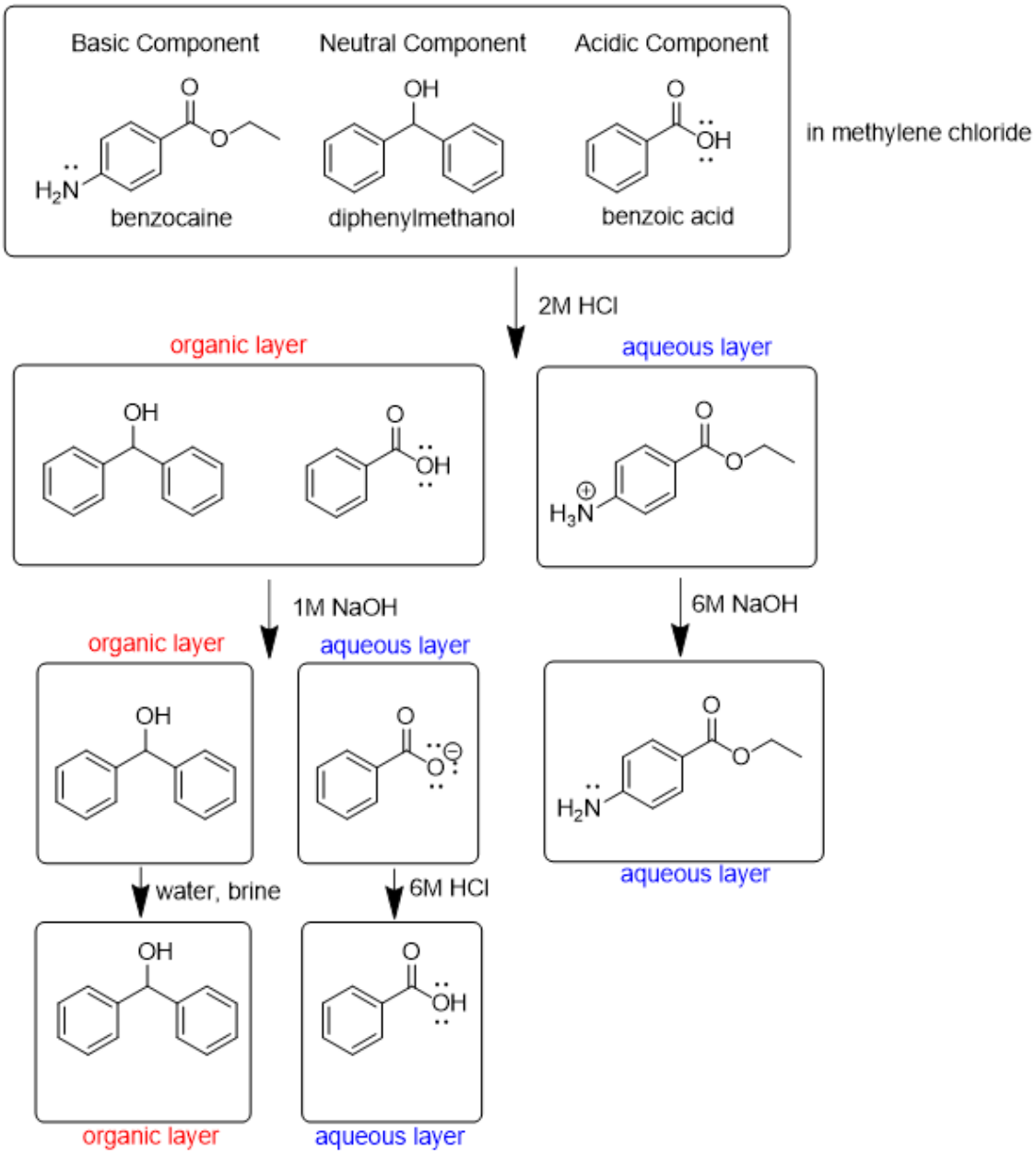
Initial weight of neutral component: _____

Final weight of neutral component recovered: _____

Melting point of recovered neutral component (range): _____

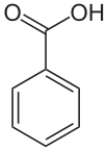
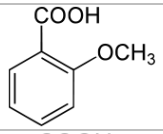
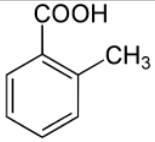
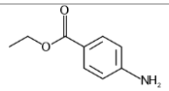
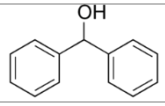
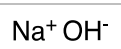
Miscellaneous Experimental Observations (Visual descriptions, texture, odor, etc…):

EXAMPLE FLOW CHART FOR TODAY'S EXPERIMENT

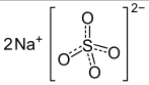


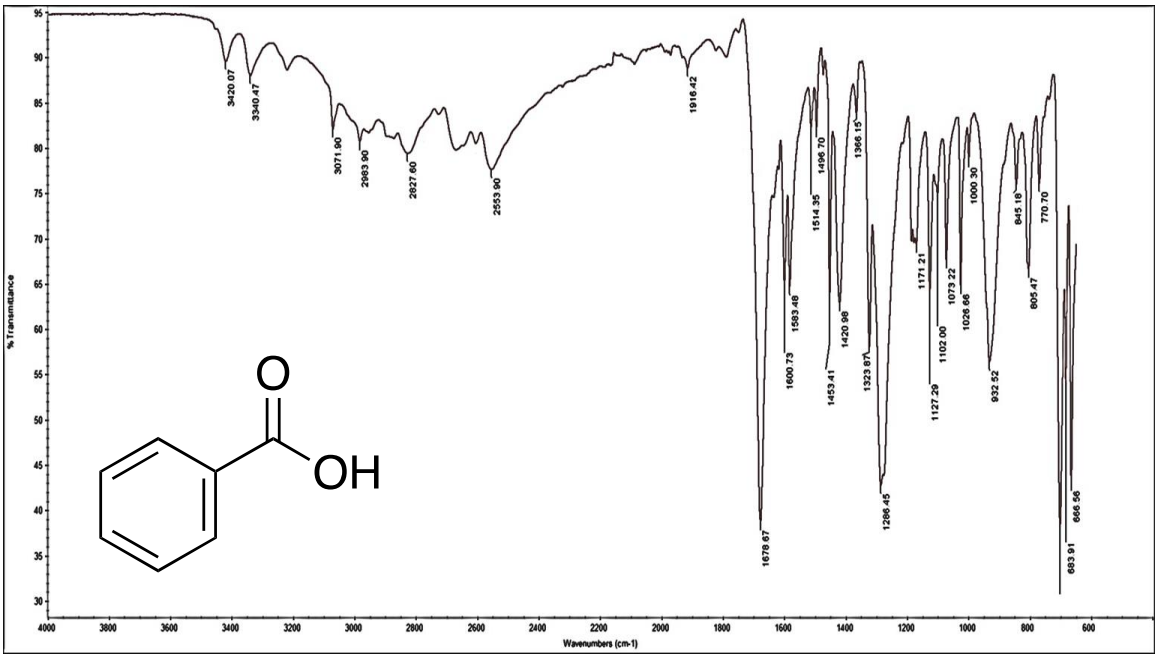
SI Figure 2.1: Example flowchart provided to students to assist in the performance of the experiment.

SI Table 2.1. Experiment Table of Reagents for Instructors

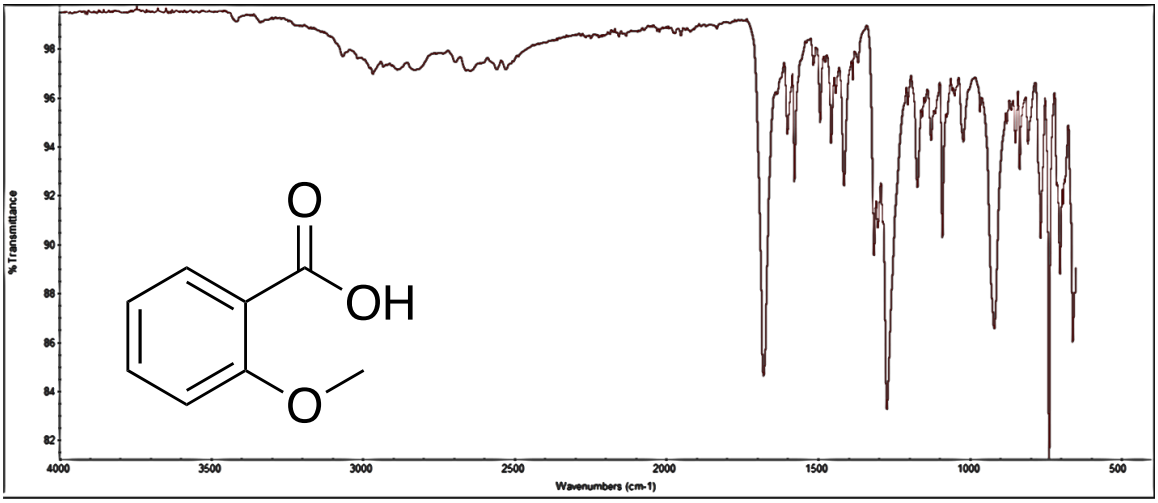
Reagent	Structure	CAS	Hazard Codes	Amount needed per Student	Mol. Weight (g/mol)	Melting Point (°C)	Boiling Point (°C)	Density (g/cm^3)	Solubility in water
Benzoic acid		65-85-0	Skin irritation (Category 2), H315; Serious eye damage (Category 1), H318; Specific target organ toxicity - repeated exposure, Inhalation (Category 1), Lungs, H372; Acute aquatic toxicity (Category 3), H402	0.5 g	122.12	122	250	1.2659	3.44 g/L
2-Methoxybenzoic acid		579-75-9	Not a hazardous substance or mixture.	0.5 g	152.15	98-100	-	-	-
o-Toluic acid		118-90-1	Not a hazardous substance or mixture.	0.5 g	136.2	104-105	259	1.06	-
Benzocaine		90-09-7	Acute aquatic toxicity (Category 2), H401; Chronic aquatic toxicity (Category 2), H411	0.5 g	165.189	89-90	310	1.17	-
Diphenylmethanol		91-01-0	Not a hazardous substance or mixture.	0.5 g	184.238	69	298	1.103	0.5 g/L
Sodium hydroxide		1310-73-2	Corrosive to metals (Category 1), H290; Skin corrosion (Category 1A), H314; Serious eye damage	Varies	40.00	-	-	-	-

			(Category 1), H318; Acute aquatic toxicity (Category 3), H402						
Hydrochloric acid		7647-01-0	Corrosive to metals (Category 1), H290; Skin corrosion (Category 1B), H314; Serious eye damage (Category 1), H318; Specific target organ toxicity - single exposure (Category 3), Respiratory system, H335	Varies	36.46	-	-	-	-
Dichloromethane		75-09-2	Skin irritation (Category 2), H315; Eye irritation (Category 2A), H319; Carcinogenicity (Category 2), H351; Specific target organ toxicity - single exposure (Category 3), Respiratory system, Central nervous system, H335, H336; Specific target organ toxicity - repeated exposure, Oral (Category 2), Liver, Blood, H373; Specific target organ toxicity - repeated exposure, Inhalation Category 2), Central nervous system, H373	20 mL	84.93	-	39.8-40	1.325	Slightly soluble

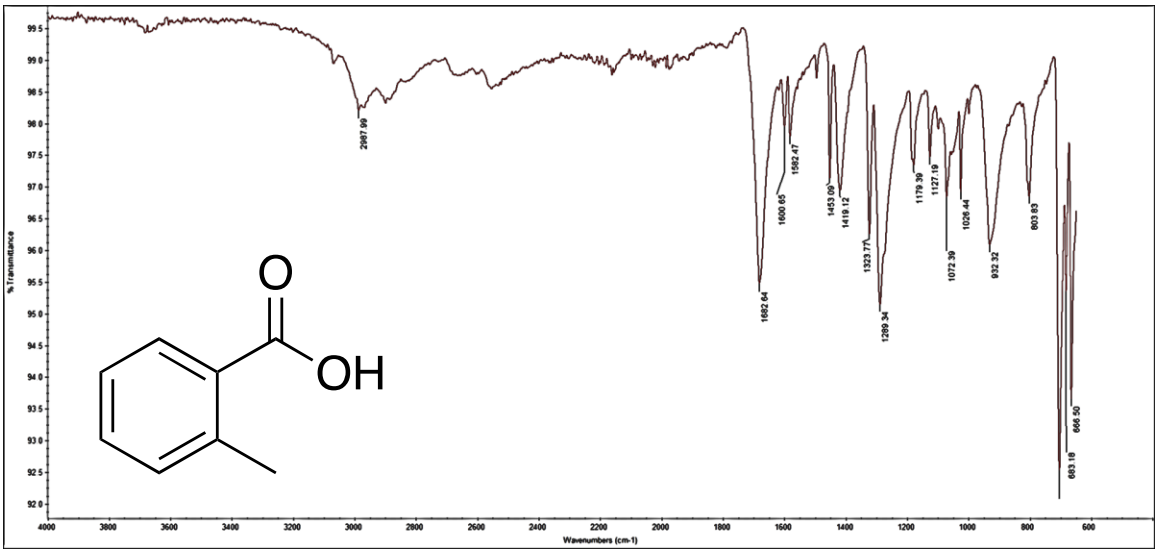
Water		7731-18-5	Not a hazardous substance or mixture.	Varies	18.02	-	100	1.000	-
Sodium sulfate anhydrous		7757-82-6	Not a hazardous substance or mixture.	Varies	140.04	-	-	-	-
Brine		7647-14-5	Not a hazardous substance or mixture.	10 mL	58.44	-	100	1.190	-



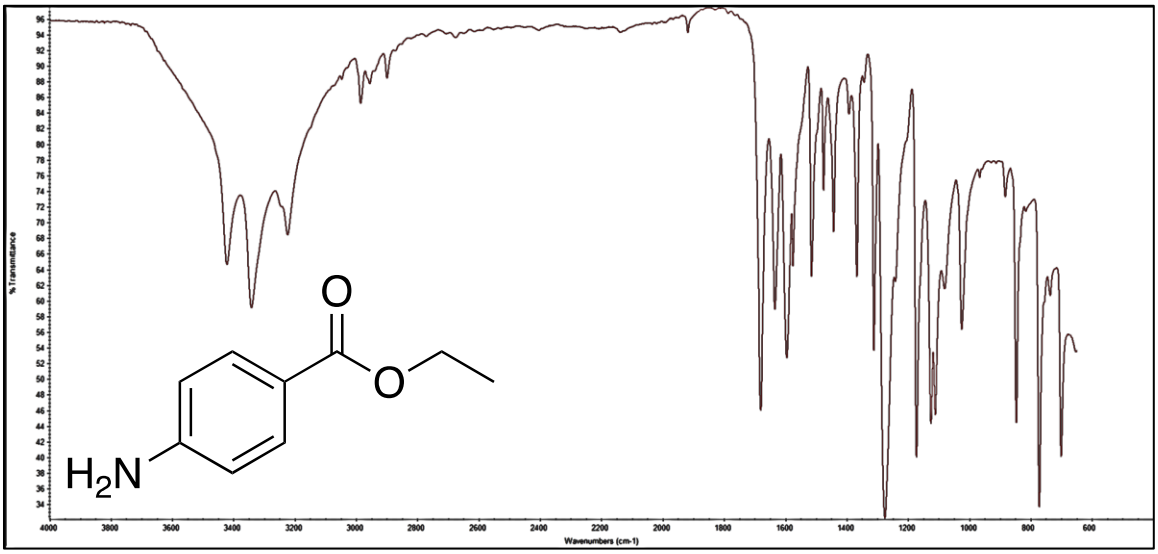
SI Figure 2.2: Student FTIR spectrum of Benzoic acid.



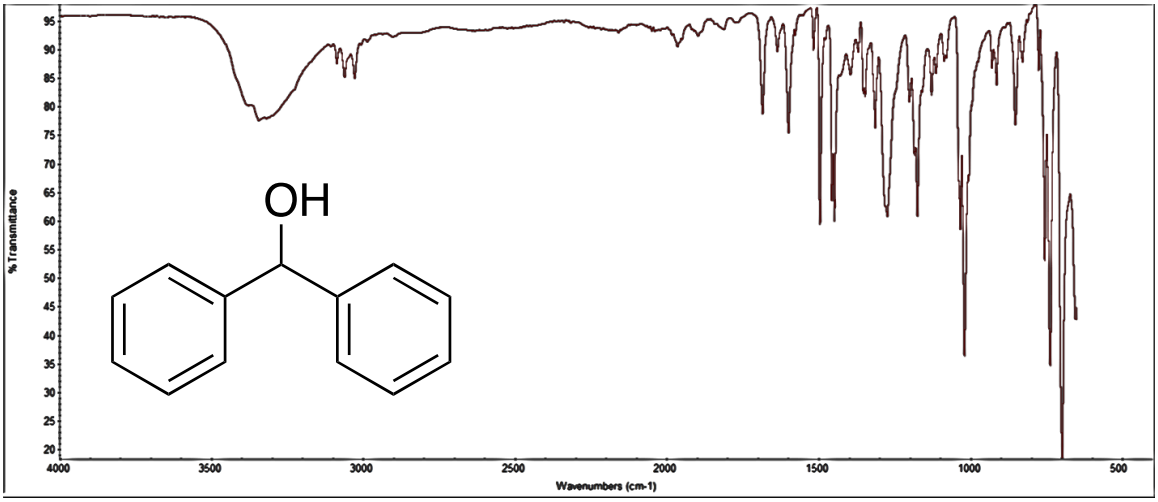
SI Figure 2.3: Student FTIR spectrum of 2-Methoxybenzoic acid.



SI Figure 2.4: Student FTIR spectrum of o-Toluic acid.



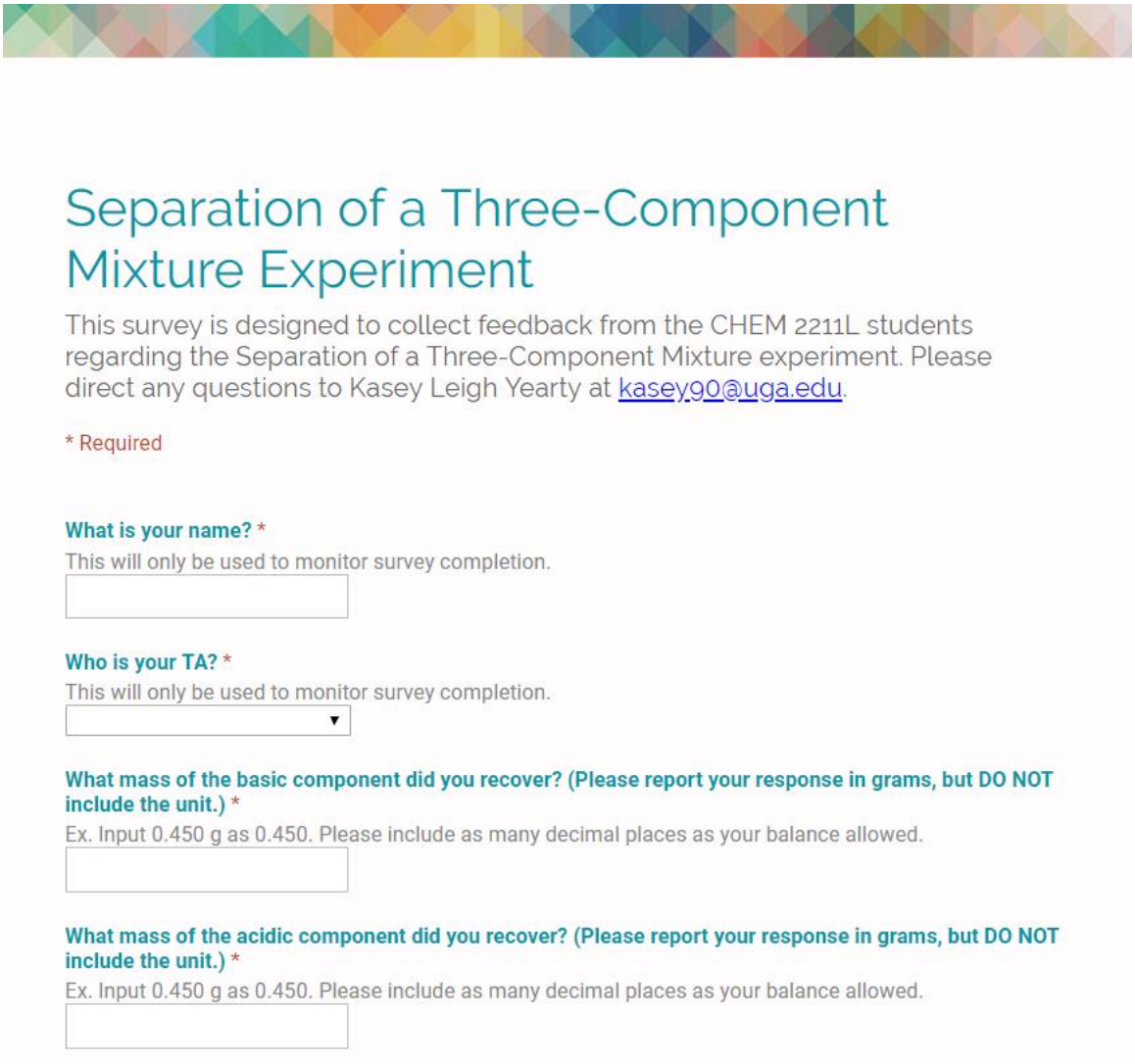
SI Figure 2.5: Student FTIR spectrum of Benzocaine.



SI Figure 2.6: Student FTIR spectrum of Diphenylmethanol.

SI Student Survey 2.1.

Survey Page 1/6



Separation of a Three-Component Mixture Experiment

This survey is designed to collect feedback from the CHEM 2211L students regarding the Separation of a Three-Component Mixture experiment. Please direct any questions to Kasey Leigh Yearty at kasey90@uga.edu.

* Required

What is your name? *

This will only be used to monitor survey completion.

Who is your TA? *

This will only be used to monitor survey completion.

What mass of the basic component did you recover? (Please report your response in grams, but DO NOT include the unit.) *

Ex. Input 0.450 g as 0.450. Please include as many decimal places as your balance allowed.

What mass of the acidic component did you recover? (Please report your response in grams, but DO NOT include the unit.) *

Ex. Input 0.450 g as 0.450. Please include as many decimal places as your balance allowed.

What mass of the neutral component did you recover? (Please report your response in grams, but DO NOT include the unit.) *

Ex. Input 0.450 g as 0.450. Please include as many decimal places as your balance allowed.

What was the code for the unknown acid that you used? *

- 1854KG2W
- 44NG256T
- 5598T26Q
- 5HG98ID9
- 6153M59T
- 8KJ23G8G
- 8T3DO5W4
- 95D6Y28D
- B854521T
- B85KA21T
- E854GN53
- F32T453A
- G54TH534
- G85W5G96
- H56N532D
- J23TH87G
- J89MA85T
- W56KS895
- Other:

What is the identity of your acidic component? *

- benzoic acid
- o-toluic acid
- 2-methoxybenzoic acid

What identification tool was MOST useful in helping you identify your acidic component? *

- Color
- IR
- 1H NMR

Please explain your previous response. *

What specific feature(s) of the identification tool selected assisted you in deducing the identity of your unknown acidic component?

What identification tool was SECOND MOST useful in helping you identify your acidic component? *

- Color
- IR
- 1H NMR

Please explain your previous response. *

What specific feature(s) of the identification tool selected assisted you in deducing the identity of your unknown acidic component?

What identification tool was LEAST useful in helping you identify your acidic component? *

- Color
- IR
- 1H NMR

Please explain your previous response. *

What specific feature(s) of the identification tool selected assisted you in deducing the identity of your unknown acidic component?

Please rank your confidence level for correctly identifying the unknown acidic component WITHOUT the melting point? *

- Most Confident
- Somewhat Confident
- Not Confident

Please rank your confidence level for correctly identifying the unknown acidic component WITHOUT the color? *

- Most Confident
- Somewhat Confident
- Not Confident

Please rank your confidence level for correctly identifying the unknown acidic component WITH ONLY the color? *

- Most Confident
- Somewhat Confident
- Not Confident

Please explain your previous response. *

Please rank your confidence level for correctly identifying the unknown acidic component WITHOUT the FTIR spectrum? *

- Most Confident
- Somewhat Confident
- Not Confident

Please rank your confidence level for correctly identifying the unknown acidic component WITH ONLY the FTIR spectrum? *

- Most Confident
- Somewhat Confident
- Not Confident

Please explain your previous response. *

Please rank your confidence level for correctly identifying the unknown acidic component WITHOUT the 1H NMR spectrum? *

- Most Confident
- Somewhat Confident
- Not Confident

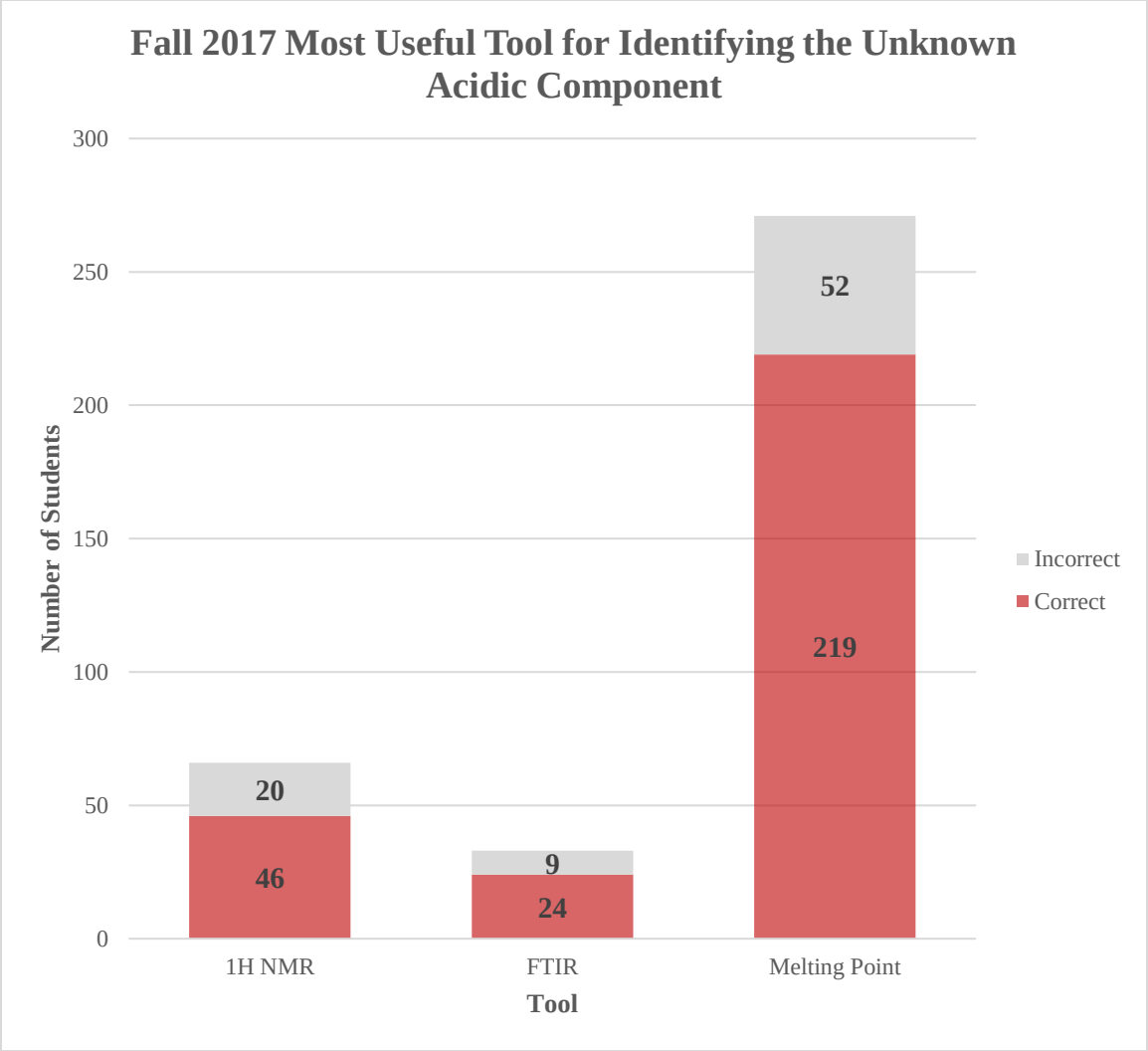
Please rank your confidence level for correctly identifying the unknown acidic component WITH ONLY the 1H NMR spectrum? *

- Most Confident
- Somewhat Confident
- Not Confident

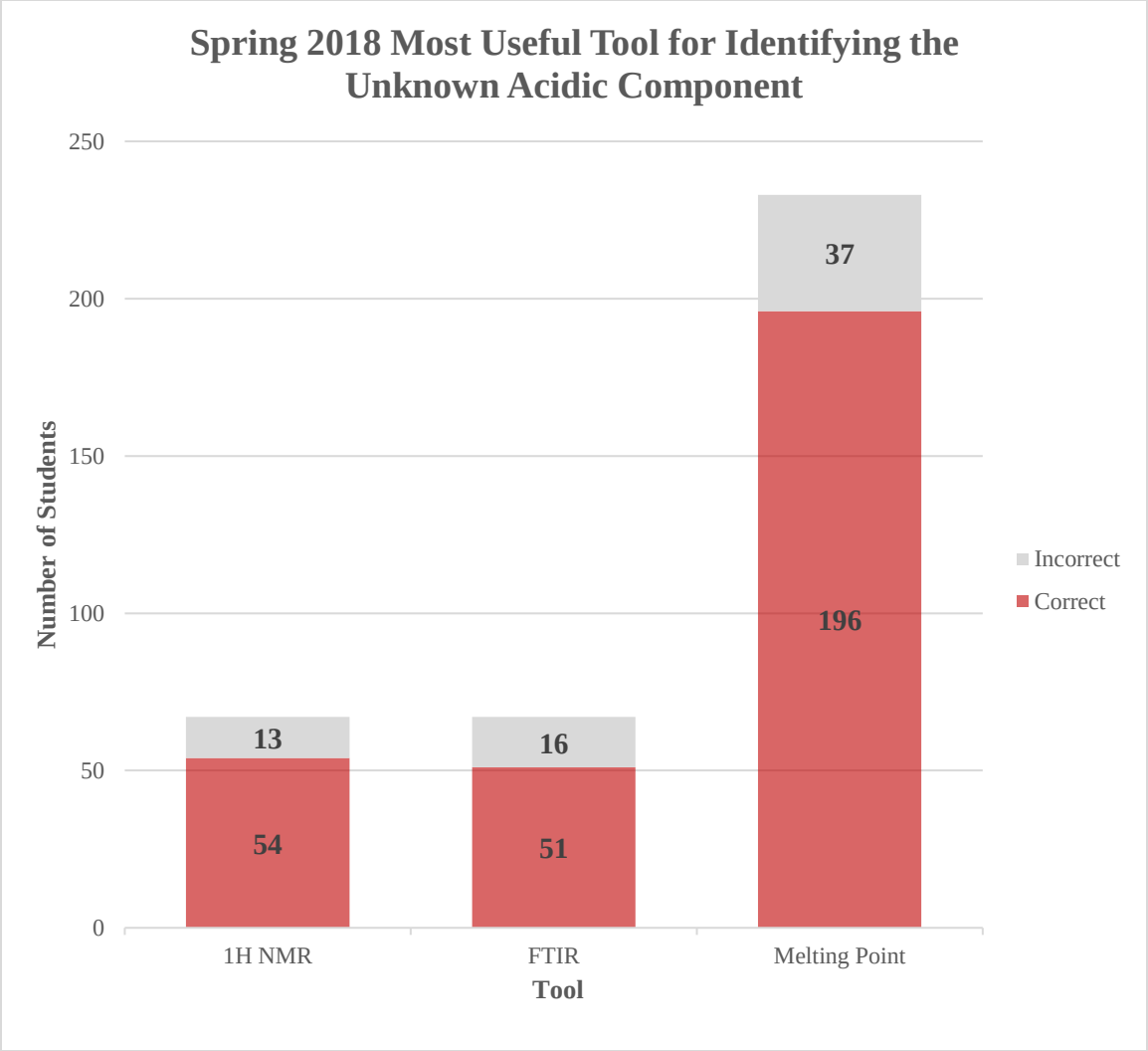
Please explain your previous response. *

Please provide any further feedback for this experiment.

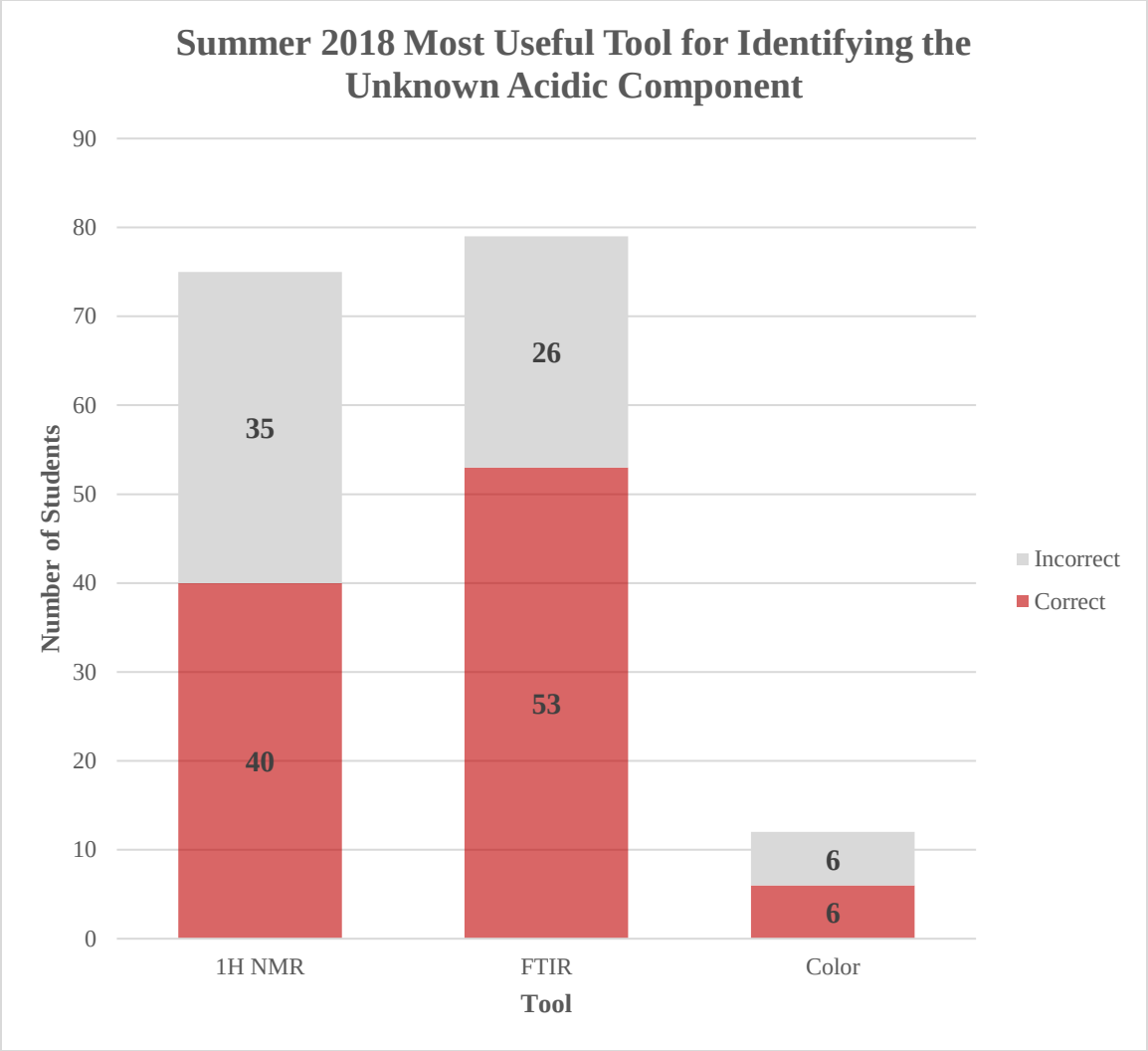
Submit



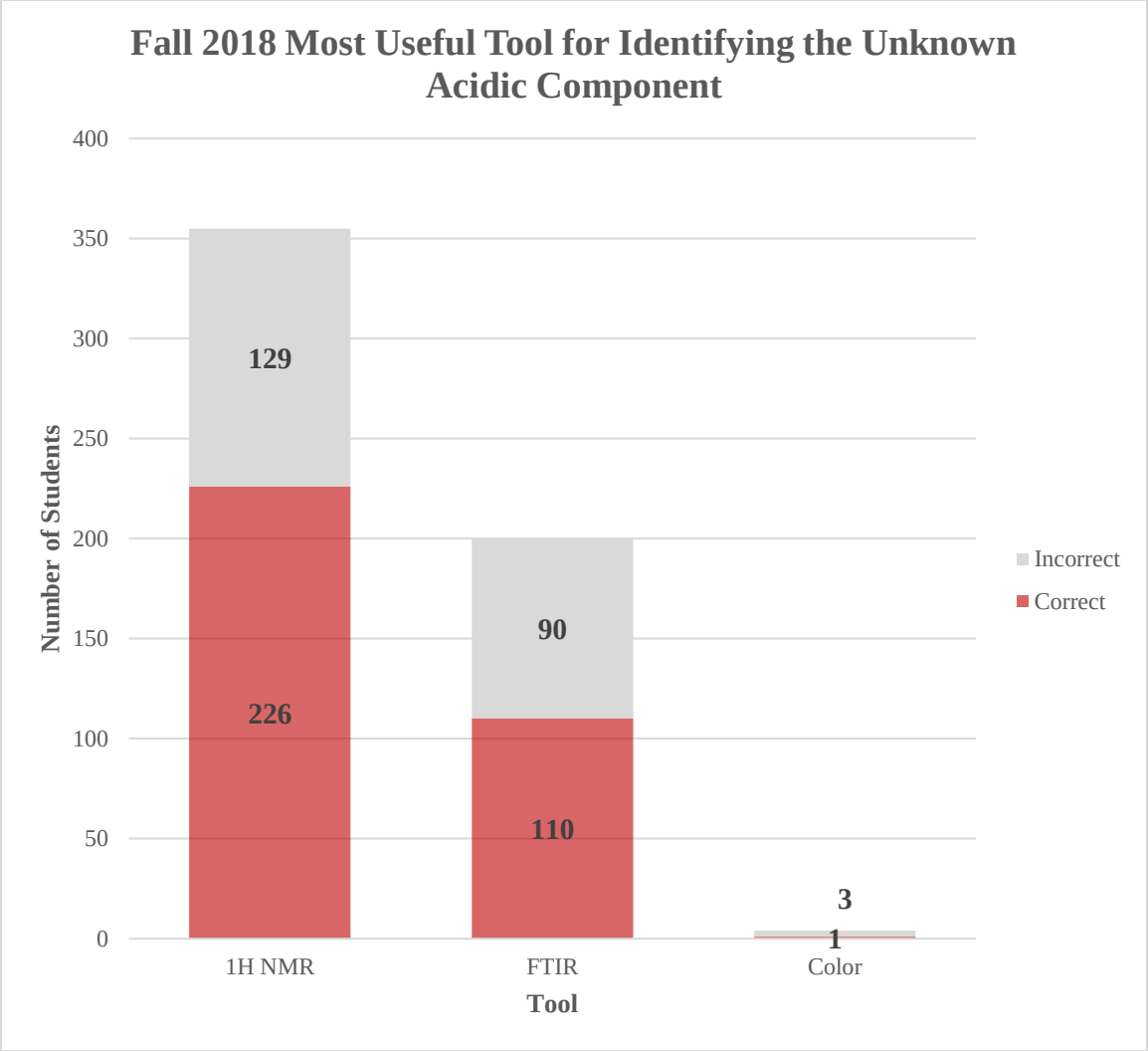
SI Figure 2.7. Fall 2017 postlab survey results for the most useful technique for deducing the identity of the unknown acidic component. N = 370 students.



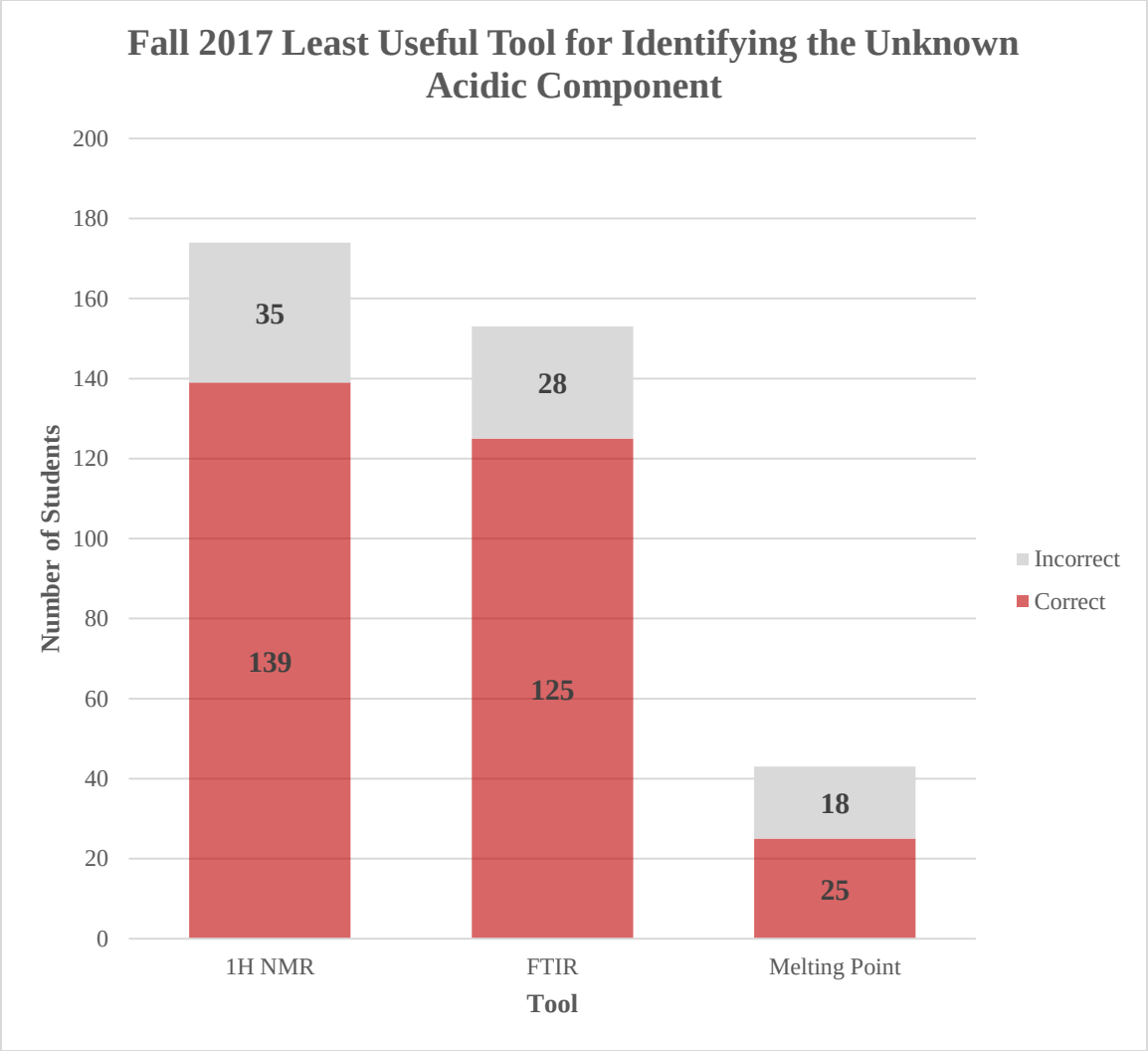
SI Figure 2.8. Spring 2018 postlab survey results for the most useful technique for deducing the identity of the unknown acidic component. N = 367 students.



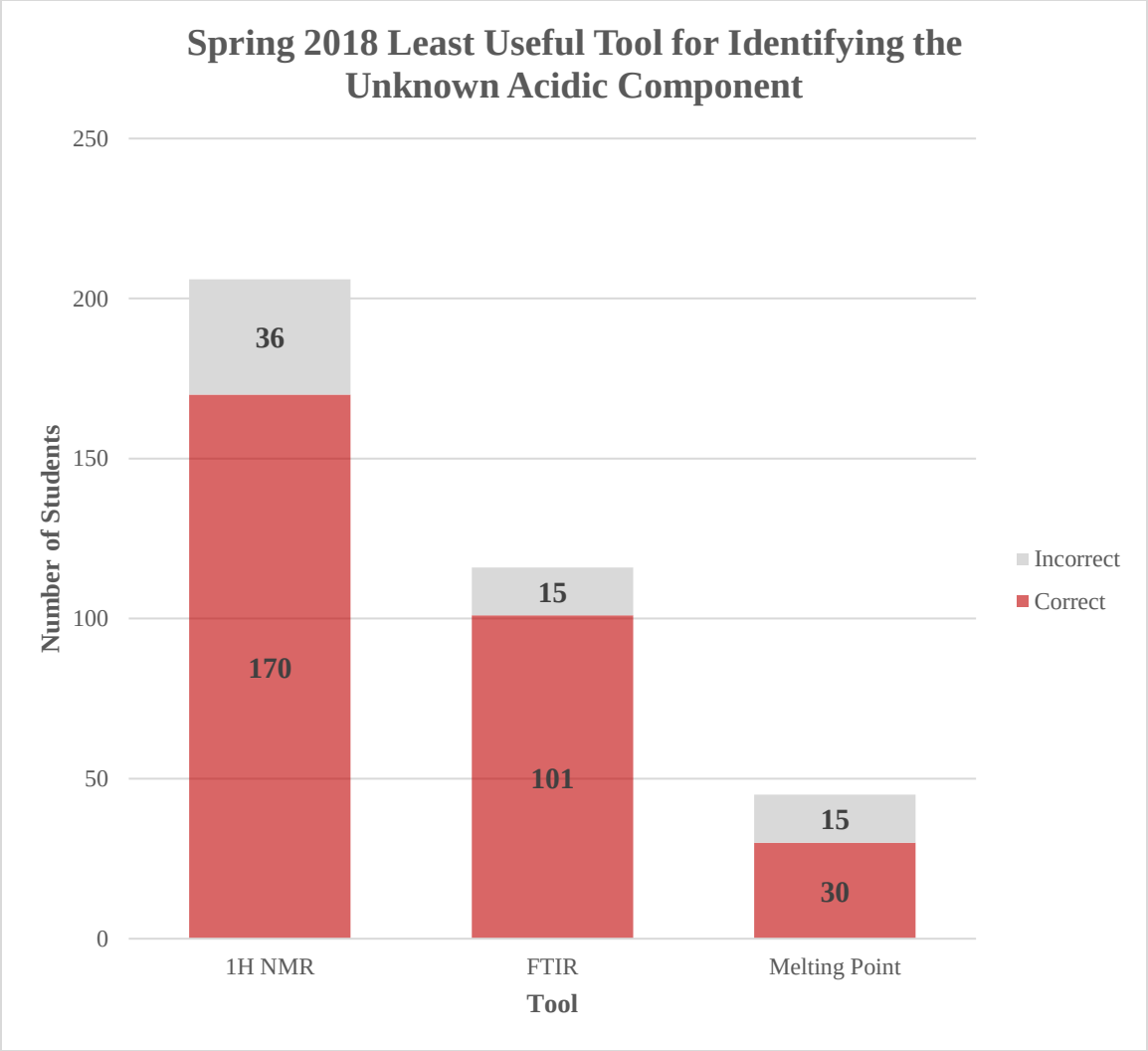
SI Figure 2.9. Summer 2018 postlab survey results for the most useful technique for deducing the identity of the unknown acidic component. N = 166 students.



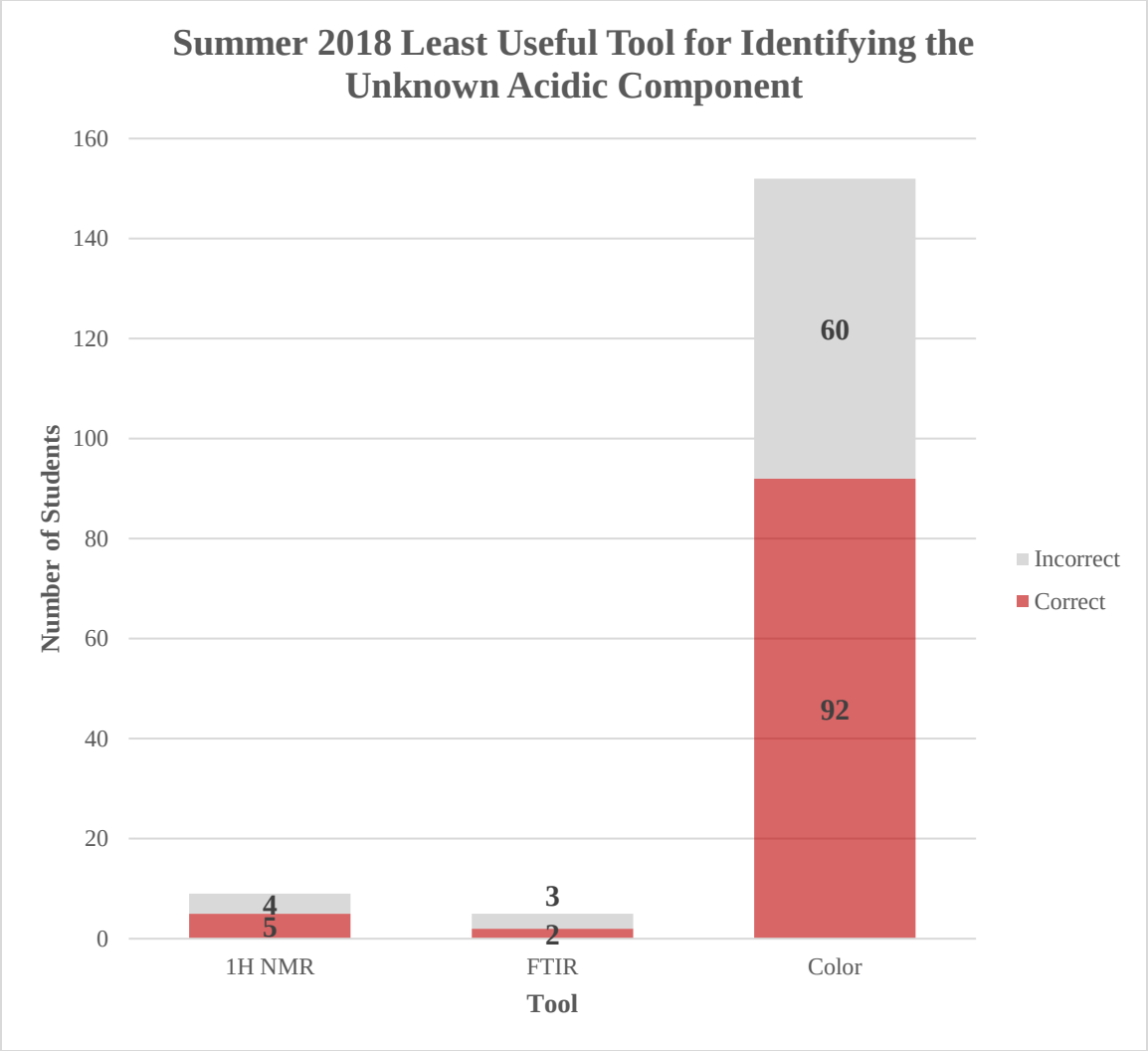
SI Figure 2.10. Fall 2018 postlab survey results for the most useful technique for deducing the identity of the unknown acidic component. N = 559 students.



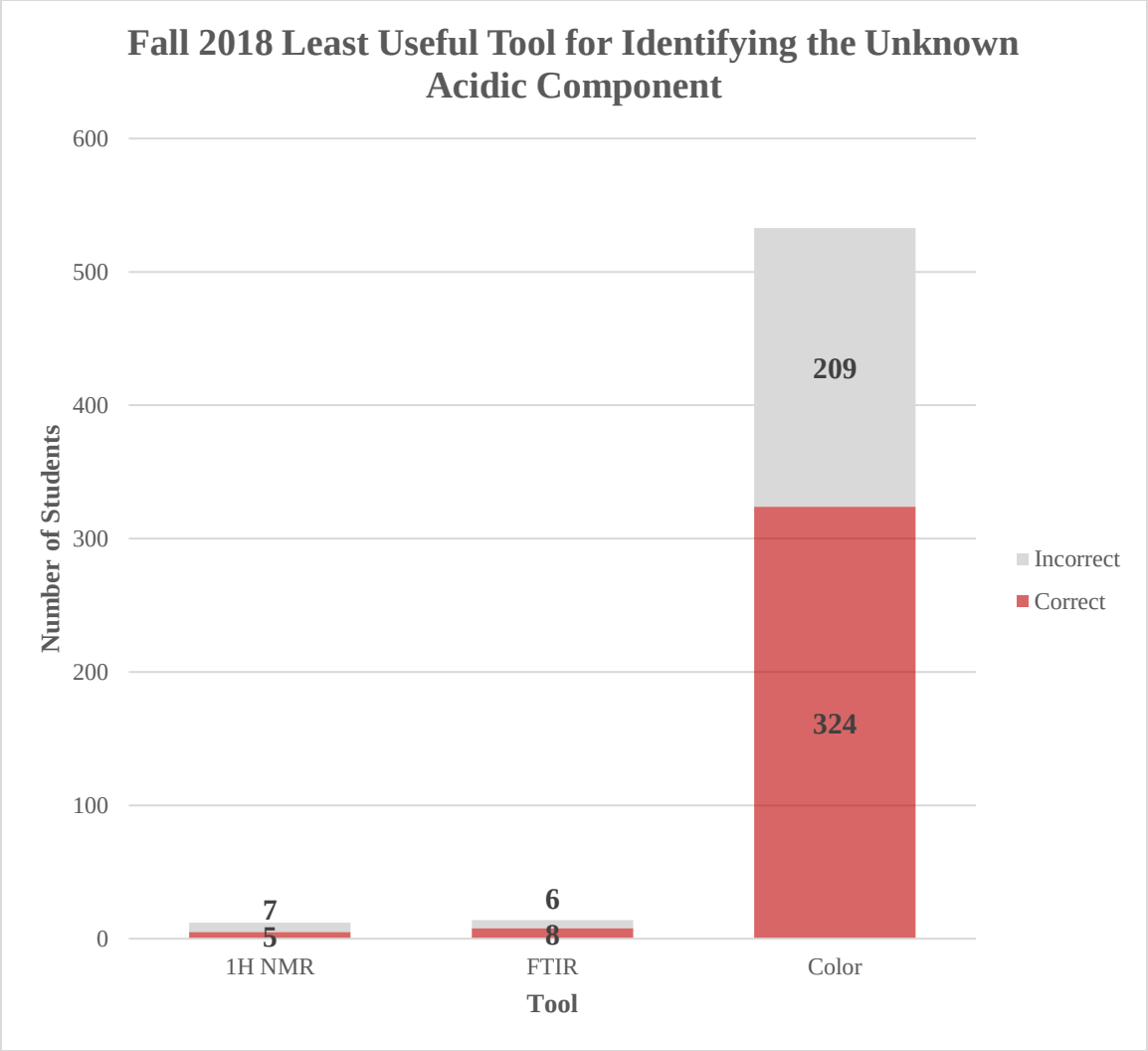
SI Figure 2.11. Fall 2017 postlab survey results for the least useful technique for deducing the identity of the unknown acidic component. N = 370 students.



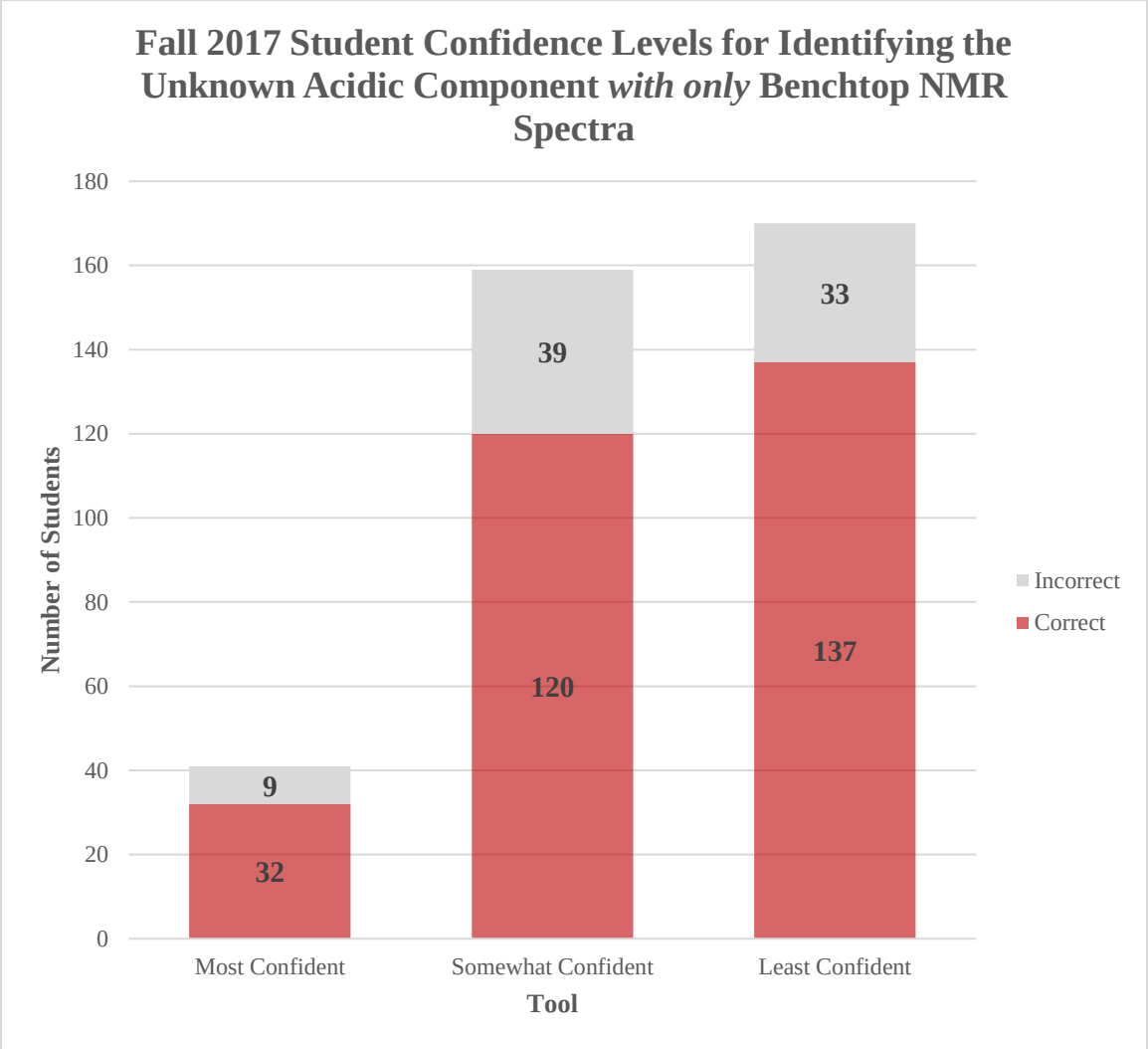
SI Figure 2.12. Spring 2018 postlab survey results for the least useful technique for deducing the identity of the unknown acidic component. N = 367 students.



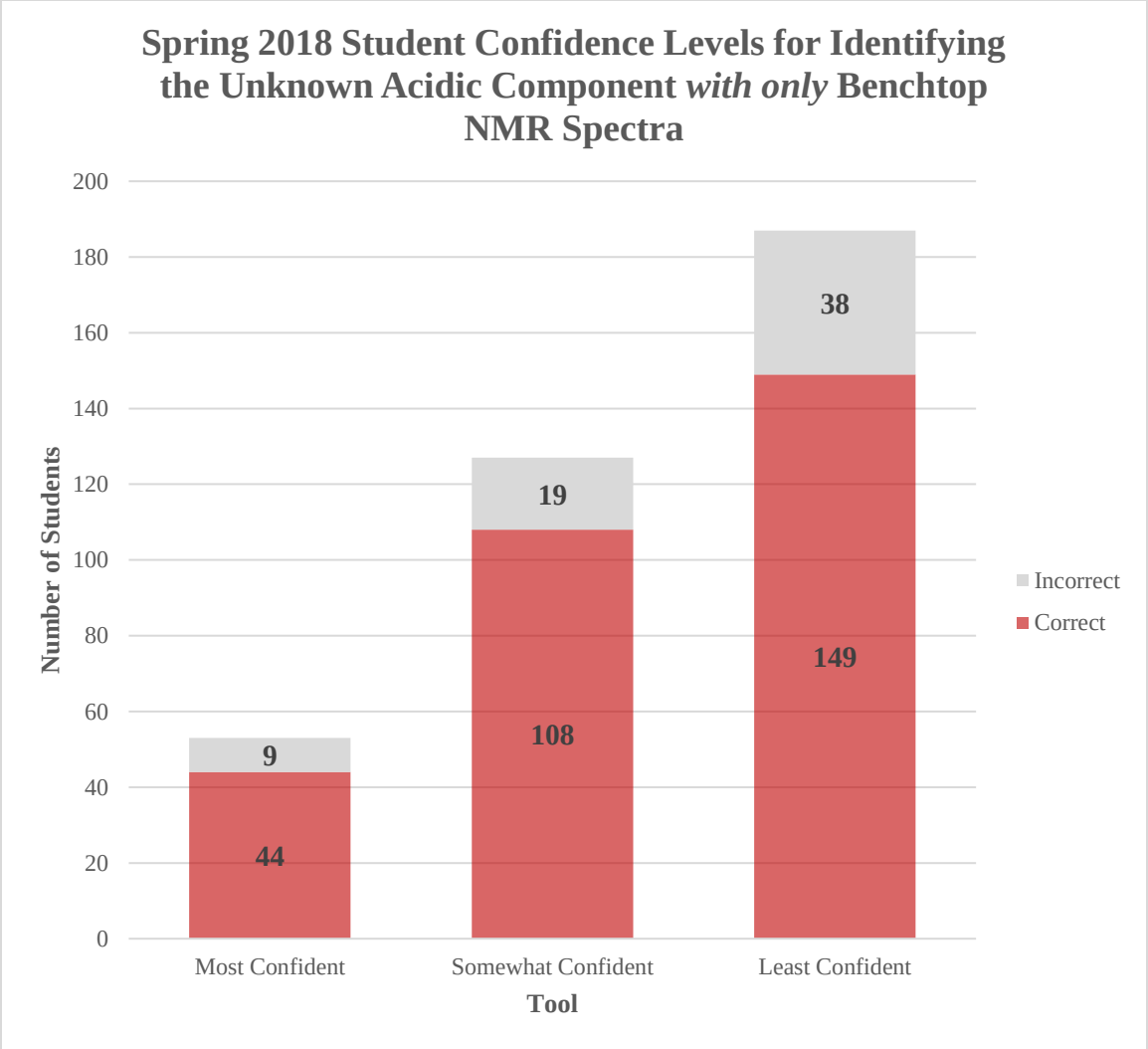
SI Figure 2.13. Summer 2018 postlab survey results for the least useful technique for deducing the identity of the unknown acidic component. N = 166 students.



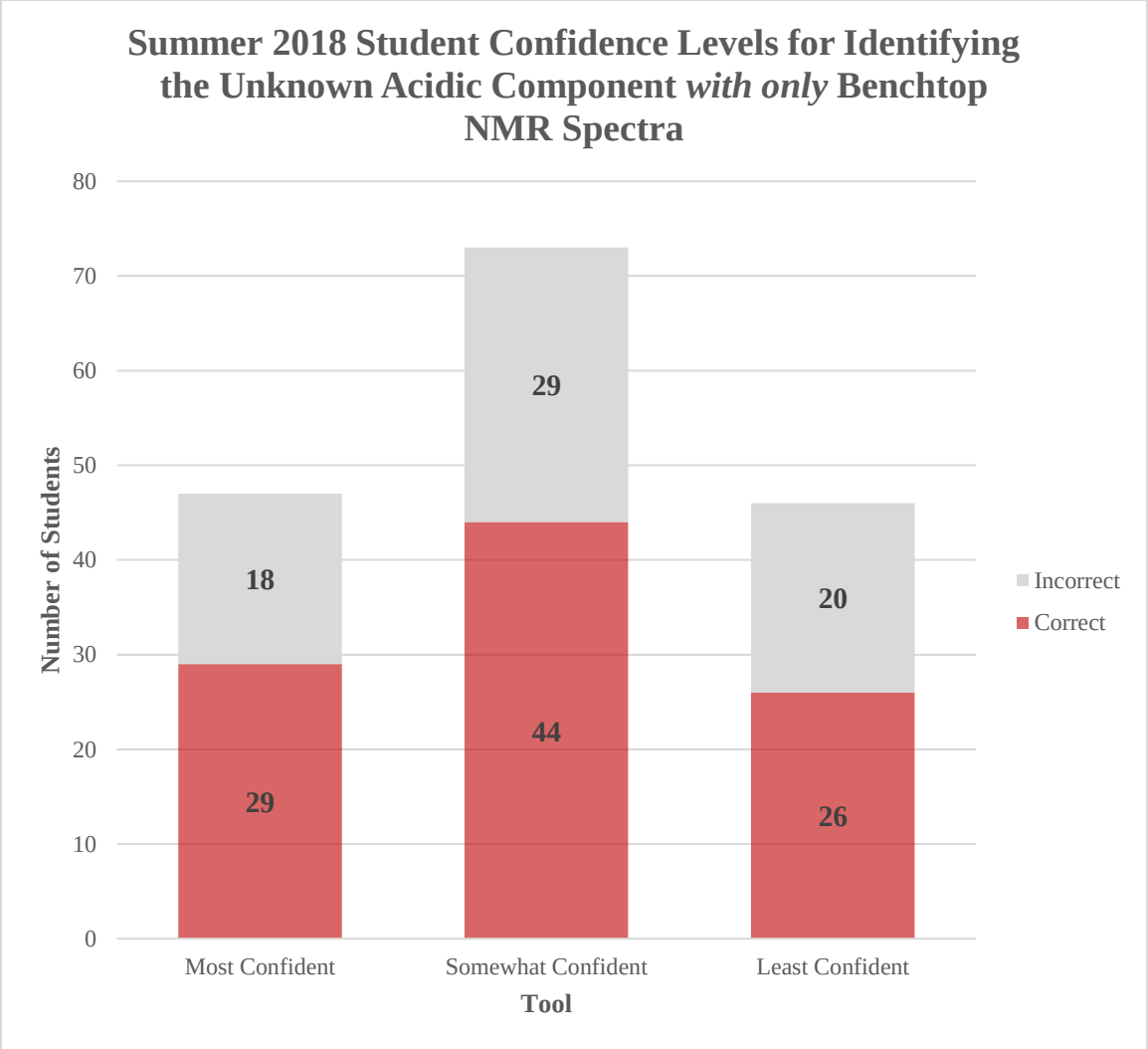
SI Figure 2.14. Fall 2018 postlab survey results for the least useful technique for deducing the identity of the unknown acidic component. N = 559 students.



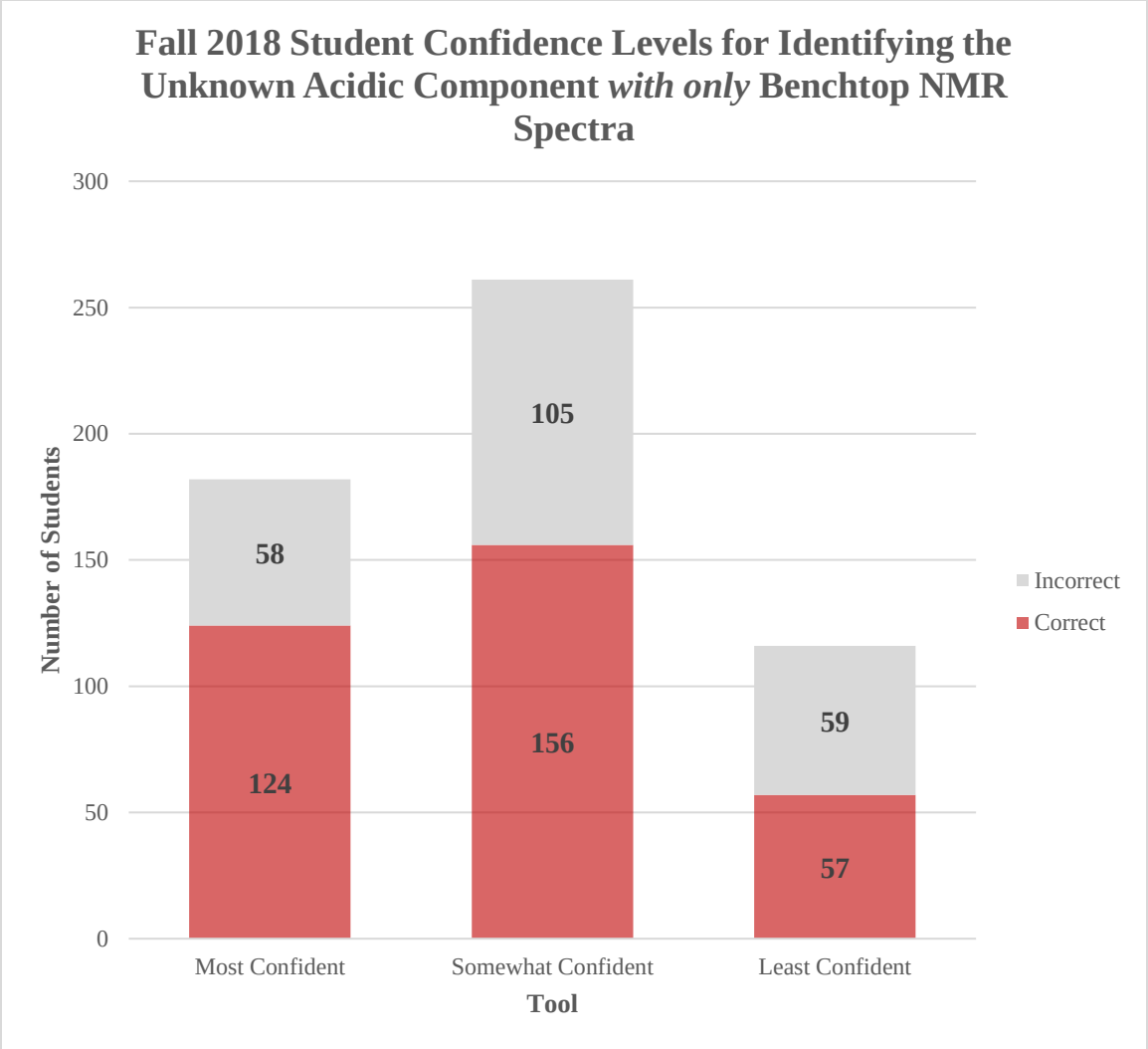
SI Figure 2.15. Fall 2017 postlab survey results for student reported confidence levels for correctly identifying their unknown acidic component *with only* benchtop NMR spectra. N = 370 students.



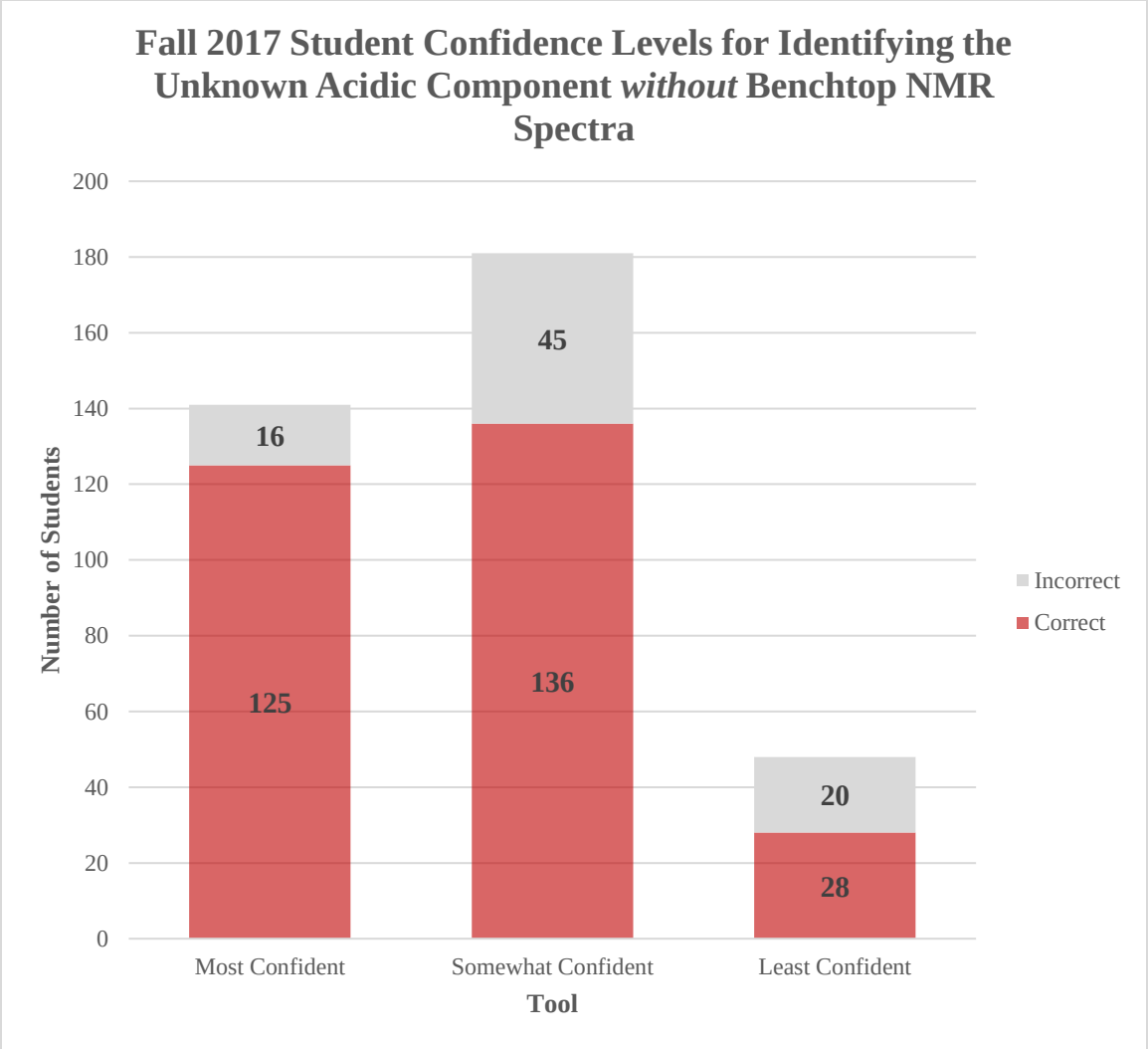
SI Figure 2.16. Spring 2018 postlab survey results for student reported confidence levels for correctly identifying their unknown acidic component *with only* benchtop NMR spectra. N = 367 students.



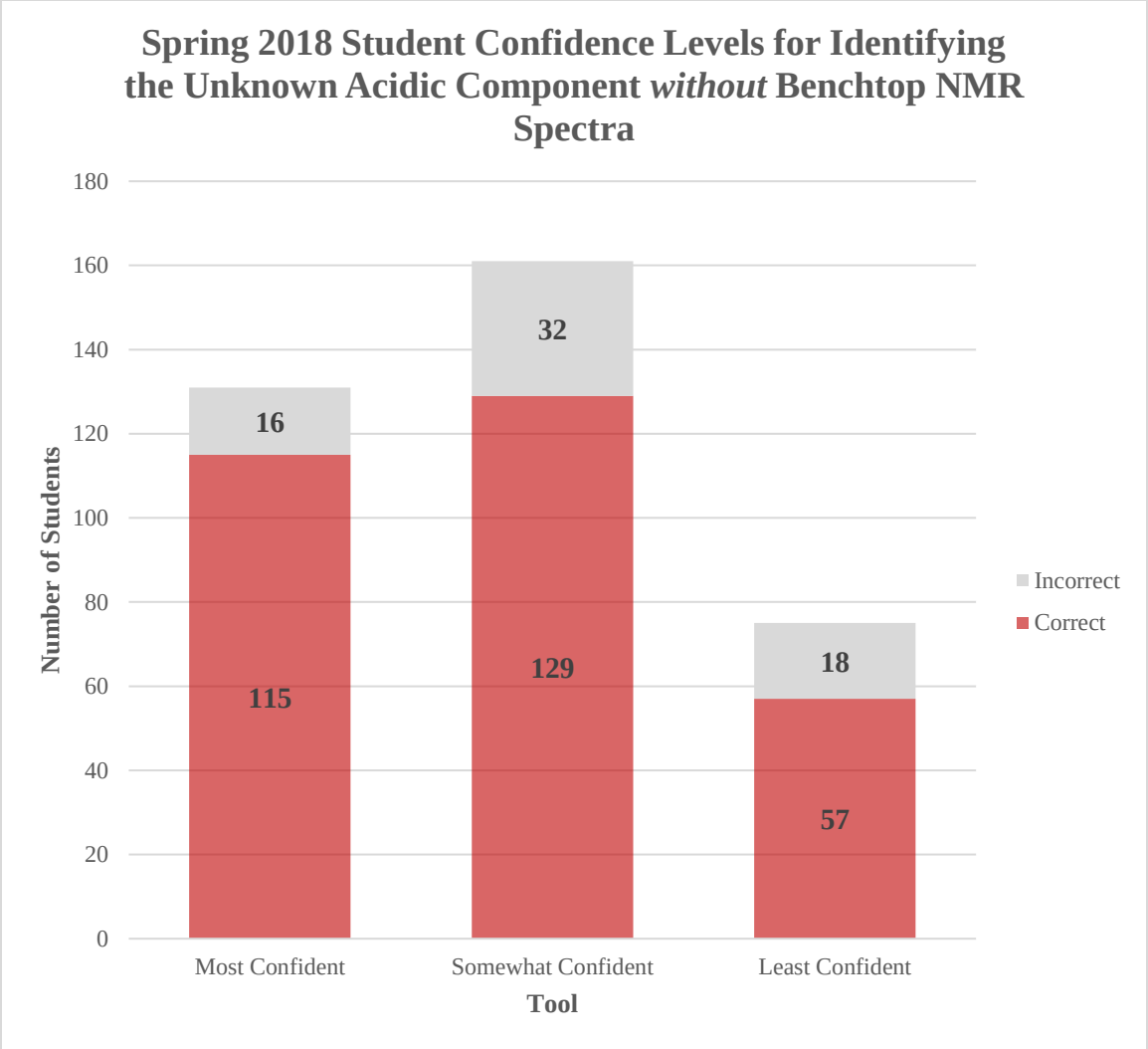
SI Figure 2.17. Summer 2018 postlab survey results for student reported confidence levels for correctly identifying their unknown acidic component *with only* benchtop NMR spectra. N = 166 students.



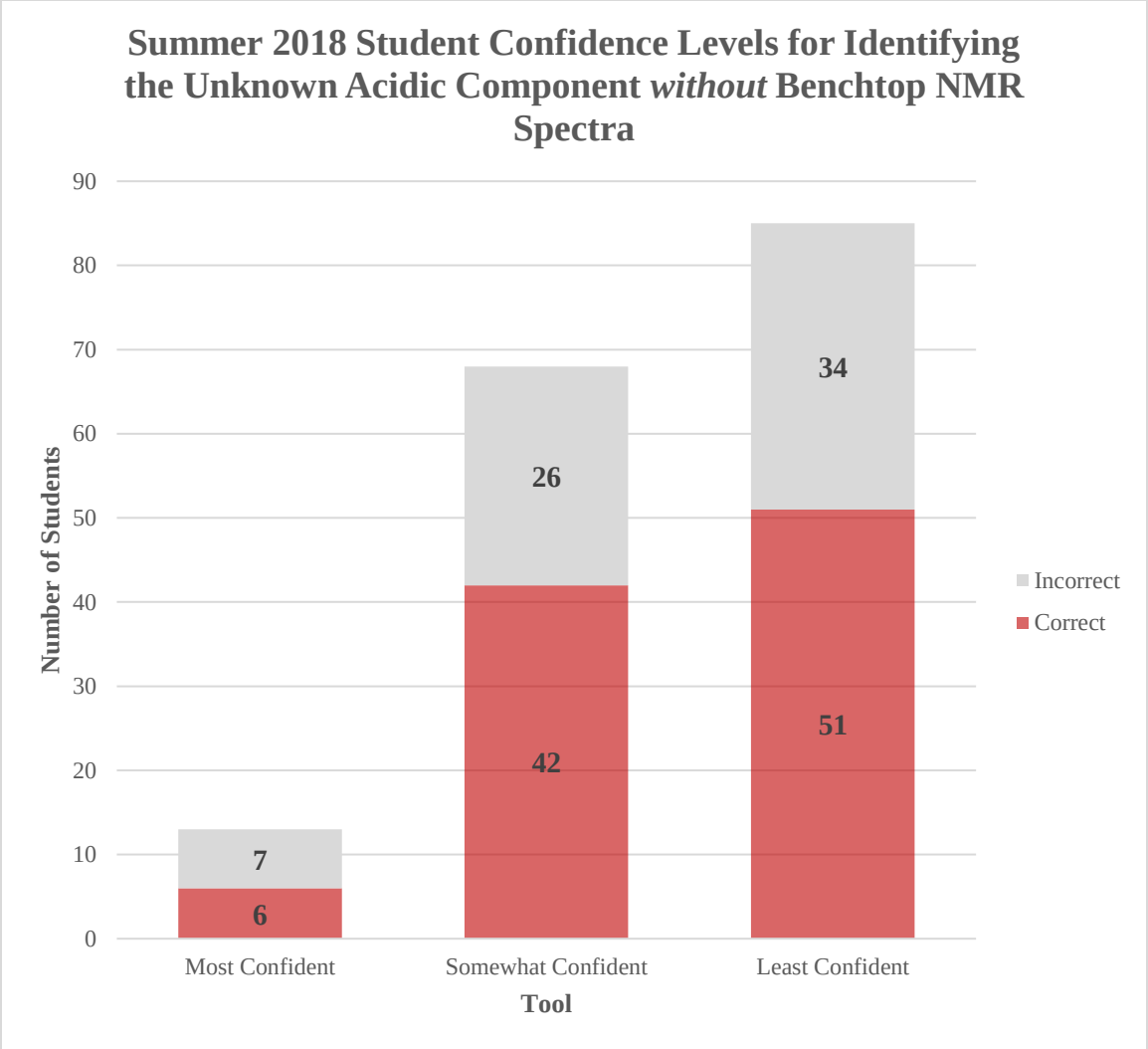
SI Figure 2.18. Fall 2018 postlab survey results for student reported confidence levels for correctly identifying their unknown acidic component *with only* benchtop NMR spectra. N = 559 students.



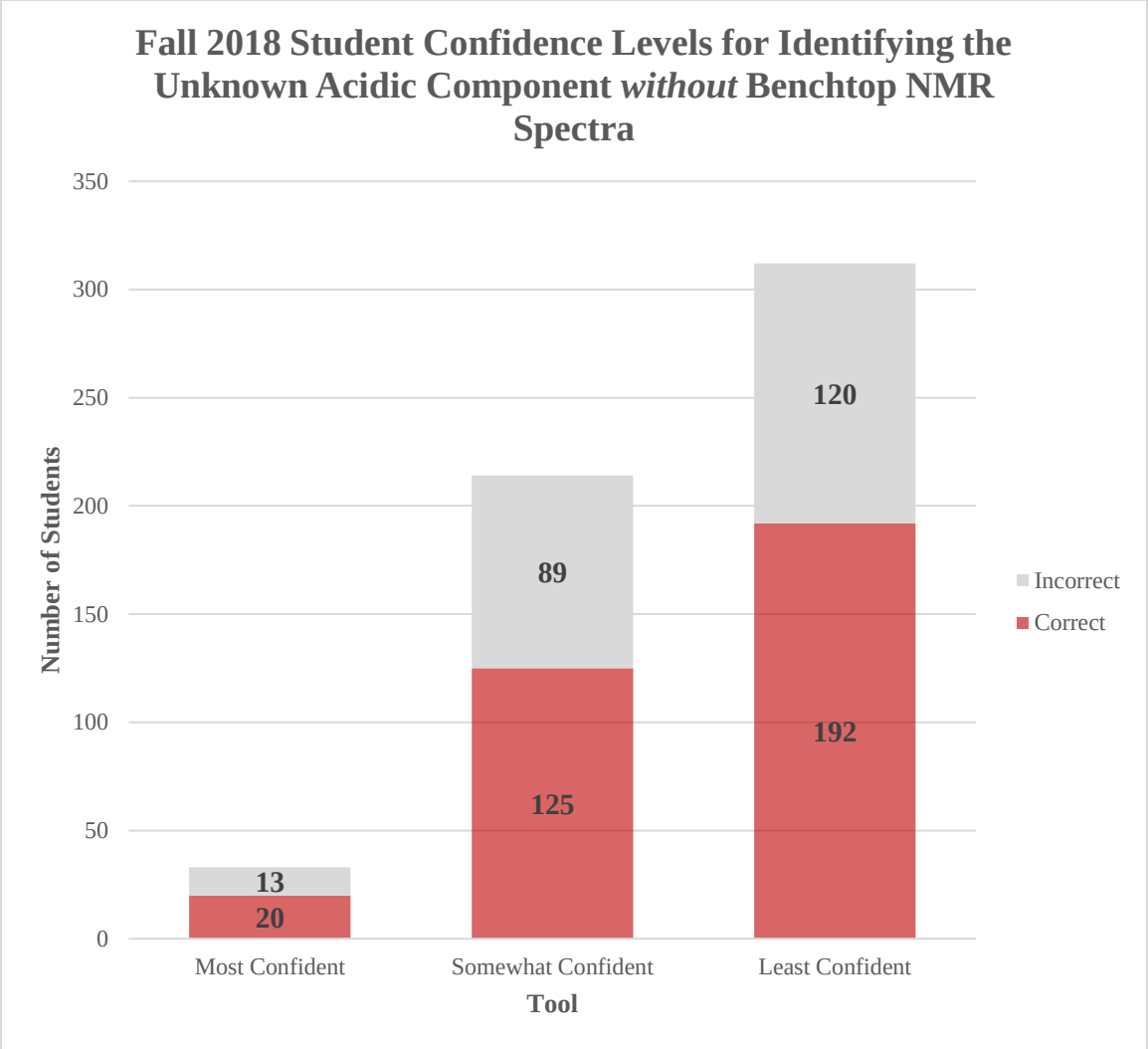
SI Figure 2.19. Fall 2017 postlab survey results for student reported confidence levels for correctly identifying their unknown acidic component *without* benchtop NMR spectra. N = 370 students.



SI Figure 2.20. Spring 2018 postlab survey results for student reported confidence levels for correctly identifying their unknown acidic component *without* benchtop NMR spectra. N = 367 students.



SI Figure 2.21. Summer 2018 postlab survey results for student reported confidence levels for correctly identifying their unknown acidic component *without* benchtop NMR spectra. N = 166 students.



SI Figure 2.22. Fall 2018 postlab survey results for student reported confidence levels for correctly identifying their unknown acidic component *without* benchtop NMR spectra. N = 559 students.

Note to Lab Coordinator 2.1

As expected with an introduction to liquid-liquid extraction, initial challenges include the confusion of aqueous and organic layers by students. With respect to the neutral component, students may occasionally confuse the drying agent used as the resulting neutral product. While this can be easily remedied, it may produce additional challenges if the student injects the drying agent into the capillary of the NMR instrument. Careful TA supervision of sample preparation is necessary for this experiment.

Inevitably, students will mix-up their white powders, insisting that the compound that produces an FTIR spectrum resembling that of benzocaine is indeed their acidic component. This can perpetuate unless the FTIR spectra, which are ideally being collected independently by the students, are checked to ensure that the file names accompanying the spectra represent the spectra collected. Additionally, this experiment is the first in which students have encountered both FTIR and ^{1}H NMR spectroscopies. A thorough training on how to collect an FTIR spectrum of a compound during the previous week's lab can increase the students' independence on the instrument during this experiment. This will give the TA more time to focus on the students as they prepare their NMR samples and inject their samples into the capillary.

Because the organic solvent used during extraction was methylene chloride, this same solvent was selected as the NMR solvent. The magnet temperature of the benchtop NMR instrument used is within several degrees of the boiling point of methylene chloride. Combined with the solvent's volatility, it is imperative that the spectra are collected immediately after sample injection. Otherwise, the solvent may evaporate, leaving the solid sample in the capillary. If this occurs, rinsing the capillary with pure methylene chloride should clear any obstructions. Because this experiment involved the greatest number of teaching assistants operating the benchtop NMR instruments, initial challenges involved summiting the learning curve for the benchtop ^{1}H NMR

instrument as sufficient operator training is essential. Training documents and programs were created by UGA operators to ensure sustainability and a gentle learning curve in the future.

SUPPORTING INFORMATION – CHAPTER 3

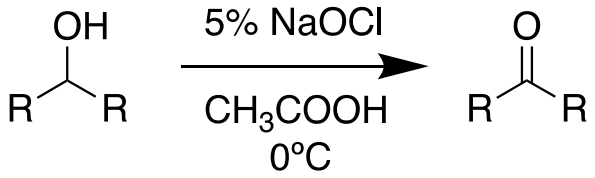
Procedure 3.1. Oxidation of an Unknown Alcohol

There are several meanings for the term "oxidation" when describing a reaction. These include:

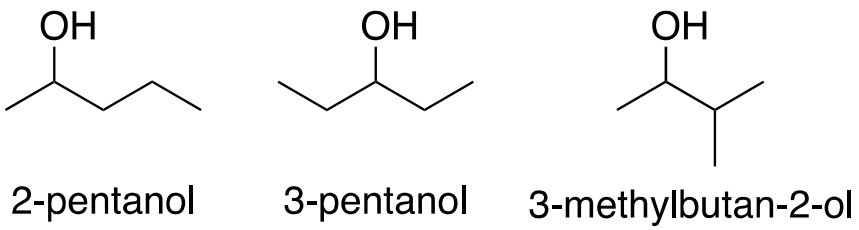
1. The addition of oxygen atoms
2. Addition of other electronegative atoms
3. Any reduction in the number of C-H bonds
4. An increase in bond order
5. A loss of electrons

When alcohols are oxidized, ketones, aldehydes, and carboxylic acids can be formed depending on reaction conditions and the structure of the alcohol. This idea has applications beyond organic chemistry. In fact, these reactions are important in the world of forensics. In a breathalyzer, the primary alcohol ethanol is oxidized to acetic acid in an oxidative environment containing sulfuric acid, potassium dichromate, silver nitrate, and water.

In this experiment, the process occurring in the breathalyzer instrument is paralleled using a mild and relatively "green" oxidizing agent, bleach (NaOCl 5% w/v in water). The starting alcohol is one of the following secondary alcohols: 2-pentanol, 3-pentanol, or 3-methyl-butan-2-ol. Below is a generic line reaction for the oxidation of a secondary alcohol using the reaction conditions in this experiment.



Potential unknown alcohols:



Following the isolation of the oxidized product, FTIR and ^{1}H NMR spectroscopy will be used to deduce the starting material.

Techniques:

Quenching

Liquid/liquid Extraction

FTIR Spectroscopy

^{1}H NMR Spectroscopy

Table of Reagents:

Gather all relevant physical data for the following compounds.

2-pentanol (structure, MW, MP, BP, density)

3-pentanol (structure, MW, MP, BP, density)

3-methylbutan-2-ol (structure, MW, MP, BP, density)

Glacial acetic acid (structure, MW, MP, BP)

Sodium hypochlorite (structure, MW)

Sodium bisulfite (structure, MW)

Sodium hydroxide (structure, MW)

Magnesium sulfate anhydrous (structure, MW)

Methylene chloride (structure, MW, BP, density, solubility in water)

Water (structure, MW, BP, density)

Brine (structure, MW, BP, density)

Hazards:

Safety glasses, lab gloves, and lab coats must always be worn. Sodium hypochlorite is the active ingredient in household bleach and will bleach colored clothing. Acetic acid and sodium hypochlorite are irritants and should be washed away immediately if in contact with skin or eyes. Use caution when working with 6M sodium hydroxide as it is caustic and may cause burns. Dichloromethane (DCM) is volatile. Take care when dispensing and evaporating it. Avoid vapors and make sure that the snorkels (fume removal arms at each student lab station) are turned on and functioning properly before dispensing any liquids. Any vapor or liquid exposure should be reported to the teaching assistant (TA) immediately. Dispose of all liquid waste in the appropriately labeled bottle in the lab hood.

Procedure:

Obtain 2.1 g of your TA-assigned unknown alcohol and record its unknown code. Prepare an ice bath to cool a 100 mL round-bottom flask containing your unknown. Add a stir bar and 1.75 mL of glacial acetic acid to the round-bottom flask. While the round-bottom is cooling in the ice bath, add 36 mL of the sodium hypochlorite (in the form of household bleach) drop-wise into the stirring solution over 10 minutes. (*Use caution while adding the sodium hypochlorite to the reaction mixture drop-wise*.) Continue to stir the reaction mixture for 20 additional minutes.

Next, a series of tests will be performed to ensure reaction completion and proper work-up. Be sure to keep the reaction mixture stirring and in the ice bath during the work-up until you reach the extraction procedure.

1. Test for Excess Hypochlorite (continue stirring)

Test the mixture for excess oxidant using potassium iodide-starch paper. Using a glass pipette, remove a drop of the reaction mixture and drop it onto the strip. If the color of the paper changes from white to a blue color, that is an indication of excess hypochlorite. If the strip does not change color, add the NaOCl in 5 mL aliquots, testing each time for a color change. Remember to

rinse your pipette with the reaction mixture before testing for excess hypochlorite; otherwise, you may be dropping bleach directly onto the paper and may receive a false positive result. Once there is a blue color change on the potassium iodide-starch paper, move onto the next test.

2. Quenching the Reaction (continue stirring)

Obtain 10 mL of the saturated sodium bisulfite solution. This will be used to quench the reaction mixture. What does quench mean? Add 4 mL of the solution to the round-bottom flask. Test the reaction mixture with the potassium iodide-starch paper by adding a drop of the solution onto the paper. Remember to rinse your pipette with the reaction mixture adding a drop to the potassium iodide -starch paper; otherwise, you may be dropping sodium bisulfite directly onto the paper and may receive a false positive result. If the paper remains white, move onto the basic wash. If the paper turns blue, continue to add the sodium bisulfite solution in 2 mL portions and test the reaction mixture with the potassium iodide-starch paper after each aliquot. Repeat until the potassium iodide-starch paper does <u>not</u> turn blue when a drop of the solution is added to it.

3. Base Wash (continue stirring)

Obtain 4.5 mL of 6 M sodium hydroxide and add it to the reaction mixture. Test the pH by adding a drop of the reaction mixture to a pH strip after each addition of base. Remember to rinse your pipette with the reaction mixture before testing the pH; otherwise, you may be dropping base directly onto the paper and may receive a false positive result. Continue to add the base in 1.5 mL aliquots and test the pH until the solution is basic. Let the mixture stir for 10 minutes.

4. Extraction

Add 10 mL of dichloromethane to extract the product. Stop the stirring and remove the stir bar from the flask. Transfer your reaction mixture to a separatory funnel and extract the organic layer. Add 10 more mL of dichloromethane to the aqueous layer and extract the organic layer again. Combine the two organic extracts and wash once with 10 mL of deionized water, followed by a second wash of the organic layer with 10 mL of brine. Dry the organic layer using anhydrous

magnesium sulfate. After drying the organic layer, filter the solution into a pre-weighed 100 mL round bottom flask using gravity filtration to remove the solid drying agent. Concentrate the sample using rotary evaporation. Record the mass of the isolated product. Obtain FTIR and ^{1}H NMR spectra of the product. Note: Two drops of tetramethylsilane (TMS) were added to 0.5 mL of the product ketone. The benchtop NMR spectrometer was prepared for analysis by first injecting an empty syringe to displace any solvent from the capillary. This was followed by injecting the sample into the injection capillary until approximately ten drops exited the outlet port.

**This procedure was adapted from Mohrig and coworkers.*[63]

Oxidation of an Unknown Alcohol Data Sheet

Code for unknown alcohol: _____

Mass of starting alcohol: _____

Volume of glacial acetic acid: _____

Volume of bleach: _____

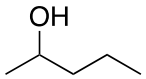
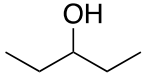
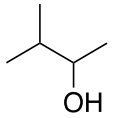
Volume of saturated sodium bisulfite: _____

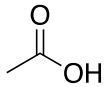
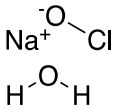
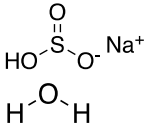
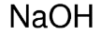
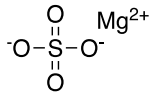
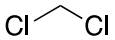
Volume of 6 M sodium hydroxide: _____

Mass of isolated product: _____

Miscellaneous Experimental Observations (Visual descriptions, texture, odor, etc…):

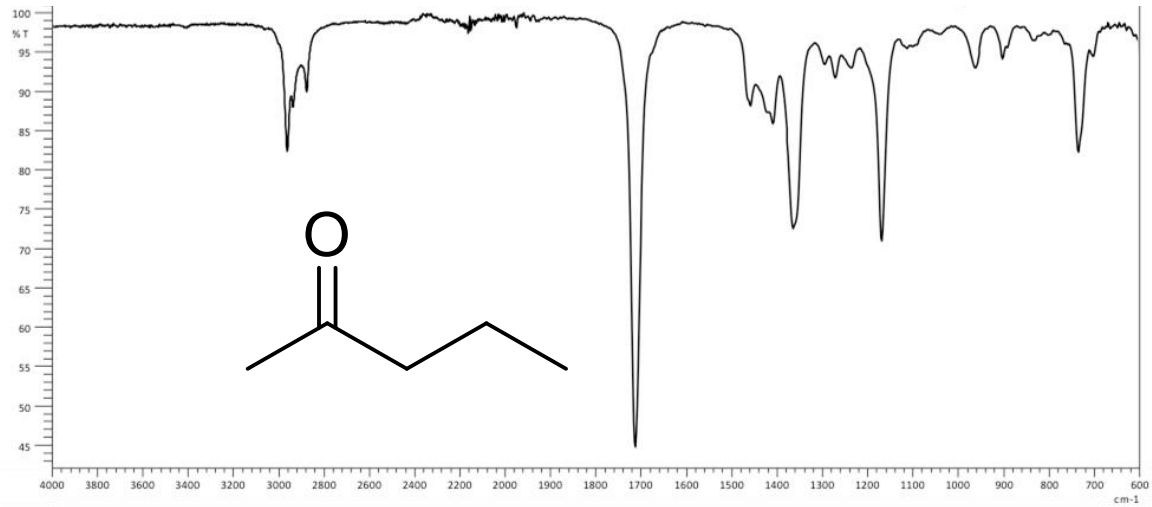
SI Table 3.1. Experiment Table of Reagents for Instructors

Reagent	Structure	CAS	Hazard Codes	Amount needed per Student	Molecular Weight (g/mol)	Melting Point (°C)	Boiling Point (°C)	Density (g/cm^3)	Solubility in water
2-pentanol		6032-29-7	Flammable liquids (Category 3), H226; Acute toxicity, Inhalation (Category 4), H332; Specific target organ toxicity - single exposure (Category 3), Respiratory system, H335	2.1 g	88.15	-73	118-119	0.812	45 g/L
3-pentanol		584-02-1	Flammable liquids (Category 3), H226; Acute toxicity, Oral (Category 4), H302; Acute toxicity, Inhalation (Category 4), H332; Skin irritation (Category 2), H315; Eye irritation (Category 2A), H319; Specific target organ toxicity - single exposure (Category 3), Respiratory system, H335	2.1 g	88.15	-63.68	114-115	0.815	59 g/L
3-methyl-2-butanol		589-75-4	Flammable liquids (Category 3), H226; Acute toxicity, Inhalation (Category 4), H332; Specific target organ toxicity - single exposure (Category 3), Respiratory system, H335	2.1 g	88.15	-	112	0.818	56 mg/mL at 25 °C

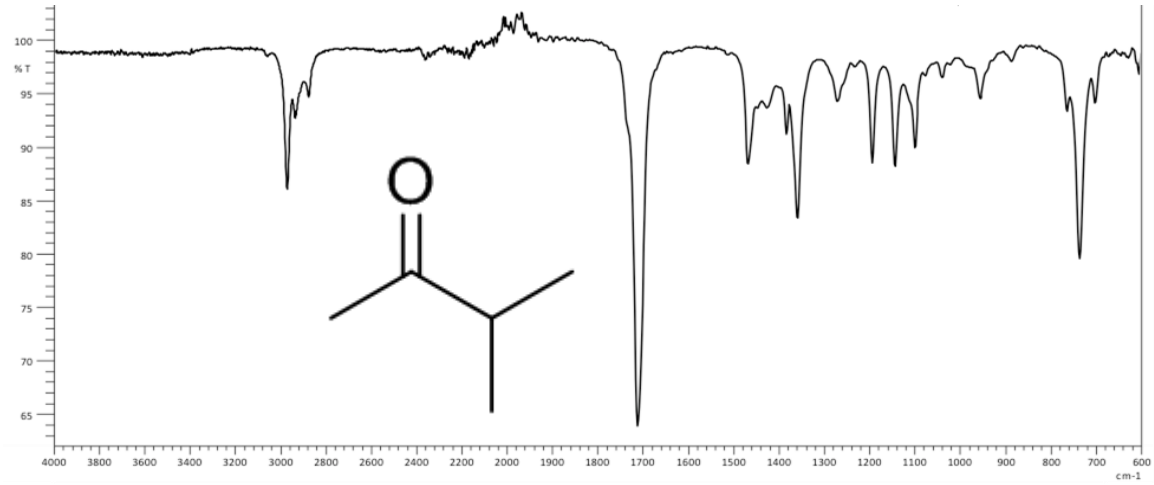
Glacial acetic acid		64-19-7	Flammable liquids (Category 2), H225; Skin corrosion (Category 1A), H314; Serious eye damage (Category 1), H318	1.75 mL	60.05	16.2	118.1	-	-
Sodium hypochlorite solution		7681-52-9	Skin corrosion (Category 1B), H314; Serious eye damage (Category 1), H318; Acute aquatic toxicity (Category 1), H400	36 mL	74.44	-	-	-	-
Sodium bisulfite solution		7631-90-5	Not a hazardous substance or mixture.	At least 4 mL	104.06	-	-	-	-
Sodium hydroxide		1310-73-2	Corrosive to metals (Category 1), H290; Skin corrosion (Category 1A), H314; Serious eye damage (Category 1), H318; Acute aquatic toxicity (Category 3), H402	At least 4.5 mL	40.00	-	-	-	-
Magnesium sulfate anhydrous		7487-88-9	Not a hazardous substance or mixture.	Drying agent (less than 5 g)	120.37	-	-	-	-
Dichloro-methane		75-09-2	Skin irritation (Category 2), H315; Eye irritation (Category 2A), H319; Carcinogenicity (Category 2), H351; Specific target organ toxicity - single exposure (Category 3), Respiratory system, Central nervous system,	20 mL	84.93	-	39.8-40	1.325	Slightly soluble

			H335; H336; Specific target organ toxicity - repeated exposure, Oral (Category 2), Liver, Blood, H373; Specific target organ toxicity - repeated exposure, Inhalation (Category 2), Central nervous system, H373						
Water		7731-18-5	Not a hazardous substance or mixture.	10 mL	18.02	-	100	1.000	-
Brine		7647-14-5	Not a hazardous substance or mixture.	10 mL	58.44	-	100	1.190	-

SI Figure 3.1. FTIR spectrum from the Shimadzu IRAffinity-1S for 3-pentanone produced by students. The structure is provided for clarity.



SI Figure 3.2. FTIR spectrum from the Shimadzu IRAffinity-1S for 2-pentanone produced by students. The structure is provided for clarity.



SI Figure 3.3. FTIR spectrum from the Shimadzu IRAffinity-1S for 3-methyl-2-butanone produced by students. The structure is provided for clarity.

SI Student Survey 3.1.

Survey Page 1/6

Oxidation of Alcohols Post-Lab Survey

This survey is intended to gain student feedback regarding the Oxidation of Alcohols experiment in CHEM 2212L at the University of Georgia. Please direct any questions regarding this survey to Kasey Leigh Yearty at kasey90@uga.edu.

* Required

What is your name? *

This will only be used to monitor the survey for completion.

Who is your TA? *

This will only be used to monitor the survey for completion.

What is the identification code for the unknown that you used? *

Please double check your response here to ensure that you have listed the correct unknown identification code.

- 4F15RW51
- 53AT2NB1
- 5AC32K5I
- 6BTF8ASR
- 8NR5CKMO
- 9TK472DL
- A2C129TL
- BT468NI1
- CA253CN8
- D4BO31PI
- FA14DTH8
- MK2RHI84
- MS17EUR2
- NL31TRF9
- P18DFWE6
- PF64A3CK
- TM43CA54
- TN51U5XN
- Other:

What was the identity of your unknown? *

- 2-pentanol
- 3-pentanol
- 3-methyl-2-butanol

What mass of the final product did you obtain? *

Please enter your responses in GRAMS with as many decimal places as your balanced allowed.

Identifying your Unknown Alcohol

This section features a series of questions designed to rank the usefulness of identification tools included the experiment and gain valuable feedback regarding your confidence in your results.

In the identification of your unknown alcohol, which tool was MOST USEFUL to you? *

- Color
- IR
- 1H NMR

Please elaborate on your previous response. *

What specific feature(s) of the tool selected assisted you in deducing the identity of your unknown alcohol?

In the identification of your unknown alcohol, which tool was SECOND MOST USEFUL to you? *

- Color
- IR
- 1H NMR

Please elaborate on your previous response. *

What specific feature(s) of the tool selected assisted you in deducing the identity of your unknown alcohol?

In the identification of your unknown alcohol, which tool was LEAST USEFUL to you? *

- ○ Color
- ○ IR
- ○ 1H NMR

Please elaborate on your previous response. *

What specific feature(s) of the tool selected assisted you in deducing the identity of your unknown alcohol?

How confident would you be in correctly identifying your unknown alcohol WITHOUT the color? *

- ○ Most Confident
- ○ Somewhat Confident
- ○ Not Confident

How confident would you be in correctly identifying your unknown alcohol WITH ONLY the color? *

- ○ Most Confident
- ○ Somewhat Confident
- ○ Not Confident

Please elaborate on your previous responses regarding the color of your product. *

How confident would you be in correctly identifying your unknown alcohol WITHOUT the IR spectra? *

- Most Confident
- Somewhat Confident
- Not Confident

How confident would you be in correctly identifying your unknown alcohol WITH ONLY the IR spectra? *

- Most Confident
- Somewhat Confident
- Not Confident

Please elaborate on your previous responses regarding the IR spectra. *

How confident would you be in correctly identifying your unknown alcohol WITH ONLY the benchtop 1H NMR spectra? *

- Most Confident
- Somewhat Confident
- Not Confident

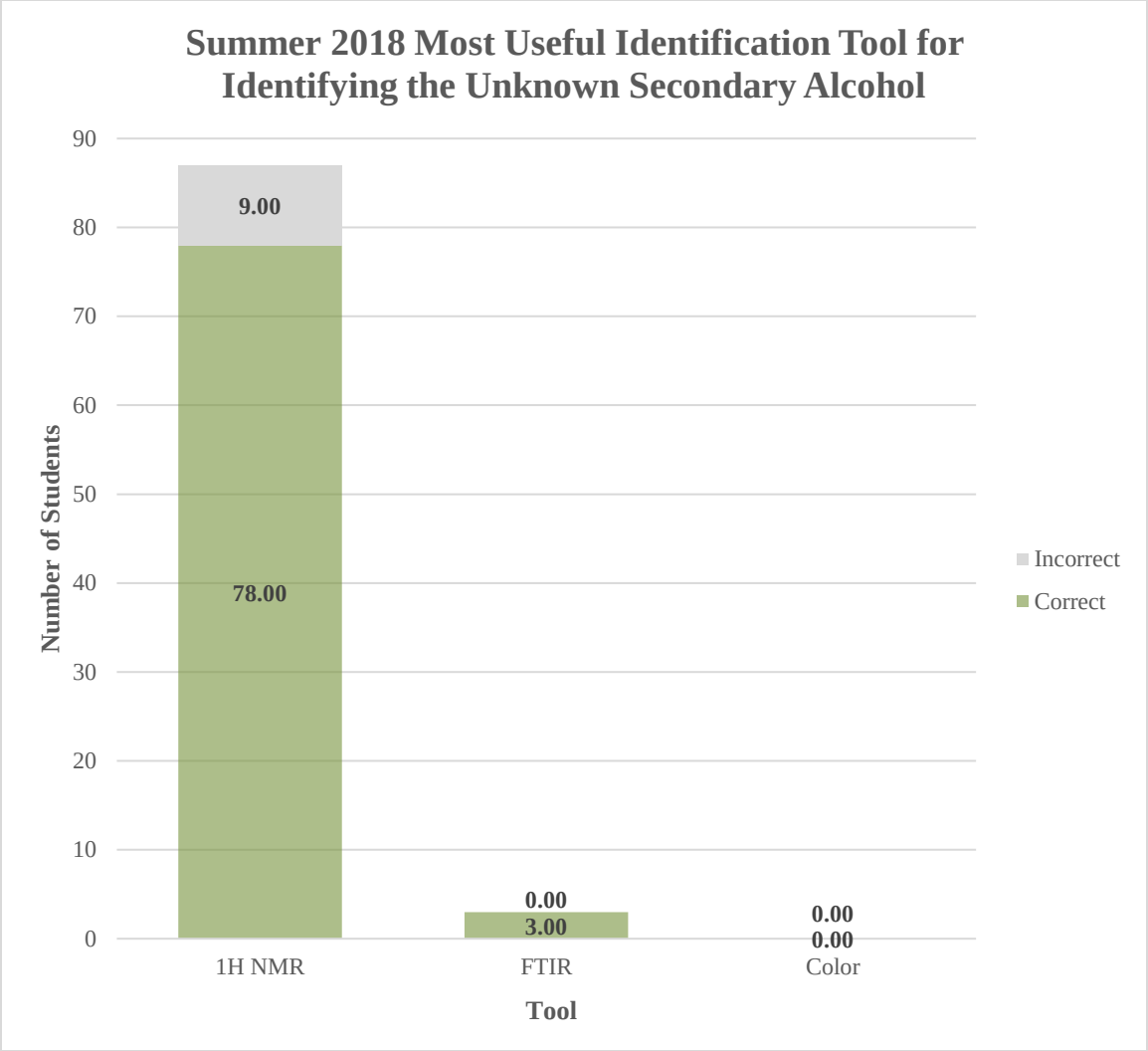
How confident would you be in correctly identifying your unknown alcohol WITHOUT the benchtop 1H NMR spectra? *

- Most Confident
- Somewhat Confident
- Not Confident

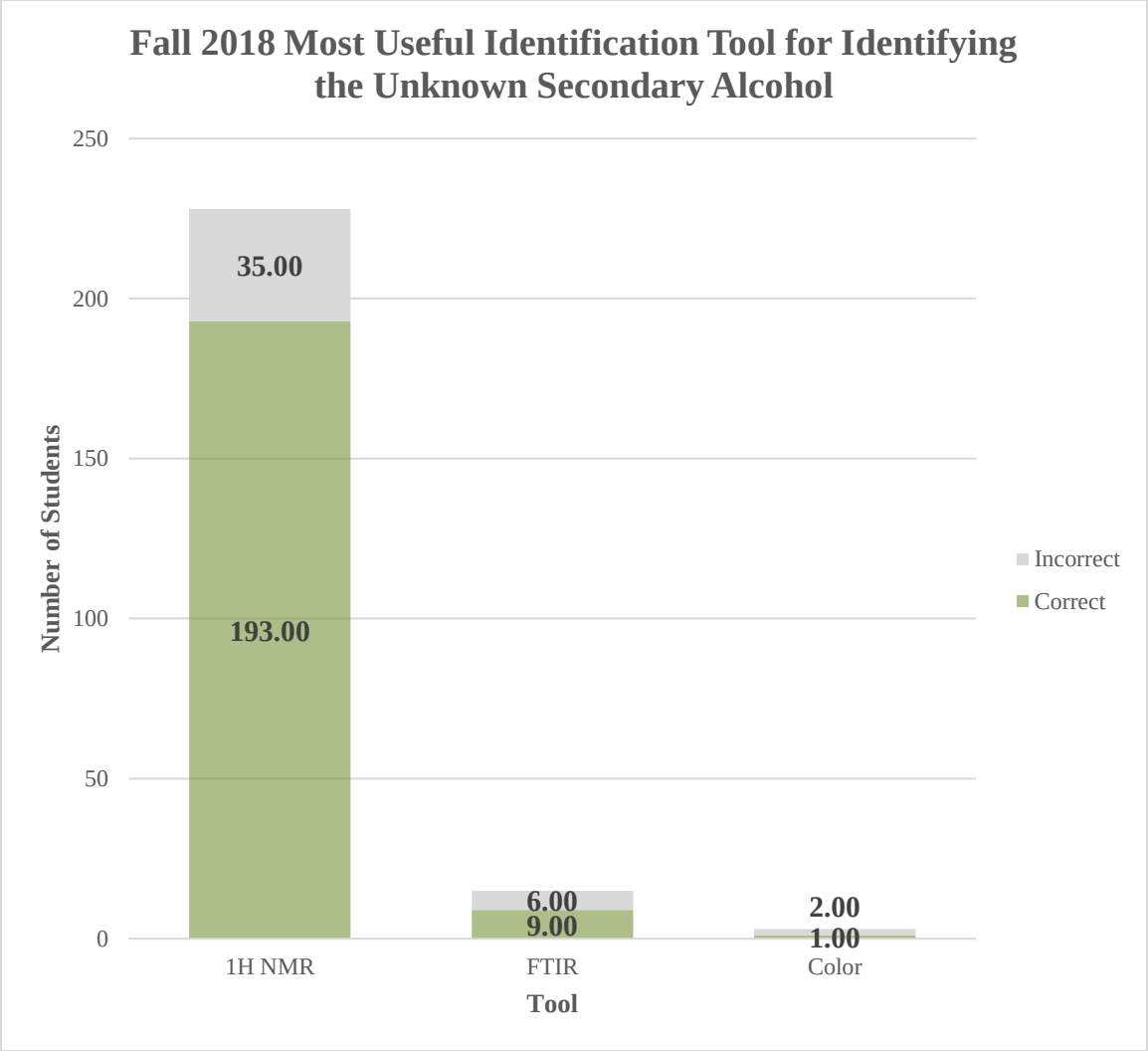
Please elaborate on your previous responses regarding the benchtop 1H NMR spectra. *

Please provide any additional feedback for this experiment.

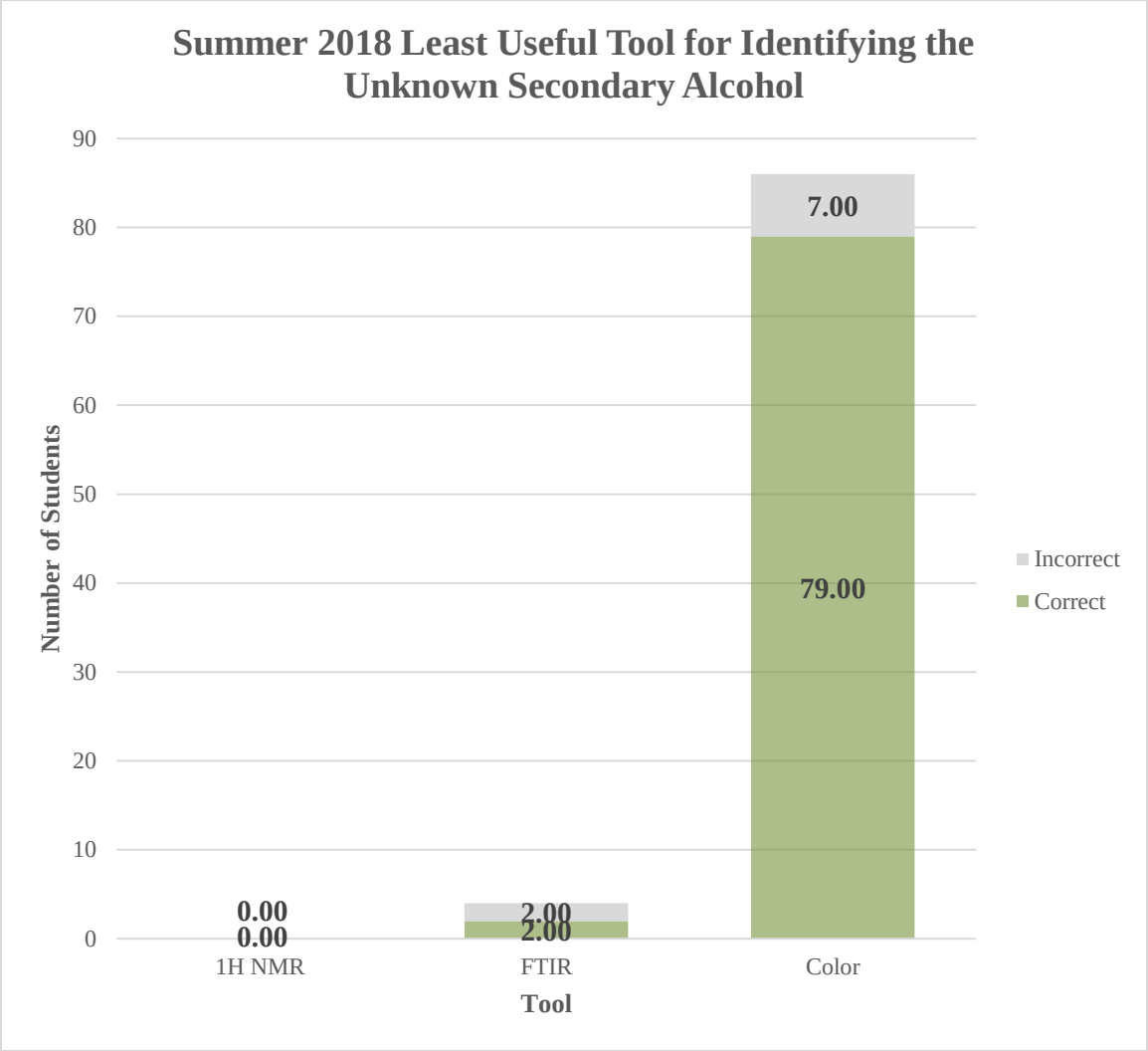
Submit



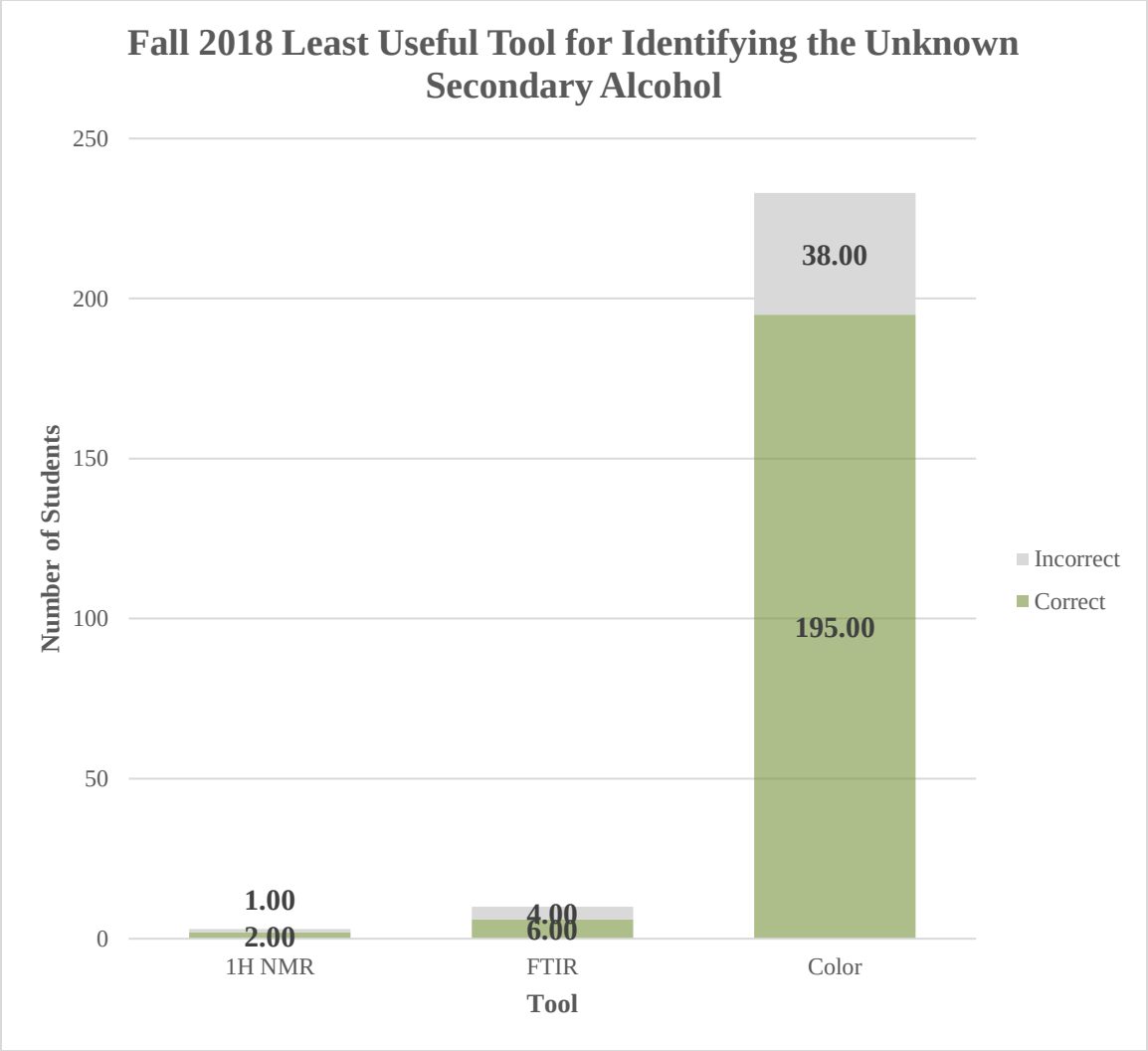
SI Figure 3.4. Summer 2018 postlab survey results for the most useful technique for deducing the identity of the unknown secondary alcohol. N = 90 students.



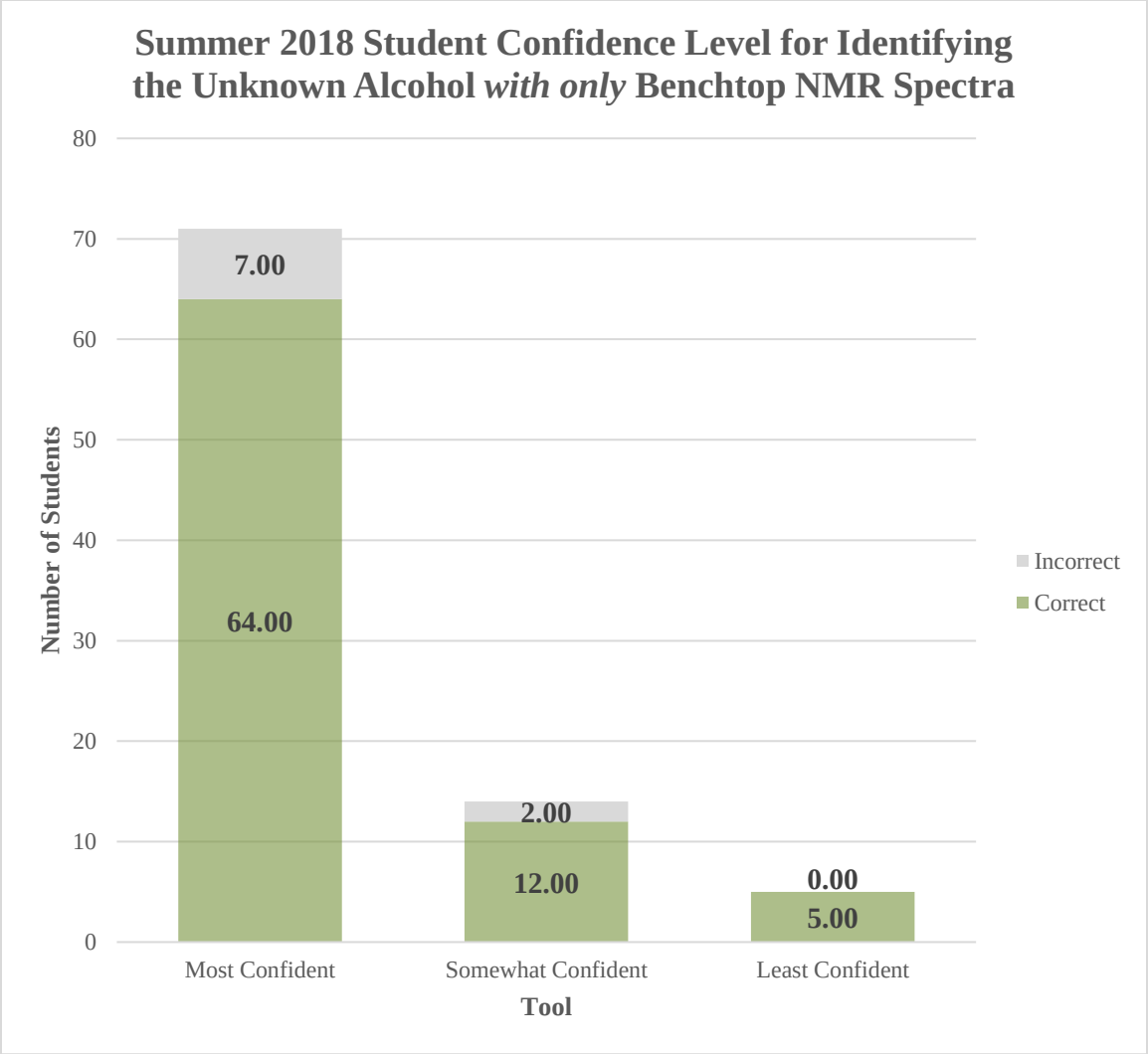
SI Figure 3.5. Fall 2018 postlab survey results for the most useful technique for deducing the identity of the unknown secondary alcohol. N = 246 students.



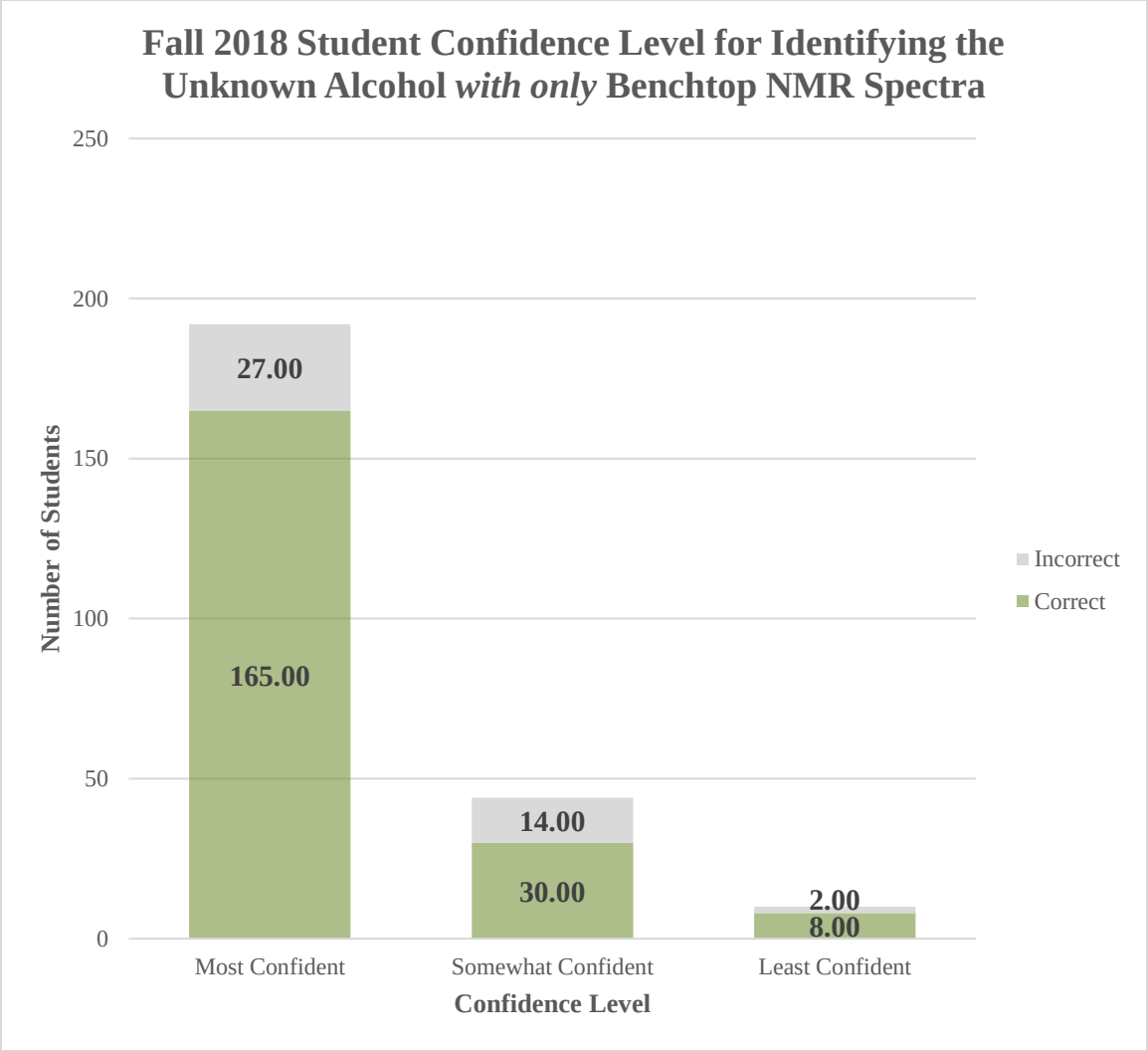
SI Figure 3.6. Summer 2018 postlab survey results for the least useful technique for deducing the identity of the unknown secondary alcohol. N = 90 students.



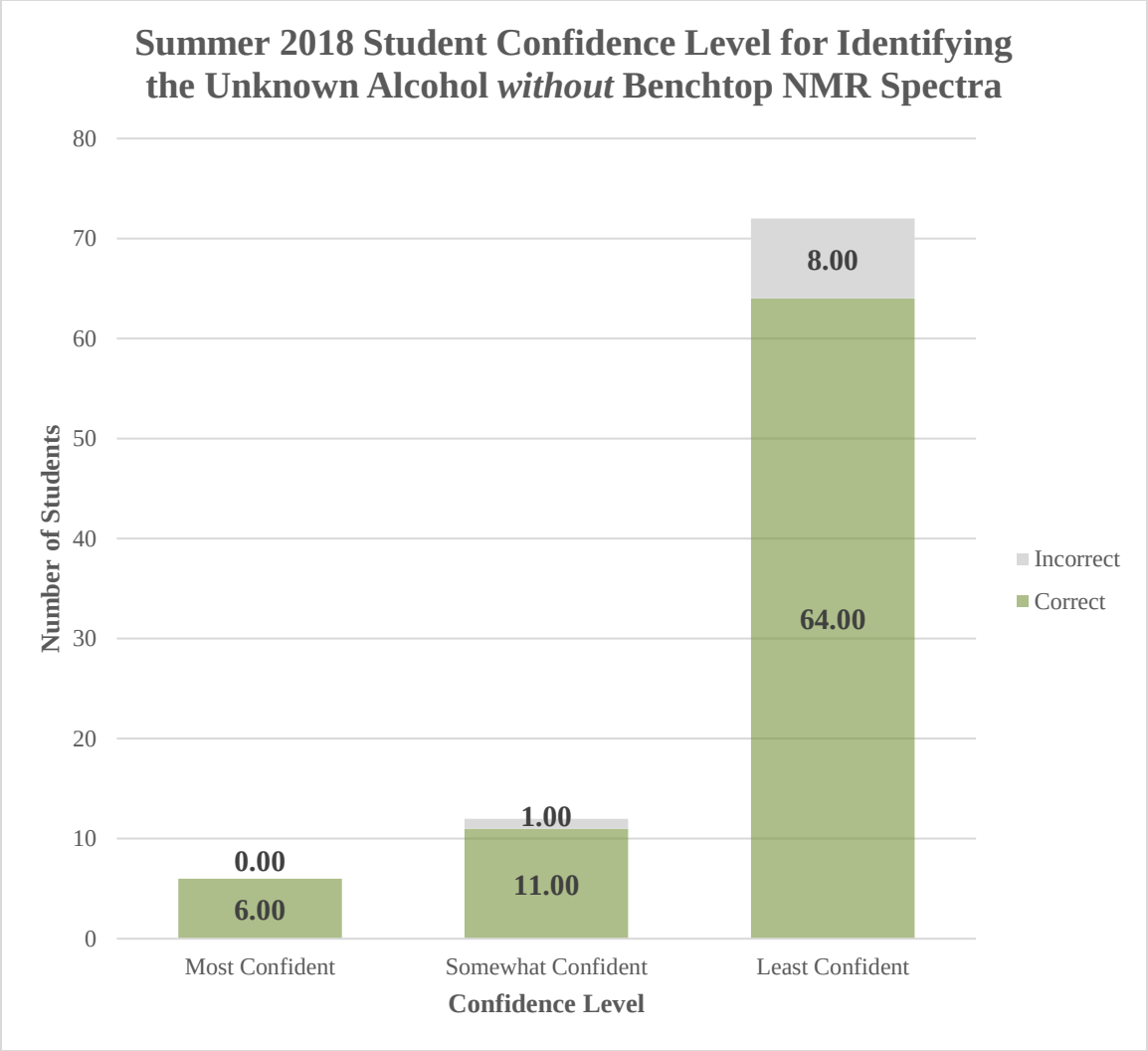
SI Figure 3.7. Fall 2018 postlab survey results for the least useful technique for deducing the identity of the unknown secondary alcohol. N = 246 students.



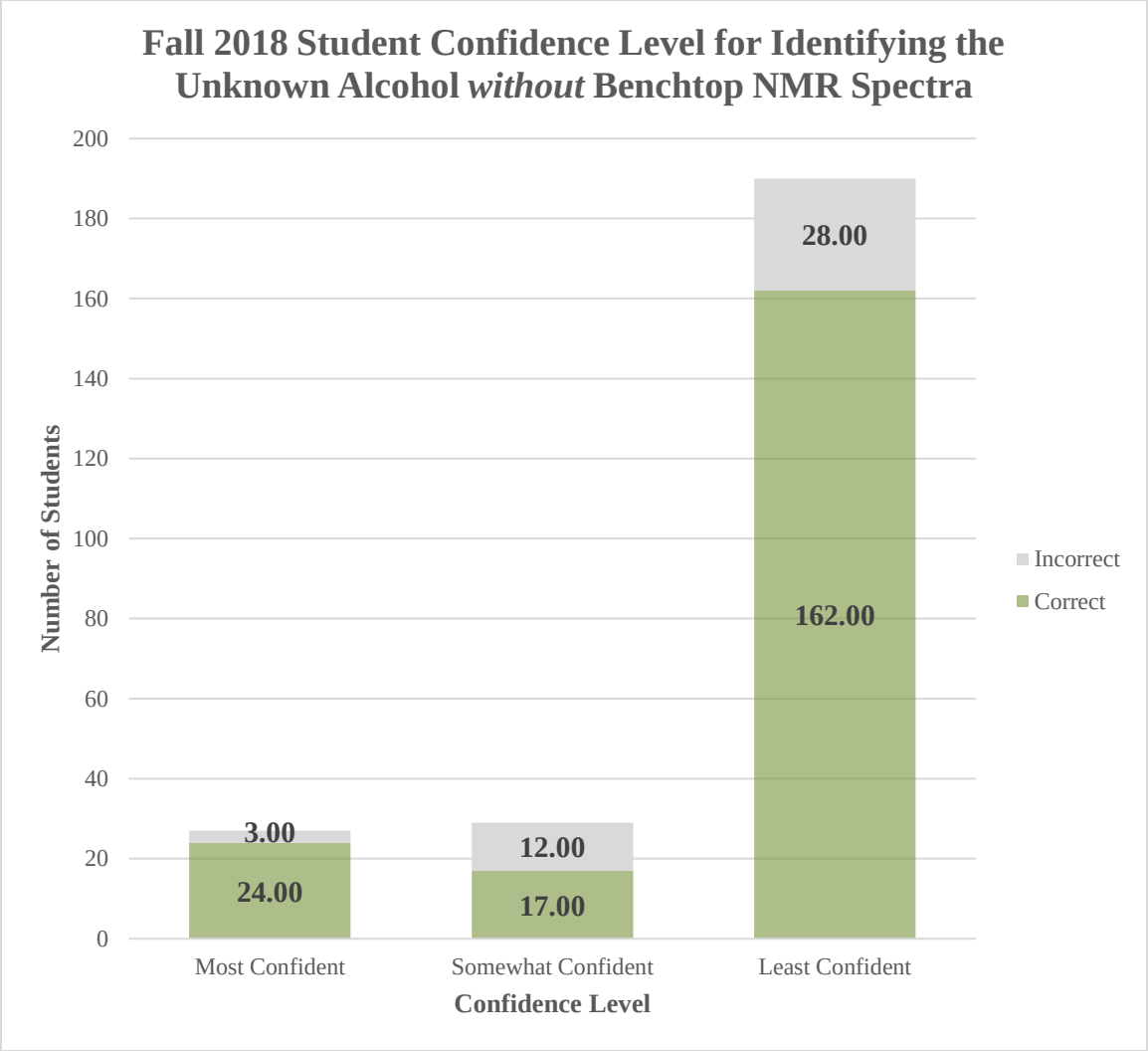
SI Figure 3.8. Summer 2018 postlab survey results for student reported confidence levels for correctly identifying their unknown secondary alcohol *with only* benchtop NMR spectra. N = 90 students.



SI Figure 3.9. Fall 2018 postlab survey results for student reported confidence levels for correctly identifying their unknown secondary alcohol *with only* benchtop NMR spectra. N = 246 students.



SI Figure 3.10. Summer 2018 postlab survey results for student reported confidence levels for correctly identifying their unknown secondary alcohol *without* benchtop NMR spectra. N = 90 students.



SI Figure 3.11. Fall 2018 postlab survey results for student reported confidence levels for correctly identifying their unknown secondary alcohol *without* benchtop NMR spectra. N = 246 students.

Note to Lab Coordinator 3.1

Initially, the researchers planned to use the Great Value brand of concentrated bleach. However, better results were obtained using the regular concentration of this same product.

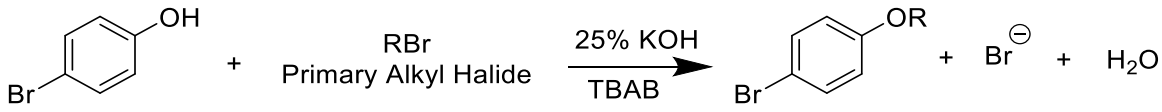
One common student error was freezing the glacial acetic acid prior to use by leaving it in the ice bath. If this is observed, it will not impact the outcome of the reaction because it will melt due to the exothermic nature of the reaction. Secondly, our initial procedure included five minutes of adding the bleach dropwise, but this was elongated to ten minutes due to students rushing this exothermic process. It is imperative that students are aware that this reaction is exothermic, and the household bleach must be added dropwise over a ten-minute period. Finally, students at the University of Georgia are actively working towards determining when they have successfully removed the solvent from their reaction mixture. This recognition can be improved with TA-guidance during the experiment.

SUPPORTING INFORMATION – CHAPTER 4

Procedure 4.1. Williamson Ether Synthesis

This week you will perform a Williamson Ether Synthesis. This reaction is a convenient way to functionalize molecules and historically involves the combination of an alkoxide ion with a primary alkyl halide to yield, unsurprisingly, an ether. Today's reaction will involve a phenoxide ion formed after the deprotonation of 4-bromophenol. Once the phenoxide ion is formed, it serves as the nucleophile in the S_N2 attack on the primary alkyl halide. The primary alkyl halide used in today's experiment will be unknown. The identity of this alkyl halide can be deductively determined by spectral analyses of the purified final product.

Example Reaction Scheme:



Possible Unknown Alkyl Halide Identities:

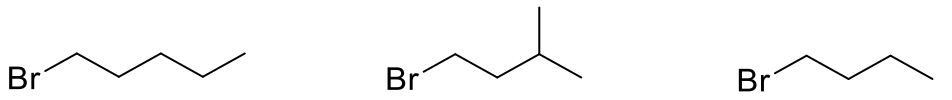


Table of Reagents:
Gather all of the indicated physical data for the following compounds:

4-bromophenol (structure, MW, MP, Density)
Potassium hydroxide (structure, MW, MP, Density)
1-bromopentane (structure, MW, MP, Density)
1-bromo-3-methylbutane (structure, MW, MP, Density)
1-bromobutane (structure, MW, MP, Density)
Tetrabutylammonium Bromide (structure, MW, MP, Density)
Diethyl Ether (structure, MW, BP, Density)
Methylene Chloride (structure, MW, BP, Density)
Water (structure, MW, BP, Density)
Sodium Sulfate (structure, MW)

Safety and Notes:

Please review online SDS sheets of all chemicals including products. Never seal a reflux apparatus air tight. Use caution to avoid inhalation when using silica gel; it is a severe respiratory irritant.

Experimental Procedure:

Preparation of the Conjugate Base of 4-Bromophenol: A TA Demonstration

Prior to gathering your chemicals for the experiment, your TA will prepare the conjugate base of 4-bromophenol as a class demonstration.

Microwave-Promoted Williamson Ether Synthesis:

Please collect 8 mL of the TA-prepared solution and place it into the white Teflon microwave vessel. (8 mL of this solution represents the 3.46 g of 4-bromophenol and 7.12 g of 25% aqueous KOH used to prepare the phenoxide.)

Add 2.90 g of tetrabutylammonium bromide (TBAB) followed by 3.02 g of your TA-assigned unknown alkyl halide to the microwave vessel. Add a stir bar to the vessel and return it to your TA. Your TA will then slide the vessel into its outer sleeve and cap the assembly. A microwave procedure will be executed to reflux the solution. (Previously, this solution was refluxed using conventional heating for 60 minutes; however, the microwave allows for a shortened reflux period of ~30 minutes including a cooling period.)

Once the reflux is complete and the vessel has sufficiently cooled, your TA will remove the assembled vessels from the microwave and open them inside of the fume hood. Your TA will then return your white Teflon vessel back to you.

Extraction:

Remove the stir bar from vessel and pour the solution from the microwave vessel into your separatory funnel. Add 10 mL of distilled water and 10 mL of diethyl ether to the separatory funnel and mix well. Separate the resulting layers into two clean, labeled beakers. Return the aqueous

layer to the separatory funnel and extract with 10 mL of diethyl ether. Separate the resulting layers into two labeled beakers. Combine the two organic layers and wash this ether layer three times with 15 mL of 5% KOH, setting aside the aqueous layer after each wash. Dry the ether layer with sodium sulfate.

Column Chromatography:

To purify the final product, a column will be used. This column will be prepared by your TA. *Use caution to avoid inhalation when using silica gel; it is a severe respiratory irritant.* Secure the pipette with a clamp. Before adding your product mixture, the column must be "packed." In order to do so, add a steady amount of methylene chloride through the top of the column using a pipette. It is **crucial** that the methylene chloride is continuously added until you are ready to use the column. This column must not be allowed to become dry. Ensure that the methylene chloride is passing completely through the column. (You can recycle the methylene chloride that is being used to pack the column by collecting all liquid in a small beaker and adding it back into the column until you are ready to use the column.) When ready to purify your product, add your product mixture into the column using a clean pipette. Once all your product mixture has been added to the column, add 2 mL of methylene chloride to the column behind the product mixture to ensure all product is collected. Once finished, remove the silica gel from column using copper wire and dispose of it into the proper waste container. If your purified product is not in a round bottom flask, please transfer it to a clean, pre-weighed round bottom flask.

Solvent Removal and Thin Layer Chromatography:

Carefully remove the dichloromethane and diethyl ether via rotary evaporation. Note that your product is also volatile, meaning heating the water bath too high may also result in the loss of your product. While one partner is watching the removal of the solvent carefully, the other partner should individually spot 4-bromophenol dissolved in methylene chloride and your alkyl bromide onto a TLC plate, leaving room for a third spot of your final purified product. After the solvent has

been removed, spot the TLC plate with a spot of the final purified product and run the plate in methylene chloride. Collect the mass of your final product.

Spectral analysis:

You will collect a ^{1}H NMR spectrum of your sample with assistance from your TA during the laboratory period. You must also collect an FTIR spectrum of your final purified product.

Experimental Procedure Modified from the following reference:

Black, S.M. "Williamson Ether Synthesis." Dixie State University. St. George, UT. www.cactus.dixie.edu/smblack/chemlabs/Williamson_ether_synthesis.pdf

Handout 4.1: TA Directions

Microwave-Promoted Williamson Ether Synthesis TA Directions

CHEM 2212L

Total Time: ~100 minutes

Prior to Class…

1. Using the table below, weigh out the appropriate amounts of 4-bromophenol and 25% KOH in two separate beakers. (Measure enough for one extra group in case someone takes a little too much.) These reagents are located under the left side of the hood closest to the MW, along with extra TBAB.

# of Student Groups	Amount of 4-Bromophenol	Amount of 25% KOH
1 group	3.46 g	7.12 g
2 groups	6.92 g	14.24 g
3 groups	10.38 g	21.36 g
4 groups	13.84 g	28.48 g
5 groups	17.30 g	35.60 g
6 groups	20.76 g	42.72 g
7 groups	24.22 g	49.84 g
8 groups	27.68 g	59.96 g
9 groups	31.14 g	64.08 g
10 groups	34.60 g	71.20 g
11 groups	38.06 g	78.32 g
12 groups	41.52 g	85.44 g
13 groups	44.98 g	92.56 g

2. Note: The unknown alkyl halides have been pre-assigned on the student handout. Please place one handout at each of your student stations.
3. This experiment can be lengthy if time is not managed appropriately. Time estimates for each task are listed throughout this document.

Upon Your Students Entering the Classroom… (5-15 minutes total)

4. Ensure that all student pairs are wearing safety glasses and lab coats.
5. Immediately upon student entry, mix the two reagents above together and stir on a stirplate until the solid is dissolved, while explaining to your students that you are preparing the conjugate base of 4-bromophenol for them. (A stir plate has already been set out for you on the bench closest to the MW.)

6. Remind your students that this can be a lengthy lab and ask them to split up to use their time more efficiently.
    a. Partner A: Collect 8 mL of solution and white Teflon insert to microwave vessel.
    b. Partner B: Collect the amounts of TBAB and pre-assigned unknown alkyl halide (pre-assigned on student handout).
    c. Remember to put the materials into the vessel in order: 1) 8 mL of solution, 2) TBAB, 3) unknown alkyl halide can be added in with a pipette to ensure that all solid TBAB is rinsed off of the inside walls of the vessel. If your students fail to remove the TBAB from the side of the vessel, use a pipette to rinse the reaction mixture down the side of the wall.
7. During this time, push your students to ensure that they are using their time wisely. A bin containing TBAB and the Unknown alkyl halide is located at each balance; therefore, this process of weighing out chemicals should take no longer than 5-10 minutes for your entire section. Please push them forward during this time period. The longer it takes for you to receive all of the vessels back, the longer the experiment will run.
8. As your students bring back the MW-vessels, provide them with a MW vessel tube number to record – located on the outside of the brown sleeve. Check each brown sleeve and cap to make sure that there is no solid or liquid present inside or outside of the pieces.
9. Ensure that each vessel is equipped with a stir bar, the inner white Teflon vessel, the brown sleeve, the white Teflon top, and the vessel cap. The ATC vessel must have the long temperature probe inserted the probe cover for the temperature to be monitored appropriately. It must also have a plastic piece inside of the cap that is not held in place.
10. Load the vessels onto the carousel, with all vents pointing towards the exterior of the MW.

The MW period… (30 minutes)

11. Execute the saved MW protocol.
    a. Admin Password: 123456
    b. When at the load screen, make sure that Methods is selected on the left side of the screen (under data) and that the type of file displayed includes *.mpr (Method). You may also need to click on the USB tab.
    c. File name: williamson ether synthesis
    d. This file will include a 5 minute temperature ramp to 100 degrees Celsius followed by a 25 minute “cook time” at 100 degrees Celsius.
12. During the MW period, please give your student their pre-lab quiz and pre-lab lecture. Please also remind them to check their separatory funnel for leaks using water from the sink. You are welcome to use this time to prepare your columns

for your students if needed (see demo column in hood). Use demo column for a class demonstration on how to use positive pressure to make the flow faster. Please direct your students to keep a hand on the adapter at all times that it is being used.

When the MW period ends… (5-10 minutes)

13. You will hear the MW turn off and can watch the temperature decrease on the screen.
14. When the temperature reaches ~ 50 degrees, remove the vessels from the MW with the vents pointing away from you.
15. Carefully open each MW vessel in the hood, again with the vent pointing away from you and have the students collect their white Teflon inner vessel.
16. **Class announcement:** *"The upcoming extraction period should take you no longer than 10 minutes to complete. Please use the diagram projected on the board to move quickly through this process."*

The extraction… (10 minutes)

17. Please ensure that the diagram from the pre-lab lecture is projected on the board.
18. Sodium sulfate is located on the common materials bench.

The column… (5 minutes)

19. The prepared columns should be provided to students. Remind them not to add solvent to the column until ready for use. Otherwise, they will continuously have to add solvent until ready to use because the column cannot dry out once solvent has been added.
20. **Class announcement:** *"These columns are expensive and are included under Research Quality Glassware. Do not break them. Please use extra caution regarding the tip at the end of the column because it is especially fragile."*
21. Students must wet the column with methylene chloride prior to use. I recommend pouring methylene chloride into two beakers in each hood to make it easier to pour quickly.
22. Show your students how to carefully use the air adapter in the hood to provide positive pressure to the column (i.e. make it go faster). The vacuum line are already in place in the hoods and the adapters are located at the column prep station in the hood next to the MW. Emphasize that putting too much pressure will create breaks in the silica, making the column ineffective.
23. Ensure that no silica or sand is passing through each column into a pre-weighed receiving beaker.

The solvent removal… (5-10 minutes)

24. Using rotary evaporation, remove the solvent. It is imperative that the diethyl ether is fully removed from the sample.
25. During this process, ask your students to spot their starting materials onto their TLC plate and run the plate. (Note: the alkyl halide may not show up. Students can run a TLC plate of their product while simultaneously collecting their product spectra.)
26. The solvent removal process is complete when approximately 5 mL of solution remains in the flask. (Note: This volume will vary based on the amount of student product in the beaker. In other words, if product was spilled during the experiment, this volume will be lower.)

Gathering the spectra… (20 minutes)

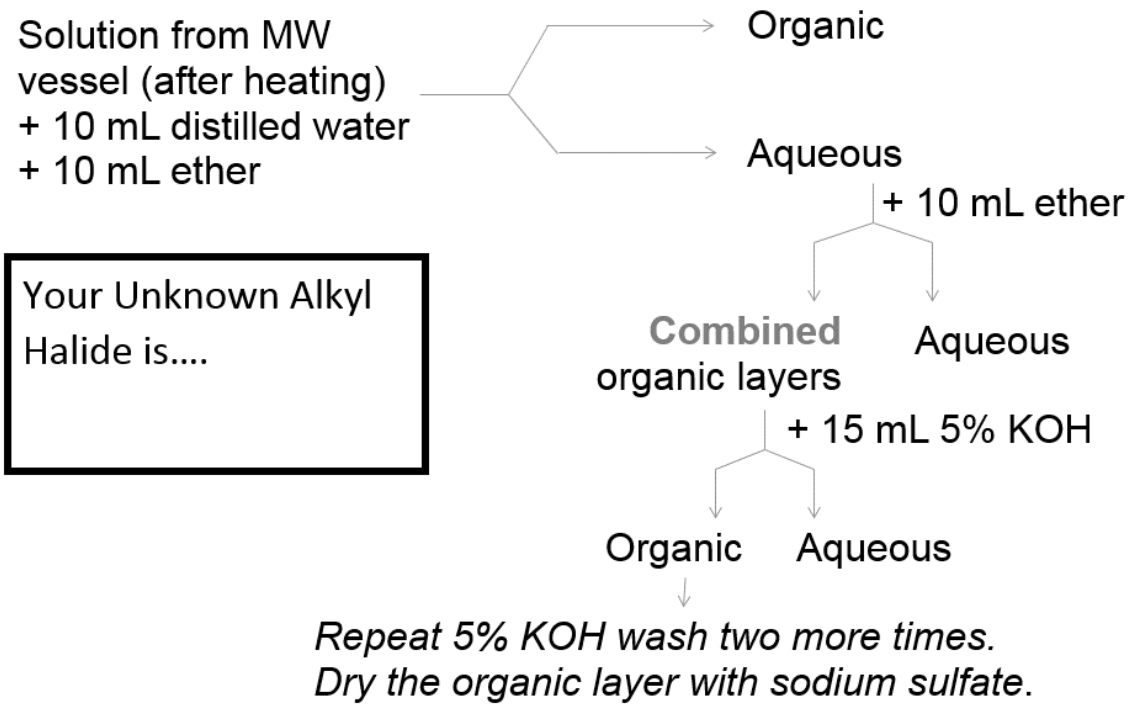
Note: Please do **not** describe for the students what information each technique will provide. This is a learning process for them and will be explored during the post-lab.

Collecting the FTIR spectra…

27. Ask students to include unknown code in their name of the file.
28. Students should be independent on this instrument and require minimal hands-on guidance. Direction sheets are posted on the wall behind each instrument for their reference.
29. Send all IR files at the end of class to all students.

Collecting the ^{1}H NMR spectra…

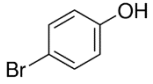
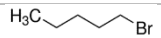
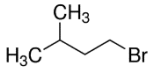
30. Ask students to provide you with an Eppendorf tube containing 1 mL of their product. Ensure that there is no solid in the tube prior to sample preparation.
31. Ask each student group to come stand next to you and insert the needle into the inlet port.
32. **NEW**: Ask the student groups to complete the injection by pushing onto the syringe **(BE SURE TO MONITOR THIS)** until 10 drops come out of the outlet.
33. Run sample using the naming protocol listed in the picoSpin guide found on top of the instrument.
34. Integrate spectra during class and send the integrated MNova files immediately following class to your students.

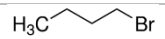
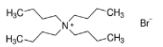
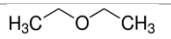


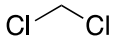
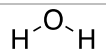
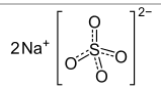
SI Figure 4.1. Example extraction handout provided to students in Spring 2018.

SI Figure 4.2. Example column prepared by students in Spring 2018. The columns were made by the Scientific Glassblowing Shop at the University of Georgia using 24/40 tubing. The column pictured is approximately 6.5 inches long.

SI Table 4.1. Experiment Table of Reagents for Instructors

Reagent	Structure	CAS	Hazard Codes	Amount needed per Student	Molecular Weight (g/mol)	Melting Point (°C)	Boiling Point (°C)	Density (g/cm^3)	Solubility in water
4-Bromophenol		106-41-2	Acute toxicity, Oral (Category 4), H302; Skin irritation (Category 2), H315; Acute aquatic toxicity (Category 2), H401	3.46 g	173.01	61-64	235-236	-	-
Potassium hydroxide		1310-58-3	Corrosive to metals (Category 1), H290; Acute toxicity, Oral (Category 4), H302; Skin corrosion (Category 1A), H314; Serious eye damage (Category 1), H318; Acute aquatic toxicity (Category 3), H402	Varies	56.11	360	1327	2.12	1210 g/L
1-Bromopentane		110-53-2	Flammable liquids (Category 3), H226; Skin irritation (Category 2), H315; Eye irritation (Category 2A), H319; Specific target organ toxicity - single exposure (Category 3), Respiratory system, H335	3.02 g	151.04	-95	130	-	insoluble
1-Bromo-3-methylbutane		107-82-4	Flammable liquids (Category 2), H225; Acute toxicity, Oral	3.02 g	151.04	-112	120-121	-	0.2 g/L

			(Category 4), H302; Skin irritation (Category 2), H315; Specific target organ toxicity - single exposure (Category 3), Respiratory system, H335; Acute aquatic toxicity (Category 3), H402; Chronic aquatic toxicity (Category 3), H412						
1-Bromobutane		109-65-9	Flammable liquids (Category 2), H225; Skin irritation (Category 2), H315; Eye irritation (Category 2A), H319; Specific target organ toxicity - single exposure (Category 3), Respiratory system, H335; Acute aquatic toxicity (Category 2), H401; Chronic aquatic toxicity (Category 2), H411	3.02 g	137.02	-	-	-	-
Tetrabutyl ammonium bromide		1643-19-2	Acute toxicity, Oral (Category 4), H302 Eye irritation (Category 2A), H319	2.90 g	322.37	102-106	-	-	-
Diethyl ether		60-29-7	Flammable liquids (Category 1), H224; Acute toxicity, Oral (Category 4), H302; Specific target organ	Varies	74.12	-	-	-	-

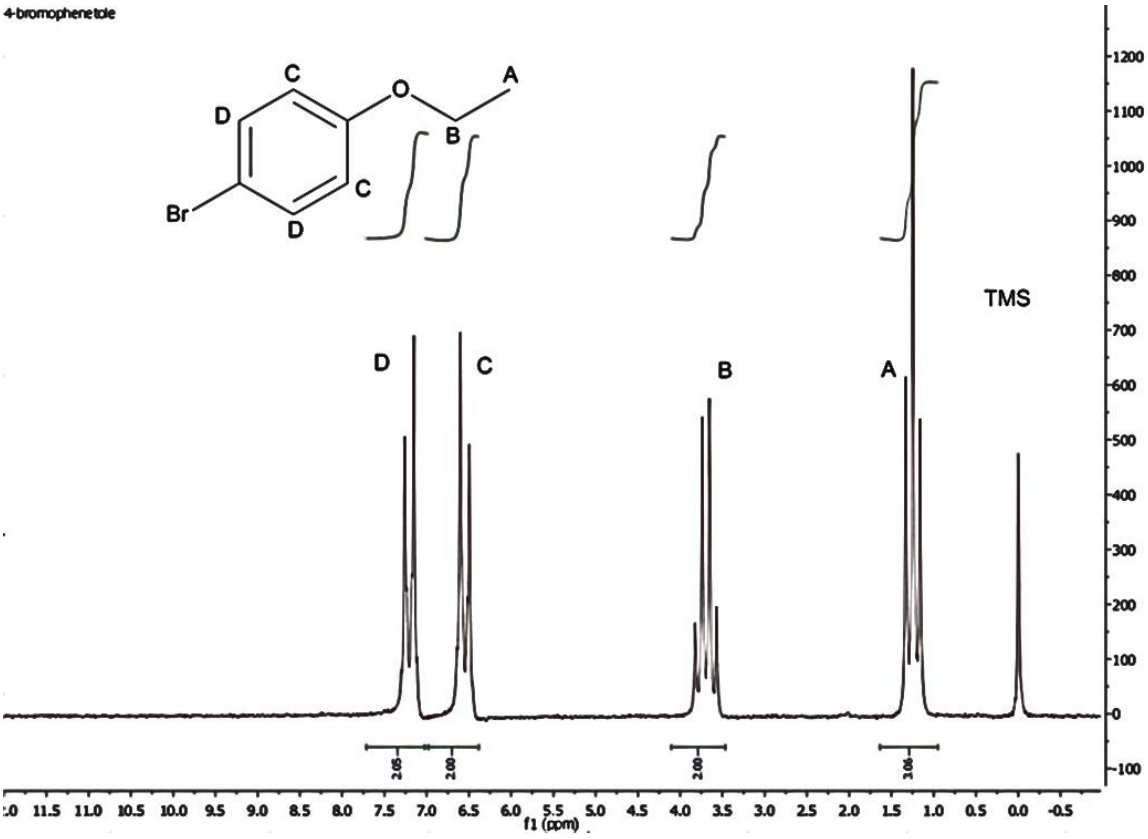
			toxicity - single exposure (Category 3), Central nervous system, H336						
Dichloro-methane		75-09-2	Skin irritation (Category 2), H315; Eye irritation (Category 2A), H319; Carcinogenicity (Category 2), H351; Specific target organ toxicity - single exposure (Category 3), Respiratory system, Central nervous system, H335, H336 Specific target organ toxicity - repeated exposure, Oral (Category 2), Liver, Blood, H373; Specific target organ toxicity - repeated exposure, Inhalation (Category 2), Central nervous system, H373	Varies	84.93	-	39.8-40	1.325	Slightly soluble
Water		7731-18-5	Not a hazardous substance or mixture.	Varies	18.02	-	100	1.000	-
Sodium sulfate anhydrous		7757-82-6	Not a hazardous substance or mixture.	Varies	140.04	-	-	-	-
Brine		7647-14-5	Not a hazardous substance or mixture.	10 mL	58.44	-	100	1.190	-

Handout 4.2. Student NMR Spectrum Analyses Directions

How to Analyze 82 MHz Benchtop ^{1}H NMR Spectra

In-lab experimental spectra do not always look exactly like the spectra predicted and studied in textbooks. Impurities and interferences often cause deviations from theoretical spectra. Therefore, when analyzing experimental ^{1}H NMR spectra, it is necessary to use good critical analysis to take into consideration signal integrals, splitting, chemical shifts, and potential contaminations simultaneously.

Shown below is a spectrum of 4-bromophenetole, a simple ether that can be identified by ^{1}H NMR analysis alone. 4-bromophenetole is not one of the unknown ethers you have synthesized in lab this week, so its analyzed spectrum is an example of how to identify an ether by ^{1}H NMR.



Handout Figure 4.1. Assigned Structure of 4-Bromophenetole with Corresponding Integrated Spectrum from the 82 MHz benchtop NMR

Things to consider:

1. Identify your TMS signal. This is an NMR reference used to mark 0 ppm.

2. There may be some residual solvents in your sample. What signals would methylene chloride and/or diethyl ether contribute to your spectrum? At what chemical shifts would you anticipate these signals?

3. Look at the triplet located around 4.0 ppm. This triplet will confirm that your ether was formed and represents the 2 protons next to the oxygen. (This triplet has been integrated to two protons for this reason.)

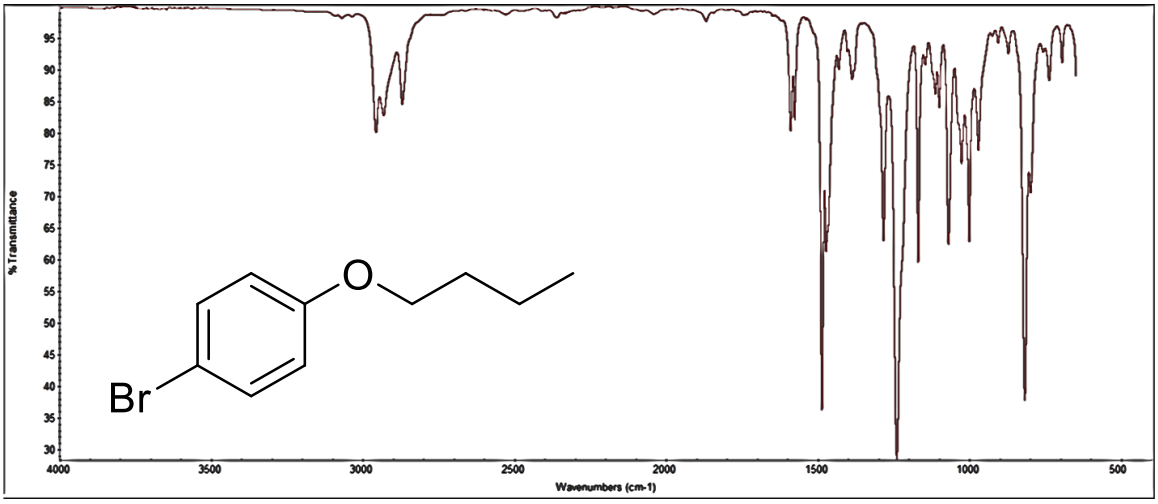
4. The two signals with the highest chemical shifts for the Williamson Ether products will be the aromatic protons. Will these doublets indicate the identity of your product?

5. After you have identified the two signals corresponding to the protons next to the oxygen of the ether and the aromatic protons, you can use the remaining signals to identify the carbon-hydrogen bonding patterns and determine what alkyl group is bonded to the oxygen.

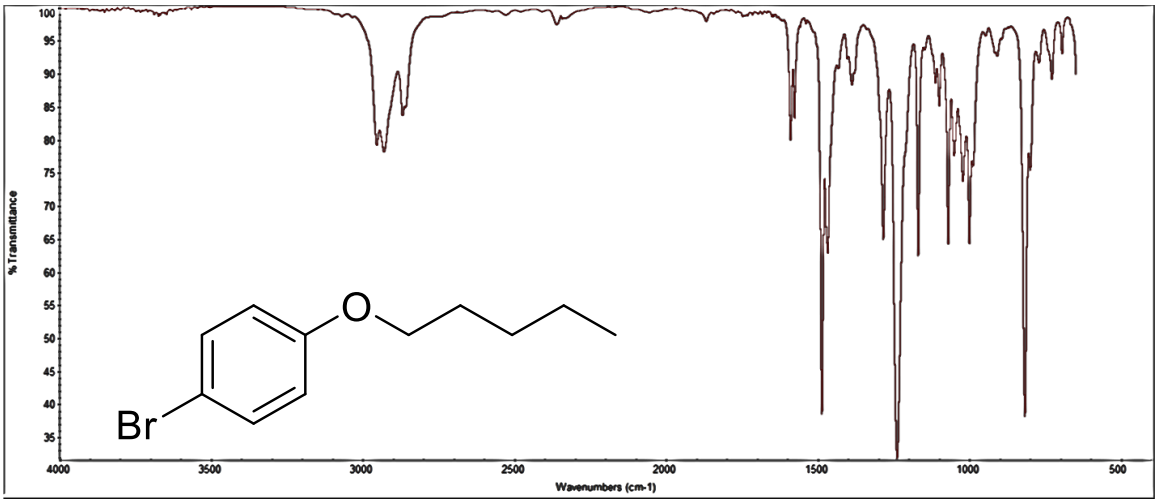
6. In the example above, there is a three-proton triplet at ~1.25 ppm, which indicates that there are 3 protons with 2 neighboring protons. Since the 2-proton signal at ~3.75 ppm is a quadruplet and there are no other split signals in the spectra, the only logical choice is that the two sets of protons are on adjacent carbons. Therefore, you can conclude that there is an ethyl group bonded to the oxygen. Because all the ethers were synthesized from 4-bromophenol, we know that this compound is 4-bromophenetole.

7. In the analysis of your unknown compound, identify all the signal integrals corresponding to the unknown alkyl group that is bonded to the oxygen. Use the splitting patterns, signal integrals, and chemical shifts to identify the alkyl group. A good place to start is to look at the signal integrals and identify the total number of hydrogens that should be in the alkyl group. Then look at potential compounds with that number of hydrogens and use the splitting patterns to match your compound to one of the possibilities. Do the predicted splitting patterns match? Secondly, methylene units

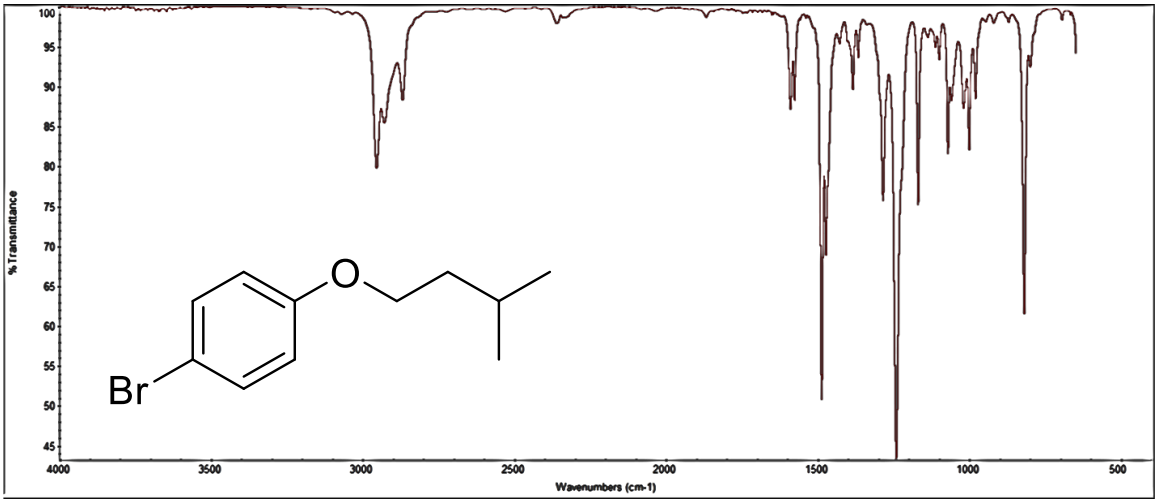
(CH_2 units) may overlap on this instrument. For example, if you have a signal that does not have distinct splitting pattern and integrates to 3 or 4 protons, you may have two signals overlapping. Even with this potential overlap, you still have enough information in your spectra to distinguish the products.



SI Figure 4.3: Student FTIR Spectrum of 1-bromo-4-butoxybenzene.



SI Figure 4.4: Student FTIR Spectrum of 1-bromo-4-pentoxybenzene.



SI Figure 4.5: Student FTIR Spectrum of 1-bromo-4-(isopentyloxy)benzene.

SI Student Survey 4.1.

Survey Page 1/8

Williamson Ether Synthesis Post-Lab Survey

This survey is intended to gain student feedback regarding the implementation of the Williamson Ether Synthesis experiment in CHEM 2212L at the University of Georgia. Please direct any questions regarding this survey to Kasey Leigh Yearty at kasey90@uga.edu.

* Required

What is your name? *

This will only be used to monitor the survey for completion.

Who is your TA? *

This will only be used to monitor the survey for completion.

What is the identification code for the unknown that you used? *

Please double check your response here to ensure that you have listed the correct unknown identification code.

- 1AZ9R21SA
- 1CFTE1HY1
- 214DTEC34
- 21KTF63XZ
- 3DRFT3C4E
- 5RMGK21P3
- 95CRLNV32
- AX21S3P6R
- B5SVL4F5T
- D34R5TY61
- K23I4U56O
- LC43T4RM1
- OJ23BR43N
- PR2G1T3C7
- UH48X5G3I
- X3AZD213D
- YT3RA29SC
- ZD391D32V
- Other:

What was the identity of your unknown? *

- 1-bromopentane
- 1-bromo-3-methylbutane
- 1-bromobutane

What mass of product did you obtain? *

Please enter your product in grams and without units. (Ex. 0.213)

Identifying your Unknown Alkyl Halide

This section features a series of questions designed to rank the usefulness of identification tools included the experiment and gain valuable feedback regarding your confidence in your results.

In the identification of your unknown alkyl halide, which identification technique was MOST USEFUL to you? *

- Color
- FTIR
- 1H NMR
- TLC

Please elaborate on your previous response. *

What specific feature(s) of the identification technique selected assisted you in deducing the identity of your unknown alkyl halide?

In the identification of your unknown alkyl halide, which identification technique was SECOND MOST USEFUL to you? *

- Color
- FTIR
- 1H NMR
- TLC

Please elaborate on your previous response. *

What specific feature(s) of the identification technique selected assisted you in deducing the identity of your unknown alkyl halide?

In the identification of your unknown alkyl halide, which identification technique was THIRD MOST USEFUL to you? *

- Color
- FTIR
- 1H NMR
- TLC

Please elaborate on your previous response. *

What specific feature(s) of the identification technique selected assisted you in deducing the identity of your unknown alkyl halide?

In the identification of your unknown alkyl halide, which identification technique was LEAST USEFUL to you? *

- Color
- FTIR
- 1H NMR
- TLC

Please elaborate on your previous response. *

What specific feature(s) of the identification technique selected assisted you in deducing the identity of your unknown alkyl halide?

How confident would you be in correctly identifying your unknown alkyl halide WITHOUT utilizing the color? *

- Most Confident
- Somewhat Confident
- Not Confident

How confident would you be in correctly identifying your unknown alkyl halide utilizing ONLY the color? *

- Most Confident
- Somewhat Confident
- Not Confident

Please provide any additional feedback regarding the incorporation of sample color in this experiment. *

How confident would you be in correctly identifying your unknown alkyl halide WITHOUT utilizing the FTIR spectra? *

- Most Confident
- Somewhat Confident
- Not Confident

How confident would you be in correctly identifying your unknown alkyl halide utilizing ONLY the FTIR spectra? *

- Most Confident
- Somewhat Confident
- Not Confident

Please provide any additional feedback regarding the incorporation of the FTIR spectra in this experiment. *

How confident would you be in correctly identifying your unknown alkyl halide WITHOUT utilizing the benchtop 1H NMR spectra? *

- Most Confident
- Somewhat Confident
- Not Confident

How confident would you be in correctly identifying your unknown alkyl halide utilizing ONLY the benchtop 1H NMR spectra? *

- Most Confident
- Somewhat Confident
- Not Confident

Please provide any additional feedback regarding the incorporation of the benchtop NMR spectra in this experiment. *

How confident would you be in correctly identifying your unknown alkyl halide WITHOUT utilizing the TLC? *

- Most Confident
- Somewhat Confident
- Not Confident

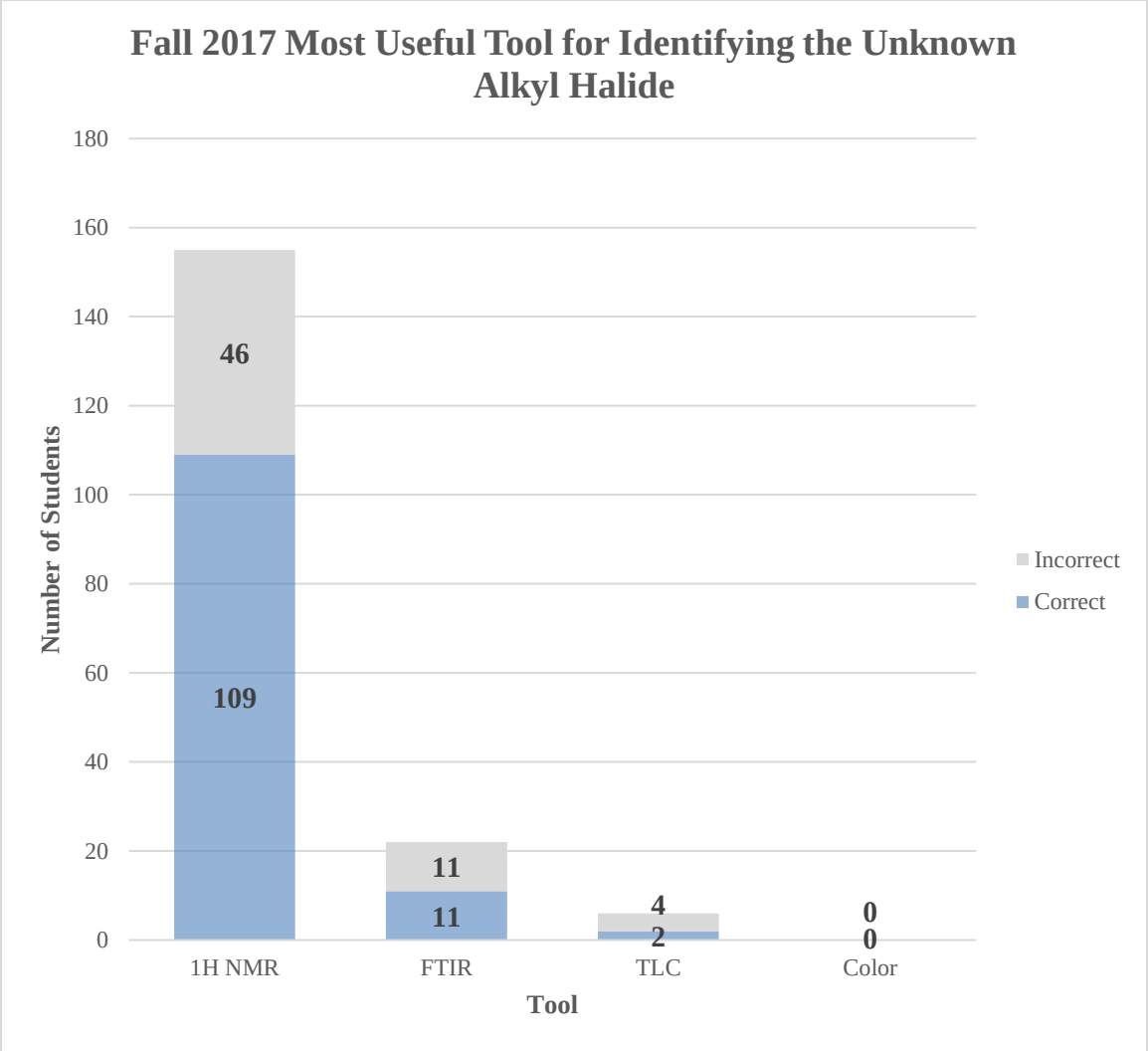
How confident would you be in correctly identifying your unknown alkyl halide utilizing ONLY the TLC? *

- Most Confident
- Somewhat Confident
- Not Confident

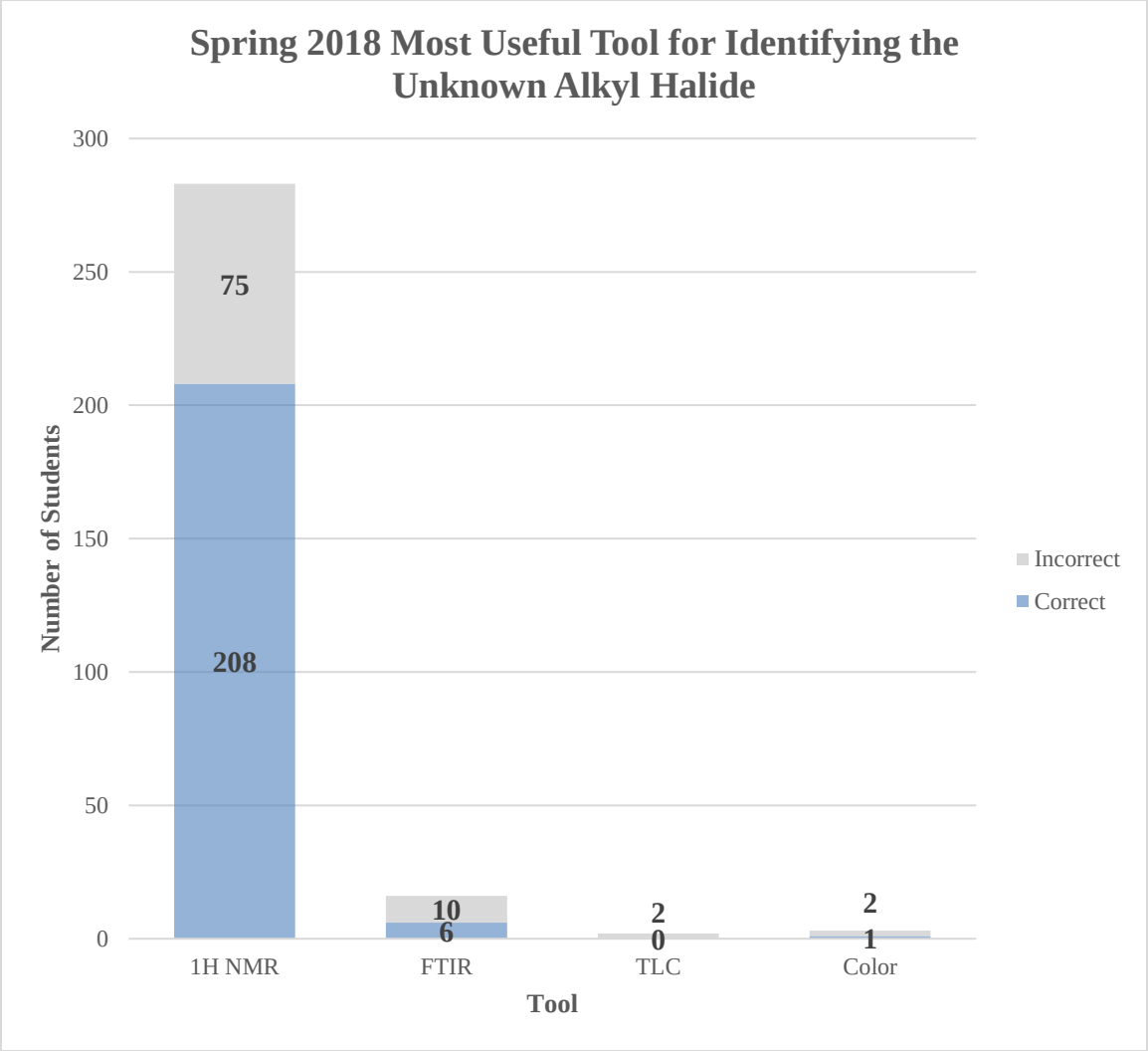
Please provide any additional feedback regarding the incorporation of the TLC in this experiment. *

Please provide any additional feedback regarding this experiment.

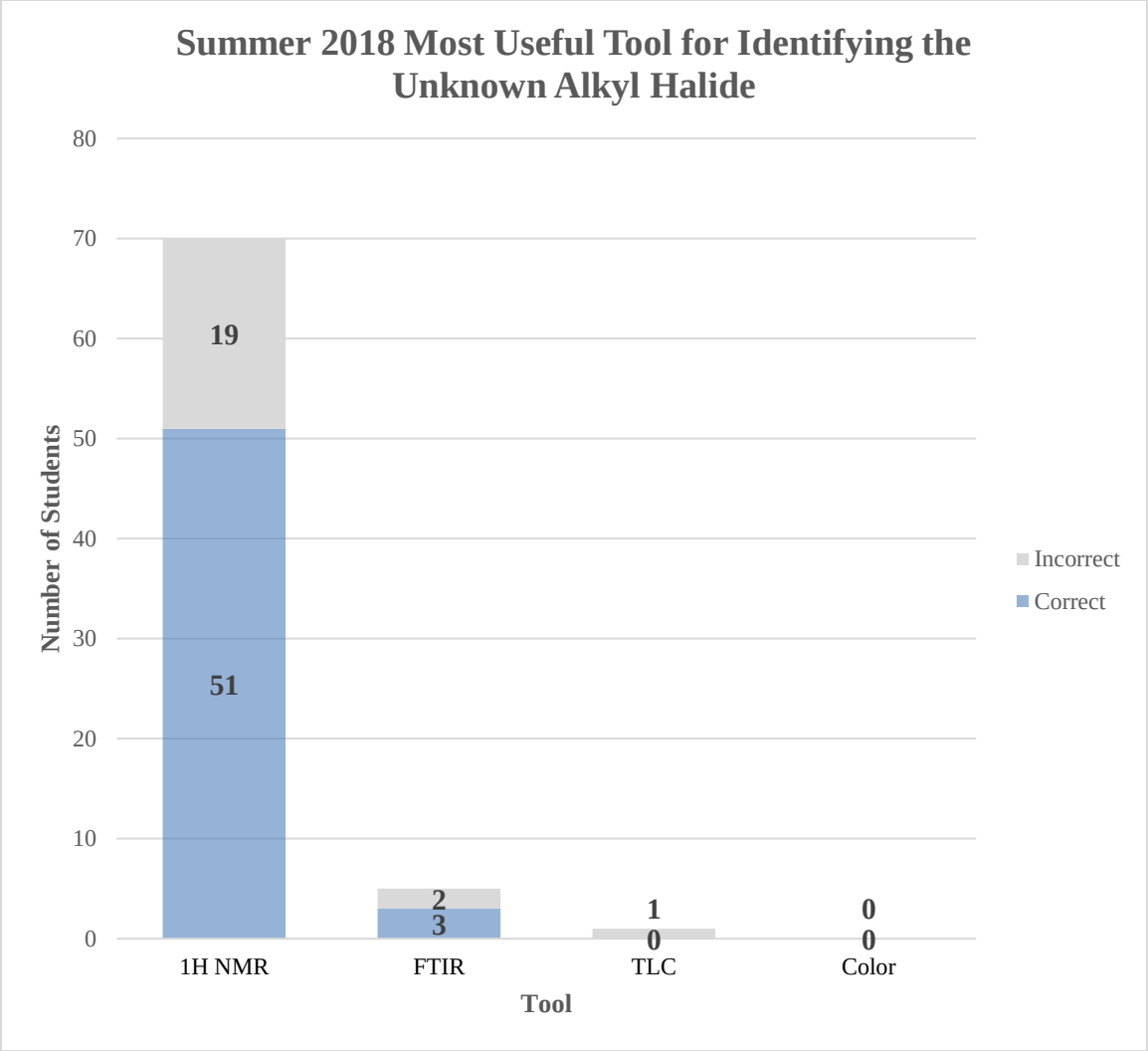
Submit



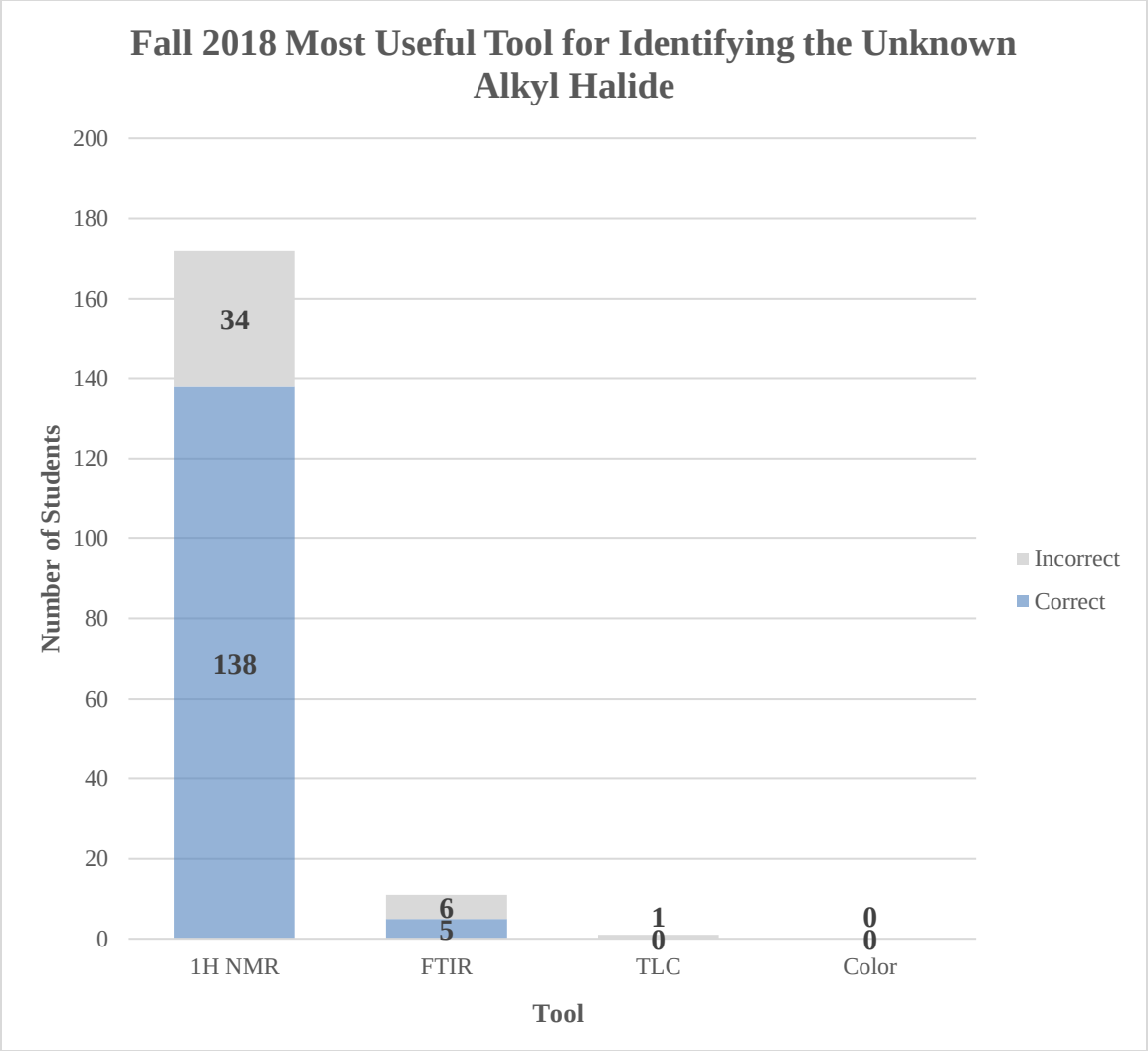
SI Figure 4.6. Fall 2017 postlab survey results for the most useful technique for deducing the identity of the unknown alkyl halide. N = 150 students.



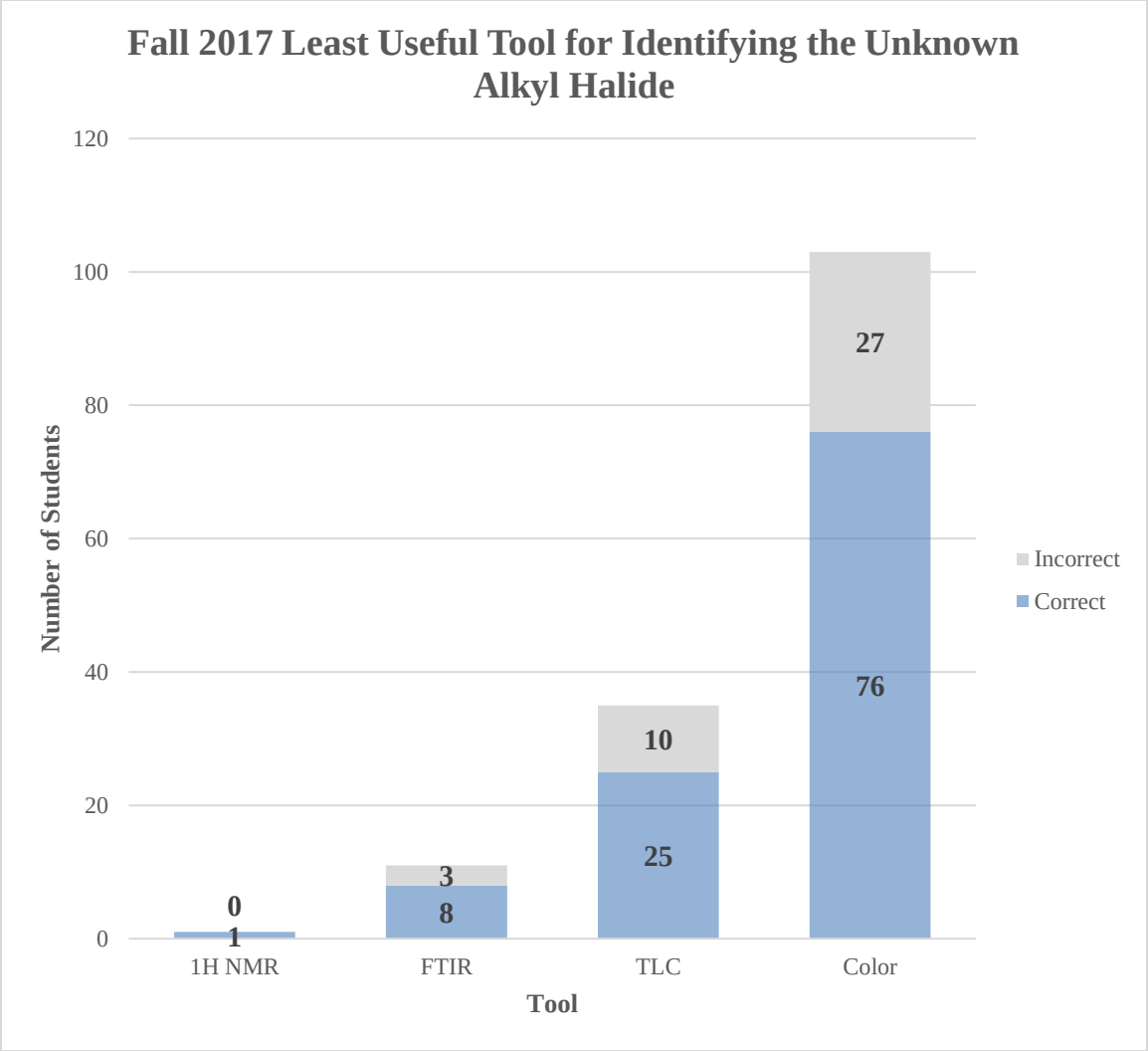
SI Figure 4.7. Spring 2018 postlab survey results for the most useful technique for deducing the identity of the unknown alkyl halide. N = 304 students.



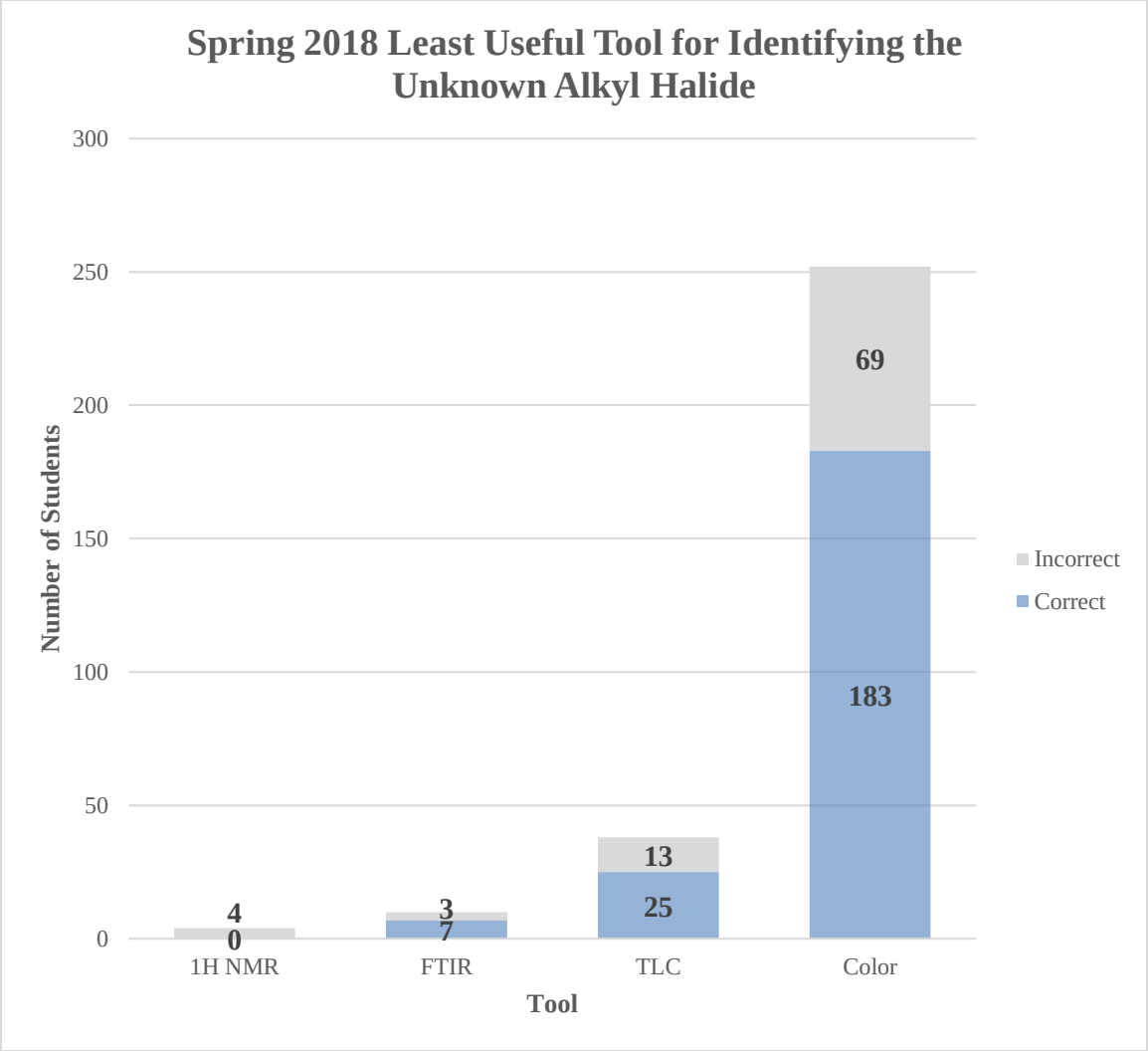
SI Figure 4.8. Summer 2018 postlab survey results for the most useful technique for deducing the identity of the unknown alkyl halide. N = 76 students.



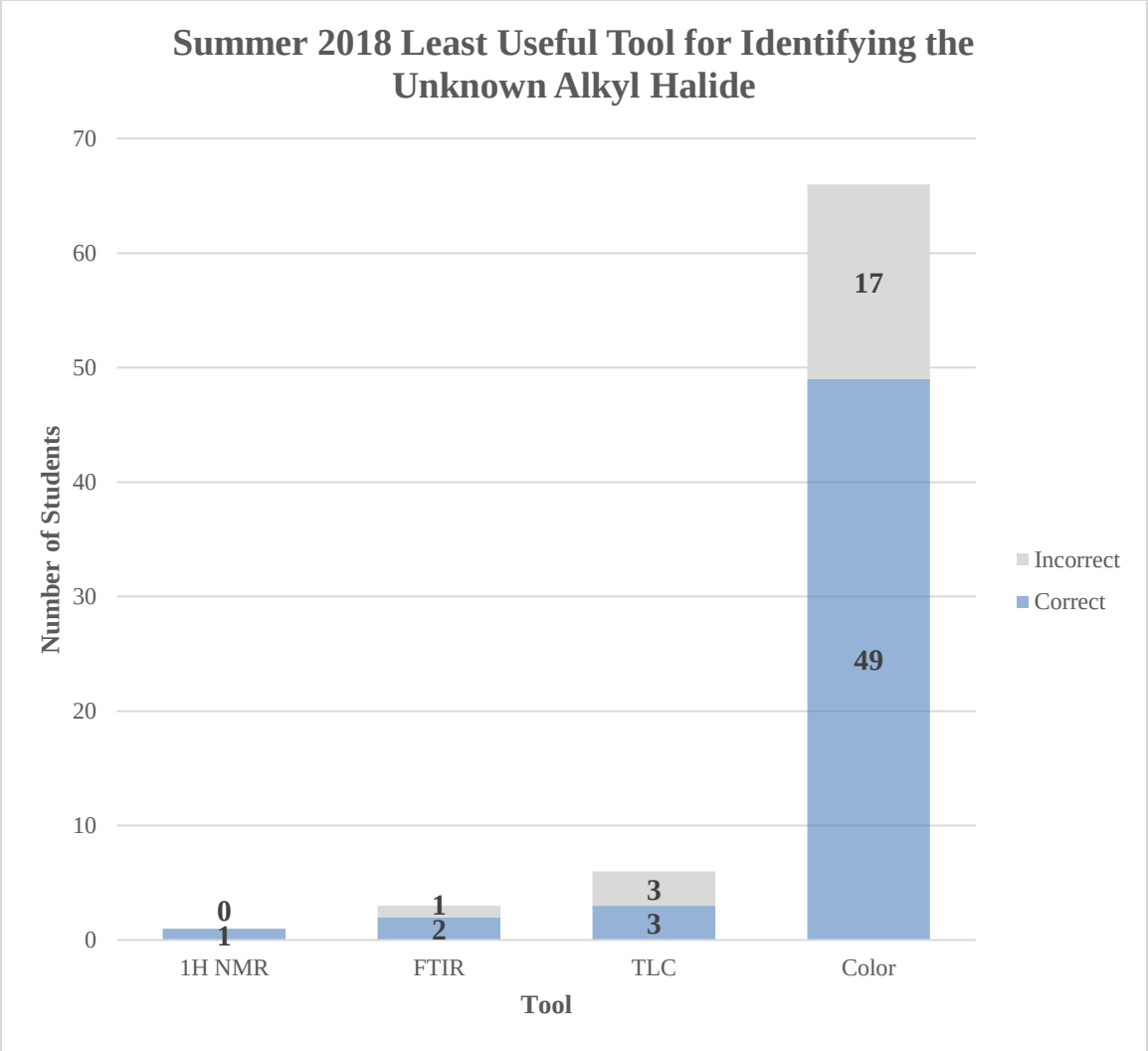
SI Figure 4.9. Fall 2018 postlab survey results for the most useful technique for deducing the identity of the unknown alkyl halide. N = 184 students.



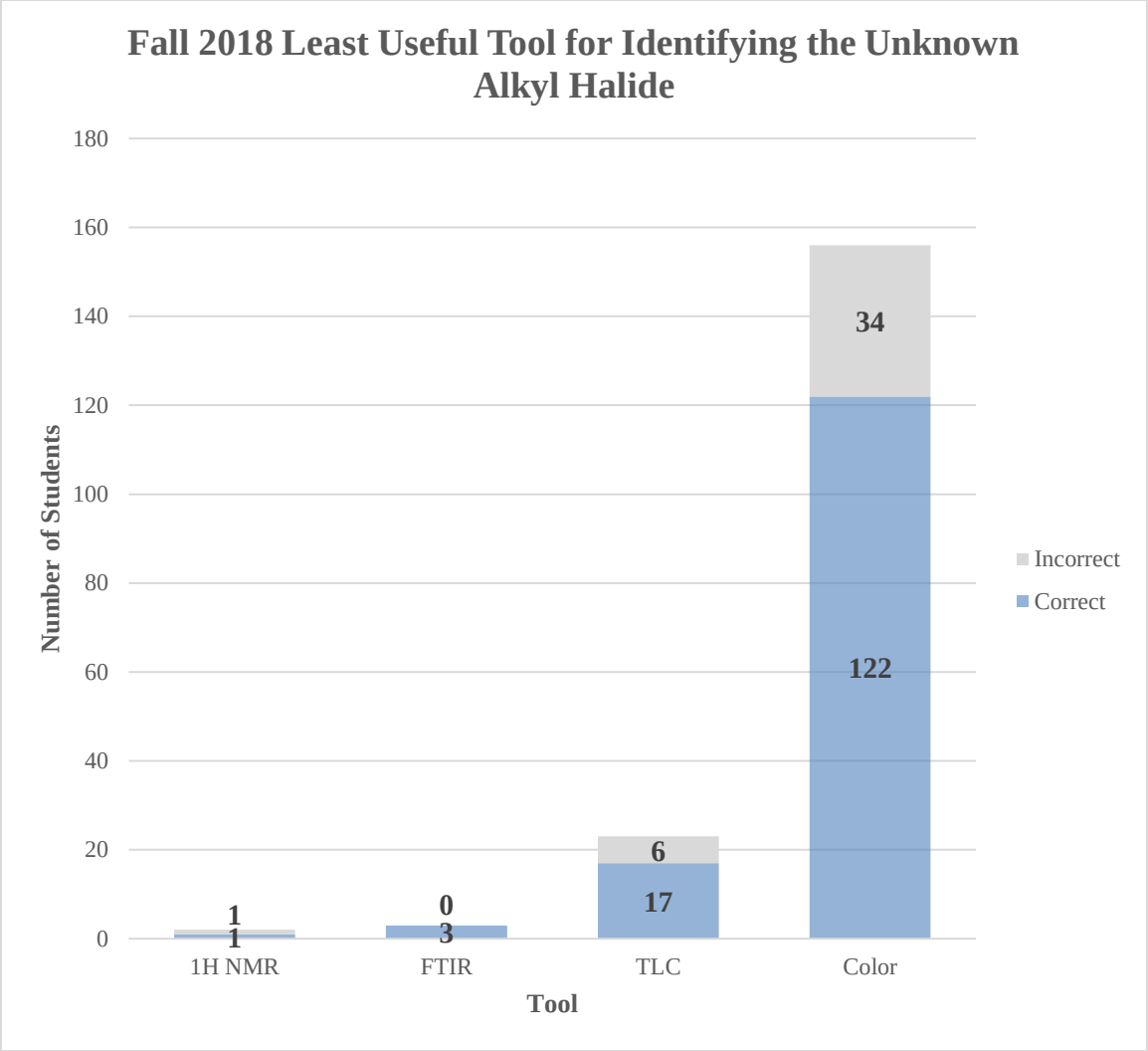
SI Figure 4.10. Fall 2017 postlab survey results for the least useful technique for deducing the identity of the unknown alkyl halide. N = 150 students.



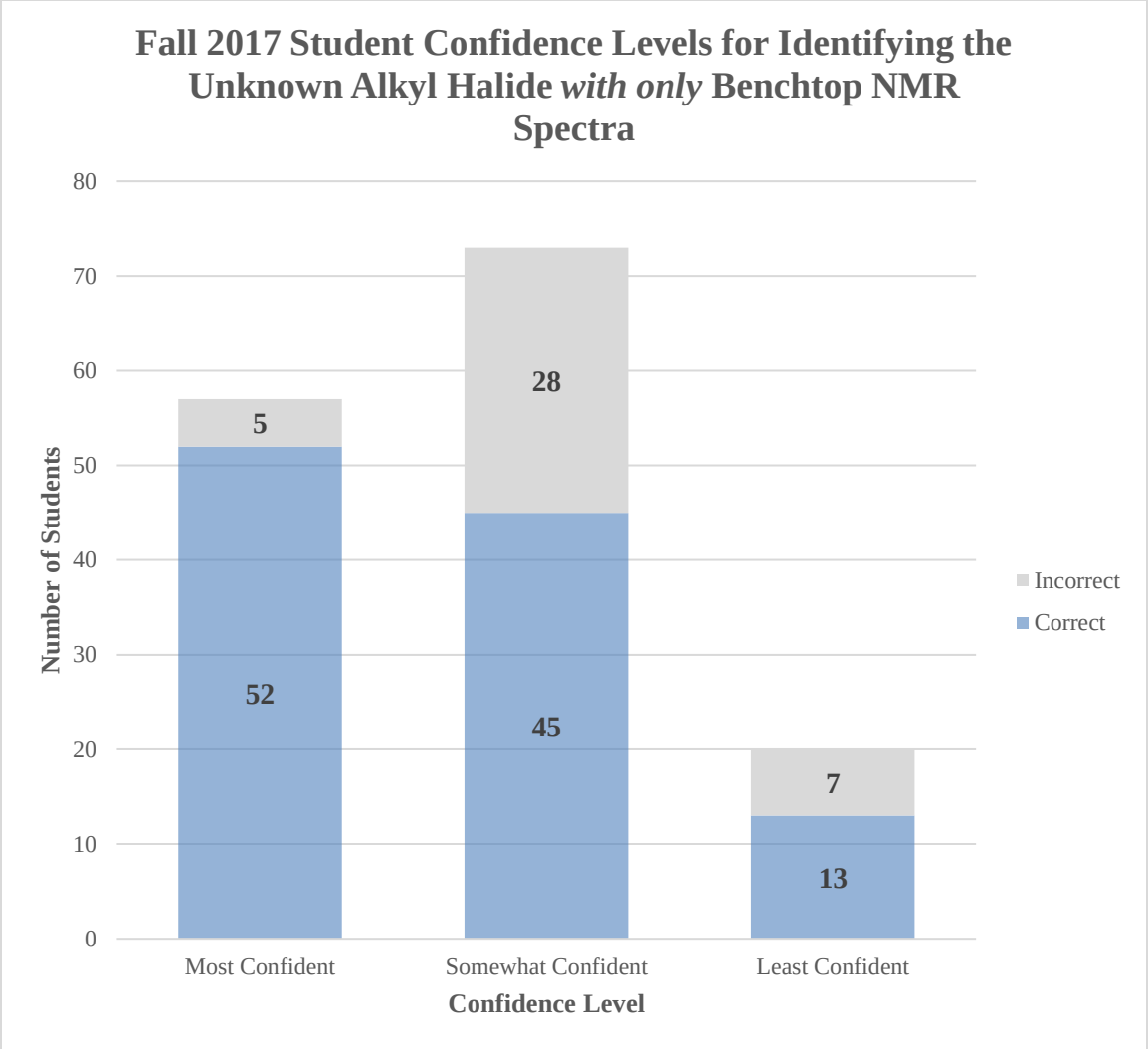
SI Figure 4.11. Spring 2018 postlab survey results for the least useful technique for deducing the identity of the unknown alkyl halide. N = 304 students.



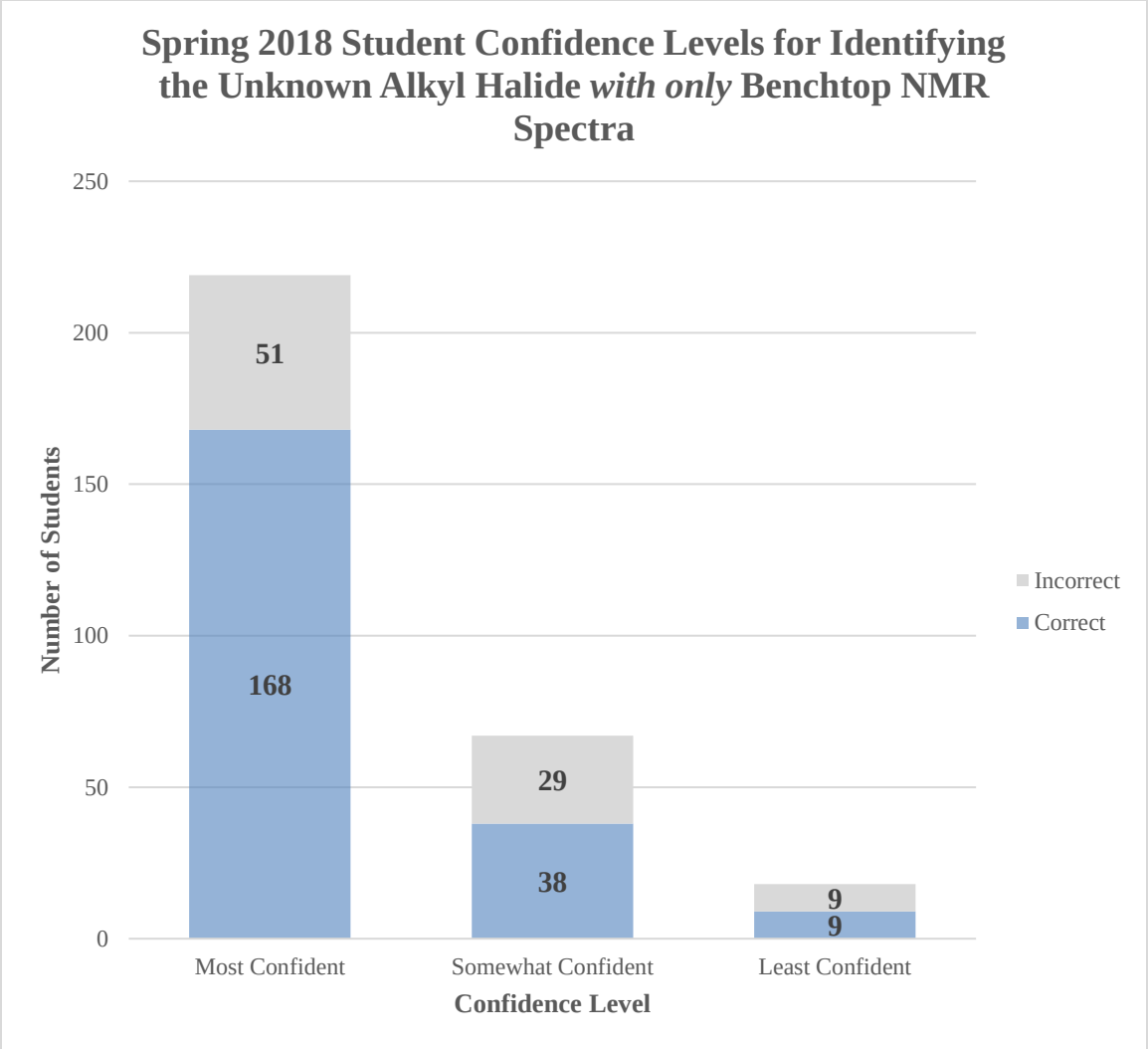
SI Figure 4.12. Summer 2018 postlab survey results for the least useful technique for deducing the identity of the unknown alkyl halide. N = 76 students.



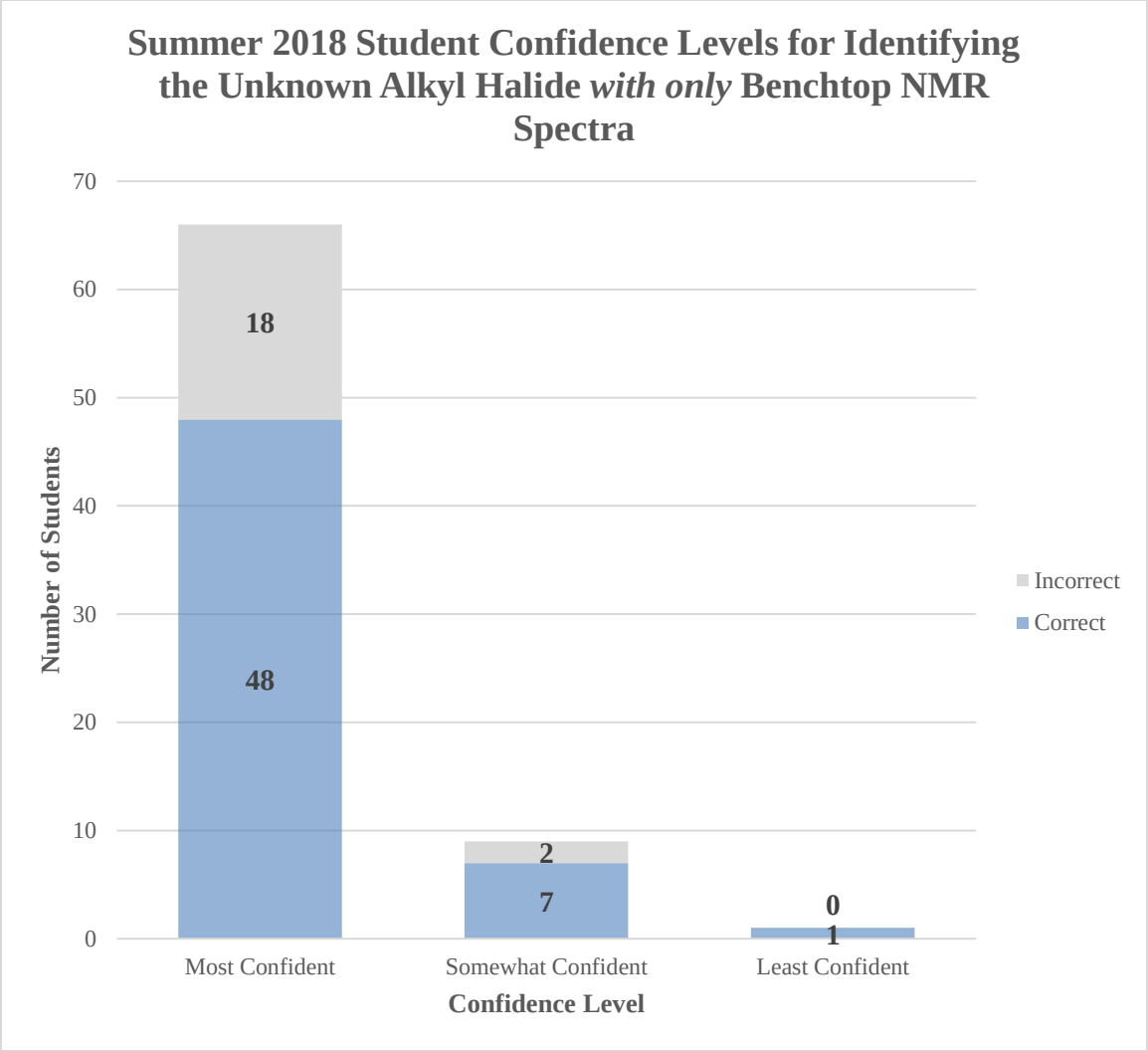
SI Figure 4.13. Fall 2018 postlab survey results for the least useful technique for deducing the identity of the unknown alkyl halide. N = 184 students.



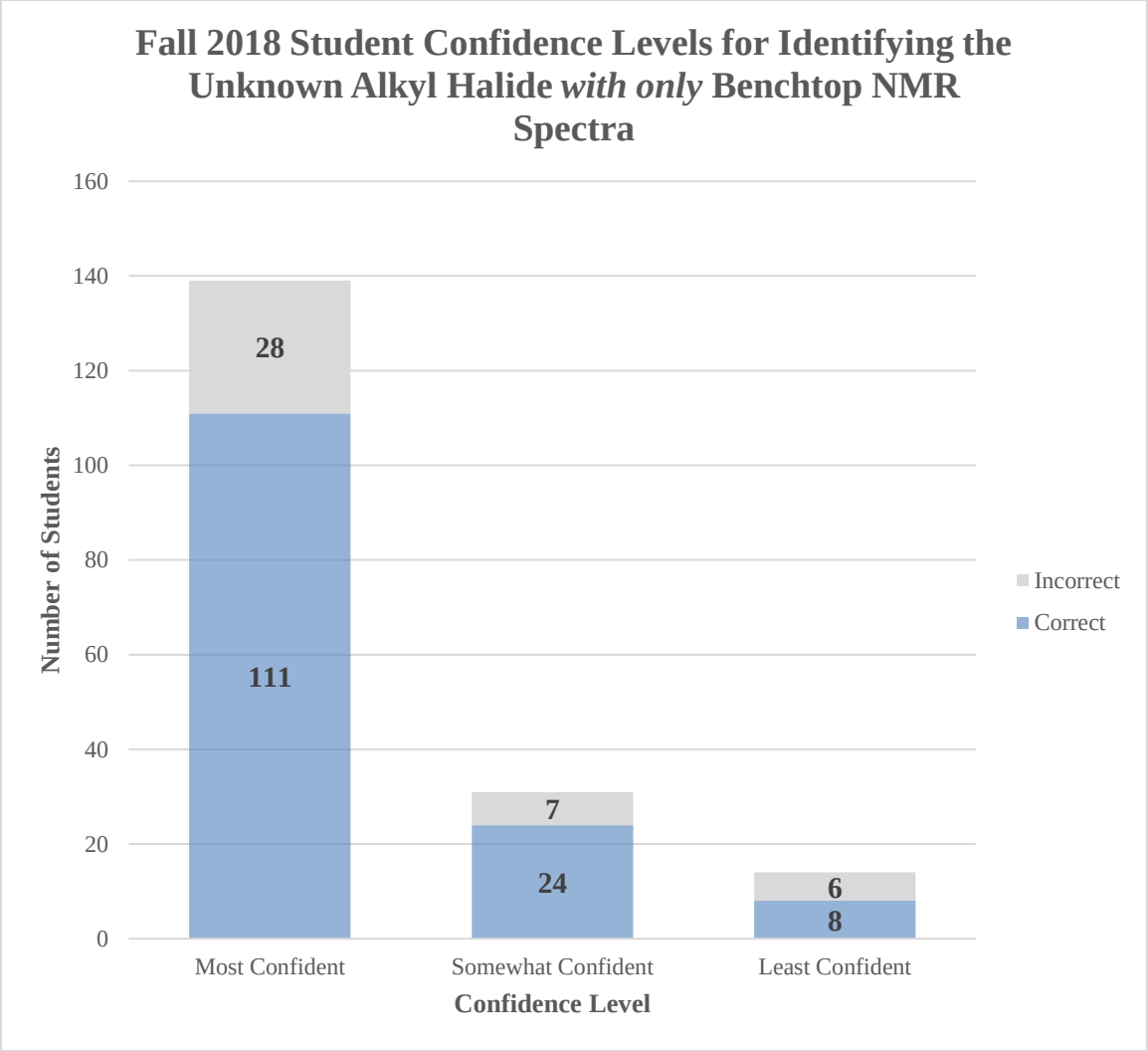
SI Figure 4.14. Fall 2017 postlab survey results for student reported confidence levels for correctly identifying their unknown alkyl halide *with only* benchtop NMR spectra. N = 150 students.



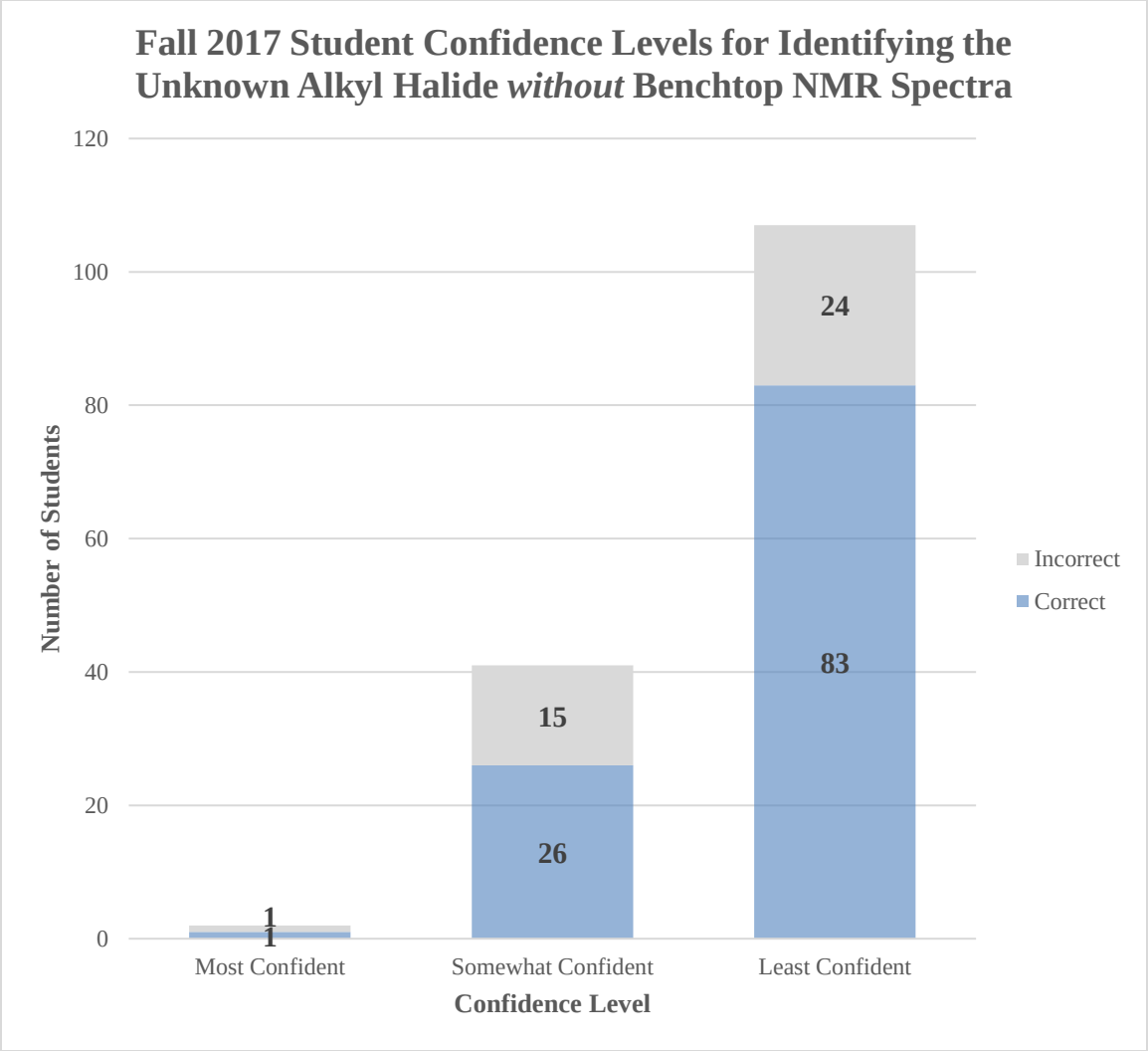
SI Figure 4.15. Spring 2018 postlab survey results for student reported confidence levels for correctly identifying their unknown alkyl halide *with only* benchtop NMR spectra. N = 304 students.



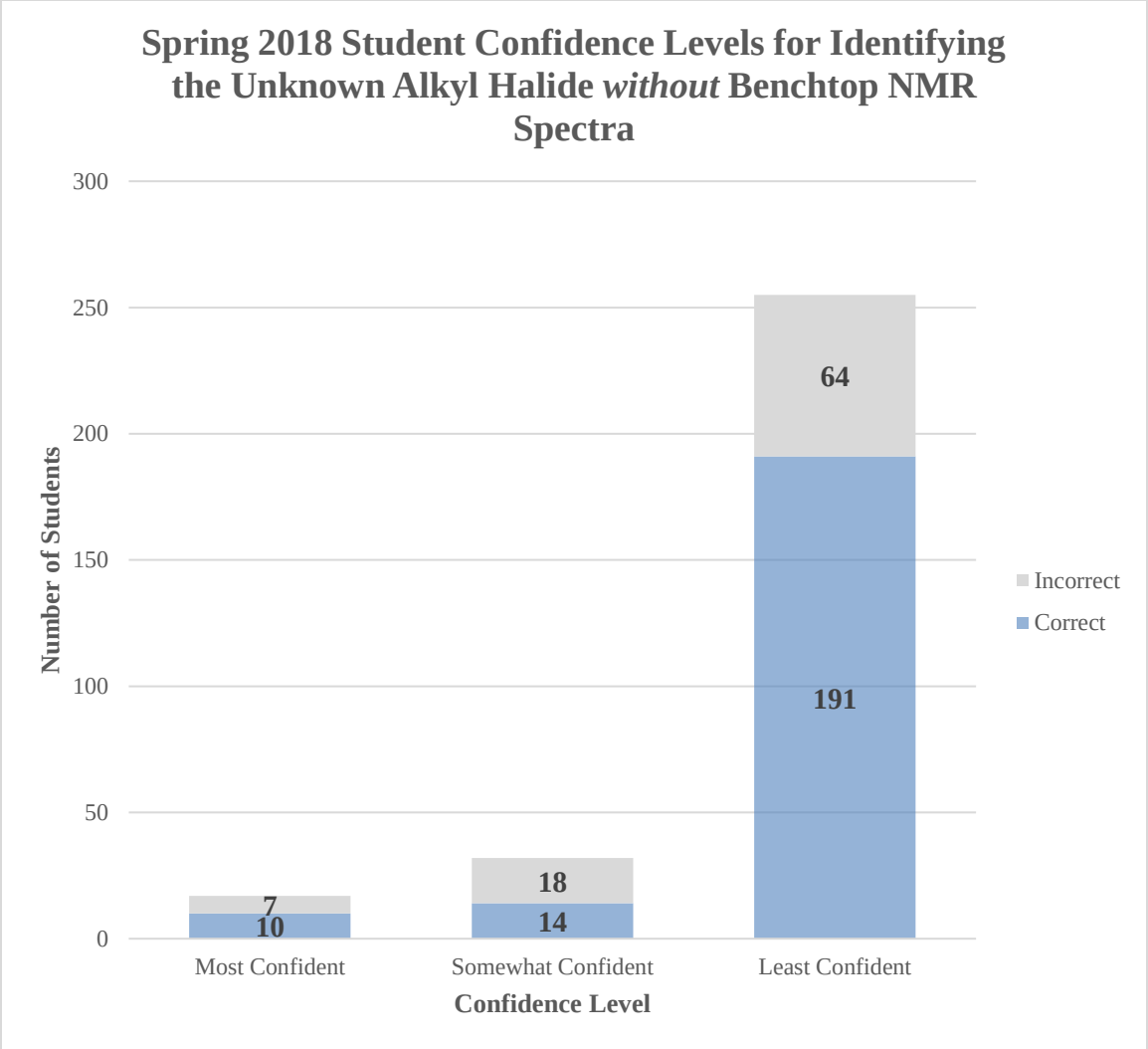
SI Figure 4.16. Summer 2018 postlab survey results for student reported confidence levels for correctly identifying their unknown alkyl halide *with only* benchtop NMR spectra. N = 76 students.



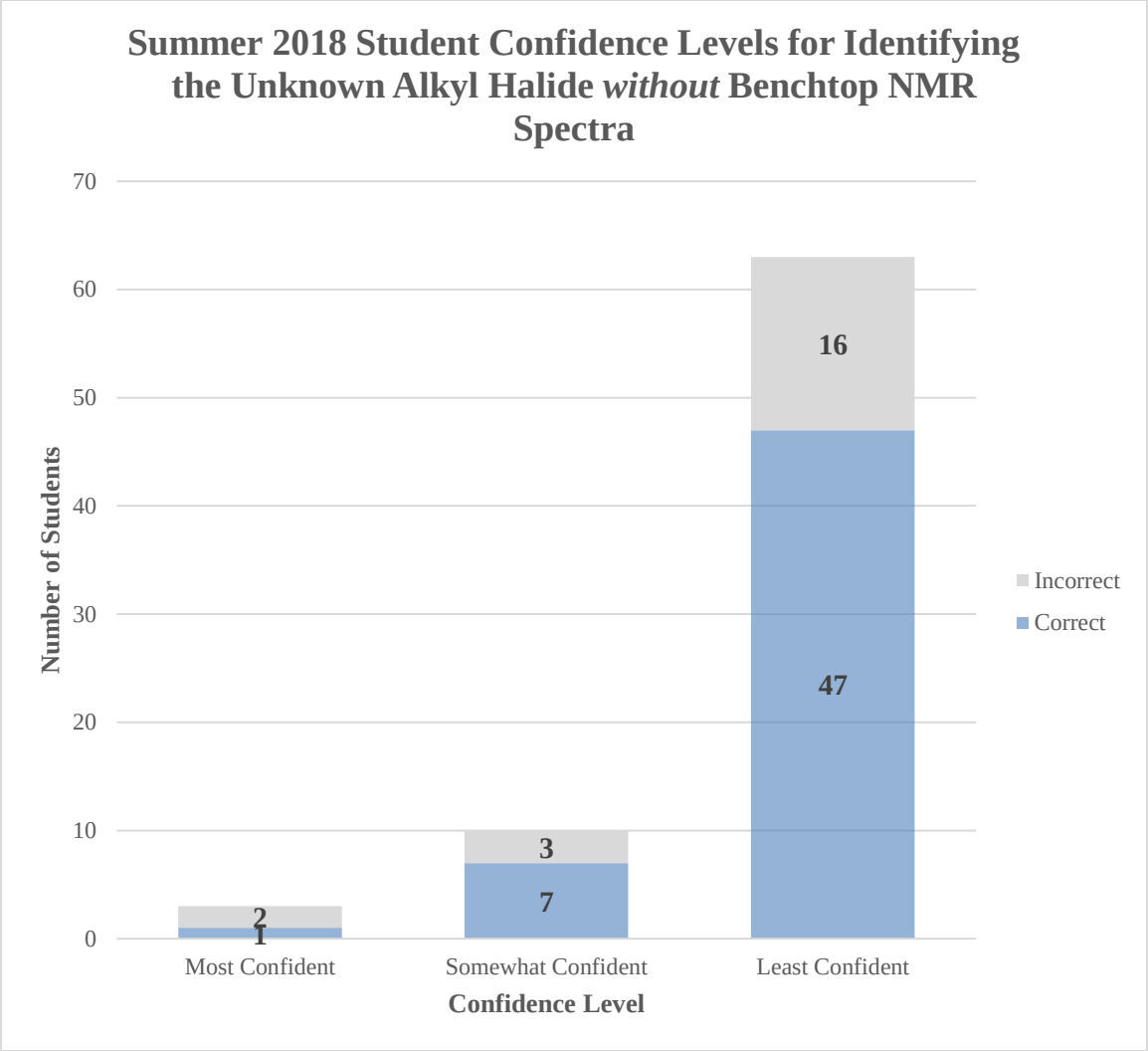
SI Figure 4.17. Fall 2018 postlab survey results for student reported confidence levels for correctly identifying their unknown alkyl halide *with only* benchtop NMR spectra. N = 184 students.



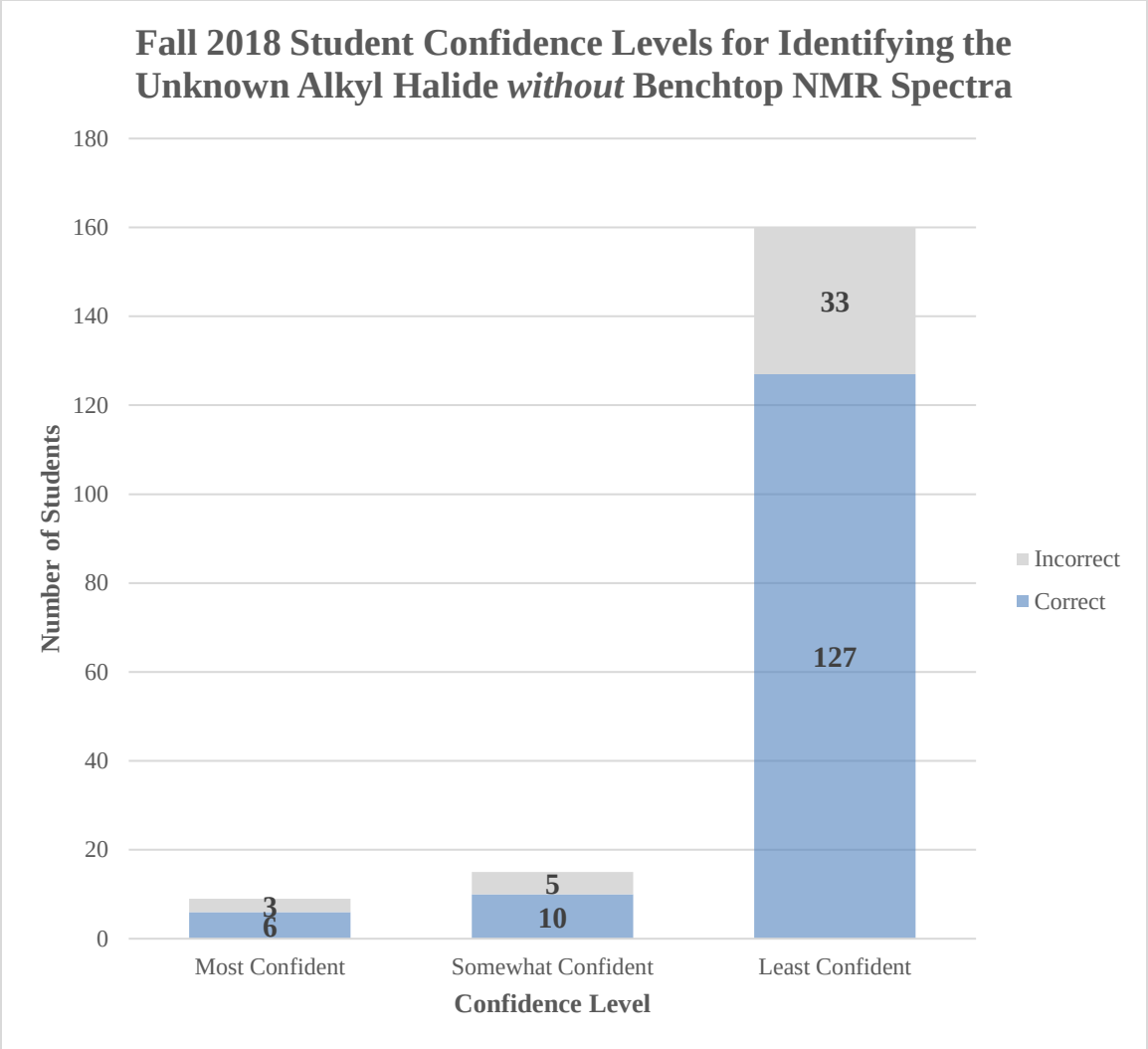
SI Figure 4.18. Fall 2017 postlab survey results for student reported confidence levels for correctly identifying their unknown alkyl halide *without* benchtop NMR spectra. N = 150 students.



SI Figure 4.19. Spring 2018 postlab survey results for student reported confidence levels for correctly identifying their unknown alkyl halide *without* benchtop NMR spectra. N = 304 students.



SI Figure 4.20. Summer 2018 postlab survey results for student reported confidence levels for correctly identifying their unknown alkyl halide *without* benchtop NMR spectra. N = 76 students.



SI Figure 4.21. Fall 2018 postlab survey results for student reported confidence levels for correctly identifying their unknown alkyl halide *without* benchtop NMR spectra. N = 184 students.

Note to Lab Coordinator 4.1.

The Fall 2017 procedure was performed as a microscale experiment without the use of the microwave promotion. $1/10^{th}$ of reagents were used for this version and conventional heating was utilized to reflux the solution for 1 hour at 100°C. Extraction solvents were halved in volume, and a test tube can be used in lieu of a separatory funnel for better visualization of the organic and aqueous phases. A Pasteur pipette was used for the column and air adapters were provided to students to add positive pressure during their elution. Initially, challenges involved summiting the learning curve for the benchtop ^{1}H NMR instrument as sufficient operator training is essential. Training documents and programs were created by UGA operators to ensure sustainability and a gentle learning curve in the future.

SUPPORTING INFORMATION – CHAPTER 5

Procedure 5.1. Fischer Esterification using Unknowns

The following reagent possibilities accompanied the laboratory experimental description. For the work described herein, students were instructed that acetic acid was the carboxylic acid used for esterification. Students were instructed to obtain an FTIR spectrum of their unknown alcohol and carboxylic acid.

Carboxylic Acids	**Alcohols**
Acetic Acid	1-Propanol
Propionic Acid	1-Butanol
Butyric Acid	Isopentyl alcohol

Students in the lab courses were paired together, and each student pair was provided acetic acid and selected one of several unknown alcohols for use during the experiment. Students recorded the identity of the carboxylic acid and the unknown code of the alcohol. 2.0 mL of acetic acid were transferred into a pre-weighed 5 mL conical vial using a microsyringe. The vial was then reweighed to determine the exact amount of acetic acid added. 1.0 mL of the unknown alcohol was added to the conical vial and the vial was reweighed to determine the exact weight of alcohol added. 5 drops of concentrated sulfuric acid were added to the vial along with a spin vane. A microscale reflux apparatus was constructed using a water-cooled condenser, an aluminum block, and a hot plate. The solution was stirred and heated gently until the liquid began to steadily boil. The reaction was refluxed for 45 minutes.

Once the reflux period was finished, the apparatus was removed from the aluminum block and allowed to slowly cool to room temperature. Once cool, the condenser was detached, and the spin vane was removed from the reaction vial. The two layers were distinguished based on the range of ester density values recorded in the table of reagents. Any visible aqueous layer was removed using a glass pipette. The remaining organic layer was washed twice with individual 1.0 mL portions of water. Subsequently, 1.0 mL of brine was added to the vial. The vial was capped (with a septum in the cap) and shaken gently. Once the layers had separated, the aqueous layer was removed via a glass pipette. The wash was repeated with a second portion of brine. Finally, the organic layer was washed with a 1.0 mL portion of 5% aqueous sodium bicarbonate solution and

stirred with a spatula until any visible foaming (CO_2 evolution) stopped. The vial was capped (with a septum in the cap) and gently shaken, venting as needed. Upon separation of the layers the aqueous layer was removed via glass pipette. This process was repeated with two additional 1.0 mL portions of 5% aqueous sodium bicarbonate. The final aqueous layer was separated from the ester-containing organic layer and the liquid ester was dried using an appropriate amount of sodium sulfate (amounts will vary based on remaining water content). The mixture stood for 5 minutes while the sodium sulfate absorbed all additional moisture in the solution. The dried ester was transferred into a tared 5 mL conical vial. Students recorded the final weight and fruity aroma of the volatile product in their lab notebook. Students determined the boiling point of the product using a Hickman still and recorded an FTIR spectrum.

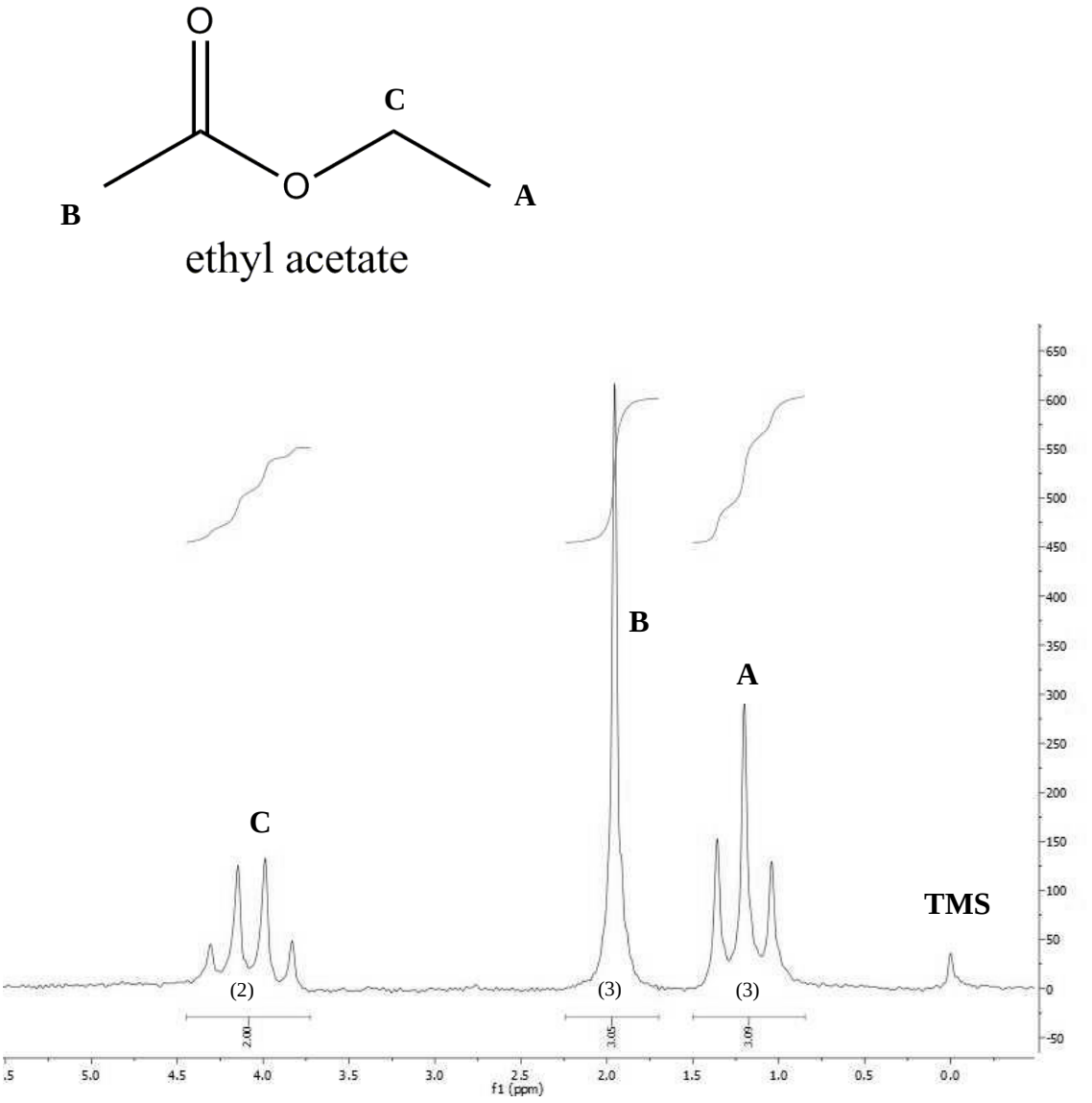
Two drops of TMS were added to 0.5 mL of the product ester. The picoSpin NMR was prepared for analysis by injecting the sample into the injection capillary until approximately ten drops exited the outlet port, displacing any residual solvents from the capillary.

Handout 5.1. Student NMR Spectrum Analyses Directions

How to Analyze PicoSpin-45 ^{1}H NMR Spectra

In-lab experimental spectra do not always look exactly like the spectra predicted and studied in textbooks. Impurities and interferences often cause deviations from theoretical spectra. Therefore, when analyzing experimental ^{1}H NMR spectra, it is necessary to use good analysis techniques to take into consideration signal integrals, splitting, chemical shifts, and potential contaminations simultaneously.

Shown below is an ethyl acetate spectrum, which is a simple ester that can be identified by ^{1}H NMR analysis alone. Ethyl acetate is not one of the unknown esters you have synthesized in lab this week, so an analyzed spectrum as an example of how to identify an ester by ^{1}H NMR.



SI Figure 5.1. Assigned Structure of Ethyl Acetate with Corresponding Spectrum from the 45 MHz PicoSpin NMR

Things to consider:

1. Identify your TMS signal.

2. There will probably be some residual water in your sample, causing a small extraneous singlet somewhere in the spectrum. Although water signals often occur between 3-5 ppm, the chemical shift changes depending upon the solvent and cannot always be predicted. Identify your water signal and disregard the signal in your analysis.

3. Look at the (not water) product signal with the highest chemical shift, which will probably be around 4.0 ppm. The hydrogens with the highest chemical shift in an ester will always be the two hydrogens on the carbon adjacent to the oxygen.

4. The next-highest chemical shift in an ester will always be the hydrogens on the carbon adjacent to the carbonyl. Find the (not water) signal with the second-highest chemical shift, around 2.0 ppm. All lab groups are using acetate as the carboxylic acid compound, which has one methyl group adjacent to the carbonyl. Therefore, the signal at 2.0 ppm should be a three-hydrogen singlet to indicate a methyl group with no adjacent hydrogens.

5. After you have identified the two signals corresponding to the hydrogens on either side of the ester, you can use the remaining signals to identify the carbon-hydrogen bonding patterns and determine what alkyl group is bonded to the oxygen.

6. In the example above, there is only a three-hydrogen triplet at ~1.2 ppm, which indicates that there are 3 hydrogens adjacent to 2 other hydrogens. Since the 2-hydrogen signal at ~4.1 is a quadruplet and there are no other split signals in the spectra, the only logical choice is that the two sets of hydrogens are on adjacent carbons. Therefore, it is known that there is an ethyl group bonded to the oxygen, and the ester is ethyl acetate.

7. In the analysis of your unknown compound, identify all the signal integrals corresponding to the unknown alkyl group that is bonded to the oxygen. Use the splitting patterns, signal integrals, and chemical shifts to identify the alkyl group. A good place to start is to look at the signal integrals and identify the total number of hydrogens that should be in the alkyl group. Then look at potential compounds with that number of hydrogens and use the splitting patterns to match your compound to one of the possibilities.

SI Table 5.1. Spring 2014 Student Data by Alcohol

Unknown	*Students*	*Correct*	*Percent*
1-Propanol	115	106	92.2%
1-Butanol	62	49	79.0%
Isopentyl alcohol	83	78	94.0%
Total	260	233	89.6%

SI Table 5.2. Spring 2015 Student Data by Alcohol

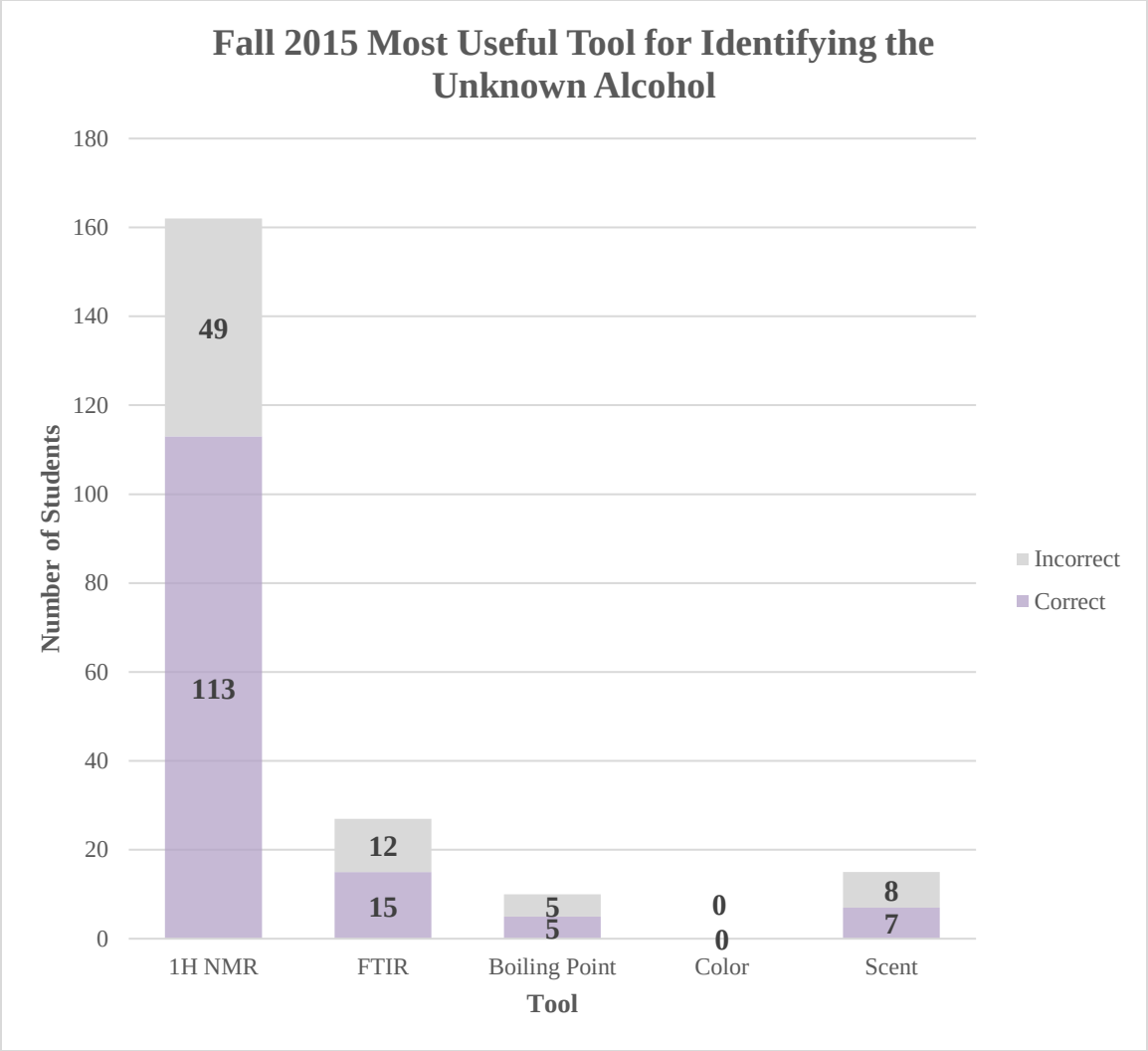
Unknown	*Students*	*Correct*	*Percent*
1-Propanol	52	47	90.4%
1-Butanol	70	25	35.7%
Isopentyl alcohol	42	38	90.5%
Total	164	110	67.1%

SI Table 5.3. Fall 2015 Student Data by Alcohol

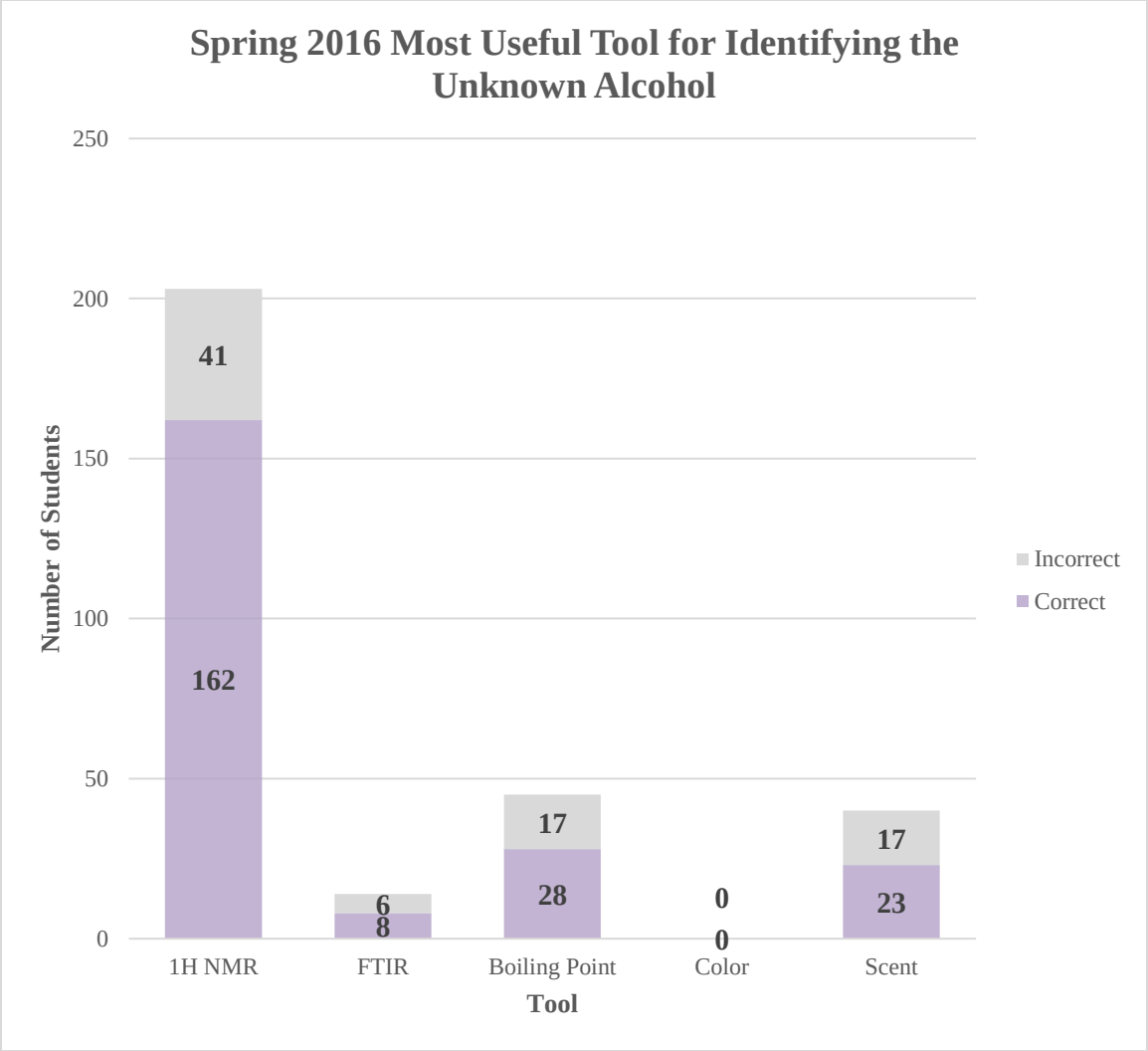
Unknown	*Students*	*Correct*	*Percent*
1-Propanol	106	89	84.0%
1-Butanol	93	40	43.0%
Isopentyl alcohol	15	11	73.3%
Total	214	140	65.4%

SI Table 5.4. Spring 2016 Student Data by Alcohol

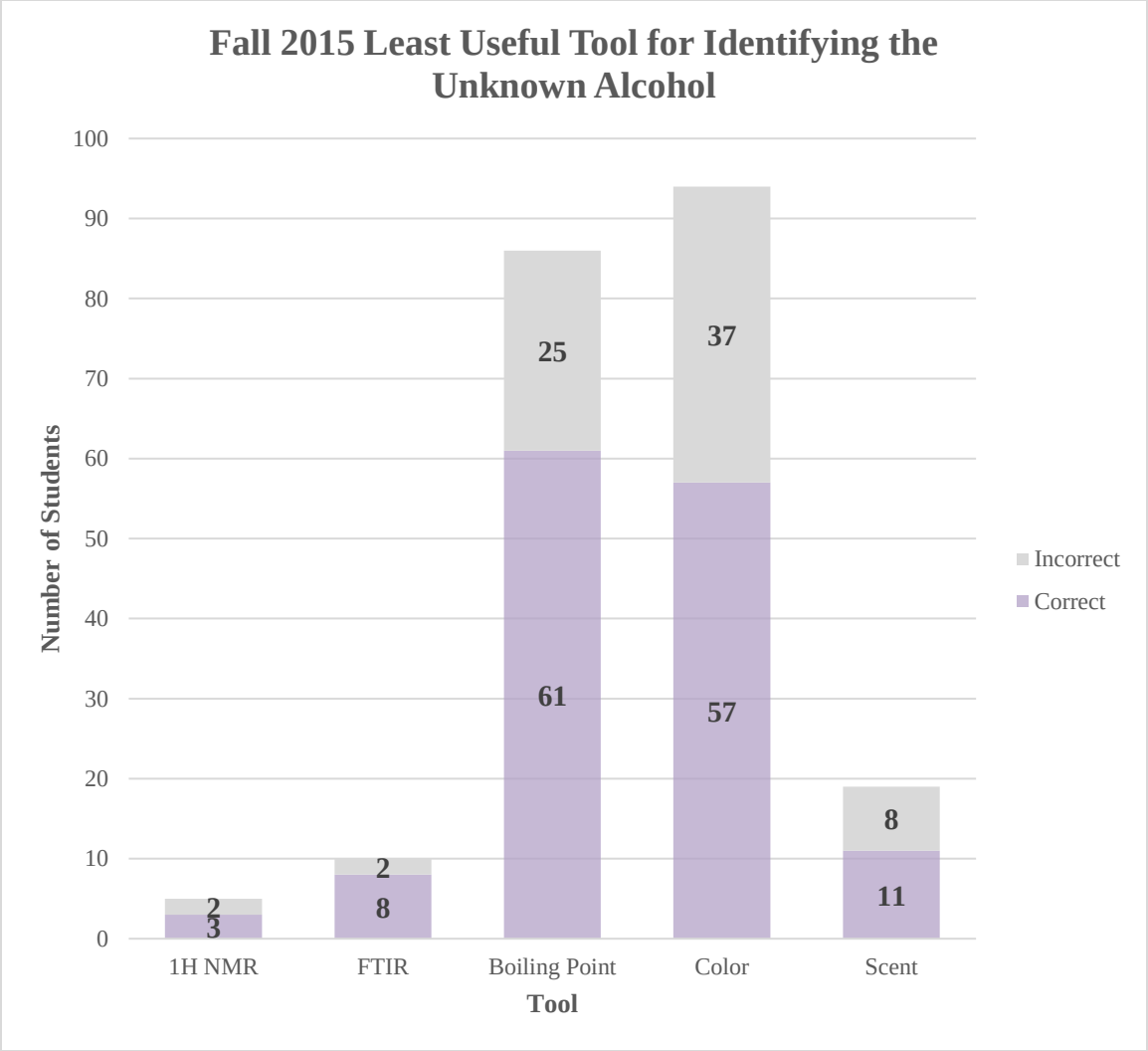
Unknown	*Students*	*Correct*	*Percent*
1-Propanol	135	94	69.6%
1-Butanol	57	46	80.7%
Isopentyl alcohol	110	81	73.6%
Total	302	221	73.2%



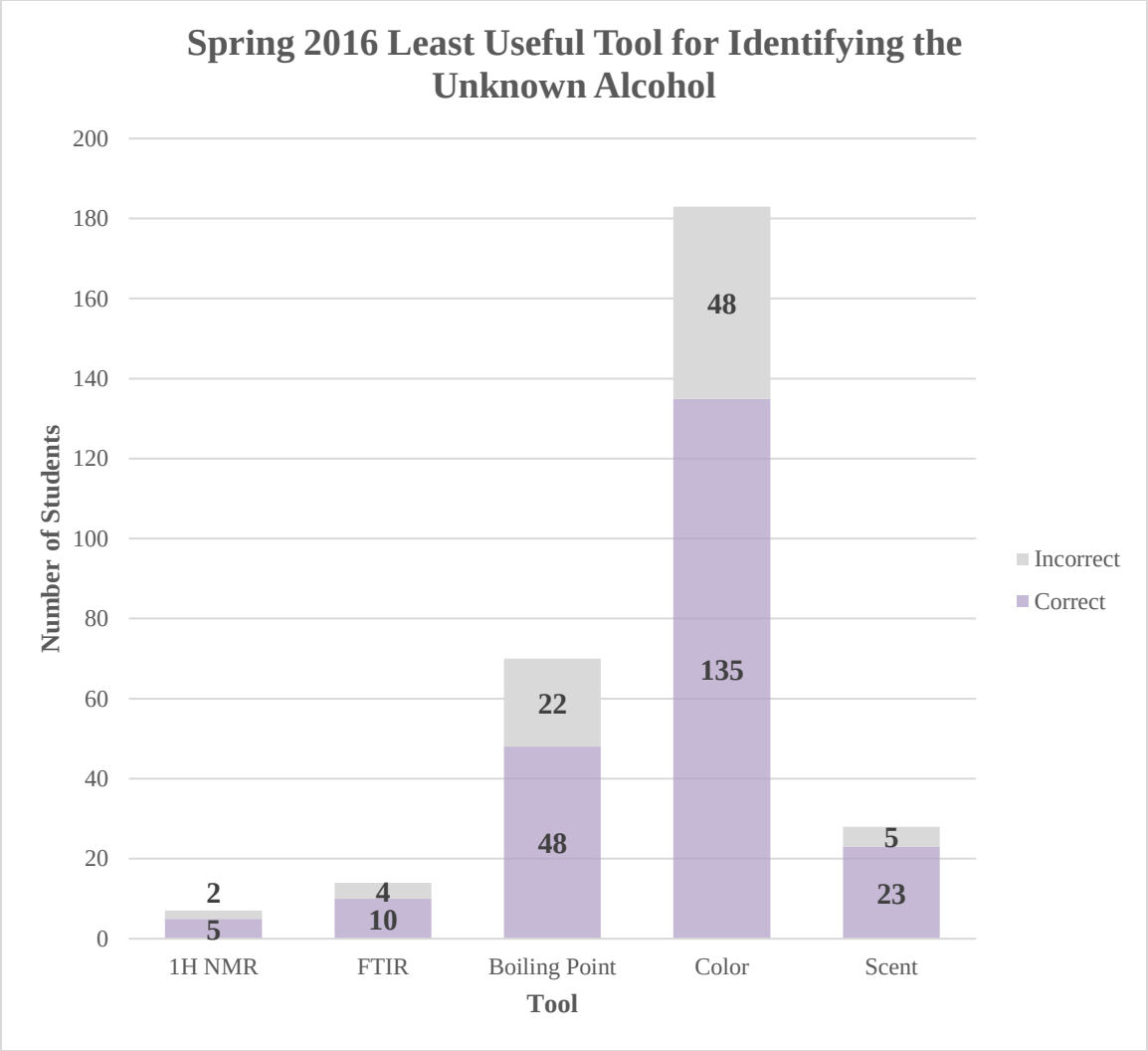
SI Figure 5.2. Fall 2015 postlab survey results for the most useful technique for deducing the identity of the unknown alcohol. N = 214 students. This survey question was not administered during the Spring 2014 and Spring 2015 iterations of the experiment.



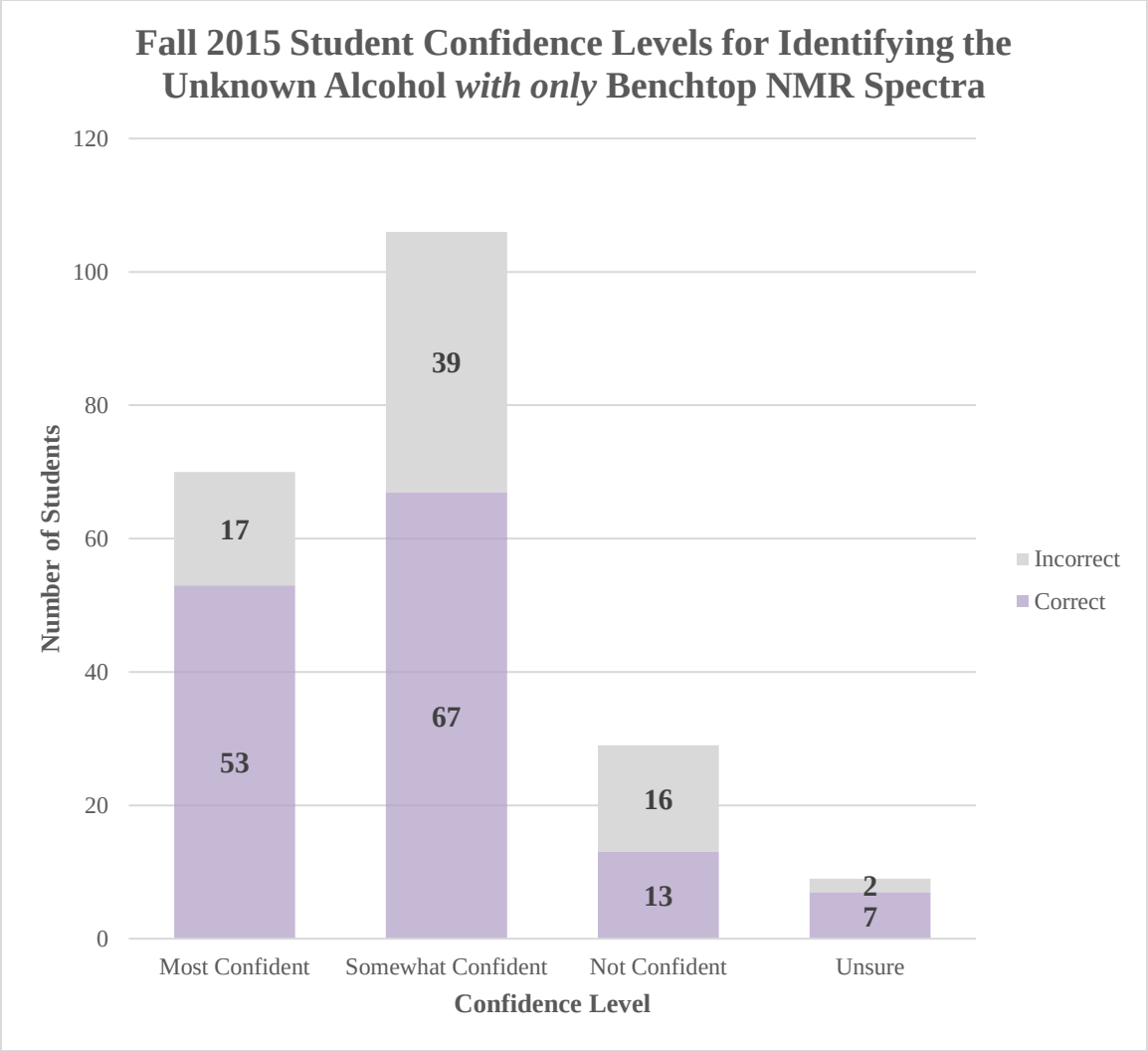
SI Figure 5.3. Spring 2016 postlab survey results for the most useful technique for deducing the identity of the unknown alcohol. N = 302 students. This survey question was not administered during the Spring 2014 and Spring 2015 iterations of the experiment.



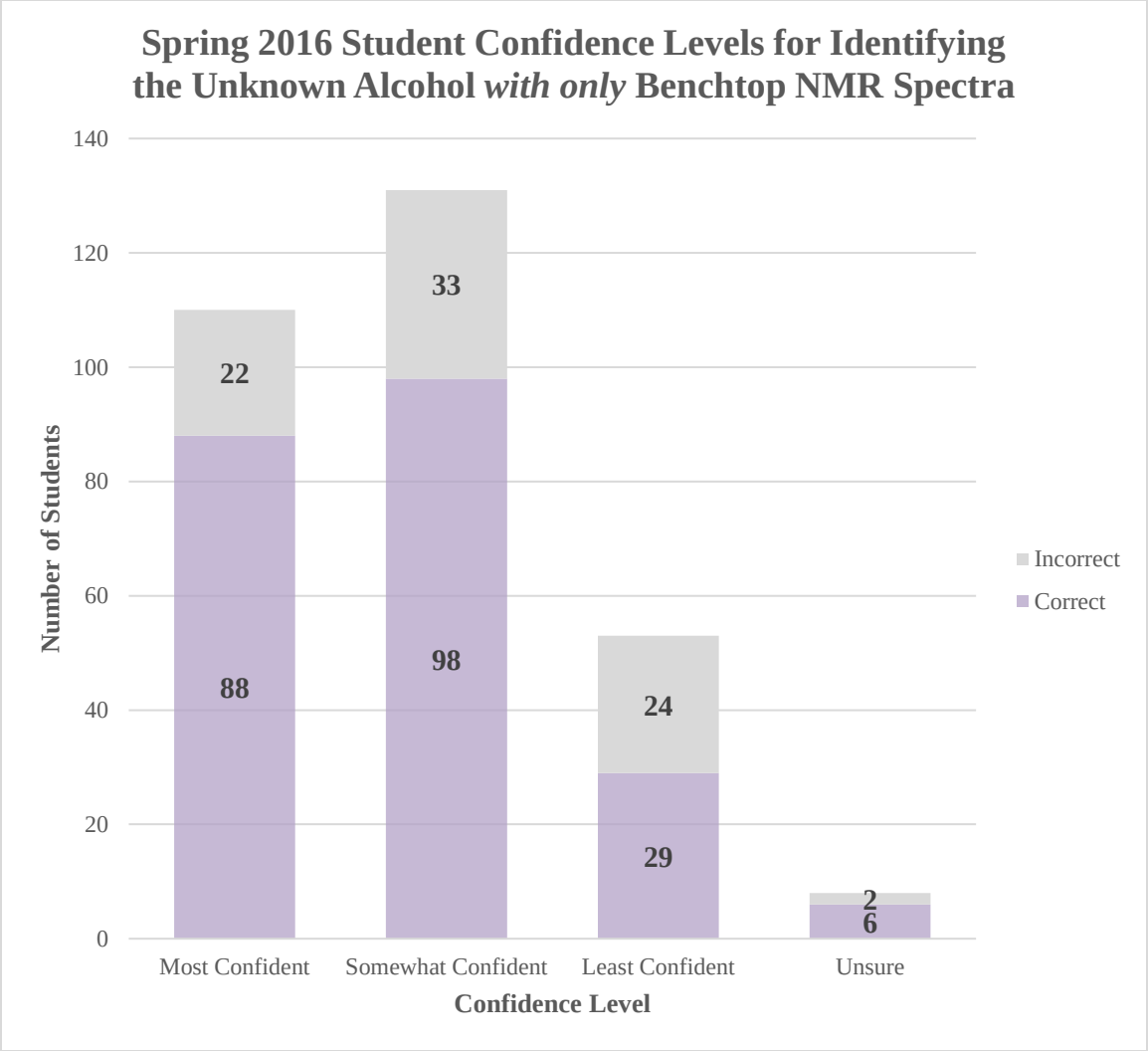
SI Figure 5.4. Fall 2015 postlab survey results for the least useful technique for deducing the identity of the unknown alcohol. N = 214 students. This survey question was not administered during the Spring 2014 and Spring 2015 iterations of the experiment.



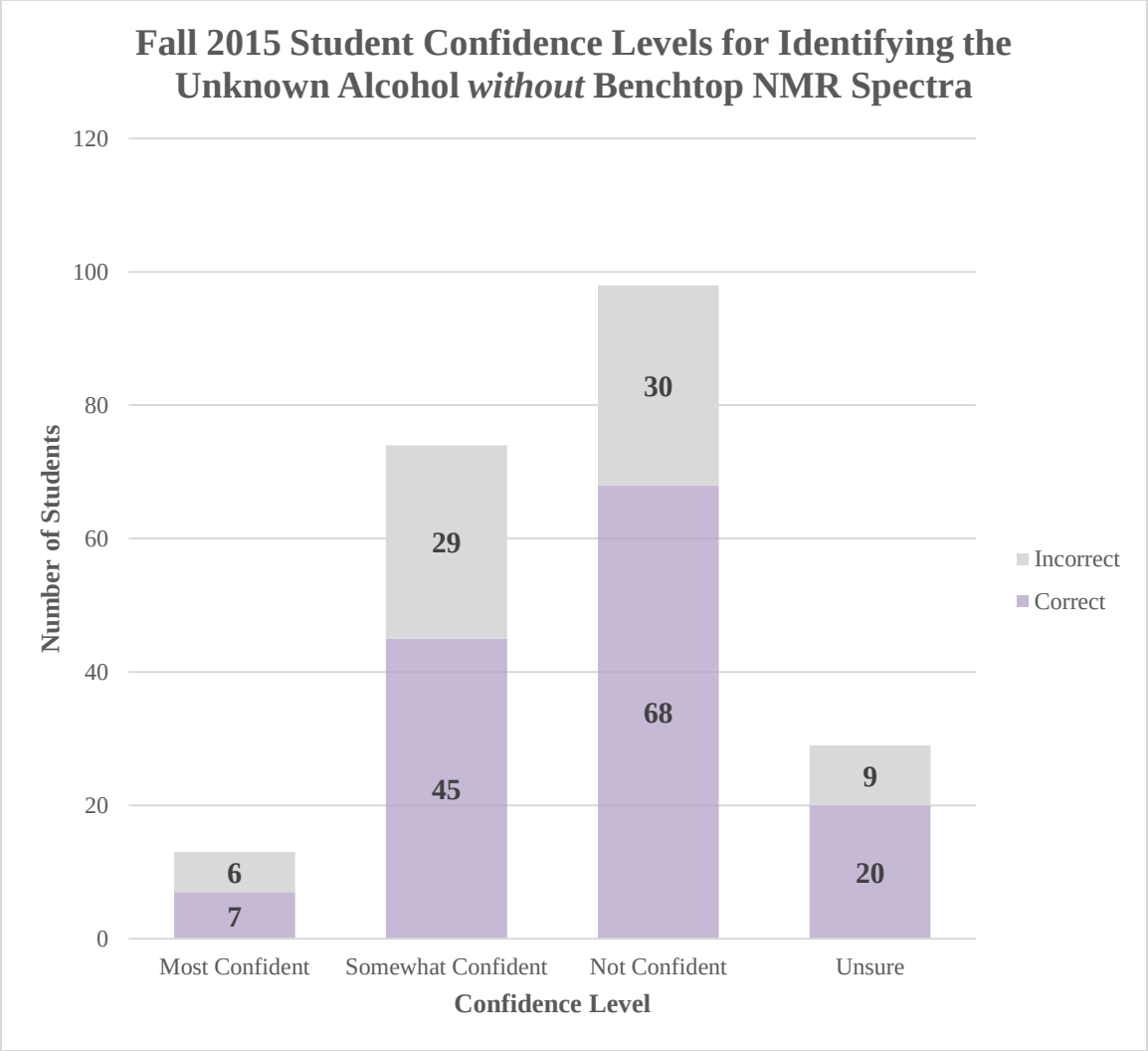
SI Figure 5.5. Spring 2016 postlab survey results for the least useful technique for deducing the identity of the unknown alcohol. N = 302 students. This survey question was not administered during the Spring 2014 and Spring 2015 iterations of the experiment.



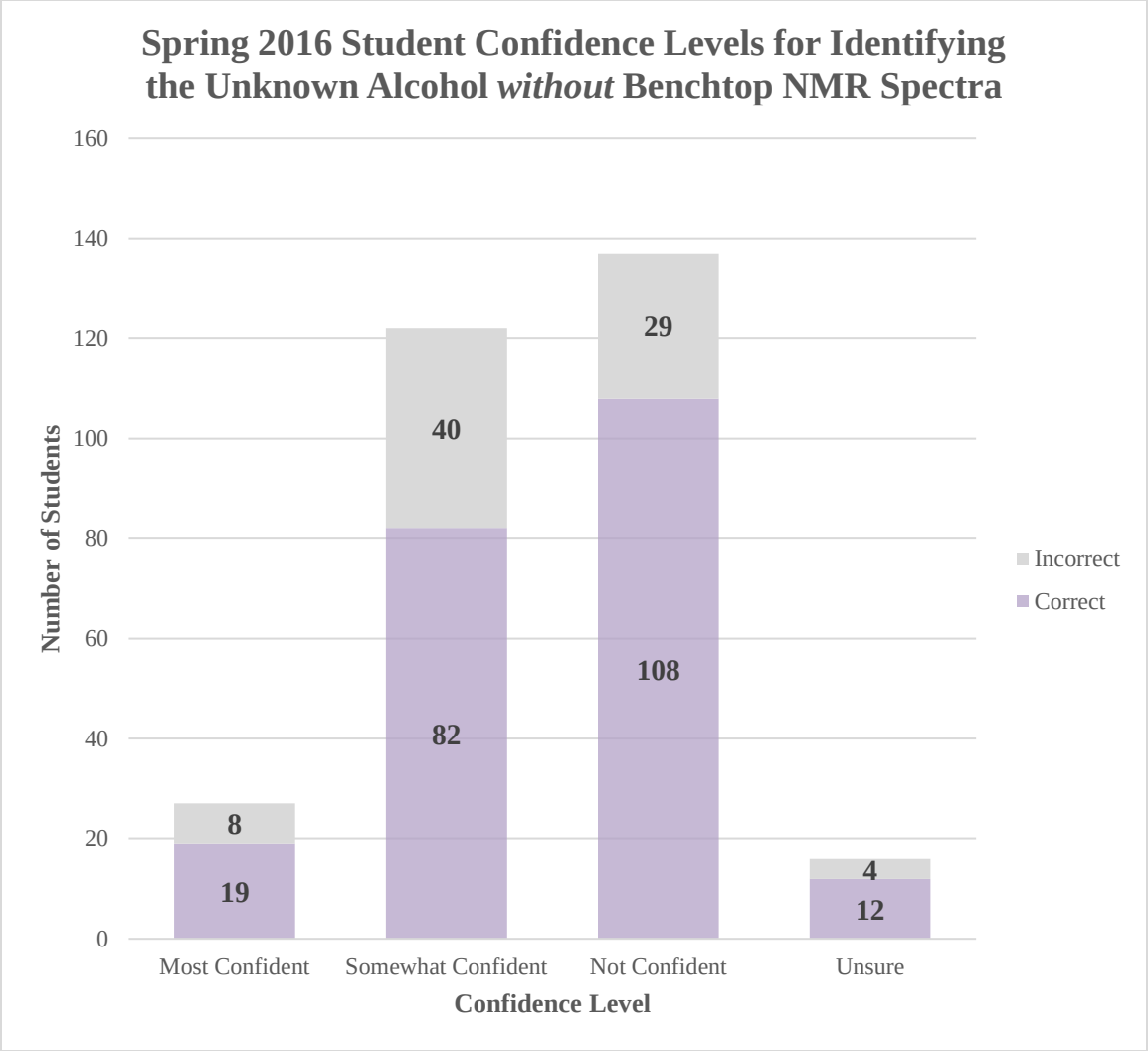
SI Figure 5.6. Fall 2015 postlab survey results for student reported confidence levels for correctly identifying their unknown alcohol *with only* benchtop NMR spectra. N = 214 students. "Unsure" was included as a response option in the earliest MOE surveys, but was removed in later surveys because of its similarity in connotation to the "not confident" response. This survey question was not administered during the Spring 2014 and Spring 2015 iterations of the experiment.



SI Figure 5.7. Spring 2016 postlab survey results for student reported confidence levels for correctly identifying their unknown alcohol *with only* benchtop NMR spectra. N = 302 students. "Unsure" was included as a response option in the earliest MOE surveys, but was removed in later surveys because of its similarity in connotation to the "not confident" response. This survey question was not administered during the Spring 2014 and Spring 2015 iterations of the experiment.



SI Figure 5.8. Fall 2015 postlab survey results for student reported confidence levels for correctly identifying their unknown alcohol *without* benchtop NMR spectra. N = 214 students. "Unsure" was included as a response option in the earliest MOE surveys, but was removed in later surveys because of its similarity in connotation to the "not confident" response. This survey question was not administered during the Spring 2014 and Spring 2015 iterations of the experiment.



SI Figure 5.9. Spring 2016 postlab survey results for student reported confidence levels for correctly identifying their unknown alcohol *without* benchtop NMR spectra. N = 302 students. "Unsure" was included as a response option in the earliest MOE surveys, but was removed in later surveys because of its similarity in connotation to the "not confident" response. This survey question was not administered during the Spring 2014 and Spring 2015 iterations of the experiment.

Note to Lab Coordinator 5.1

Initially, challenges involved summiting the learning curve for the PicoSpin instrument as sufficient operator training is essential. Once the UGA operators understood these programs, maintenance was straightforward; however, the initial learning curve was steep. Training documents and programs were created by UGA operators to ensure sustainability and a gentle learning curve in the future.

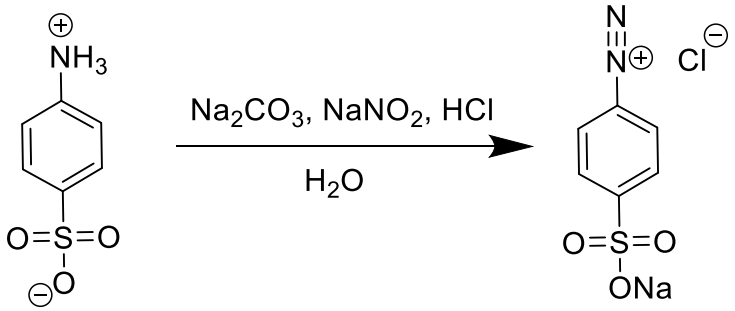
SUPPORTING INFORMATION – CHAPTER 6

Procedure 6.1.

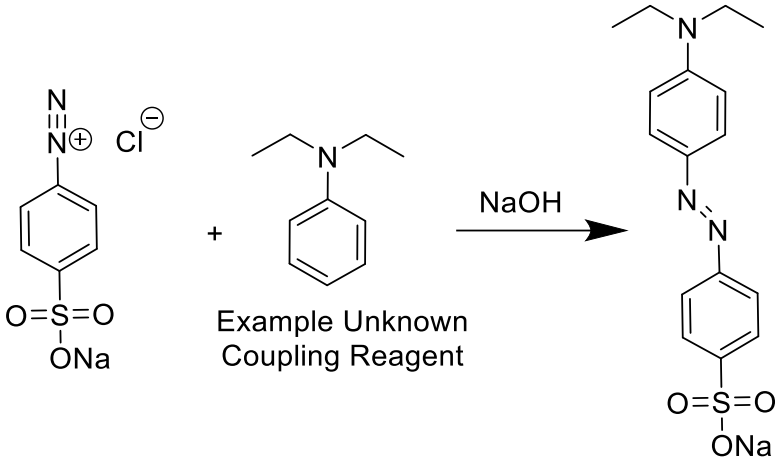
Synthesis of Azo Dyes

Azo dyes are commonly used as colorizing pigments for fabrics. The azo group is designated as the R–N=N-R' connectivity within the molecule. These compounds can be prepared through the coupling of an aryl diazonium cation with a coupling reagent through an electrophilic substitution. This experiment is a part of a cross-course collaboration to generate commercially available products. In consideration with both the Chemistry and Art departments, students performing this experiment will synthesize azo dyes for future experiments conducted with the UGA Chemistry in the Arts course (CHEM 1110). CHEM 2312/2412L students will prepare dyes in a multi-outcome experiment and study the resulting spectra to deduce the unknown coupling reagent with which they began the experiment. In the Chemistry in the Arts course, students discuss the colors of the visible light spectrum and analyze the dyes using UV-Vis spectroscopy. By exploring the same materials in vastly different ways, students in both fields will come to better understand the complimentary and interdisciplinary roles in their processes.

Preparation of the Diazotized Sulfanilic Acid:

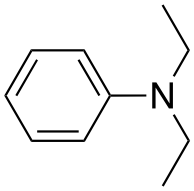


Preparation of the Azo Dye:

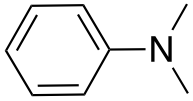


Possible Unknown Coupling Reagent Identities:

N,N-diethylaniline



N,N-dimethylaniline



phenol

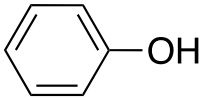


Table of Reagents:
Gather all the indicated physical data for the following compounds:
Sodium carbonate (structure, MW, MP)

Water (structure, MW, BP, density)

Sulfanilic acid (structure, MW, MP)

Sodium nitrite (structure, MW, MP)

Hydrochloric acid (structure, MW, density)

N,N-dimethylaniline (structure, MW, MP)

N,N-diethylaniline (structure, MW, MP)

Phenol (structure, MW, MP)

Glacial acetic acid (structure, MW, BP, density)

Sodium hydroxide (structure, MW, concentration)

Sodium chloride (structure, MW, MP)

Ethanol (structure, MW, BP, density)

Safety and Notes:

Lab coats, gloves, and safety glasses must always be worn while in the lab. Please review online SDS sheets of all chemicals including products. **The diazotized sulfanilic acid must remain cooled in an ice bath until it is to be used.** Use caution when working with sodium nitrite. Report any spills or accidents immediately to your TA. All generated waste must be collected in the appropriately labeled hazardous waste container.

Experimental Procedure:

Preparation of the Diazotized Sulfanilic Acid

In a 50 mL Erlenmeyer flask, dissolve 0.58 g of anhydrous sodium carbonate in 25 mL of water. Add 2.0 g of sulfanilic acid monohydrate to the solution and heat it carefully until it dissolves. A small amount of suspended material may render the solution cloudy. Cool the solution to room temperature, add 0.75 g of sodium nitrite, and stir until the solution is complete. Pour this mixture, while stirring, into a 100 mL beaker containing 16 mL of ice water to which 2.5 mL of concentrated hydrochloric acid have been added. Caution: add the HCl dropwise to maintain a temperature of 0-5˚C. The diazonium salt of sulfanilic acid should soon separate as a precipitate. **Keep this suspension cooled in an ice bath until it is to be used.**

Preparation of the Azo Dye

In a small beaker or Erlenmeyer flask, mix together 1.4 mL (if liquid) or 1.4 g (if solid) of the unknown coupling reagent and 1.0 mL of glacial acetic acid. Add this solution dropwise to the cooled suspension of the diazotized sulfanilic acid in the 100 mL beaker. Stir the mixture vigorously. In a few minutes, a precipitate should form. Keep the mixture cooled in an ice bath for about 15 minutes to ensure completion of the coupling reaction.

Add 15.0 mL of a 10% aqueous sodium hydroxide (NaOH) solution. Do this slowly and with stirring, as you continue to cool the beaker in an ice bath. Check with pH paper to make sure that

the solution is basic. If it is not, add more base until the solution is basic. Heat the mixture slightly to dissolve most of the newly formed dye. When all (or most of it) the dye is dissolved, add 5.0 g of sodium chloride and cool the mixture in an ice bath. The dye should then recrystallize. Isolate the dye using a Büchner funnel.

To purify the product, transfer the filter cake to a beaker containing 20 mL of ethanol. Heat the ethanol until gently boiling. Maintain the solution at a gentle boil for 5 minutes, stirring it constantly. Note: not all the dye will dissolve, but the salts with which it is contaminated will dissolve. Filter the solution again using a clean Büchner funnel to isolate the purified dye. Transfer the dye onto a clean, pre-weighed, and labeled watch glass. Place the watch glass in the oven for 10 minutes at 110˚C to fully dry the dye.

Experimental Procedure Modified from the following reference: Altig, Jeff. "Diazo Coupling: A Synthesis of Methyl Orange." New Mexico Tech. http://infohost.nmt.edu/~jaltig/Diazo.pdf

Spectral analysis:

You will collect an FTIR spectrum of your product. Please save the entire sample in a labeled vial with your name and TA **CLEARLY** written. A ^{1}H NMR sample of the product will be run on the 400 MHz instrument in Chemistry and the spectra will be returned to you via your TA. What information did you gather from the FTIR spectrum? Was there any remaining starting material based on the FTIR spectrum? If so, what steps could you take to remove the excess starting material(s)? What information did you gather from the ^{1}H NMR spectrum? Was there any remaining starting material based on the ^{1}H NMR spectrum? Were any solvents depicted in the ^{1}H NMR spectrum?

Special Note:

The prepared dyes must be cleaned carefully from the lab glassware, your bench, and any other equipment used. Please consult your TA for the best method of removing this rich color from your materials and workspace.

Azo Dye Synthesis Data Sheet

Amount sodium carbonate used: _____

Amount water used: _____

Amount sulfanilic acid used: _____

Amount sodium nitrite used: _____

Amount hydrochloric acid used: _____

Amount unknown coupling reagent used: _____

Amount glacial acetic acid used: _____

Amount sodium hydroxide used: _____

Amount sodium chloride used: _____

Amount ethanol used: _____

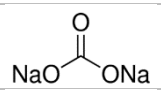
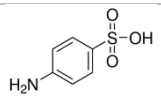
Mass of the clean, labeled watch glass: _____

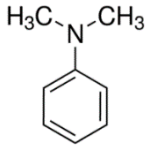
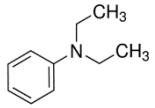
Mass of the watch glass with the purified product: _____

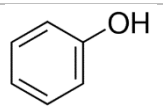
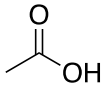
Mass of the purified product: _____

Miscellaneous Experimental Observations (Visual descriptions, texture, etc…):

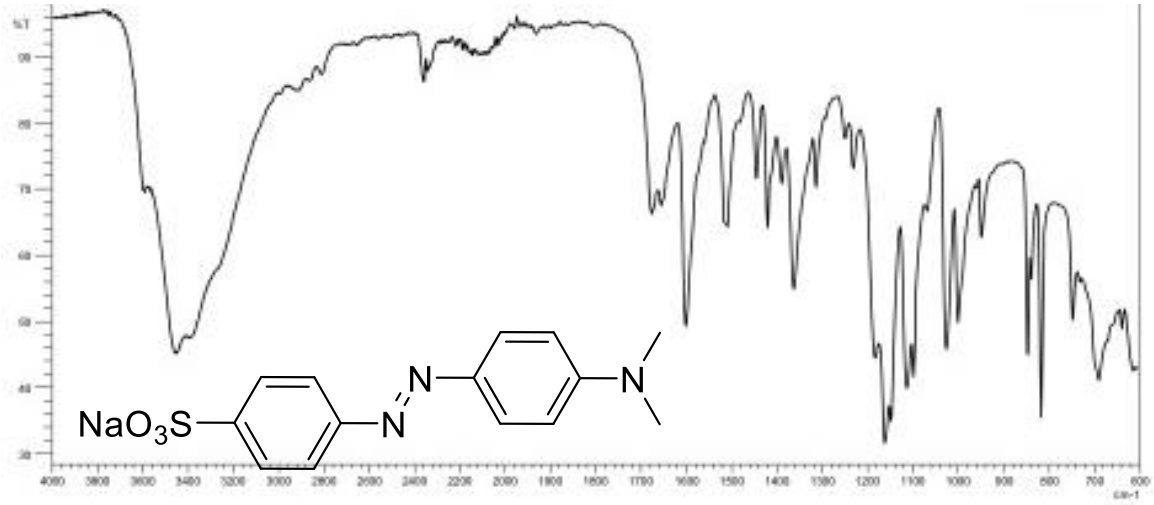
SI Table 6.1. Experiment Table of Reagents for Instructors

Reagent	Structure	CAS	Hazard Codes	Amount needed per Student	Molecular Weight (g/mol)	Melting Point (°C)	Boiling Point (°C)	Density (g/cm^3)	Solubility in water
Water		7731-18-5	Not a hazardous substance or mixture.	Varies	18.02	-	100	1.000	-
Sodium carbonate		497-19-8	Eye irritation (Category 2A), H319	0.58 g	105.99	851	-	-	1 M
Sulfanilic acid		121-57-3	Skin irritation (Category 2), H315; Eye irritation (Category 2A), H319; Skin sensitisation (Category 1), H317; Acute aquatic toxicity (Category 3), H402	2.0 g	173.19	>300	-	-	-
Sodium nitrite		7632-00-0	Oxidizing solids (Category 3), H272; Acute toxicity, Oral (Category 3), H301; Eye irritation (Category 2A), H319; Carcinogenicity (Category 1B), H350; Acute aquatic toxicity (Category 1), H400	0.75 g	69	271	-	-	-
Hydrochloric acid		7647-01-0	Corrosive to metals (Category 1), H290; Skin corrosion (Category 1B), H314; Serious eye damage (Category 1), H318; Specific target organ toxicity - single	2.5 mL	36.46	-	-	-	-

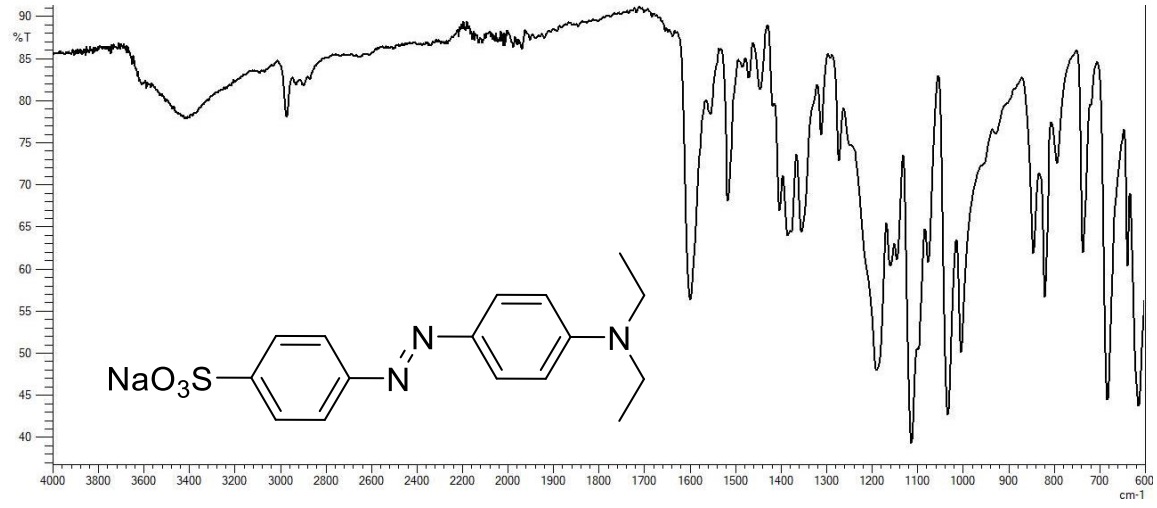
			exposure (Category 3), Respiratory system, H335						
N,N-dimethyl aniline		121-69-7	Flammable liquids (Category 4), H227; Acute toxicity, Oral (Category 3), H301; Acute toxicity, Inhalation (Category 3), H331; Acute toxicity, Dermal (Category 3), H311; Eye irritation (Category 2A), H319; Carcinogenicity (Category 2), H351; Acute aquatic toxicity (Category 2), H401; Chronic aquatic toxicity (Category 2), H411	1.4 mL	121.18	1.5-2.5	193-194	0.956	-
N,N-diethylaniline		91-66-7	Flammable liquids (Category 4), H227; Acute toxicity, Oral (Category 3), H301; Acute toxicity, Inhalation (Category 2), H330; Acute toxicity, Dermal (Category 3), H311; Acute aquatic toxicity (Category 2), H401; Chronic aquatic toxicity (Category 2), H411	1.4 mL	149.23	-	217	-	-

Phenol		108-95-2	Acute toxicity, Oral (Category 3), H301; Acute toxicity, Inhalation (Category 3), H331; Acute toxicity, Dermal (Category 3), H311; Skin corrosion (Category 1B), H314; Serious eye damage (Category 1), H318; Germ cell mutagenicity (Category 2), H341; Specific target organ toxicity - repeated exposure (Category 2), H373; Acute aquatic toxicity (Category 3), H402; Chronic aquatic toxicity (Category 2), H411	1.4 g	94.11	-	-	-	-
Glacial acetic acid		64-19-7	Flammable liquids (Category 2), H225 Skin corrosion (Category 1A), H314 Serious eye damage (Category 1), H318	1.0 mL	60.05	16.2	118.1	-	-
Sodium hydroxide	NaOH	1310-73-2	Corrosive to metals (Category 1), H290 Skin corrosion (Category 1A), H314 Serious eye damage (Category 1), H318 Acute aquatic toxicity (Category 3), H402	Varies	40.00	-	-	-	-

Sodium chloride	NaCl	7647-14-5	Not a hazardous substance or mixture.	5 g	58.44	-	-	-	-
Ethanol	CH_3CH_2OH	64-17-5	Flammable liquids (Category 2), H225; Eye irritation (Category 2A), H319	20 mL	46.07	-	-	-	-



SI Figure 6.1: Student FTIR Spectrum of Methyl Orange.



SI Figure 6.2: Student FTIR Spectrum of Ethyl Orange.

SI Figure 6.3: Student FTIR Spectrum of Phenol dye.

SI Student Survey 6.1.

Survey Page 1/5

Synthesis of Azo Dyes Post-Lab Survey

This survey is intended to gain student feedback regarding the implementation of the Synthesis of Azo Dyes experiment in CHEM 2312H/2412L at the University of Georgia. Please direct any questions regarding this survey to Kasey Leigh Yearty at kasey90@uga.edu.

* Required

What is your name? *

This will only be used to monitor the survey for completion.

Who is your TA? *

This will only be used to monitor the survey for completion.

What is the identification code for the unknown that you used? *

Please double check your response here to ensure that you have listed the correct unknown identification code.

- Unknown A
- Unknown B
- Unknown C
- Other:

What was the identity of your unknown? *

- N,N-diethylaniline
- N,N-dimethylaniline
- phenol

What mass of product did you obtain? *

Please enter your product in grams and without units. (Ex. 0.213)

Identifying your Unknown Coupling Reagent

This section features a series of questions designed to rank the usefulness of identification tools included the experiment and gain valuable feedback regarding your confidence in your results.

In the identification of your unknown coupling reagent, which identification technique was MOST USEFUL to you? *

- Color
- FTIR
- 1H NMR

Please elaborate on your previous response. *

What specific feature(s) of the identification technique selected assisted you in deducing the identity of your unknown coupling reagent?

In the identification of your unknown coupling reagent, which identification technique was SECOND MOST USEFUL to you? *

- Color
- FTIR
- 1H NMR

Please elaborate on your previous response. *

What specific feature(s) of the identification technique selected assisted you in deducing the identity of your unknown coupling reagent?

In the identification of your unknown coupling reagent, which identification technique was LEAST USEFUL to you? *

- Color
- FTIR
- 1H NMR

Please elaborate on your previous response. *

What specific feature(s) of the identification technique selected assisted you in deducing the identity of your unknown coupling reagent?

How confident would you be in correctly identifying your unknown coupling reagent WITHOUT utilizing the color? *

- Most Confident
- Somewhat Confident
- Not Confident

How confident would you be in correctly identifying your unknown coupling reagent utilizing ONLY the color? *

- Most Confident
- Somewhat Confident
- Not Confident

Please provide any additional feedback regarding the incorporation of sample color in this experiment. *

How confident would you be in correctly identifying your unknown coupling reagent WITHOUT utilizing the FTIR spectra? *

- Most Confident
- Somewhat Confident
- Not Confident

How confident would you be in correctly identifying your unknown coupling reagent utilizing ONLY the FTIR spectra? *

- Most Confident
- Somewhat Confident
- Not Confident

Please provide any additional feedback regarding the incorporation of the FTIR spectra in this experiment. *

How confident would you be in correctly identifying your unknown coupling reagent WITHOUT utilizing the benchtop 1H NMR spectra? *

- Most Confident
- Somewhat Confident
- Not Confident

How confident would you be in correctly identifying your unknown coupling reagent utilizing ONLY the benchtop 1H NMR spectra? *

- Most Confident
- Somewhat Confident
- Not Confident

Please provide any additional feedback regarding the incorporation of the benchtop NMR spectra in this experiment. *

Please provide any additional feedback regarding this experiment.

Submit

Note to Lab Coordinator 6.1

This experiment was widely enjoyed by students because of the bright colors produced; however, traces of these bright colors are easily left behind on surfaces touched by the students, glassware used, and personal belongings. The TAs who directed the individual implementations of these experiment reminded the students of the possibility (and likelihood) of staining during the previous week's experiment. The TAs also thoroughly checked all instruments, workstations, and glassware for cleanliness during check-out procedures. It is also of note that the diazotized sulfanilic acid is unstable and should be kept in an ice bath at all times. Attempts should never be made to isolate this reactive intermediate.

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