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Laboratory Experiment

Students Thinking Like Physical Chemists Using an Inquiry-Based NMR Experiment

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ABSTRACT: A revised version of a traditional physical chemistry laboratory experiment has been developed to enhance student discussion in the laboratory and to improve students' connections between physical chemistry concepts and real molecular systems. In this experiment, students explore the keto−enol tautomerization of 2,4-pentanedione. However, unlike in prior versions of this experiment, students follow a line of inquiry about data collection and interpretation. Students are provided many structured opportunities to discuss and collaborate on the analysis of data. A general outline of the experiment is provided that highlights areas of student decision-making and inquiry-based learning about the thermodynamics of this equilibrium system. A description of student activities and outcomes shows that students are afforded a number of opportunities to build their own understanding and make decisions about experimental design.

KEYWORDS: *Upper-Division Undergraduate, Laboratory Instruction, Physical Chemistry, Inquiry-Based Learning, Problem Solving/Decision Making, Constructivism, NMR Spectroscopy*

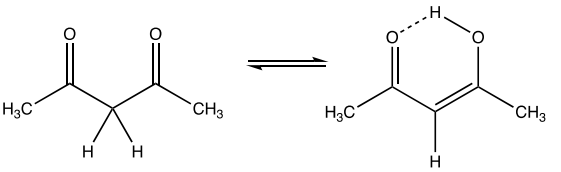
INTRODUCTION

One of the primary purposes of the chemistry teaching laboratory is to provide students with exposure to the techniques and forms of analysis used in the various chemistry disciplines. Additionally, instructors will use the laboratory as a venue to develop detailed conceptual material concurrent with student work in the chemistry classroom. In the field of physical chemistry, it can be a challenge to achieve both of these goals successfully. For the first task, state of the art or even state of the practice research equipment is often expensive and complex. As a result, students often receive limited instrument exposure that would allow them the ability to understand what the equipment is doing to a sample. For the second task, fundamental physical chemistry concepts and the development of theoretical models often do not lend themselves to experimental explorations that can be done in a 3 or 4 h lab period. What has resulted is that many physical chemistry experiments rely on the use of instruments to measure a particular chemical property with the student being left (usually after the lab period is over) to convert the measurement into an already known and often well-determined quantity, such as the bond length of a diatomic molecule or the enthalpy of combustion of a particular hydrocarbon. While the exposure to instruments is of value to undergraduate students, this particular kind of activity does not really teach students what physical chemistry exploration is about. Rather, this type of experience instills the sense that physical chemistry is all about getting the right measurement.

The experiment described herein, the study of the keto−enol tautomerization process in 2,4-pentanedione using nuclear magnetic resonance has been part of the physical chemistry laboratory curriculum for several decades and has been discussed many times in this journal and other sources.[1−9] The ketone form of 2,4-pentanedione readily tautomerizes into its enol form as shown in the reaction scheme below (Scheme 1).

From the early NMR work on this system, the enol has been understood to be stabilized by an internal hydrogen bond,[10] but both forms are typically present in solution in an equilibrium ratio that is dependent on the polarity of the solvent. What is new in this "recasting" of the standard physical chemistry experiment is the way that students approach their exploration,

Scheme 1. Tautomerization Reaction of 2,4-Pentanedione from Diketone to Cyclic Enol Form



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for indeed this experiment is written here as an exploration of a topic with which some students may already have familiarity from organic chemistry. The difference from the traditional student experience is that students are required to think about physical chemistry through answering, during the lab period, a series of questions about this system in a way that makes the details of the instrument and gathering the exact numerical results secondary to the conceptual understanding of the thermodynamics of a chemical process and how the chemical environment can affect that process.

There are two main goals in providing this revision. First, it combines three previously separate analyses of the 2,4-pentanedione system into one unified set of explorations. Second, the revision to this experiment follows a methodology that has been previously described in the POGIL-PCL (Process-Oriented Guided Inquiry Learning-Physical Chemistry Laboratory) model.[11−13] Three important aspects of the POGIL-PCL model will be discussed here. First, the experiment starts with a question and provides a structure for students to follow a line of inquiry using experimental data to answer the questions as they proceed. Second, the students collaborate with the entire class to develop a full understanding of the system, and much of the understanding is developed through peer-to-peer discussions and discussions with the instructor during the laboratory session. Finally, there are several places where students are asked to make decisions and provide justifications for modifications to a basic experimental protocol, requiring them to use their own chemical understanding of the system they are exploring.

EXPERIMENTAL WORK

For background information on this experiment, instructors will find that this experiment is primarily based on the many details for exploring this system using a high field NMR system described by Grushow and Zielinski[1] and the manuscript by Marsh and co-workers[5] which discusses an exploration into substituent effects on the NMR spectrum of 2,4-pentanedione. The experiment as traditionally presented in textbook form[3] provides a significant amount of theoretical exposition and specific directions on which solutions to make and how to analyze the spectrum with limited opportunity for discussion at the beginning of a traditional lab class other than safety precautions and additional instruction on how to use the instrument. The structure of this revised experiment is developed to promote discussion among students as they develop a framework for understanding how 2,4-pentanedione behaves in solution. Nothing in the previously published experiments on this system asks students to make predictions, revise their theoretical model, or consider the properties of the solutions in order to make decisions about how to analyze their samples.

To begin with, this experiment starts with a question: "What environmental factors affect an NMR spectrum?" By the time most students reach the physical chemistry laboratory, they usually have had a reasonable opportunity to analyze NMR spectra of both known and unknown samples in their organic chemistry lab. Indeed, it is often the case that students, fresh from their experiences in organic chemistry lab, are better at interpreting unknown NMR spectra than their physical chemistry instructors who have not had to identify an unknown compound using NMR in many years. The experiment specifically builds on the students' prior experience by asking students to predict and discuss what the NMR spectrum of 2,4-pentanedione will look like after drawing the diketone in their lab notebooks. In most cases, students will reasonably predict the spectrum with two peaks: one for the six terminal methyl protons and one at higher frequency for the two methylene protons. While most student predictions will likely prove incorrect, there is no effort to correct them at this point because one task in the analysis will have the students reconcile their predictions with the experimental outcome. After a class discussion of their predictions, teams of students (usually two or three each) are given the task of preparing an appropriate NMR sample of 2,4-pentanedione in two different deuterated solvents. The use of two different solvents deviates from students' prior NMR experience in the organic lab where student samples were typically obtained using a single solvent, usually $CDCl_3$. No explanation is given for why different solvents are used, other than "Let's see what happens." One new challenge is that students are asked to prepare a sample of a specific concentration: 0.20 mole fraction. This is a challenge because most students who have hands-on experience with high field NMR in organic chemistry are not used to preparing a sample of a specific concentration. The 0.20 mole fraction is used primarily for historical consistency because earlier versions of this experiment relied on a high concentration to make sure that a strong signal was observed. However, it also serves the purpose to make a quantitative sample that is easily prepared by mass even though both the solute and solvent are liquids. Concentration dependence is a factor in this system that could be explored later in the experiment. Details of the concentration dependence are further discussed in the literature.[1]

After generating the samples and obtaining the spectra, the students follow through a line of questioning in the lab manual. The line of questioning is referred to as "thinking about the data" (TATD) and is an aspect of all POGIL-PCL experiments.[11−13] As students work on the TATD questions, they develop their own understanding of how to analyze this NMR spectrum to determine an equilibrium constant for the enolization process. Through discussions with other student teams that are prompted by the lab manual, students discover that the solvent does have an effect on the equilibrium constant for this system. This deviates from the traditional approach to this experiment which would didactically explain how to use peak integrations in a specific way to determine an equilibrium constant for the reaction in Scheme 1. Exploring the line of questioning can take up to an hour with students working in small teams to answer questions about the spectra, identifying differences from their predictions, and comparing their results with other teams in the class who used different solvents. Most of this analysis time is spent by students working together with very little instructor intervention except for clarification.

At the end of this section of work, student teams are asked to predict what will happen to the NMR spectrum and equilibrium constant when a substituent, such as a $-Cl$ or $-CH_3$, replaces a proton in the 3-position of the molecule. This next round of hypothesis generation requires students to integrate some understanding of organic chemistry with the new knowledge they have just developed. However, there is another significant barrier to analysis for students because there is no longer a proton at the 3-position of the enol form of the substituted compound. Integration of the NMR signals of the methylene and vinyl protons was used to determine the equilibrium constant in the first cycle. The absence of a vinyl signal in the 3-subsituted enol requires the students to devise a different mechanism to determine a relative population of each tautomer. However, the TATD questions scaffold the solution to this

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problem, and students figure out how adjust their method of analysis through discussion with their peers.

In the final piece of the experiment, students explore the temperature dependence of the equilibrium constant for one of their samples. This part of the experiment is reliant upon the temperature dependent capabilities of the NMR instrument, which may not be feasible at every institution. If variable temperature NMR is not available, then the experiment can end after the second cycle of inquiry. However, continuing on with the experiment is desirable because it demonstrates for students a new line of inquiry after the solvent and substituent effects have been investigated. Many students in physical chemistry are familiar with the equations

$$\Delta G^\circ = -RT\ln K_{eq} \quad (1)$$

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ \quad (2)$$

and they usually see very quickly how to utilize these equations to determine ΔH° and ΔS° by combining them to form

$$\ln k_{eq} = -\frac{\Delta H^\circ}{RT} + \frac{\Delta S^\circ}{R} \quad (3)$$

From eq 3 the student teams figure out what data they will need to develop a van't Hoff plot to determine values of ΔH° and ΔS° from the slope and y-intercept of a plot of $\ln K_{eq}$ vs $\frac{1}{T}$. This is also different from a traditional implementation which would just provide eq 3 and specific instructions for obtaining spectra at specific temperatures. Furthermore, in this implementation, students are required to think critically about the solvent systems they are using as they must choose a set of temperatures that is appropriate for their solvent. This aspect of the experiment then requires students to consider an appropriate temperature range to use in the NMR. It also provides students with the opportunity to recognize the capabilities of the equipment with which they are working and potential safety considerations. For example, students who use DMSO-d_6 should recognize that experiments at lower than room temperature would not work well based on the freezing point of that solvent. Similarly, experiments with a low boiling solvent, such as acetone-d_6, should not be performed much above room temperature. Specific questions in the experimental write-up ask students to think about these considerations and provide students with the opportunity to use their chemical understanding to make appropriate decisions.

Everything described to this point is part of the student experimental manual which is available as Supporting Information. An instructor's handbook is also available which provides guidance to the instructor on how to coach student teams in their work (Supporting Information). As written, this experiment typically takes two 3 h lab sessions and some additional time in a third session to analyze fully and discuss the temperature dependent data after they have been collected. That is simply because the acquisition of temperature dependent data typically takes a longer time frame. While our system, a Bruker 300 MHz NMR with gradient shimming using TopSpin 3.5pl7, is automated, that automation does come with additional lag time while the system changes temperature and ensures that the temperature in the magnet is stable for each spectrum. However, at this point in the experiment, students understand how to determine an equilibrium constant. Because they have developed for themselves the necessary method of analysis and the equations for the relationship between K_{eq} at various temperatures and ΔH° and ΔS°, students typically analyze these newer data sets very quickly. The final discussion after collecting the temperature dependent data typically takes less than an hour.

Instructors, of course, do not need to stop there. There are other aspects of this system that could be explored as further extensions. Some extensions that have been proposed by students as capstone experiences for the laboratory course include the exploration of the concentration dependence of equilibrium constants (mentioned earlier) or the exploration of the NMR signals using the ^{13}C nucleus, as discussed by Grushow and Zielinski.[1] The effect of substituents on the terminal carbons was also explored[8] by students who had an interest in physical organic chemistry. Another exploration proposed by students is the use of computational chemistry to examine the structures and energetics of the tautomers in gas and "solution" phase.

Any of these extension explorations are ready sources for independent work after the structured portion is completed. Indeed, many users of POGIL-PCL experiments find that student-developed extensions are a useful way to provide a capstone experience to a physical chemistry laboratory course. Again, each step of the line of experimental inquiry is developed by the student teams rather than having it be laid out for them in a ready-made procedure.

HAZARDS AND SAFETY PRECAUTIONS

Specific compounds mentioned in this manuscript and the Supporting Information include the following solvents:

acetonitrile-d_3 (CAS 2206-26-0)
acetone-d_6 (CAS 666-52-4)
benzene-d_6 (CAS 1076-43-3)
carbon tetrachloride (CAS 56-23-5)
cyclohexane-d_{12} (CAS 1735-17-7)
DMSO-d_6 (CAS 2206-27-1)
and solute compounds:
2,4-pentanedione (CAS 123-54-6)
3-chloro-2,4-pentanedione (CAS 1694-29-7)
3-methyl-2,4-pentanedione (CAS 815-57-6)

All compounds are volatile organic compounds. All NMR sample preparation should be carried out in a well-ventilated laboratory or fume hood. Contact with skin should be avoided as many of these compounds are irritants and can be absorbed through the skin. Some solvents, benzene and carbon tetrachloride in particular, are also carcinogenetic and may cause organ damage from prolonged exposure. Further precautions, as mentioned above, should be taken when performing temperature dependent NMR experiments so that the samples remain in a liquid phase throughout. DMSO, for example, will freeze at temperatures just below room temperature. For elevated temperature NMR studies, it is recommended that after sample tubes are prepared, they are gently heated in a water bath to the highest experimental temperature before use in the NMR to make sure that the NMR tube cap does not pop off because of increased vapor pressure.

STUDENT BEHAVIOR AND IMPLEMENTATION

From the previous discussion and close examination of the instructor handbook (see the Supporting Information) for this experiment, readers will find a number of places where students need to engage in decision-making based on how their experimental measurements and analysis have progressed. The TATD questions help to scaffold their line of inquiry, but an important aspect of this implementation is that we observe

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students "behaving like physical chemists" and not necessarily like students. This phrase is put in quotations because it was coined during one of the POGIL-PCL workshops,[14] and many trained users of these experiments have since agreed with this observation. The primary focus of this experiment is to get students to behave like a physical chemist: generating predictions, comparing their models with data, revising their understanding, and further exploring a line of inquiry. In the rest of this section, specific activities that students use during this experiment are highlighted to show that this implementation is different from the traditional implementation.

Initial Predictions and Preparations

Prior to most traditional experiments, students may be asked to read background material about an experimental technique, consider safety hazards, read an entire experimental procedure, and perhaps even copy the procedure into their lab notebook. In this implementation the preliminary activities and the discussion of the prediction of the NMR spectrum rely on students' prior experiences rather than material handed to the students by the instructor. Also, during the discussion time, the student teams develop the details of their own experimental protocols within the parameters set out in the student manual. The protocols are discussed as a class and agreed to before the experiment begins. This activity allows the students to take ownership of the experiment as it is conducted. The details of the protocol then receive a mild confirmation from the instructor, just to make sure that appropriate data will be collected and that students are not creating an unsafe laboratory situation.

Data Analysis

This is the section that has the greatest divergence from the traditional version of this experiment. As described earlier, the TATD questions guide students through the analysis of the NMR spectrum of this tautomeric system. A few students may have a sense that 2,4-pentanedione readily tautomerizes, but they rarely expect to observe both forms in the same spectrum. The analysis of the spectrum with two related species does require them to work through some details. This is done by the student teams as they work through the TATD questions and then discuss as a class, with teams sharing their results. The data-sharing aspect is important for two reasons. First, it allows teams to confirm that their results are reasonable and make sure that everyone is working with an analysis that is appropriate. Second, when possible, different teams are assigned different deuterated solvents from the nonpolar cyclohexane-d_{12} to the very polar DMSO-d_6 and acetonitrile-d_3. The teams are asked to compare the equilibrium constants obtained in these different solvents and discuss what affect solvent polarity might have on the tautomeric equilibrium. This experiment has been taught several times in this format, and it has been seen that the students figure out, through their discussions as a team and with little instructor intervention, that a polar solvent favors the diketone form more than a nonpolar solvent. The students further rationalize this behavior based on the structure of the diketone compared to the internally hydrogen-bonded enol form. The development of this understanding arises from the students working together, thus internalizing their understanding rather than using the experiment as a means to confirm prior knowledge. The other two sections of the experiment, as described earlier, further require collaboration among teams and discussion of the different results each team generated. The use of this jigsaw strategy in gathering and analyzing this data further develops the students' ability to work with one another to answer the lab questions. In each phase of the experiment, the students are discussing among themselves how to interpret the data and create a model understanding of the system.

Student-Reporting Activity

It should be clear at this point that, by design, most of the data analysis and discussions occur *during the lab period* under the supervision of the instructor. This structure requires the students to learn almost everything they need to know about the system through structured discussion *before* they leave the laboratory. This means that there is little analysis work to be done without some class discussion. This has resulted in a marked improvement in student comprehension observed in the lab reports submitted within 1 week after the last discussion session. It has been observed over the recent implementations of this experiments that students focus more on the concept of how the solvent environment affects the equilibrium rather than making sure the values for the equilibrium constants match accepted values.

A final observation worth noting about this framework of experimentation is that, as in other experiments that have been developed by the POGIL-PCL community,[15] the student discussion that takes place in the laboratory is often quite animated as students are taking ownership of their understanding of the system through the exchange of ideas and ways to model their understanding. I would assert that this behavior by the students is very similar to the active discussions about data and models that occur between professional research scientists in the physical chemistry discipline. I will leave it to those who are better trained in observing and analyzing student behavior in educational settings to characterize student activity. However, as a trained physical chemist, I find the student activity in this and other POGIL-PCL experiments to be very similar to discussions that researchers, undergraduate or postgraduate, have as they work to create understanding and connections between their prior understanding and new data as they are gathered in a research setting.

Implementation

This inquiry-version of the NMR analysis of 2,4-pentanedione was first tested at Rider University in 2016 and has been utilized four different times in the intervening years, with over 35 students using the experiment as devised. In the first two, revisions were undertaken as a result of student feedback. Additionally, the experiment has been tested and reviewed by the POGIL-PCL community during two separate workshops,[14,15] one in which over a dozen physical chemistry faculty followed the student instructions, developed their own data, and reviewed the line of questioning as students. After each review session, feedback for the author was generated and incorporated into the materials that are found in the Supporting Information. Following these workshops, a number of members of the POGIL-PCL community have also reported using this experiment in their own courses.

CONCLUSION

The description of the experimental work and student activity described above clearly indicates a level and type of activity by the students that are counter to the traditional forms of this experiment or most other physical chemistry teaching experiments. In a traditional experiment, students are often given specific instructions on chemical preparations and measurement conditions. Furthermore, the model equations for data analysis are given up front, and students are given instructions of what to

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do with the data. In many cases, the students do not have a further opportunity to explore the specified system, nor are they encouraged to build their own conceptual models or equations because those are given to the student directly. In contrast, the experiment described here emphasizes student predictions and discussion of methods to model experimental results. It is the active work by students to develop and discuss how to model the data that is the greatest divergence from traditional teaching experiments. Rather than directly providing the theoretical framework to analyze the data that they collect, the lab manual guides student teams to develop their own understanding and theoretical model framework in order to describe this equilibrium system. Students then refine their theoretical models after conducting additional experiments. At all stages, data are analyzed through student team discussions that are monitored by the instructor. During these discussions, students develop a deeper understanding of the equilibrium system while making specific decisions about both experimental design and the direction for the analysis of the resulting data. By the end of the laboratory exercises, not only are students able to explain what they did in the experiment and what was learned, they also can often articulate additional research questions to pursue in a subsequent experimental cycle or extension as discussed above.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available at https://pubs.acs.org/doi/10.1021/acs.jchemed.2c00589.

Student experiment manual (PDF)

Instructor handbook (PDF)

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Notes

The author declares no competing financial interest.

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