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Teaching with the Case Study Method To Promote Active Learning in a Small Molecule Crystallography Course for Chemistry Students

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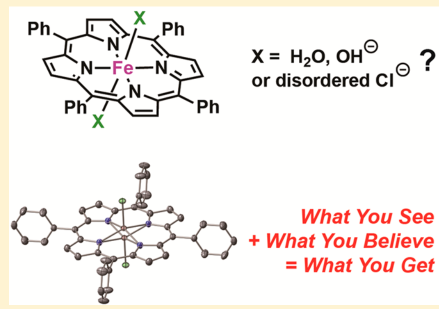
Ⓢ *Supporting Information*

ABSTRACT: Implementing the case study method in a practical X-ray crystallography course designed for graduate or upper-level undergraduate chemistry students is described. Compared with a traditional lecture format, assigning small groups of students to examine literature case studies encourages more active engagement with the course material and stimulates improved class discussion. In particular, a judicious selection of case studies either from high-profile publications or from literature directly pertaining to students' fields of research allows students to draw an immediate connection between the lecture material and their own academic/research interests.



KEYWORDS: *Upper-Division Undergraduate, Graduate Education/Research, Inorganic Chemistry, Collaborative/Cooperative Learning, Problem Solving/Decision Making, X-ray Crystallography*

X-ray crystallography, and as a result crystallography education, has changed dramatically thanks to the availability of modern technology and software.[1] It is now easier than ever for "non-crystallographers," such as inorganic chemists, to perform structure analysis routinely using small molecule single-crystal X-ray diffraction.[2−4] The accessibility of structure analysis to chemists is beneficial for research, as crystallography is, in many ways, the ultimate tool for structure determination at atomic level resolution in three dimensions. Modern software and electronic educational resources[5,6] have also made *teaching* crystallography much easier.[7−9] However, many chemists, including chemistry students and postdoctoral researchers who now routinely perform small molecule crystallography, are not trained in the details of diffraction physics, and usually approach structure solution/refinement software as a "black box".[10] It is important to impress upon students who have learned chemical crystallography the point that "*careful crystal structure determination is at best a measurement of the precision of the fit of the structure model used to the experimental data obtained, which sometimes may lead to serious errors.*"[11] In teaching small molecule crystallography to graduate or upper-level undergraduate chemistry students, we have found that the case study method, in which students actively evaluate potential errors or ambiguities in published crystallography data from chemistry literature, is the most effective way to help students understand such key concepts. Herein, guidelines are described for the use of literature case studies in a practical crystallography course for chemistry students, which may be of use to educators in the field.

■ BENEFITS OF CASE STUDY DISCUSSION FOR A CRYSTALLOGRAPHY CLASS

The benefits of the case study method have been demonstrated in a variety of disciplines,[12] and have been widely discussed in the context of science education,[13,14] but to our knowledge, case studies are not widely used in crystallography courses. "Classic" examples of ambiguity in structure refinement are often discussed, and can readily be found in textbooks in the field,[15−17] but are typically addressed in a lecture format. To improve our own crystallography course,[18] we sought (1) to develop a more active way for students to participate in learning, and (2) to utilize modern literature examples that more directly connect to students' own interests and/or research. The case study method was identified as an ideal approach to achieve these educational goals. Rather than the traditional lecture method (one way spoken communication from instructor to students), case study discussion is an interactive teaching method and provides contextualized learning, in which the key skills relevant to the course are situated in a meaningful context.[19] The use of contemporary literature cases also helps to reinforce the idea that a careful, critical analysis of crystal structure data/refinement is a necessary part of using crystallography as a research tool.[20] Analysis of recent literature engenders discussion about common errors and pitfalls during problematic small-molecule structure determination in the real world.

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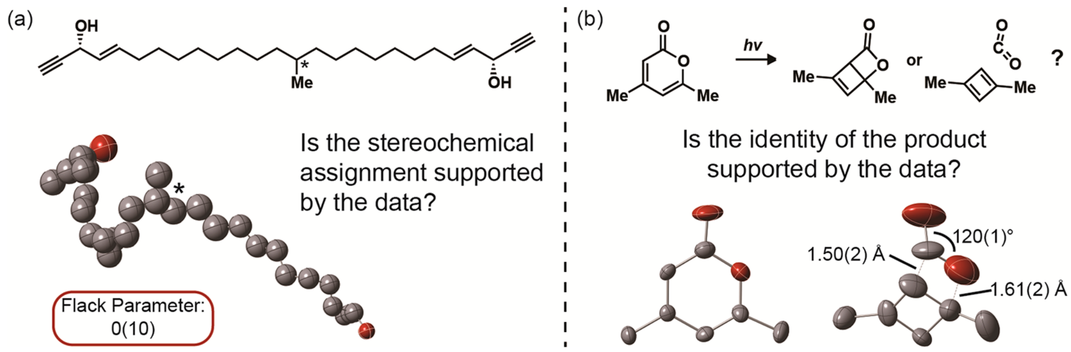

Figure 1. Examples of case studies from the chemistry literature with key guiding questions for students (all structures are plotted with 50% probability ellipsoids, and H atoms are omitted for clarity).

■ GUIDELINES FOR DESIGNING CASE STUDIES

Through trial and error, some general guidelines were developed that can increase the effectiveness of case study discussion in the context of an X-ray crystallography class for chemistry students. The development of case studies in our class was shaped by considering the established components of experiential learning methods:[19]

1. The learning uses real-world situations, problems, equipment, or actions to the extent possible.
2. The situations involve complex, ill-defined problems that do not have a simple answer and may even have more than one possible answer.
3. The situations involve the learners in solving a problem that reflects the kinds of problems they would encounter in the real world using the real tools of the discipline.
4. The instructor is a resource, but not the leader of the problem-solving task.
5. When the learners have come to a solution, they spend an equal amount of time reflecting on how they reached their solution and getting feedback about the quality of their proposed solution.

The specific guidelines outlined here pertain to *timing*, *format*, *case study selection*, and *guidelines for students*.

Timing

It is important that students have already received a sufficient background in the theory and practice of structure solution and refinement prior to case study discussion. In our course, lecture and laboratory are conducted simultaneously, and by approximately two-thirds completion of the semester-long course, students will have learned topics such as careful space group selection, twinning, and disorder refinement. Through laboratory exercises, students will have addressed introductory examples of each type of problematic refinement, and will be familiar with common small molecule crystallography software such as SHELX,[21] PLATON,[22] and OLEX.[23] During the final third of the semester, students refine increasingly difficult structures that feature combinations of the problems described above. Case study discussions are the most fruitful after students are well versed in small molecule crystallography software and have experience refining structures. Students are experienced enough to work mostly independently, and the case studies provide guiding examples for the types of problematic refinement that occur in real-life research situations.

Format

Students are divided into small groups of three or four. Usually, each small group is assigned a different case; however, for cases that involve an ambiguous refinement (rather than simply an incorrect structure determination), two groups may be assigned to the same case and debate each side of the "argument" through careful reanalysis of the data. Each group is given approximately 2 weeks to complete the assignment, which consists of a short (~15−25 min) oral presentation, followed by in-class discussion, as well as a written report summarizing both the oral presentation and resulting in-class discussions. Students are taught how to obtain published crystallographic information (online supporting information, request from CSD, etc.), examine their quality (cif validation, reconstruction of ellipsoid plots, etc.), and search for additional related literature. They are then provided with the original literature report and asked to examine the quality of the crystallography data, and given several guiding questions that they answer in the oral report. While students are preparing case discussions, the teaching staff serves as an available resource, but students lead the problem-solving task. The course teaching staff checks on each group's progress regularly, and provides additional guidance if necessary. As much as possible, students should work independently to arrive at their own conclusions and possible solutions to any perceived problems. After each group's oral presentation, a discussion is opened with the entire class to examine what can be learned from the case study, including additional points that may have been omitted from the oral presentation. The subsequent written report then serves to summarize both the oral presentation and the in-class discussion.

Case Study Selection

Case study selection can focus on recent literature examples in the field that feature ambiguous and/or problematic small-molecule structure refinement. Cases where a debate already exists in the literature are particularly useful, as they provide students with ample information to consider multiple possible solutions. For example, the "crystalline sponge" method for small-molecule structure determination generated widespread interest and discussion in the chemical community,[24,25] and made for an engaging case study discussion (Figure 1a). One group assessed the merits of the method, while another group identified shortcomings and possible improvements. After in-class discussion of the case, students concluded that a major strength of the crystalline sponge method is that it can be used to determine the absolute configuration for compounds, such as liquids, that cannot easily (or ever) be crystallized under

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practical conditions. However, through a close analysis of the supporting crystallographic information, they realized that the authors may have overused constraints and restraints for geometric and anisotropic displacement parameters, as well as employed void electron-density squeezing programs. In addition, students identified that a stereochemical assignment of miyakosyne A based on the given crystallographic data was likely unreliable. Indeed, several months after the class ended, a corrigendum was published acknowledging that the data did not support the initial stereochemical assignment[26] and a variety of subsequent papers have been published to address the limitations of the initial method.[27−29]

The case study method can also be used to introduce advanced crystallography techniques that may relate to student's research interests. If students are already active in a research group, the instructor can consult directly with the students or their research advisors to gather ideas for potential case studies. For example, some students in our course showed great interest in learning about photocrystallography because of projects in their research group that used this technique.[30] A case was therefore chosen for discussion regarding X-ray crystallographic monitoring of intermediates during a photochemical reaction of 4,6-dimethyl-α-pyrone (Figure 1b).[31] While the authors claimed that 1,3-dimethylcyclobutadiene and CO_2 were generated and crystallographically characterized, subsequent re-evaluation suggested that the data might be better interpreted as a Dewar β-lactone structure.[32−34]

Additional literature case studies that have been successful include the following: a case for the refinement of the aquohydroxyiron(III) derivative of tetraphenylporphine complex, one of the great classic crystallographic errors regarding misassignment of one disordered Cl atom as two O atoms;[35] a literature debate over correct space group assignment;[36,37] and a literature discussion over assigning a surprising chemical transformation based on X-ray crystallography evidence.[38,39] A set of example prompts are provided that may be given to students for each case study described here (Supporting Information). It is recommended that instructors use more than one case study per course, because additional practice will allow students to improve their new skills and build their confidence with using and interpreting crystallography data in real-life research situations.

Such case studies can also fit into an introduction to crystallography that has been integrated into a more general undergraduate course such as advanced physical, inorganic, or organic chemistry, which may be useful for schools that do not offer a dedicated course on crystallography. As others have noted in the literature, such a brief introduction can be feasible and beneficial for an undergraduate lecture or laboratory course.[40−43] In this situation, case study selection should avoid problems that students may not be equipped to evaluate, such as crystallographic data quality or space group selection. Instead, case studies may focus on the question of whether structures make "chemical sense," and students can evaluate crystallographically determined parameters such as bond lengths and angles. For example, the case examining the photochemical reaction of 4,6-dimethyl-α-pyrone (Figure 1b) would be fully appropriate for discussion in an upper-level undergraduate organic chemistry course, without the need for detailed examination of the crystallographic data files.

Guidelines for Students

Aside from the guiding questions, some guidelines for students are provided to keep the case study discussions on task. A danger that arises when students critically evaluate literature data is that it can be appealing to simply criticize, which is not the point of the exercise. The aim is for students to develop a better understanding of the *advantages and limits* of small-molecule crystallography, which is why students typically present both sides of an ambiguous structure determination and suggest additional experiments (using other common spectroscopic techniques in chemistry such as NMR, GC−MS, XRF, etc.) that could overcome limitations of crystallographic data. Additionally, students are explicitly instructed to focus only on the crystallography aspect of the literature case studies and not to give their opinions on the research in general, etc. These simple guidelines lead to spirited and productive class discussions.

■ IMPACT ON A CRYSTALLOGRAPHY CLASS

The key goal in introducing case study discussions in a crystallography class was to emphasize to students that, during problematic small-molecule structure refinement, X-ray crystallography alone may *not* provide an unequivocal result. In many cases, it is important to collect other information about the chemical structure of the analyzed molecule beforehand, because "What you see (from the Fourier difference map) + What you believe (the geometry of your structure) = What you get."[15] If the model that you believe is wrong, the conclusion that you make from the crystallographic data may also be wrong, such as the miyakosyne A case in crystalline sponge method.[26] Students develop a more mature understanding of the strengths and limitations of crystallography as an experimental science through a hands-on analysis of crystallographic data in contemporary chemistry research.

An additional outcome of case study discussion, which may or may not be explored at the instructor's discretion, is the analysis of "bigger" questions in science pertaining to the reliability of data, the review process, and scientific knowledge in general. The idea that ambiguous or incorrect data has been published may be surprising to some younger students, who are used to simply learning "facts" in science courses. If deemed appropriate by the instructor, case study discussions such as the ones described here can be a platform for a broader discussion of Nature of Science themes and the pitfalls of *experimental* science and data analysis in general.[44]

Finally, an aim of using case studies is to give students the ability to transfer what they learn in class to their own research projects. For example, students in our Spring 2013 class generated enough interest in the crystal sponge method such that Harvard research groups actively pursued more fundamental studies aimed at developing this method into a practical tool.[28,29] The use of contemporary case studies also puts crystallography in the context of real research and shows students how crystallography can be used appropriately along with other experimental techniques to address research problems. The more that students are exposed to real-world problem-solving in the classroom, the greater the probability that they will be able to apply what they have learned to their own research. Compared with a traditional lecture format, incorporation of case study discussion in a crystallography class not only promotes increased student participation and interest

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the course material, but also increases students' ability to use crystallography as a tool in their own research.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available on the ACS Publications website at DOI: 10.1021/acs.jchemed.5b00629.

Example case studies and prompts for students (PDF, DOC)

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Notes

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