Crystallographic Structure Determination: An Experiment for Organic Analysis and Other Nontraditional Venues

Allen D. Hunter

Abstract

Single crystal diffraction analysis is a technique being increasingly utilized by non-specialists. To give students an introductory experience in this method, a one to two hour lecture and a three hour lab are described for use in courses such as organic analysis, biophysical chemistry, and instrumental methods. This class emphasizes the practical aspects of diffraction analysis, especially how routine structures are solved, how the results are prepared for publication as graphics and tables, and how reliable these results are. The student employ x-ray diffraction analysis software (i.e. SHELXTL) to solve the structures of compounds from supplied crystallographic data sets. Three data sets appropriate for this experiment are provided (i.e. for $PhCH_2$-NH-$CHPh$-$P(O)(OH)(OEt)$, (^{6}-1,4-$C_6H_4(NH_2)(NMe_2)$)$Cr(CO)_3$, and $Pd(Ph_2PCH_2CH_2PPh_2)(S_2C_2(CN)_2)$) as is a link to a Youngstown State University Structure Center WEB page (i.e. http://xray1.wb.ysu.edu/~scenter/structure.html) where additional properly formatted crystallographic data files may be downloaded.

Keywords

laboratory instruction, instrumental methods, crystallography, crystall growth, laboratory computing, interfacing

Supplementary Materials

No supplementary materials available

Full Text

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Allen D. Hunter

Department of Chemistry, Youngstown State University, Youngstown, OH 44555-3663

Background and Rationale

X-ray crystallography is first introduced to undergraduates in freshmen chemistry, where they are taught the principles of Bragg's law of diffraction and the solid-state structures of simple inorganic solids. It is generally discussed again in upper-level physical and inorganic chemistry courses and in instrumental methods courses where the principles of single crystal diffraction analysis (*1*) and powder methods (*2*) are covered in more detail. Indeed, at least a dozen papers on X-ray crystallography have appeared in this *Journal* already this decade (*1–12*). In departments with the necessary equipment, one or more laboratory experiments are often carried out in which the students use *powder* X-ray diffraction data to identify unit cell symmetry and dimensions or to identify unknown solids. The results of X-ray diffraction analyses are also used extensively as the reported source of molecular structure information in upper-level inorganic, organic, and biochemistry courses (*3*). However, laboratory experiments on *single-crystal* diffraction methods are much less commonly taught to undergraduates (*1*). Where they are taught, they are typically part of an entire quarter- or semester-long X-ray crystallography course that serves both seniors and graduate students.

Until relatively recently, single-crystal X-ray diffraction analysis was an instrumental method carried out almost entirely by specialists. Recent advances in crystallographic software and inexpensive high-speed personal computers now make it possible for nonspecialists to have a much greater involvement in the solution of crystal structures of small molecules. In addition, diffractometers are now frequently equipped with high-intensity X-ray sources (e.g., from rotating anodes or focusing optics) and area detectors (e.g., imaging plate and charge coupled device, CCD, detectors). These hardware innovations produce very high raw data collection rates, often approaching or even surpassing one complete data set a day. Thus, the small staffs typical of departmental crystallography facilities often have the ability to collect far more data than they have the time to analyze. This has resulted in growing pressure (and opportunity) to have synthetic chemists participate more fully in the crystallographic work on their structures. Their contributions typically range from preparing the graphics and crystallographic tables for their papers to solving routine structures with the aid of the staff crystallographer. This trend has been accelerated by the simple economic fact that, if one can get a single crystal, it is often both faster and less expensive to determine a structure from crystallographic data than by using conventional "sporting methods" (elemental analysis, IR,

UV–vis spectroscopy, one- and two-dimensional multinuclear NMR, and low- and high-resolution mass spectroscopy).

Given these changes, it is no surprise that there is increasing interest in teaching nonspecialists, even at the undergraduate level, to interpret X-ray diffraction results, know their limitations, and be involved in the final stages of data refinement and the preparation of results for publication. Organic chemists and biochemists are now coming to rely on crystallographic data almost as much as inorganic chemists traditionally have (*1*). A lab project involving small-molecule diffraction analysis that would be suitable for use in upper-level organic, inorganic, and biochemistry lab courses was therefore developed.
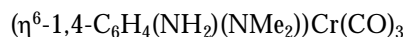
Laboratory Project

This lab project has been taught to a variety of students including chemistry majors taking our organic analysis lab course, biochemists taking our biophysical lab course, and high school chemistry teachers taking a summer professional development lab course on modern spectroscopic and structural methods. These students had all previously seen the principles of X-ray diffraction in their general chemistry classes and usually had some additional coverage of powder diffraction in various physical, inorganic, and instruments classes. To supplement this background, the students were given between one and two hours of lecture on single-crystal diffraction analysis before the start of the lab. This material included a quick review of the principles of diffraction, the relationship between raw X-ray data and the final structural results, the steps in an X-ray diffraction analysis, and the strengths and limitations of X-ray derived structural data.

The three-hour scheduled lab time begins with a 15-minute tour of our single-crystal diffraction facility with quick explanations and demonstrations of how the various parts of diffractometers work. The students are then introduced to the X-ray structure solution package (we use SHELXTL from Siemens Analytical, but other packages are available [*3*]). This is done by demonstrating a typical diffraction analysis on an example structure (this takes about 1 hour). The students then work in pairs or small groups to solve data sets on their own.
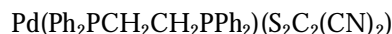
The data sets used typically include examples of organometallic, coordination, and organic compounds. They are chosen from structures determined in our department that are particularly well behaved crystallographically (either direct methods or Patterson methods work reliably with their default settings, there is no twinning or disorder in the structure, etc.). Three compounds whose data we commonly use are

$$PhCH_2–NH–CHPh–P(O)(OH)(OEt)$$

$(\eta^6\text{-}1,4\text{-}C_6H_4(NH_2)(NMe_2))Cr(CO)_3$

and

$Pd(Ph_2PCH_2CH_2PPh_2)(S_2C_2(CN)_2)$

(see Table 1). Each data set is composed of the two files needed to begin the structure solution. One file contains the experimental structure factors and the other contains the information on the molecular identity, presumed molecular formula, space group, any assigned atoms' coordinates, occupancies, displacement parameters, etc.[1] These data sets, along with those for other compounds appropriate for this exercise, may be downloaded from the Youngstown State University Structure Center Web site (*http://xray1.wb.ysu.edu/~adhunter/ YSUSC/xraydpst/index.html*). Several examples are also available for download from the electronic version of this manuscript in *JCE Online*.

Students use these input files to generate a direct methods or Patterson method trial solution, using the XS program in SHELXTL. They then use molecular graphics (the XP program in SHELXTL) to evaluate this solution. If it looks reasonable, they then assign the first few peaks on the electron density map to specific atoms using their chemical intuition and by considering peak intensities and interpeak distances and geometry. If they are in any doubt about the atomic identity of an electron density peak, they are encouraged to delete it ("if in doubt, chuck it out"). They often find this difficult to do and otherwise tend to "over-assign" peaks at the early stages of refinement. It is explained that if the questionable electron density peak is real, it will return in the next refinement cycle. However, if it isn't real, they may not be able to refine their data to a satisfactory solution. They then use a least squares program (e.g., the XL program in SHELXTL) to refine their assignments. The assignment and refinement stages (using XP and XL, respectively) are repeated in several sequential stages: (i) the non-hydrogen atoms in the structure are identified from electron density maps and assigned, and their positions are refined with isotropic displacement parameters;[2] (ii) the non-hydrogen atoms are converted to anisotropic displacement parameters and these are refined; and (iii) the hydrogen atoms are found in the electron density maps and refined with isotropic displacement parameters.[3] This process is continued until the solution has converged sufficiently that the atomic positions and displacement parameters are no longer shifting in each refinement cycle.

On completion of the structure determination, students generate a variety of views of the resulting molecule and print tables of bond lengths and angles using the XP and XCIF programs in SHELXTL, respectively. This process is generally complete by the end of the laboratory period. In most cases, students voluntarily return to complete one or more additional structures.

Merits of This Exercise

One might reasonably ask what benefit the students get from such an abbreviated exercise, given that while completing the project they do not fully understand the theory behind much of what they are doing. Substantial benefits I've seen include (i) students develop a real interest in crystallography sufficient for many of them to subsequently enroll in a full quarter-long course on solid-state diffraction methods, (ii) they develop a qualitative appreciation for the source of much

Table 1. Example X-ray Crystallographic Data Files

Name of Compound in Exercise	Proposed Chemical Formula and Chemical Structure	Data Files from JCE Online
Fun1	$PhCH_2\text{–}NH\text{–}CHPh\text{–}P(O)(OH)(OEt)$	Fun1.ins Fun1.hkl
Fun2	$(\eta^6\text{-}1,4\text{-}C_6H_4(NH_2)(NMe_2))Cr(CO)_3$	Fun2.ins Fun2.hkl
Fun3	$Pd(Ph_2PCH_2CH_2PPh_2)(S_2C_2(CN)_2)$	Fun3.ins Fun3.hkl

of our detailed structural knowledge,[4] (iii) they learn that compounds don't always have the structure that spectroscopic data imply,[5] and (iv) students love this experiment, it is fun!

This experiment is more popular with students than any other I have ever used and I'm convinced that it could be very widely adopted, since it only requires one or more PCs, the appropriate structure analysis package, and some data sets that are readily available from the *JCE Online* version of this paper, from the Youngstown State University Structure Center Web page at *http://xray1.wb.ysu.edu/~adhunter/ YSUSC/xraydpst/index.html*, or from the Web sites of many crystallographers.

Notes

1. For this lab exercise, the students don't determine their own space groups. In my experience, this takes at least six hours of lecture and lab time and, when not done as part of a complete crystallography course, leads to more confusion than enlightenment.

2. This typically takes two or three XP/XL cycles.

3. This typically takes between two and six XP/XL cycles.

4. This really drives home the fact that these are *experimental* values and are independent of the bonding theory used to explain them. The students all know this in theory, but it still often takes them as a surprise in practice.

5. In one of the structures a hydrogen atom is not attached to the expected heteroatom—it has undergone an internal acid–base reaction.

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