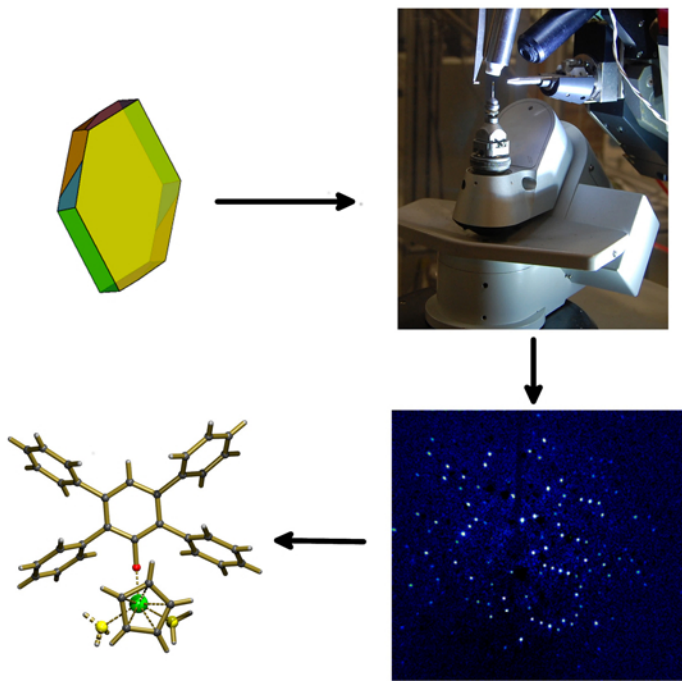


Crystallography for Chemists



Phillip E. Fanwick

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By

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FOREWORD

Crystallographic methods have been very important in the development of modern chemistry. Unlike NMR, crystallographic education in the chemistry curriculum remains at best minimal and frequently non-existent. There are historical and practical reasons for this failure. However, this has led to the situation where most chemists cannot really interpret crystallographic data. This extends from graduate students to journal editors. The goal of this book is to provide assistance and insight into crystallography in a language that chemists can understand. It should be suitable for advanced undergraduate and beginning graduate students.

There have been several motivations for producing this book. The first was my experience in organizing a session on crystallographic education at the American Chemical Society's Biennial Conference on Chemical Education in 2006. Both crystallographers and chemists warned me that there is no interest in this topic and to expect few to attend. It surprised me when I entered the room for the session to see it fairly full. I gave my talk on the importance of crystallographic education and it was received enthusiastically. The first question I was asked is what book I would recommend for such a course. I listed the standard texts but was told that they were too advanced. Faculty from small colleges pointed out that they had no experience with crystallography and found it difficult to understand the topic with enough depth to teach it. They needed a book that would be the main teaching tool and not just a reference.

A second motivation was the graduate course on applied crystallography I taught for many years at Purdue. This provided a platform where I could try different approaches to instruction in crystallography. I quickly learned that most of the students enrolled were synthetic chemists who only wanted to use crystallography as an analytical method. They did not have much interest in the theory of crystallography or topics they could not apply to their research. I always taught this course in a computer lab so the students could run programs instead of studying their input and output. One unintended consequence of providing students with computers was that I received an instant evaluation on my teaching abilities and their interest in the topics covered. If I walked around the lecture room and found most of

the students were checking their email, the news, or sports, I knew this lecture was not of interest. Much of what I learned from this experience is in this book.

Before stating what this book is, let me stress what it is not. This is not, nor was it meant to be a comprehensive text on crystallography. There are already many excellent books at various levels and there is no reason to reinvent the wheel. Nor is this book a reference book used to answer all questions concerning crystallography. Some will complain it is not suitable for training professional crystallographers. However, that is not the intent.

There have been several guiding philosophies in organizing this book. First, was to make it as non-mathematical as possible. Equations are provided when they can provide insight. Statements are presented as facts rather than proved. This is in keeping with what I have observed in teaching. The concepts of typical programs are explained. There is no discussion of the algorithms, formulas, and approaches. Many programs will be considered black boxes where the input and output is more important than what is happening in the program.

The discussion of crystallographic programs presents a problem in writing a book such as this. It is a conscious decision to not spend much time on software. There are several justifications for this decision. First, there are many programs available for running diffractometers, processing data, and solving and refining structures. It is not the place of this book to endorse any of them. Besides, today most software has excellent manuals typically on the internet and in the case of SHELXL there is even a text on its use. The one exception to the above involves SHELXL. This program is the most widely used crystallographic program. Therefore, the appropriate commands are placed in square brackets during discussions of refinement. However, only the name of the command is given and its application and usage will require research elsewhere. With advances in computers and artificial intelligence, software is changing rapidly. No book can keep up with the changes. Undoubtedly, new software will become available which will pass into common usage.

Many topics are introduced and some readers will desire more detail. It is hoped that the references provided will allow for further exploration. Also, as much as possible, terminology and concepts are not used until introduced. This creates some unusual wording in the early chapters.

Chapters 1 to 4 are an introduction that provides information on understanding crystallographic data and results. They should be useful to all chemists even

if they do not perform crystallographic experiments. Chapter 5 introduces the concepts of real and reciprocal space. One theme of this book is the nature of these two spaces which are related by Fourier transforms. This is essential to crystallography. Chapters 6-8 deal with symmetry. Basic symmetry operations are quickly introduced and previous knowledge of the concepts of symmetry will be useful. Chapters 9 to 12 deal with the process and equipment used to go from a crystal to a crystal structure. They will be most useful to those who will actually collect crystallographic data and refine structures. Chapter 13 deals with the determination of absolute structure and absolute configuration and is important to those working with enantiomeric compounds. Chapter 14 concerns crystals that do not have perfectly repeating motifs. Lastly, Chapter 15 is about diffraction methods beyond X-rays and single crystals.

There are several who have provided graphics that have been used in this book. Larry Falvello and Esteban Urriolabeitia of the University of Zaragoza provided the NMR spectra used. I am grateful to Margret Kastner for the use of drawings found on her Crystallographic Courseware web page. It is a wonderful resource for those learning crystallography. I also thank Kevin Cowtain of York University for allowing me to reproduce figures from his web page <http://www.y.sbl.york.ac.uk/~cowtan/fourier/fourier.html>. Lastly I thank the International Union of Crystallography for permission to print pages from the **International Tables of Crystallography, Volume A**.

I never had any formal education in crystallography (and some say it shows). There are a great many people who have taught me much over the years. First, is my friend Larry Falvello who has always answered my ignorant questions with wonderful and frequently humorous explanations. He has helped me to gain insight into the crystallographic experiment. I also thank David Watkin for his help over the years. David has written many articles which clearly explain the workings of crystallography beyond the scope of this book. I also thank Ton Spek for many interesting conversations over the years from which I have gleaned much. I am also most grateful to Mary Hoekstra who proofread this manuscript. Lastly, I thank my wife and soul mate Karen, for her encouragement, patience, and help in assembling this text. I do not think I would have ever taken on this project without her being by my side.

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CHAPTER 1

SINGLE CRYSTAL X-RAY CRYSTALLOGRAPHY AS A METHOD OF CHEMICAL ANALYSIS

During the last fifty years, X-ray crystallography has been an important chemical analytical tool capable of routinely solving problems that would be very difficult by other methods. In this chapter, an example of such an analysis will be discussed as well as the strengths and weaknesses of the technique.

For all but the last chapter, it will be assumed that a high quality crystal was the sample and X-rays were the radiation for the diffraction experiments.

1.1 A Case Study

In 1958 Kotel'nikova and Tronev¹ reported the preparation of a compound of the formula $(C_5H_5NH)^+HReCl_4$. The addition of the hydrogen ion to the chemical formula was required because the oxidation state of the rhenium was determined to be +2. Later a single crystal structure of this compound was published and the result is shown in Figure 1.1.² The major portion of the publication deals with the difficulties in obtaining structural results in 1963. However, there are comments on several chemical aspects that are worthy of discussion. The most noteworthy comments are:

“It should be noted that the Re-Re distance = 2.22 Å is less than the Re-Re distance in the metal.”

“The decrease in the Re-Re distance in this structure, compared with the Re-Re distance in the metal, indicates that the valence electrons of rhenium also take part in the formation of the Re-Re bond. This may explain the diamagnetism of this compound.”



Figure 1.1 $\text{Re}_2\text{Cl}_8^{2-}$

Possible positions for the H^+ ion are provided. However, since there is no solvent or other base that could be protonated, the existence of this ion in a crystal would be unusual. Even with a crystal structure and other supporting chemical analyses, the bonding and even the chemical formula of the $\text{Re}_2\text{Cl}_8^{2-}$ ion failed to be established.

The reported results interested Professor F. Albert Cotton who quickly published three papers dealing with this ion. The first dealt with the chemical formula.³ Electrochemical analysis revealed that the rhenium was in the +3 oxidation state and no hydrogen cation was required to balance the charge. This made the formula from the crystal structure consistent with the chemistry. In the second paper, the structure of the potassium salt of $\text{Re}_2\text{Cl}_8^{2-}$ was determined.⁴ This was both a check on the previously reported structure and provided an improved structure. This structure confirmed the previously reported details. The Re-Re distance was 2.241Å while the Cl-Cl distance across the Re-Re bond averaged to 3.32Å which is nearly twice the chlorine van der Waals distance.

The third paper reported on the bonding in the octachlorodirhenate ion.⁵ Unusual features of this ion included the very short rhenium-rhenium distance and the eclipsed configuration of the chlorine atoms when looking down the Re-Re bond. The chlorine atoms are essentially at the minimal non-bonding distance from each other and this results in a Re-Re-Cl angle of 103.7°. Since there are 8 electrons available from the two rhenium atoms that are not involved in the Re-Cl bonding, it was suggested that the bond order between the rhenium atoms was 4. Such a bond would be composed of a σ bond, two π bonds, and a δ bond. For

maximum overlap of the δ bond the chlorine atoms would need to be in an eclipsed configuration as observed. The important point is that the stability provided by the δ bond was greater than the repulsive forces of the chlorine atoms. Hence, the shape of the molecule and the geometrical parameters determined by the structure were used to elucidate the metal-metal bonding.

This is hardly a unique example of the use of crystallography to solve chemical mysteries. There may have been other methods that would have eventually led to the geometry, formula, and bonding in this novel dimetallic ion. However, the information would be more indirect, require much more interpretation, and take more time. The results would have had greater uncertainty and not contained as much information. Crystallography provided a definitive structure and accurate geometrical parameters in a short time. It is for these reasons that crystallography has become an essential tool for chemists and changed the nature of chemical analysis.

1.2 Crystallography and Chemical Analysis

1.2.1 Qualitative and Quantitative Analysis

Qualitative and quantitative analyses are the determinations of what elements are present in a compound and the relative ratios of each element. It appears that crystallography would be perfect for providing this information, but that is not totally correct. From Figure 1.1 it appears that the formula can easily be determined from a crystal structure, since all the atoms are assigned an element. However, these assignments are made by the researcher determining the crystal structure; they are not uniquely provided by the crystallography.

This ambiguity results from the nature of the X-ray crystallographic experiment. The graphical results such as Figure 1.1 falsely imply that crystallography is like a giant microscope able to observe the atoms. Even if that were true, it is not clear how the atomic number could be directly observed. However, the actual result of the X-ray crystallographic experiment is the calculated value of the electron density at any location within the crystal. Throughout most of the crystal the electron density is at or near zero. It is only in some small locations where the electron density is significant. It is assumed this is where the atoms are located.

There is a problem however. There is no simple direct relationship between the electron density and the atomic number of an element in a crystal. There are several reasons for this, most of which have to do with the movement of the atoms in a crystal. All atoms are vibrating even at 0 K. The greater the movement of an atom, the more the electron density will be decreased because of the increasing volume caused by the atomic displacement. There are also problems such as multiple atoms at a site or disorder in the structure which will affect the electron density.

A common example of unusually low electron density is observed for the trifluoromethyl group. This group in some crystals rotates about the C-C bond. If the displacements are small, this will simply lower the electron density and the fluorine atoms will appear to have less electron density than even the carbon atom neighboring them. It is also possible that there will be two sets of positions where the fluorine atoms are located. The electron density observed in the structural analysis will display the density averaged over the entire crystal. In this case, six half fluorine atoms will be observed around the central carbon and the observed electron density will be half of what would be expected. It is also possible that there is nearly free rotation around the C-C bond and the fluorine atoms will be smeared out into a ring of density. It is possible (though not necessarily likely) that the electron density will be so low as to not be observed above the noise. In this case, it will be difficult to assign locations for the fluorine atoms.

How are the element types assigned to the calculated electron density? In most cases there is external information about the sample synthesis, and other analyses are available. This information can be used to guide both a qualitative and quantitative crystallographic analyses. There is always the possibility the crystal contains unexpected fragments such as molecules of solvation. These can usually be assigned, given more information. Therefore, a correct crystal structure contains the chemical formula of the contents of the crystal and not just the fragment that is of interest. It must be emphasized that elemental assignments add a bias to the experiment, not only can that produce an incorrect result but sometimes spectacularly incorrect chemistry as will be discussed later.

For unknown samples the problem is more difficult. The organic part is usually the easiest to assign. First, most elements in an organic fragment have a consistent number of bonds about them and a well-established geometry. The bond order can be determined by the bond length. Besides,

the difference in an incorrect electron density assignment is significant. For example, if a carbon atom is assigned as a nitrogen atom the electron count is too great by 17% while as an oxygen the overage is 33%. This difference makes a significance in the quality of the structure and can readily be observed in a drawing of the molecule that includes atomic displacement parameters (see Chapter 4).

For inorganic compounds or fragments, elemental assignment is much more difficult. First, heavier elements have variable coordination numbers. Their bond distances are not as consistent as main group elements. If the rhenium atom in the structure discussed in Section 1 were replaced by next heaviest element osmium, the electron difference would only be 1.3%. Lastly, substitution of heavier elements does not significantly affect the quality of the structure. Structures containing second or third row transition metals can be "titrated" by trying different elements at the metal location. Invariably, the best fit does not contain the correct element. In the end, if there is any question about the composition of a crystal, further analytical means must be employed to determine what elements are present. For the rest of this text, the assumption is that the elements have been correctly identified and the atoms in the structure have been correctly assigned, except as noted.

1.2.2 Structural Isomerization

The greatest strength of crystallography is to provide unequivocal evidence of the arrangement of the atoms in a molecule. Structural isomers are molecules with the same chemical formula but different connectivities, while stereoisomers have the same connectivity but differ in their three dimensional orientations. Obviously, the drawing of a molecule from a crystal structure analysis provides proof of the isomer.

Crystallography is almost too good at determining isomers. There are standards that must be met if a structure is to be considered a quality structure. This includes standards for quality and quantity of data collected. Also, the calculations required for a finished structure and the quality of the final results are equally specified. The problem is that frequently the isomer can be determined satisfactorily from even the most rudimentary data and calculations. This provides frustration because the structural results may not be publishable, yet the nature of the isomer has been determined. There is a consensus that the quality of the entire structure must be considered and not just some area of interest. Since a

crystal structure is considered indisputable evidence of the arrangement of atoms in the crystal, low quality structures cannot provide this certainty, even if they appear to provide the desired information. It is essential that the proper amount of high quality data be collected and that all calculations be completed before any conclusions can be drawn from a structure. This at times appears to be overkill, but it has proved essential to eliminating incorrect structures.

1.2.3 Geometric Parameters

A quality crystal structure provides accurate geometrical parameters for the contents of the crystal. These include bond distances, bond angles, torsional angles (the dihedral angle between two sets of planes formed by three atoms in which two planes contain two atoms in common), planarity of a group of atoms, and other special parameters which define the shape of unsaturated rings, sugars, *etc.* These parameters may be calculated for molecules or molecule like ions or non-bonded atoms. Likewise, parameters between fragments in a crystal can be determined. This includes intermolecular hydrogen-bonds and π - π interactions.

As shown in the example at the beginning of the chapter, knowledge of intramolecular distances can be used to determine the strength of a bond and its bond order. This is important for the elucidation of functional groups in the molecule. Unusual bonds such as metal-metal bond orders can be assigned. The effect of interactions such as hydrogen bonds on carbon-oxygen and carbon-nitrogen bonds can be studied. While similar results can be obtained from vibrational spectroscopy or NMR, the results provided by a crystal structure are much easier to interpret.

1.2.4 Optical Isomerization

One important use of crystallography is to determine the absolute configuration of optically active molecules. This is important in many cases, such a pharmaceutical compounds. Crystallography is essentially the only technique that can provide this information.

There are certain requirements for this determination to be made. First, the crystal must be enantiomorphically pure. Frequently, crystals grown from non-pure materials will be racemic and therefore no determination can be made. Second, a high quality data set is required for this experiment to succeed. Lastly, the choice of X-ray wavelengths must be considered so

that the calculations will provide a definitive result. All of this will be discussed in Chapter 13.

1.2.5 Other Uses

In no way does the above discussion reflect the total extent of what can be done using crystallography. There are experiments for studying the surface of a crystal. This information can be important to the creation of electronic devices. Changes in the crystal, such as reactions, can be studied using time-resolved crystallography. Experiments have been performed where the geometry of an electronic excited state has been determined. These experiments however are usually performed at national laboratories where high intensity synchrotron X-ray sources are available that allow data collection to be completed in seconds. In the end, crystallography is an extremely versatile technique able to provide analyses for a wide variety of chemical and solid state problems.

The above is based on crystal structures from single crystals. However, one of the most important analytical crystallographic tools is powder crystallography. If crystalline materials are ground up into a fine powder, then the diffraction pattern of this powder can be obtained. The pattern can be matched to previously determined patterns to ensure the material is the correct crystalline phase. Unexpected peaks can be used to establish the presence of impurities. If the powder pattern of the impurity is known, then its concentration can be determined. This type of analysis is very important in pharmaceutical manufacturing where, in general, not only the identity and purity of a compound is required, but also the precise crystalline form. Differences in the crystal structure can change the stability of the pharmaceutical, as well as its efficiency as a drug.

1.3 Limitations of crystallography

There are several important limitations to the crystallographic analysis that must be kept in mind. It appears obvious, but a crystallographic result only provides information about the crystal sample studied. Clearly, if a crystal of a minor product is used, it will not provide any data about the major product of a chemical reaction. Also, some compounds react during crystallization and the crystal may be completely different from the original product.

The second limitation is that the structure only provides information about the packing and geometry of the components in the solid state. The formation of a crystal introduces strong intermolecular forces that can distort a molecule or in some cases even alter the isomer. It can be expected that geometrical information from crystallography may not agree with data from studies done in the gas phase or in solution. In many cases the agreement is excellent.

CHAPTER 2

SCATTERING AND DIFFRACTION— WHAT IS GOING ON WHEN RADIATION INTERACTS WITH A CRYSTAL

In order to understand what is happening in the diffraction experiment, it is important to build a model for the interaction of the radiation and the sample being studied. In this chapter the concept of scattering of radiation will be introduced. The use of constructive interference and diffraction to produce the observed data will be explained. The importance of translation will be emphasized. Finally, the concept of the primitive unit cell will be introduced. The chapter will be presented for X-ray radiation, though much of what is presented can be extended to other forms of radiation.

2.1 Scattering of Radiation

The theory of scattering of radiation by a free electron was first reported by J. J. Thompson in 1906.⁶ This theory was based on classical mechanics and assumed the scattering was elastic *i.e.* the wavelength of the scattered wave was the same as the exciting radiation. Also, relativistic effects were not included. The discussion here will be further simplified in that the polarization of the scattered wave will be ignored. This simplified approach gives a good starting place as to the interaction of the X-ray radiation with the electron and provides a model that can be built upon to understand crystallography.

When the free electron encounters the electromagnetic radiation, it moves opposite to the amplitude of the applied field because of the repulsive nature of the interaction. Since the electron, a charged particle, is now moving, it should emit radiation. The emitted radiation will have the same wavelength as the exciting source but be 180° out of phase. Since this is a new wave it will be emitted from the free electron in all directions. This new radiation is called scattered radiation and it occurs at all exciting wavelengths.

It is also interesting to look at the intensity of the scattered radiation. The intensity will be very much weaker than that of the exciting radiation. A few centimeters from the free electron, the ratio of the intensity of the total scattered radiation to that of the incident radiation is on the order of 10^{-24} . This value is only slightly less than Avogadro's number. The electrons in a chemical sample will produce considerable scattered intensity. One last point is that if the primary beam is completely unpolarized, then the intensity will fall off by the factor $(1+\cos^2\theta)/2$ where θ is the angle between the incoming beam and the scattered beam.

Obviously, scattering by an atom is more complex. First, the electrons in an atom can hardly be considered free. There are attractive forces with the nucleus and repulsive interactions between them. Classical physics is not a valid description for these electrons. However, the model developed for the free electron can be applied to the atom. The biggest difference is in the calculation of the intensity of the scattering which is much more complicated. However, atoms with more total electrons will scatter more strongly.

2.2 Diffraction in One-dimension

At first, the fact that atoms will weakly scatter X-ray radiation appears to be of little use in determining a crystal structure. If an X-ray beam is directed at any matter regardless of its state, there will be randomly scattered radiation from the sample. The greater the atomic number of the atoms in the sample, the more intense this scattering will be. Waves can interact by constructive or destructive interference as shown in Figure 2.1. Most of the scattering away from the incident beam will be eliminated by destructive interference,

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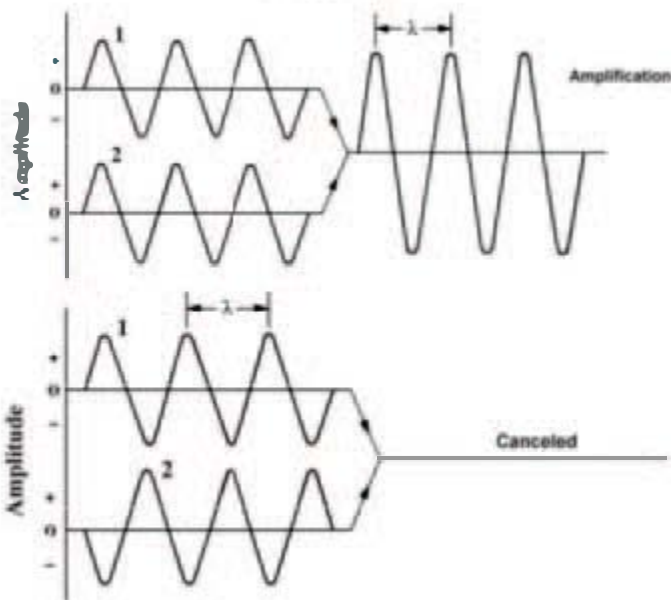


Figure 2.1 Interactions between waves

However, more complicated effects will occur if the atoms or molecules are lined up in a regular repeating pattern. The result of such an interaction is shown in Figure 2.2. The repeat distance between the arrangement (in this case the atoms) will be the vector a . If the length of a is on the order of the wavelength emitted, then interference effects will be observed. The repeat distance in a crystal is typically measured in Angstroms (\AA) which is 10^{-10} meters. While the Angstrom is not an SI unit, it is very convenient to use in crystallography. Typical bond distances are on the order of a few Angstroms and repeat distances in crystals typically range from 3 to 100 \AA . Since the wavelength of commonly used X-rays is from 0.5-2 \AA , they will produce interference interactions when multiple waves interact. Two waves can interact either constructively or destructively as shown in Figure 2.1. Constructive interference will occur whenever two waves are in-phase. The result will be a new wave.

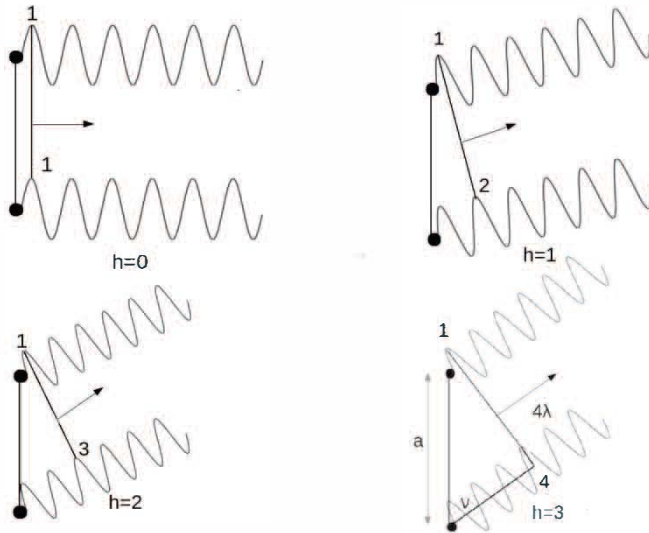


Figure 2.2 Constructive Interference

The case where the incident radiation is perpendicular to the line of the atoms is first studied. The scattered radiation will come out in all directions and will interfere with other waves scattered by other atoms. However, except for the case where the waves are in phase, they will interact destructively and no intensity will be observed. Obviously, scattered waves in the direction of the primary beam will be in phase. The intensity of such scattered X-rays will be very weak compared to the primary beam and cannot be observed. However, as Figure 2.2 illustrates, at certain angles ν the scattered beam from one atom will differ by exactly some integer multiple of wavelengths, and constructive interference will take place. The number of wavelengths difference will be assigned the symbol h which must be integral. If $h=0$ then the scattered beam will be along the primary beam. If $h=1$ then there will be a difference of one wavelength between the scattered radiation. Higher numbers work similarly.

From Figure 2.2 it can be observed that there must be a relationship between the wavelength of the X-ray radiation, the separation distance $|a|$ and the angle ν between a and the diffracted wave. It is obvious that a is the hypotenuse of a right triangle and h times the wavelength (λ) is the side adjacent to ν . Thus, $h \cdot \lambda / |a| = \cos(\nu)$. This provides a simple equation for

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diffraction. If an X-ray sensitive film is placed perpendicular to the primary beam, then various lines representing the diffracted beams will be observed. Let θ be the angle between the primary beam and the diffracted beam. The distance between diffracted beams is given by $\sin(\theta)$ times the distance to the film.

However, even in one-dimension this result is too simple. It was assumed that the primary beam was perpendicular to \mathbf{a} , which requires the total phase shift to occur only in the diffracted beam. If the primary beam makes an angle μ with \mathbf{a} , then a phase shift as illustrated in Figure 2.2 can also take place for the primary beam. The phase shift for either the primary beam or the diffracted beam need not be an even number of wavelengths as long as the sum is. This creates the condition

$$|\mathbf{a}|\cos(\mu) + |\mathbf{a}|\cos(\nu) = h\lambda \quad (2.1)$$

This equation is called the Laue Equation and it provides the most liberal description of the conditions for diffraction in one dimension.

In order to place some restrictions on the Laue diffraction, it is useful to make the angles ν and μ equal and call this new angle Λ . In this case, the Laue Equation reduces to $2|\mathbf{a}|\cos(\Lambda) = h\lambda$. (2.2)

A second way to approach this is to add imaginary lines P perpendicular to \mathbf{a} (see Figure 2.3). Initially, the lines will be spaced at $|\mathbf{a}|$ from each other. The angle θ will be the angle between the incoming beam and P and the same for the outgoing beam. The angle Λ was defined previously as the angle between the diffracted radiation and the line defining the distance between the atoms. This means that $90 - \Lambda = \theta$. The cosine of 90 minus an angle is equal to sine of the angle. Therefore, changing to θ and relabeling $|\mathbf{a}|$ as d converts equation 2.2 into

$$2d\sin(\theta) = \lambda \quad (2.3)$$

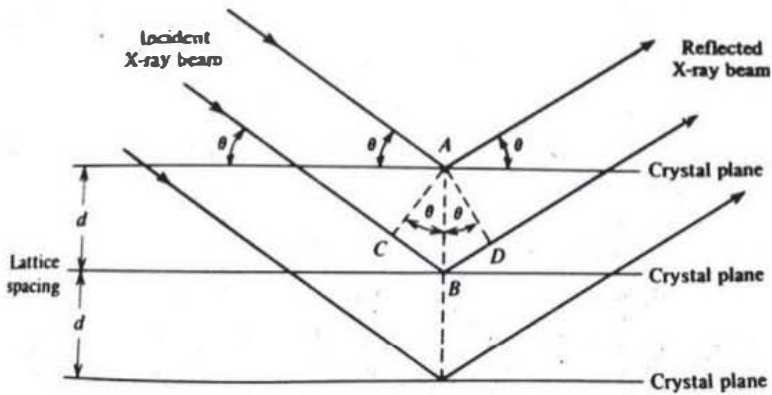


Figure 2.3 Bragg's Law

This is the well-known Bragg's Law if higher and much weaker orders of diffraction are ignored. For the beams to be in phase the length of CB plus BD must be a multiple of the wavelength. It should be pointed out that in Figure 2.3 it appears the primary beam is reflecting off the line P and Bragg's Law is just an example of the familiar equation for reflection that the angle of incidence is equal to the angle of reflection. However, this is not simply reflection but a complicated diffraction process. It also should be pointed out that crystallographers frequently call their data reflections even though that is only what appears to be happening.

The genius of William Lawrence Bragg and his father William Henry Bragg was that they derived an explanation for the different diffracted beams without using phase differences. Since the line P does not exist, it can be modified by changing the distance between the lines by dividing $|a|$ by integers and using this new distance in equation 2.3. The modified Bragg's Law becomes $2(|a|/h)\sin(\theta) = \lambda$ where $|a|/h$ is the distance between the lines P. This is a much easier equation to work with as it relates the angle θ to distances within the crystal. It should be pointed out that in the one-dimensional case P is a line and is perpendicular to the direction of stacking making the distance between lines P easy to figure out. Things become somewhat more difficult in three dimensions as P becomes a plane and the distances between planes are not as simple to determine. It must also be emphasized that the line P is an abstraction and has nothing to do with where the atoms are with respect to the line. The result of both the Laue and Bragg descriptions of diffraction is that the location of the diffracted

radiation is determined only by the repeat distance $|a|$ and has nothing to do with what pattern is being repeated along the line.

There are some easy conclusions that can be drawn from Bragg's Law. First, as h gets bigger then $\sin(\theta)$ will increase and the angle between the incident beam and the observed diffracted beam will increase. Also, as the wavelength used increases the diffracted beams will become further apart. Lastly, as the magnitude of a increases, the distance between diffraction intensities will decrease. This is the well-known reciprocal relationship.

2.3 The Primitive Unit Cell

The derivation of the diffraction of X-ray radiation requires that there be a regular repeating pattern. In the example just discussed, this is in one dimension but for a solid obviously this should be in three dimensions. It turns out crystals are composed of just such a repeating pattern. The properties of crystals such as the way they allow light to pass through them are because of this regular structure. In general, non-crystalline solids are not transparent unless they are very thin. Yet even large crystals are 'crystal clear.' Also, non-crystalline solids can be cut smoothly in any direction. Crystals, on the other hand, can only be cleaved along certain planes.

In considering the one-dimensional array of atoms, it is observed that the array is made up of a unique pattern that is translated along the a vector. In the previously considered array the translation vector was called a (see Figure 2.4a). The vector a is the basis vector for a one-dimensional coordinate system. The familiar Cartesian coordinates have basis vectors whose magnitude is 1. However, here the magnitude is $|a|$. This means that if we pick a particular place on the one-dimensional pattern, then adding or subtracting an integer results in a translation to an equivalent position. This is because the basis vector has length $|a|$ and any integer translation with respect to this basis vector simply shifts to an equivalent point down the line. If x is a decimal fraction greater than zero and less than one, it refers to a point between the equivalent origins of the coordinate system and x is called a fractional coordinate. Its distance to the origin of the coordinate system is given by $x|a|$. The repeating pattern can be considered a one-dimensional unit cell.

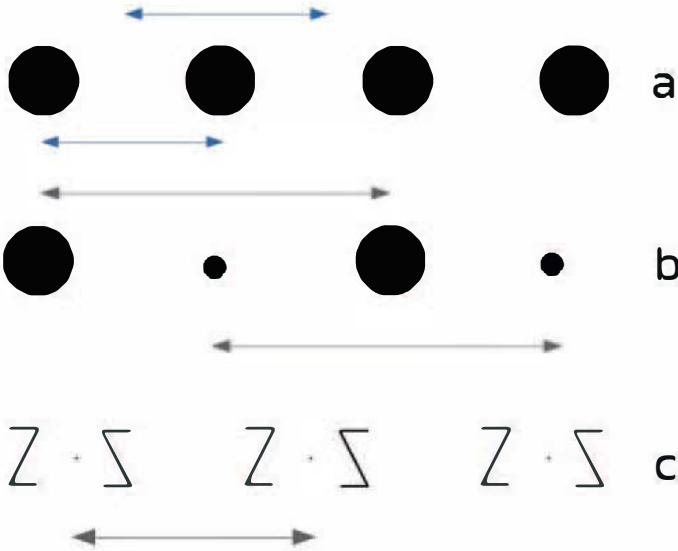


Figure 2.4 One-Dimensional Unit cells

The one-dimensional unit cell will be more complicated and $|a|$ will increase as the number of atoms increases. There is also the question as to where to place the origin. If the array is made up of atoms or ions, it appears easiest to place the origin for the pattern on one of the atoms. However, for linear molecules it is much less clear. Should the origin be placed on an atom, midway between the bonded atoms, or at some other place? Actually, for the cases being discussed, it makes no difference. The only requirement is that the one-dimensional array is formed by translating the basic pattern by $|a|$. Note when two different atoms are placed with the same separation as in Figure 2.4b, the length of the repeat distance doubles as the old a now translates an atom from one type to another.

Figure 2.4c represents a one-dimensional arrangement of Z shaped objects. In creating crystals, nature tries to minimize the cell volume to pack the components efficiently. So, in 2.4c turning one Z upside down with respect to the other may make sense in providing maximum packing efficiency. There is only one type of object in this linear arrangement. The other is related by a symmetry operation between the two objects. This is represented by the dot between them. The two form a pair which is the basic building block of the pattern. Therefore, it makes sense to use the dot as the origin for the axis system.

The discussion of 2.4c illustrates some important points about unit cells. First, an atom does not need to occupy the origin of the unit cell. In the vast majority of structures there is no atom at the origin. Second, a primitive unit cell can contain more than one formula unit in the unit cell. In this example there are two. Lastly, in most cases the origin of the unit cell is determined by the symmetry operations, not the contents.

The one-dimensional idea can be extended to two and even three dimensions. Possible repeating patterns in two dimensions are shown in Figure 2.5. Note that in this figure two different repeating patterns have been selected as unit cells. A second vector called b becomes the basis vector in the second direction. It should be noted that in both of the repeating patterns displayed, the vectors a and b are not orthogonal *i.e.* they do not make a 90° angle with each other. This angle will be called γ . It can be shown that the area of the parallelogram is given by $|a||b|\sin(\gamma)$. While the two potential cells have different shapes, the area of the parallelograms is identical. In fact, any cell that has this minimal volume is acceptable as a valid primitive unit cell.

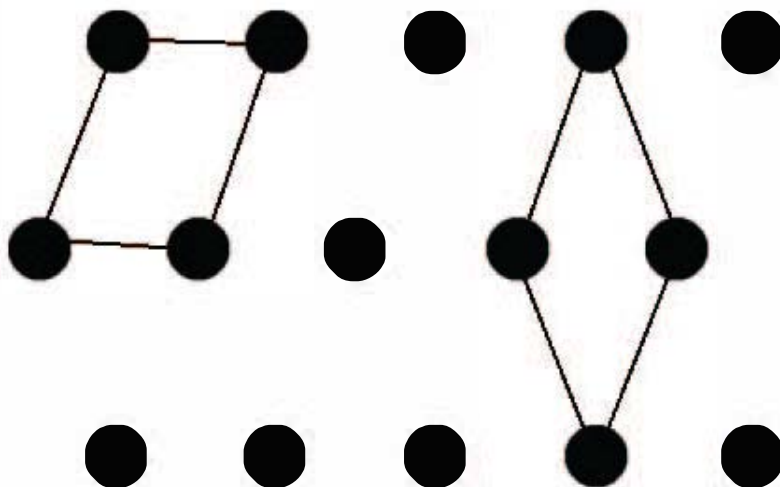


Figure 2.5 Choices for a unit cell

In three dimensions, it takes six parameters to define the unit cell. Three are the basis vectors a , b , and c . Three angles are also required. The angle α is the angle between b and c , β between a and c and γ between a and b .

The easiest way to remember this is that an angle name is the Greek equivalent of the axis **not** involved in the angle.

The unit cells presented here are called primitive because they represent the smallest volume that when repeated forms the crystal lattice. However, for some cells additional translation within the unit cell can be added that will result in a unit cell with higher symmetry. These are called centered cells and will be discussed when unit cell symmetry is considered. This means the primitive unit cell will not always be the cell reported in the final crystal structure.

Since the unit cell axes are typically not identical in three-dimensions, the physical properties of the crystal will depend on the direction of measurement. When properties differ when measured in different directions, they are called anisotropic. If the direction has no effect, it is called isotropic. The existence of anisotropy only occurs naturally in crystalline solids.

2.4 Diffraction in Three-dimensions

Diffraction in three dimensions is much more complicated than in one. If the Laue Equation is to be used, three equations like equation 2.2 are required. In this case, h was an integer that described the offset between waves that constructively interfered along the a -axis. Two new integers are required for similar interactions along b and c . These are assigned k and l , respectively. Likewise, two more equations are required where the angles are measured from b and c . Therefore, the Laue conditions are fulfilled whenever all three equations are satisfied and at the point in space where the beams intersect. The diffracted waves in three dimensions form spots in space wherever the conditions are satisfied. However, this is not an easy set of equations to work with.

Bragg's Law provides a simpler approach to diffraction in three dimensions. In the one-dimensional approach the trick was to create the line P which is perpendicular to a . By using $|a|/h$ as the distance between lines, the location of the various diffraction intensities can be determined. In three dimensions P must be converted into a plane called the Bragg plane. The various Bragg planes will be defined by the three Miller indices h , k , and l . Each index will indicate the plane intersects the axis a , b , and c at coordinates $1/h$, $1/k$, and $1/l$. The plane (1,2,3) intersects a at 1, b at $1/2$ and c at $1/3$. A value of zero means the plane is parallel to that axis. The

plane $(1,0,0)$ is the plane containing the \mathbf{b} and \mathbf{c} axes since it never intersects these axes.

What is important is the distance d_{hkl} between the set of planes. Calculating this distance is more difficult than might be imagined. Take the $(1,0,0)$ plane. It would be expected that the distance between these planes which contain \mathbf{b} and \mathbf{c} would be the length of the a -axis. This may or may not be correct. For some unit cells the a -axis is not perpendicular to \mathbf{b} or \mathbf{c} and therefore is not perpendicular to the bc -plane. The perpendicular would need to be calculated and this is difficult in non-Cartesian axes. Later the concept of reciprocal space and the reciprocal lattice will be introduced to make the calculation of d much easier. Until then, it will be assumed that d can be calculated.

If d_{hkl} is known, then Bragg's Law reduces to $2d_{hkl}\sin(\theta)=n\lambda$. Note that addition of n to the equation. The integer n represents the order of the diffraction, which in the case of X-ray crystallography is usually treated as one and can therefore be ignored. However, for very intense radiation it is possible that second order diffraction ($n=2$) or even higher orders will be present with reduced intensity. In nature, $n=2$ results in a double rainbow. If we treat d as a vector and know the alignment of the crystal, then diffraction will be observed when d bisects the angle between the incoming and diffracted beam. This means it is possible to calculate the diffracting position for any indices hkl .

It is clear that the diffracting position is well-defined by Bragg's Law. However, that does not mean there is only one orientation of the crystal that will satisfy it. The only requirement is that the diffraction vector bisect the angle between the incoming primary beam and the outgoing diffracted beam. However, there is still one degree of freedom. Rotation around the diffraction vector will not change this geometry. Therefore, the same hkl diffraction spot can be observed at many positions during the data collection. This means that it is possible to collect a given reflection at different positions.

Lastly, it must be emphasized that the Bragg planes are an abstraction introduced to make the calculations easier. They are simply a function of the unit cell parameters and have nothing to do with the contents of the unit cell. There is no relationship between the location of the cell contents and the Bragg planes. Also, as mentioned above, the concept that the primary beam is being reflected by a Bragg plane like light by a mirror does not describe what is physically happening.

2.5 Review and Using Diffraction Data

This chapter represents a typical description of X-ray diffraction. It appears that the emphasis has been placed on explaining the existence and location of the diffraction spots. However, the original idea was to use the diffraction to calculate the position of the atoms in the crystal. A piece is still missing.

A review of this chapter will highlight the points made so far. When an X-ray beam interacts with an atom, the atom will produce new intensity which will have the same wavelength as the exciting radiation and be 180° out of phase. If there is no order to the solid, this scattered radiation will be of little use. However, if the material forms a regular array as in a crystal, then interference effects will be observed. The Bragg and Laue approaches were developed to provide a method of calculating where the diffracted beams will be observed. The concept of the unit cell was also introduced. The crystal is formed by translating the unit cell in three dimensions. The directions for translation are the unit cell parameters which form the basis vectors for a coordinate system. These basis vectors are not required to be orthogonal which can greatly complicate any calculations using them. The location of the diffraction spots in space will depend only on the unit cell parameters.

However, none of this has answered the question of where the atoms are in the crystal. If all the unit cells are identical then the problem is reduced to finding all the atoms in a single unit cell. In fact, this problem can be further simplified if the crystal has multiple formula units in the cell related by symmetry. In this case it is only necessary to position the atoms in the unique part of the unit cell called the asymmetric unit to form the entire unit cell.

The key to positioning the atoms is that the diffracted beam is created by constructive interference of waves of differing intensity. The intensity difference is because of the different number of electrons in each scatterer. The observed diffraction is a Fourier transform of the electron density in the unit cell. The indices (h,k,l) are Fourier summation factors and the amplitude of these data are the Fourier coefficients. The information concerning the location of the cell contents is contained in the intensities measured and their phases. It is possible to talk of two Fourier domains like in Fourier spectroscopy. One is real space which is defined by the unit cell parameters and has a dependent value of the electron density (ρ) at any location x,y,z inside the unit cell. The other domain is reciprocal space

which will represent the data. Reciprocal space cannot be physically observed. First, it has dimensions of inverse length. The dependent variable in this space is the amplitude of the scattered wave. This is not a continuous space but only has non-zero values where the indices (h,k,l) are integral. The data obtained is a representation of reciprocal space.

It should be mentioned at this point that unlike Fourier spectroscopy, the transformation from reciprocal to real space cannot be done by a simple mathematical calculation. This is because the collected data are missing the phase information. Thus, a great many calculations called refinement must be done to get the information from the data. It also needs to be pointed out that it is also possible to do a Fourier from real to reciprocal space. This means that if the contents and locations of all the atoms in the unit cell are known it is possible to calculate the intensity data. The methods for doing this will be explained in later chapters.

The above is just one of many equivalent ways of explaining X-ray diffraction. Richard Feynman in his book on quantum electrodynamics offers up a brief explanation of X-ray diffraction which uses a totally different explanation.²

CHAPTER 3

CREATING CRYSTALLOGRAPHIC DATA

In this chapter the equipment needed to make crystallographic measurements, the sample requirements, and the raw output will be discussed. In most cases, this will serve as a brief introduction. Later these topics will be examined in greater detail.

3.1 Equipment Required to Obtain Single Crystal Data

Like any experiment involving the interaction of electromagnetic radiation with matter, three items are required to obtain data. The first is a source of the radiation; the second is something to hold and orient the sample; the third is a detector to measure the intensity of the radiation. The requirements for making measurements on single crystals are no different.

In the laboratory setting X-ray tubes are used to produce radiation by bombarding a pure metal anode with a high energy electron beam from a filament. The target metals most used are copper, molybdenum and rarely silver. Each produces a different wavelength. The advantages and disadvantages of each will be discussed in a later chapter.

Depending on the geometry and nature of the X-ray tube, the final beam may have various diameters. Standard tubes use currents in the range of 20-60mA and produce beams with diameters from 1.0 to 0.4 mm. These tubes are being replaced by micro-focus tubes, which produce a much smaller beam (0.1 mm in diameter), a higher flux, and use much less power (typically 1mA or less). The higher output is achieved by using a dot instead of a filament to produce the electron beam, focusing the electron beam and then using X-ray optics to focus the output X-rays.

The sample holder for the crystal called a goniometer is quite expensive as it is built to very high tolerances. The motions of the goniometer are controlled by a computer and the device is a robot for positioning the crystal very accurately at any given angle. The source, goniometer and

detector compose a diffractometer. A diffractometer is shown in Figure 3.1. The X-rays come from a tube on the right and then pass through a collimator to make the beam more coherent. The goniometer which moves the crystal is in the middle and the detector is to the left. The crystal is mounted on an adjustable head and is located in the center of all the equipment. The black tube above the collimator is a microscope with a digital camera which is used to align the crystal into the beam. The metal piece to the left of the crystal is the beam stop or beam trap which catches the primary beam so it is not observed in the images. The metal tube descending above the crystal provides a beam of cold nitrogen gas to allow for data collection down to 80K.

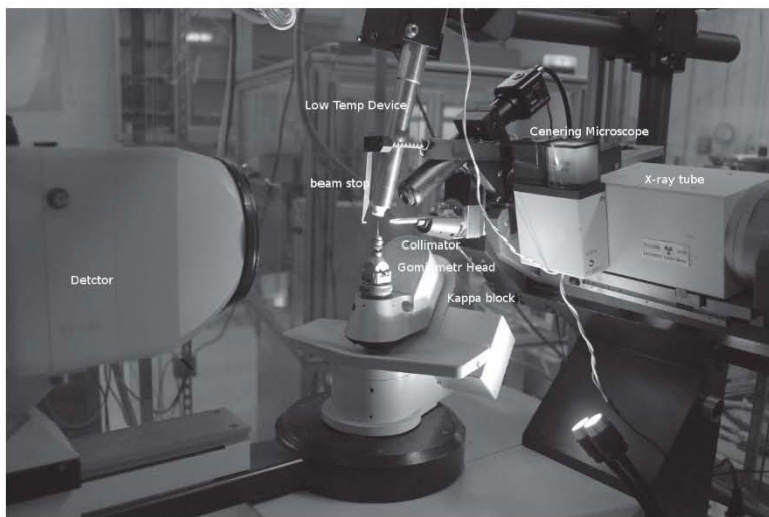


Figure 3.1 A Diffractometer

Last is the detector. Today most diffractometers use an area detector. This is a device equivalent to a digital camera. Figure 3.2 is the image or frame recorded with the area detector shown.

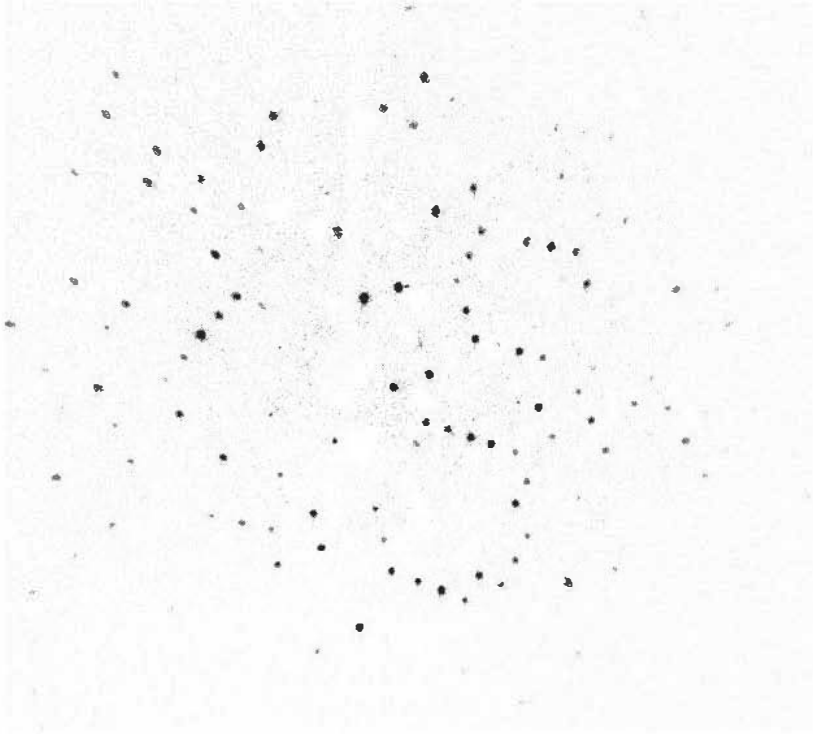


Figure 3.2 A diffraction image

3.2 The Crystal Sample

Once the equipment is available, the only other requirement is a sample. The crystal needs to be of high quality to obtain good results. The most obvious characteristic of good crystals is that they are composed of faces.

The faces should be planar and their intersection should be a straight line. If the crystal is not too dark, then it should be transparent. The crystal should look like a miniature gemstone. Crystals to be used are normally studied with a microscope and should look like the crystals in Figure 3.3.

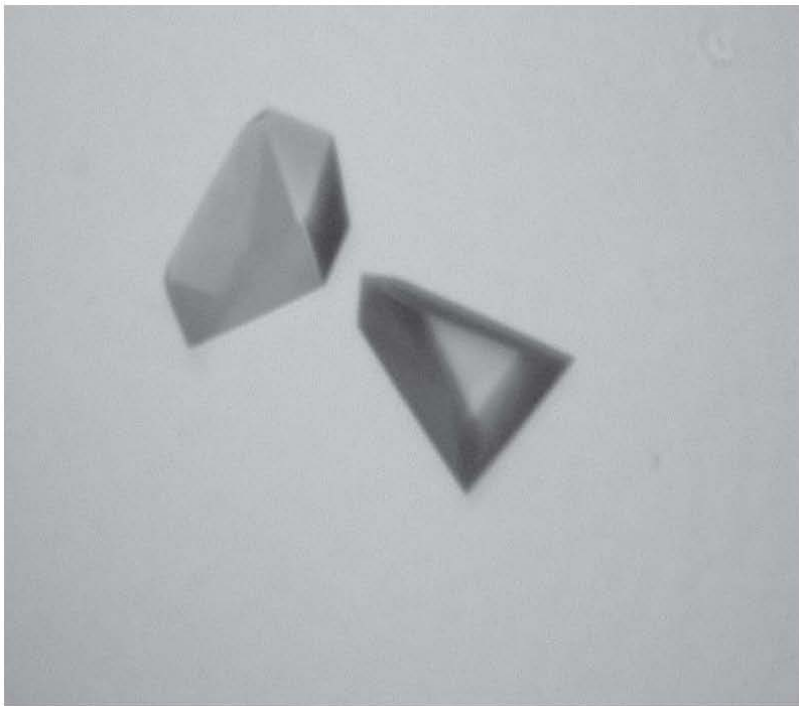


Figure 3.3 Good quality crystals

The quality of the diffraction spots from an image taken on the diffractometer can also be used to determine the quality of the crystal. Figures 3.2 and 3.4a display images from a high quality crystal. Note the spots are small, round, and have little overlap. Figure 3.4b is a marginal crystal. While the left side of the image looks fine, the diffraction spots on the right side are becoming less circular and beginning to overlap. This crystal probably could be used for data collection but the quality of the data will not be as high as for 3.4a. The crystal in 3.4c is not very good. The spots are becoming more irregular and diffuse. This is a sample that will not produce a satisfactory structure. Also note in 3.4c that there is a large amount of scattered X-ray intensity suggesting there is a large amount of non-crystalline material in the beam.

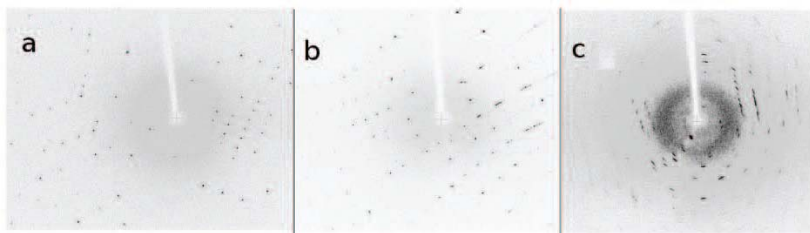


Figure 3.4 Images from three different samples

The size of the crystal is important. It should be scaled to the diameter of the X-ray beam. Typically, this will be about 0.3mm on an edge. Using crystals that are too small will result in weak data that will not provide a quality structure. However, the X-ray beam has a definite size and using crystals significantly larger than the beam will produce not only more intensity but also more problems. In fact, using crystals that are too large may make the measurement of the intensities unreliable. Shape is also an important consideration. Very thin plates or long needles may not place a sufficient volume in the X-ray beam and produce weak data.

At one time the crystal sample had to be a single crystal. That means all the unit cells were aligned with their basis vectors all in the same direction. It was impossible to use a sample composed of two or more crystals to increase the sample size. However, modern diffractometers and software now can determine samples composed of multiple crystals. Such crystals are called non-merohedral twins. In the simplest case, these are composed of two crystals which will each produce a different set of diffraction spots. However, as the sample is composed of two crystals with two distinct lattices, most spots will be weaker than for a single crystal of the same size except where the spots overlap.

There is one last requirement. As emphasized in Chapter 1, it is important to know what elements are likely present in the unit cell. This will save problems with incorrect element assignments and make the calculations easier.

Since the crystals used are relatively small, it would appear it should be easy to obtain suitable ones. However, it can be difficult to obtain samples of sufficient size. Today, obtaining high quality crystals may be the most difficult part of the crystal structure experiment. Some compounds produce crystals which are very thin plates or long, skinny needles. It is hard to get enough sample into the X-ray beam to give anything but weak

data. Some crystals are layers of slightly misaligned planes. If the alignment is only off by a small amount, they will diffract. However, the spots will be very broad and such crystals are usually unsuitable. In the extreme, each layer may be one molecule thick and result in a two-dimensional crystal such as graphite. Some compounds will never crystallize because they do not form stable enough crystals. It may take many attempts and much patience to produce an acceptable sample.

While modern diffractometers and software can work with smaller and poorer quality crystals, they can only do so much. There is no way to measure data that is weaker than the noise of the instrument or background. While some tricks can be used that will appear to improve the refinement, these will be noticed and may be questioned when trying to publish the structure. It cannot be emphasized enough that **the quality of a crystal structure can never be better than the quality of the crystal used!**

3.3 Crystallographic Data

3.3.1 Data from a Structure Study

There are four types of data that represent a crystal diffraction experiment. First, is the intensity data that are obtained from the diffractometer. Secondly, is scientific metadata. These are data needed to analyze the crystallography but not directly used in the crystallographic calculations. An example of this would be the temperature during data collection. Third, is the information that is directly determined by the crystallographic refinement. Last is data calculated from the refinement data. Each will be discussed below.

Before discussing data it is necessary to understand how the error in the data is reported. In a scientific measurement, the error typically is reported as a standard deviation. This is calculated from multiple measurements of a value. In general, the diffractometer data are only measured once. The values of the error in the data are obtained from a numerical calculation. At one time these computed errors were referred to as the estimated standard deviation (esd). However, it was recommended by a working group of the International Union of Crystallography (IUCr) that these errors would be better called standard uncertainties (s.u.).⁹ S.u.'s are given by an integer in parentheses after a number and represents the error(s) in the last place(s). If the s.u. has a value so that $1.95 \leq \text{s.u.} < 9.5$ then the s.u.

is a single integer between 2 and 9. If the s.u. is between $9.5 \leq \text{s.u.} < 1.95$ then an extra figure is reported and the s.u. is two digits between 10 and 19. In this case the s.u. represents the error in the last two places. Some examples are 2.065(3) is basically the same as 2.065 ± 0.003 while the number 2.0653(17) is 2.0653 ± 0.0017 . Almost all numbers in a crystallographic report will have a standard uncertainty attached to them.

The data from the diffractometer are quite simple. The cell parameters and their errors are reported. Secondly, is the orientation matrix. This is a 3×3 matrix that allows an orientation of the crystal to be calculated for a set of Miller indices. This matrix is not widely used and there are other ways to incorporate the orientation information into the data file. Lastly, a file of the data collected is produced. This file will contain h, k, l, I , and $\sigma(I)$. The values of hkl define the diffracting Bragg plane, I is the integrated (total) intensity of the diffraction spot and $\sigma(I)$ is the uncertainty in the intensity. This data file can contain thousands of entries and is usually large.

There is a good deal of scientific metadata required to publish a crystal structure. This includes the temperature where the unit cell parameters were determined and the data were collected. Then there is the description of the crystal. This would include the habit, the color, and the size of the crystal. There are other items like the type of diffractometer used, the software the diffractometer uses, *etc.* which are helpful in evaluating the quality of the resulting structure. Some of this metadata will be standard to a particular diffractometer. Others may be available to the diffractometer software by communication with peripheral equipment such as a low temperature device. Others need to be provided. Most diffractometer software will ask for needed data at the start of an experiment and store the information to include it in a metadata report. If this is not included as a computer file, the information should be written down as it will be required later.

The data from the diffractometer after correction is the input for a long set of calculations referred to as structure solution and refinement. The output of the refinement makes up the description of the unit cell. This data includes the position of every atom in the asymmetric unit of the unit cell reported in fractional coordinates as well as the s.u.'s. The rest of the contents of the unit cell will be obtained by applying symmetry operations which are properties of the space group which is determined as part of data processing. In general there are three parameters so far which must be refined for each atom.

Beyond the position, the motion of the atoms must be considered. The vibration of the atoms decreases their scattering power because it disrupts the exact translation of the atoms. The vibration can be modeled in two ways. It can be calculated so that the vibrational displacement is identical in all directions. In this case only a single number that defines the radius of the sphere of vibration is required. This is called isotropic refinement. If isotropic refinement is used, this adds one parameter to the atoms' refinement. However, for most atoms the isotropic model is an oversimplification. Atoms tend to move more freely perpendicular to bonds than along bonds. The number of bonded neighbors will affect the freedom of movement. To allow more freedom in the vibrational displacements, anisotropic refinement is done. If an atom is refined anisotropically, there are six parameters. The first three define the principal axes of an ellipsoid that replaces the sphere while the last three define the orientation of the ellipsoid. Given the power of today's computers most atoms except hydrogen atoms are refined anisotropically. These vibrational parameters are called the atomic displacement parameters (adp's) though at one time they were referred to as temperature factors. The adp's only should reflect the movement of the atom in the crystal. Unfortunately, the values may also include any systematic or refinement errors.

While all the above data makes up the crystal structure, little of it is useful to chemists. Fortunately, from the coordinates of the atoms and the unit cell parameters, the molecular geometry of the contents can be calculated as well as their errors. This geometric information includes bond distances, bond angles, torsional angles, least squares plane fits for groups of atoms, distances and angles between planes as well as the distance for an atom to the plane. Beyond these are various specialized values that describe various arrangements of rings such as sugars which can be obtained. Thus, most of the data used by chemists are derived data which are not accurate until the structure refinement is completed.

3.3.2 CIF

In order to standardize and simplify the reporting of all the types of crystallographic data, the Crystallographic Information File (CIF) was developed in 1991. While at first the CIF may appear to be difficult to understand, it is important that anyone working with any crystallographic data, whether from studies done in-house or from elsewhere, be able to understand and interpret a CIF.

Data reported in the CIF consists of two parts. First is the data name which begins each line. This is a long string beginning with an underscore (`_`) and describes the data being reported. Multiple entries of identical type data can be done in a loop. The data names are controlled by a committee of the International Union of Crystallography (IUCr) referred to as The Committee for the Maintenance of the CIF Standard (COMCIFS) and are spelled out in a CIF dictionary. The dictionary is more than a list of data names but a complete description of what is to be reported, units, data type, and possible values. There is a core dictionary and various specialized dictionaries found at <http://www.iucr.org/resources/cif/dictionaries>. An example is the entry for the temperature at which the data were collected¹¹

```
_diffn_ambient_temperature (numb, s.u.)
```

The mean temperature in kelvins at which the intensities were measured.

The permitted range is 0.0 -> infinity

Note this contains several important pieces of information. First is the data name itself. After the name is the data type which in this case is numeric and it must contain an s.u. The definition follows and includes the fact that the units for the measurement are Kelvin. Lastly, the possible values for the temperature are given. In a CIF this would appear as a line such as

```
_diffn_ambient_temperature 150.0(2)
```

The format of the CIF is very exacting. Each line (except in a loop) must begin with the data name entered with no typos or upper case letters beginning in column 1. The actual datum can be placed one or more spaces after the data name. The format for numbers is obvious. Integers must be entered without a decimal point. The other type of data are character data. If the character string fits on the line following the data name and has no blank spaces, it can just be entered. There are two ways of treating blank spaces. First, the blanks can be replaced by the underscore character. Secondly, the entire string can be enclosed in quotes (`'`). It is sometimes desirable that character data extend over several lines. This is done by entering a semi-colon (`;`) on the line following the data name and then entering the character data on lines following the semi-colon. A last line containing a semi-colon is used to close the string. There must be an entry for each data name. If there is no value than a question mark (`?`) can be entered for either numeric or character data. It can be questioned why lines without data are used at all. This is mainly because

most CIFs are created by a computer program and the use of the question mark makes the programming easier and also makes the CIF file more readable.

Sometimes there is a need to enter values or comments that have no defined data name. This can usually be done using the names that have special details as part of the name. For example, the name `_diffm_special_details` is where unusual aspects about the data collection can be placed and `_refine_special_details` allows for added comments on the refinement. Almost every class of data name has a special_details name. However, creating CIF data names not in any dictionary is unacceptable.

As mentioned above, a loop can be used to enter repetitive data even involving multiple data names. The loop is started by entering `loop_` on a line. The loop ends when a blank line is encountered. Following the `loop_` are one or more lines containing data names. After all the names, the actual data values are entered. All the data for each entry must be placed on a line separated by blank spaces. There must be exactly as many entries on a line as there are data names defining the loop or an error will result. It is not unusual that some data names will only apply to some entries in the loop. In this case a period (.) is used to indicate an undefined value. Only one level of loop is allowed.

The CIF format allows for more than one structure to be reported in a CIF. The `data_` statement defines the structure whose data are being reported. For example, if you called a crystal `cry1` then the data statement for this data would be headed with `data_cry1`. The CIF must begin with a `data_` statement. The data applies until another `data_` is encountered. The CIF may include entries for authors' names and addresses, phone numbers, *etc.* which only need to be entered once for the multiple structures being reported. A `data_global` heading can be placed at the start of the CIF file for such repetitive data.

Recently the data in the CIF file has been expanded to include the refinement instruction file and the file containing the diffraction data used. This means the data needed so that anyone can refine the reported structure or produce new graphics is contained in the CIF file.

There is a lot of software for creating and checking the format of a CIF. The easiest way for checking and correcting the format is ENCIFER which is part of the program MERCURY available at www.ccdc.cam.

www.cam.ac.uk/Community/csd-community/encifer. MERCURY is included in the Cambridge Structural Database and a more limited version can be downloaded for free. The program is available for WINDOWS, MAC, and LINUX operating systems. ENCIFER will only check the formatting of the file and not whether the values reported are sensible or consistent. On the IUCr website is additional software for reading and writing CIFs which may be added to locally written programs.

This is a brief introduction to CIF. There are many data names that can be used. Beyond that, there are names that allow an entire manuscript to be input into a CIF. The use of additional specialized dictionaries extends CIF to handle all types of crystallographic experiments. A 20 page PDF guide to CIF can be obtained from the website

<https://www.iucr.org/resources/cif/documentation/cifguide>.

3.3.2 Graphic Output

Most chemists view crystallographic results first and foremost by a drawing of the cell contents. A wide variety of programs is available for all operating systems to produce the graphics. Some are commercial but many programs are free or free for academic users. To get an idea what is available

go to <https://www.iucr.org/resources/other-directories/software/search>

and search for graphic software appropriate for your operating system.

Graphics are typically drawn in one of the four formats illustrated in Figure 3.5. The simplest is the line drawing shown in a. A common drawing format is the ball and stick shown in b. The drawing in c is a space-filling model. While not useful for viewing a molecule, it can be useful when looking at the surface of a molecule or when looking for cavities in the unit cell. The last drawing displays the atomic displacement parameters. Carol Johnson created the first program for producing these drawings at The Oak Ridge National Laboratory in 1965.¹² The program was called Oak Ridge Thermal-Ellipsoid Plot program or ORTEP. Today almost any drawing which illustrates adp's is called an ORTEP drawing even though many are created by programs other than ORTEP.

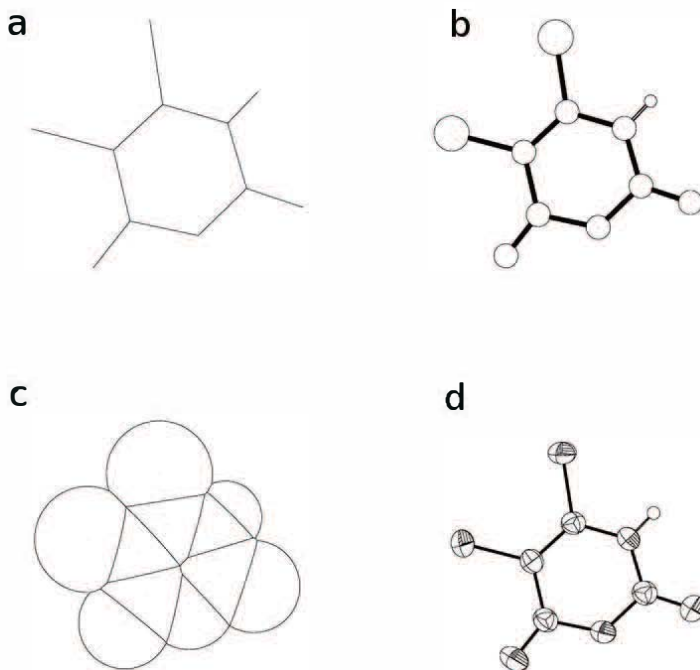


Figure 3.5 Common Molecular Graphics

3.3.3 Publishing Crystallographic Data

Publishing a crystal structure at times appears to be very difficult. There are a myriad of requirements. Frequently reviewers ask questions that appear to be technical and sometimes irrelevant. The goal of this section is to try to give approaches that can make publication easier.

First, it is very important that the requirements for the journal intended for publication are known. These will either be found in the notes for authors or in a separate document. The requirements will include what needs to be submitted; what can be placed in the body of the manuscript; and what is supplementary material. In some journals which are mainly concerned with organic compounds, only a sentence that the isomer was determined via X-ray crystallography can be included. Other journals will require that there be a detailed experimental section describing the data collection and refinement.

● One major difference between journals is whether the CIF file is to be deposited with the Cambridge Structural Data Centre (CCDC) as part of the submission process. Depositing a CIF can be done even if you do not have a license to the CSD. An account must be created and then log in at <https://www.ccdc.cam.ac.uk/deposit> and follow the instructions given. Journals that do not require deposition as part of submission will deposit the CIF file with the CCDC upon acceptance.

The question of what data must be reported in the CIF and appropriate values also needs to be considered. Most journals do not provide their own standards but use the ones specified by **Acta Crystallographica, Section C**. These can be found at <http://journals.iucr.org/c/services/cif/requirements.html> while the page <http://journals.iucr.org/c/services/cifinfo.html> has a wide variety of information about CIF files and publication. The website at <http://journals.iucr.org/c/services/stdswrefs.html> provides a list of references for most commonly used software.

Sometimes a structure will not be good enough to meet all the requirements specified by the journal or as part of validation (discussed in the next chapter). Everything should be done to try to meet these standards. The next question is whether the structure supports the chemistry based on it. A low quality structure of a routine organic compound may provide the isomer. ● On the other hand, if molecular geometries are to be compared to previous structures, then a higher quality structure will be required. If the structure suggests a new chemistry, then it must be of the highest quality.

When the standards are not met, this should be discussed in the paper. To fail to do so suggests the authors are hoping the problems will not be noticed. For example, the crystal was not of high quality. If after repeated attempts the sample studied was the best that could be obtained this should be noted. Likewise, if several approaches were tried during refinement with the one submitted being the best, it should be noted in the experimental section.

CHAPTER 4

WORKING WITH AND VALIDATING CRYSTALLOGRAPHIC DATA

In this chapter the methods of comparing geometrical data from crystallographic studies will be discussed. Crystallographic databases will be briefly introduced. Methods of ensuring the data in a structure are consistent and meet the standards will be considered. Finally, incorrect structures will be examined.

4.1 Comparing Results

Because the data collected has an estimated error, all the parameters obtained from a structure will also have standard uncertainties, s.u.'s. For comparison, using the values without the s.u. does not provide a true measure of the agreement or difference. It is usually assumed that values that differ by more than 3 s.u. (99.7% certainty) can be considered statistically different. Values that differ by less than 3 s.u. should not be reported as different.

For example, consider the CIF loop below:

```
loop_  
_geom_bond_atom_site_label_1  
_geom_bond_atom_site_label_2  
_geom_bond_distance  
_geom_bond_site_symmetry_1  
_geom_bond_site_symmetry_2  
_geom_bond_publ_flag
```

C1 C6 1.373(3) . . ?

C1 C2 1.398(3) . . ?

F1 C7 1.321(3) . . ?

F3 C7 1.313(3) . . ?

F2 C7 1.317(3) . . ?

This loop defines bond distances between atoms. The first three entries are the two atom names involved in a bond. The site symmetry entries are used when atoms are related by symmetry operators in the cell. Here, there are no symmetry operations to be applied so nothing is entered as signified by the periods. The last value is the publication flag. For a few crystallographic journals, the entire manuscript is contained in the CIF. The publication flag indicates whether the distance should be included in a table of bond distances that is automatically created in the body of the manuscript. The values can be y or n for yes and no. The value of '?' indicates no value is given and is equivalent to no.

The value of the C1-C6 bond length is to be compared to the C1-C2 bond. The difference between the two lengths is 0.025\AA while the s.u. is 0.003 . Since 0.025 is greater than 0.009 (3xs.u.) it can safely be concluded that these bonds have different lengths. Next, the three carbon-fluorine bonds in a CF_3 group are compared. It would be expected that all should be the same length but there is a slight variation. The maximum difference is 0.008\AA while the s.u. is 0.003 . This difference is less than 3xs.u. and therefore it cannot be stated there is a difference in these bond lengths. If the numbers to be compared have different s.u.'s then the largest s.u. value should be used.

This is one example where the quality of the data becomes important. The more precise the data, the smaller the s.u.'s should be. Clearly, with smaller s.u.'s differences can be determined with greater statistical certainty.

4.2 Crystallographic Databases

There is obviously a need to compare geometrical parameters and other information with what is in the literature. Several databases have been created composed of crystallographic results that make this an easy task.

While the following discussions are hardly complete, they provide some idea of what is available.

4.2.1 The Cambridge Structural Database

The oldest and most used database for chemists is the Cambridge Structural Database (CSD) available from the Cambridge Structural Data Centre on the web at <https://www.ccdc.cam.ac.uk/>.¹³ This database and the associated software are released each year in November. There are several ways to obtain the database either for individual computers or for web access. The price varies depending on the country where the purchaser resides and whether the user is academic or industrial. If you are not aware of the availability of this software at your university or place of employment, you should check to see if there is a site license that will allow the database to be installed on local computers or if it can be accessed from a website. The software is available for all three personnel computer operating systems.

The organization of the CSD is a bit different from most chemical databases. Rather than the records being by publication, they are by structure. Each structure is identified by a six letter refcode. Refcodes that end with additional numbers indicate that they are from different publications of the crystal structure either by the original or new authors. The CSD only contains structures that have at least one organic carbon somewhere in the unit cell. For example, sodium chloride will not be found in the CSD but the ethanol solvate of calcium chloride is an entry. As of November 2017 the database contained nearly 891,000 entries. The CSD refers to structures containing a metal and an organic fragment as organometallic which is different from the usual chemical definition. If a structure has been reported more than once, then each report will be a separate entry. Each entry contains the scientific metadata and the refinement data. In addition, the publication data such as authors and journal of publication are part of the record. The database generally derives geometrical parameters from the coordinates. However, the geometrical parameters reported in the CIF file are compared to the values given in the publication when the database entry is created to ensure they are consistent. The database can be searched by one or a combination of logically combined queries.

CONQUEST is the main program for searching the CSD. Selecting an icon from the desktop or entering `cq` on the command line starts the

program. Once running, CONQUEST has a graphical user interface (GUI) and the data are entered by using the mouse or typing into an entry box. While most of the input is intuitive, there is extensive help included in the GUI. In fact, the help even includes tutorials on use of the CONQUEST.

While CONQUEST provides for searching on formulas, this is not the major method for chemical searches. Typically, a target fragment is drawn in the GUI. The drawing comprises atoms connected by bonds of a specified bond order. If the bond order is unknown, the bond type 'any' can be used. The drawing can contain one or many atoms. Rings and templates for common fragments are provided. The great advantage of searching on a fragment is that it provides a great deal of freedom in the chemical composition. Where the full coordination sphere of an atom has not been specified, then any number of atoms can be bound. For example, if just a benzene ring without hydrogen atoms is the target, then any compound with any substituent at any position will be found in the search. This would include benzene itself, phenol, hexachlorbenzene and any phenyl group for example. To keep the searches manageable and useful, the drawing should be specific enough to only find compounds of interest.

There are several features that can make searching on a fragment easier. For example, it is possible to search on all the elements in a column or a row of the periodic table. It is also possible to create a new combination element by combining any two or more elements. In addition, it is possible to limit the number of atoms bonded to an atom or the number of hydrogen atoms attached to narrow the search.

Several search criteria can be combined into one search. If several criteria are selected, they will be joined by an 'and' as the default. For example, if compounds of a certain type published by a particular author are to found, then two queries are set up. One would be a drawing of the compound and the other the name of the author. Both would be selected and the search would find entries that meet both criteria. It is also possible to create more complex logic that includes 'or' and 'not.' This can narrow the output.

In general, the CSD does not contain some information that could be useful though it is being upgraded to be more complete. First, the actual diffraction data are not stored. This can usually be obtained from the supplementary material of the publication. Until recently, the atomic displacement parameters were not part of the structural data available. The CSD data for a given structure or group of structures can be output as a CIF. However, a drawing such as an ORTEP will not illustrate the adp's.

Essentially, only ball-and-stick formats will be available. The last missing information is the s.u.'s for the geometrical parameters. As discussed above, this would appear to make comparisons difficult. However, since the CSD usually contains multiple entries for structures of any type, true statistics can be obtained from the many entries. In addition, the s.u.'s can always be obtained from the publication cited.

To calculate statistical data from the CSD it is important that the geometrical parameters be defined before the search is run. Atoms that define the geometrical parameters are entered as 3D parameters when building a drawing. If two atoms define a 3D value, it will store all the bond distances for every entry that matches the search criteria. If there are multiple examples of this parameter in a single entry, then all will be reported. Note the two atoms that define a bond do not have to be bonded to each other. If three atoms are selected, bond angles will be stored and four atoms will define a torsional angle. Selecting all the atoms in a ring will calculate either the centroid or the best fit plane. These can then also be used to define geometrical data to be included in a statistical analysis. The centroid is used like any other atom. The planes are somewhat different. If two planes are selected then the angle between the planes will be stored. If an atom and a plane are selected then the distance from the plane to the atom will be used.

After the CSD is searched, the 3D results must be saved and exported to the program MERCURY for analysis.¹⁴ Under the File tab in CONQUEST there are selections for storing and analyzing data. One will export the data and start MERCURY. In MERCURY, it is possible to do many statistical analyses. The simplest is basic statistics. It is also possible to draw histograms of the result. If two different parameters are selected, then it is possible to do a scatter plot which displays how these parameters are correlated.

A statistical analysis for the carbon-oxygen bond distances reported for terminal iron carbonyl compounds will be used as an example. To search in CONQUEST, a sub-structure drawing was entered. It consisted of an iron atom bound by a single bond to a carbon. Since the bond order between the carbon and oxygen atom is not clear, the bond type 'any' was used. To restrict this fragment to the compounds desired, the number of atoms bonded to both the carbon and oxygen was limited. The carbon was only allowed to bond to two atoms (the iron and oxygen) and the oxygen to one. The carbon-oxygen distance was then defined as a 3D parameter and a search run. The search returned 45,975 C-O bonds. The results were

then passed to MERCURY and basic statistics were calculated. An abbreviated output of the results is given below.

Name	Count	Minimum	Maximum	Mean	Std.Dev	Median
DIST1	45975	0.627	1.759	1.145	0.023	1.143
Low Outliers		High Outliers				
252		509				

The C-C distance was labeled as DIST1 in CONQUEST. The mean distance was 1.145 with a standard deviation of 0.023. The median distance was 1.143. Since the mean and median agree, it suggests the mean is not being distorted by several extreme values or outliers. Also, note that since the standard deviation is calculated from many values, it is a true standard deviation and not an s.u. The bond distance values range from a low of 0.627Å to a high of 1.759Å. Both the low and high values are not reasonable. A carbon-hydrogen bond determined by X-ray analysis has a typical length of about 0.9Å and it is hard to believe a larger atom such as oxygen could form a shorter bond. A carbon-carbon single bond is typically about 1.54Å making the upper limit equally unlikely. These structures are dubious and should not have been published. However, the position of the CCDC is that data from all published structural studies should be included in the database and should not be rejected or edited by the CCDC. The results also suggest the smallest 252 and the 509 largest distances are statistical outliers and could be omitted. While this would probably not change the mean distance much, it should decrease the standard deviation which is greater than expected for an s.u. from refinement data.

4.2.2 Other Crystallographic Databases

There are several other crystallographic databases that may be useful to chemists. Probably the next most used after the CSD is the Inorganic Crystal Structure Database (ICSD).¹⁵ Information about obtaining and using this software can be found at http://www2.fiz-karlsruhe.de/icsd_home.html. The contents of this database are the opposite of the CSD as it does not contain organic structures. The software runs only in Windows but there is a web version which when licensed can be run through a web browser. Because this database deals mostly with solid state compounds, there is no drawing component in the GUI. Structures can be found using either the complete or partial formula or information such as

the cell type. In November 2017 this database contained about 188,000 entries.

A new addition to the crystallographic databases is the Crystallography Open Database¹⁶ which is online at <http://www.crystallography.net/cod/>. This database is described as an “Open-access collection of crystal structures of organic, inorganic, metal-organic compounds and minerals, excluding bio-polymers.” As of November 2017 there were 386,081 entries. While not as complete as the CSD, there are several advantages to this software. First, it is free. Second, complete CIF files for structures can be downloaded which contain the adp’s and the s.u.’s and the diffraction data can be obtained for newer entries. This database can also be used for depositing CIFs before publication. The database consists of a collection of CIFs which the software can search. For newer structures they are the full CIF submitted either to the database before or after publication and may also include the reported diffraction data. For older entries, the CIF files are very abbreviated and may not contain adp’s. This is less consistent and the search software is more primitive than the CSD but it sometimes can provide more information.

The Protein Data Bank (PDB) is searched mostly by structural biologists but may be of interest to some chemists. It contains structures of proteins, nucleic acids, and other large assemblies. Structural data comes not only from X-ray crystallography but also nmr spectroscopy and cryo-electron microscopy. It can be searched for free on-line at <https://www.rcsb.org/pdb/search/home.do>.

There are several other specialized databases that are available but not typically used by chemists. The most important is the Powder Data File from the International Center for Diffraction Data at <http://www.icdd.com/index.htm> and will be discussed in Chapter 15.

4.3 Ensuring Structures are Correct

As already pointed out, the crystal structure analysis involves making many decisions. Computer programs make some and crystallographers others. It is possible to create an incorrect structure and sometimes even non-existent compounds. In this section, methods of checking to ensure the validity of a structure will be discussed.

4.3.1 CheckCIF

The program CheckCIF was written by Antony Spek as part of the program PLATON.¹⁷ While the results from CheckCIF can be frustrating as they appear to always find fault with any CIF, it is an invaluable tool for testing the validity and quality of a structure.

There are two ways to check a CIF. First, a copy of the program PLATON can be obtained from <http://www.cryst.chem.uu.nl/xraysoft/>. For installation on the Windows operating system, the site <http://www.chem.gla.ac.uk/~louis/software/platon/> provides additional required software. It should be noted that PLATON is frequently upgraded and must be kept current if it is to be used. The program is started with the CIF file as input and then the Validation button under the REPORTS column is selected. CIFs can also be validated using CheckCIF at the website <https://checkcif.iucr.org/>.

The first function of CheckCIF is to check for agreement between the various data entered in the CIF. For example, does the formula for the contents of the unit cell agree with the number of atoms reported in the refinement data? Do the geometrical parameters agree with values calculated from the atomic coordinates and the cell constants? There are many such checks and any discrepancies are reported. The second check determines if the reported data agree with the best practices of crystallography. Do the values fall in the ranges required by **Acta Crystallographica Section C**? Lastly, there are checks to ensure the data are chemically and physically reasonable.

The output of CheckCIF validation is reported in a file with the suffix .chk. At the top of the report is a comparison of many of the values reported with those calculated by CheckCIF. Slight differences may suggest round off error but large deviations suggest a problem. Then comes a series of alerts divided into four categories. The most severe problems are identified as A-alerts. Most journals today will not publish structures with A-alerts without some justification why the alert should be ignored. Obviously these represent severe problems which must be addressed. Alerts at the B level represent potentially serious problems that should be investigated further. C-level alerts are less serious potential problems that should be checked. They might not be problems at all. Finally, there are G-level alerts which are usually warnings that should be considered. Over the years Dr. Spek has frequently changed the alert levels of different problems to correspond with the frequency of their

occurrence and their perceived seriousness. This is one reason it is important to keep PLATON up to date.

The CIF system provides a way of responding to CheckCIF alerts. While CheckCIF is very good at evaluating errors, it will not always be correct. For example, sometimes a low quality crystal is all that can be obtained and must be studied. This will produce a lower quality structure and some high level CheckCIF alerts. If this structure unquestionably supports what is claimed in a manuscript, then it may still be fine if its limitations are recognized. Responses can be entered into the CIF file via Validation Response Form (VRF). An example of a VRF from the IUCr page <http://journals.iucr.org/services/cif/checking/checkfaq.html#dvrf> is

```
_vrf_PLAT_220_global
```

```
;
```

```
PROBLEM: Atom C(6B) has ADP max/min ratio ..... 5.20
```

```
RESPONSE:
```

```
Atom C6 of the ring (B) was found to be disordered; see
```

```
  _publ_section_exptl_refinement
```

```
;
```

The value 220 in the heading of PLAT_220 is the error number reported by CheckCIF. The response is obviously the justification for the problem which is manually entered. VRF's are typically placed after the first data_ block. They can be entered by editing the CIF or using PubCIF.¹⁸ PubCIF is a program for easily editing CIFs and ensures the format will be correct. It can be downloaded at <http://journals.iucr.org/services/cif/pubcif/#download>. The latest version of PLATON will produce a .vrf file containing all the serious problems that require a response. The response can be entered using a text editor and then copied to the CIF being submitted.

Many chemists have trouble dealing with CheckCIF when submitting structures for publication. One cause of this anxiety is that many manuscripts are not reviewed by experienced crystallographers. These reviewers use CheckCIF as a binary test and not as a guide for evaluating structures as was intended. It is important to understand the problem

causing the alert reported by CheckCIF. The IUCr site <http://journals.iucr.org/services/cif/datavalidation.html> has a full list of all the CheckCIF errors and when an error is clicked, a full explanation is provided in a window. For example, the PLAT220 error in the VRF above provides

“This test reports on a larger than usual Ueq range for the specified element type in the non-solvent/anion part of the structure. Too high or too low Ueq's may be an indication for incorrectly identified atomic species (i.e. ● versus N).”

If there is still some question as to the correctness of a CheckCIF error then more advice should be obtained from an experienced crystallographer. If the error appears to not apply to this study, then it can be challenged with a VRF. Some journals do their own CheckCIF and occasionally report alerts that are not found in the submitter's check. This is usually because the journal is using an obsolete version of CheckCIF. This problem can be avoided if the submission contains the author's original CheckCIF result as supplementary material.

4.3.2 Using ADP drawings as a check

The addition of atomic displacement ellipsoids to a molecular drawing increases the amount of information available. ORTEP drawings contain all the information of a ball-and-stick drawing plus much more. The ellipsoids ideally just display the motion of the atoms in the crystal. However, many mistakes and systematic errors will also be displayed in these ellipsoids. There are several checks that should be made when examining an ORTEP type drawing. First, is the overall size of the ellipsoids. Second, are any ellipsoids too large or small as compared to the other atoms? Third, is whether the direction of the long axis of the ellipsoid can be used to diagnose problems. Last, the overall shape of the ellipsoid could indicate a problem.

It is difficult to say what the average size should be for an ellipsoid in an ORTEP drawing. The size of the ellipsoids will be a function of the temperature of the crystal during the data collection. For this reason, it is important to know the temperature at which the data were collected. At lower temperatures the ellipsoids will be smaller. A second factor that needs to be considered is the probability used in calculating the ellipsoid in the drawing. In this calculation a factor is included for the probability the nucleus is within the ellipse. This probability is reported as a percentage. For many years it was standard to use 50%. However, there is

no requirement for this percentage. Some authors use 30%. In any case, the percentage should be part of the caption for the figure. This information should be available for each ORTEP in a manuscript. Without it, any analysis of adp size is futile. Structures with unusually large adp's frequently have problems that should be investigated. However, large adp's can be hidden by using a small percentage.

The relative sizes of the ellipsoids in an ORTEP also should be carefully studied. Heavier atoms will have smaller ellipsoids. Atoms bonded to one or two atoms will have more freedom of movement than atoms in a ring or having a higher coordination number. Lastly, for long organic chains, the adp's for atoms in the chain should become larger the further from the anchor point. This is like a line of skaters going around in a circle. The outer part of the line must move faster than the inner part to rotate as a line.

One of the biggest causes of unusual sized ellipsoids is a mistake in the assignment of an atom's element type. As has been explained, X-ray diffraction results from the electron density in the crystal. If too many or too few electrons are added at an atomic position, then the density will be adjusted by changing the volume resulting in unusual adp's. Too many electrons increases the volume to try to reduce the density. This will result in large ellipsoids. Too few electrons results in a volume decrease. In fact, an unusual ellipsoid size is what the PLAT220 warning above is pointing out for atom C6.

An example of this is given in Figure 4.1, This was first shown in Margret Kastner's excellent **Crystallographic Courseware**¹⁹ and has been redrawn from the CIF obtained from the COD.²⁰ This is the same molecule shown in Figure 3.5. The figure on the left side is for the correct element assignments while the one on the right has the carbon and oxygen atom types swapped. It is clear on the right the ellipsoids of the assigned carbon atoms are too small while the oxygen atoms are too large. This is just what would be expected. This displays the effects of atoms assigned with the wrong element type. While one would expect that the chlorine atoms might be slightly smaller than the carbon atoms, this is not obvious in the drawing. Because the chlorine atoms only form one bond, they can move more easily than the carbons in the ring. This explains the discrepancy. Lastly, it might be expected that hydrogen atoms should have the largest ellipsoids because they are very light and only form one bond. However, in most ORTEP drawings the hydrogen atoms are assigned an arbitrarily small radius. This is done so they do not obscure the more important

details of the molecule. Also, note that the carbons display the σ 's using one format and the other atoms use a different one. This can be controlled by the input to the drawing program.

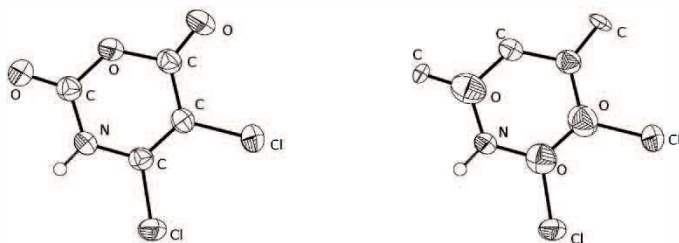


Figure 4.1 ORTEPs for a correctly and incorrectly assigned molecule

The direction of the longest axis for a distorted ellipsoid is also important. The largest vibrational force constants are stretching modes. This is why the stretching frequencies in IR Raman spectra are always at higher frequencies than the corresponding bending modes. Therefore, the ellipsoids should never be elongated along a chemical bond. If this is observed it suggests there is a problem which is frequently a disorder. Also, if all the ellipsoids have the same orientation, this is proof of a systematic error. Frequently the cause of this is how the absorption in the crystal was corrected.

Lastly, all the ellipsoids should have reasonable shapes. Ideally they should be as close as possible to a sphere unless there is some explanation as to why the vibrations are anisotropic. If any atoms are very elongated (prolate) this suggests possibly there are two disordered atoms represented by a single atom. The ellipsoids should never be saucer shaped (oblate). This suggests a problem with the data.

4.4 Incorrect Structures

Because a crystallographic experiment ultimately provides geometrical data and a drawing of the unit cell contents, many assume that all published structures must be correct. Unfortunately, this is not the case. Decisions made by the crystallographer, sometimes influenced by bias, can result in an incorrect structure. Such structures can do great damage to chemistry in that they may create non-existent compounds or support incorrect theories. This is why every structure needs to be evaluated as to

its correctness. Examining cases of erroneous structures can provide lessons on what to look for.

The development of the topic of wrong structures and their importance was brilliantly articulated by Richard Harlow.²¹ Much of what follows here is a restatement of his ideas. I would classify incorrect structures into four categories. First, is the analysis that produces a structure that is unlikely given the chemistry. The second class results from an incorrect assignment of an element. Third, are structures that have crystallographic problems such as disorder which led to either incorrect refinement or interpretation. Last are what Dr. Harlow calls fuzzy structures. These are not necessarily incorrect but their quality does not unequivocally support the conclusions made.

4.4.1 Structures Incompatible with their Synthesis

One thing that must be correct in any crystal structure is that the contents of the crystal must be in agreement with the compounds used in the synthesis and crystallization. This error is rare, yet it happens occasionally. Also, it is very difficult to diagnose with crystallographic validation programs. The simplest example would be to report the existence of an element or solvent that was never used. However, the discrepancy can be more subtle as the example below will point out.

A submitted manuscript described the structure of a metal-fluorine anionic complex with a hydronium (H_3O^+) as the cation. CheckCIF did not have any significant alerts and the ORTEP drawing displayed nothing out of the ordinary. The only minor problem was that the hydrogen atoms on the hydronium ion were disordered and there was additional density around the oxygen atom that could be hydrogen atoms. It was pointed out by a reviewer that the compound had been synthesized at a pH of 8.5. While not impossible, it is unlikely that an acid salt would be synthesized in a basic solution. When all the hydrogen atoms around the oxygen were removed, it was clear that there were four areas of electron density appropriate for a hydrogen atom, and they formed a tetrahedron about the presumed oxygen atom. The oxygen was changed to a nitrogen and the refinement improved. The hydronium ion was an ammonium ion. An Inorganic Crystal Structure Database search confirmed this was a previously published structure. This database was not searched routinely for submitted manuscripts.

4.4.2 Incorrect Assignment of an Element

Exciting and novel chemistry can be reported if an atom is assigned the wrong element. Because crystallography is held in such high regard, most will accept the structure as proof of unusual chemistry even if it appears unlikely.

A report of a novel transition metal chemistry will exemplify this. It was reported that the metals silver and copper sigma-bonded to the 1-carbon of 2,4,6-triphenylbenzene.²² This was important for several reasons. The metals were one coordinate and behaved like main group elements. This had never been observed. In addition, the metal-carbon distances were surprisingly short. There were problems with the report. Few details were given about the structure. No drawing displaying the adp's was included in the manuscript to allow the assignments to be examined. It was very hard to determine if this really was an extraordinary result

This research was later repeated and the structures re-determined.²³ Figure 4.2 shows an ORTEP of the original result on the left and the correct structure the right (hydrogen atoms omitted). The key problem in the original structure is the size of the silver atom as compared to the carbons. It is not obvious in the drawing but the silver atom actually has a larger adp than would be expected. Since this atom is much heavier, it should have a smaller amplitude of vibration, yet it is the largest ellipsoid in the drawing. Part of the justification is that it is the only atom with a coordination number of one and therefore can move freely. In the drawing on the right, the structure has been refined with the presumed silver replaced by bromine. The ellipsoid is now comparable to the other atoms. In addition, the quality of the refinement improves and the distance between the bromine and carbon is within the expected range. An identical result was obtained when the assumed copper atom was replaced by a chlorine.

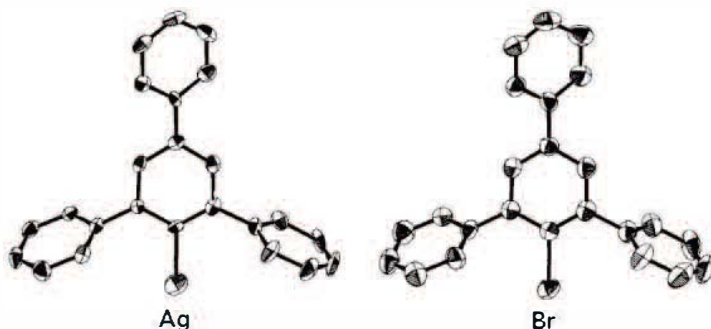


Figure 4.2 A structure with an incorrectly assigned element. All unlabeled atoms are carbon.

While this result is not recent, manuscripts with incorrect element assignments are still submitted and occasionally published. Most do not produce results as novel as the example above. CheckCIF may suggest a problem with the sizes of the adp's, however, it cannot provide definitive proof that an element assignment is incorrect. It is imperative that if there is any question about the assignment of the elements in a structure, the formula be confirmed by additional chemical analysis.

4.4.3 Misinterpretation of Structural Results

As emphasized, the result of an X-ray crystal structure is the electron density in the unit cell and not the location of the atoms. This can be complicated by disorder in the crystal. Ideally, each unit cell is exactly the same as every other cell except translated in space. However, nature is not always so obliging. In some cases, a single site can be occupied by different elements in different cells. An example is a solid compound composed of Al^{+3} randomly substituted by Cr^{+3} ions occupying the same location. Obviously this means that some unit cells will differ from others. The way this is handled is that the coordinates for each atom occupying the same site are made identical and the amount of each element present is refined. The site is disordered in the "typical" cell since one location is a combination of two elements. It is clear if the element is assigned only by the electron density it will be incorrect because the observed density is the average of the two elements multiplied by their relative ratios. More than two atom types can disorder and even a void (empty site) can be included.

There are other forms of disorder. A common one is where a molecule can exist randomly in the crystal in two different conformations. In this case, the structure will display sets of partial atoms. Again interpretation is required to work out and understand the true nature of the structure.

Misinterpretation can result in the creation of non-existent molecules. Such is the case with the rhodium complex shown in Figure 4.3.²⁴ This is a surprising compound. First, rhodium in the +2 oxidation state is unusual. Also, such complexes would not be expected to have square planar geometry. The most obvious problem with the ORTEP drawing is the ellipsoids for the chlorine atom. There is a symmetry element located at the rhodium atom that relates the two chlorine atoms so in reality there is only one refined atom. The two PPh₃ ligands have a similar relationship. Not only are the chlorine ellipsoids very elongated but the longest axis is along the Rh—Cl bond. This structure was re-investigated and not surprisingly the original interpretation was incorrect.²⁵ The elongated chlorine atom is actually a carbon monoxide ligand disordered with the chlorine. The Rh—C distance is shorter than the distance to the chlorine while the Rh—● distance is longer. The highly prolate ellipsoid extends over all three atoms. When the disorder was modeled correctly, the refinement improved and all the adp's made sense. In addition, the oxidation state of the rhodium became +1 which is nearly always square planar. The structure was correct but its interpretation produced a non-existent molecule.

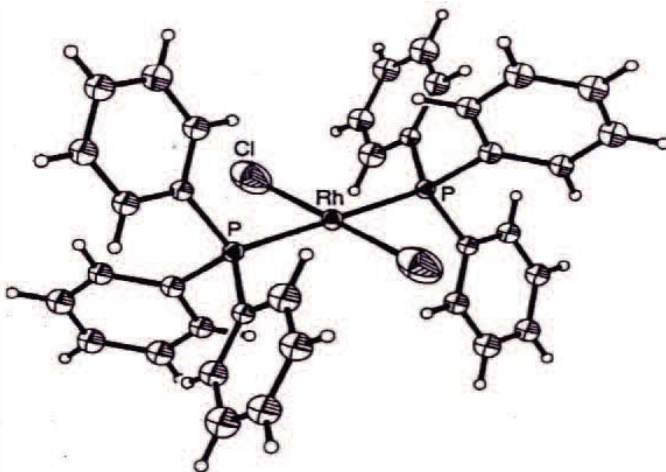


Figure 4.3 An incorrect structure caused by disorder.

Failure to account for disorder has resulted in not only bogus molecules but was even used to support a theory. This involved the concept of bond stretch isomerization. This theory suggested that there were isomers that were geometrically the same but differed in a bond distance. A molecule which was disordered was assumed to be an example of this type of isomerism. However, when the disorder was accounted for, it was not true. The publication by Gerard Parkin discusses the history of this disorder.²⁶

4.4.4 Fuzzy Structures

There is a whole class of structures which Richard Harlow refers to as fuzzy structures. These are not incorrect structures but for one reason or another do not unambiguously answer a question. This might occur because the quality of the crystal used was poor and resulted in a poor structure. It may be because the structure is so disordered that it cannot be interpreted unequivocally. In fact, Dr. Harlow claims, 'The problem with fuzzy structures is that it is difficult to decide whether they are interesting structures or wrong structures.'

While there are many examples of fuzzy structures, a relatively recent controversy will be used as an example. In 2015, the structure of $[\text{K}(\text{crypt-222})]^+(\text{CF}_3)$ was reported.²⁷ The cryptand ligand was used to isolate the potassium ion from both chemical reaction and electron

exchange. The trifluoromethyl anion is extremely reactive and thermally unstable. Therefore, growing and working with these crystals was difficult. It was later suggested that this structure did not unambiguously support the claims made for it.²⁸ The crystals were not of high quality and thus the data were not collected to the required limits. Furthermore, both the cation and anion were disordered. This is the perfect fuzzy structure. This disagreement has yet to be fully resolved.

4.5 Final Comments

Crystallography is not an infallible method and because of this, the results of the experiment need to be fully provided. Where problems appear, they need to be dealt with or explained. Any chemist submitting a crystallographic result should either provide all the required information for evaluation or be ready to respond to problems. Using methods like CheckCIF can highlight potential problems. However, there are examples where the CheckCIF alerts are not really a problem and other times problems are not found that are significant.

As a user of crystallographic data, it is important to realize a reported result could be incorrect. Studying the geometric parameters and the alert's can expose significant problems.

Finally, remember the comment of the astrophysicist and skeptic Carl Sagan, 'Extraordinary claims require extraordinary evidence.' If the structure supports previously unknown chemistry, then it must be beyond question. Almost always, when a structure disagrees with known chemistry it is the structure that is wrong.

CHAPTER 5

REAL AND RECIPROCAL SPACE

In this chapter the nature of real and reciprocal space will be explained.

Mathematics for working with vectors and matrices will be reviewed. The relation between the two spaces will be introduced.

5.1 A Brief Review of Vector and Matrix Mathematics

This treatise is not intended to be mathematical. When working with crystallographic data, it is useful to review some basic concepts.

5.1.1 Some Trigonometric Function Values

When mathematical formulae concerning unit cell axes are reported, they will only be given for the most general case where the basis vectors are neither unitary nor orthogonal. These formulas can be simplified for coordinates where the angles have special values by invoking the following trigonometric values.

$$\cosine(90^\circ) = \text{sine}(0^\circ) = 0.0$$

$$\text{sine}(90^\circ) = \cosine(0^\circ) = 1.0$$

$$\cosine(60^\circ) = 0.5$$

$$\cosine(120^\circ) = -0.5$$

5.1.2 Vectors

A vector is a quantity possessing both magnitude and direction. A vector can be represented by a line with an arrow on the end that defines its direction. A vector is denoted in bold for example \mathbf{v} . Note if the direction

of the vector is changed by 180° then this would be $-\mathbf{v}$. The length or magnitude is indicated by $|\mathbf{v}|$ and is a number (scalar).

An important operation involving vectors is the dot product given by

$$\mathbf{v} \cdot \mathbf{w} = |\mathbf{v}| |\mathbf{w}| \cos(\theta) \quad \text{where}$$

θ is the angle between the two vectors

The dot product provides a way to determine a vector's length. If a vector is dotted into itself the value will be the square of the length of the vector since the cosine of zero is one. Of course a method is needed to determine the value of the dot product if this is to be applied.

There are several ways a vector can be written. One is as coordinates. The coordinate (x, y, z) defines the end of the vector starting with its tail at the origin. If these coordinates are defined by set of basis vectors which are neither unitary nor orthogonal and the relationships are as defined in Chapter 2 for the angles between them then

$$\begin{aligned} \mathbf{v} \cdot \mathbf{w} = & x_v x_w a^2 + x_v y_w ab \cos(\gamma) + x_v z_w ac \cos(\beta) + y_v y_w b^2 + \\ & y_v x_w ab \cos(\gamma) + y_v z_w ac \cos(\alpha) + z_v z_w c^2 + z_v x_w ac \cos(\beta) + \\ & z_v y_w bc \cos(\alpha) \quad (5.1) \end{aligned}$$

This equation contains a notation that will be invoked from now on. The basis vectors \mathbf{a}, \mathbf{b} , and \mathbf{c} will be denoted by a bold letter while their magnitude will be represented by the equivalent non-bold letter. For Cartesian coordinates all the cosine terms are zero and the basis vector lengths are one. In this case the dot product of the vectors is three terms $x_v x_w + y_v y_w + z_v z_w$ which is the well-known formula for a dot product. This equation can also be simplified if the same vector is dotted into itself to give the square of the magnitude of the vector.

5.1.3 Transformations

Sometimes vectors or axes need to be transformed. This includes swapping unit cell basis vectors, transforming coordinates, or transforming hkl values. This is the realm of linear algebra and matrix mathematics. In the following section the mathematics that is needed to perform such conversions will be briefly discussed without attempting to provide

extensive instruction in manipulating matrices. Those who are familiar with this mathematics will have a deeper understanding of these methods.

The easiest way to represent a transformation is by using a matrix which is an array of numbers. Since real space is three-dimensional the matrix for these transformations is a square 3x3 matrix. This means it has three horizontal rows and three vertical columns. The individual numbers that compose the matrix are labeled as below

$$\begin{pmatrix} a_{11} & a_{12} & a_{13} \\ a_{21} & a_{22} & a_{23} \\ a_{31} & a_{32} & a_{33} \end{pmatrix}$$

If this matrix is multiplied into a column vector consisting of x,y,z, the result is

$$x' = a_{11}x + a_{12}y + a_{13}z$$

$$y' = a_{21}x + a_{22}y + a_{23}z$$

$$z' = a_{31}x + a_{32}y + a_{33}z$$

A summary of this is that the new, transformed value of x indicated by x' has the a₁₁ component of the old x, the a₁₂ component of the old y and the a₁₃ component of the old z. The same is true for y' and z' except that the rows two and 3 are used. A simple example would be if the x values are to be swapped with the y values. The matrix representing this transformation would be

$$\begin{pmatrix} 0 & 1 & 0 \\ 1 & 0 & 0 \\ 0 & 0 & 1 \end{pmatrix} \quad (5.2)$$

The square matrix has additional properties that are important. The first is the determinant. This is a number which can be calculated for any square matrix. For a 3x3 matrix the determinant is given by

$$\det = a_{11}a_{22}a_{33} + a_{12}a_{23}a_{31} + a_{13}a_{21}a_{32} - a_{31}a_{22}a_{13} - a_{32}a_{23}a_{11} - a_{31}a_{21}a_{12} \quad (5.3).$$

The determinant of the transformation matrix in 5.2 is -1. When a transformation is applied to the basis vectors defining a unit cell, the absolute value of the determinant times the old cell volume is the volume of the transformed cell. The transform in 5.1 has no effect on the cell volume which is what would be expected if the **a** and **b** axes were swapped. The fact that this determinant is negative means the coordinate system has been changed from a right-handed to a left-handed system or *vice versa*. It is important in crystallography that any transformation maintain the handedness of the coordinate system and therefore should always have a positive determinant. Anytime two axes are interchanged then the determinant will be negative. In the case above if any of the non-zero values are changed to -1, then the determinant will remain positive. However, when a basis vector is rotated by 180° the angle between the new basis vector and the unchanged ones becomes 180° minus the original value. Obviously, if the original basis vector was orthogonal to a vector, the transformed vector will still be orthogonal. If we make the one in the first row -1 it would indicate the new **x** would be the old **-y**. A cyclical swap (*i.e.* abc becomes bca) always gives a positive determinant.

A special case is a matrix with a determinant of zero. Such a matrix is said to be singular. A matrix will be singular if two rows or two columns are either equal or related by a multiplier. A transformation matrix must not be singular if it is to be valid. A transformation that is singular essentially reduces the original three-dimensional cell to a two or even one-dimensional space.

5.2 Real Space and Unit Cells

As previously discussed, the domain of real space is the actual crystal. This space is defined by three basis vectors **a**, **b**, and **c** which represent distances between translationally equivalent coordinates. These vectors will have a non-unitary length and may not be orthogonal. Their relationship is given by the angles α , β , and γ . The volume enclosed by one unit of each of the three basis vectors is a unit cell. These vectors define the coordinate system within the unit cell. The dependent value at any location is the electron density given the symbol ρ_{xyz} .

The absolute location of any point within the crystal can be defined by coordinates based on **a**, **b**, and **c**. First, the coordinates within a given unit cell must be determined. Since the unit cell is bounded by the three basis vectors, the location within a given cell can always be defined by three

numbers between 0.0 and 1.0. Then the number of translations along each unit cell direction to the particular cell chosen measured from an origin must be determined. This will always be an integer and can be positive or negative. The combination of the two values will make up the absolute location in the crystal.

When dealing with coordinates within a single unit cell, only the decimal part (fractional coordinate) is required. Furthermore, since all the unit cells must be exactly the same, there must be an exact equivalent location in every unit cell. An equivalent location is one where the environment at the fractional coordinates is identical in all cells. This gives rise to a unique unit cell mathematics. Any integer can be added or subtracted from a fractional coordinate to give an equivalent position. Thus, x is equivalent to the coordinate $x-1$. This implies that a values of 0.7 and -0.3 are equivalent. However, in absolute terms the position of -0.3 is not in the same unit cell as the positive coordinate. It is important to keep in mind whether the coordinates being applied are for equivalent or absolute positions.

Because the unit cell basis vectors are not Cartesian, it is frequently difficult to impossible to perform advanced mathematical calculations using the fractional coordinates. The fact that the basis vectors do not have a length of one can be easily compensated for by using a_x , b_y , and c_z as lengths. The lack of orthogonality is more difficult to deal with. It is possible to transform the fractional coordinates to Cartesian coordinates. There are many transformation matrices which will accomplish this but one that is commonly used is

$$N=1 \cdot \cos^2(\alpha) - \cos(\beta)^2 \cos^2(\gamma) + 2 \cdot \cos(\alpha) \cos(\beta) \cos(\gamma)$$

$$\begin{pmatrix} a & b \cos(\gamma) & c \cos(\beta) \\ 0.0 & b \sin(\gamma) & c [\cos(\alpha) - \cos(\beta) \cos(\gamma)] / \sin(\gamma) \\ 0.0 & 0.0 & c * N / \sin(\gamma) \end{pmatrix} \quad (5.4)$$

This matrix has several interesting properties. First, its determinate is the volume of the unit cell. Secondly, the transformation from the resulting Cartesian coordinates back to fractional coordinates is the inverse of this matrix.

5.3 Reciprocal Space and Reciprocal Cells

Several important points from Chapter 2 need to be emphasized. First, the diffraction data are related by a Fourier transform from real space. Each datum must be labeled by three integer coordinates h , k , and l which will become the Fourier summation indices. The values hkl are called the Miller indices. The diffraction data can only be measured at certain orientations of the crystal, with respect to the incoming and diffracted beam. The hkl values will either be used to determine how to orient the crystal for diffraction to be observed or may be calculated from the known location of a diffraction spot and the orientation of the crystal.

The key to the orientation process is the vector \mathbf{d} the diffraction vector which is the vector that is perpendicular to the Bragg plane that is defined by a set of Miller indices. Figure 5.1 illustrates the family of planes that would be labeled $\{1,2,3\}$. Note the brackets indicate this is a family of planes and not a single plane or vector. The location of the plane in real space is the plane intersects the x -axis at 1, the y -axis at $1/2$ and the z -axis at $1/3$. The fractional coordinates of the intersection of the plane is the inverse of the h , k , and l values. Therefore, the vector \mathbf{d} , will provide all the information needed to position the crystal, or assign the diffraction spot

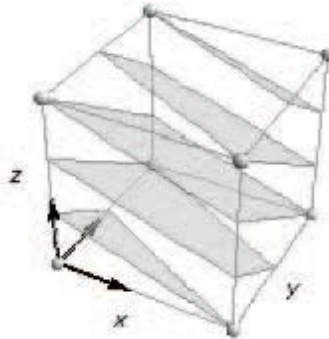


Figure 5.1 The $\{1,2,3\}$ family of planes.

If Bragg's Law is written as $\sin(\theta) = \lambda/2|\mathbf{d}|$ then the problem of orienting the crystal to observe diffraction only requires knowledge of the vector \mathbf{d} . The crystal must be positioned such that the diffracted beam makes an angle θ to a Bragg plane family. The angle θ can be calculated from the magnitude of \mathbf{d} using Bragg's Law. The vector \mathbf{d} must also be perpendicular to the

plane and bisect the incoming and diffracted beams. Calculating just the magnitude of \mathbf{d} let alone its direction in real space is not a simple problem.

To make working with the diffraction vector easier, a new space is defined. This is called reciprocal space and values associated with reciprocal space are indicated by a superscript *. A reciprocal cell can be created which is defined by basis vectors \mathbf{a}^* , \mathbf{b}^* , and \mathbf{c}^* which are related by the three angles α^* , β^* , and γ^* . The relationship between the reciprocal and real vectors is as follows (remember $\mathbf{v} \cdot \mathbf{w} = \mathbf{w} \cdot \mathbf{v}$)

$$\mathbf{a} \cdot \mathbf{a}^* = \mathbf{b} \cdot \mathbf{b}^* = \mathbf{c} \cdot \mathbf{c}^* = 1$$

$$\mathbf{a} \cdot \mathbf{b}^* = \mathbf{a}^* \cdot \mathbf{b} = \mathbf{a} \cdot \mathbf{c}^* = \mathbf{a}^* \cdot \mathbf{c} = \mathbf{b} \cdot \mathbf{c}^* = \mathbf{b}^* \cdot \mathbf{c} = 0$$

Since all the vectors have a non-zero length, the only way the dot products between real and reciprocal axes can be zero is if the axes are perpendicular. From above, it can be seen that \mathbf{a}^* is perpendicular to \mathbf{b} and \mathbf{c} requiring \mathbf{a}^* to be perpendicular to the bc -plane. Any vector $h\mathbf{a}^* + k\mathbf{b}^* + l\mathbf{c}^*$ must be perpendicular to the planes given by $\{hkl\}$ and its length is the reciprocal of d i.e. $1/d$. Bragg's law can now be written as $\sin(\theta) = \lambda |\mathbf{d}^*| / 2$ where the magnitude of \mathbf{d}^* is given by

$$(|h^2 a^{*2} + k^2 b^{*2} + l^2 c^{*2} + 2hka^*b^* \cos(\gamma^*) + 2hla^*c^* \cos(\beta^*) + 2klb^*c^* \cos(\alpha^*)|)^{1/2} \quad (5.5)$$

Placing the vector \mathbf{d} in the correct position for diffraction involves the reciprocal axes. The exact calculations are beyond the scope of this text.²⁹ However, the calculations all involve a transformation matrix called the orientation matrix. This matrix consists of the projection of the reciprocal axes onto an orthogonal coordinate system centered on the diffractometer. As different manufacturers define the x , y , and z axes differently, the orientation matrix may not transfer from one diffractometer to another. Once the orientation matrix is determined, then any set of Miller indices can be transformed into this Cartesian vector using the diffractometer coordinate system as the basis by multiplying the orientation matrix into the column matrix of h , k , and l . From this, the crystal can be positioned such that it is in the required diffracting position. A similar approach can be used to determine the indices from an observed diffraction spot.

It should be apparent that all operations on diffraction equipment are done using the reciprocal cell. Indexing of the crystal is accomplished by determining a set of integral Miller indices that will fit the observed

diffraction points. Data collection is done using the reciprocal cell. Reciprocal space is the domain of diffraction and data.

Obviously it is important to be able to convert between reciprocal and real cell constants. The equations in Table 5.1 give the formulas for these conversions. The formulas are written for the most general case where none of the axes are orthogonal and can be simplified by inserting the values discussed in section 5.1 for other axes.

Table 5.1 Real and Reciprocal Relationships

$$a^* = bc \sin(\alpha) / V$$

$$b^* = ac \sin(\beta) / V$$

$$c^* = ab \sin(\gamma) / V$$

$$\cos(\alpha^*) = [\cos(\beta) \cos(\gamma) - \cos(\alpha)] / \sin(\beta) \sin(\gamma)$$

$$\cos(\beta^*) = [\cos(\alpha) \cos(\gamma) - \cos(\beta)] / \sin(\alpha) \sin(\gamma)$$

$$\cos(\gamma^*) = [\cos(\alpha) \cos(\beta) - \cos(\gamma)] / \sin(\alpha) \sin(\beta)$$

$$V^* = 1/V = a^* b^* c^* \{ 1 - \cos^2(\alpha^*) - \cos^2(\beta^*) - \cos^2(\gamma^*) - 2 \cos(\alpha^*) \cos(\beta^*) \cos(\gamma^*) \}^{1/2}$$

$$a = b^* c^* \sin(\alpha^*) / V^*$$

$$b = a^* c^* \sin(\beta^*) / V^*$$

$$c = a^* b^* \sin(\gamma^*) / V^*$$

$$\cos(\alpha) = [\cos(\beta^*) \cos(\gamma^*) - \cos(\alpha^*)] / \sin(\beta^*) \sin(\gamma^*)$$

$$\cos(\beta) = [\cos(\alpha^*) \cos(\gamma^*) - \cos(\beta^*)] / \sin(\alpha^*) \sin(\gamma^*)$$

$$\cos(\gamma) = [\cos(\alpha^*) \cos(\beta^*) - \cos(\gamma^*)] / \sin(\alpha^*) \sin(\beta^*)$$

$$V = 1/V^* = abc \{ 1 - \cos^2(\alpha) - \cos^2(\beta) - \cos^2(\gamma) - 2 \cos(\alpha) \cos(\beta) \cos(\gamma) \}^{1/2}$$

Several aspects of reciprocal space must be stressed. The units for a^* , b^* , and c^* are inverse distance usually \AA^{-1} . This cannot obviously be observed and is in fact an artifact like the Bragg planes which makes the mathematics easier. Also, short vectors in real space are long vectors in reciprocal space and vice versa.

There is a certain irony in using reciprocal space. The desired information is the location of the atoms or their electron density in real space. However, there is still no microscope with the resolution required to observe this directly. On the other hand, reciprocal space which is an artificial construct can readily be observed in the arrangement of the diffraction spots. In fact, if the crystal is moved in the proper way or certain pixels are selected from a set of images, it is possible to observe a two-dimensional image with the reciprocal lattice as a regular grid. A synthesized precession is given in Figure 5.2 displays the two-dimensional reciprocal space where $h=0$, b^* is horizontal and c^* is vertical. Clearly the b^* and c^* axes are perpendicular.

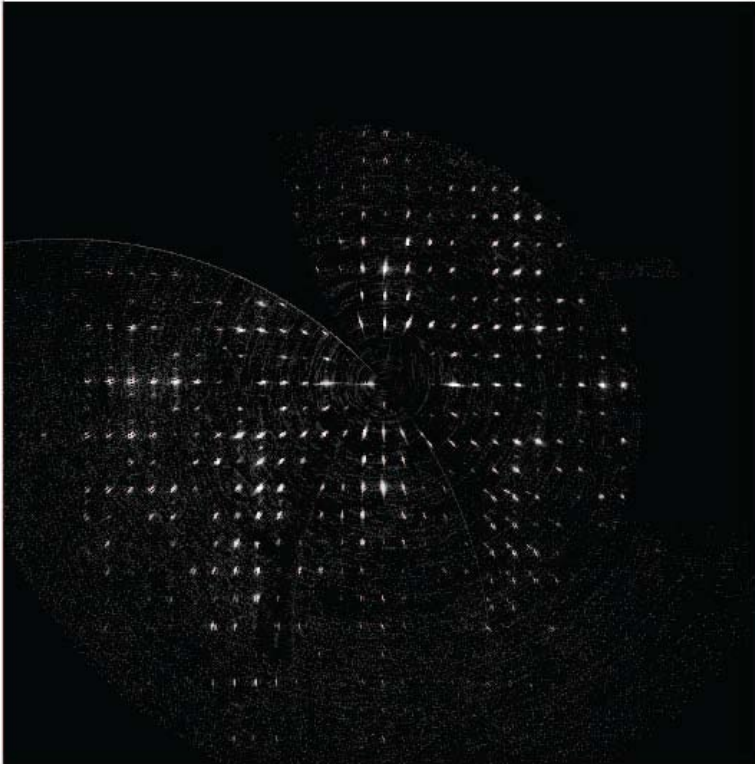


Figure 5.2 A precession photograph displaying $0kl$.

CHAPTER 6

SYMMETRY OPERATIONS AND UNIT CELLS

In this chapter simple and complex symmetry operations will be defined. Translation as a symmetry operation is introduced. The classes of unit cells and cell centering will be topics.

6.1 Basic Symmetry Operations

A symmetry operation is defined as an operation that leaves an object or group of objects in an equivalent, indistinguishable position. There are three basic symmetry operations for a single object which are based on a plane, a line and a point.

6.1.1 Symmetry Notation

There are two terminologies used to describe symmetry operations. The one familiar to most chemists is the Schönflies notation used first by spectroscopists and then expanded to molecular orbitals. While this system is useful for single molecules, the notation is not broad enough to allow for a complete characterization of all the symmetry types for crystals. Therefore, a more complete system called Hermann-Mauguin(H-M) notation is used. The difference between the two systems is not only in nomenclature but even affects the definition of a symmetry operation. In the beginning, the more familiar Schönflies notation will be used and the H-M equivalent will be indicated in square brackets. Later, they will be interchanged.

6.1.2 The Rotation Axis

The rotation axis as its name suggests is an imaginary line running through the center of an object around which an object can be rotated. The amount of the rotation will be classified by an integer n where the rotation is a $360^\circ/n$. A rotation axis where n is equal to 3 is referred to as a 3-fold

rotation and the rotation is 120° . In general, n can be any number from 1 to infinity. For real objects a 360° rotation is equivalent to rotating the object all the way around and can be applied to anything no matter what its shape. The value infinity applies to objects that can be rotated by any amount and still be in an indistinguishable position. This applies to a sphere or a cylinder. A rotation operation changes the values for the coordinates of the axes in the plane perpendicular to the axis of rotation and does not affect the coordinate along the axis of rotation. Because of the need to fill space, only a small subset of rotations is allowed in crystals. The values are limited to $n=1,2,3,4,6$.

Rotation is the only symmetry operation that can actually be carried out on a solid object without having to deconstruct the object. Also, like all symmetry operations it can be carried out repeatedly while leaving the object apparently unchanged.

The rotation axis is indicated simply by C_n [n in H-M]. A 3-fold axis is designated by C_3 [3]. In either notation this only describes the operation but provides no information about its direction. Repetitive rotations are indicated by a superscript. Thus, C_3^2 [3^2] indicates two three-fold rotations of 120° or a 240° rotation. Note that $3^3=1$ as it represents a full 360° rotation.

6.1.3 The Mirror Plane

The symmetry operation based on a plane is the mirror. This operation takes anything on one side of the plane and transfers it across to the other side at the same distance from the mirror. What is observed is a mirror image. For this to be a symmetry operation, initially there must be equivalent items on both sides of the mirror. The mirror must run through the center if it is being applied to a single object. For a single line to be related by a mirror plane the line must be perpendicular to the mirror or in the mirror plane. Also, applying a mirror changes the handedness of an object. When you observe a right hand in a mirror, the image is that of a left hand. If an object is planar, the plane of the object will always be a mirror plane. If the object is not planar, it will be impossible to perform a mirror reflection without rearranging the object which is impossible for a solid object. The mirror operation changes the coordinates of any axis not in the mirror plane while keeping the coordinates within the plane unchanged.

Mirrors are labeled by whether they are perpendicular to a rotation axis or the axis is located within the plane. In Hermann-Mauguin notation a plane is simply indicated by m while in Schönflies it is labeled as σ . A plane perpendicular to an n -fold rotation axis is designated by $\sigma_h [n/m]$. A four-fold axis with a mirror perpendicular would be indicated by $4/m$ in Hermann-Mauguin notation which is read as “four over m .” Any plane that is not perpendicular to a rotation axis is just m . In Schönflies notation σ_v designates a plane that contains two axes while σ_d contains one axis and bisects the remaining two perpendicular axes. H-M does not make this distinction in the designation for non-horizontal mirrors.

Lastly, it should be noted that reflection through a mirror plane can only be done once. A second reflection simply results in the starting orientation. In equation form this means $m^2=1$.

6.1.4 The Inversion Center

The symmetry operation based on a point is the inversion center. For an object this is the center of the coordinate system and requires all points (x,y,z) must be identical to $(-x,-y,-z)$. The presence or absence of a center of inversion is very important in crystallography. If inversion is one of the symmetry elements, then the symmetry is called centric; otherwise acentric or non-centrosymmetric. Cartesian coordinates are acentric because they are positive in one direction from the origin and negative in the other. The Schönflies notation for an inversion center is i while the nomenclature for H-M will be discussed in the next section.

6.1.5 The Improper Rotation

It is possible to create new symmetry operations which are combinations of the three simple operations introduced above. The improper axis of rotation is such a combination operation. However, the definition is different in Schönflies and the Hermann-Mauguin notation. In Schönflies, an improper rotation is given the symbol S_n and consists of a $360^\circ/n$ rotation followed by reflection through a mirror plane perpendicular to the rotation axis σ_h . In H-M the improper rotation is a rotation followed by inversion. The symbol for an improper rotation is the value n with a bar above it. Thus $\bar{2}$ is a 180° rotation followed by inversion. This results in the symbol for inversion being simply $\bar{1}$. It should be noted that the bar

symbol is sometimes given as \bar{n} since creating a number with a bar above it can be difficult on many word processors.

Because of the difference in the definitions of the improper rotation, there is no equivalence between the Schönflies S notation and the H-M. The following are some equivalences

$$\bar{1} = S_2 = i \quad \bar{2} = \sigma_h \quad \bar{3} = S_6^5 \quad \bar{4} = S_4^3 \quad \bar{6} = S_3^2$$

6.1.6 The Identity Operation

It may appear silly, but there is a need for an identity operation. This is not applying any symmetry operation at all. This is required since the combination of all the unique symmetry operations must be a closed group. This requirement is equivalent to the number zero in addition and subtraction. In H-M notation identity is simply indicated by 1. However, in Schönflies notation the symbol E is used. This is because Schönflies notation is applied not only to real objects but to quantum mechanical wave functions. If a spin wave function such as that of an electron is rotated by 360° the value changes sign. Therefore, the operation E can be different from a 360° rotation. All real objects no matter how irregular have at least identity as a symmetry operation.

6.2 Translation

6.2.1 Translation as a Symmetry Operation

It has been emphasized several times that crystals are solids with a regular translation and that diffraction only occurs because of these translations. The result of translation is that there is a unique space called the unit cell bounded by three vectors that are the directions of translation. If the position in any unit cell is given by (x, y, z) then (n_1x, n_2y, n_3z) , where n_1, n_2 , and n_3 are any positive or negative integer, is an identical position in a different unit cell. It could be claimed that an integral translational shift produces an equivalent position and therefore translation is a symmetry operation in a crystal.

Translation does have one aspect that makes it different from the symmetry operations previously discussed. All the above operations can be performed unlimited times without resulting in any obvious change in

the object. In fact, any combination of the previous transformations will also leave the object indistinguishable. However, translation has limits. Eventually, the surface will be reached and translations will no longer be possible as there will be no more unit cells. There are several approaches that can be applied so that translation can still be considered a symmetry operation. There are typically at least one million cells along any axis of a crystal and the surface can simply be ignored. For calculations, the Born-von Karman boundary conditions can be imposed. This requires that translation in any direction by an extremely large number of unit cells results in a return to the starting position.

If translation is included as a symmetry element, then it is clear that it must be applied to a set of items and not just a single object. If translation is not included then the symmetry is called point group symmetry as a single object can be manipulated but cannot be moved to a different location. This requires that all the symmetry operations have a common origin which is a point inside whatever is being studied. Symmetry including translation is called space group symmetry because the objects can not only be transformed into themselves but also moved to equivalent locations where other identical objects are located.

Once it is accepted that translation is a symmetry operation it can be utilized like any other operation. It can be combined with the operations defined previously to produce new symmetry operations. Since these operations will involve translation, they can only exist in space groups.

6.2.2 Screw Axes

The screw axis is a combination of a rotation followed by a translation along the axis of rotation. The nomenclature for a screw is n_m where n is the rotation of $360^\circ/n$ while m/n defines the translation. Since the screw axis is along a cell axis, the absolute amount of translation is given by the length of the axis times m/n . The symmetry element n/m is read as n sub m or nm .

The simplest screw axis is the 2_1 (read as either two-of-one or 2 sub 1). This operation requires 180° of rotation followed by a translation half-way along the rotation axis. Obviously a second 2_1 operation rotates the object back to the original position and shifts it one unit along the axis. Since all unit cells are the same, a translation of one is a move to the next unit cell. The 2_1 operation is illustrated in Figure 6.1 This and all similar figures

were copied from the Crystallographic CourseWare website¹⁹ and used with the author's permission. Obviously before the screw axis is applied there must be an identical object at the appropriate coordinate half-way along the screw axis or it would not be a symmetry operation.

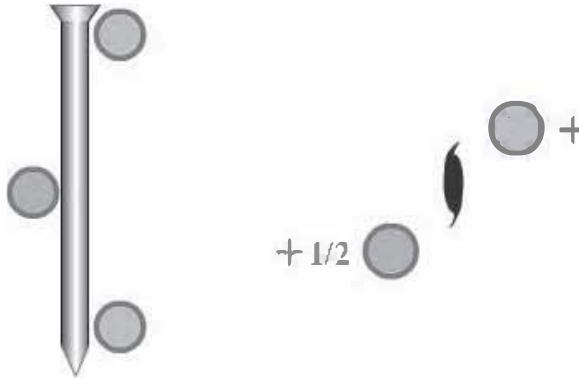


Figure 6.1 A 2-fold screw axis viewed perpendicular to and along the direction of translation

There are two related operations for a three-fold screw axes as illustrated in Figure 6.2. The 3_1 screw operations consists of a 120° rotation followed by a translation of $1/3$ the length of the rotation axis. The second application of the symmetry results in a 240° rotation plus $2/3$ of the length. Finally, the third application results in simply a shift by 1 unit which is simply a translation. In Figure 6.2 which covers two unit cells the second three applications of the screw axis are labeled with the '...

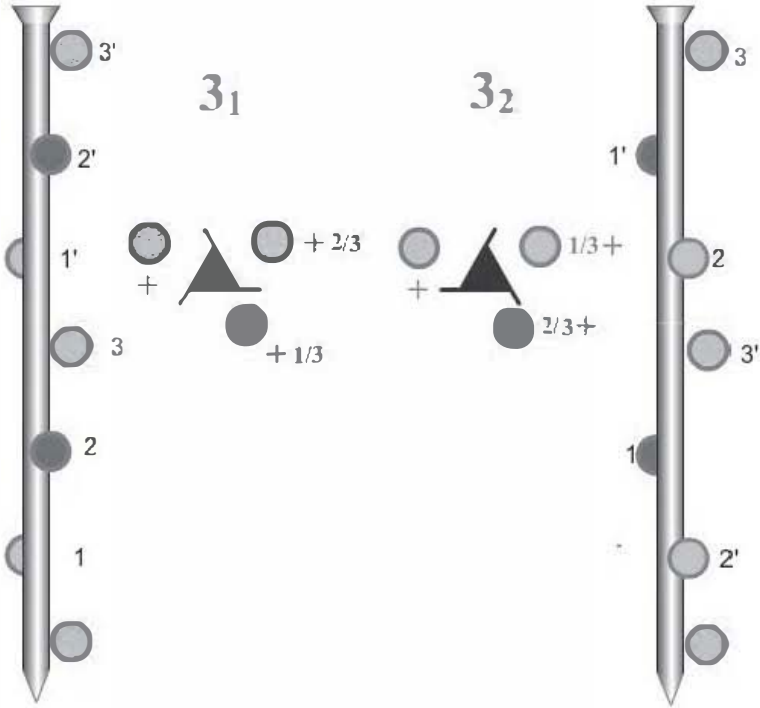


Figure 6.2, Three-fold screw axes. The numbers indicate the position after that many successive application of the screw axis.

The related operation is noted by 3_2 . In this case the rotation is followed by a translation of $2/3$ of the lattice vector. The second operation results in the 240° rotation followed by a translation of another $2/3$ for a total of translation of $4/3$ or $1 \frac{1}{3}$. This translation results in moving into the neighboring unit cell. However, since all unit cells must be identical, whatever is located at $4/3$ must also be at $1/3$. The operations of the 3_2 screw axis are indicated in Figure 6.2 while the operations denoted with a ' are equivalent positions required by translation. The 3_1 and 3_2 screw axes represent counterclockwise and clockwise screws.

The four-fold screw axes are illustrated in Figure 6.3. Here the 4_1 and 4_3 screw operations are again a pair of opposite handed screws. The 4_3 operation translates through three cells for successive applications. There is also the 4_2 operation. This is a 90° rotation followed by a translation of half the cell vector. In this case, after two applications the translation has

moved exactly one unit cell length and has rotated 180° . This means that there must be another symmetry related object across the axis of rotation before any translation and is related by 180° as is illustrated in Figure 6.3. The 4_2 operation requires there be a 2 fold rotation along the same axis.

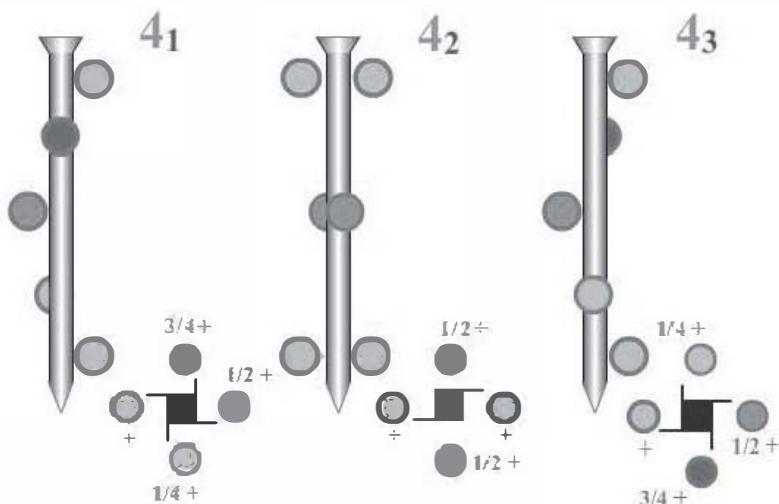


Figure 6.3 The four-fold screw axes

The six-fold screw axes work in similarly. The 6_1 - 6_3 and 6_2 - 6_4 axes are again opposite handed screws. For 6_2 or 6_4 operations after three successive operations there has been a cumulative rotation of 180° and a translation of one unit cell length. So like the 4_2 operation, there must be pairs of objects which creates a 2-fold rotation colinear with the screw axis. Likewise, two applications of the 6_3 operation produces a rotation of 120° and a translation of one unit cell. This requires that there be a three-fold rotation colinear with the screw axis.

6.2.3 Glide Planes

The combination of a mirror and translation produces a glide plane. The symbol for a glide plane defines the direction of the translation. For most glide planes the translation is $1/2$ the indicated vector length. The vector for translation is defined as a, b, c, or n. The first three are translations along the unit cell axis defined by the designated letter. The n-glide is a

translation of $1/2$ along the diagonal of the plane that makes up the mirror as shown in Figure 6.5. Notice, in H-M notation the actual direction of the perpendicular to the mirror has yet to be defined. However, this is no different from for any other operation introduced so far. In any case, the translation must be completely in the plane of the mirror and may not contain any component along the perpendicular.

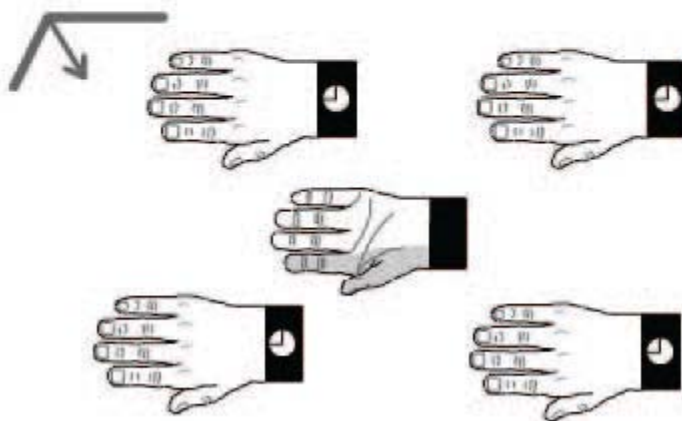


Figure 6.5 The n-glide. The translation is along the diagonal.

There is one other glide plane which does not appear frequently. This is called the diamond glide and is given the symbol d . The diamond glide can only occur in F or C centered cells (which will be discussed later in this chapter). The definition of the diamond glide is reflection through a mirror perpendicular to an axis followed by a translation of $1/4$ along the cell diagonal. An example would be a diamond glide perpendicular to c . This would change the coordinates x, y, z to $x+1/4, y+1/4, \bar{z}+1/4$ where \bar{z} is the same as $-z$. The current preferred nomenclature for indicating translations is to place the coordinate first and the translational quantity second. In the example above the change in z could also be reported as $-z+1/4$.

6.3 Symmetry and Unit Cell Types

6.3.1 Defining the Unit Cell Vectors

Point group symmetry is applied to a single object. For point groups, all the symmetry operations must pass through a single origin. In general, the coordinate system used in point group symmetry is the standard Cartesian coordinates. However, it is obvious that these axes only share the symmetry of the object if it has 1, 2, or 4-fold symmetry. If a three-fold rotation is applied along z , then the x and y axes do not go into themselves or swap but into combinations of the two. This is not a problem in dealing with point groups.

However, in crystallography the problem is more difficult. Even if the arrangement inside the unit cell contains no symmetry, there is the requirement that the axes possess translational symmetry. Therefore, when a rotation is applied it is mandatory that each axis a , b , and c go into either themselves or entirely into another axis. This means that the cell vectors will be consistent with the internal symmetry of the unit cell. This is why these axes may be non-equal in length and non-orthogonal. In addition, the cell must form a right-handed set of axes.

However, the cell parameters cannot contain all the information about the space group. First, a translation of one unit cell in either positive or negative direction will always be a valid translational symmetry operation. This applies to all three axes. The cell axes will fail to distinguish between the three types of rotation operations (proper and improper rotations and screw axes) or between the two reflection operations (mirror and glide plane). These fine details of the space group can only be obtained by determining the symmetry of the cell in either real or reciprocal space. However, there are conditions that the symmetry operations will force on the relationships between the cell axes. The unit cells can then be divided into cell classes depending on these relationships.

6.3.2 How Cell Parameters are Determined

In order to identify the cell class, it must be understood how the cell constants are determined on a diffractometer. While different algorithms are used by different manufactures, they all accomplish the same basic task. Only the input and output for these programs will be briefly discussed as the actual calculations are beyond the scope of this book.

In order to determine a unit cell, some diffraction data must be found. Assuming an area detector is used, then this is just a matter of collecting a few images. The exact locations of the observed data must be determined accurately. The problem is then one of finding a set of three reciprocal vectors such that the Miller indices of all the observed data are nearly integral. In fitting all the data a cell length may be adjusted by an integral value if all the hkl do not fit all the data. In addition, most software tries to find the smallest such vectors with angles as close to 90° as possible. The above assumes that all the data used in the calculation form one reciprocal cell grid. Some samples contain more than one axis system and special calculations are required to exclude the data from these other lattices from the cell calculation.

At this point in the cell determination a fitting procedure is employed. The object is to find cell constants that minimize the difference between the hkl's for the observed data (which may be fractional) and the ideal location based on integral hkl's. As part of this calculation, the values of the cell constants will change slightly and a standard uncertainty (s.u.) will be calculated for each parameter. The better the quality of the crystal and the better it is centered on the diffractometer, the lower the s.u. The parameters will have the values calculated which may be slightly off from those required by symmetry as discussed below. For example, in some symmetries angles are required to be exactly 90° . The values obtained from the indexing will be close (typically better than 0.01°). At some point either the software or the crystallographer must decide whether the parameters fit a cell class. Some software, allows for the fitting procedure to be reapplied with constraints so parameters will have exactly the correct values required by symmetry. In any case, the cell constants reported and used in calculations should have the values required by symmetry. If a parameter is required to have a specified value, its s.u. must not be reported as it does not have an error.

6.3.3 Cell Classes

6.3.3.1 Triclinic Cells

The triclinic class, also called anorthic, is the lowest symmetry. The two triclinic space groups contain either no symmetry or an inversion center. In either case, there are no restrictions on the cell parameters. Since there are many possible triclinic cells for a given set of reflections, there needs

to be a standard for the reported cell.³⁰ The standard triclinic cell has all the cell angles either acute or obtuse.

Many definitions for a triclinic cell use the following relationships for the cell parameters:

$$a \neq b \neq c \quad \alpha \neq \beta \neq \gamma \neq 90^\circ$$

It must be remembered that symmetry defines equivalent coordinates and cannot create non-equal conditions. Since, there are no restrictions on the cell parameters for a triclinic cell, it is possible that two parameters are nearly identical or that a cell angle is within error 90° . Such values would just be accidental and not a result of any symmetry.

6.3.3.2 Monoclinic Cells

In monoclinic cells there is a two-fold rotation and a mirror perpendicular to it (2/m). The convention is to make **b** this unique axis. Since this rotation axis must be perpendicular to the a,c plane, the angles α and γ must be exactly 90° . There are no symmetry restrictions on the beta angle and it therefore can take on any value. The standard monoclinic cell has an obtuse beta angle.

6.3.3.3 Orthorhombic Cells

The axes of an orthorhombic cell each display 2/m symmetry. This means that the cell must be composed of three mutual perpendicular basis vectors. There is no requirement on the lengths of the a, b, and c-axes, and they may have any value required to ensure translational symmetry. Since all three axes are two-fold rotations, there is no principal axis. The ordering assignment of **a**, **b**, and **c** will depend on the space group. The axes must be orthogonal requiring $\alpha = \beta = \gamma = 90^\circ$.

At this point it is interesting to ask how can an orthorhombic cell definitively be differentiated from a monoclinic cell where the beta angle is accidentally 90.0° . The answer is that it cannot be based only on the cell parameters. In fact a search of the Cambridge Structural Database found that there were 225 monoclinic cells where all three cell angles were within 0.01° of 90.0° . This works out to a percentage of 0.052%. It is most likely that a cell with different cell lengths which are orthogonal is orthorhombic. However, it always should be kept in mind that it could be monoclinic. The information that will finally differentiate the two cell

classes is the symmetry of reciprocal space which will be observed in the intensities of the data.

6.3.3.4 Tetragonal Cells

The tetragonal cell contains a four-fold axis along **c**. This requires that **a** and **b** be equivalent by symmetry and 90° from each other. In addition, the c-axis must be perpendicular to the ab-plane resulting in the requirements that $a=b$ and $\alpha=\beta=\gamma=90^\circ$. It should be emphasized that the 4-fold symmetry operation rotates **a** into **-b** and *vice versa*. However, it never directly interchanges **a** and **b**. An orthorhombic cell can have two axes that are accidentally equal and appear tetragonal.

6.3.3.5 Trigonal Cells

The trigonal cell is the three-fold equivalent of the tetragonal cell. Again the principal axis of rotation is along the c-direction. This requires the symmetry of the unit cell to be $a=b$, $\alpha=\beta=90^\circ$, and $\gamma=120^\circ$.

The angle of 120° causes several problems. First, there must be three axes in the plane perpendicular to **c** so that rotation always carries an axis into an equivalent axis. However, since a plane is two-dimensional, it can only contain two independent axes. The third axis must be a combination of **a** and **b** and is not often used in real space.

The second problem is determining the equivalent positions. In a tetragonal cell when any point (xyz) is rotated clockwise by 90° the result is (-yz). This is not so clear for the trigonal axes. In fact, a rotation of 120° transforms (xyz) to (-y,x-y,z). The derivation of this is more involved than needs to be presented here. The next chapter will provide where such information can be found.

6.3.3.6 Hexagonal Cells

The hexagonal cell has a six-fold axis along **c**. The unit cell vectors are identical to those of the trigonal class. This means that hexagonal cells can not be distinguished from the trigonal class simply on the basis of their cell parameters.

6.3.3.7 Cubic Cells

The highest symmetry cell is the cubic cell. Cubic cells are defined by having a 3-fold rotation axes along each of the cell diagonals. For one such diagonal the rotation will take x into y, y into z and z into x. The

other diagonals will involve one or more negative axis. In any case, the interchange of axes and the need for all diagonals to be three-fold rotations creates the requirement that $a=b=c$ and $\alpha=\beta=\gamma=90^\circ$. Cubic cells are the only class with Cartesian coordinates though the basis vectors do not have a length of one.

6.3.3.8 Rhombohedral Cells

The rhombohedral cell is frequently listed as a basic cell class. This cell represents a cube that has “collapsed” along one of the diagonals. The result is that the cell lengths are all the same as are the angles. However, in this case the angles are not required to be 90° and usually are not. Today rhombohedral cells are reported as centered cells (see next section) of the trigonal class and have trigonal cell parameters.

6.3.4 Cell Centering

Until now translational operations have only been allowed to translate between unit cells. All other symmetry operations are permitted to relate objects within a cell resulting in unit cells containing more than one formula unit. A cell without internal translational symmetry is referred to as a primitive cell and always represents the smallest possible volume for a cell. Primitive cells are indicated by their space group name beginning with a capital P.

Sometimes it is possible to increase the symmetry of the unit cell by adding internal translation. Such cells will then have some asymmetric units related by translations. This will increase the cell volume. If N is the number of translational operations added, then the volume will increase by the multiple $N+1$. Since centering is added only to increase the symmetry of the unit cell, the centered cell must possess a higher symmetry than the primitive cell. For example, adding centering to a monoclinic cell to transform to a centered monoclinic cell is not valid as it does not increase the cell symmetry.

It is important that the unit cell used and reported has the highest symmetry. The cell class not only defines the cell parameters and the number of asymmetric units but also the optical, electrical, mechanical, thermal, and other physical properties of the crystal. In addition, for the calculations to proceed correctly, it is important that all the atoms being refined be independent and not related by a symmetry element.

A well-known example of a centered cell is NaCl. This crystal is face-centered. In this case, there is an atom at each corner and one in the center of each face of the unit cell. However, the presence of an atom at the center of each face is not a requirement of centering. The four translations for a face-centered cell are x,y,z ; $x+1/2,y+1/2,z$; $x+1/2,y,z+1/2$ and $x,y+1/2,z+1/2$. These translations can be summarized as $(0,0,0)$; $(1/2,1/2,0)$; $(1/2,0,1/2)$; $(0,1/2,1/2)$ for each equivalent position. If the starting point is $(0,0,0)$ then these translations produce an atom at the center of each face. Most molecular crystals do not contain an atom at the origin so the effect of centering does not create an atom at the center of a face. Also, since there are three new translational symmetry elements the face-centered cell volume must be four times larger than the related primitive cell.

In Figure 6.4 a face-centered cubic cell is drawn with dashed lines while the rhombohedral primitive cell is represented with solid lines. The rhombohedral cell only contains one three-fold rotation axis while the resulting cubic cell contains four. The properties of a cubic cell are independent of direction (isotropic) while this is not true of a rhombohedral cell. The physical properties of an NaCl crystal require the cell must be cubic.

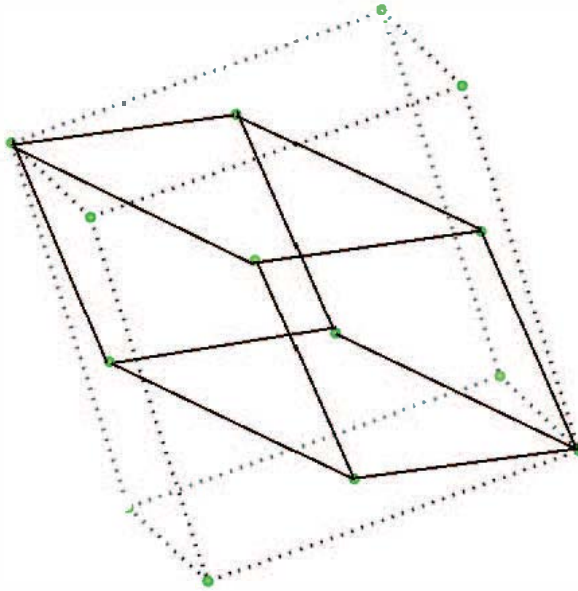


Figure 6.4 The primitive and F-centered cell.

There are five basic types of centering used. They are

ID	Type	Translations
A	a-centered	$(0,1/2,1/2)$
B	b-centered	$(1/2,0,1/2)$
C	c-centered	$(1/2,1/2,0)$
I	body-centered	$(1/2,1/2,1/2)$
F	face-centered	A+B+C

The position of the zero in the translation (if present) indicates the centering type. The zero for x for the translation creates an a-centered cell. The space group for a centered cell begins with the capital letter indicated by ID above. The space group for NaCl is $Fm\bar{3}m$.

When there is a glide plane in a face that is also a centered face, then the translation will create a second glide in that face. This is referred to as a double glide plane and in 1992 it was suggested such glide planes be labeled as an e-glide. This changed five space group names as follows

new name	Aem2	Aea2	Cmce	Cmme	Ccce
old name	Abm2	Aba2	Cmca	Cmma	Ccca

The new names are used in the latest tables of real space symmetry but have not caught on. Most programs continue to use the old names but one should be aware of both.

As mentioned above rhombohedral cells are no longer reported in the rhombohedral axes but as trigonal centered cells with rhombohedral (R) centering. The translations are $(2/3, 1/3, 1/3)$ and $(1/3, 2/3, 2/3)$. The resulting cell has a volume that is three times greater than the primitive cell.

CHAPTER 7

POINT GROUPS AND SPACE GROUPS

In this chapter a review of point groups will lead to the concepts of space groups. The point group symmetry operations and groups will use the Schönflies notation while the crystallographic Hermann-Mauguin notation will be in square brackets. The nomenclature will be reversed for space groups.

7.1 Groups

Before proceeding, the concept of a mathematical group must be understood. A group is a set of elements along with operators that convert a member of the group into another member of the group. The number of elements may be very much greater or less than the number of operations. There are four laws that define a group. First, any valid operation must transform one element of the group into another element that is also a member of the group. Second, the operations must be associative. This means $(a \rightarrow b) \rightarrow c$ must equal $a \rightarrow (b \rightarrow c)$ where the arrow represents an operation. Third, there must be an identity element in the group e such that $e \rightarrow a = a \rightarrow e = a$. Last, there must be an inverse element such that $a \rightarrow b = b \rightarrow a = e$. There is no requirement that the order of the operations be commutative *i.e.* $a \rightarrow b$ does not have to equal $b \rightarrow a$. Groups that are commutative for all operations are called abelian groups (which is the source of the physics joke Q: What's purple and commutes? A: An abelian grape).

A prime example of a group is the collection of all positive and negative integers. Only one operator addition will be considered. First, this group is infinite. Secondly, it is clear that it is abelian. The identity element will be zero. Adding two integers together will always create a new integer. If subtraction is used as the operation, then the integers still form a group but the group is not abelian since $3-2 \neq 2-3$.

Symmetry operations can form a group. The elements are the various equivalent orientations of the object. The operators are all the symmetry operations. If the symmetry operations are applied to a single object, it is called a point group. In this case the operations must all pass through a common origin located within the object.

7.2 Point Group Nomenclature

A collection of elements that defines all the symmetry in an object makes up the operations in a point group. Each point group has a Schönflies name. The first consideration is what is the highest rotation axis. If there is no rotation axis the point group will either be C_i [$\bar{1}$] or C_m [m] for an inversion center or mirror, respectively. If there is no symmetry, the point group is C_1 [1].

The principle axis is the rotation with the largest value of n . Once the principal axis is determined, the next question is are there 2-fold rotations perpendicular to this axis. If they exist, then the group name begins with D otherwise C . If there are mirrors that include the rotation axis and one of the other Cartesian axes, they are classified as v for vertical mirrors otherwise d for diagonal. If there are both v and d mirrors, v has preference. The other question is there a mirror plane perpendicular to the principal axis of rotation which is then labeled as h . For C type point groups the possibilities are C_n , C_{nv} or C_{nh} where n describes the principle axis of rotation. For D type groups the possibilities are D_n , D_{nh} , and D_{nd} . There are also point groups S_n where the principal axis is an improper rotation. Notice this shorthand will not contain all the operators but just those needed to distinguish between different point groups. There are also special space groups where there are more than one principle axis that is larger than two-fold. The two most common are T_d and O_h for a tetrahedron and octahedron.

Two examples will provide an example of naming the space group of a molecule. First, consider the V-shaped molecule water. There is a 2-fold rotation that runs through the oxygen and bisects the two hydrogen atoms. There is no horizontal mirror perpendicular to this rotation but there are two mirrors containing the rotation axis. One is the plane of the molecule itself and the other the plane that bisects the molecule. Since there are no 2-fold rotations perpendicular to the single rotation axis, this is an example of a C class. Since, the two mirrors are perpendicular and contain the

Cartesian axes, they are classified as vertical mirrors. Water is a member of the point group C_{2v} [2mm].

Next, let's examine the square plane. This might be a square piece of cardboard or a square planar ion like PtCl_4^{2-} . The principal axis is a four-fold rotation. There are two-fold rotations and a mirror plane perpendicular to this four-fold axis. Last, there are both vertical and diagonal mirrors. The point group therefore is D_{4h} [4/mmm].

7.3 Symmetry Operations and Equivalent Positions

Once the name of a symmetry group is known, the next thing to be determined is the symmetry operations that belong to this group. This is fairly easy since this information is listed at the top of a character table for the group. These tables can be found in any quick search of the web.

The first example will be the operations for C_{2v} . A web search for "character table C_{2v} " returned over 50,000 hits. The top line of the table is

$$C_{2v} \quad E \quad C_2 \quad \sigma_v \quad \sigma_v'$$

The C_{2v} is the name of the point group. The $E[1]$ is always the first element and is the identity operator. $C_2[2]$ is a two-fold rotation. It can be placed along any axis. For this example the y-axis will be the rotation. Note there is no $\sigma_h[m]$ operation so the two mirrors include the rotation axis. They are the xy and yz planes. Again, it makes no difference which plane represents which operation. There are several other things worth noting that will be important later in space group symmetry. Since this group does not contain the inversion operation $i[\bar{1}]$ it is non-centrosymmetric. There are four operations and this is the order of the group given the symbol h. Third, not all the operations are unique. The line formed at the perpendicular intersection of two mirror planes is always a two-fold rotation. Therefore, the two-fold rotation is created by the two vertical mirrors.

The second property of the group that is needed are the equivalent positions. These are the coordinates generated by symmetry for any point (x,y,z) . For C_{2v} these are not difficult to figure out. The identity operator does not change (x,y,z) . The 2-fold rotation along y takes x to -x, z to -z and does not change y. So the position (\bar{x},y,\bar{z}) is an equivalent position. If the first vertical mirror is the xy plane, this will generate an equivalent position of (x,y,\bar{z}) . Lastly, the yz plane will generate (\bar{x},y,z) . It should be

noted if we apply the two mirrors the result will be (\bar{x}, y, \bar{z}) or the same as the rotation. $((x, y, \bar{z})$ followed by (\bar{x}, y, z) .

The character table for the square plane is as follows:

D_{4h} E 2C₄ C₂ 2C₂' 2C₂" i 2S₄ σ_h 2σ_v 2σ_d

At first, it appears that there are only ten operations ($h=10$). However, the number two in front of some operations indicates there are two related operations. For example, the 2C₄ represents the counter-clockwise and clockwise 90° rotations or C₄¹[4] and C₄³[4³]. For spectroscopy and molecular calculations they are equivalent. However, for crystallographic purposes where they both are required to determine equivalent positions they need to be treated separately. The next C₂ is the 2-fold rotation along the 4-fold axis and represents C₄². The 2C₂' are rotations about the x and y axes while the C₂" are about the two equivalent diagonals. The mirrors along the respective directions that include the 4-fold axis are σ_v and σ_d, respectively. The operator i is inversion ($\bar{1}$) while σ_h (/m) is the mirror perpendicular to the principal rotation axis. Finally, the S₄ operations are the improper rotations along the 4-fold rotation axis. Remember, in spectroscopy an improper axis is a rotation followed by σ_h while in crystallography it is a rotation followed by inversion. If the number of operations is now counted including the number preceding the symbol h is equal to 16.

The equivalent positions can again be worked out by inspection. The counterclockwise four-fold rotation moves -y to x and x to y. For the two C₄[4] operations along z they are $(\bar{y} \ xz)$ and $(y \ \bar{x} \ z)$. The equivalent positions for the 2C₂" are (yxz) and $(\bar{y} \ \bar{x} \ z)$. Others can be worked out similarly or by doing simple drawings.

7.3.1 Trigonal/Hexagonal Axes

For the previous examples the equivalent positions could be readily determined from the symmetry operations with some thought. When Cartesian axes are used, the three-fold/six-fold equivalent positions can be derived from a formula that only requires the rotation angle and involves projections along x and y. However, in crystallography, these symmetries produce two axes related by 120° and the methodology for deriving the equivalent positions is much more difficult and cannot be done by inspection. The results for a C₃ [3] in the trigonal axes are

$$(x, y, z), (\bar{y}, x - y, z), \text{ and } (\bar{x} + y, \bar{x}, z).$$

The six-fold rotation will also require the additional equivalent position (\bar{x}, \bar{y}, z) . This is the two-fold rotation that is C_2 and each of the original three-fold position are multiplied by this. The result is to add three more positions

$$(\bar{x}, \bar{y}, z) | (y, \bar{x} + y, z) | (x - y, x, z)$$

7.3.2 Three-fold Axis Along Cell Diagonals

In cubic crystals the four diagonals of the cube are three-fold rotations. There will be one rotation that is located that bisects the **a**, **b**, and **c** axes and will change (x, y, z) to (y, z, x) and (z, x, y) . A second one will bisect $-x$, $-y$ and z and will give $(\bar{x}, \bar{y}, z), (\bar{y}, z, \bar{x}), (z, \bar{x}, \bar{y})$. The two others will begin with (\bar{x}, y, \bar{z}) and will follow the axis swapping used in the first two examples.

At first, it may appear odd that a three-fold rotation could swap the three Cartesian axes. However, a chemical example will illustrate how this works. Consider a tetrahedral molecule like methane. It is common to think of this shape as a trigonal pyramid. It can also be thought of as a cube with the carbon in the middle and the four hydrogen atoms at alternate corners of the cube. Therefore, the four carbon-hydrogen bonds are along the four diagonals of the cube. Since there is a three-fold rotation around each carbon-hydrogen bond, there must be one along each diagonal.

7.3.3 Improper Rotations

As mentioned previously, the definition for an improper rotation is different in point group and space group symmetry. For point groups the improper rotation is defined as a rotation followed by reflection through a mirror perpendicular to the rotation. Assuming the rotation axis is along a cell axis this reflection will simply negate (take x to $-x$) the rotation axis direction. In space group symmetry an improper reflection is a rotation followed by inversion. Inversion negates all three axes. The result is that the two designations for improper rotations have different equivalent positions.

The S_4 operation is a C_4 followed by σ_h . If the four-fold rotation is along z then the point group can be calculated by $(x,y,z) \rightarrow (-y,x,z) \rightarrow (-y,x,-z)$. On the other hand, the $\bar{4}$ results in $(x,y,z) \rightarrow (-y,x,z) \rightarrow (y,-x,-z)$. This is either a clockwise S_4 or an S_4^3 .

The situation is again more complex for the 3-fold and 6-fold improper rotations whose equivalent positions are listed in Section 7.3.1. First consider the $\bar{3}$ operation. Using the method in the previous paragraph it can be determined this operation results in $(x, y, z) \rightarrow (-y, x-y, z) \rightarrow (y, -x+y, -z)$. Just concentrating on the xy coordinates, it is observed that the final position is a 60° clockwise rotation. Therefore, $\bar{3} = S_6^5$. Likewise, it can be shown that $\bar{6} = S_3^2$.

7.4 Space Groups

While there are an infinite number of point groups, the number of space groups is limited to 230. Even with this restriction, the Schönflies notation is not adequate because it provides no way to label symmetry operations involving translation. In general, the point group of an object can be determined by inspection. The character tables list the symmetry elements in the point group and this is used to determine if the object belongs to that group. While space group symmetry could be determined this way, it very rarely is. It is usually found from the symmetry of reciprocal space to be discussed in the next chapter. The reverse of character tables for point groups, space groups tables list the equivalent positions and the symmetry operations must then be determined. The main source of space group symmetry is **The International Tables for Crystallography, Volume A (ITC-A)**³¹ which will also be discussed in greater detail in the next chapter. The equivalent positions for a space group can also be calculated using various programs.

7.4.1 Triclinic System

Typically, space groups, like point groups, are classified by their principal rotation axis or the axis perpendicular to a mirror. Since triclinic cells do not contain rotations or mirrors, no cell axis is included in the space group name. The two possible triclinic space groups either have no symmetry (P1) or an inversion center ($\bar{1}$)

7.4.2 Monoclinic System

Monoclinic cells have one unique axis. The ITC-A lists two settings for each monoclinic space group. The first setting has the unique axis along **c** while the second setting **b**. Today it is standard procedure to use the second setting unless there is strong justification. There is one symmetry code listed in a monoclinic space group name and it is along the unique axis.

A monoclinic space group name will begin with the capital letter indicating centering and then one symmetry designation. However, in order to indicate which axis is unique, the space group name may be expanded to a full name such as $P 1 2_1 1$ or $P 1 1 2_1$ to indicate the **b** or **c**-axis is unique, respectively.

7.4.3 Orthorhombic System

The space group for an orthorhombic cell will always contain three symmetry designations. The first one will be the symmetry along the **a**-axis, the second along **b**, and the third along **c**. If any operations include a rotation then it must be two-fold.

7.4.4 Tetragonal System

All tetragonal space groups must have a 4-fold rotation, improper rotation, or screw axis. After the centering identifier, there must be the number 4 in some form. Since the unique axis in a tetragonal cell is parallel to the **c**-axis, the first position in the Hermann-Mauguin symbol identifies the symmetry operations along the **c**-axis.

There are actually two classes of tetragonal space groups. The first has no two-fold rotations in the plane perpendicular to the **c**-axis or any similar mirrors. Space groups in this class have the single symmetry operations relating to **c**. An example would be $I4_1/a$.

The second class obviously has operations not allowed in the first class. Therefore, two additional symmetry designations need to be included. The second position indicates the symmetry involving the **a** and **b**-axes. Since, the four-fold rotation relates one axes into the other, they must contain identical symmetry operations and this element is the same for both axes. The last position describes any symmetry elements involving the two

diagonals $(1,1,0)$ and $(-1,1,0)$ in the ab -plane. Again since the four-fold relates one to the other they must be identical. A tetragonal space group in this class is $P4_2/mbc$. The $4_2/m$ indicates a 4_2 screw axis along c with a mirror perpendicular to it ($/m$). The second position b indicates a glide plane in the bc -plane with a translation along b . The fact that it is in the first position indicates the perpendicular to the plane is a . There must also be an a -glide plane in the ac -plane which in this case is a translation along a and which is perpendicular to the b -axis. The last position c indicates a glide plane composed of a plane containing a diagonal in the ab -plane and the c -axis. There must also be an equivalent plane rotated 90° about c from this plane. Again the notation covers two planes related by the four-fold rotation. In both cases the glide plane translation is along c .

In the low symmetry space groups monoclinic and orthorhombic the three positions (if used) in the Hermann-Mauguin refer to a , b , and c and define the direction of the symmetry operation. In higher symmetry, the first position is the principal axis of rotation which is c .

7.4.5 Hexagonal System

The hexagonal system space groups are very similar to the tetragonal system. The first position must always contain a 6. Again there are two classes. The first only has one symmetry element such as $P6/m$. In the other class there are two additional symmetry designations. The second element again defines the symmetry along the three axes (two independent) in the ab -plane. The third position can be understood by looking at Figure 7.1. For a hexagon, the negative of one cell axis bisects the other two positive axes. Therefore, there is no unique diagonal as in a tetragonal cell. In the drawing vectors connect the vertices of the hexagon. Three are the positive axes and three the negative axes. However, there is a second set of symmetry elements that connect the mid-point of the edges. There are three such axes that make a 30° angle with a and b . The planes that contains these new symmetry element can be classified as $(2,1,0)$, $(-1,2,0)$ and $(-1,1,0)$. The third symmetry position in the H-M name are c ; a , b and the third dependent axis; and the $(2,1,0)$ plane and those related to it by successive 120° rotations,

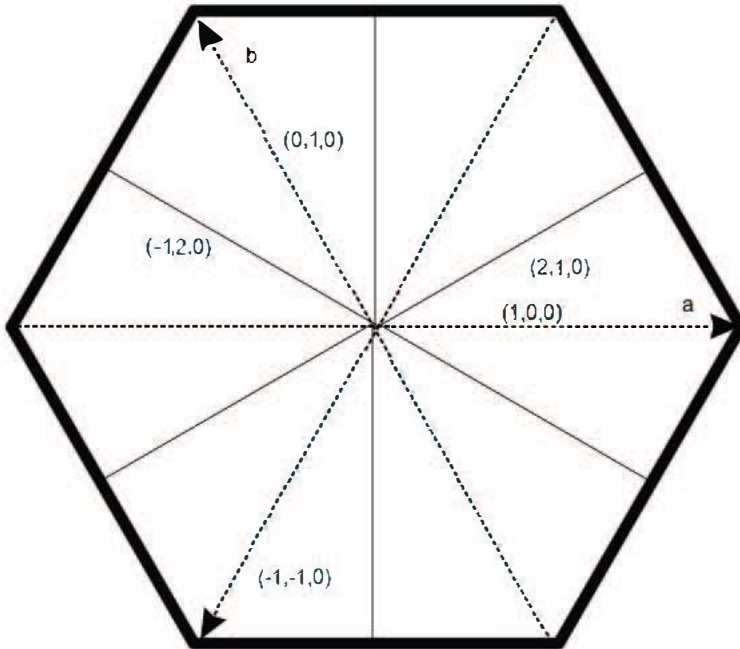


Figure 7.1 Symmetry Axes for a Hexagon.

7.4.6 Trigonal System

The Hermann-Mauguin notation for trigonal systems is nearly identical to that for the hexagonal system. The first position is again the principal rotation axis which will be parallel to c and have a 3 in it. Again one class of trigonal cells has only one entry after the centering symbol. If there are three entries, then they are as for the hexagonal system. The second position defines the symmetry about the axes while the third defines the symmetry about the $(2,1,0)$ and related planes.

However, there is a difference for the trigonal system. There can only be symmetry about the axes or bisecting planes but not both. Therefore, there is only one set of symmetry operations. This would suggest one class. However, either the second or third position will be a 1 indicating no symmetry. If there is symmetry along the axes then the third position will be 1 while if along the bisecting planes then the second position will be 1. These two situations can be told apart when looking at the symmetry of

the data. Therefore, it is convenient to consider them as two classes $\bar{3}m1$ and $\bar{3}1m$.

Today, rhombohedral cells are always reported in the trigonal R-centered form. They therefore will either belong to the class $\bar{3}m1$ as the third alternative is inconsistent with the R-centering.

7.4.7 Cubic System

The defining characteristic of all cubic cells is the presence of three-fold rotation symmetry along the four cell diagonals. The Hermann-Mauguin notation for cubic cells is quite different from any other lattice class. The key notation will be a 3 in the second position which defines the symmetry about the four equivalent diagonals. The first position will be the symmetry along the three equivalent axes while the third will be along the face diagonals. There are two classes of cubic cells $m\bar{3}$ and $m\bar{3}m$.

7.5 Unit Cell Translations and Equivalent Positions

If there is a center of inversion, this will nearly always be placed at the origin. Several high symmetry groups have two settings where the origins are different. For computational purposes, the one where the inversion center is at the origin is the one that is used. Therefore, the equivalent positions for an inversion operation are given as (x,y,z) and $(\bar{x}, \bar{y}, \bar{z})$.

However, the nature of fractional coordinates and the requirement that all unit cells be identical will generate additional inversion centers. This is because -0 is the same as 0 and $-1/2$ is the same as $1/2$ since adding or subtracting 1 creates an equivalent position. The result is that for the space group $P\bar{1}$ where the only symmetry is an inversion center there are eight independent coordinates for the inversion centers in the cell: $(0,0,0)$, $(1/2,0,0)$, $(0,1/2,0)$, $(0,0,1/2)$, $(1/2,1/2,0)$, $(1/2,0,1/2)$, $(0,1/2,1/2)$, and $(1/2,1/2,1/2)$. It must be emphasized that this works for inversion centers because this operation involves a single point. It cannot be directly applied to rotation or reflection operations.

Sometimes it is necessary to provide information about two atoms that are identical but related by an inversion center. If the two are related by an inversion center at the origin, then their positions will be given by (x,y,z) and $(\bar{x}, \bar{y}, \bar{z})$. However, it is possible they could be related by one of the seven other inversion centers. In this case, $(\bar{x}, \bar{y}, \bar{z})$ would not be the

position of the second atom. An example, assume an atom is located at $(0.45, 0.45, 0.45)$. The related atom by the origin inversion center would be $(-0.45, -0.45, -0.45)$. The distance between them would be 0.9 times the length of the diagonal of the cell. This is not likely to be a chemical bond distance. However, if 1.0 is added to the new position, the second coordinated are $(0.55, 0.55, 0.55)$. In this case the atoms are related by the inversion center at $(1/2, 1/2, 1/2)$ and are only 0.1 times the length of the diagonal apart. To specify how the new position was obtained it is necessary to define a new, non-standard equivalent position. To do this, the symmetry operation used and the translation applied needs to be provided.

There are two approaches used. In the body of a manuscript when distances and angles of symmetry-related atoms are mentioned, the new equivalent position must be specified explicitly. The specific code is referenced by a lower case superscript Roman numeral. In the example above, the atom at $(0.45, 0.45, 0.45)$ the atom might be labeled C5. Then the symmetry-related atom would be indicated in the text as 'C5ⁱ [symmetry code: (i) $-x+1, -y+1, -z+1$].' Once the symmetry code is assigned a number (in this example i) it can be used on any atom that is related by the same symmetry operation by simply appending the number as a superscript. If more codes are need they are labeled ii, iii, iv, ... and defined and used as needed.

Symmetry codes in the CIF file are handled differently. Every CIF has a loop of all the equivalent positions for the space group used. These will even contain the operations related by centering. At first this may appear to be redundant information but to create a new symmetry code the order of the list is important and may not be standard. For the space group $P\bar{1}$ the loop will be

```
loop_
```

```
_space_group_symop_operation_xyz
```

```
'x, y, z'
```

```
'-x, -y, -z'
```


Remember, a loop always requires a blank line to terminate it. There are two symmetry operations listed here where identity would be considered 1 and inversion 2. The numbers are obtained from the order of the lines. To make a symmetry code, first the number of the symmetry operation is listed. If there is no translation, then this number is the entire code. The translation is indicated by three integers after the number separated by an underscore (`_`). These numbers are the translations with 5 added to them. This is done so that the integers will always be positive for ten cells in each direction. Therefore, in the example above the CIF translation code would be `2_666`. The 2 specifies that symmetry operation 2 was used. The 666 becomes 111 after subtracting the offset of 5 which is a translation of one along each cell axes.

7.6 From Point Group to Space Group

It is interesting to see how point groups can be expanded into space groups. Figure 7.2 is a diagram for $4/mmm$ (D_{4h}). As shown previously, this group contains 16 symmetry operations ($h=16$). The figure illustrates the minimum number of operations to define the group. The square at the center represents the 4-fold rotation perpendicular to the plane of the drawing. This includes the 2-fold rotation that is part of the four-fold. The bracket at the lower right indicates the plane of the drawing is a horizontal mirror $/m$. The two axes and two diagonals along with the axis of rotation form four vertical mirrors. All the other symmetry operations can be generated by combining the operations in the drawing. Any object that will fit at the center and contains all the indicated symmetry can then be assigned at a minimum to the group $4/mmm$.

Just fitting this pattern does not prove the object has $4/mmm$ symmetry. The object could have additional symmetry operations not in this group. When the symmetry of an object is reported it is always the highest possible symmetry that is used. For example, an octahedron would contain the $4/mmm$ symmetry but in addition has many additional elements. Thus, $4/mmm$ is not the highest symmetry for an octahedron. However, $4/mmm$ is a sub-group of the full symmetry.

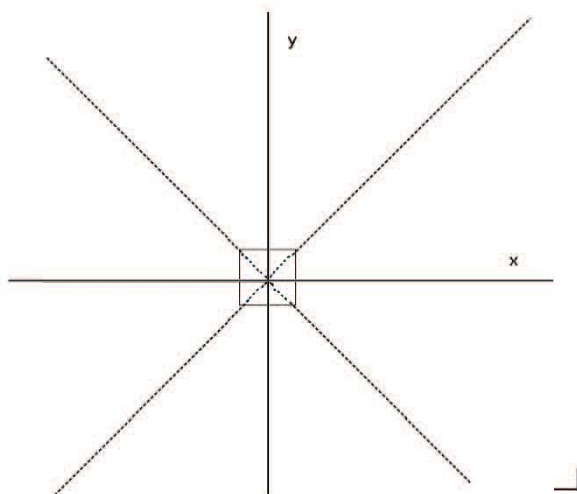


Figure 7.2. The point group $4/mmm$

Obviously, when dealing with point groups, the object must be located at the origin. Space groups have no such requirement. For example, how could water be placed in a cell with $4/mmm$ symmetry? Obviously, it cannot be placed at the origin as there is no four-fold rotation in a water molecule. However, four water molecules could be placed as shown in Figure 7.3 (note: water does not normally crystallize in a tetragonal cell—this is just for educational purposes.). The two-fold rotation of the water aligns with the two-fold rotation along the axes. In addition, the mirrors in the water share the mirror planes of the space group. The water is located at a position where some of the symmetry of the space group and the symmetry of the molecule are shared. It is said to be located at a special position. The special position in this example has the full symmetry of water or $2mm [C_{2v}]$. As a consequence of this arrangement there is only one unique hydrogen atom as the second is related by symmetry. Therefore, the two \bullet -H bond distances must be identical. In addition, there is only one unique water molecule in the cell. The other three are all related by applying symmetry operations.

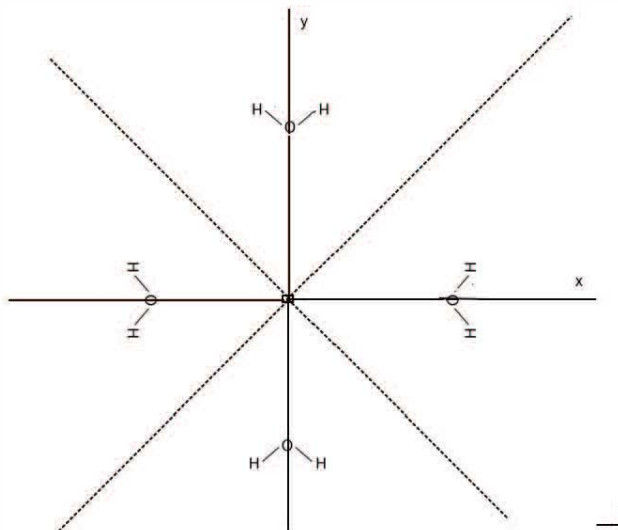


Figure 7.3 Water arranged in $4/m\bar{3}m$ on a $2mm$ special position.

A few terms need to be defined. The number of formula units in the unit cell is given by Z which in this case is $Z=4$. The definition of Z depends on how the formula unit is defined. As an example, consider a molecule that hydrogen bonds to a symmetry-related molecule to form a dimer in the crystal. If the monomer is used as the formula unit, Z will have one value while if the dimeric formula is used, Z will be half of the value for the monomer. The asymmetric unit is the unique part of the cell which is transformed by the cell's symmetry operations to produce the full cell. The number of asymmetric units in a unit cell is equal to h the number of symmetry operations. The parameter Z' is the number of formula units in the asymmetric unit and is equal to Z/h . For the proposed water structure $Z'=0.25$ ($4/16$). When Z' is less than one it means the molecule resides on a special position. Z' can also be greater than one which means there is more than one formula unit in the asymmetric unit.

Figure 7.4 shows a second arrangement of eight water molecules in the $4/m\bar{3}m$ space group. In this case the molecules have been moved off the axes but share the plane of the paper. Since Z' in this case is 0.5 , the molecule is still located at a special position with site symmetry of m . A plane of the water molecule is in the $/m$ plane of the space group. There are now two independent hydrogen atoms and the two O-H bond lengths

can be different. However, if the water molecules are rotated by 90° around the vector that bisects the H-O-H angle, then the two hydrogen atoms are now related by the $/m$ mirror. In this case there is again one unique hydrogen atom and only one O-H bond distance.

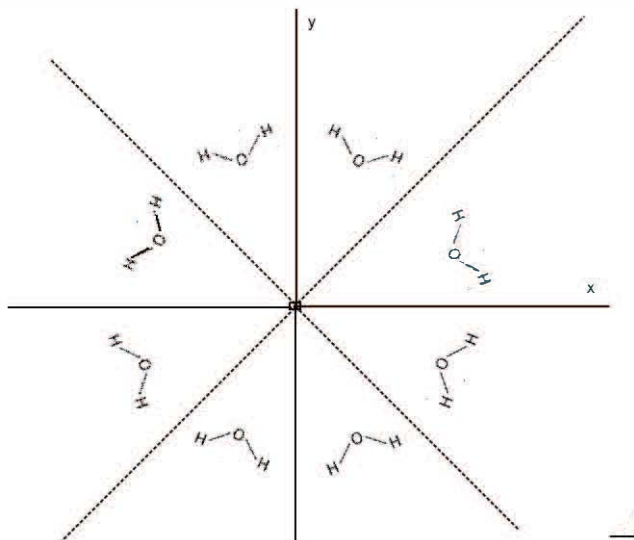


Figure 7.4 A different arrangement of water in $4/m\bar{3}m$ on an m special position.

The last case is to move the eight molecules below the $/m$ mirror and add eight additional water molecules above, so they are related by the mirror. In this case $Z=16$ and $Z'=1$. The site occupied by the water molecules now has no crystallographically imposed symmetry and is called a general position. Any molecule can be positioned at a general position since the site symmetry is 1. If a molecule is located at a general position, then all the geometrical parameters are independent.

The site symmetry is very important if physical properties are studied in a crystal. The crystal will act as a perturbation to the isolated molecular symmetry. Many times symmetrical molecules do not crystallize at sites with high symmetry. An example is benzene. Benzene has a six-fold rotation axis and six equal C-C bonds in the gas phase and might be expected to crystallize in a hexagonal cell. In fact, benzene crystallizes in an orthorhombic cell and is centered on an inversion center.³² The C-C

bond lengths in the initial report were 1.39(2), 1.37(7), and 1.39(5). The reduction of symmetry can have consequences in the spectroscopy. States that are doubly degenerate in the isolated molecule may be split by the crystal symmetry. This can result in the spectrum displaying split peaks. This perturbation is frequently referred to as solid state effects.

7.7 A Detailed Look at the Space Group P2₁/c

The space group P2₁/c is the most common space group for molecular compounds. Structures in this space group account for 34.4% of the entries in the Cambridge Structural Database.³³ In this section, the symmetry for this space group will be studied in detail and various methods which can be used to analyze any space group will be applied.

The four equivalent positions for P2₁/c where **b** is the unique axis from the ITC-A are

$$(x,y,z) (\bar{x},y+1/2,\bar{z}+1/2)(\bar{x},\bar{y},\bar{z})(x,\bar{y}+1/2,z+1/2)$$

The first thing to do to analyze any space group is to remove the translations which reduces it to a point group. The equivalent positions then become

$$(x,y,z) (\bar{x},\bar{y},\bar{z})(x,\bar{y},z)$$

These can be assigned as follows:

1. Identity: 1 [E]
2. A two-fold around **b**: 2 [C₂]
3. An inversion center: $\bar{1}$ [i]
4. A mirror perpendicular to **b**: /m [σ_h]

These operations define the point group as C_{2h}. There are several monoclinic space groups that belong to this point group. This is one of the reasons Schönflies notation is not used in space group notation.

The translations removed in the first step can now be replaced. Since the name P2₁/c indicates that there is a 2₁ screw axis along **b** and a c-glide in the plane perpendicular to **b**. The screw axis consists of a two-fold rotation followed by a translation of 1/2 along **b**. The glide plane is a mirror

followed by a translation of $1/2$ along \mathbf{c} . Adding the translations to the second and fourth positions gives $(\bar{x}, y + 1/2, \bar{z})$ and $(x, \bar{y}, z + 1/2)$. When compared to the original positions they do not agree. The second result is missing a $+1/2$ on z while the last one is missing $+1/2$ on y .

To understand the origin of these added translations, the location of the symmetry elements must be determined. Since this is a space group, there is no requirement they pass through the origin. Start with the c -glide. The position given above would be correct if the mirror plane was $(x, 0, z)$. However, this is not the case. The plane is actually located at $(x, 1/4, z)$. Therefore, reflection through the mirror changes the y coordinate unless its value is 0.25 , Figure 7.5 illustrates a mirror at $y=1/4$. In this case reflection results in the y value changing from its original value to $-y+1/2$ where $1/2$ is twice the mirror offset. In general, if a mirror is perpendicular to an axis at a coordinate p , reflection will result in a coordinate of $2p$ minus the original coordinate. A similar argument can be made for the screw axis which has the coordinates of $(0, y, 1/4)$ which will produced in $-z+1/2$. When these corrections are applied the reported coordinates are duplicated.

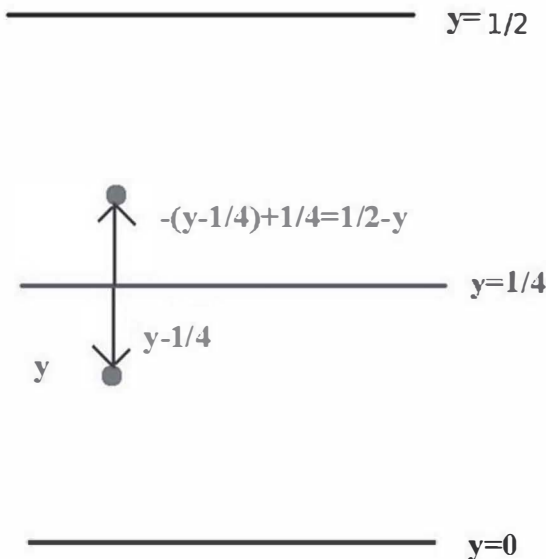


Figure 7.5 A Mirror offset at $y=1/4$.

CHAPTER 8

SYMMETRY IN RECIPROCAL SPACE

In this chapter, the effects of symmetry on the intensity data will be examined. Space group pages from the **International Tables for Crystallography, Volume A** will be studied.

8.1 Centric vs Acentric Cells

An important distinction in collecting data and assigning space groups is whether the space group has a center of inversion. Up to this time it has been assumed that the only source of the diffraction intensity is the interference of scattered photons as developed in Chapter 2. If this were true then the diffracted intensity would have the relationship $I(hkl) = I(\overline{hkl})$. This is Friedel's Law. However, there is a second weak source of intensity which is referred to as anomalous scattering. The source of this intensity is absorption followed by the emission of a photon. Since these photons will most likely be out of phase with the scattered photons, they will change the intensity because of interference. In centered cells this phase change is canceled out by symmetry. However, in acentric cells it must be accounted for. Friedel's Law does not strictly apply in acentric cells. However, the contribution of the anomalous scattering is quite weak and $I(hkl) \approx I(\overline{hkl})$.

Many space groups occur as centric--acentric pairs where the difference in the symmetry operations is the inversion center. Examples of pairs of space groups are $P\overline{1} - P1$, $C2/c - Cc$, and $Pnma - Pna2_1$. Unfortunately, the effect of anomalous scattering is usually not strong enough to distinguish between the pairs of space groups. To refine the structure, the actual space group must be known. There are statistical methods that are used to determine centricity, but they require knowledge of the chemical

formula to be successful. Newer *ab initio* methods can determine the space group as part of the initial calculations.

Some further comments on centric–acentric space group identification. Centric cells are more common unless the molecule is enantiomorphic and pure.³⁴ Therefore, if in doubt start with the centric group. If the structure refines in this space group, it is proof that the cell is centric. Orthorhombic pairs such as Pnma-Pna2₁ cause problems because the ordering of the cell axes is different in the two space groups. In the case cited the **b** and **c** axes as well as **h** and **k** for each reflection need to be exchanged. Some centric space groups such as P2₁/c have no acentric equivalent which makes space group identification much easier.

8.2 Equivalent Reflections

The symmetry of reciprocal space is directly related to that of real space with some changes. First, in reciprocal space all the symmetry elements pass through the origin. Also, translation in real space does not apply in reciprocal space. However, the translational elements in real space do create systematic presences/absences which will be discussed in the next section. The general positions can be equated to reflections with equal intensity. In P2₁/c the four equivalent positions ignoring translation are (x,y,z) (\bar{x},\bar{y},\bar{z})(\bar{x},\bar{y},z)(x,y,z). Therefore, the reflections hkl, ($\bar{h}\bar{k}\bar{l}$), ($\bar{h}kl$), and ($h\bar{k}l$) all should have equal intensity. Of course, there will be some statistical variation caused by the uncertainty.

In general there is a 1:1 correspondence between (xyz) and (hkl) with the exception again being trigonal/hexagonal cells which will be discussed later. The equivalent positions in real space will produce data with identical intensity for related values of hkl. An example of this is Friedel's Law where (xyz), ($\bar{x}\bar{y}\bar{z}$) produces the equivalent conditions noted above. These equivalences allow for the assignment of the proper class to a data set independent of the cell constants. For example, it was mentioned in Chapter 6 that a monoclinic cell could have a beta angle of 90°. A monoclinic cell has only a mirror which is perpendicular to the b-axis. Since the equivalent positions for the mirror are (xyz) and ($\bar{x}\bar{y}z$) then the data must reflect the relationship $I(hkl)=I(\bar{h}\bar{k}l)$. The axes **a** and **c** have no symmetry and no relationships. An orthorhombic cell has mirrors perpendicular to all three axes resulting in $I(hkl)=I(\bar{h}\bar{k}\bar{l})=I(h\bar{k}l)=I(\bar{h}kl)$. If the data for a cell which appears to be orthorhombic has only one mirror and not three, then it is monoclinic. Of

course there is no certainty that the unique axis will be **b** and it is possible that the axes will have to be interchanged.

Equivalent positions for trigonal/hexagonal cells are frequently reported using an additional index labeled *i* along with *hkl*. The value for *i* is always $-(h+k)$. Older data sometime reported the indices as (*hkil*).

The cell class is today determined at various stages either on the diffractometer or when processing the data. The programs that make this analysis are intelligent and rarely make a mistake if the data are of reasonable quality. An old, stand-alone program for determining the cell class for a data file in SHELX format is LAUE by Louis Farrugia and was originally part of the WinGX package.³⁵ The Fortran source code is freely available from the IUCr Crystallographic Software Museum³⁶ and when run, nearly instantly gives information that allows for the class to be determined.

Some comments need to be made before displaying output from LAUE. The name comes from a time when what has been called the class in this text was called the Laue Class. However, the definition of a Laue Class has changed since this program was written.³⁷ Today there are only two trigonal Laue Classes $\bar{3}$ and $\bar{3}m$ not the three previously discussed or listed in the LAUE program output. The term Laue Class has been avoided. The second concept is that of an R-factor. An R-factor is a decimal fraction or percentage indicating the ratio of a difference in values divided by the sum of a value used in the calculation. In this case, the R-factor is *R*_{merge} which was once known as *R*(int). The formula for *R*_{merge} is $\sum_j (\sum_i (I_j) - \langle I \rangle) / \sum_i (\sum_j \langle I \rangle)$ where *i* is over every reflection in the data set and *j* is over every symmetry equivalent observation, *I* is the intensity of each reflection and $\langle I \rangle$ is the mean of the intensity of the set of equivalent reflections of *j*. In other words the numerator is the difference between the reflection and the mean value for all the intensities that should be equivalent and the denominator is the sum of the mean intensities. For a good data set *R*_{merge} is less than 0.12.

The output from program LAUE can now be evaluated. The program calculates *R*_{merge} using the equivalent reflections of each class. For the data reported here the cell parameters were *a*=*b*=33.151, *c*=16.683Å,

$\alpha=\beta=\gamma=90.0^\circ$. These parameters appear to define a tetragonal cell. The LAUE output is

Laue class	R(int)	N(obs)	N(ind)
-1	0.072	23307	9773
2/m	0.601	24926	5787
mmm	0.617	24987	3278
4/m	0.094	24994	3174
4/mmm	0.626	24994	1685
-3(rhomb)	0.411	24062	8720
-3m(rhomb)	0.748	24990	5002
-3(hex)	0.544	23995	7030
-3m1(hex)	0.772	24984	4160
-31m(hex)	0.772	24991	4129
6/m	0.551	24882	4362
6/mmm	0.781	24996	2369
m-3	0.761	24998	2733
m-3m	0.768	24996	1454

Highest diffraction symmetry with reasonable $R(\text{int}) = 4/m$

Here Laue Class is the old definition. It can be seen that the $R(\text{int})$ (R_{merge}) value for -1 (triclinic) is acceptable. Since triclinic cells can at best only have an inversion center, every data set will merge well to -1. Notice 2/m (monoclinic) and mmm (orthorhombic) have large values for $R(\text{int})$. In fact the only value that is acceptable is for the class 4/m. Indeed, this cell was solved in the space group $I4_1/a$.

A second use of the equivalent data is to minimize data collection. Data are classified as being in one of eight octants which are as follows: $[hkl], [\bar{h}kl], [h\bar{k}l], [hk\bar{l}], [\bar{h}k\bar{l}], [\bar{h}k\bar{l}], [h\bar{k}l], [h\bar{k}l]$. If a cell is centric, then the first four octants are related to the second four by the inversion center (each value of h , k , and l is multiplied by -1). Therefore, it is only necessary to collect four octants and not eight. Of course, it must be assured that the four octants collected do not contain equivalent data. Diffractometers today have excellent algorithms for determining efficient data collection. Some laboratories write their own data collection routines. With the speed of data collection now only hours, there is no reason not to collect all eight octants if diffractometer time is available. In most cases this will produce a large amount of redundant (equivalent) data. However, having redundant data will produce data with greater precision and smaller

s.u.'s for the refined parameters. At some point the intensity of redundant data will be merged so that only a single value is used in the calculations.

8.3 Systematic Presences and Absences

8.3.1 Centered Cells

The effect of any symmetry operation involving translation on the reflection data is to cause some reflections to have zero intensity. This will create a set of reflections that will all have certain related hkl values where the intensity will be zero. The hkl conditions that result in zero intensity are called systematic absences while the observed relations are referred to as systematic presences.

The best example of why these absences occur is found in centered cells. In a primitive, centric monoclinic cell there are four asymmetric units. If there is only one formula unit in this asymmetric unit then $Z=4$ and $Z'=1$. In a C-centered monoclinic cell there are an additional 4 asymmetric units created by the centering. For this cell, Z will be eight but Z' still is one and only one formula unit must be structurally characterized. In order to contain the additional formula units the cell volume must double. The number of unique reflections for a crystal is proportional to the volume of the cell. This suggests that the C-centered cell will provide twice as many data as the primitive cell. However, the number of atoms to be refined will be the same. Centering cannot double the data to parameter ratio (this ratio is defined as the number of unique data used in the refinement divided by the number of parameters refined). If this were the case more data could be obtained by simply doubling any cell length which is clearly not true.

Figure 8.1 shows a primitive a, b and its centered cell A, B equivalent. The following is derived from Ladd and Palmer.^{3*} It can be seen that

$$A=a+b \text{ and } B=a-b$$

The indices H and K will refer to the centered cell and h and k to the primitive cell. If the indices behave like the axes then

$$H=h+k \text{ and } K=h-k.$$

If the two indices are added, $H+K=2h$. For a cell centered on a face, the sum of the two indices in that face must always be even.

C-centering produces a systematic presence of hkl , $h+k=2n$ or the equivalent systematic absence of $h+k=2n+1$. Therefore, for any hkl , the data will only have a non-zero value when $h+k$ is even. This is an example of a systematic presence. Because of the systematic presence only half the data will have a non-zero intensity and the data/parameter ratio will be the same as for the related primitive cell.

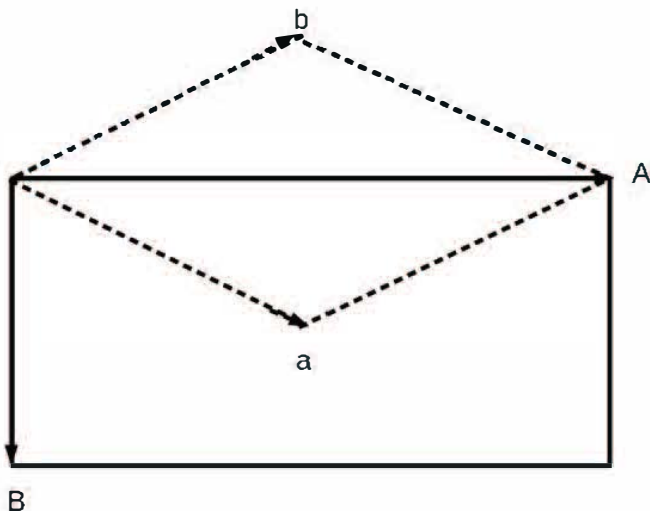


Figure 8.1 Centering in 2-dimensions.

The systematic presences for various types of centering which effect all hkl are:

A-centered: $k+l=2n$ B-centered: $h+l=2n$ C-centered: $h+k=2n$

I-centered: $h+k+l=2n$ F-centered: A +B+C centered

R-centered: $-h+k+l=3n$

8.3.2 Other Systematic Presences

Since glide planes and screw axes both contain a translational component, they will result in systematic presences. Unlike centering, these effects will only be observed for certain sets of reflections. For a glide plane the absences involve the set of reflections that has a zero value of the Miller index that corresponds to the axis perpendicular to the plane. For example,

for a c-glide in a plane perpendicular to **b** the hkl values affected will be (h0l). If the translation is 1/2 along c then the total systematic presence is given by h0l, l=2n. The 0 occupies the Miller index equivalent to the axis perpendicular to the mirror. The index in the presence represents the axis that is the direction of the translation. For an n-glide, the presence is indicated by the sum of the two h, k, or l values that form the diagonals in the mirror plane. Assuming the plane described above was an n-glide then the systematic presence would be h0l, h+l=2n. A d-glide will work similarly except since the translation is 1/4 of the diagonal length the condition would be h0l, h+l=4n.

Screw axes absences are akin to glide planes. The class of hkl that is affected by the screw has two zeros and affects values for the index that is along the screw axis. For a 2₁ screw along **b** the 0k0 data will be affected. The value of n used for each screw axis is as follows

$$2_1 \quad 2n$$

$$3_1 \ 3_2 \quad 3n$$

$$4_1 \ 4_3 \quad 4n$$

$$4_2 \quad 2n$$

$$6_1 \ 6_3 \quad 6n$$

$$6_2 \ 6_4 \quad 3n$$

$$6_3 \quad 2n$$

Therefore, the 2₁ screw axes along **b** has the systematic presence 0k0
k=2n.

8.3.3 Manual Space Group Determination

As pointed out, only glide planes and screw axes provide systematic presences which can be used to determine the space group of a unit cell. Fortunately, most molecular structures crystallize in space groups which contain such symmetry operations. Therefore, usually the space group can be narrowed to two or three choices.

The simplest way to do this is record any systematic pattern observed for the following sets of hkl for monoclinic and orthorhombic cells (triclinic only has an inversion center and no systematic pattern)

$hkl, 0kl, h0l, hk0, h00, 0k0, 00l$

A pattern based on hkl with two zeros is not always indicative of a screw axis. This is because a glide plane that has a presence of $h0l \ 1=2n$ will include $00l \ 1=2n$ which appears to be a screw axis. For tetragonal cells an additional check must be done on hhl. For trigonal hexagonal cells the sets are hkl, $h\bar{h}l$ and hhl. For cubic cells hkl, 0kl and hhl are examined. However, for cubic cells a, b, and c are all identical so 00l also means h00 and 0k0, etc. Generally because of the high symmetry, cubic data sets are quite small and there is no certainty that h00, 0k0, and 00l will all be present in the data.

In trying to determine the space group several things must be kept in mind. The reflections to be examined will be spread throughout the data listing. If the data set is stored as a computer file, it may be possible to do several sorting operations to simplify finding the needed data. This requires knowledge of file sorting methods. The second point is that the systematic absences are unlikely to have intensities of exactly zero. This is especially true for data collected at low Bragg angles. The problem then is to determine which reflections are actually absences. This is done by using the sigma (s.u.) of the data. The ratio of the intensity to its sigma ($I/\sigma(I)$) is used as a statistical indicator. At a very minimum this ratio should be greater than three to be considered non-zero. This is frequently referred to as three sigma data. For heavy atom structures a cutoff of up to ten sigma may be appropriate. In the end, the appearance of a pattern should be given equal importance to just the intensities. However, crystals containing very heavy atoms may display pseudo-symmetry. This is because the symmetry involving just the heavy atom may be quite a bit higher than the overall crystal. If a significant number of the expected absences have intensities greater than three sigma, this may be the case. It takes some experience to evaluate the pattern of the absences.

Another common problem is evaluating the absences for a screw axis along a short unit cell length. Generally data along a cell are collected to an index of one or two greater than that cell length. Imagine a monoclinic cell with a b length of around 5Å. The data collected along b will be (010), (020), (030), (040), (050), (060), and maybe (070). Note there are only three or four reflections which have odd indices and could be the

basis for systematic absences. Frequently, the intensity of the (010) reflection may be slightly greater than 3σ , meaning there are only two or three data to establish the pattern. It is possible to fail to identify this pattern.

Once the patterns are established there are several ways to proceed. The absences can be used to establish screw axes and glide planes and their direction. However, this requires remembering what the expected conditions are. **The International Tables for Crystallography Volume A (ITC-A)** provides a table to help determine the space group. This is Table 3.1.4.1 which is divided by cell class. One can take the systematic presences and look for them in this table and it will provide the space group name and number for all the possible space groups that fit this pattern.

Orthorhombic cells present one additional problem. Whether done by hand or using the ITC-A there is no guarantee that the ordering of the axes from the data collection is correct for a standard cell. In fact, the table in the ITC-A provides the name of the non-standard cell but the correct space group number. These axes will have to be interchanged so that the space group is a standard one.

8.3.4 Automatic Space Group Determination

If humans have problems determining a space group, so will computers. There are many programs that will analyze the data and suggest a space group. These will also provide the information about the various classes of hkl examined. Programs that prepare the input for structure solution and refinement frequently perform space group analysis. An example is the program XPREP which is used to create input files for the SHELX programs which is part of the SHELXTL package. There are also stand-alone programs such as PLATON and ABSEN³⁹ which will use a SHELX formatted reflection data file and refinement input files to determine the space group. In addition, the program will either convert the cell constants and hkl's of orthorhombic cells so they are in the standard space group or provide input that can be used to change the indices during refinement.

The problem of determining the true absences is harder for a computer program than a human. There are two basic approaches used. In the first, the program stores the probability distribution for each space group. That information can then be used for borderline systematic absences to weight

the result to the most probable space group. This approach is used in XPREP. The other approach is to use a fairly high value of $I/\sigma(I)$ such as ten. Then if even a single reflection violates a systematic absence, the absence is considered not to exist. This is the method used in ABSEN. Both methods can produce incorrect space group determinations. If there is some question as to the correct space group, it is advisable to try more than one program.

Occasionally a data set fails to provide any space group or suggests a space group that does not contain any systematic presences. For molecular crystallography, it will not be possible to determine the structure in the recommended space group. This always indicates a problem. The data will rarely be of such low quality that the absences cannot be determined. If the lattice appears to show higher symmetry the crystal may be twinned. A discussion of twinned crystals will be given in Chapter 14.

8.4 The International Tables for Crystallography

The standard source for information about space group symmetry is **The International Tables for Crystallography-Volume A (ITC-A)**. There are many tables and discussions that provide detailed information needed for working with space group symmetry. Probably the most referred to pages are those providing information about each of the 230 space groups. In addition, for some space groups information is given on alternative settings and symmetries.

The **ITC-A** is an essential reference for anyone who does crystallographic experiments. There are several ways to access the **ITC-A**. The volume can be purchased from many sources. It is also possible to purchase on-line access from the IUCr. This is then used like any on-line journal. Lastly, it is possible to purchase a brief teaching edition.⁴⁰ This contains the most commonly used tables and space groups. However, since it is not complete, it is possible that needed information will be missing.

The pages providing data on $P2_1/c$ are reproduced in Figure 8.2. The top line lists the short name for the space group ($P2_1/c$), the name in Schönflies notation ($C2h^5$ where the 5 indicates it is the fifth space group in that symmetry), the crystal class ($2/m$), and the lattice class (monoclinic). The second line contains the unique space group number (14) for $P2_1/c$, the full Hermann-Mauguin name ($P1\ 2_1/c\ 1$), and the Patterson map symmetry (see Chapter 11.3.3). The next line provides some additional information. In this case it states the unique axis is **b** and

the cell choice is the first of several possibilities. Below this are several diagrams which can be complex and will not be explained here. Below the diagrams are two interesting pieces of information. First, is that the origin is located on an inversion center and secondly that an asymmetric unit is defined by the $0 \leq x \leq 1$; $0 \leq y \leq 1/2$; $0 \leq z \leq 1/2$.

The second page provides the details of the space group symmetry. The first columns are labeled Multiplicity, Wyckoff Letter, and site symmetry. The multiplicity indicates how many times an atom at the given coordinates will occur in the unit cell. The Wyckoff Letter is a designation of the symmetry element. While it is not used much in chemical crystallography, it is still used in geological and solid state crystallography. The site symmetry is the symmetry operation at the coordinates defined.

The first line in this table is always for the general position. Therefore, the order h will be equal to the number of symmetry operations in the space group and the site symmetry will be 1. Next comes the equivalent positions for an atom located at this site. Finally, the systematic presences will be listed at the far right. In this case they are $h0l$: $l=2n$, $0k0$: $k=2n$, and $00l$: $l=2n$. The first presence is from the c -glide while the second is from the screw axis. The condition on $00l$ is not unique but part of the glide plane.

The following lines are the information for the special positions. For $P2_1/c$ the only special positions are inversion centers ($\bar{1}$). As previously discussed there are eight of them only in this case symmetry in the space group combines them into four pairs. Generally, the systematic absences for these special positions can be ignored as they rarely come into play for molecular crystals.

Figure 8.3 lists alternative cell choices for $P2_1/c$; $P2_1/a$ and $P2_1/n$. $P2_1/a$ is $P2_1/c$ with the a and c -axes interchanged. This is not considered a standard space group and the axes and cell constants should be interchanged. $P2_1/n$ is more complex. Most diffractometer indexing programs try to produce a unit cell which is as close to orthogonal as possible. This can result in a monoclinic cell where the c -axis is not the direction of the glide plane instead the diagonal of the ac -face. Since a glide along the diagonal of a plane is an n -glide, the space group becomes the $P2_1/n$. In this case, the c -axis length and the beta angle will be different from the cell where the glide plane translation is along c . The directions of the translations are typically not known until after the data collection is completed and the

space group determined. While $P2_1/n$ can be converted into $P2_1/c$, it is not straightforward to calculate the cell constants for the new space group. Therefore, the use of the n-glide in place of the c-glide is accepted as a standard for monoclinic crystals.

International Tables for Crystallography (2006). Vol. A. Space group 14, pp. 184–191.

$P2_1/c$

C_{2h}^5

$2/m$

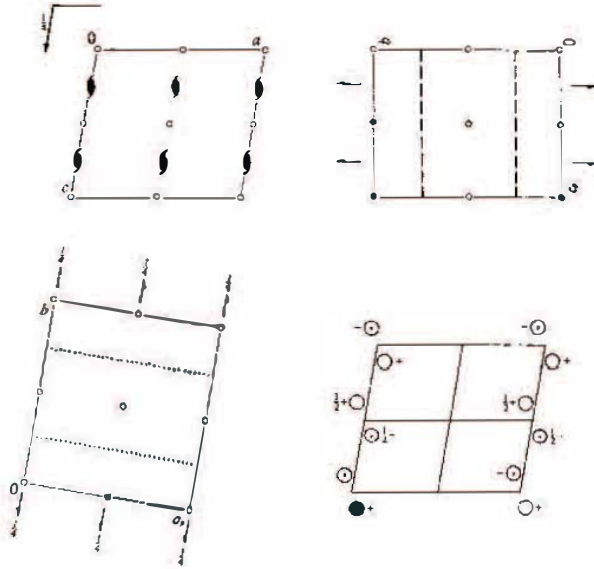
Monoclinic

No. 14

$P 1 2/c 1$

Patterson symmetry $F 1 Z m 1$

UNIQUE AXIS b . CELL CHOICE 1



Original $\bar{1}$

Asymmetric unit $0 \leq x \leq 1; 0 \leq y \leq 1; 0 \leq z \leq 1$

Symmetry operations

- (1) 1
- (2) $2(0, \frac{1}{2}, 0) \parallel b, y, z$
- (3) $\bar{1}(0, 0, 0)$
- (4) $c(x, \frac{1}{2}, z)$

CONTINUED

No. 14

 $P2_1/c$ Generators selected (1), $t(1,0,0)$; $t(0,1,0)$; $t(0,0,1)$; (2); (3)

Positions

Multiplicity	Wyckoff letter	Site symmetry	Coordinates	Reflection conditions
4	e	1	(1) x, y, z (2) $\bar{x}, y + \frac{1}{2}, z + \frac{1}{2}$ (3) \bar{x}, \bar{y}, z (4) $x, \bar{y} + \frac{1}{2}, z + \frac{1}{2}$	General: $h0l : l = 2n$ $0k0 : k = 2n$ $00l : l = 2n$ Special: as above, plus $hkl : k + l = 2n$
2	d	$\bar{1}$	$\frac{1}{2}, 0, \frac{1}{2}$ $\frac{1}{2}, \frac{1}{2}, 0$	$hkl : k + l = 2n$
2	c	$\bar{1}$	$0, 0, \frac{1}{2}$ $0, \frac{1}{2}, 0$	$hkl : k + l = 2n$
2	b	$\bar{1}$	$\frac{1}{2}, 0, 0$ $\frac{1}{2}, \frac{1}{2}, \frac{1}{2}$	$hkl : k + l = 2n$
2	a	$\bar{1}$	$0, 0, 0$ $0, \frac{1}{2}, \frac{1}{2}$	$hkl : k + l = 2n$

Symmetry of special projections

Along [001] $P2_1/gm$ $a = a, b = b$

Origin at 0, 0, 0

Along [100] $P2_1/gg$ $a = b, b = c,$ Origin at $x, 0, 0$ Along [010] $P2_1$ $a = c, b = a$ Origin at 0, $y, 0$

Maximal non-isomorphic subgroups

I [2] $P1c1 (Pc, 7) 1; 4$ [2] $P121 (P2, 4) 1; 2$ [2] $P1(2) 1; 3$

IIa none

IIb none

Maximal isomorphic subgroups of lowest index

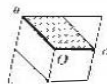
IIc [2] $P12/c1 (a = 2a, 0, a = 2a, c = a + c) (P2/c, 14); [3] P12/c1 (b = 3b) (P2/c, 14)$

Minimal non-isomorphic supergroups

I [2] $Pnna (52); [2] Pmna (53); [2] Pcca (54); [2] Pbam (55); [2] Pcen (56); [2] Pbcm (57); [2] Pnmm (58); [2] Pbcn (60); [2] Pbca (61); [2] Pnma (62); [2] Cmc (64)$ II [2] $I12m1 (C2m, 12); [2] C12c1 (C2c, 15); [2] I12c1 (C2c, 15); [2] P12/m1 (c = $\frac{1}{2}$ c) (P2/m, 11); [2] $P12/c1 (b = 4b) (P2/c, 13)$$ Figure 8.2 The Space Group $P2_1/c$ (used with permission of the IUCr <http://it.iucr.com>)

CONTINUED

No. 14

 $P 2_1/c$ $P 1 2/n 1$ UNIQUE AXIS b , CELL CHOICE 2● origin $\bar{1}$ Asymmetric unit $0 \leq x \leq 1; 0 \leq y \leq \frac{1}{2}; 0 \leq z \leq 1$ Generators selected (1); $r(1,0,0)$; $r(0,1,0)$; $r(0,0,1)$; (2); (3)

Positions

Multiplicity
Wyckoff letter
Site symmetry

Coordinates

4	e	$\bar{1}$	(1) x, y, z	(2) $\bar{x} + \frac{1}{2}, y + \frac{1}{2}, \bar{z} + \frac{1}{2}$	(3) \bar{x}, y, \bar{z}	(4) $x + \frac{1}{2}, \bar{y} + \frac{1}{2}, z + \frac{1}{2}$
---	-----	-----------	---------------	---	---------------------------	---

2	d	$\bar{1}$	$\frac{1}{2}, 0, 0$	$0, \frac{1}{2}, \frac{1}{2}$
---	-----	-----------	---------------------	-------------------------------

2	c	$\bar{1}$	$\frac{1}{2}, 0, \frac{1}{2}$	$0, \frac{1}{2}, 0$
---	-----	-----------	-------------------------------	---------------------

2	b	$\bar{1}$	$0, 0, \frac{1}{2}$	$\frac{1}{2}, \frac{1}{2}, 0$
---	-----	-----------	---------------------	-------------------------------

2	a	$\bar{1}$	$0, 0, 0$	$\frac{1}{2}, \frac{1}{2}, \frac{1}{2}$
---	-----	-----------	-----------	---

Reflection conditions

General:

 $h0l : h + l = 2n$ $0k0 : k = 2n$ $h00 : l = 2n$ $00l : l = 2n$

Special: as above, plus

 $hkl : h + k + l = 2n$ $hkl : h + k + l = 2n$ $hkl : h + k + l = 2n$ $hkl : h + k + l = 2n$ $P 1 2/a 1$ UNIQUE AXIS b , CELL CHOICE 3● origin $\bar{1}$ Asymmetric unit $0 \leq x \leq 1; 0 \leq y \leq \frac{1}{2}; 0 \leq z \leq 1$ Generators selected (1); $r(1,0,0)$; $r(0,1,0)$; $r(0,0,1)$; (2); (3)

Positions

Multiplicity
Wyckoff letter
Site symmetry

Coordinates

4	e	$\bar{1}$	(1) x, y, z	(2) $\bar{x} + \frac{1}{2}, y + \frac{1}{2}, \bar{z}$	(3) \bar{x}, y, \bar{z}	(4) $x + \frac{1}{2}, \bar{y} + \frac{1}{2}, z$
---	-----	-----------	---------------	---	---------------------------	---

2	d	$\bar{1}$	$0, 0, \frac{1}{2}$	$\frac{1}{2}, \frac{1}{2}, \frac{1}{2}$
---	-----	-----------	---------------------	---

2	c	$\bar{1}$	$\frac{1}{2}, 0, 0$	$0, \frac{1}{2}, 0$
---	-----	-----------	---------------------	---------------------

2	b	$\bar{1}$	$\frac{1}{2}, 0, \frac{1}{2}$	$0, \frac{1}{2}, \frac{1}{2}$
---	-----	-----------	-------------------------------	-------------------------------

2	a	$\bar{1}$	$0, 0, 0$	$\frac{1}{2}, \frac{1}{2}, 0$
---	-----	-----------	-----------	-------------------------------

Reflection conditions

General:

 $h0l : h = 2n$ $0k0 : k = 2n$ $h00 : h = 2n$

Special: as above, plus

 $hkl : h + k = 2n$ $hkl : h + k = 2n$ $hkl : h + k = 2n$ $hkl : h + k = 2n$

Figure 8.3 Alternative Settings for $P2_1/c$ (used with permission of the IUCr <http://it.iucr.com>)

Figure 8.4 is the table for the space group $C2/c$. Everything is as previously discussed except that the c -centering changes some things. The table indicates there are eight equivalent positions for the general position but only four are listed. The line above this is $(0,0,0) + (1/2,1/2,0) +$. These are the centering translations and are only listed for centered cells. This indicates that the equivalent positions are generated by adding each of the two values to the positions listed. Therefore, the position (x,y,z) is actually two positions. The first adds zero to each coordinate and results in (x,y,z) . The second is formed by adding $1/2$ to x and y to create $(x+1/2,y+1/2,z)$. Thus, the four positions listed are actually eight. Note $C2/c$ contains a two-fold rotation axis at $(0,y,1/4)$ which is also at $(1/2,y+1/2,1/4)$ and two additional positions related by symmetry. Since a rotation axis involves a line, the equation must involve any value for the axis parallel to the rotation and fixed values for the other coordinates. For a mirror, two axes are allowed any value while one is fixed.

International Tables for Crystallography (2006), Vol. A, Space group 15, pp. 192–199.

$C2/c$

C_{2h}^6

$2/m$

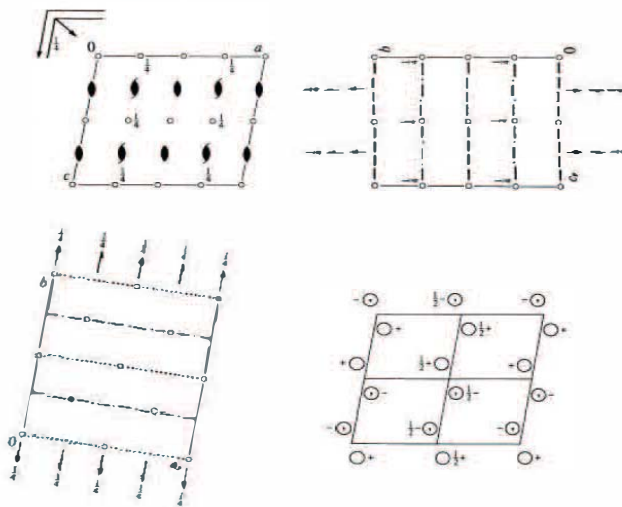
Monoclinic

No. 15

$C12/c1$

Patterson symmetry $C12/m1$

UNIQUE AXIS b , CELL CHOICE 1



Origin at $\bar{1}$ on glide plane c'

Asymmetric unit $0 \leq x \leq \frac{1}{2}; 0 \leq y \leq \frac{1}{2}; 0 \leq z \leq \frac{1}{2}$

Symmetry operations

For $(0, 0, 0)+$ set

(1) 1 (2) $2 \parallel 0, y, \frac{1}{2}$ (3) $\bar{1} \parallel 0, 0, 0$ (4) $c \parallel x, 0, z$

For $(\frac{1}{2}, \frac{1}{2}, 0)+$ set

(1) $i(\frac{1}{2}, \frac{1}{2}, 0)$ (2) $2(0, \frac{1}{2}, 0) \parallel x, y, \frac{1}{2}$ (3) $\bar{1} \parallel \frac{1}{2}, \frac{1}{2}, 0$ (4) $m(\frac{1}{2}, 0, \frac{1}{2}) \parallel x, y, z$

CONTINUED

No. 15

C2/c

Generators/selected (1) $t(1,0,0)$; $t(0,1,0)$; $t(0,0,1)$; $t(\frac{1}{2},\frac{1}{2},0)$; (2) (3)

Positions

Multiplicity
Wyckoff letter
Site symmetry

Coordinates

$(0,0,0) + (\frac{1}{2},\frac{1}{2},0) +$

Reflection conditions**General:**

8 f 1 (1) x,y,z ; (2) $\bar{x},y,\bar{z} + \frac{1}{2}$; (3) \bar{x},y,\bar{z} ; (4) $x,\bar{y},z + \frac{1}{2}$

$hkl : h+k=2n$

$h0l : h,l=2n$

$0kl : k=2n$

$h\bar{h}0 : h+k=2n$

$0k0 : k=2n$

$h\bar{h}0 : h=2n$

$00l : l=2n$

Special as above, plus

no extra conditions

4 e 2 $0, y, \frac{1}{2}$ $0, \bar{y}, \frac{1}{2}$

$hkl : k+l=2n$

4 d $\bar{1}$ $\frac{1}{2}, \frac{1}{2}, \frac{1}{2}$ $\frac{3}{2}, \frac{1}{2}, 0$

$hkl : k+l=2n$

4 c $\bar{1}$ $\frac{1}{2}, \frac{1}{2}, 0$ $\frac{3}{2}, \frac{3}{2}, \frac{1}{2}$

$hkl : k+l=2n$

4 b $\bar{1}$ $0, \frac{1}{2}, 0$ $0, \frac{3}{2}, \frac{1}{2}$

$hkl : l=2n$

4 a $\bar{1}$ $0,0,0$ $0,0,\frac{1}{2}$

$hkl : l=2n$

Symmetry of special projections

Along $[001]c2mm$

$a = a$, $b = b$

Origin at $0,0,0$

Along $[100]p2gm$

$a = \frac{1}{2}b$, $b = c$

Origin at $x,0,0$

Along $[010]p2$

$a = \frac{1}{2}c$, $b = \frac{1}{2}a$

Origin at $0, y, 0$

Maximal non-isomorphic subgroups

- I** [2]C1c11(Cc, 9) (1; 4)+
 [2]C121(C2, 5) (1; 2)+
 [2]C1(P1, 2) (1; 3)+
- IIa** [2]P12/n1(P2/c, 14) 1; 3; (2; 4) + $(\frac{1}{2}, \frac{1}{2}, 0)$
 [2]P12/c1(P2/c, 14) 1; 4; (2; 3) + $(\frac{1}{2}, \frac{1}{2}, 0)$
 [2]P12c1(P2c, 13) 1; 2; 3; 4
 [2]P12n1(P2c, 13) 1; 2; (3; 4) + $(\frac{1}{2}, \frac{1}{2}, 0)$

IIb none

Maximal isomorphic subgroups of lowest index

- IIc** [3]C12c1($b=3b$)(C2/c, 15); [3]C12c1($c=3c$)(C2/c, 15);
 [3]C12c1($a=3a$ or $a=3a, c=-a+c$ or $a=3a, c=a+c$)(C2/c, 15)

Minimal non-isomorphic supergroups

- I** [2]Cmc/m(63); [2]Cmce(64); [2]Cccm(66); [2]Ccce(68); [2]Fddd(70); [2]Ibam(72); [2]Ibca(73); [2]Imma(74);
 [2]I4/a(88); [3]P31c(163); [3]P3c1(165); [3]Bc167)
- II** [2]F12m1(C2/m, 12); [3]C12m1($c=3c$)(C2/m, 12); [2]P12c1($a=\frac{1}{2}a, b=\frac{1}{2}b$)(P2/c, 13)

Figure 8.4 Space Group C2/c (used with permission of the IUCr <http://it.iucr.com>)

Figure 8.5 are the pages for the orthorhombic space group $Pnma$. It is readily seen that everything is more complex here. However, there is nothing different from the previous space groups tables.

International Tables for Crystallography (2006), Vol. A, Space group 62, pp. 298–299.

$Pnma$

D_{2h}^{16}

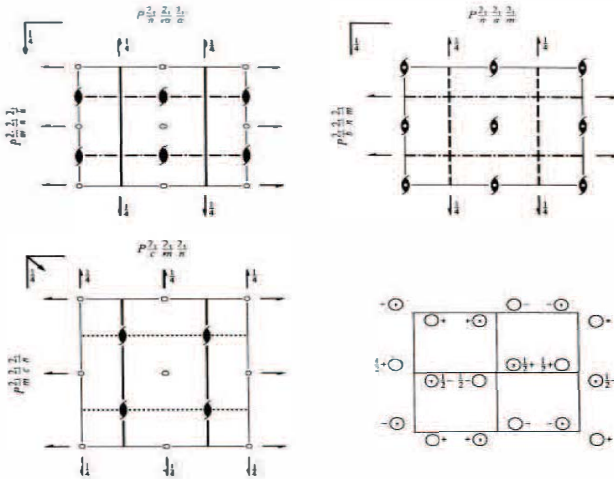
mmm

Orthorhombic

No. 62

$P 2_1 / a 2_1 / m 2_1 / a$

Pattern symmetry $Pm\bar{m}m$



Origin at $\bar{1} | 0 | \bar{1} | 2 | 1$

Asymmetric unit $0 \leq x \leq \frac{1}{2}, 0 \leq y \leq \frac{1}{2}, 0 \leq z \leq 1$

Symmetry operations

- (1) $\bar{1}$
- (2) $2(0, 0, \frac{1}{2}) \parallel z, 0, z$
- (3) $2(0, \frac{1}{2}, 0) \parallel y, y, 0$
- (4) $2(\frac{1}{2}, 0, 0) \parallel x, \frac{1}{2} + x, \frac{1}{2}$
- (5) $\bar{1} \parallel 0, 0, 0$
- (6) $a \parallel x, y, \frac{1}{2}$
- (7) $m \parallel x, \frac{1}{2}, z$
- (8) $n(0, \frac{1}{2}, \frac{1}{2}) \parallel \frac{1}{2}, y, z$

Generators selected (1); $r(1, 0, 0)$; $d(0, 1, 0)$; $r(0, 0, 1)$; Ω ; (3); (5)

Positions

	Multiplicity	Wyckoff letter	Site symmetry	Coordinates	Reflection conditions		
8	<i>d</i>	$\bar{1}$	(1) \bar{x}, y, z (3) $\bar{x}, \bar{y}, \bar{z}$	(2) $\bar{x} + \frac{1}{2}, \bar{y}, z + \frac{1}{2}$ (6) $\bar{x} + \frac{1}{2}, y, \bar{z} + \frac{1}{2}$	(3) $\bar{x}, y + \frac{1}{2}, \bar{z}$ (7) $x, \bar{y} + \frac{1}{2}, z$	(4) $x + \frac{1}{2}, \bar{y} + \frac{1}{2}, \bar{z} + \frac{1}{2}$ (8) $x + \frac{1}{2}, y + \frac{1}{2}, z + \frac{1}{2}$	OKl : $k + l = 2n$ hk0 : $h = 2n$ h00 : $h = 2n$ 0k0 : $k = 2n$ 00l : $l = 2n$ Special: as above, plus no extra conditions hkl : $h + l, k = 2n$ hkl : $h + l, k = 2n$
4	<i>e</i>	$\bar{2}m$	x, y, z	$\bar{x} + \frac{1}{2}, y, z + \frac{1}{2}$	$\bar{x}, \bar{y}, \bar{z}$	$x + \frac{1}{2}, y, \bar{z} + \frac{1}{2}$	
4	<i>b</i>	$\bar{1}$	0, 0, $\frac{1}{2}$	$\frac{1}{2}, 0, 0$	0, $\frac{1}{2}, \frac{1}{2}$	$\frac{1}{2}, \frac{1}{2}, 0$	
4	<i>a</i>	$\bar{1}$	0, 0, 0	$\frac{1}{2}, 0, \frac{1}{2}$	0, $\frac{1}{2}, 0$	$\frac{1}{2}, \frac{1}{2}, \frac{1}{2}$	

Symmetry of special projections

Along [001] $P2gm$ a = $\frac{1}{2}$ a b = b ● origin at 0, 0, z	Along [100] $e2mm$ a = b b = c ● origin at $x, \frac{1}{2}, \frac{1}{2}$	Along [010] $P2gg$ a = c b = $\frac{1}{2}$ a ● origin at 0, y, 0
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Maximal non-isomorphic subgroups

- I** [2] $Pn2_1a$ ($Pna2_133$) 1: 3; 6; 8
- [2] $Pum2$ ($Pmn2_131$) 1: 2; 7; 8
- [2] $P2ma$ ($Pmc2_126$) 1: 4; 6; 7
- [2] $P2_12_1$ (19) 1: 2; 5; 4
- [2] $P112/a$ ($P2/c14$) 1: 2; 5; 6
- [2] $P2/n11$ ($P2/c14$) 1: 4; 5; 8
- [2] $P12/m1$ ($P2/m11$) 1: 3; 5; 7

- IIa** none
- IIb** none

Maximal isomorphic subgroups of lowest index

- IIc** [3] $Pnma$ ($a=3a$) (62); [3] $Pnma$ ($b=3b$) (62); [3] $Pnma$ ($c=3c$) (62)

Minimal non-isomorphic supergroups

- I** none
- II** [2] $Amma$ ($Cmcm$, 63); [2] $Bhmm$ ($Cmcm$, 63); [2] Cmc ($Cmce$, 64); [2] $Imma$ (74); [2] $P4_2/mfbam$ (55); [2] $Pbma$ ($c=2c$) ($Pbcm$, 57); [2] $Pnam$ ($a=2a$) ($Pmna$, 59)

Figure 8.5 Space Group *Pnma* (used with permission of the IUCr <http://it.iucr.com>)

CHAPTER 9

X-RAYS AND DIFFRACTOMETERS

In this chapter, the equipment, methods, and software for obtaining crystallographic data will be examined in more detail.

9.1 X-rays

9.1.1 The nature of X-rays

X-rays were a serendipitous discovery by Wilhelm Röntgen in 1895. They were named X-rays because they were mysterious and not immediately understood. It was also quickly discovered that X-rays could expose photographic film. Their use for medical diagnosis was instantly recognized and most of the early work was devoted to finding better ways to produce them.

Initially, there was a question whether X-rays were particles or waves. William Bragg proved they were electromagnetic radiation. The wavelengths are in the range of 0.1 to 100 Å. Therefore, they are very high energy. Beyond film, they can be detected by radiation detectors such as Geiger counters and other detectors.

X-rays react with matter in the same way other forms of electromagnetic radiation do. They can be absorbed. Since this interaction involves the electrons, increasing the atomic number of the atom or its density will increase the amount of absorption. Atoms with larger atomic numbers absorb greater amounts of X-rays. The wavelength of the X-rays also affects the amount of absorption. The shorter the wavelength (the higher the energy) the lower the absorption.

As discussed previously, X-rays can also be scattered. This is the primary source of the diffracted intensity. X-rays also can be absorbed and then emitted. This gives rise to anomalous scattering which is important in

determining the absolute configuration of optically active crystals and molecules.

9.1.2 X-rays from Conventional X-ray Tubes

X-rays are produced whenever a charged particle with sufficient kinetic energy interacts with matter. The source of the X-rays used in most laboratories today is various types of X-ray tubes. Originally, ions were used as the particle source but it soon proved more efficient to use an electron beam which is all that will be discussed. The most common source for X-rays in the laboratory is the hot cathode tube, which was introduced in 1913. The X-ray spectrum of each element contains two parts. First is the bremsstrahlung or braking radiation. This is the radiation caused by the high-speed electrons slowing down because of interactions with matter. Since this is not a quantized process, the spectrum is broad. Below some minimum energy, the electron collisions will produce no X-rays at all. The intensity and width of the bremsstrahlung increases with increasing kinetic energy of the electrons impacting the target and the maximum shifts to shorter wavelengths.

On top of the bremsstrahlung radiation are strong peaks whose wavelengths are characteristic for each element. In fact, the British physicist Henry Moseley derived an equation which related the wavelength of these lines to the atomic number. The X-ray spectrum of a typical tube is shown in Figure 9.1. The broad radiation is the bremsstrahlung. Atop the bremsstrahlung are two peaks. The one at shorter wavelength is called K_{β} , while the more intense radiation is K_{α} . Typically, the K_{α} radiation is used for crystallography because it is the most intense. The K_{α} radiation can be resolved further into a doublet. The two wavelengths making up the peak are labeled $K_{\alpha 1}$ and $K_{\alpha 2}$.

The X-ray tube is designed to produce X-rays with constant intensity. The cross section of a tube is shown in Figure 9.2. The tube basically consists of a filament as the source of the electrons and an anode which is the target typically made of a pure element. The element used in the anode will determine the wavelength of the K_{α} radiation. The size of the filament will determine the size of the beam. Most X-ray tubes contain four beryllium windows where the X-rays emerge. Beryllium is used because it has an atomic number of four and has a low absorption coefficient. The shape of the X-rays beam produced is determined by the size and shape of the filament. Two different beams are obtained. If the plane of the window

is parallel to the filament, the beam will be a line referred to as the line source. This is frequently used in powder diffraction work but is not suitable for single crystal experiments. If the window looks down the filament, then the beam is called the point source which is what is needed for single crystal experiments. The beam shown in Figure 9.2 is a point source. One modern change to tube construction is that some tubes use ceramic instead of glass to enclose the bottom of the tube.

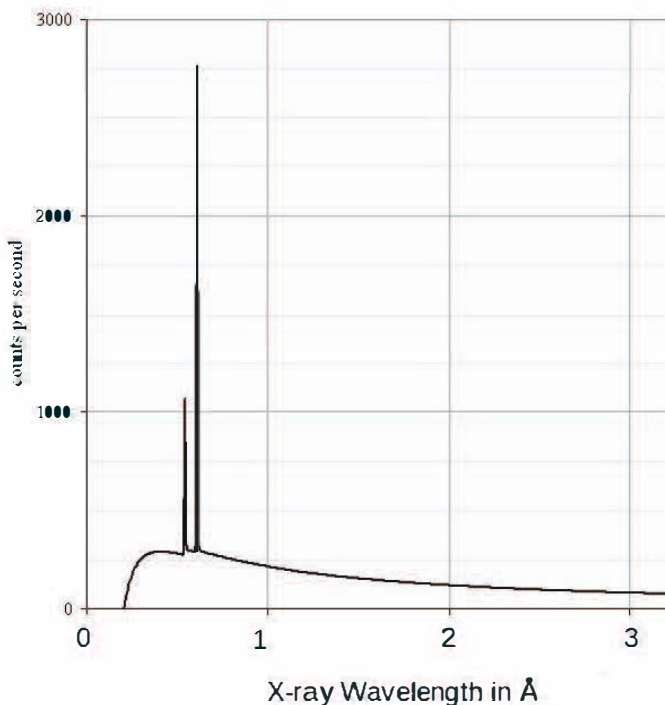


Figure 9.1 Output from a molybdenum X-ray tube.

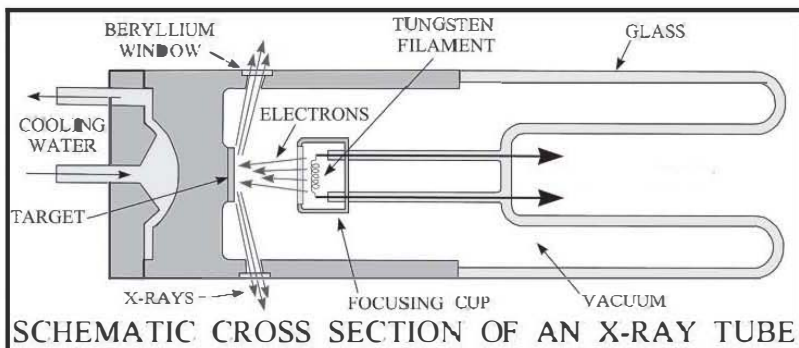


Figure 9.2 Cross section of an X-ray tube.

The X-ray tube will not produce X-rays unless energized to create an electron beam. A steady source of high voltage is required and the electronics which provide the power are referred to as the X-ray generator. The potential between the filament and the target is between 40-60kV. The anode is kept at ground while the filament is at the higher voltage. No current is forced through the filament as both ends are at the same voltage. However, the electrons in the filament are attracted by the voltage difference and are emitted from the filament as a beam. There is a current setting which determines the maximum number of electrons that can flow from the filament circuit. Conventional X-ray tubes have a total power rating of 2-3kW depending on the element used in the anode and the construction. The current is the wattage divided by the accelerating voltage and is between 20-50mA.

There are several additional features in the conventional X-ray tube that must be considered. Less than 1% of the energy delivered to the tube produces X-rays. The rest is converted into heat. This creates several problems. The area bombarded by the electron beam can get hot enough to melt. Metals with higher melting points can be exposed to a greater current. This heat problem also requires the anode be cooled. In conventional tubes this is accomplished by water flowing over the back surface of the anode. This creates a new danger as having water around high voltages can be very dangerous. X-ray generators used with water-cooled tubes are all equipped to shut down the power to the tube if the water flow drops below a set level.

A second problem is arcing. The distance between the filament and the anode in the tube is fairly small, on the order of millimeters. If the tube

were open to air, arcing would occur between the two. A high vacuum is used as an insulator. The tubes also contain small bars of various alloys called getters which remove oxygen and nitrogen to maintain the high vacuum. In addition, all X-ray generators contain a circuit which will shut down the tube if the current quickly rises to an unreasonable value. In most cases, arcing is a sign that the tube has reached the end of its lifetime and needs to be replaced.

The X-rays generated come off the anode in all directions. Many of the X-rays produced do not even get through the windows. Beyond that, crystallographic experiments require a coherent beam, one traveling in one direction. As shown in Figure 9.2 this is not what the tube produces. To form a coherent beam, the point focus beam is shaped by a collimator. This is a long metal tube with an entry hole nearest the tube window and a smaller exit hole through which the X-rays emerge. There are various sized collimators for a diffractometer. The size of the entry hole is determined by the type of X-ray tube used while the size of the collimator is the size of the exit hole. Generally collimators range from 0.2 to 0.7 mm.

Modern instruments all contain some form of monochromator to try to make the output of the tube more monochromatic and eliminate the K_{α} radiation. Some use X-ray optics which serve both to monochromate the beam and also focus the intensity into a smaller spot. These are used on micro-focus tubes which will be discussed later. The most commonly used method is to employ a monochromator placed between the tube window and the collimator. This is simply a crystalline material that is aligned so that the output of the tube is a diffraction spot. This diffracted beam will then be considerably more monochromatic than the original beam. Of course, intensity will be lost in this process. It is possible to create a monochromator with a crystal of silicon that can separate the two K_{α} lines. However, such a monochromator has several problems. First, it must be carefully aligned and is sensitive to many environmental factors. Secondly, since silicon will absorb X-rays, the loss of intensity will be large. Therefore, most diffractometers use graphite. The width of the radiation monochromated by graphite will be broader than for silicon. Graphite will not separate the K_{α} lines and the radiation will not be strictly monochromatic. It will also include some neighboring bremsstrahlung. However, it will not include the K_{β} lines.

The last part of the X-ray source is a shutter which can absorb all the radiation produced and stop the X-ray beam. This is computer controlled

so that it can be opened and closed as needed during data collection. It will also be closed if interlocks are triggered suggesting a problem with the system.

The conventional tube is contained in a tube shield that allows the position of the beam to be adjusted both horizontally and vertically. If a crystal monochromator is used, the tube must be aligned so the beam makes the proper Bragg angle with the crystal. The alignment is usually done such that the beam is centered to better than 0.01mm. The tube position must also be adjusted so the most intense beam emerges from the collimator. The alignment process should only be undertaken by someone who is experienced in performing this maintenance.

9.1.2 Micro-focus X-ray Tubes

The intensity of the diffracted X-rays is weak. The more intense the X-ray source is the smaller the sample that can be studied and also the better the data. Interestingly, this has been accomplished by making the size of the point source smaller and using less power in the tube. This class of tube is referred to as a micro-focus tube.

The basic concept of a micro-focus tube is to replace the wire filament with a much smaller point source. It requires great care in manufacturing to produce a cathode which will stay focused at the same spot on the anode regardless of changing conditions. In addition, magnets are used to further focus the electron beam. The result is an X-ray beam which is much smaller in diameter but has more photons/area. The voltages used in this type of tube are the same as in a conventional tube. However, the current is much lower from <1ma to 2ma. The total power is reduced from 2-3Kw to 30-100w. Since this power level is much smaller, most micro-focus tubes are air cooled simplifying the installation and support equipment needed.

At about the same time micro-focus tube technology developed so did the field of X-ray optics. There are several methods used to focus the beam. All involve diffraction that focuses the spot emanating from the tube into a smaller, more intense beam. The spot size for a micro-focus tube is typically on the order of 0.1mm versus 0.4mm for the best conventional tube and the number of photons in the beam is greater by at least 100. The small size of the beam may create problems when using larger crystal and also can present problems in aligning the beam.

9.1.3 The Rotating Anode

The limitation in the power applied is keeping the anode cool enough so it will not melt. One approach is to rotate the anode rapidly so that only one small area of the anode is heated at any time. Systems that make use of this technology are called rotating anodes. While these sources are brighter than even micro-focus tubes, they have many drawbacks.

For the rotating anode to be usable for a long time, the entire cavity containing the filament and anode must be able to be opened for maintenance. This means the vacuum must be maintained with vacuum pumps. The anode is a heavy cylindrical piece of metal. Since it is spun at rates of up to 6,000 rpm (100 rotations a second), it must be carefully machined and balanced. It is also necessary that cooling water flow through the anode while it is spinning. Obviously, there must also be a motor attached to the anode to spin it. To achieve all this requires precise manufacturing. In addition, the filaments must be changed when they finally burn through. This requires significant maintenance. Like all non-tube sources, the position of the beam is not adjustable requiring the entire diffractometer be moved for alignment.

One advantage of the rotating anode besides greater intensity is that the beam size can be selected. This is accomplished by using electromagnets to increase the size of the electron beam. Increasing the electron beam size allows an increase in the power. However, since the X-ray beam is now larger, the flux/mm decreases.

At one time rotating anodes were the only solution for working with small samples in the home laboratory. However, because of the maintenance requirements and cost they are being replaced with micro-focus sources which are becoming the standard source on most new equipment.

9.1.4 Metal Jet X-ray Sources

Recently, a new technology has become available that further increases the power and decreases the spot size of the X-ray beam. These sources are called metal jet sources. These are rotating anodes where the solid anode is replaced by a liquid jet of melted metal. The main metal used is gallium (melting point 29.8°C) either pure or as an alloy which is liquid at or near room temperature. Since the anode is already a liquid and moving, the power load can be much greater than even for a rotating anode. The X-ray

beam size is readily adjustable and beams even smaller than 0.1mm can be obtained. Currently, metal jet sources are sold as a complete package including electronics. However, it is not inconceivable that a tube like metal jet source could be developed which would allow for installation on existing equipment.

9.1.5 More Intense Sources

It is possible to generate more intense X-ray beams. However, the sources that produce them do not use an electron beam focused on an anode to produce the X-rays but instead involve particle accelerators. They are not suitable for installation in a home laboratory but are typically only available at government research laboratories. The discussion here is simply to provide the minimum information as to the output of these sources. Information about what is available or obtaining access for a particular facility will not be covered.

9.1.5.1 Synchrotrons

A synchrotron is a special particle accelerator in which particles travel around a closed loop. In the production of synchrotron radiation, electrons are the particle accelerated in a storage ring. The particles are kept in the loop by bending magnets. Frequently, the electrons are accelerated to near the speed of light by a linear accelerator. The diameter of the loop is typically in the hundreds of meters range with some having diameters of over 1km. There is a list of synchrotron radiation facilities with their size and energy at <https://nucleus.iaea.org/sites/accelerators/Pages/Synchrotron.aspx>. These radiation sources produce a broad range of wavelengths from far ultraviolet through the whole spectrum of X-rays. The radiation exits from many beamlines around the synchrotron so multiple experiments can be performed simultaneously. Each experiment can select a single wavelength and this radiation is monochromatic.

The intensity of synchrotron X-rays is several orders of magnitude greater than even a rotating anode source. For chemical crystallography this means data can usually be collected in less than a half hour. It also means that much smaller crystals can be studied. However, it must be remembered that this higher intensity will not turn poor quality crystals into good samples. As the solid state chemist Robert Scheidt of Notre Dame University once commented to me, "Small crystals frequently have problems beyond dwarfism." Synchrotron radiation is also monochromatic

and can be linearly or circularly polarized. These properties allow experiments to be performed at a synchrotron that cannot be done using X-rays generated from laboratory sources.

At one time there was a great demand for experiment time at synchrotron diffraction beamlines. However, the demand from biological crystallographers has decreased and beam time today is frequently available. To collect a diffraction data set at a synchrotron, it is best to contact the facility to find out about availability and how to conduct the experiment.

9.1.5.2 Free Electron Lasers

The brightest X-ray source is the free electron laser (fel). Like the synchrotron, this source produces the entire wavelength range of X-rays. The most recently constructed fel took over 10 years to plan and build and cost over 1.5 billion dollars. It is a pulsed source so it can be used for timing experiments. At the time of writing, there are only three such X-ray facilities in the world so getting beam time is difficult. It is not clear yet how this technology will expand chemical crystallography.

9.1.6 X-ray Wavelengths

The choice of wavelength used in a diffraction experiment can make a significant difference in the result. The X-ray wavelengths used in most diffraction studies in Å are Cu=1.54178, Mo=0.71073, Ag=0.56086, and Ga=1.3414. The most widely used sources are copper and molybdenum.

There are several considerations that must be made in choosing the wavelength to use. Since copper has a longer wavelength, the diffraction spots will have larger Bragg angles and be further apart. For very large unit cells this may be important so that spots do not overlap. On the other hand, the longer wavelength limits how many data can be collected in the working range of 5-80° in theta for most diffractometers. This is illustrated by the completeness requirements from **Acta Crystallographica, Section C**. $\sin_{\max}(\theta)$ must be greater or equal to 67° for data collected with copper radiation but only 25° if molybdenum radiation is used. Obviously the molybdenum data set can continue out much further than the copper. Since the greater the \sin_{\max} the greater the atomic resolution, it is possible to get higher resolution when molybdenum radiation is used. Besides resolution, truncating the Fourier series has other consequences. When crystals containing heavy elements are used, this truncation can cause ringing as is observed in the truncated FT-NMR data.

The second major difference is in the absorption of the radiation by the atoms in the crystal. The shorter the wavelength the less absorption or the more penetrating the X-rays are. Tungsten X-rays typically used in dentistry and medicine have a wavelength of about 0.15\AA . For medical diagnostics it is important that the X-rays penetrate to varying degrees so that the image displays contrast between different densities of tissues. In crystallography absorption can be both helpful and a problem. If the sample absorbs too highly, then the measured intensities will need to be corrected for the absorption. On the other hand, if the absolute configuration of an organic molecule is to be determined, the sample must have some absorption to produce sufficient anomalous scattering.

In most cases molybdenum and copper radiation can be used interchangeably. If the sample contains mostly heavy atoms (atoms with a large atomic number), molybdenum or even silver radiation is preferred. To determine very high resolution data molybdenum is the choice. Copper radiation generally is used for organic crystals. While one radiation may be preferable, the use of either common radiation is frequently acceptable.

9.1.7 Safety

X-ray sources are intrinsically dangerous. Not only is there the radiation but also the very high voltages produced. Only those with sufficient training and experience should work on this equipment.

The d.c. high voltage that is used in a tube should be treated with great respect. Even after the generator is powered down it is capable of providing dangerous voltages. This is because capacitors are employed to convert the current to d.c. These capacitors store charge and can release current. This is akin to what happens when you turn off a computer. In that case it takes 10-20 seconds before the monitor loses the signal. The decay for the high voltage generator can take much longer. Whenever work is done on a power supply or a tube, the cable to the X-ray tube should be removed and grounded by touching the side of the tube shield.

The X-rays used in crystallography generally do not present a great danger if the equipment's safety features are working. First, the energy of the X-rays used is much lower and less penetrating than medical X-rays. The beam is quite small and it is hard to expose much skin to it because there is little room between the collimator and the beam stop. All diffraction equipment has numerous safety interlocks that will close the shutter or turn off the generator if an unsafe operation is detected. An example might

be opening the enclosure where the diffractometer is housed when the shutter is open.

The biggest chance of X-ray exposure is during and after maintenance. During operations such as alignment it may be necessary to override the interlocks. It is important that these protections be restored immediately after maintenance is completed. The other potential problem occurs when the X-ray pathway is repaired. If it is not reassembled correctly, there is a small probability of a leak. After any work is completed on the X-ray source and its associated components, a radiation detector should always be used to ensure that the background is low when the shutter is closed. Fortunately, diffraction equipment must meet stringent safety standards and the chance of exposure to X-rays is low.

9.2 Diffractometers

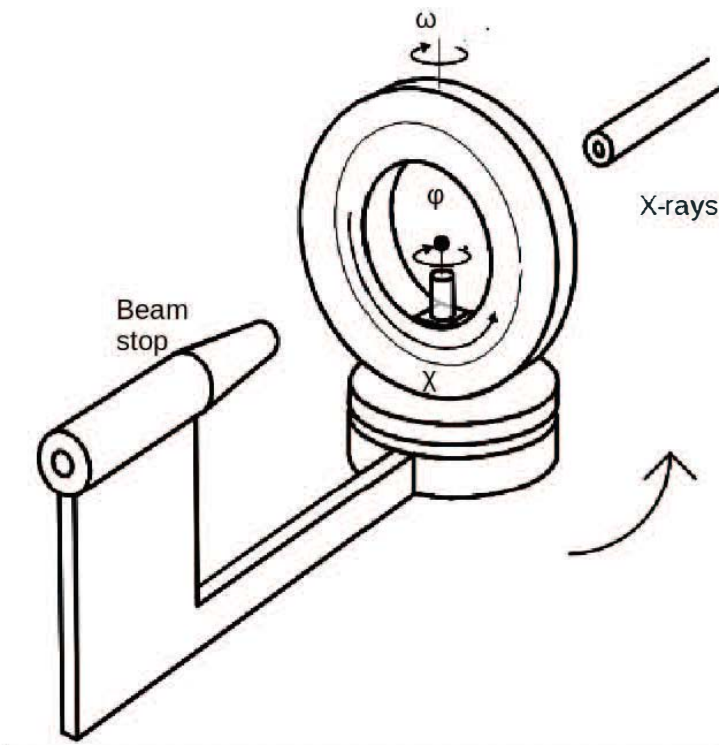
The part of the diffractometer used to orient the sample is complex. This is sometimes referred to as the goniometer (from the Greek word γωνία [gonia] meaning angle). The goniometer is a series of arcs that can be precisely moved to obtain any desired orientation of the crystal. The diffractometer is computer controlled. Over the years as computers have become more powerful, diffractometer software has greatly improved and modern instruments are capable of automating analyses. Diffractometers are precise instruments and care must always be taken not to upset the alignment or damage them. Diffractometers come in both three circle and four circle types. One of the arcs moves the detector while the other two or three involve movements of the crystal. The circles of the diffractometer are all moved by motors which are capable of very fine movements. The angle setting is read by an encoder which is accurate to less than 0.05° .

The object of the diffractometer is to place the crystal in the correct diffracting position such that the diffraction vector bisects the incoming and diffracted beam for hkl . To accomplish this the calculations make use of the Eulerian angles introduced by the eighteenth century Swiss mathematician Leonhard Euler. The angles define the rotation of body to position a vector along a fixed Cartesian coordinates (XYZ). In the case of the diffractometer XYZ are imposed onto the diffractometer. One problem is that the direction of XYZ is arbitrary and may differ for different manufacturers. If the desired position of the diffraction vector can be calculated in terms of XYZ then the crystal can be rotated through three axes so that it is in the proper orientation.

The key to the Euler calculation is the orientation matrix. This consists of a 3x3 matrix where the first column is the projection of \mathbf{a}^* on X, Y, and Z respectively, the second column is the equivalent for \mathbf{b}^* and the last is for \mathbf{c}^* . The length of each column gives the length of the respective reciprocal axis while the angle between the column vectors are the reciprocal angles. The orientation matrix therefore describes not only the orientation of the crystal but also the reciprocal cell constants. When the orientation matrix is multiplied into a column matrix containing the desired values of hkl for a reflection, the result is the coordinates of the vector in XYZ with all the diffractometer angles set at zero. The angles required to place the crystal in the diffracting position are then calculated using the formula worked out by Euler.

9.2.1 Eulerian Geometry

There are two different geometries used for diffractometers. The oldest geometry is the Eulerian cradle shown in Figure 9.3. The most obvious feature of this diffractometer is the χ -circle which is the vertical circle in the middle of the unit.



All angles at zero as drawn.

Figure 9.3 An Eulerian Cradle

The three angles on the Eulerian cradle directly correspond to the three Eulerian angles. The first is χ (chi) which allows the crystal to be rotated with the incoming X-ray beam as the axis. The zero value of χ is when the sample is vertical and at the bottom of the circle. The χ -circle can be rotated around the vertical diameter. This angle is called ω (omega) and is at zero when the plane of the χ -circle is perpendicular to the beam. The angle ω has a limited range of values before the χ -circle will collide with either the collimator or the beam stop. The third angle is a rotation about the crystal itself. This angle is called ϕ (phi). There is no required zero for ϕ but once defined, this zero point cannot change during a given

crystallographic experiment. Three circle goniometers have omega and phi but have a fixed value of chi.

There are several disadvantages to the Eulerian cradle. The χ -circle greatly restricts access to the crystal especially from above. To solve this some goniometers have a quarter circle with a range of χ from -10 to 100° . While this opens access to the crystal, it limits the range of chi as it is impossible to set chi to values greater than 100° . The second problem is controlling the motor and reading the position for the phi axis since this axis rotates about chi. Several solutions have been used to solve this problem but all either restrict phi motion while chi is moving or involve a cable which is pulled along. Lastly, the rotation axes for the arcs must have a common center which is where the crystal and X-ray beam intersect. The tolerance in this alignment is usually 0.02mm or less. The χ -circle makes maintaining this alignment more difficult. The alignment can be affected by environmental changes such as temperature.

9.2.2 Kappa Geometry

Because of the drawbacks of the Eulerian cradle, a new geometry called kappa geometry was invented by the Dutch engineer Siem Poot. A picture of a kappa geometry diffractometer was given in Figure 3.1 and is reproduced here as Figure 9.4. The most obvious difference to the Eulerian cradle is the obvious lack of a χ -circle. The movement of the crystal from vertical to horizontal is accomplished by a new angle kappa about an inclined kappa block. The maximum value that the crystal can be rotated from the vertical is determined by the angle of the kappa block which is typically around 50° . This means that the maximum value from the vertical is 100° . The value of the angle of the kappa block must be determined very accurately and is provided by the manufacturer and stored in the software.

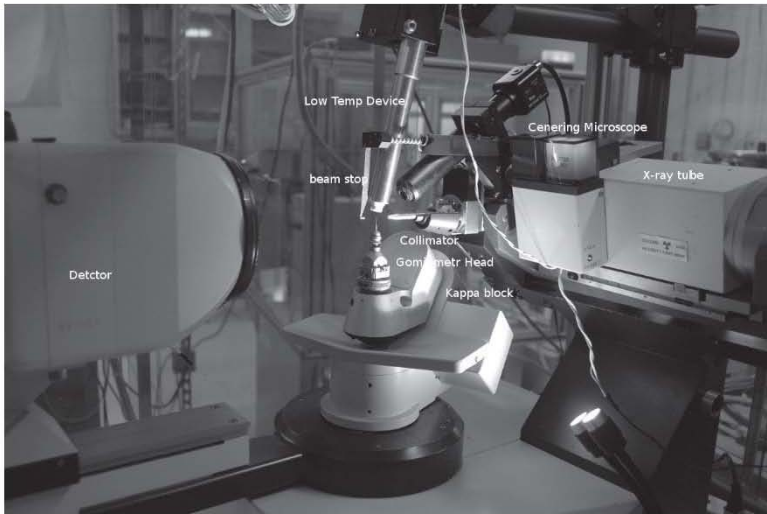


Figure 9.4 Kappa Geometry Diffractometer.

The corresponding kappa angles are calculated from the Eulerian angles. Ω and ϕ are the same motions as in the Eulerian cradle but will have different values from the Eulerian angles for an identical orientation. The three Eulerian angles are referred to as ϕ , ω , and χ while the kappa angles are ϕ_{ik} , ω_{ik} , and χ_{ik} .

The kappa geometry alleviates some problems of the Eulerian cradle. It is completely open on the top giving access to the crystal sample. Because the ϕ axis is directly attached to the kappa block, it can easily be connected to the electronics. The design also offers greater stability than the χ -circle. While the kappa geometry has a more limited range of χ than a full Eulerian cradle, it also allows greater motion in ω . In the end, the range of vectors that can be brought into the diffracting position is about equal for the two geometries.

9.2.3 Theta, Two-theta, and d-spacing

The last axis of rotation on the diffractometer involves moving the detector. The axis of this rotation is the same as for ω . The detector is moved to create the Bragg angle for the diffracted beam.

In the diffracting position, the diffraction vector \mathbf{d} bisects the angle between the incoming and diffracted beam. The Bragg angle θ is the angle between the Bragg plane perpendicular to \mathbf{d} and the incoming beam. It makes an angle of $90^\circ - \theta$ with \mathbf{d} . One way to achieve this angle is to move the detector and X-ray beam such that they make the appropriate angles when \mathbf{d} is in the horizontal plane defined by the incoming and diffracted X-ray beams. However, moving the X-ray source is not an efficient way to accomplish this geometry. If the X-ray source is moved, maintaining the strict alignment required is difficult. It also means moving the high voltage cable and maybe the water lines that cool the tube. For sources other than X-ray tubes the beam cannot be moved at all.

The solution to the problem is shown in Figure 9.5. Because the crystal is small and the diffractometer can move the crystal precisely, it is far easier to move the crystal than the source. The angles ϕ and χ are first adjusted so that the diffraction vector is perpendicular to the beam and in the required plane as illustrated at the top of Figure 9.5. The crystal is rotated about ω by the Bragg angle so that the incoming beam makes an angle of θ with the Bragg plane. If the detector is now moved by θ , it is parallel with the Bragg plane and must be moved another θ so it makes an angle of θ with the plane. Therefore, the total angular rotation of the detector is 2θ . When collecting data the center of the detector is at an angle of 2θ from zero defined as being aligned with the X-ray source. Most diffractometers require and report values of two-theta for the detector angle though CIF files use theta.

A second method for indirectly reporting the theta angle is by reporting the magnitude of the diffraction vector \mathbf{d} which is called the d -spacing. The theta value for any value of d can be calculated from Bragg's Law $\theta = \sin^{-1}(\lambda / 2d)$. The great advantage of d -spacing is that it is independent of the X-ray wavelength used. However, the diffractometer requires an angle be calculated. In the past chemical crystallographers tended to use theta and biological crystallographers d -spacing. However, the distinction between the two branches of crystallography has greatly diminished and today many programs are shared. The trend appears to be towards d -spacing. Notice that d -spacing and theta share a reciprocal relationship. The larger the value of theta the smaller the value of d . To confuse things further high resolution data has large values of theta and therefore small values of d .

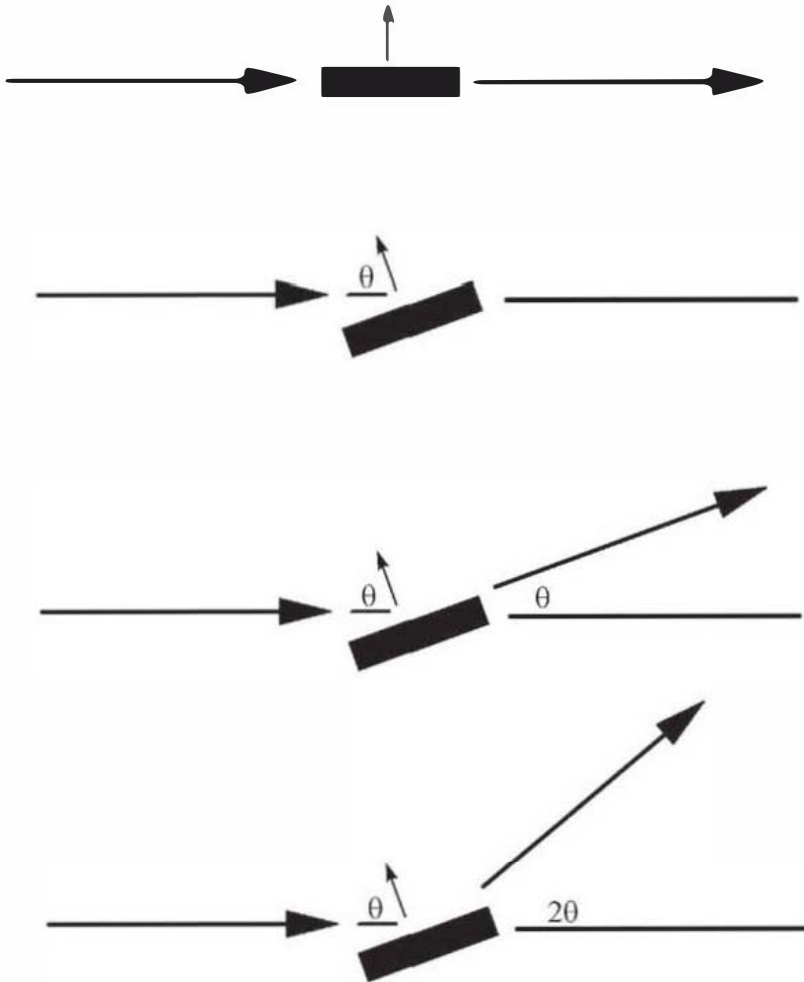


Figure 9.5 The angle 2θ

9.2.4 Detectors

The detectors used for X-ray diffraction have greatly improved over the years. The original detector was photographic film. For many years, a scintillation crystal was used to convert X-rays into visible light that were detected by a photo-multiplier tube. Since this provided no ability to

determine the location of the intensity, only one diffraction spot could be measured at a time. A variety of slits was used to keep the opening to the detector small. This type of detector is called a point detector.

Today, area detectors are used. These are like digital cameras in that they have an array of pixels that can each measure intensity. The location of the diffraction is known from the pixel excited and its intensity determined for that pixel is stored. This requires a large file for each image as it contains the numeric value of the intensity for each pixel. The diffraction spots are much larger than a single pixel and the intensity must be obtained from many pixels. Area detectors have evolved from digital arrays that detected light emitted from a phosphor when it was struck by X-rays to today's detectors which are excited directly by X-ray photons.

While this is not meant to be an in-depth discussion of detector technology, there are some concepts that must be introduced. Readout time is the time required to record the intensity of all the pixels. The older detectors had readout times of several seconds to minutes. Detectors are always counting even during readout. This meant that the shutter needed to be closed during readout. In addition, the shutter used had to be relatively high speed so the exposure time over the entire detector surface was uniform. The readout time for the present generation of detectors is almost instantaneous so there is no shutter operation required while reading the frame. A second measure of the detector is dynamic range. This is the range from how few photons the detector can measure to the maximum number of counts that can be stored. Again, the dynamic range has increased with every new generation of detector. The last specification is for the level of noise. Again, modern detectors have very low noise.

The size of the detector face is also important. Most detectors used can cover the required range of two-theta for molybdenum radiation. Both the positive and negative values of two-theta are recorded in a single image. This means that typically both hkl and $\bar{h}\bar{k}\bar{l}$ are collected without moving the detector. This will not be true for copper radiation and the detector must be moved to extend its range. Therefore, the bigger the size of the detector the quicker data collection.

9.3 Low Temperature Data Collection

There are many advantages to collecting data at lower temperatures. Since the crystal is inside a beam of cold, inert gas, usually nitrogen, even the most reactive crystals are reasonably stable. The reduction in the

molecular vibrations will increase the intensity of the high angle data and the $I/\sigma(I)$ ratio. It is also easier to mount crystals for low temperature data collection.

There are some drawbacks however, First, a low temperature device is needed. This delivers a stream of cold nitrogen gas at a constant temperature over the crystal. Either liquid nitrogen must be provided or a nitrogen separator and refrigeration system needs to be used. In rooms with high humidity, the formation of ice on the crystal may be a problem even though a column of very dry air is used to try to isolate the crystal from the room environment.

Most laboratories have standard conditions for low temperature data collection. However, temperature can have a pronounced effect on the quality of the data. Many crystals undergo phase transitions upon cooling and have a different unit cell than that determined at room temperature. Some phase changes are very sharp. If the phase change is sharp, at the temperature of the change the sample will not be crystalline and will not diffract. More common is a broad phase change. Data collected at temperatures where both phases exist will produce lower quality data. Also, the effects of the plunge to a lower temperature can cause the crystal to develop fractures resulting in broad diffraction spots or to even explode. The low temperature device can be run at room temperature if the nitrogen beam is needed to protect the crystal. If the diffraction spots are sharp at room temperature and broader when cooled, then a higher temperature should be used.

The nozzle of the low temperature device is shown in Figure 9.6. The nozzle is composed of two concentric tubes. The inner tube emits the stream of cold nitrogen. The outer tube puts out a column of very dry (dew point below -60°C) air. If the flow rates are evenly matched, the two beams can travel 8-10mm without mixing. The nozzle is adjusted so the crystal is located within the cold stream at all times.

For lower temperatures, there is equipment designed to use liquid helium as the coolant. These units can cool the crystal to 20K or less. However, because of the increasing costs of liquid helium, experiments at these extremely low temperatures are expensive. Helium cooled units are needed for data collection for experimentally determining the electron density in the crystal. They are also useful for crystals where there are large movements of parts of a molecule in the crystal.



Figure 9.6 The tip of a low temperature device.

CHAPTER 10

FROM CRYSTALS TO DATA

In this chapter selecting and mounting crystals and data collection will be discussed. Data integration and reduction and other corrections will be introduced.

10.1 The Crystal Sample

10.1.1 Growing Suitable Crystals

It would seem it should be easy to obtain suitable crystals for diffraction studies since the samples used are small (0.1-0.4mm). Ideally they will be equidimensional. Today obtaining high quality crystals may be the most difficult part of a crystal structure. Some compounds produced crystals which are very thin plates or long, thin needles. It is hard to place enough of these samples in the X-ray beam to give anything but weak data. Some crystals are actually layers of slightly misaligned planes. If the alignment is only off by a small amount they will diffract, but the spots will be broad. In the extreme, each layer may be as little as one molecule thick and result in a two-dimensional crystal such as graphite. Some compounds will never crystallize because they do not form stable enough crystals. It may take many attempts and much patience to produce an acceptable sample. However, even after repeated attempts an ideal crystal may not be obtained and therefore the entire analysis will need to balance what can be determined from the best sample obtained versus what the requirements are for a quality structure. The question then becomes is low quality knowledge better than no knowledge.

There are several excellent websites that provide insight and procedures and that information will not be duplicated here. **Growing Crystals That Will Make Your Crystallographer Happy** by Paul Boyle (http://xray.chem.uwo.ca/crystal_growing/GrowXtal.html) is a very good place to start. Martin Lutz has a useful page **Tips for Crystal Growing** (<http://www.cryst.chem.uu.nl/lutz/growing/growing.html>). A web search will provide many additional sites. There is a 1994 review article by Jürg

Hulliger which is a thorough review of crystallization.⁴¹ It contains many useful references and some astute quotes.

The vast majority of crystals for diffraction studies are grown from solution. The choice of the solvent is very important. The solute must only be moderately soluble in the solvent used. If the compound is too soluble, then the crystallization will occur too quickly as the final small volume of solvent evaporates. If it is not soluble enough, then it will be hard to produce the required equilibrium between the solution and crystal phases required for good crystal growth. Today, the use of mixed solvents has become routine. A second consideration that seems almost obvious, is that the solvent used should not react with the compound being crystallized. For example, chlorine containing organic solvents such as methylene chloride or chloroform can transfer chlorine atoms to reactive compounds.

It must also be recognized that if the solid is a mixture of compounds, then the one that forms the most stable crystal is what will crystallize. An example is an alcohol as the solvent for the crystallization of a molecule with a carboxylic acid group. The resulting crystals may contain the ester even if it exists in negligible quantities in the solution. As the ester is removed from the solution phase, the equilibrium will shift to produce more ester. Another example, is enantiomorphic compounds. Generally, the racemate will form more stable crystals and even a small amount of the other enantiomer will produce some racemic crystals. Starting with pure materials always improves crystallization.

10.1.2 The Thermodynamics of Crystal Growth

The growth of a crystal can be considered the synthesis of a super molecular assembly. As such, the process of crystallization is related to any chemical reaction where the atoms are replaced with the formula unit of the crystal. The growth of a crystal will be controlled by both thermodynamic and kinetic factors. The thermodynamics of crystal growth provides insight into why crystal growing is so difficult.

If a process is to occur spontaneously, the change in the Gibbs Free Energy (G) must be less than or equal to zero. The equation that expresses this is $\Delta G = \Delta H - T\Delta S$ where H is the enthalpy (sign convention is negative for exothermic), T the temperature in Kelvin and S the entropy. For the vast majority of chemical reactions the entropy term is small and can be ignored as it is typically much less than the enthalpy. However, forming a crystal requires a very disordered arrangement of molecules to form an

extremely ordered array. There is a very large decrease in the entropy during crystallization which must be offset by the enthalpy of crystallization if the process is to occur.

In a chemical reaction the formation of chemical bonds provides the energy for the reaction. There are similar sources of energy in a crystal. The strongest interaction results from extended covalent bonds between the atoms in the crystal. Diamond is an example of such a crystal structure. Almost as strong is the electrostatic interaction between ions especially if the charge is localized over a small area. Neither of these interactions hold most molecular (or molecular ion) crystals together. An important interaction here can be the formation of hydrogen bonds. Another frequent interaction is between the π -electrons in aromatic rings, This is referred to as π - π interactions. Molecules with dipole moments can interact through an electrostatic interaction between the positive and negative ends of the molecule. In addition, there are always van der Waals forces which are weak, short range attractions. However, if none of these interactions can provide enough stabilization to overcome the entropy term, then a crystal will not form spontaneously under any conditions.

10.1.3 Selecting a Crystal

This topic was discussed briefly in Chapter 3 Section 2. That information will not be repeated here.

A large number of crystals should be examined before selecting the one to be analyzed. Crystals can be placed on a slide and viewed under a microscope. Air sensitive crystals can be placed in a drop of mineral oil or other protectant such as paratone (parabar) or a fomblin oil. Crystals can be manipulated with sewing needles or glass fibers. The quality range of the crystals can then be observed. It is also important to determine the average shape and color of the crystals. Crystals that differ from the average should be avoided as they might be a byproduct. The crystallographic study only provides information on the sample used and not on the bulk material.

The size of the crystal is important. It should be scaled to the diameter of the X-ray beam. Typically, the crystal will be about 0.3mm on an edge. Using crystals that are too small will result in weak data that may not be reliable. However, the X-ray beam has a definite size determined by the size of the collimator and using crystals significantly larger than the beam will not produce more intensity. Crystals that are too large may cause

problems and make measurements of the intensities unreliable. Shape (morphology) is also an important consideration. Very thin plates or long needles may not place a sufficient volume in the beam and result in weak data. Large crystals can sometimes carefully be cut with a scalpel or single-edged razor blade. However, the quality of the resulting crystal may be lower. With thin plates, they will frequently lose crystallinity as the loosely bound layers delaminate. Whenever, possible it is best to use crystals without cutting.

Another tool for studying crystals that are transparent is the polarizing microscope. This is a microscope with a polarizer above and below the sample in a crossed orientation. Two polarizers are said to be crossed if their planes of polarization are perpendicular. In this case, no light is able to pass through both polarizers. This results in a black background. However, when most crystals are placed between such polarizers, light will come through the crystal. When rotated there will be a position every 90° where the crystal becomes very dark. This is referred to as extinction and it is proof that the sample is crystalline. Trigonal, tetragonal, and hexagonal samples will always be dark when the c-axis is parallel to the light tube. Cubic crystals will always be dark. Non-crystalline samples such as glasses will never extinguish. If there is any doubt, the sample should be mounted and some data collected on the diffractometer.

While modern diffractometers and software can work with weaker and poorer quality crystals, they can only do so much. There is no way to measure data that is weaker than the noise of the instrument and background. While some tricks can be used that will appear to improve the refinement, these will be noticed when trying to publish the structure and will be questioned. It cannot be emphasized enough that **the quality of a structure can never be better than the quality of the crystals used!**

10.1.4 Mounting the Crystal

Once a crystal is selected it must be securely placed on the diffractometer and then centered so it remains in the beam when the arcs are repositioned. The device that mounts to the diffractometer and holds the sample is usually called a goniometer head. The gonio- prefix suggests it has arcs for changing angles. These were used at one time so that the crystal could be rotated around a real or reciprocal axis. Modern diffractometers allow for the crystal to be randomly oriented so these arcs are no longer needed or included. These heads should properly be called

XYZ heads but the older name is widely used. There is an excellent presentation at https://www.bruker.com/fileadmin/user_upload/4_PDF_Docs/X-ray_Diffraction_Elemental_Analysis/SC-XRD/Webinars/Bruker_PDS_Fast_Groove_Structure_Determination_I_Crystal_Mounting_2012_1031.pdf which covers selection, handling, and mounting of crystals.

An XYZ head is shown in Figure 10.1. All diffractometers accept a common threaded head base which has a slot that fits over a pin so it only can be oriented one way. The z direction adjusts the height of the crystal while x and y are two perpendicular movements perpendicular to z. The actual part of the head which the crystal is placed may be a tube with a screw. This tube accepts 3mm (1/8 inch) mounting pins. The pins can be made by cutting copper pipe to a length of about 15mm or machined pins can be purchased. The other mounting method is to use a magnet to hold the mounts. Heads can either be purchased with the required magnet (as shown in Figure 10.1) or an adapter purchased that fits into the goniometer head can be used. The magnet is strong enough to keep the associated holder firmly in place.



Figure 10.1 An XYZ goniometer head

There are two basic systems used to mount the crystal into a holder. The first makes use of a glass or quartz fiber. These fibers can be quickly

pulled from a thin rod. For glass, a Bunsen burner can be used as the heat source. For quartz, a hotter flame is required which means using oxygen with either gas or hydrogen. The fiber is fixed in the 3mm pin. For room temperature work the fiber can be attached with glue or wax. However, wax shrinks at low temperatures allowing the fiber to move. Therefore, low temperature mounts should be made with a glue such as epoxy resin. Quartz fibers are better for low temperature work as they do not change length as much as glass when cooled. Since, the fibers should have a smaller diameter than the crystal to be mounted, they are very thin and easy to break. Quartz fibers are more brittle than glass. Crystals can also be mounted in special glass capillary tubes to protect them from air or maintain them in the presence of solvent.

For room temperature work, the crystal is typically attached with some form of glue. Epoxy resin, super glue, and even varnish have been used. Whatever the adhesive, it must create a bond that will hold the crystal firmly in place. For low temperature work, grease may be employed. While vacuum grease works, the silicon in its formulation will create more scattering of the X-ray beam. Hydrocarbon greases such as Apeazon are a better choice. The crystal should be mounted so it extends upright from the end of the fiber and not on the side of the fiber like a flag on a flagpole. Crystals may be pulled into the drop of glue while drying. It is easier to use grease as the crystal can be repositioned more easily.

Magnetic bases, nylon loops or mounts can be used. These are more expensive than fibers but offer many advantages. Mounting is much easier. Because the nylon is not as fragile as thin fibers, it can be handled more easily. The use of grease as the adhesive works even at room temperature. The mounts come in various sizes so larger crystals have greater support than small ones. They fit into the magnetic bases allowing quick and easy mounting and removal from the diffractometer without removing the head.

It at first appears odd that glue, nylon, and fibers can be placed in the X-ray beam. It must be remembered that X-ray diffraction is not a chemical analysis but an analysis of the crystalline phase. Only crystals will give rise to diffraction spots and none of the materials mentioned above is crystalline. However, many metals are crystalline and should not be near the X-rays even if thin enough not to absorb the beam. Amorphous materials will scatter X-ray radiation. For that reason, glues or fibers containing heavier atoms will produce greater scatter and therefore higher backgrounds. The nylon used for mounts is specially formulated to

produce minimal scattering. Whatever system is used for mounting, the amount of amorphous material in the beam should be kept to a minimum.

10.2 On the Diffractometer

In this section, the steps for obtaining a data set will be described. The actual programs to be used will differ between manufacturers and even versions. Some packages are fairly automatic proceeding nearly on their own through all the steps. Others use menus to run the programs as needed. In any case, using the diffractometer software will require training.

10.2.1 Centering the Crystal

Once the crystal is in place on the diffractometer, data collection is nearly ready to begin. First the crystal must be centered in the X-ray beam. This is another task that appears to be inconsequential but spending a little time can pay dividends. The less well centered the crystal is the more systematic error will be observed in the data.

All diffractometers have a microscope for centering the crystal. There is always a grid or crosshairs displayed which is used to center the crystal. At one time optical microscopes were used. Today there is usually a digital camera on the microscope and the result is displayed on a monitor used for communication with the diffractometer. Centering the crystal first involves placing the plane of two of the three goniometer movements perpendicular to the microscope. If this is not done, the adjustments will not be independent and will affect the movement not in the plane. There is usually software which will move the diffractometer angles to the appropriate position. Typically, the z goniometer movement is vertical and the other motion horizontal. The goniometer head is then adjusted so the crystal is centered. The image may be out of focus at this point because the third movement is far from centered. The focus of the microscope should never be adjusted since when centering is complete it will be in focus. At this point the crystal is rotated 90° in phi which brings the plane containing z and the third movement perpendicular to the microscope. Again, the crystal is centered. This continues with additional 90° rotations and adjustments until the crystal is always centered in the beam.

Occasionally, after two full rotations the crystal still does not appear to be stationary. There are two causes for this. First, the goniometer head, the

mounting pin, magnet, or the fiber or nylon mount are not firm. Check that the goniometer head is firm when pushed. If the crystal moves, either the head is not screwed down tight enough on the diffractometer or the head is defective. Do not over tighten the head as the excessive torque could ruin the diffractometer alignment or the drive motors. Instability in the crystal mounting may be caused by glue that did not dry correctly or failed to adhere to the sample.

The other cause of alignment failure is that the crosshairs do not accurately indicate the center. This can be overcome easily. Center the crystal at one position and note the tick mark the right (or left) edge makes. Rotate the crystal 180° and again determine where the new edge crosses the right (or left) tick mark. The average of the two values gives the tick mark where the edge should be aligned and the negative of half the difference between the two values is the true center. For example: a crystal is centered such that the edge is at 5 tick marks to the right. When rotated 180° the edge is now 3 tick marks to the right. The true center would place the edge at 4 tick marks. The true center of the crosshairs is at the negative of $(5-3)/2$ or 1 tick mark to the left. If that is used as the true center then the other horizontal movement can be centered. To center the height of the crystal there is usually an alternate diffractometer position where z is horizontal and the other movements vertical. Since the true center is known for the horizontal crosshairs, this can be used to center z . The position of the crosshairs should not be reset by a casual user but reported to whoever maintains the diffractometer.

10.2.2 Preliminary Data

There are two approaches for data collection. One is to begin collecting images without any preliminary frames. The outstanding macromolecular crystallographer Michael Rossmann labeled it "The American Method—shoot first and ask questions later." This is possible but there are advantages in small molecule crystallography to acquiring some preliminary data. First, these images can be examined to ensure the sample is crystalline and is of sufficient quality to produce data. The images can be used to determine the unit cell. If the crystal will not produce a cell at this point, it is probably unsuitable for data collection.

It is important to realize the chemical contents of the crystal being examined are not fully known at the beginning to the experiment. The unit cell can be used to provide some data about the crystal. First, the

Cambridge Structural Database or Inorganic Crystal Structure Database as appropriate can be searched to determine if the cell belongs to a previously characterized crystal. The CSD always searches on the primitive cell. Therefore, the centering type must be known for a cell parameter search. The cell angles are only used for reducing a centered cell to its primitive equivalent and are not used in the actual search. It is therefore advisable to “and” a second search criteria of the Crystal System found under the Space Group button. This second search will reduce the number of incorrect matches.

A second check is to determine if the cell volume is consistent with the proposed chemical formula. The average volume of all atoms excluding hydrogen has been determined. For organic compounds it has been reported as 17 or 18\AA^3 for each non-hydrogen atom.⁴²⁴³ For inorganic crystals where the packing is less dense a value of 20 is probably more appropriate. These are just rough estimates and should be treated as such. Bulky side chains will increase the average volume while large numbers of aromatic rings may reduce it.

When the proposed atomic formula is to be verified, the observed cell volume is divided by the calculated volume of the formula unit (excluding hydrogen atoms). This ratio should be close to an integer which is the value of Z for the cell. If the number of atoms in the cell is slightly too large, this can be due to the presence of solvent molecules which were not included in the expected formula. However, if Z is very far from an integer, it suggests this formula is incorrect. If the cell is much too small for the expected contents then the crystal is probably not even related to the expected compound. Frequently it is a small inorganic salt or some other compound used in the synthesis.

The other use of the unit cell and orientation matrix is to calculate an efficient data collection strategy. Because higher symmetry crystals have more equivalent hkl 's, fewer data need to be collected for these crystal classes. Some laboratories prefer to use a single routine for all crystals that may collect all eight octants. When using copper radiation it is important that any routine not be designed for molybdenum radiation. This will result in a data set that will be incomplete.

10.2.3 Data Completeness

The importance for measuring data out to high resolution (low value of maximum d -spacing) cannot be overstated. However, it is not easy to illustrate with crystallographic data what happens as the d_{max} (resolution) increases. Because Fourier Transform NMR (FT-NMR) has many properties similar to diffraction data it can be a model. No attempt is made here to teach NMR.

10.2.3.1 FT-NMR

The desired output from a nuclear magnetic resonance experiment is a spectrum plotting intensity versus frequency. This is referred to as the frequency domain. This data could be collected by obtaining the intensity of the signal while scanning the frequency (or in the particular case of NMR the magnetic field). However, obtaining such a scan can take many seconds. Since the NMR signal is weak, many scans may be required to obtain a spectrum with enough intensity.

A second approach is to work in a Fourier transfer domain called the time domain. In this case, the sample is exposed to a pulse of radiation. The interference pattern over time is then recorded. This is referred to as the free inductive decay or fid. A fid is shown in Figure 10.2. It is nearly impossible to determine what the sample was from looking at the fid. The most obvious feature of the fid is that the intensity of the signal decays with time. The intensity of the fid is both positive and negative at different times. Data can be collected using multiple pulses as long as the delay between pulses allows the fid to reach essentially zero intensity. In the displayed fid the collection time was 5.4 seconds. The frequency domain spectrum is obtained by performing a Fourier transform on the fid data. Since the fid is a continuous function, this transformation involves an integration. The theoretical limits for the Fourier transform are from 0 to ∞ seconds. Obviously 5.4 seconds is well short of this but the signal intensity is approaching zero so longer times are unlikely to produce a signal that is anything but noise.

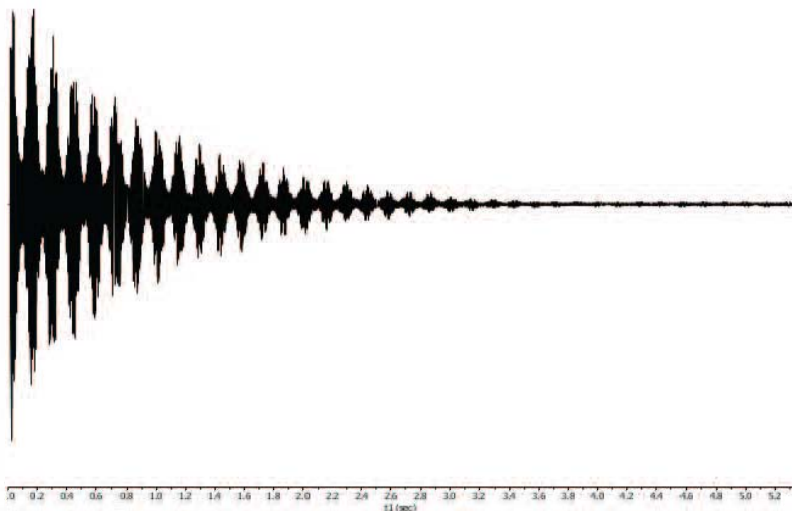


Figure 10.2 A fid for an FT-NMR spectrum.

The question then becomes how do we determine if the time for the decay is long enough and what happens as the time is shortened. The Fourier transform of the fid in 10.2 is shown in 10.3. The spectrum can now be recognized as that of ethanol. It is evident in the spectrum that there are no problems with the time used. The peaks are well-formed and sharp. The baseline is flat and there are no values where the intensity is less than zero.

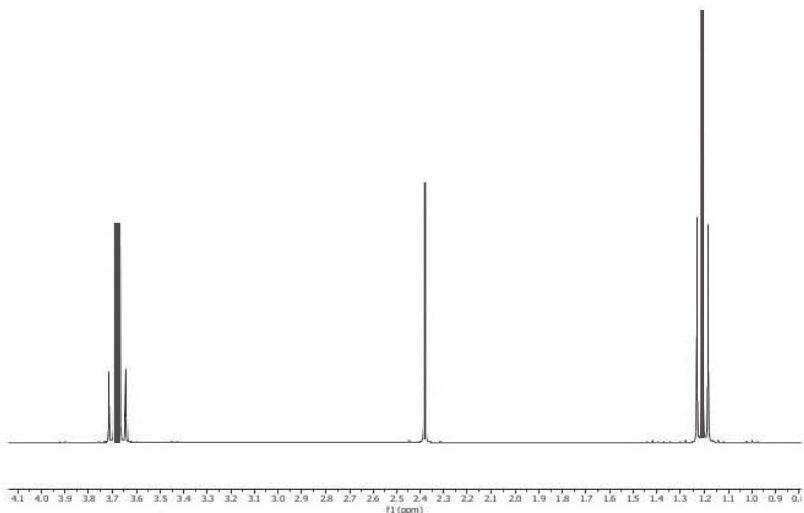


Figure 10.3 NMR obtained from the fid in Figure 10.2.

An equivalent result is shown in Figure 10.4 where the decay time was reduced to only 0.29 seconds. The difference with the 5.4 second spectrum is striking. The baseline in this case is not flat but displays what is called ringing. In the ringing and in the baseline the intensity is negative at some frequencies. The peaks have become wider and less intense. The area under the peaks should be the same however in both spectra. Further reduction in the data collection time will cause the peaks to become broad enough they will overlap and not be distinguishable as multiplets.

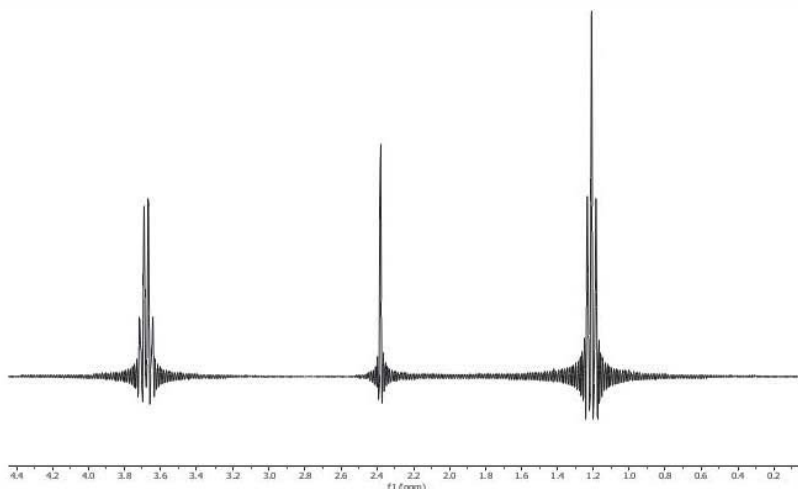


Figure 10.4 NMR spectrum returned from a brief time.

Taking data for longer times is also not that helpful. All instruments and experiments have a level of noise. When the intensity of the data becomes weaker than the noise, then only noise will be observed. Of course, if a single pulse such as for the neat ethanol in the previous figures is used, weak data will simply not provide reliable values as input to the Fourier transform. If many pulses are averaged, then the noise should average to zero which is no different from not collecting this data.

10.2.3.2 X-ray Diffraction Data

The situation for diffraction data is quite similar to that of FT-NMR even though the origin of the signal is different. Here, real space replaces the frequency domain and reciprocal space replaces the time domain. Of course, the spaces in crystallography are now three-dimensional. In reciprocal space hkl replaces time. The intensity of most diffraction experiments decreases with increasing values of θ just as in NMR. The exception is for diffraction by neutrons. In both the methods being compared the signal is fairly weak. In X-ray diffraction, the intensity of the diffraction can be increased by longer exposures. However, just as in FT-NMR if the signal intensity is less than the noise, longer exposures will not produce reliable data.

The crystallographic Fourier transform is different than for NMR. First, the data are not continuous but only occur where the indices hkl are integer. Instead of an integral the Fourier transform here is a triple sum over the Miller indices. The sum limits should be $-\infty$ to ∞ or zero to ∞ for centric crystals because of Friedel's Law. Obviously, no data set will be that complete. In fact, it cannot be. This is because for Bragg's Law θ can never be greater than 90° . At this angle the diffracted beam is traveling in the same path as the incoming beam and will be impossible to measure. On the diffractometer this would require a 2θ value which puts the center of the detector at the incoming beam. Obviously, the detector cannot collide with the collimator or beam stop. In any case the theoretical values for d_{\max} is 0.35\AA for molybdenum radiation but only 0.75\AA for copper. This means that when using copper radiation the data will always be truncated to a greater degree.

The effect of truncating the data in the diffraction experiment is similar to what was seen in FT-NMR. First, the electron density in real space will become more diffuse. Eventually, the density peaks will merge and it will be difficult to distinguish individual atoms. However, this takes a considerable truncation of the data. Another problem is that the ringing observed in the NMR spectrum can also be observed in the electron density. It will be most noticeable near heavy atoms. This is why copper radiation is not used for structures containing third row transition metals.

One other problem of truncating the data set is that it will reduce the number of data collected. The refinement of the structure involves the use of non-linear least squares. For this calculation to provide correct statistics it is essential that there be sufficient data (observations) for each variable refined.

Sometimes the data must be truncated. Truncating even a small amount in d -spacing can eliminate a large amount of data. The number of data in the range of $0.9 > d > 0.8$ (for copper $49.0 < \theta < 55.2^\circ$ or molybdenum $22.6 < \theta < 25.5^\circ$) represents about 29.5% of all the data from $\infty > d > 0.8$. However, if these data are so weak they cannot be measured accurately, it can badly affect the quality of the structure. The range of the data can be altered during the refinement, but even a small change can greatly affect the total number of data.

10.2.4 Data Collection

With all the preliminaries out of the way, it is time for data collection. As mentioned above, today the setup is almost automatic. The most important questions now are the exposure time for each image and the frame width. Both are usually determined automatically. It is possible to increase the exposure time to increase the $I/\sigma(I)$ ratio. The increase in this ratio is proportional to the square of the increase in time. To double $I/\sigma(I)$, the exposure time must be four times greater.

During the collection of an image, the crystal is rotated about an axis either omega or phi. The extent of rotation is the width of the frame. Again, this is usually automatically determined. The greater the width, the more diffraction spots will be on the image. If too many spots are on a given image, they may overlap making it impossible to determine the intensity of each one. A smaller width is used with molybdenum radiation than copper. This is because the spots for copper radiation are more spread out and there are fewer on each frame. Again, many laboratories have their own standards for frame widths.

10.2.5 Face Indexing

For crystals containing significant absorption a correction will be required. The details of this will be discussed later in this chapter. For crystals with severe absorption, the shape and size of the crystal should be defined by assigning Miller indices to as many external faces as possible and measuring the distance of the face to some origin. Different diffractometers have different methods for identifying faces so the software and methods will not be discussed here. However, this indexing should be done before the crystal is removed from the diffractometer while the orientation matrix still applies. If the crystal is mounted again then it will have to be re-indexed so that a correct orientation matrix can be obtained before the faces are assigned.

10.3 Integration and Scaling

The steps described below must be carried out before the data from the diffractometer can be used for calculations. They are listed as separate steps. However, on some program packages different steps are combined into one or more programs. The actual sequence will depend on the make of diffractometer and programs used.

10.3.1 Integration

The data stored during data collection are the intensity of each pixel for each image. This must be processed so the numerical data needed for the calculations are obtained. The required data are the hkl of each datum, its intensity and its standard uncertainty (s.u.). The process of converting the image data to numerical data is called integration. Each diffractometer will have at least one if not more programs for doing integration. The algorithms used for determining the intensity and s.u. differ from program to program and are usually proprietary. Integration is the first example encountered of a program that is referred to as a black box. The user needs knowledge of what input is required and how to interpret the output, but will not have detailed knowledge of the exact nature of the calculations. Many programs used in crystallography are black boxes.

The only critical piece of information for integration beyond the orientation matrix is the number of pixels that define a spot since the diffraction spot will be larger than a single pixel. Again, this will frequently be determined automatically. If the spot size is too large, the boundary of one peak may overlap a nearby peak. If it is too small, part of the spot may not be included in the integration. Also, the spot size will need to increase with increasing two-theta. This is because the X-ray radiation used is actually the two closely spaced peaks, $K_{\alpha 1}$ and $K_{\alpha 2}$. At low angles, the diffraction from these two wavelengths will not be resolved and the spot will appear slightly broadened. At higher angles the two diffraction peaks will begin to resolve and the overall spot will become broader. At very high angles the two individual peaks may be resolved completely. This is more of a problem with copper radiation where higher angles of theta are used.

One problem that needs to be dealt with during integration is spots that are not entirely contained within a single image. For example, the spot could be centered on the boundary between two images and some intensity will be in two consecutive images. These spots are called partials and while they complicate integration, they are useful in determining the exact values of the angles for that spot.

10.3.2 Data Reduction, Frame Scaling, and Merging

The results of integration are raw data that must be further corrected before the final data are obtained. It should be noted the data collected is

called intensity data and is frequently labeled I . It must be converted into the amplitude of the structure factor F or more commonly the square of the amplitude F^2 . Making these corrections is called data reduction.

The value of F^2 is related to the measured intensity by two factors; the polarization correction p and the Lorentz factor L so that $F^2=I/Lp$. The polarization factor arises because the X-ray beam is unpolarized when a tube is the source of the X-rays. In this case the polarization factor has the value of $(1+\cos^22\theta)/2$. The Lorentz factor is a function of the geometry of the diffractometer and how the beam is produced and treated. It is provided for the diffractometer used and will be stored in the program used for data reduction.

A second correction that can be made is frame scaling. This adjusts for changes in intensity between frames. This variation can be caused by movement of the crystal, decay of the sample during data collection, or absorption. Frame scaling is used to improve the quality of the data and remove systematic errors.

The next step on some programs is to merge the data. Each hkl may have been collected many times during the data collection process. This is because of different orientations of the crystal and occurs from rotation around the diffraction vector. In addition, symmetry equivalent reflections can also be merged to increase the redundancy. At one time the data were merged once during the data processing. The advantage was that it created smaller data files and reduced computer time. With larger disks and faster computers, it is more common today to merge the data in the refinement program each time it is run. Keeping the individual measurements separate has advantages especially if further processing to the data is needed.

The last step is to format the data and output it as needed for the programs to be used. There may be options for what format to use and in what form the data are to be stored. For example, most programs today expect the data file to contain F^2 and $\sigma(F^2)$.

10.3.3 Correcting for Absorption

Correcting for absorption produces more arguments among crystallographers than almost any other topic. When using point detectors each datum was usually collected only once at one particular set of goniometer angles. Since there were no redundant data, the correction was important. Typically, a data set collected with an area detector will have a great many

redundancies each collected with the crystal in a different orientation. Just merging these values provides an adequate correction in many cases where the absorption is not large.

10.3.3.1 The Absorption Coefficient

The absorption of X-rays by materials of different density and elemental composition makes X-ray images useful for medical and other non-invasive analyses. However, they are a nuisance in diffraction as they lower the intensity of the diffraction anisotropically. The amount of absorption is given by the absorption coefficient μ of the crystal. This is determined by the wavelength of the radiation, the atomic numbers of the elements in the cell and the percentage of the density of the crystal provided by each element. The absorption coefficient increases irregularly with increasing atomic number and increasing wavelength of the radiation. The cross section for selected elements in copper and molybdenum radiation respectively is C--89.9 and 19.5; Cl--6240 and 678; Ba--57400 and 9650. While μ can be manually calculated, it is usually given in the output of the programs if the formula is provided. The absorption coefficient has units of reciprocal length usually cm^{-1} . The percent transmission for a path length is then given by $e^{-\mu l}$ where l is the path length. Of course if the chemical formula used in calculating μ is incorrect its value will be incorrect.

10.3.3.2 Empirical Corrections

The object of any empirical absorption correction is to try to construct a function called the absorption surface which provides the value for correcting any reflection given its orientation. There is no general formula for this function as it will be a property of each crystal and how it is mounted. The function is approximated by some series and is evaluated to minimize the differences in intensity between equivalent reflections, R_{merge} . One method was to use a trigonometric series composed of the diffractometer angles.⁴⁴ Today, the method of using spherical harmonics proposed by Robert Busing is applied.⁴⁵ All of these methods require truncation of the series so the function is approximate but adequate for crystals with small to medium levels of absorption. Once the absorption surface is defined, then it is simply a matter of applying the calculated correction. This is done by dividing the observed intensity by the correction for the orientation of the crystal where a reflection was measured. Since this calculation does not make use of the absorption coefficient, it can be applied even if the formula is not known. Therefore,

it is frequently part of the scaling program. In this way orientation information does not need to be stored in the data file.

There is a problem with reporting empirical corrections. The CIF standard for reporting the extent of an absorption correction is to define the minimum and maximum correction by their transmission factors. Empirical corrections cannot provide this information as they do not use μ or calculate a path length. These programs produce a result in which the maximum transmission is 1.0 and the minimum is smaller. Since the intensity is divided by the correction, a factor of one will have no effect while smaller numbers will increase the intensity. A second method is to normalize the corrections such that the average correction is one. In this case the values of the correction will range from numbers greater than one to less than one. However, it is unreasonable to think that there is no absorption which is what a value of 1.0 applies or even worse that the reflection has negative absorption. This scaling is done so there will be no change in the scale factor.

In order to meet the CIF standard, an estimate of the transmission must be made. The smallest external dimension of the crystal and the absorption coefficient are applied. An approximation is then made that the maximum transmission is a path length along the minimum size of the crystal. The minimum transmission is then calculated by applying the ratio of the maximum and minimum calculated corrections. Most programs today calculate estimated transmission values either as part of the empirical correction or when the CIF file is produced. However, if the maximum transmission is reported as 1.0 or greater, CheckCIF will report an alert which will need to be addressed.

10.3.3.3 Numerical Corrections

For crystals with large absorption, the empirical method may not provide an adequate correction. In this case, a numerical correction sometimes referred to as a face indexed correction will be required. This requires that the Miller indices of the bounding faces of the crystal sample and their distances from some common point be reported. This data can then be drawn and should provide a view of the crystal. In addition, the orientation of the crystal to the incoming and diffracted beam must be known. This is done by providing the orientation matrix or more frequently six direction cosines. These can be included in the data file or as a separate file. The direction cosines are usually calculated by the program that produces the

data file and are omitted unless requested by the input. An accurate value of the absorption coefficient is also required.

The concept for the numerical correction is to divide the crystal into segments. The distance the incoming beam and diffracted beam travel from or to each segment can be calculated as shown crudely in Figure 10.4. The transmission along the resulting distances can then be used to calculate the transmission from each segment and then summed to produce the total correction. The smaller the segments the better the correction. Of course the quality of this correction will depend mostly on how well the shape of the crystal is defined. This limits numerical corrections to crystals with well-defined faces.

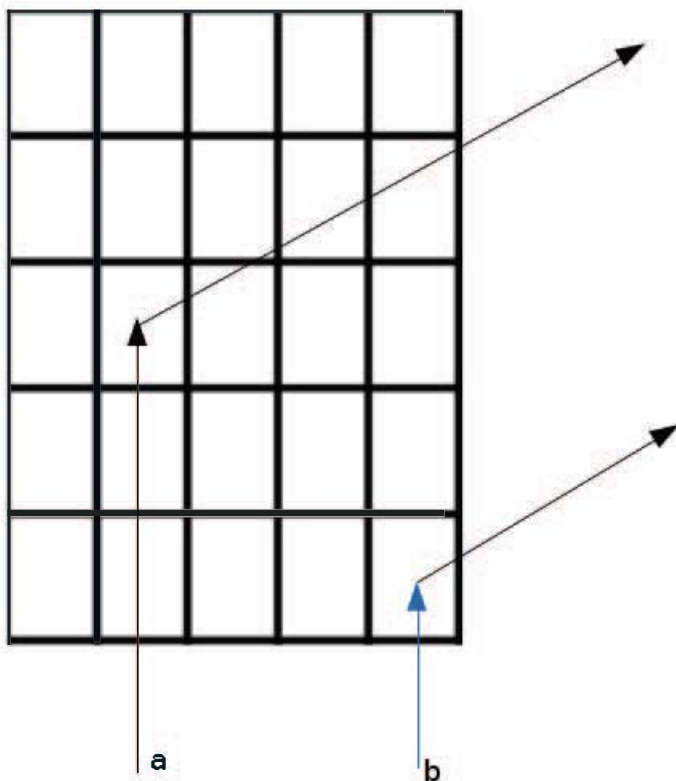


Figure 10.4 The basis of a numerical absorption correction.

It is important that the reflection data used in the numerical correction not be previously corrected by an empirical correction. Also, the data cannot be merged in any way as this will make the orientation information useless.

10.3.3.4 Evaluating Absorption Corrections

Not every crystal requires an absorption correction. Data from crystals containing only first row elements and hydrogen need not be corrected. However, today most programs that produce a reflection data file have an empirical correction built in. There is no real reason not to apply this correction. However, it should be expected that the ratio between the minimum and maximum correction should be small. If this ratio is large it suggests there is a problem with the data or the correction.

For crystals with small absorption and fairly equivalent dimensions, an empirical correction is more than adequate. However, for very thin plates or tiny needles then a numerical correction may be required. This might also be the case for crystals that contain heavy elements and are highly absorbing.

The best test of whether an applied correction has improved the data is the value of R_{merge} . The value of R_{merge} before and after the absorption correction should be provided by the software used. If the correction does not decrease R_{merge} , the correction is either inadequate or incorrect. In the end, some experience is required to select the right correction and evaluate its efficiency.

10.4 Analysis of the Diffraction Data

Usually at this point, an analysis of the reflection data will be made. This will determine, the cell centering and the space group. The program may provide information about the quality of the data and will usually create two or more files. First, is the data file. Instruction file(s) containing the data and commands need for structure solution and refinement programs will be created. This final analysis may be part of the diffractometer software or be a stand-alone program.

● One important analysis is the nature of the data. A table from the program XPREP (widely used but unfortunately not freely available) for an organic structure is given below

Resolution	#Data	#Theory	Redundancy	Mean I	Mean I/s	Rmerge	Rsigma
2.78 - 1.87	463	464	4.11	54.8	47.66	0.0227	0.0163
1.87 - 1.48	676	677	4.16	21.4	38.61	0.0266	0.0184
1.48 - 1.29	673	673	4.01	14.4	30.75	0.0272	0.0217
1.29 - 1.18	629	630	3.69	12.0	25.47	0.0324	0.0253
1.18 - 1.09	704	705	3.44	12.9	24.28	0.0340	0.0269
1.09 - 1.03	614	618	3.20	13.3	23.24	0.0341	0.0289
1.03 - 0.97	772	772	3.05	8.1	17.83	0.0420	0.0379
0.97 - 0.93	662	662	2.90	5.3	13.51	0.0554	0.0509
0.93 - 0.90	553	553	2.76	5.3	12.98	0.0581	0.0537
0.90 - 0.87	650	650	2.70	4.2	10.98	0.0687	0.0655
0.87 - 0.84	741	741	2.56	3.4	8.84	0.0779	0.0790
0.84 - 0.81	838	838	2.46	3.5	8.67	0.0797	0.0831
0.81 - 0.79	624	624	2.41	2.9	7.45	0.1017	0.1009
0.79 - 0.77	704	705	2.29	3.3	7.61	0.0891	0.0963
0.77 - 0.75	790	792	2.21	2.9	6.52	0.0966	0.1110
0.75 - 0.74	434	436	2.19	3.0	6.54	0.0981	0.1131
0.74 - 0.72	871	877	2.08	2.8	6.07	0.1022	0.1243
0.72 - 0.71	514	519	2.03	2.9	6.00	0.1143	0.1277
0.71 - 0.70	526	536	1.99	2.7	5.52	0.1116	0.1364
0.70 - 0.69	544	700	1.47	2.3	4.77	0.1206	0.1666

0.79 - 0.69	4383	4565	2.03	2.9	6.21	0.1016	0.1215
Inf - 0.69	13180	13371	2.78	10.1	15.88	0.0346	0.0365

The data are divided into groups by d-spacing. Such groups of data are referred to as shells. The next two columns represent the number of data collected and the number of data possible in that shell. The percentage of collected data should be near one. Notice for the shell **0.70-0.69** the data are only 71% complete. The redundancy column tells the average number of times a reflection or an equivalent reflection was collected. Rsigma is the sum of the sigma of the intensity for each reflection divided by the sum of the intensities. Both Rsigma and Rmerge should be as small as possible. The final row is a summary for the entire data set. Note the mean intensity and mean $I/\sigma(I)$ decrease with decreasing d-spacing while Rmerge and Rsigma increase.

This table can be helpful in analyzing problems with the data. Normally the Rsigma should be quite low (less than **0.03**) for the first shell and increase with increasing resolution. This is because of the corresponding decrease in the intensity. The Rmerge values starting large and remaining constant or getting larger is an indication the quality of the data is not good. This may be because of problems with the crystal, the data collection or the integration. It could also be caused by extreme absorption that will need to be corrected later by a numerical correction. If such data are used, the structure will probably not refine satisfactorily and may well not be publishable.

CHAPTER 11

SOLVING THE STRUCTURE

The first calculation in a crystallographic study done is to solve the structure. The need for this calculation results from the phase problem. It is necessary to make complex calculations to obtain some or all of the atom positions in the cell. Three methods for solving a structure will be discussed briefly. They involve working in real space, working in reciprocal space or alternating between the two. This discussion will only consist of what needs to be understood for the software and will not go into the details of how the results are achieved. In many respects, structure solution is the ultimate example of black box software.

11.1 The Phase Problem

The F presented in Figure 10.2 is the Fourier transfer of the desired spectrum. The amplitude of the F at any point can be positive or negative. This sign is required if the Fourier transform is to be calculated from the F . The only sign freedom is whether to multiply the entire F by -1 . Changing all the signs simply inverts the spectrum (all intensities are less than zero).

The data obtained in the crystallographic experiment are not the amplitude of the data but the intensity. This is proportional to the square of the amplitude. To obtain the amplitude or structure factor called F it is necessary to take the square root of the intensity. However, when this is done all the sign information is lost. The location of the electron density in the unit cell cannot be obtained from a Fourier transform without knowing at least all the signs. For acentric crystals this is even more complex as the anomalous scattering can change the phase even more. The lack of phases is referred to as the phase problem. At this point only centric crystals will be considered though the methods have been extended to non-centric crystals.

The importance of the phases cannot be underestimated. This can be observed in the optical transforms shown in Figure 11.1 provided by Kevin Cowtan at York University in the United Kingdom on his excellent website.⁴⁶ The two images a and b are of a duck and a cat. They can be Fourier transformed using methods similar to what is described below to create optical transforms. The calculated transform includes both amplitude and phase data. When the reverse transform to return to an image is performed using the intensities of the duck and the phases of the cat, the result is mostly a cat with some problems with the background as shown in e. Likewise, when the intensities of the cat and the phases of the duck are used the image appears to be a duck (d). Obviously, the phases are very important to the Fourier transform.

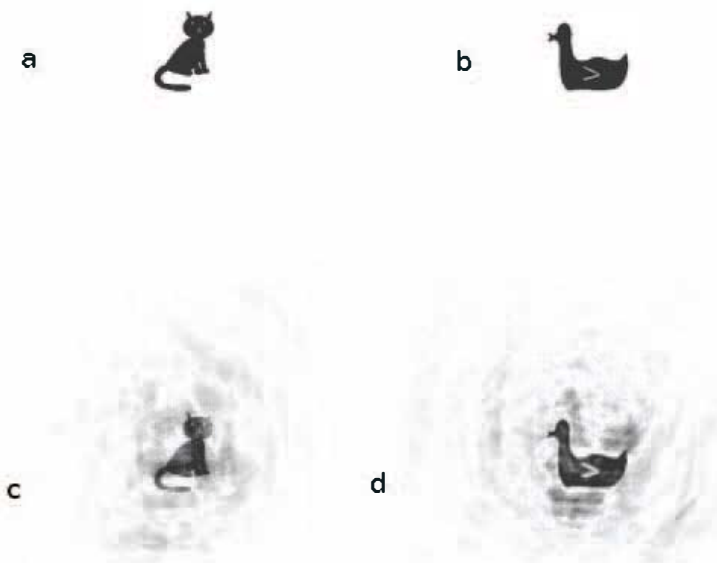


Figure 11.1 A and B are images of a cat and duck. Images C and D are created using the phases from the image above and the intensity from the other image.

11.2 Crystallographic Fourier Transforms

The transforms between reciprocal and real space will be important to understanding both structure solution and refinement programs to be discussed in this and the next chapter. Therefore, the approach and formulas used will be discussed briefly.

11.2.1 From Reciprocal to Real Space

Reciprocal space represents the data collected while real space is the unit cell. To determine the contents of the unit cell, the diffraction data must be transformed to real space. The formula for the density at any point xyz in the cell is given by the equation

$$\rho_{xyz} = 1/V \sum_{hkl} F_{hkl} \cdot \exp[-i2\pi(hx + ky + lz)] \quad 11.1$$

where ρ is the electron density, V the cell volume and F is the structure factor obtained from the data. This states that the electron density at any fractional coordinate inside the unit cell is given by the sum over all the hkl 's in the data set of the structure factors (including phases) times the exponential involving hkl from the summation and xyz of the fractional coordinates for the electron density. This formula determines the density at any location or range of locations.

The results of this calculation are referred to as a Fourier map. Generally, the map consists of a grid of fractional coordinates and the density calculated at each grid point. The grid points are separated by 0.25 to 0.5 Å expressed in fractional coordinates. This map can be printed. Two directions at a fixed value of the third direction are printed on a page. The next page contains a similar output except with a step of one grid in the third direction. At each grid point in the page, there is a number for the electron density. It is also possible to create a contour map where values of similar density are connected. This is much like a meteorological map of atmospheric pressure where the contours are called isobars. At one time the individual two-dimensional contour maps were drawn on plexiglass providing a three-dimensional view of the electron density. Today the data at the grid points are interpolated to obtain an exact location of the maximum of the electron density. This location is referred to as a peak. The geometrical relationship involving other peaks or atoms can be calculated.

Since the unit cell is made up of identical asymmetric units which are related by internal symmetry, it is not necessary to calculate the Fourier map for the entire unit cell. The much smaller volume of the asymmetric unit is used. This reduces the number of grid points that must be evaluated and speeds up the calculation and the storage needed for the Fourier map.

11.2.2 From Real Space to Reciprocal Space

While it may not appear obvious, it is frequently necessary to convert the unit cell and its electron density to calculated values for the diffraction data. This will be referred to as the inverse transformation.

While the inverse transformation could be done similarly to the previously discussed transformation, there are some problems. First, since real space is continuous, it would involve integrals and not sums. Secondly, electron density is typically added to the cell by positioning atoms. How is this density to be added?

This problem can be simplified by making use of a property of Fourier transforms. The Fourier transform (F_t) of a sum is the same as the sum of the Fourier transforms of the components that make up the sum. In equation form $F_t(\Sigma f) = \Sigma F_t(f)$. Therefore, it is possible to sum the Fourier transform of the electron density to calculate the observed data. The density for an element is calculated using quantum mechanics and then transformed. The transformed density is then called the atomic scattering factor f . Atomic scattering factors can also be calculated for simple geometries of electron density so regions of uniform density which are not atomic can be used. The atomic scattering factor is usually spherical though recently non-spherical scattering factors have been used.

The values for the atomic scattering factor are a function of the X-ray wavelength, and the atomic number of the element. For X-rays, the value of the atomic scattering factor always is the atomic number at $\theta = 0^\circ$ and falls off with increasing theta. The scattering factor decreases faster for lighter elements. Therefore, at $\theta = 0^\circ$ the contribution to the total scattering by an atom is its atomic number. However, at high angles the heavy elements dominate the scattering. A light atom such as hydrogen contributes little to the low angle data and nearly nothing at higher angles. Figure 11.2 is a plot of some atomic scattering factors versus 2θ .

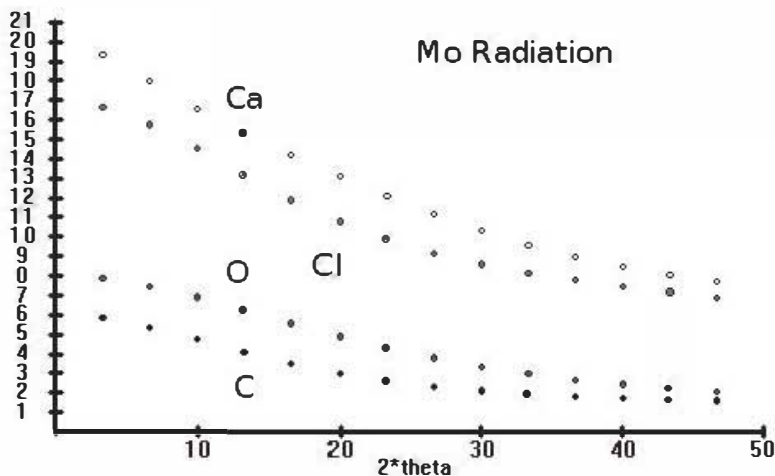


Figure 11.2 Scattering factors for several elements.

The observed reduction in the intensity with increasing resolution for a crystal is not only because of the atomic scattering factors but also because of the vibrations of the atoms which further spread out the electron density. This is accounted for in the atomic displacement parameters adp 's. Therefore, the atomic scattering factor must be adjusted to include this added reduction. The adjusted atomic scattering factor is labeled f' . Unfortunately, there are two related systems for adp 's. One system is labeled as U which is the root-mean-square of the magnitude of the atomic motion. The mean amplitude for vibration is given by the square root of U . This means U has units of \AA^2 . The calculation of f' is given by $f' = f \cdot \exp(-8\pi^2 U (\sin^2 \theta / \lambda^2))$. Because of the negative sign, the exponential term will become smaller as theta increases. The other method used for adp 's is the B 's where $f' = f \cdot \exp(-B \cdot (\sin^2 \theta / \lambda^2))$. The U 's are smaller than the B 's by a factor of $8\pi^2$ which is about 80. The value of B for well-behaved carbon atoms at room temperature is about 4 or 0.05 for U . Increasing the value of the adp will cause the scattering factor to diminish quicker with theta.

The value for the value of F with indices hkl can be calculated from the f' using the formula

$$F_{hkl} = \sum_i f_i' \left| 2\pi \left[\cos [hx_i + ky_i + lz_i] + i \sin [hx_i + ky_i + lz_i] \right] \right|$$

The sum i is over all the atoms in the unit cell. The calculated F_{hkl} (referred to as F_c versus

Fo for the observed value) includes the phase information. Note that i need not include all the atoms in the cell. However, the fewer atoms used the less accurate the value of Fc will be. This function is imaginary.

11.3 Structure Solution Methods

So at this point it appears the collected data cannot be used to obtain the crystal structure since there are no phases. Obviously there are ways of solving the phase problem. They may entail directly calculating the phases, analyzing a Fourier map generated using no phase information, or hybrid methods. This step is referred to as solving the structure and it is critical if the structure is to be determined.

11.3.1 Charge Flipping

In 2003-2004 the Hungarian mathematician Gabor Oszlanyi suggested a method of solving structures without knowledge of either the chemical contents or the space group of the unit cell⁴⁷ He called it charge flipping and it has greatly improved and simplified solving structures.

The method appears to be quite simple. Initial phases are estimated for each diffraction datum either arbitrarily or by some method. A Fourier map of the entire unit cell based on these phased data is then calculated and the locations of all the electron density peaks determined. Initially it will not display anything that looks like a chemical fragment. Any negative peaks of electron density simply have their sign changed. This is the charge flipping part of the method. A reverse Fourier transform is then applied from the new electron density to provide new phases for the data. The cycle is begun anew and repeated until the procedure converges to a structure. In practice, the algorithm is somewhat more complicated in that some weak data must also be charge flipped so that the calculation will converge to a solution.⁴⁸

The result of a charge flipping solution in the program PLATON (command Flip Patt) is shown in Figure 11.3. The ordinate axis plots R values (in percent) where $R = \frac{\sum |F_o - F_c|}{\sum |F_o|}$. The lower the value of R the better agreement between the observed and calculated data. The value of R begins at over 70% and ends at less than 20% with a sudden decrease when the correct phasing is found.

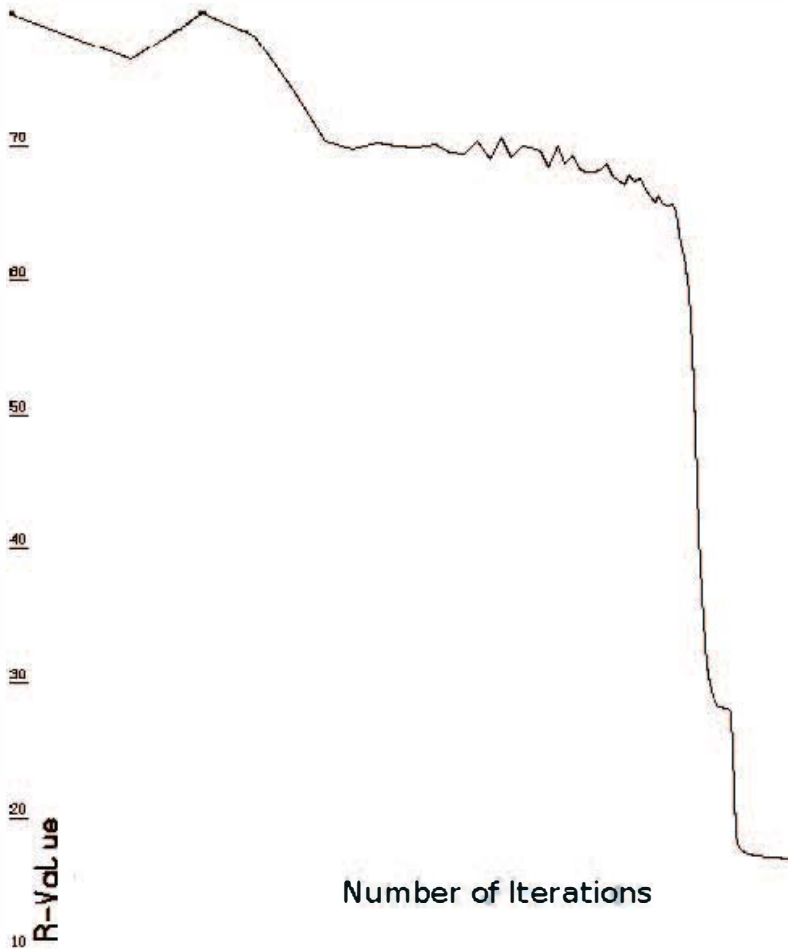


Figure 11.3 Output from PLATON/FLIPPER

Once a set of phases is found, the charge flipping can be stopped but a second step must be performed. Charge flipping works on the entire unit cell without symmetry. For the solution to be used, the space group must be determined from the results and a Fourier map calculated using the calculated phases to provide the location of the electron density. The density then must be converted to atom assignments assuming the highest density represents the element with the greatest atomic number.

There are several program packages that can apply the charge flipping method. As already mentioned the program PLATON can be used. Lukas Platinus created the programs SUPERFLIP and EDMA and associated software.⁴⁹ SUPERFLIP does the charge flipping while EDMA does the unit cell analysis. The programs can be downloaded at <http://superflip.fzu.cz/>. Probably the most used program is George Sheldrick's SHELXT⁵⁰ that can be downloaded from <http://shelx.uni-hac.gwdg.de/SHELX/>. This program is easy to use and very fast. It has one other nice feature. If peaks are found where the electron density is greater than what would be expected for any element in the provided formula, the program assigns the halogen closest in atomic number to this electron density as a placeholder so that further calculations will be reasonably correct. The user should never assume that the program has determined the presence of these halogen atoms, and they will need to be replaced by the correct element as determined by the chemical reactions and the reactants used.

Charge flipping programs are powerful. The method has been used to solve a completely unknown crystal found in a laboratory.⁵¹

11.3.2 Direct Methods

Over the years methods have been developed to assign phases directly in reciprocal space. The mathematics behind these methods is quite complicated. Herbert Hauptman and Jerome Karle won the 1985 Nobel Prize in Chemistry for the development of equations that could be programmed. The programs developed from their research opened up, improved, and simplified chemical crystallography. This is especially true for studies of organic compounds which were very difficult to solve before direct methods were available. They have been superseded by charge flipping though some crystallographers still prefer direct methods.

Because of their complexity, direct methods programs represent the most extreme example of a black box. The discussion here will be perfunctory and provide only enough information, so they can be employed and their output understood.

First, for reasons to be explained later, it is important to find reflections that have significantly higher values of F or F^2 than would be expected for a given d -spacing. This cannot be done by simply sorting the F values and using the most intense. The falloff of F with resolution means that an

apparently weak high angle reflection might be more intense than expected. To determine the relative intensities a new factor E the normalized structure factor is introduced. The E value is the F value divided by the expectation value of F at the d -spacing for the reflection. The expectation value for a reflection $\langle F^2 \rangle$ at a given value of θ is given by $k\varepsilon \sum f_i^2 \exp[-2B \sin^2(\theta)/\lambda^2]$. The sum is over all the atoms in the formula. In this equation k is an overall scale factor and B a single adp applied to all the atoms. The value ε is symmetry enhancement factor for some classes of hkl . It depends on the space group of the unit cell. Values can be found in the **International Tables for Crystallography, Volume B**, Table 2.1.3.3. The value of E is $F/\langle F \rangle$

Before the values of the E 's or E^2 's can be calculated, the appropriate values for B and k need to be estimated. They are usually obtained from a Wilson Plot. A typical Wilson plot is shown in Figure 11.4. The curved line is the data and the straight line represents the best linear least squares fit. The data should make a curve as observed and the fit is obviously not great. However, it is good enough to provide a rough value of B needed to calculate the E 's. It is also possible to obtain k from the y-intercept. If the fit line is nearly vertical or even has a negative slope, it strongly suggests there are problems with the data. The E 's are typically scaled such that the average value of E is one. Therefore, E 's with values much greater than one are strong reflections regardless of the value of F . Since the expectation value of F is summed over the chemical contents of the cell, the chemical formula must be known. The presence of unexpected heavy atoms or the absence of such atoms when they are included in the formula will generate incorrect values for E and direct methods may not work at all.

Direct methods work on mathematical formulas that come from two aspects of real space. First, the electron density cannot be negative. Second, the electron density is not evenly distributed throughout the cell but localized at specific coordinates within the unit cell. From these conditions relationships between the E 's can be developed. The oldest one is the Sayre equation which is $E_{hkl} = \sum_{h'k'l'} E_{|h'k'l'|} \cdot E_{|h-h', k-k', l-l'|}$ where all the E 's have been assigned signs. At first this appears to be nearly useless as the signs of all the other E 's need to be known to calculate a value. However, it does suggest that there is a relationship between the phases for all the diffraction data.

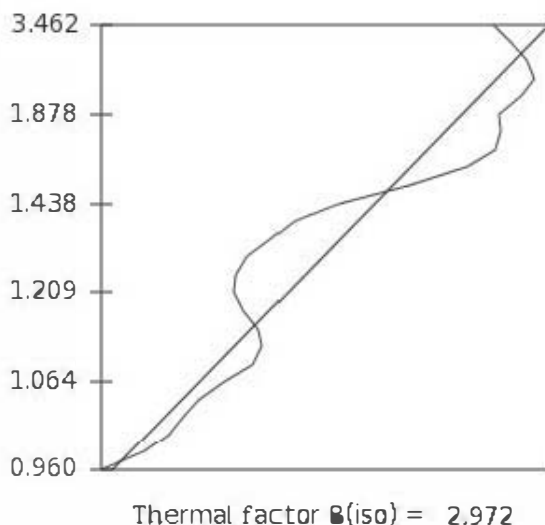


Figure 11.4 A Wilson Plot

For centrosymmetric structures this can be reduced to $S_{hkl} \approx S_{hkl} \cdot S_{-h,-k,-l}$ where S is the sign + or - one. If two large E 's on the right side of the equation both have the same sign then the sign of F_{hkl} must be positive. The reflections in the above equation are referred to as a triplet Σ_3 . These ideas were further extended by Hauptman and Karle in probability equations for determining the signs of strong triplets and then later extend to methods for acentric structures. These later formulas were the basis for software that made direct methods available for structure solution. Some modern programs even use quartets or sets of four reflections.

The approach used by most direct methods programs is to calculate the E 's and then find several large E 's that can be used to generate values for much of the remaining data. These starting E 's are assigned all sign possibilities and then the calculation is done to generate as many of the phases as possible. The number of solutions is then 2^{n-1} where n is the number of E 's in the starting set. For five starting reflections sixteen possible solutions are calculated.

At the time direct methods programs came into being, these calculations were lengthy and would have been considerably longer if a Fourier map had to be generated for each possible solution. Therefore, it was important to develop a test of the quality of a potential solution in reciprocal space

before calculating a Fourier map. This included evaluating the constancy of the resulting E^2 's, whether the result correctly predicted the intensity for weak reflections, and other tests. The result was reported in one number called the combined figure of merit (CFOM). The solutions with the best CFOM were most likely to be the correct solution. If these programs were designed for today's computers, they would probably just calculate a Fourier map for each solution which could then be evaluated as to whether it made chemical sense. It should be remembered that charge flipping does a forward and reverse Fourier transform for each cycle and there may be several hundred cycles run before it provides a solution. This suggests calculating a single Fourier map should not take much time.

The first direct methods program package that found widespread use was MULTAN introduced in the early 1970s by Declercq, Germain, Main, and Wolfson⁵² and modified extensively over the years. The two most widely used direct methods programs are George Sheldrick's SHELXS⁵³ and the SIR⁵⁴ package by the Sir Group. For SHELXS the closer the CFOM is to zero the better the solution while in the SIR programs the closer to three the better the solution. The program SHELXD⁵³ is the ultimate direct methods program for small molecules. It is an absolute brute force method generally trying 1000 or more solutions. If it fails, then nothing else is likely to work. It is also the only solution program capable of solving data from twinned crystals.

When looking at the Fourier maps calculated from the data with phases from the calculation, realize it may not be accurate. The phases of some reflections may not be determined correctly. It is not uncommon to see extra atoms or there may be missing atoms. These problems will be taken care of later during refinement.

11.3.3 Patterson Methods

It is possible to calculate a Fourier map without assigning any phases. This is called a Patterson map. However, this map will not be a map of electron density versus position. Instead, it will consist of all the vectors between any two atoms in the unit cell where the height at a given coordinate is proportional to the atomic numbers of the two atoms at the ends of this vector. At the origin of the map will be a large peak which is the sum of all the zero length vectors between an atom and itself. At first, it does not appear that there is anything useful that can be obtained from such a map but in fact when the symmetry of the unit cell is considered it is possible to

derive the positions of a few heavy atoms. For this reason Patterson methods are sometime called heavy atom methods. While it is not likely that the entire contents of the asymmetric unit will be obtained from this method, it is possible to find at least 15% of the electron density which is all that is needed to proceed with refinement.

An example will make this clearer. Consider a crystal with one heavy atom in the formula unit that crystallizes in $P\bar{1}$. In this space group there are two symmetry operations x, y, z , and $\bar{x}, \bar{y}, \bar{z}$. If there is an atom at the first position there is also one at the second. The vector between the two is either $2x, 2y, 2z$ or $2\bar{x}, 2\bar{y}, 2\bar{z}$. This means that the Patterson map is always centric no matter the symmetry of the unit cell. The coordinates of the heavy atom are given by $0.5(2x, 2y, 2z)$. The space group tables in the ITC-A list the symmetry of the Patterson map.

As the number of symmetry operations in the space group increases so do the number of vectors. The space group $P2_1/c$ has four equivalent positions x, y, z ; $\bar{x}, y + 1/2, \bar{z} - 1/2$; $\bar{x}, \bar{y}, \bar{z}$; and $x, \bar{y} + 1/2, z - 1/2$. When the vectors are calculated from these positions, there are three major peaks $2x, 2y, 2z$; $2x, 1/2, 2z + 1/2$; and $0, 1/2 + 2y, 1/2$ and their inverses (remembering $1/2$ is the same as $-1/2$). The $2x, 2y, 2z$ peak will have half the intensity of the other two peaks. By adding and subtracting these vectors the position for the heavy atom can be found.

As the number of symmetry operations increases further and/or the number of heavy atoms increases, the number of vectors will increase. This makes solving the Patterson function much more difficult. Fortunately, there are several programs that can perform the calculations to obtain positions. One is DIRDIF by Paul Beurskens *et al.* and the other is PATSEE by E. Egert and G. Sheldrick.⁵⁵ Neither program is new but both work well to solve Patterson maps.

Today, Patterson maps are not widely used to solve structures. However, calculating the Patterson map can still provide important information about the unit cell contents. If the Patterson map is devoid of high peaks, it strongly suggests that there is no heavy atom in the unit cell while if there are intense peaks, it suggests a heavy atom is present. This can provide information needed for direct methods calculations. The map can also be compared to the expected symmetry as a check on the space group.

11.4 When No Solution Is Found

Sometimes even when all the methods are tried, no chemically reasonable solution will be found. There are several approaches that can be tried to get a solution.

1. Try charge flipping methods. Give the program as much freedom as possible to test different space groups and even crystal classes.
2. Make sure the formula is close to correct. In organic compounds that only contain first row elements, the presence of a solvent such as chloroform or methylene chloride will introduce relatively heavy atoms that may cause problems with direct methods programs.
3. Make sure the crystal class is correct. This should be determined by examining the intensities of the equivalent reflections and not just the cell parameters.
4. Ensure the space group is correct. Look to make sure the systematic absences are actually there. A frequent source of problems is a screw axis on a short cell axis. Check to see if adding a screw axis transforms the space group into a common one. The other problem is also possible where a screw axis has been included which should not be there. A common example is $P2_12_12_1$ instead of $P2_12_12$.
5. Try a brute force program like SHELXD.

If all the above do not produce a solution, the problem is in the data. Check that the Rmerge values are reasonable. Also examine the Wilson plot to determine if it appears correct and the calculated value of D (around 4) is reasonable.

Lastly, the problem may be the crystal is actually some form of twin. Problems of twinning will be dealt with in Chapter 14. Common signs of twinning are high values for Rmerge or the systematic absences do not appear to fit any space group in that crystal class or there are no systematic absences at all. Twinned structures will not solve routinely unless more information about the twinning is supplied.

Today's programs are extremely powerful and will almost always find a solution if one is to be had. It may take trying several programs to arrive at the solution. However, with diligence most structures today are solved routinely.

CHAPTER 12

STRUCTURE REFINEMENT

When modern programs are used to solve a crystal structure, they frequently provide the coordinates of all the atoms in the formula unit. This may provide enough information to answer questions about the composition and geometry of the compound studied. However, this is only the beginning of the calculations needed to complete a structure. The parameters obtained at this point are crude and refinement is needed to improve the accuracy of the structure and to insure all the electron density has been accounted for. A more thorough review of crystallographic refinement is the article by David Watkin.⁵⁶

12.1 Refinement Software

There are several refinement software packages available for performing the needed calculations. The most popular package for chemists is SHELXL written by George Sheldrick.⁵³ This program is available at no cost to academic users. There is a website devoted to this program where there is information for downloading, instructions for use and even FAQ's.⁵⁷ The use of SHELXL is so extensive that there is even a book on structure refinement using this program.⁵⁸ When discussing refinement, the appropriate SHELXL command will be given in []. However, this will just be the name of the command and will not contain any additional input that may be required. This information should be obtained from the references previously mentioned.

SHELXL is a command-driven program and does not contain a graphical user interface (GUI). Some users are not comfortable entering commands and using a text editor. Several GUIs have been developed that simplify the use of SHELXL. One such program is SHELXLE⁵⁹ can be downloaded from <https://www.shelxle.org/shelx/eingabe.php>.

A second program OLEX2 began as a SHELXL GUI.⁶⁰ and its website is <http://www.olexsys.org/>. However, it has grown steadily and should now

be considered a powerful refinement package in its own right. It even has added its own least squares software in addition to using SHELXL. Since these programs are based on SHELXL all accept SHELXL commands. All the programs mentioned so far are available for Windows, Linux and Mac.

There are two other excellent packages which for whatever reason have not found widespread use among chemists. One is CRYSTALS which was first written by David Watkin of Oxford University and has been continued on by a group there.⁶¹ This program is fully graphical. While it does not use SHELXL code, it does have software so files can be interchanged between the two packages. It is only available for the Windows operating system and is free to both academic and commercial users. The program JANA2000 by Luckas Palatinus is another package available at the website <http://jana.fzu.cz/>. It has many features for working with structures with crystallographic problems.

Whatever software is used, there will be a learning curve before it can be used even routinely. Beyond that are features that enable unusual problems to be handled. Reading the manuals and understanding the program is essential if the results are to be correct.

12.2 Least Squares Methods

The object of refinement is to build a model of the electron density by adjusting the locations and adp's of atoms such that the data calculated from these parameters provides the best agreement with the observed data. While several approaches were tried in the history of crystallography, today all refinement is done with non-linear least squares methods. In this section, the nature of the familiar linear least squares will be first discussed. Then the differences with the non-linear calculation will be highlighted. Finally, the importance of weighting will be explored.

12.2.1 Linear Least Squares

The method of linear least squares (also called linear regression) is commonly used to determine the best slope and intercept of a straight line. The slope and intercept will be considered parameters to be determined. The linear reference here does not refer to the straight line but the fact that the parameters to be determined all occur in a sum and therefore form a set of linear equations. The method can be applied to any system that meets this requirement. For example, the best fit for parameters in the following

equation form $y = \sum a_i x^i$ can be obtained. Some equations can be made linear by applying an inverse operation. Thus $y = e^{(mx+b)}$ can be reformulated as $\ln(y) = mx + b$.

The input data for a linear least squares calculation are the values of the measured variable (the dependent variable) and the values at which it was measured (the independent variable). In the discussion here, y is the dependent value and x the independent one. The function that ideally relates y to x is also required. This fitting method is called least squares because the object is to minimize the value of $\sum (Y_o - Y_c)^2$ where Y_o is the measured value and Y_c is the value calculated from the function for a given independent value. The output of the calculation is the parameters fit and their errors. A single calculation is sufficient and no initial values for the parameters are required. The number of observations (pairs of x, y) are important if the errors in the parameters are to have any validity. Clearly, any two points define a straight line and no least squares calculation is needed to determine the slope and intercept in this case. It is only when many data are used that the actual errors and even the shape of the function can be determined. A rule of thumb is that ideally there be a minimum of 7-10 data points for fitting a straight line. Using fewer may not greatly alter the calculated parameters but will have an effect on the errors. It should be noted that for some experiments it may not be possible to obtain that many data points.

A second problem is whether the function used to calculate the values is a valid fit for the data. A line can be fit to any data regardless if the data have a linear relationship. An example of this is the Wilson plot in the last chapter where a line is fit to data that clearly are not linear. An additional factor the correlation coefficient can be calculated to determine how well the formula applied fits the data. For linear least squares the value of the correlation coefficient ranges from -1 to +1. An absolute value of the correlation coefficient near one means there is a strong probability the function used is correct. The smaller the absolute value is the less likely the function describes the relationship between the observed and calculated data.

It is possible to improve the fit and the correlation coefficient by adding additional terms. For example, the term ax^2 could be added to the equation for a straight line to introduce some curvature. If there are sufficient data, this will lower the correlation coefficient simply because it provides another parameter to adjust. However, an improvement in the fit does not

ensure the function is correct or even statistically better than the simpler form.

12.2.2 Non-Linear Least Squares

Non-linear least squares also involves trying to minimize the sum of the square of the differences between the observed and calculated data. However, it is a very different method from linear least squares. To demonstrate the method, the problem of fitting multiple Gaussian peaks to an observed spectrum will be examined. The intensity of a spectrum made up of component Gaussian peaks is given by

$$I_x = \sum_1^n A_i \exp -\left(x - b_i/c_i\right)^2$$

where the sum is from 1 to the number of component peaks. In this equation I is the intensity at x ; A is the amplitude of the component Gaussian peak; b is the location of the centroid of the peak; and c is related to the peak width. It is clear this function is not linear and therefore linear regression cannot be applied so non-linear methods must be used to obtain the three parameters A , b , and c .

There are many differences between linear and non-linear least squares. The non-linear method does not provide values for the parameters, only shifts that when added to the original parameters will lower the sum of the squares. Therefore, this is not a case of performing one calculation but many iterative ones. Each such iteration is called a cycle. Since the method does not provide values but only changes to the previous data, initial values must be provided. These initial values must be reasonably close to the correct values or the sum of the squares will be so large that the calculated shifts will be meaningless.

The next question is how to measure if the fitting process is improving the fit. One way is to graph the differences between the calculated and observed intensities. It is more useful to find numbers that provide a summary of this information. The quality of the fit can be measured as a fraction using the R-factor. There are two R factors. The first is just the sum of the absolute values of the differences divided by the sum of the observed data as given by

$$R_1 = \frac{\sum (|I_o - I_c|)}{\sum |I_o|}$$

while the second R factor is given by

$$R_2 = \frac{\sum (I_o - I_c)^2}{\sum I_o^2}$$

The sums are over all the data points used. The numerator for R_2 is the sum that is being minimized by the least squares calculations. Like linear least squares, the calculation will also produce values for the errors for each parameter. These errors are estimated from the calculation and are not exact. At one time they were called estimated standard deviations but are now called standard uncertainties (s.u.'s). While not calculated this way, the s.u. for a parameter can be thought of as how sensitive the overall fit is to changes in that parameter. If the quality of the fit is very sensitive to changing a parameter, that parameter will have a small s.u. while if it is insensitive, the s.u. will be large.

As with the linear case, it is also important to question whether the model being fit has anything at all to do with the results. In the linear calculation this is indicated by the correlation coefficient. For non-linear least squares the equivalent value is the goodness-of-fit (GooF). The range of the GooF is from zero upwards. For a proper fit the value should be one. This GooF is also sensitive to the weight scheme used (see below) and so is a measure of the validity of the weighting.

Non-linear calculations can be run forever and will always produce some small shift in the parameters. Therefore, a way is needed to determine if the calculations are providing meaningful changes or the calculation has converged. Convergence is indicated by the maximum shift/error. The shift is defined as the value of the new calculated parameter minus the value of the original. For each parameter the absolute value of the shift divided by its s.u. (referred to as the shift over error) is readily obtained. The fitting program typically reports the largest absolute value. If this value is considerably less than one, then the changes in the parameter just amount to noise and the fitting cycles can be stopped. Usually values of 0.05 or less are expected for the maximum shift/error in the final cycles.

In fitting spectra it is possible to add more component peaks than needed to obtain a good fit. This will usually result in the least squares calculation moving the unneeded peak so it is centered well beyond the range covered in the data. The intensity of this added peak will contribute little to the resultant intensity in the observed spectrum.

12.2.3 Weighted Least Squares

The least squares fitting procedure described so far assumes that the error in each measurement is identical. This is rarely the case. If each datum is collected multiple times, the standard deviation σ can be calculated. The fit can then be weighted frequently using $1/\sigma^2$ as a weighting factor. The larger the weight the more importance assigned to that datum in the calculation. Other weighting schemes can be used as long as they are statistically valid.

There are several assumptions in using $1/\sigma^2$ as the weight. First, the value of the standard deviation should arise from the accuracy of the measurement and not a systematic error. Second, the standard deviations must have a statistically valid distribution. For example, if the data were acquired using different instruments with different precision, then the standard deviations will not be distributed correctly, and they will not provide valid weights. The data on the more precise instrument will be given more importance, which may or may not be correct. Lastly, the weight may not contain any connection to the fitting process. Obviously, a calculation where the weight is related to the difference between the observed and calculated values will not be acceptable. While such an obvious weighting scheme is usually easily detected, it is possible to build this bias into complicated schemes and not be aware of it.

The weight takes on an additional importance in non-linear least squares. The values of the dependent variable can cover a much larger range than for most linear relationships. For example, for a UV-Visible spectrum the molar absorptivity may range from zero to over 4,000 with most values being small numbers. If the sum being minimized is not adjusted, then the weak values will contribute essentially nothing to the sum and therefore be ignored. Assume for example that the difference between each calculated and observed value is 5% of the observed value. A value of 4,000 will contribute 200 to the sum while a value of 10 will only contribute 0.5. The resulting fit will accurately agree with the peak maxima but will ignore the baseline. Therefore, the weighting is also used to scale the values so all data make relatively equal contributions to the fit. The s.u.'s on large values will be significantly larger than for smaller values and therefore the large values will be down weighted.

12.3 Crystallographic Least Squares

Crystallographic least squares involves using the inverse Fourier transform introduced in the last chapter to calculate values of the structure factor F from the location of the electron density in real space. The equation for this is given by

$$F_c = \sum_i f_i \exp(-8\pi^2 U |\sin 2\theta / \lambda|^2) \quad (12.1)$$

$$\left(2\pi (\cos(hx_i + ky_i + lz_i) + i \sin(hx_i + ky_i + lz_i)) \right)$$

where i is the sum over all the atoms in the unit cell, f_i is the atomic scattering factor for the atom i , and xyz are its fractional coordinates. U represents the atomic displacement parameter (adp) ideally caused by atomic vibrations and will be more thoroughly discussed in the next section. For this function, F_c is the dependent variable and hkl are the independent variables. Therefore, the object of the least squares calculation is to calculate better values for x , y , z , and U to minimize $\sum (w(F_o - F_c)^2)$ where w is the weighting factor. For technical reasons most crystallographic refinement programs today tend to store and minimize the square of the structure factors. This changes the sum being minimized to $\sum (w|F_o^2 - F_c^2|^2)$. The result is that for the simplest model, the refinement of an atom requires four parameters (x, y, z and U the isotropic adp) to be adjusted.

12.3.1 ADP's

The movement of the atoms due to vibrations causes the scattering power to decrease as a function of increasing θ . In this section the parameter U will be used exclusively even though some programs may still use the related B where $B = 8\pi^2 U$.

When a single U is refined, the vibrational displacement is assumed to be identical in all directions and therefore is isotropic. Using equation 12.1 with a single value for U is called isotropic refinement. This is usually the method used in the early stages of refining a structure until all the non-hydrogen atoms have been added. However, it is not reasonable to expect that displacements are isotropic.

Anisotropic refinement involves replacing the single U value with $U_{11}h^2a^{*2}+U_{22}k^2b^{*2}+U_{33}l^2c^{*2}+2U_{23}klb^*c^*+2U_{13}hla^*c^*+2U_{12}hka^*b^*$ where there are now six U components, hkl , and the reciprocal cell lengths. Refinement of an anisotropic atom now takes nine parameters. The U values 11, 22, and 33 represent the magnitude of the vibrational displacement along the unit cell axes a , b , and c . These provide the lengths of the axes of an ellipsoid. The other three U values indicate how the ellipsoid is oriented. It is also possible to derive U_{eq} which is the value of an equivalent isotropic parameter. This is not the average value obtained from $(U_{11}+U_{22}+U_{33})/3$ but is readily calculated using a simple formula. It is not necessary that all atoms be refined anisotropically as it is possible to mix isotropic and anisotropic refinement in a structure. However, most journals require that all non-hydrogen atoms be refined anisotropically in the reported structure.

While there is a physical meaning for the various adp 's, the values are not restricted to any range in the least squares refinement. For an isotropic atom, U can refine to a negative value even though this does not describe a real vibration. First if U is negative it means the vibrating atom actually scatters with a greater magnitude than that of a stationary atom. The U value is the square of the root-mean-square of the vibrational displacement. Since it is not possible to take the square root of a negative number, the radius of vibration cannot be determined. There are similar impossible values for anisotropic parameters. A negative isotropic U or a set of anisotropic U parameters which does not produce real displacements is called non-positive definite. This almost always indicates a problem with the structure or data and cannot be published.

Ideally, the adp 's should adjust the atomic scattering factor f for vibration. However, they can also adjust for any systematic error in the structure. For example, failure to correct for absorption can result in ellipsoids that are all oriented in the same direction. As mentioned in Chapter 4, the adp 's will also increase or decrease if the atomic scattering factor used is not correct for a given atom. Elongated ellipsoids may be indicative of a disorder where two atoms are too close to be resolved. Any abnormality in the size or direction of the adp ellipsoids when plotted should always be investigated.

The value of U or U_{eq} for a carbon atom in an organic molecule at room temperature should be about 0.05. The larger the atomic weight of an atom the smaller the U value will be. The adp will also be a function of

temperature becoming smaller as the temperature is decreased. This is why for many years α_p 's were referred to as temperature factors and the displacement ellipsoid was called the thermal ellipsoid. The TE in ORTEP stands for thermal ellipsoid.

12.3.2 Accessing Refinement Quality

Crystallographic non-linear least squares employs three evaluations of the quality of the fitting process. These are R_1 which may also be called R and R_2 also known as R_w plus the goodness-of-fit. Each of them provides different information about the refinement.

R_w is the easiest to understand and probably the most important. Assuming that values of the data used in refinement are F^2 , then R_w is given by

$$\sum \left(w(F_o^2 - F_c^2) / \sum (wF_o^2) \right)$$

The reason for its importance is that the numerator of R_w is the sum that is being minimized by the least squares calculation and therefore is very sensitive to problems in the data or refinement.

The most used definition for R is unusual and the reason for this will be discussed below. It is defined as

$$\sum (|F_o - F_c|) / \sum |F_o|$$

Even when the refinement is done using F^2 , the R value is usually reported based on the structure factor. The reason for this is historical. At one time refinement was done on F and many chemists thought a crystal structure was acceptable if the value of R was 0.07 or less. R factors based on F^2 are always larger than for F . At the conclusion of refinement they are about twice as large. This created problems with referees who did not fully understand the change. So the basis for the calculation of R remained F and not F^2 so that the numbers provided would be consistent with older calculations. A second change in newer programs was to use all the data for refinement while earlier only data larger than some $F/\sigma(F)$ cutoff was used. Again, many programs use a cutoff when calculating R for consistency. Some programs create CIFs with four different R -factors. These are based on F and F^2 with and without a cutoff.

The GooF is also an important indicator of both the quality of the refinement and the quality of the weights. At the early stages it is more sensitive to incorrect solutions or other problems than the R-factors. When all the electron density is accounted for, it becomes more sensitive to the weights used. A value of the GooF significantly below 1.0 suggests the data are being over weighted which will mean the errors obtained may not be valid.

It must be emphasized that no one value can fully explain the quality of a crystal structure. The R-factors will be affected by the quality and size of the crystal used, uncorrected absorption or other problems, and any systematic errors. The s.u.'s observed in the geometrical parameters are also an important measure of quality. There are many tricks for lowering the R-factor. While they can reduce its value they do not improve the quality of the structure. This should be taken into account not only when doing structural refinement but even more so when reviewing the work of others.

12.3.3 Least Square Weights

The problem of appropriate and statistical weights has been treated extensively. A good discussion can be found in Jack Dunitz's book on crystallography.⁶² As pointed out, it is not clear if the s.u.'s for the data follow any statistical distribution. Many approaches have been tried to produce valid weighting schemes. The simplest is that $w=1/\sigma^2$. It has been found that using $1/\sigma^2$ still gives too much importance to the very intense data. A common scheme added a second term so that $w=1/[\sigma^2|Fo|^2 + \{pFo\}^2]$. The factor p usually has a typical value of 0.1 and should never be more than 0.2.

The commonly used SHELXL has a more complicated weighting scheme.

The formula used is

$$w=1/[\sigma^2|Fo|^2 + \{aP\}^2 + bP] \text{ where } P=1/3\max\{0, Fo^2\} + 2/3Fc^2.$$

The use of P rather than just Fo^2 produces better weights during the early stages of refinement. The second term is equivalent to the p factor while the third term affects mostly weak data. The value for b is usually zero or close to it. The full SHELXL weight has two more terms— a constant

and a term e that weights as a function of $\sin\theta/\lambda$. These additional terms are almost never used.

Most crystallographic refinement programs have either a standard weighting scheme or one that is preferred. This should be used for routine operations. The program may provide new values for the weighting scheme which will bring the GooF closer to one. These can be substituted for the initial value during the final refinement cycles. If the GooF remains much greater or less than one this suggests a problem with the data which must be investigated.

12.3.4 Other Refined Parameters

Besides the four or nine parameters refined for each atom there are several other parameters that will or may be refined as needed. The one that will always be refined is the scale factor. The value of the calculated data will depend on only the atomic parameters and the atomic scattering factors. However, the observed data will depend on the size of the crystal, the intensity of the X-ray beam, and other factors. In order to compare the observed and calculated data, the observed data must be scaled. The scale factor does this. Depending on the refinement program used, the observed data may either be divided or multiplied by this factor. When properly scaled, F^2 will have units in electrons squared for X-ray diffraction.

It is expected a full atom will occupy a site. The scattering factor will then be multiplied by one to express the scattering power of that atom. However, sometimes the site is not fully occupied or occupied randomly by two different elements. In this case a site occupation factor (sof) also known as a multiplicity factor may be refined. In a completed structure the sof should be greater than zero and less than or equal to one if refined. Refinement of the sof can also be used to try to determine the atomic number of an incorrectly assigned atom. If the sof of an atom is refined, the approximate atomic number of the atom is the product of the value of the sof (which in this case can be greater than one) with the atomic number of the refined atom.

It would be expected that the sof would be 1.0 for all atoms that fully occupy a site. However, this is not the case. The calculation of F_c involves a sum over all the atoms in the cell. However, only the atoms in an asymmetric unit need be provided as the rest can be calculated from the equivalent positions. Therefore, every atom will be expanded into a set

consisting of all the atoms in the cell. This is a problem for atoms on a special position. Consider an atom on an inversion center at $(0,0,0)$ in a unit cell. When inversion $(-x,-y,-z)$ is applied to these coordinates, its position is not changed. The atom is transformed into itself by the symmetry. To keep the composition correct, the *sof* for this atom is assigned 0.5 so that symmetry produces an identical half atom and a total occupancy of 1.0. The occupancy of an atom on a special position will be the multiplicity of the special position divided by the number of symmetry operations for a general position. Crystallographic programs will automatically take care of this when an atom is added for refinement.

Another parameter that is sometimes refined is an extinction correction. Extinction is observed in reflections with high intensity in very high quality crystals. It results from interference between the diffracted beams. This is negligible for most data and only affects the most intense peaks whose measured intensity will be less than would be expected. A variety of methods have been developed for correcting for extinction. Generally, the refinement program will indicate if this correction is likely to be required and an additional parameter is then refined.

12.3.5 Correlation

One problem with non-linear least squares is that there is an assumption that all the parameters being refined are independent of each other. When this is not the case the method has problems calculating better values. This is because the calculation involves finding the determinate of a matrix and dividing by this number. If any two rows or columns of a matrix are identical or multiples of each other, the determinate will have a value of zero and the division cannot be done. In most cases it will be close to zero which will cause enormous shifts. When this happens, the structure will fall apart (diverge).

The extent to which two parameters are related is defined by the correlation coefficients. The largest values are typically included in the refinement output. A value of zero indicates no correlation between two parameters while a value of one indicates the two parameters are actually one, related parameter. It is not unusual to see the value of the scale factor highly correlated to a parameter like the *adp* of a heavy atom. However, when atomic parameters are highly correlated to those of similar atoms in the structure, it suggests problems.

The usual cause of correlation is an incorrect space group. This almost always occurs for space groups where there are both centric and acentric groups with the same systematic absences. E statistics can give an estimate about the presence or absence of a center of inversion. They are based on probability and can be incorrect. One reason why is because the values of E are based on the supposed chemical formula which may be totally incorrect. A centric space group has twice the number of symmetry operations as the related acentric space group. This means atoms that should be related by symmetry are not related in an incorrect non-centrosymmetric cell. This causes Z' to be twice as large. Fragments which are on a general position in the centric cell become two apparently independent fragments in the acentric cell. Fragments that would be located on a special position in the centric cell become situated on a general position in the acentric cell. In either case, twice as many parameters are needed for refinement in the acentric cell and half of these parameters are not really independent which will cause problems.

The ORTEP plots of molecules with large correlations will also usually show this problem. To avoid the correlation problem, the refinement will result in half of the parameters being incorrect. These will be displayed as strange looking rings and half the atoms will have unusual displacement ellipsoids. If lucky, one ring will look fine and the potentially symmetry related one will be distorted. However, there is no guarantee that all the distorted parameters will be in a single ring and two distorted rings may be observed.

In any case, when there are numerous large correlation coefficients and the ORTEP displays odd features, the space group should be examined. If it is acentric, it should be determined if there is an equivalent centric space group. Solution and refinement should then be tried in the centric space group. Unfortunately, for orthorhombic centric/acentric pairs, the axes may need to be swapped to obtain the standard space group. Also as discussed previously, a lower R-factor for the acentric refinement is not proof that this space group is correct. If in doubt, start with a centric space group. If the structure cannot be solved, then switch to the non-centric space group. If using charge flipping programs, make sure that both centric and acentric space groups are tried to ensure the correct space group is obtained.

12.3.6 Constraints and Restraints

There are many times a value or a set of related values needs to be constrained. A constraint means a value has one unique value. It is best explained by examples.

The simplest and most mundane constraint is where a single value cannot vary at all. An example is when an atom is located on an inversion center. If the atom moves even slightly from the coordinates of the center, the inversion symmetry will create two atoms. To prevent this, the coordinates are not refined and are reported without an s.u. since there is no error in their value. Refinement programs all can indicate a possible parameter should not be refined. Modern program packages will automatically take care of constraining the coordinates for atoms at special positions.

A slightly more complex constraint is required for the case where two different elements can occupy the same location. The actual coordinates should be the same but the values and s.u.'s should be determined by both the atoms. Because the parameters will be the same, they cannot both be refined or the least squares calculation will diverge. Again the program needs to be told to refine these different atoms at the same coordinates with the same adp's [in SHELX: EXYZ, EADP]. Beyond that the sof's can be refined to determine the fraction of each element at that site. This requires a constraint so that the sum of the two sof's add up to 1.0. Again an instruction(s) is required to set a constraint [FVAR].

A third example of the need for a constraint is for some special positions in high symmetry space groups. For example, in the space group $P\bar{3}1m$ there is a special position x, x, \bar{z} . This means the fractional coordinate along the b axis must be identical to that along a . Again the refined values of x and y and therefore their s.u.'s should depend on both axes even though they must end up identical. However, they cannot be given the same value without resulting in extreme correlation. This refinement is handled by creating a constraint between the two necessary identical values.

Modern refinement programs also include the ability to add restraints. Unlike a constraint, a restraint does not force the values being restrained to have a definite relationship but just tries to keep them from being too different. You can consider a constraint to be like a metal bar. It forces two objects at the end to be separated by exactly the length of the bar. On the other hand, a restraint is like a spring. The objects at the end can differ

from the length of the spring. However, the further they move from the length of the spring, the more force the spring will exert to bring them back to the length of the spring. An example of a restraint might be maintaining a bond length near a certain distance [DFLX]. The refined bond length will not have to be exactly the distance for the restraint but the further it tries to deviate from the requested bond distance the more force will be exerted to keep it in check. Besides requiring the desired parameter value, the restraint instruction needs to know how tightly the parameter is to be restrained.

Restraints are mainly used in dealing with structures that are disordered and will be discussed in more detail in Chapter 14. They are one way to keep structures from diverging during refinement. However, they can be misused to force a structure into a preconceived geometry. There are CIF headings for dealing with restraints so their appropriateness can be gauged. However, today it is required that the actual refinement program instruction file be included in the final CIF file which makes interpreting the restraints straightforward.

12.4 Difference Fourier Map

After the least squares cycles have completed, it is customary to calculate a difference Fourier map. This is the results for Fourier transform using as input $F_o - F_c$ where the phases for F_o are those calculated for F_c . This is equivalent to calculating a Fourier map on F_o and then subtracting the map calculated based on F_c . The map based on the observed structure factors will contain all the calculated electron density within the accuracy allowed by the applied phases. The map using the calculated data will only show the electron density accounted for in the current model. The difference Fourier can then be used to find missing atoms. Any positive peak in the difference Fourier will be a location where there is electron density not accounted for. A negative peak indicates density in the model that is not in the observed data. The intensity of the peak is roughly equal to the atomic number of the atom though typically slightly less. Obviously atoms accounting for significant negative peaks should be removed from the model. The difference Fourier map is how missing atoms are added to the model and unneeded atoms removed.

The difference Fourier peaks that are atoms can be added to the model in two ways. In graphical refinement packages, they can usually be assigned names on a drawing of the molecule and the peaks. The program

PLATON can also be used to do this. It is also possible to calculate a table of bond distances and angles which includes these peaks. They can then be added to the model manually. The program used to add the peaks should make sure that the soft and constraints required for a special position are applied.

There are peaks that are not caused by missing atoms. These are peaks less than 0.8\AA from a refined atom and are referred to as ghost peaks. They are most frequently observed around heavy atoms and may have several origins. If the atomic refinement is isotropic, they will result from trying to fit an ellipsoid with a sphere. There will be two positive peaks and two negative peaks. These do not represent any problem and should disappear when the atom is refined anisotropically. A second cause of ghost peaks is an absorption problem. In this case, many atoms will be surrounded by ghost peaks. The direction of the vector from the atoms to the ghost peaks will be nearly parallel. This is a problem that needs to be corrected. The last type of ghost peaks are observed at the end of the refinement around the heavy atoms. This is the equivalence of ringing in the FT-NMR and is caused by truncation of the atomic scattering factor. The problem is most pronounced in heavy atom structures collected with copper or other longer wavelength radiation. There is really no way to eliminate these peaks. The CIF file will report the greatest positive and negative peaks. If these are close to atoms, there is usually no problem. However, large peaks that are not ghosts do represent a serious problem. These structures should not be published.

12.5 Refinement of Hydrogen Atoms

The way hydrogen atoms are refined is still somewhat under dispute. At one time *Acta Crystallographica*, Section C preferred that hydrogen atoms be treated using the riding model. The hydrogen atoms are added at calculated, ideal positions and move as the atom they are bound to moves. The isotropic *adp* is usually some multiple of that of the atom the hydrogen is riding. When this model is used there are no s.u.'s for any of the hydrogen parameters. Because there are no parameters refined for the hydrogen atoms, it is always appropriate to use the riding model when there is minimal data.

The iconoclastic crystallographer Richard Harlow stated "I have a lot of confidence in structures where the hydrogen atoms were found and refined to reasonable positions (e.g. $0.85 < C-H < 1.05\text{\AA}$) and with reasonable

thermal parameters (e.g. $2.0 < B_{\text{iso}} < 6.0 \text{ \AA}^2$). The hydrogen atoms appear to be very sensitive indicators of a reliable structure and simply don't refine well if there are even modest errors in the data or the model, or if the data is insufficient for the structural analysis." "3 In addition to a good check on the structure's quality, refinement of hydrogen atoms also provides s.u.'s and allows the atoms to refine to non-ideal geometries which may be real.

One problem is that the s.u.'s for hydrogen parameters determined by X-ray diffraction are always at least an order of magnitude greater than for other atoms. This is because the location of the one electron does not greatly affect the quality of the structure. The large value of the uncertainty is intrinsic to using X-rays and does not reflect a problem that can easily be corrected. Also, the observed bond distances for bonds involving hydrogen obtained using X-rays are always shorter than the distances obtained by other methods. This is because the distance involves the electron and not the nucleus. For most atoms, the nucleus is centered in the electron cloud. However, the single electron for hydrogen is polarized toward the atom it is bound to and the bond distance is shorter. One approach to deal with these problems would be to use non-spherical atomic scattering factors.

How should hydrogen atoms be refined? The riding model is certainly acceptable for hydrogen atoms bound to carbon unless there is some reason to expect a deviation from the idealized geometry. On the other hand, hydrogen atoms bound to other elements should be refined isotropically. As has been emphasized previously, geometrical parameters without s.u.'s cannot be accurately interpreted. Tables of hydrogen bonds with idealized hydrogen positions and no standard uncertainties are almost meaningless. If there is any question about the presence of a hydrogen atom that hydrogen must be refined. The distance and Δp offer proof that it is present.

12.6 Refinement in Practice

Generally refinement involves repeated least squares calculations followed by a difference Fourier map and then adjustment of the model until all the electron density is accounted for and the maximum shift/error is less than 0.05. Today's refinement packages have all that is needed to carry out the calculations, adjust the model, and provide the information to assess the progress.

Crystallography programs generally have two methods of storing all the data and input required for the calculations. All programs will have a file that stores the diffraction data [hkl]. SHELXL uses only one additional file [.ins] that includes all the crystal information, atomic parameters and instructions needed for the refinement. Since this is the only record of the data, some metadata may also be stored in this file [SIZE, TEMP]. Other packages may have a file with all the crystal information and another with the refinement parameters. Data are read from these files as needed.

Before any refinement is begun, data must be transferred or entered manually from the results of the structure solution. Most structure solution packages can write data that can directly be used in refinement. This might be in SHELX or other formats.

There is standard information that makes up the crystal and atomic data that are needed for refinement. While not essential, a title [TITL] is usually provided so the output is labeled with some identification as to the structure studied. Cell constants and their s.u.'s must be provided [CELL, ZERR]. The wavelength of the X-ray radiation is also required data [CELL] either as a wavelength or the element symbol of the anode. The symmetry information is required. This can be entered in several ways. Some programs can convert the space group name or number into the symmetry operations. Others require each operation be entered [SYMM]. SHELXL only requires the unique operations be added. Therefore, operations created by a center of inversion or centering are not entered. However, this means the program needs to know if the space group is centered and/or centric [LATT] The formula must be provided. This can either be the chemical formula or the contents of the unit cell as for SHELXL [SFAC, UNIT]. To convert from a chemical to a unit cell formula, the value of Z is needed [ZERR]. Programs today will provide the needed atomic scattering factors for commonly used wavelengths from the given information. However, if unusual wavelengths are used additional information may need to be entered [SFAC].

Some instructions are needed to direct the program as to what calculations are to be performed and what output is desired. The number of least squares cycles to be done must be provided [L.S.]. Is a CIF file to be generated [ACTA]? Other instructions such as converting isotropic atoms to anisotropic atoms [ANIS], adding riding hydrogen atoms [HFLX], and many other diverse instructions may be included. Finally, the values and in some programs the type of the weighting scheme must be provided [WGHT].

Lastly comes the parameters to be refined. This will also include a scale factor [FVAR] followed by the name, xyz, a dp, and so of information about the atoms. In some programs the atomic number of the atom can be determined from the first one or two characters of the atom name. In SHELXL a number is used and relates to the position on the SFAC card. Generally some method is used to mark the beginning or end of the atoms list [HKLF]. Also the input must inform the program if the data are F or F². An instruction is used to indicate the end of the input [END].

When the refinement program is finished it will produce a new set of atomic parameters that need to be used in the next set of cycles. The refinement should always be examined before the refinement data are upgraded to make sure the result is reasonable. Typically, once the parameters are updated, the original values are lost. SHELXL produces a new file .res which is renamed to .ins for the next calculation.

CHAPTER 13

DETERMINATION OF ABSOLUTE CONFIGURATION

One of the most important uses of X-ray crystallography is to determine the absolute configuration of an enantiomorphous molecule. While this has become fairly routine, the method must be understood to prevent incorrect assignments.

13.1 Absolute Structure and Absolute Configuration

Absolute structure is a property of every non-centrosymmetric crystal. The online dictionary defines absolute structure as "The spatial arrangement of the atoms of a physically identified non-centrosymmetric crystal and its description by way of unit cell dimensions, space group, and representative coordinates of all atoms."⁶⁴ The cell parameters of the two possible absolute structures are identical. Only the internal arrangement of the cell contents differs. What this means is that there are two ways to construct the cell. The space group $Pna2_1$ with equivalent positions (x,y,z) , $(x+1/2, -y+1/2, z)$, $(-x,-y,z+1/2)$, $(x+1/2,y+1/2,z+1/2)$ will be used as an example. First, it will be noticed that this is indeed acentric as the inversion operation $-x,-y,-z$ is not present. Second, notice that for all four equivalent positions z is always positive. This means that the direction of positive z cannot be determined without the coordinates of at least one atom being assigned. The two possible arrangements cannot be determined from the data as will be discussed below. Since there is no inversion operation it means Friedel's Law is not exactly obeyed.

Note that the space group $Pna2_1$ has glide planes perpendicular to both the a and b -axes. Since a glide plane contains a mirror operation, a pure enantiomorphous molecule cannot crystallize in this space group. The mirrors of the glide plane would relate one enantiomer into the other.

Since Friedel's Law does not apply, it is still necessary to determine the absolute structure in this space group.

There is a sub-group of acentric space groups that do not contain symmetry operations that change enantiomers. These space groups can only contain no symmetry (1), rotation axes, or screw axes. Since improper rotation operations are composed of a rotation followed by inversion, these rotations are not allowed for crystals containing enantiomorphically pure compounds. The 65 space groups in which optically pure molecules can crystallize are called Sohncke groups. They are easily recognized from their space group name which cannot contain any letters (after the capital centering letter) or numbers with a bar over them. It should be pointed out that most biological molecules crystallize in Sohncke groups as they are almost always enantiomorphically pure.

When the absolute structure of a Sohncke group is determined, the absolute configuration of the contents are also determined. X-ray diffraction determines the absolute structure for all crystals that crystallize in non-centrosymmetric space groups. If the space group is a Sohncke group then the absolute configuration (optical isomer) of the contents is also determined.

13.2 Determination of Absolute Structure

If all the intensity measured during data collection were generated from scattered photons, it would be impossible to determine the absolute structure. However, there is a second source of intensity, anomalous scattering, that makes this possible. An excellent review of the whole process was written by Flack and Bernardinelli.⁶⁵

13.2.1 Anomalous Scattering

The following model for the origin of anomalous scattering is not rigorously correct. However, it is useful in understanding the nature of anomalous scattering and drawing some conclusions.

When discussing scattering it was pointed out that all the scattered photons are 180° out of phase with the incident beam. This simplifies many of the interactions as the resulting diffraction only depends on the change in direction of the scattered wave and not the phases. However, there is a second weak source of photons arising from a different mechanism that

produces photons whose phase is different from the scattered ones. This process is referred to as anomalous scattering.

A simple model for anomalous scattering is that it is equivalent to emission of photons in the UV-Visible wavelengths. First, the sample must absorb the exciting radiation. The larger the absorption the more intense the emission. Second, once the photon is absorbed the sample is in an excited state which has a definite lifetime before a photon is emitted. The emitted photon will be out of phase with the scattered photons unless the lifetime is some multiple of the frequency. Third, the emitted photons will have equal intensity in all directions. The emitted photon is a new photon and as such has no memory of the direction of the incident photon.

These three characteristics are also true of photons resulting from anomalous scattering. Each element has a cross section for absorption for the X-ray wavelength used for the experiment. This is related to the absorption coefficient. In general, the cross section increases with increasing atomic number and decreases with decreasing X-ray wavelength.

The equivalence to the light emission lifetime means that the emitted photons will be out of phase with the scattered photons. It is this phase change which will allow the absolute structure to be determined. There is no simple relationship between the atomic number of the element being considered, the wavelength of the X-rays used and this phase shift. It must be calculated for each element and radiation.

The fact that these anomalous photons have an intensity that is independent of direction is identical for emitted light photons. This means that the intensity of the anomalous scattering unlike the normal X-ray diffraction is independent of θ the Bragg angle. Therefore, the ratio of the intensity of the anomalous scattering to the diffraction scattering will be greatest at larger values of θ .

13.2.2 Adding Anomalous Scattering to the Atomic Scattering Factor

Earlier the concept of the atomic scattering factor f was used for entering electron density in reciprocal space to the model being refined. The atomic scattering factor for a specific reflection in reciprocal space is a function of the atomic number of the atom involved, the wavelength of the X-ray radiation and the Bragg angle for the reflection. The atomic scattering

factor can be expanded by including two additional terms for the anomalous scattering. These additional terms like the original one must be calculated.

The first term is f' and indicates the increase or decrease involved in adding anomalous scattering. As such its value can be positive or negative. The second term f'' is an imaginary term that reflects the change in the phase. The full formula for the scattering factor used when anomalous scattering is accounted for is given by $f + f' + i f''$ (13.1).

In a centric crystal Friedel's Law is exactly obeyed. This is because the inversion center requires that x, y, z must be symmetrically equivalent to $\bar{x}, \bar{y}, \bar{z}$. This cancels out the f'' term. However, for acentric crystals Friedel's Law is broken. The structure factors of the reflections F_{hkl} and

F_{-h-k-l} are called Friedel pairs. If the absolute structure is correct the sign for f'' will always be positive producing the best agreement between F_o and F_c while if incorrect a negative sign will produce better agreement. This provides the basis for approaches used to determine the absolute structure.

13.3.3 The Effects of Anomalous Scattering

The values of f' and f'' are small as compared to the atomic scattering factor. Examples are

ELEMENT	Mo radiation		Cu radiation	
	f'	f''	f'	f''
C	0.003	0.002	0.018	0.009
S	0.333	0.125	0.558	0.123
Ni	0.339	1.112	-3.003	0.509
Pt	-1.703	8.391	-4.593	6.926

The fact that copper radiation is absorbed more than molybdenum is evident in the larger values for copper. The values for anomalous scattering will produce the greatest change in the total f when applied to high angle (small d) data. If the quality of the crystal is good and the noise is low, this can be observed. For the anomalous scattering to be measurable it must be greater than the noise level. The values for molybdenum radiation are so small that the effect is generally not able to be measured accurately for organic compounds. As the atomic numbers

increase so does the magnitude of the anomalous scattering, making the determination of the absolute structure easier and more accurate.

If the incorrect absolute structure for a crystal with a non-centrosymmetric space group is refined, then the value of f'' should be subtracted instead of added. There are three ways to fix this problem. One is to make a right-handed unit cell left-handed. While this will change the sign of f'' it will also result in the atomic positions producing the incorrect absolute configuration. This is why it is important to always ensure the cell is right-handed when it is indexed or transformed. The second approach is to change the sign of f'' . This results in the same problems as changing the cell handedness. The only way to obtain the correct coordinates for the absolute structure is to change the absolute structure to its enantiomer.

For most space groups the handedness of the absolute cell can be changed by simply changing the coordinates of each atom from xyz to \overline{xyz} . Program packages have a command to do this [move]. However, if there is a screw axis with a rotational component greater than 2, then the space group must also be changed to invert this screw axis. For example, if a structure is solved in the Sohncke space group $P3_1$ then the space group must be changed to $P3_2$ and the coordinates inverted to change the absolute structure.

There are several space groups where a simple inversion of the coordinates does not produce the opposite absolute structure. They are $Fdd2$, $I4_1$, $I4_122$, $I4_1md$, $I4_1cd$, $I\bar{4}2d$, and $F4_132$. These space groups are not common. Details for the needed transformations can be found in the SHELXL manual.⁵⁷

In general, the programs used to solve a structure have no ability to select the correct absolute structure. The absolute structure must be confirmed during refinement.

13.3 Determination of Absolute Structure in Practice

13.3.1 From a Known Fragment or Atom

It must be emphasized that the crystal model used in refinement for enantiomorphous compounds must be totally correct or totally incorrect. This means all the optically active centers must all be right or all be wrong. The model never contains some correctly assigned centers and some incorrectly assigned ones. If the enantiomer of any fragment in the

structure is known, then this can be used to assign the absolute structure to the entire cell without resulting to anomalous scattering. Likewise, if the r_s configuration for any atom is known, this can also be used. The absolute structure can be determined from the absolute configuration of a known molecule.

The CIF dictionary recognizes these situations, and they can be reported as values under the heading `_chemical_absolute_configuration`. These are:

`rm`--Absolute configuration established by the structure determination of a compound containing a chiral reference molecule of known absolute configuration.

`syn`--Absolute configuration has not been established by anomalous-dispersion effects in diffraction measurements on the crystal. The enantiomer has been assigned by reference to an unchanging chiral centre in the synthetic procedure.”

Other possible values are:

`ad`--Absolute configuration established by anomalous-dispersion effects in diffraction measurements on the crystal.

`rmad`--Absolute configuration established by the structure determination of a compound containing a chiral reference molecule of known absolute configuration and confirmed by anomalous-dispersion effects in diffraction measurements on the crystal.

`unk`--unknown”

Examples of a chiral reference molecule commonly include salts of enantiomorphically pure tartrates, citrates, *etc.* Likewise the inclusion of a resolved molecule in a crystal containing two different molecules would fall under this category. The use of a single chiral center must be done with some care to ensure that there is no chance of racimization during the syntheses or crystallization.

13.3.2 From Examination of Reflections most affected by anomalous scattering

The first attempt to determine the absolute structure was reported in 1930 by Coster, Knol, and Prins.“ The crystal studied was zincblende, one crystalline form of ZnS. They collected careful data and by examining the differences in the observed and calculated structure factors for the high

angle Friedel pairs most affected by anomalous scattering, they were able to assign the absolute structure. Several points should be noted. Zincblende crystallizes in the cubic space group $F\bar{4}3m$ which is not a Sohncke group. Only the absolute structure can be determined. There are no optically active components in this crystal and yet it has an absolute structure. Since the absolute structure of the crystal and not the absolute configuration is being determined, atoms with large anomalous scattering coefficients do not need to be bonded to the optically active component. The large anomalous scattering of a bromine ion can be used to help determine the absolute configuration of an optically active organic compound even though it is not directly connected to the organic fragment.

The first experiment to determine the absolute configuration of an organic moiety was reported by Bijvoet in 1951.⁶⁷ The sodium, rubidium double salt of tartaric acid was characterized. To ensure maximum anomalous scattering zirconium $K\alpha$ X-rays were used. Again by examining those reflections with the largest differences between Friedel pairs, the absolute structure and therefore the absolute configuration of the tartrate ion were established.

While this method for establishing the absolute configuration works, it requires a good deal of manual examination of data and is not readily programmed for a computer. The Bijvoet experiment was repeated in 2008 using modern equipment and was proved correct upon detail examination.⁶⁸

13.3.3 From the R-factor Ratio Test

The R-factors can be used to determine if the correct absolute structure has been assigned. The R-factor from refinement with the correct absolute structure should in theory be lower than that for the incorrect structure. However, there still needs to be a test to ensure the statistical significance of the difference between the two R-factors. Walter Hamilton in 1965 published an R-factor ratio test to make this determination.⁶⁹

In practice, for many structures this method will not be successful. First, if the anomalous scattering is lower than the experimental noise, it is likely the two R-factors will be the same or the difference will not be statistically meaningful. In addition, there are assumptions made in the derivation of the R-factor ratio test that may also not apply. Lastly, this test like most

tests for absolute structure will be most successful when the Friedel coverage (fraction of reflections that have a Friedel pair) is high. This means the data set must contain roughly twice the data than for a similar centric structure.

Hamilton's test is also somewhat difficult to apply. The best approach is to read the manuscript introducing the test and use the tables published there. For all the cited reasons, this test is almost never employed anymore to determine the absolute structure. In fact, the test has been completely removed from the latest additions of the **International Tables for Crystallography**.

However, the R-factor ratio test can still be of some use. This is when two different models are refined and one model has a lower R-factor. However, if the best model has more refined parameters, the change in the R-factor may simply be because of the increase in parameters. The R-factor ratio test can be used to determine if the observed change between the two models is statistically meaningful or just an artifact from the change in the number of parameters. This can be useful when trying to decide which model is correct.

13.3.4 From the Roger's Parameter

The first test to add a refined parameter to indicate the correctness of the absolute structure was suggested by Donald Rogers in 1981.⁷⁰ He suggested a parameter η be refined so that the atomic scattering factor was given by $f + f' + \eta i f''$. If η refined to +1, then the absolute structure was correct while if it refined to -1 it was incorrect. Intermediate values suggest that the anomalous scattering is too weak to allow the absolute structure to be determined.

Again, while this method was successful, it had several drawbacks. First, the Roger's parameter did not change greatly with each least squares cycle and was very slow to converge to the final value. Also, like the other methods, it worked best when the Friedel coverage was large. While it never found widespread use, it still suggested there was a parameter that could be refined to determine the absolute structure.

13.3.5 From the Flack Factor

In 1983 Howard Flack introduced a new parameter which could be refined and would indicate the correctness of the absolute configuration.⁷¹ The parameter is called the Flack factor and is given the symbol x . While there are several ways to think about this parameter a nice definition from Martin Lutz is $F(hkl) = (1-x)|F(hkl)|^2 + x|F(\bar{h}\bar{k}\bar{l})|^2$ (13.2).⁶³ If the absolute structure is correct then the value of x will be zero while if incorrect the value will be one. The Flack factor has become the principal method for determining absolute structure.

The first thing that made the Flack factor useful was that it could be used even if the Friedel coverage was zero. However, when used with little or no Friedel pairs, it had to be checked more carefully. The values of the Flack factor for the two absolute structures would be expected to be related by $1-x$. However, this was not always the case when the extent of the Friedel coverage was low so both absolute structures needed to be refined. Also, when the Friedel coverage was minimal, values well outside the expected range of 0 to 1 were sometimes obtained. These could indicate that the absolute configuration could not be determined from the data but sometimes gave a reasonable value when the cell was inverted.

The value of the x factor if it is not zero or one has little significance. A value of 0.2 does not suggest that the probability of the absolute structure is more likely to be correct than incorrect. In addition, the s.u. of the Flack factor needs to be considered. For the Flack factor to provide any information, the value of x must be within 3 s.u. of either zero or one but not the other. An example is an x value of 0.2(3). In this case the tolerance is ± 0.9 (three times 0.3). That means that both zero and one are within 3 s.u. of the x value and it is unreliable. Flack suggested that for a correct absolute structure the x value should be less than 0.07 unless it was totally clear the structure was enantiomorphically pure in which case it could be as high as 0.1.⁶⁵

A Flack factor near 0.5 with a low s.u. is always suspicious. While it could be a racemic twin (discussed below), it could also suggest the structure is actually in a centric space group. This is particularly likely if the space group has a related centric group with identical systematic absences.

The other possible case is that the Flack factor has an unacceptable value and a small s.u. This is usually indicative of an inversion twin. In this case,

there are domains of each absolute structure in the crystal studied. Since the cell constants for the two absolute structures are identical, this condition cannot be observed in the indexing. This problem is dealt with by refining the structure where F_c is calculated by equation 13.2. The value of $1-x$ is the fraction of the cells that have the absolute structure being refined [TWIN, BASF].

There are several points that must be made about the existence of inversion twins in acentric space groups where the absolute structure is to be determined. First, both absolute structures are present in the crystal. This means the material crystallized was not enantiomorphically pure. Second, the extent of the twinning does not necessarily represent the degree of racemization in the bulk material. It would be necessary to complete crystal structures on several crystals to determine how reproducible the twin is. NMR or separation techniques would be preferable methods for analyzing the extent of enantiomorphous impurity.

In 2013, Simon Parsons *et al.* published a new method for calculating the Flack factor that in many cases gave lower s.u. values than the Flack method.⁷² This factor calculated by the newer method is called the Parson's z factor and its interpretation is identical to the Flack factor.

13.3.6 From Bayesian Statistics

In 2007, Hooft *et al.* introduced a new method of determining the absolute configuration.⁷³ The method requires that the Friedel coverage be high so it cannot be used if there are few Friedel pairs. The method has been imported to PLATON as BIJVOET. Standard SHELXL files can be used as input.

The program examines the Friedel pairs using a statistical analysis. The output contains values for the Flack x parameter and the Parson z parameter. In addition, a new Flack-like parameter called the Hooft y parameter is calculated. This is again interpreted like the Flack factor. In addition to these parameters, the program provides several calculated probabilities. If it is assumed that the absolute structure is either correct or incorrect, then the probability of it being correct is reported. A second calculation is made adding the possibility the crystal is an inversion twin. In this case three probabilities are reported: correct, twinned, and incorrect.

The reported probabilities must be considered using the 3s.u. standard. For a normal distribution 3s.u. would have a probability of 0.9973. Therefore, to be consistent with other crystallographic statistics, it would be expected that for the result to be correct, the probability should be no lower than 0.99.

13.4 Determination of Absolute Structure in Practice

Using modern instruments, the determination of the absolute structure has become almost routine. First, the quality of the weak data is very good because of the amount of redundant data collected and the low noise in the detectors. Second, the Friedel coverage is very high because of the wide range covered by an area detector. Even when no special allowance is made to collect the Friedel pairs, the coverage is usually over 80%. The Flack or Parsons parameter are usually provided at the end of the last refinement cycle.

Below is the formatted output from a light atom organic analyzed by PLATON/Bijvoet Pair. Numbers are reported where $E-10$ is 10^{-10} .

Absolute Structure Analysis

Flack Factor	-0.02 +/- 0.110
Hooft Parameter	-0.02 +/- 0.050
Parson's Parameter	0.03 +/- 0.030
Friedel Coverage	92%

Assuming No Racemic Twinning is Present

Probability Absolute Structure is Correct 1.000

Probabilities Allowing for Racemic Twinning

Probability Absolute Structure is Correct	1.000
Probability Absolute Structure is Incorrect	0.9E-91
Probability Crystal is a Racemic Twin	0.2E-24

It is apparent from all the parameters that the absolute structure has been correctly determined. This is confirmed by the probabilities which for both two and three possibilities have a value of 1.000 for the current model.

What follows is a similar analysis for a different light atom organic molecule. This was done using molybdenum radiation.

Absolute Structure Analysis

Flack Factor	-0.4 +/- 0.80
Hooft Parameter	-0.6 +/- 0.60
Parson's Parameter	-0.5 +/- 0.50
Friedel Coverage	93%

Assuming No Racemic Twining is Present

Probability Absolute Structure is Correct 0.965

Probabilities Allowing for Racemic Twining

Probability Absolute Structure is Correct 0.762

Probability Absolute Structure is Incorrect 0.028

Probability Crystal is a Racemic Twin 0.210

It is clear that the absolute structure cannot be determined from this data. All three of the parameters have very large values for their s.u.'s and the values are closer to 0.5 than either 0.0 or 1.0. The only indication that the absolute structure might be correct is the probability ignoring racemic twining. However, the value of 0.965 is well outside the 0.997 required for definitive proof. The set of three parameters does not support any possibility. In this case, the anomalous scattering from molybdenum radiation was not intense enough to allow any determination. This data should have been collected using copper radiation and would probably establish the absolute structure.

CHAPTER 14

DISORDER AND TWINNING

Disorder and twinning are two effects where a crystal is not a regular array. Disorder arises from a variation of the arrangement of the contents in different unit cells while twinning stems from the arrangement of the cells. Crystals are not always as orderly as proposed up to this point. A very nice discussion on the nature of these problems and their alleviation can be found in the Ph. D. thesis of Marcus Neuberger.⁷⁴

14.1 Disorder

Disorder is when there are different contents or arrangements of the atoms in the unit cells that make up the crystal. Since the crystallographic experiment requires that all unit cells be identical, the reported unit cell is the average of all the unit cells that compose the crystal. Several types of disorder will be considered: partial occupancy, different elements located at the same coordinates, disorder by symmetry, and multiple conformations for a molecule. All are encountered in performing crystal structure analysis.

14.1.1 Disorder Caused by Partial Occupancy

The case where a particular site is occupied by an atom, ion, or molecule only in some unit cells is not uncommon. The locations that are not occupied are voids. In solid state compounds, these can occur so that the charge on ions can be balanced. In molecular crystals they can result from solvent evaporating from the crystal. When there are voids in only some unit cells the chemical formula will not be integral.

The refinement of this type of disorder is very straightforward. The f (multiplicities) of the atoms are refined. If there are several atoms that

form a molecule such as a solvent then the sof of all the atoms making up that molecule must be constrained so that they are all identical [FVAR].

14.1.2 Disorder Caused by Different Elements

There are occasions where more than one element type can be at a location in the crystal. This might be because a solid state compound has a mixed composition where two or more atoms or ions have the same coordinates. In this case, the disorder is handled by refining each element with identical coordinates and adp's. The least squares refinement program must also be told that the atomic parameters are to remain the same [EXYZ, EADP] to prevent correlation. In addition, the sof's of these atoms with identical parameters must be constrained so they add up to 1 (or if at a special position the appropriate fraction).

In molecules, it is also possible that the two disordered elements possess different bond distances with the atom they are bonded to. In this case, the atoms may be refined independently and just their sof constrained. If the distance between the two equivalent atoms is small, restraints may be required to prevent correlation from diverging the refinement. This will be discussed later.

14.1.3 Disorder Caused by a Symmetry Element

In most unit cells, there are multiple asymmetric units related by the symmetry operations of the space group. If there is minimal interaction between the contents of the asymmetric units, then the contents will try to be evenly spaced away from any special position. Therefore, if there are voids between the principal components, they will tend to be located close to a special position. Frequently solvent molecules may occupy these voids and end up located on a special position that is inconsistent with the point group symmetry of the solvent. This will create a disorder.

A simple example might be methylene chloride located on an inversion center. The carbon will be located at the special position. It will be surrounded by a square plane of chlorine atoms. Two of these will be part of one component of the disorder and two will be created by the site symmetry. The sof of the carbon atom will be 0.5 because it is located at a special position as discussed previously. Each of the two refined chlorine atoms will also have an sof of 0.5 so that the total occupancy for the four chlorine atoms is two. The sof of the chlorine atoms must be exactly 0.5

because of the symmetry and cannot be refined. Adding hydrogen atoms to this model is difficult. The positions of the two hydrogen atoms cannot be calculated by most programs as they are confused by the apparent square planar geometry. The positions could be calculated by hand. Another approach is to begin with a rigid group (discussed in section 14.1.5). The last resort would be not to add hydrogen atoms but include them in the reported chemical formula. A solvent that is frequently found on an inversion center is water.

Symmetry disorders can be quite complex. They are hard to visualize because they will appear to contain extra atoms and extra bonds. An example of a complicated disorder is a toluene molecule located about an inversion center as shown in Figure 14.1. Some non-existent bonds have been omitted in the drawing to make the arrangement clearer. The two configurations are differentiated by the bond shade. The inversion center is located at the dot in the middle.

This disorder is not common but there are examples in the CSD. Note that three atoms take part in only one disorder while two are involved with both disordered solvents. The *sof* of the atoms must be adjusted to account for this. The two that belong to both parts are assigned an *sof* of 1.0 while the other three are assigned 0.5. The total occupancy of the five atoms adds up to 3.5 and when doubled because of the symmetry, equals 7 the number of carbons in a toluene.

This disorder also highlights some problems encountered when refining disorders. First, it is very difficult to add hydrogen atoms to this fragment. For example, the carbons on the extreme top and bottom of the figure represent both the methyl group and also the carbon *para* to it. Secondly, it is clear that the toluene is distorted from the ideal geometry. This is not unusual in a disordered fragment in that the refinement attempts to fit what is given as best it can. The geometry could be improved by using restraints or rigid groups to obtain better geometry and including the hydrogen atoms. However, if the toluene is not a major focus of the crystal structure, it can probably be reported as shown if appropriate comments are included in the experimental section.

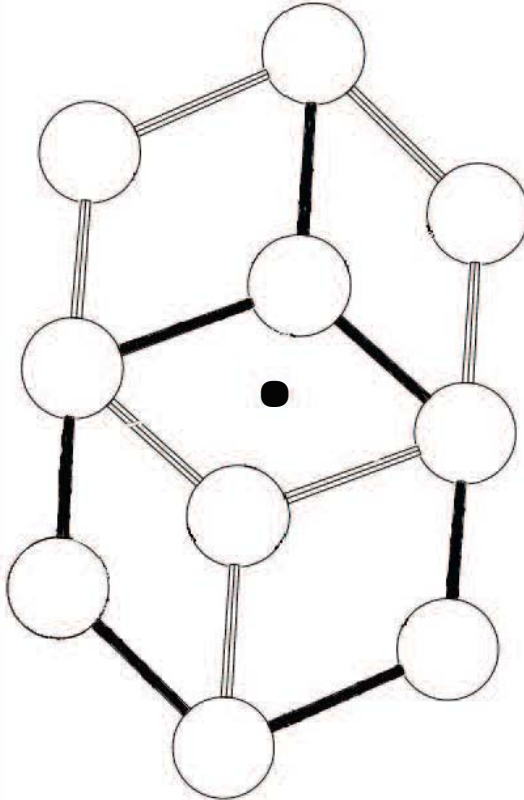


Figure 14.1 A toluene molecule disordered about an inversion center.

14.1.4 Disorder caused by Multiple Configurations

The most commonly observed disorder is caused when a molecule can exist in a crystal in two or more configurations. This will result in two or more arrangements of some atoms. While this disorder could be ignored, it should be modeled if the structure refinement is to produce good statistics. This is another example where the entire unit cell must be modeled even if the chemical information can be obtained from a less complete model.

It is important to consider the origin of this type of disorder. The treatment of bonding energies by a parabola resulting from the harmonic vibration model is well-known. Frequently a parabola is drawn to represent the relationship between geometrical parameters and energy. The x-axis

represents some geometric variable. It is typically a bond distance but could also be a bond angle or torsion angle. The location of the minimum in the parabola represents what is considered the bond distance or angle. The y-axis is in energy. If the geometric parameter is to be changed to a new value of x then the amount of additional energy required is given by the corresponding y value. Generally, diagrams for bond distances have very narrow curves as it requires significant energy to change this distance. Parabolas for angles are broader. Lastly, it should be clear that a parabola is being used to simplify the concepts. Clearly if a bond distance is increased too much the bond will break.

The energy diagrams are usually calculated in the gas phase by accounting for all the attractive bonding energies and all the repulsive electrostatic interactions within the molecule. In this case only the intramolecular interactions need to be accounted for. The situation is more complex in a crystal. This is because intermolecular forces must also be included. Figure 14.2 displays a potential well with two minima. Even in a crystal, this type of well has not been observed for bond distances. At one time it was suggested that there could be two bond distances between atoms in a crystal which was labeled bond stretch isomerization but this has now been disproved. However, it is quite possible that for bond angles, torsion angles or other deformation modes, the potential energy curve below could be correct.

There are certain features that should be noted in Figure 14.2. There are two minimum and these should be the observed values for the geometric parameters plotted along the x-axis. These define the two possible, stable configurations. The two minimum are not at the same energy. This means that there should be more molecules with the geometry described by the lower energy curve than in the higher one. Lastly, there is a barrier between the two minima. This barrier is important in determining the nature of the disorder.

If the barrier is low, then there may be enough thermal energy at room temperature to allow for the molecules to convert between the two configurations. This is called a dynamic disorder. However, if the barrier is large or the temperature is low, such movement cannot occur and the result is a static disorder. If there is a configurational disorder, it pays to collect data at the lowest possible temperature to prevent movement.

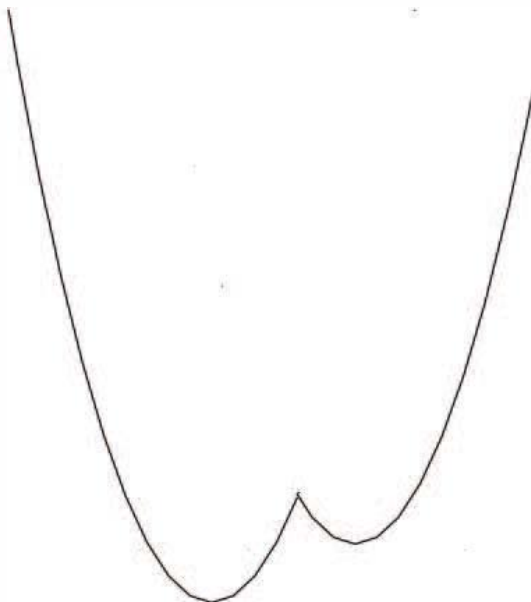


Figure 14.2 A potential well with two minima.

A disorder is indicated either in the adp 's for the atoms involved or observed in the difference Fourier map. The ellipsoid may be very prolate (one very long axis) if two disordered atoms are close to each other and cannot be resolved. Most refinement programs will suggest splitting the disordered atoms in two at new positions. In addition, the sof 's for these split atoms will need to be lowered to 0.5 and should then be refined and constrained. Refinement on this new model will either proceed reasonably smoothly or the adp 's of the split atoms will again be very prolate and need to be split. At this point a decision needs to be made. If the disorder is dynamic, then the single elongated atom may be the best way of modeling the atoms. While this may not be pretty, it provides a reasonable fit to the actual atomic motion. If nature creates a disordered crystal, it can certainly create atoms whose adp 's produce a prolate ellipsoid. If the data were obtained at room temperature, data collection at low temperature might improve the appearance especially if this is the result of a dynamic disorder. On the other hand, it is possible that the potential well is very broad with numerous shallow minima. In this case, the atoms will not have a well-defined value for the geometrical parameter and the electron density will be smeared out.

The other possibility is that the additional atoms refine satisfactorily. In this case routine refinement can be continued. Some restraints may be required to keep the geometry reasonable or prevent correlation during refinement. This will be discussed in the next section.

14.1.5 Refinement of Disordered Atoms

There are several approaches that can be used for dealing with disordered fragments. The fragment may consist of a side chain, a disordered ring, or an entire molecule such as a solvent or ion. Working out the best way to model a disorder can be difficult and may require trying more than one approach. Fortunately, there are several approaches available.

One approach is to refine the disordered atoms as a rigid group. In this case the ideal coordinates, usually in Cartesian coordinates, are added as a fragment [FRAG; FEND]. Ilia Guzei has provided a large collection of coordinates for most common fragments at <http://xray.chem.wisc.edu/Projects/IdealizedMolecularGeometry.html>. The fragment is fitted as best as possible to the observed atoms that form the group [AFIX]. The program will then idealize the positions of the observed atoms, add coordinates for any missing atoms (entered with coordinates 0,0,0), and treat these atoms as a rigid group. In general, there are a minimum of six parameters required to refine such a group. Three will determine the position of the center of the group and three more will be used to orient the group. In addition, a parameter may be added to allow the bond distance between the atoms to refine to a single value assuming there is only one bond type. If possible, the adp's of the atoms in the group should be refined individually to determine how well the rigid group models the atoms.

When used to fit a disorder, two or more rigid groups will be used. Care will need to be taken that the occupancy of the atoms is correct. It is important there are proper constraints for the sof's, so they sum up to a full or partial fragment. One advantage of rigid groups is that atoms in different groups can be placed quite close to each other without worry about correlation since the individual atomic coordinates are not refined. The disadvantage of rigid groups is that they only provide an idealized geometry and not one obtained from the structural refinement. However, if the disorder is extreme this may be satisfactory.

Generally, even in the best of circumstances, disordered fragments will not provide ideal geometric parameters. This is because the presence of two or more atoms may lead to correlation or other effects during the refinement calculations. Some of these problems can be overcome by using restraints to control the geometry. The restraints can involve limiting the bond distances [DFIX], the bond angles [DFIX between non-bonded atoms] or making bond distances equivalent [SADI]. Remember, the parameters involved in a restraint are not required to have the same value but are prevented from differing by too much. SHELXL also allows restraints to be set for all the atoms in two or more fragments using the SAME command. This sets restraints for all the bond distance and angles between all the atoms in these fragments. Lastly, it may be necessary to restrain the anisotropic u 's to be more spherical [ISOR]. Restraints are frequently used in the refinement of disorders but the extent of the restraint should not be so tight that the geometry is forced.

A second problem in dealing with disorders is in creating tables of geometrical parameters. Clearly bonds and angles involving atoms in two different disordered fragments should not be reported. Refinement programs typically have a way to define which atoms belong to a particular disordered fragment [PART]. There may even be a method to keep atoms disordered by symmetry from adding extraneous values to the CIF.

14.1.6 Non-atomic Treatment of Disorder

Up until now, electrons were always added to the structure by adding atoms-- actually atomic scattering factors. However, it is possible to treat some extreme disorders by adding electrons within a region. In this case the assumption is made that the electron density throughout the region is constant.

The refinement package CRYSTALS makes use of this approach. A volume containing the electron density may be along a line, in a ring, or along the surface of a sphere.⁷⁵ The ring can be used to model something like a rotating CF_3 group while the sphere could represent a completely disordered symmetric fragment such as the ions BF_4 or PF_6 . In these cases, the total number of electrons in the volume is known. The refinement is similar to rigid group refinement in that the position of the center of the region is refined. It may also be necessary to refine the orientation of a ring. This method can account for the electron density due to a completely

disordered fragment. However, the downside is that it provides no geometrical information about the atoms involved. This may not be a significant problem. Refinement by placing large numbers of partial atoms around a central atom and then using tight restraints so that refinement is satisfactory probably does not provide better geometric data.

An extension to this idea was developed by Ton Spek to treat disordered solvents in crystals and was programmed into PLATON as SQUEEZE.⁷⁶ In this case neither the volume nor the number of electrons is known. SQUEEZE first searches the unit cell to locate large voids that contain no electrons and are at least the van der Waals radius from the atoms surrounding the void. This calculation is done by expanding the cell and applying the symmetry equivalent positions, so that all the atoms in the cell are in the list. Frequently, multiple voids are found which are symmetry related but they are always treated as independent. Then the program adds electrons to each void until the R-factor of the model is minimized and converges. SQUEEZE then calculates the scattering of these electrons for each reflection which can be used to adjust the observed diffraction intensity to eliminate the calculated electron density.

The use of SQUEEZE should be a last resort. It should never be used to remove the disordered part of a molecule or to remove any contents that are chemically important. It should not be used if a reasonable atomic model for the disorder can be determined such as the toluene in Figure 14.1. However, there are times when the method is invaluable in refining a structure.

There are several steps that must be done to report a structure where SQUEEZE was used. This is done automatically in newer versions of SHELXL. If other programs are used, the CIF should be checked to ensure the SQUEEZE data are included. The headings for these data all begin with “_platon_squeeze.” It is also a good idea to comment in the experimental section that SQUEEZE was used. The biggest problem is what to do about the chemical formula. SQUEEZE only provides the number of electrons in the void and no chemical information. If only one solvent was used during crystallization and the electron count and volume is consistent with that solvent, then its chemical formula could be added to the reported formula. However, if mixed solvents were used or the void may only be partially occupied or multiply occupied, any formula is simply a guess. In one structure SQUEEZE reported four symmetry related voids each containing 170 electrons. The solvents used were thf, pentane, toluene, and diethylether. Clearly, there must be multiple solvents

in each void. It is certainly not clear which solvents are present and to what degree. There is a difference of opinion whether a guess should be included in the formula or simply ignored. Again, if nothing is included in the reported chemical formula that fact should be highlighted in the experimental section.

14.2 Twinning

14.2.1 Comments

Twinning describes a crystal where there are two (or occasionally more) reciprocal lattices present. It is important to consider not only the orientation of the lattice but also the intensity at each hkl of each lattice. The lattices may completely overlap which is called twinning by merohedry or may exist as easily observed separated lattices. In either case, special refinement techniques must be used. If the twinning is ignored, then not only will the refinement quality be low but the derived geometrical parameters may be incorrect.

The relationship between the different lattices is called the twin law. This may be a symmetry operation that is in the crystal but not in the space group of the unit cell. In this case the twin law will be a symmetry transformation along the cell axes. This is the case for merohedral twins. To refine this type of twin, the twin law usually must be determined. On the other hand when the crystal sample was not single but composed of two (or more) crystals, the twin law(s) can be determined by indexing both sets of reflections. No twin law will be required.

In some cases the solution and refinement of twinned samples is straightforward. Other times it is very difficult to determine the twin law and therefore to refine the structure. In some merohedral twins it may be difficult to determine the true space group. In these cases, solving the crystal structure will be difficult. Complicated twins will require knowledge and experience beyond that of most chemists who do their own crystallography. Such problems should be given to a crystallographer who has experience working with these difficulties. There are specialized programs for analyzing twinned crystals. In addition, twinning has a specialized vocabulary. The Online Dictionary of Crystallography entry on twinning provides pointers to many of the terms used as does a review by Martin Lutz.⁷⁷

Twins are neither a rare nor common phenomenon. There are some minerals and crystals which only exist as twinned samples. Twins are also frequently encountered in crystals obtained after a solid state phase transition. In this case, the structure of the previous phase may provide data that can be used for solving the twinned structure. However, it is always best to work with a sample that is not twinned if possible even though refinement of twins can provide results that are equivalent.

14.2.2 Non-overlapping Lattices

Crystals that contain two or more lattices which are not superimposed are called non-merohedral twins. This class of twins is different from other types and is generally easily treated. The only reason that the two lattices must be accounted for at all is that randomly hkl's from the two lattices will overlap. The hkl's involved will not be related as this is completely accidental. Obviously, the measured intensity of these overlapping spots will be much greater than if there was no overlap.

Area detector diffractometers make it much easier to recognize such twinning. After some initial images are collected, the unit cell is determined. It is then possible to display the images and indicate where the calculated spots should be. The presence of many diffraction spots which do not fit the pattern suggests there is probably a second indexing that will fit the non-indexed intensity. It is possible to index just those spots. It may also be possible to restrict the new lattice parameters to those previously obtained. This assumes the crystal is composed of one cell type. This provides the second lattice.

After the data are collected, it is integrated for each of the component lattices. Finally, a special program for processing data from this type of twin is used. Two data files are typically produced. One contains the data from a single lattice as if no twinning were present. The other lists the hkl's, intensity, and standard uncertainty for each component. An integer is used to specify which twin domain the data belongs to. Where the data overlap, the different hkl's are listed followed by the same intensity. An indicator is provided so that the fact they overlap is noted.

When twin data has been obtained as above, then structure solution and refinement is begun with the data for the single component. Only in the final cycles is the mixed data file used. In addition, a refined parameter must be added so that the relative amount of each component can be

determined [BASF]. If this value is low, it may be possible to finish the structure as if it were not twinned and obtain nearly as good results.

A second way of dealing with this type of twin is using the program PLATON and the TwinRotMat function. The data from a single component is used as input. This calculation requires a crude CIF file and a file containing the observed and calculated data [.fcf]. PLATON can calculate a twin law and also produce a twinned data file. This method works but not as well as obtaining the twinned data from the diffractometer.

14.2.3 Overlapping Twins

Merohedral (overlapping) twins are twins where the two lattices overlap exactly. This means there is only one diffraction pattern to index. While the hkl 's overlap, the intensities of the overlapping spots are not correct. Therefore, the collected intensity data appear regular with respect to crystal class and space group. The twin law in this case is a symmetry operation that relates the two lattices but is not an operation within the crystal class or space group. The twin law can be an inversion center, a mirror or a rotation operation. These twins are best considered in reciprocal space. There are two reasons for this. First, all symmetry operations in reciprocal space pass through the origin. Secondly, the equivalent hkl 's for a crystal class are well determined. The twinning will increase the symmetry and add new equivalent reflections that do not belong to any space group or crystal class.

A related class of twins is called pseudo-merohedral twins. This occurs when an accidental similarity for cell parameters makes the crystal symmetry look higher than it is. An example might be an orthorhombic unit cell where two axes are nearly equal in length. There might be regions where these two axes are swapped and the crystal will appear to have tetragonal symmetry. However, the slight differences in the cell lengths may make the spots along the two axes involved elongated. Care must be taken when this data are integrated that the spot size used covers the elongation.

14.2.3.1 Inversion Twins

As discussed in the last chapter, inversion twins are common and easily handled. However, they can also provide an understanding of twinning in general.

The twin law must be known to process any merohedral type twin. Integration cannot be used to separate the individual twin intensities since the spots completely overlap. Therefore, the twin law is needed to assign the total intensity to each individual component of the twin. For an inversion twin, the twin law is the inversion operation which makes all the data more closely obey Friedel's Law.

The end result is that the effect of inversion twinning is minimal. Since I_{hkl} and $I_{\bar{h}\bar{k}\bar{l}}$ only differ by the small contributions of anomalous scattering, the values of F or F^2 are only slightly distorted, Solution and refinement proceeds smoothly ignoring the twinning. The result of the twinning only is considered at the very end of refinement. The twin law is entered [TWIN] and a parameter refined to represent the extent of the twinning [BASF]

14.2.3.2 Other Overlapping Twins

There are several publications that provide a good overview of more complicated twinning. Simon Parsons has an excellent introduction⁷⁸ and a publication on refining twins in SHELXL is also very useful.⁷⁹ This paper also provides an excellent checklist of warning signs of twinning on page 448.

There are several important warning signs that are indicative of a twin. First, is that there appear to be no systematic absences. Molecular or molecular ion compounds rarely crystallize in such space groups. For example, space groups such as $Cmnm$ or $P4/mnm$ would be unusual for molecular compounds.

The relative intensities of the spots whose intensity is effected by the twinning is also important. If the amount of the second component is reasonably small, then the structure will solve and refine as if it is not twinned. Like the inversion twin, the twin refinement does not need to be done until the very end. However, in many cases it is likely that if the twinning is ignored altogether it could result in inaccurate geometrical parameters and large s.u.'s.

If the ratio of the twinning domains is about 1:1, then the data will always look as if it is from a higher symmetry crystal class. However, in this case there will be no satisfactory space group and solution will be impossible using most solution programs.

The last case is where the twin ratio does not fall into either of the above cases. In this case it will be possible to observe the true crystal class and space group though many of the systematic absences will be present but weak. However, because of these intensity problems the structure will probably not solve or refine routinely.

In order to refine merohedral twins it is necessary to obtain the twin law. This must be done by studying the data for strong-weak intensity patterns. Presently, there are no programs for deriving the twin law. In addition, even when the twin law is known it cannot be entered into most solution programs. The lone exception is SHELXD which can solve twinned structures.

As emphasized above, working with most merohedral twins requires more knowledge and experience than the casual chemist-crystallographer has. These problems should be turned over to an experienced crystallographer who will frequently be able to provide a satisfactory structure.

14.3 Other Crystallographic Complications

There are several other crystallographic problems that may be encountered which should not be handled by inexperienced crystallographers. In many cases they are probably not recognized or treated and usually have little effect on the structural information.

One rare example are modulated structures.⁸⁰ These are structures that may have added translational components along some axes. Another is working with diffuse scattering.⁸¹ Again, this can provide information about the nature of the crystal but is not of great importance to most chemists.

CHAPTER 15

OTHER DIFFRACTION METHODS

So far the methods discussed have used a high quality crystal as the sample and X-rays as the radiation. Experiments can be performed on polycrystalline samples. Both high energy neutrons and electrons can replace the X-rays. In this chapter, these methods will be introduced. The discussion will not be in great depth. These methods can provide data beyond the structural data that have been discussed so far. However, the discussion here will emphasize the structural aspects of these techniques.

15.1 Powder Diffraction

Powder diffraction is totally a misnomer. The sample used is composed of crystals ground up into a fine powder. The sample is really polycrystalline microcrystals. The technique will provide no output for samples that have no crystallinity. Therefore, material such as flour or sawdust will not produce a signal. In fact, the mere presence of a signal from a powder is proof that there is something crystalline in the sample. While powder diffraction does not supply as complete a data set as a single crystal, it can be used when a single crystal for analysis cannot be obtained. A web search on “introduction to X-ray powder diffractometry” will provide a plethora of references.

The powder sample is ideally composed of microcrystals that pack randomly in all orientations. However, even after grinding, the microcrystals may maintain the morphology of the larger crystals. Needles and plates are less likely to pack randomly and therefore may have a preferred orientation. Originally the samples were packed into capillaries and the X-rays were passed through the sample. This is called transmission mode. Most modern diffractometers reflect the X-ray beam off the sample in reflection mode. In this case the sample is evenly distributed on a solid surface.

Because the sample is composed of many microcrystals, the diffraction pattern does not radiate out as spots but as a cone from the source. When a two-dimensional detector is placed in the diffracted beam, circles of diffraction are observed with the beam at the center. The Bragg angle can be easily calculated from the radius of the circle and the distance from the detector to the sample. In fact, the Bragg angle and the intensity are the only information from such a pattern. If the sample has no preferred orientation, then the intensity around a circle should be constant.

There are several consequences of the appearance of powder diffraction. If the diffraction around the ring is constant, then data only needs to be measured along a radius starting at the center. Clearly, the intensity at any distance moving in either direction along a diameter from the center should be the same so only a radius is required. The powder pattern is usually given as a plot of intensity versus theta. Figure 15.1 is the powder pattern for NaCl while Figure 15.2 is the synthesized pattern for a small inorganic compound.

XRD Pattern of NaCl Powder

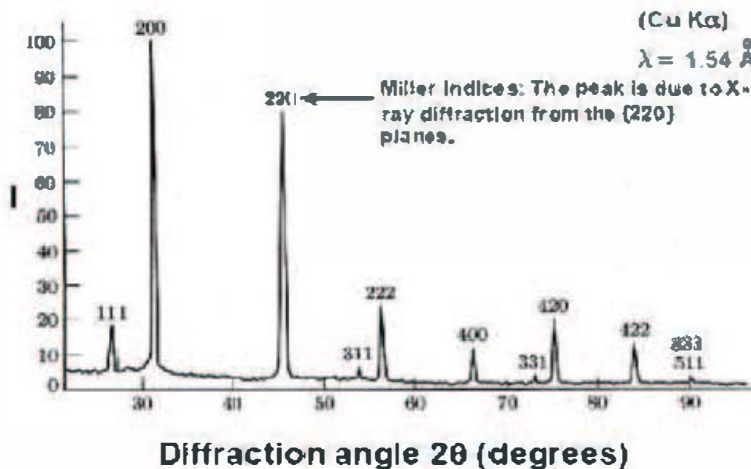


Figure 15.1 The Powder Pattern of NaCl.

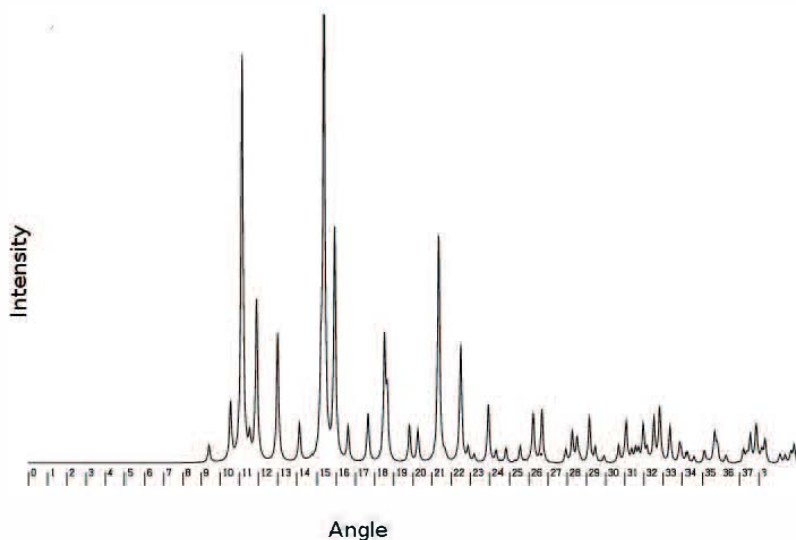


Figure 5.2 A simulated powder pattern

The biggest difference between powder and single crystal diffraction is in the resolution. Because each hkl has essentially a unique position in space for a single crystal, peak overlap is rare unless the spots are very broad. However, when the same data are reduced to only a theta value, overlap is likely. There are several ways to minimize this overlap. As previously explained, the radiation produced by X-ray tubes is not monochromatic. It consists of a background radiation and several sharp peaks. Even the peaks are doublets which are usually not resolved by typical monochromators. In powder diffraction diffractometers slits are used to try to create as monochromatic an X-ray beam as possible. Slits also narrow the output of the diffraction. It is important to use as long a wavelength as possible for collecting powder data. Typically, copper or even chromium radiation is used. This will produce the greatest differences in theta for the various peaks. However, when X-ray tubes are used as the source, the radiation will not be monochromatic increasing the peak width and increasing overlap. If minimum peak width is required, synchrotron radiation, which is monochromatic, should be used.

Of course, the great advantage of powder diffraction is that it does not require a sizable, high quality crystal. It can also measure the properties of the bulk material and not just a small sample. The main use of powder diffraction is to determine if a sample is a known compound and crystalline phase and to look for impurities. It is akin to routine NMR but for crystalline solids.

The major use for powder diffraction patterns is as a fingerprint of a crystalline phase. This is important information for several reasons. First, pharmaceuticals are approved and patents awarded for a particular crystal form. It is important during manufacturing to ensure the product is the correct form. It is easy to compare a quickly obtained powder pattern to the expected pattern to ensure the product is correct.

Powder diffraction is also used extensively in the analysis of solid state and hydrothermal syntheses. These techniques perform synthesis in an inert tube and at high temperatures. Determining whether any reaction has occurred and what the products are is done by powder diffraction. Combinatorial methods where multiple reactants are tested can be automated and the patterns obtained using a robotic sample changer.³²

Powder diffraction can also be used to identify unknown solids. A good library of known patterns is required. The most complete set of patterns is sold by the International Center for Diffraction Data as the Powder Diffraction File (PDF).³³ The latest databases consist of several products PDF4+ for inorganic compounds, PDF4+/organics for organic and organometallic compounds and PDF4+/minerals. The organic database can be used to identify pharmaceuticals and narcotics. While there are smaller free databases, none match the completeness of the PDF.

Like other fingerprint methods such as mass spectrometry or chromatography, powder patterns can be used to identify mixtures of solids. Most powder diffractometers include such software. In addition, stand-alone software can be obtained. Obviously, patterns for the components must be available for the determination of a mixture. The PDF will allow multiple components to be identified. If the combined powder pattern is of high quality, the ratio of the components may be determined.

While matching patterns offers one way of identification, indexing the unit cell provides information that is more readily searched. It also does not involve the relative intensity of the peaks, which can change for different

samples if they are not properly prepared. There are many good indexing programs for powder patterns. Some software can even index the components of mixtures. The software has improved greatly over the last few years and determination of cell parameters from powder data is now more routine.

It is also possible to calculate a powder pattern from the atomic parameters and cell constants determined from a single crystal study. Many programs can perform this calculation including PLATON. The pattern calculated is not as exact as one measured since the width of the peaks must be estimated. The wavelength used in calculating the powder pattern does not need to be the same as used in the single crystal data collection. Figure 15.2 represents a calculated pattern for copper radiation from a structure collected with molybdenum radiation.

It is possible to determine the entire structure from powder diffraction. The refinement method is referred to as Rietveld refinement. In most cases it will not be possible to determine the intensities of the individual hkl reflections. There are several programs such as SIRPOW²⁴ that are designed to solve structures from powder data. Rietveld refinement adjusts the structure so that the total calculated pattern is in agreement with the observed pattern.²⁵ This is quite different from single crystal refinement. For small unit cells and high quality data (preferably from a synchrotron) the results can be quite acceptable.

Powders are also studied for non-structural data. Powder textures can be studied and quantified by diffraction. A related technique small-angle X-ray scattering (SAXS) is used to study interactions on the micro or nano scale.

15.2 Neutron Diffraction

In 1924 Louis de Broglie proposed that matter could be considered as waves. The wavelength for such a wave is given by $\lambda=h/mv$ where h is Planck's constant, m the mass of the matter and v its velocity. For most matter, the value of mv is so large that the wavelength is so small as to be negligible. However, for light atoms and sub-atomic particles it is possible to obtain wavelengths in the Angstrom region which are comparable to X-rays. It should be possible to obtain a diffraction pattern using neutrons. The first experiments with neutron scattering were carried out in the 1930s. It was not until the late 1940s when nuclear reactors became

available as sources, that there was sufficient flux (intensity) to make use of neutrons in diffraction experiments.

Since the velocities of the neutrons are random, the neutron source unlike X-ray sources does not produce any preferred wavelength. Nuclear reactors produce a continuous source of neutrons. However, to use the neutrons from a reactor requires very large crystals. Neutron powder diffraction has been used to avoid this problem. More modern neutron sources are pulsed. The neutrons are generated when light atom nuclei are accelerated and collide with a heavy metal target. The accelerated particles are not continuously produced but pulsed at regular intervals. Therefore, white radiation is used as the source. The wavelength can be determined by the time it takes for the diffracted neutrons to reach the detector. The faster the time the shorter the wavelength.

Working with neutrons is somewhat different than X-rays. First, it is hard to build a shutter to stop the neutron beam. As neutrons are not charged they penetrate matter to a much greater extent. It is also difficult to detect neutrons. Most charged particles and electromagnetic radiation are detected because of their charge. The penetrating ability of neutrons requires very special detectors. Today there are area detectors that can be used for neutron data collection.

For years, the lack of intense sources and sensitive detectors, limited neutron diffraction to very large crystals. These crystals were sized in centimeters instead of millimeters. Obtaining such large crystals was very difficult to impossible, limiting this technique. But in the last few years, there have been improvements in both the intensity of the neutron sources and in the sensitivity of the detectors. These new sources are called spallation sources and they are just coming on-line now. The International Atomic Energy Agency lists a total of ten such sources worldwide but not all are equipped for diffraction experiments.³⁶ However, more such sources are being built and hopefully will enable greater use of neutron diffraction. The experimental requirements are given for the single crystal diffractometer at the Oak Ridge Spallation Neutron Source located in the United States.³⁷ This instrument is capable of handling X-ray diffraction sized crystals with unit cells lengths of less than about 50\AA . The bandwidth of the white radiation is typically either $0.5\text{-}3.5$ or $4.0\text{-}7.0\text{\AA}$. Data collection times are on the order of minutes.

One major difference between neutron and X-ray diffraction is that neutrons are diffracted directly by the nucleus. The neutron equivalent of the X-ray scattering factor is the scattering length. The scattering length is different for each isotope of an element and an average value is used when the element is not isotopically pure. Unlike the X-ray scattering factor, the scattering length is not a function of θ the scattering angle and therefore high angle data are more easily measured for neutrons. The scattering length has no regular variation with atomic number. The isotopes ^1H and ^7Li both have negative scattering lengths. This means that their scattering is out of phase with the incident beam. Different phasing does not happen for Bragg scattering of X-rays. This also means diffraction by ^1H will decrease the intensity of the diffraction. Therefore, compounds with large amounts of hydrogen may be difficult to study. On the other hand ^2H deuterium has a positive scattering length making it easy to discriminate from the lighter isotope. The element vanadium has a nearly zero scattering length and therefore is difficult to detect in neutron crystallography. Because of the penetration of the uncharged neutrons, absorption is not a problem.

The structures to be studied by neutron diffraction are usually first determined using X-rays. This provides basic atomic parameters that can then be refined using the neutron data. Because the hydrogen atoms now contribute strongly to the overall scattering, their parameters can be refined and the adsorbates even treated anisotropically. The distances involving hydrogen atoms will always be longer in neutron studies than X-ray. This is because neutrons measure the actual inter-nuclear distance while X-rays measure the center for the electron density which is typically polarized for hydrogen.

The chemical use of neutron diffraction frequently involves hydrogen atoms. The aim of many neutron studies is to measure the distances and bond angles involving hydrogen. It is also useful for the study of heavy metal hydrides, because hydrogen atoms frequently do not appear larger than the noise around the metal in the difference Fourier map when X-rays are used. Neutron data have been invaluable for distinguishing between dihydrides and coordinated hydrogen molecules. Neutron studies are frequently required to determine the location of deuterium atoms after substitution reactions. This is especially important in inorganic compounds where there may be no good NMR handle.

There are other experiments done with neutrons that have no easy X-ray equivalence. First, because neutrons are a particle, they have a magnetic and electric moment even though they are uncharged. By careful

experimentation, the magnetic moment can be used to determine the magnetic structure of a crystal. Since this diffraction will fall off as a function of the Bragg angle, a form factor is required. Magnetic structures are much more complex than atomic ones and are described by one of the 1651 magnetic (Shubnikov) groups.

Neutrons can also be used to study the atomic and molecular motions in a crystal. This is done by neutron inelastic scattering studies. Inelastic scattering is scattered radiation that has a wavelength different from the exciting radiation. The Raman spectrum is the equivalent inelastic scattering for visible light.

15.3 Electron Diffraction

In 2017 Lukas Palatinus *et al.* published a paper in *Science* where they reported they had characterized two very small crystals using electron diffraction.²² The structures were of sufficient quality that the hydrogen atoms had been located in the difference Fourier maps and refined. While electron diffraction had been used previously, this was the first report where the quality of the resulting structures was equal to what is obtained from X-ray diffraction.

The two structures determined were paracetamol (acetaminophen) and a disordered, solid state cobalt compound. The size of the paracetamol crystal was reported at $0.001 \times 0.0005 \times 0.0005$ mm which is much smaller than any sample that could be studied with X-rays. The final R_w for this structure was 0.098. Obviously, this method opens up crystallography to a whole new class of crystals that in the past have not produced samples that were large enough for analysis with X-rays.

Like neutron diffraction, electron diffraction uses a particle moving at high velocity to produce wave behavior. The two techniques have almost inverse experimental problems. For example, because of their lack of charge, neutrons do not normally do any damage to the crystal even after long exposure. Electrons quickly destroy the crystal. For the organic sample reported, the crystal had to be moved with respect to the beam after each exposure while for the inorganic sample six crystals were used. The electron beam used as the source was produced by an electron microscope and was monochromatic. Samples must be placed in a high vacuum in the electron microscope which can cause loss of solvent. The

data reported by Palatinus were collected at 100K which should prevent this problem.

The major problem in electron diffraction, is that the beam is so intense that effects ignored in X-ray diffraction are commonly observed. One example is multiple diffraction. Bragg's Law is $2d\sin(\theta) = n\lambda$. The n represents the order of diffraction which up to now has always assumed to be one. Occasionally the second order diffraction can be observed but is too weak to affect the data. With electrons many values of n provide sufficient intensity which alters the intensity of the first order diffraction. Care must be used in the design of the experiment and the integration software to account for these added contributions. Other factors such as extinction and absorption can also be more important in electron diffraction and must be eliminated either in the diffraction geometry or in the integration.

This technique is obviously in its infancy but has the potential to revolutionize crystal structure analysis. The most important improvement over X-rays is that microcrystals could be structurally characterized. This opens the technique up to compounds that do not grow large enough crystals and may mean that the drudgery of trying to obtain larger crystals would be eliminated. Additionally, individual crystals in a mixture of microcrystals could be examined instead of the entire sample using powder diffraction. This would be important in patent cases to ensure that a known crystalline material is not part of a competitor's product. The diameter of the beam of an electron microscope is usually less than 10^{-5} mm so very small areas of the crystal can be examined. These results can determine if different phases or regions with different packing patterns are present. However, the experimental setup and the software will have to be improved so these studies can be done routinely.

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