

Chemical Crystallography: From Inception to Maturity

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The use of single crystal X-ray diffraction to determine the structure of a chemical compound has been historically classified as 'Chemical Crystallography'. The methodologies, the accuracy in experiments coupled with the modern computer gadgets and advances in technology makes this branch of science an unequivocal provider of accurate and precise measurements of molecular dimensions. Structure determination by powder diffraction, crystal engineering, charge density analysis and studies on molecules in excited states are the recent add-ons.

Introduction

Following the discovery of X-rays by Wilhelm Konrad Röntgen in 1895 approximately seventeen years later Walther Friedrich, Paul Knipping and Max von Laue demonstrated that crystals diffract X-rays. They wrote in their classic 1912 paper "If X-rays really are electromagnetic waves, it would seem likely that the structure of the crystal lattice would give rise to interference phenomenon, resulting from the atoms being excited to either free or constrained vibration. In fact the interference phenomenon should be similar in nature to those known for optical grating spectra." The definition of a crystal in this context is a three-dimensional solid with a regularly repeating internal arrangement of atoms. Structures of chemical compounds are in general, built from a collection of bonded atoms to represent a molecule or an ionic solid. The basic building block referred, as the unit cell is the representation of the internal regularity in the crystal and could be generated by an atom, several atoms, a molecule, an ion or several molecules or ions depending on the internal symmetry of the unit cell. X-ray diffraction then is the interference between X-rays scattered by the electrons in the

Keywords

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various atoms at different locations in the unit cell. This becomes an observable effect as spots of differing intensities on a photographic film when the diffraction is reinforced by the repeat of the unit cells in the crystal. W L Bragg demonstrated that the measurement of the diffraction patterns yield the electron density and hence the arrangement of atoms in the crystal. The first X-ray analyses were on alkali halide crystals and interestingly the alternating cations and anions arranged like a chessboard pattern was demonstrated. Conventional chemists did not readily accept this first chemical crystallography experiment. In fact H E Armstrong wrote an article even as late as 1927 opposing the non-existence of NaCl molecule by saying “Chemistry is neither chess nor geometry, whatever X-ray physics maybe... it were time that chemists took charge of chemistry once more...”. However, with the accumulation of more and more crystal structures it became evident that chemical crystallography would become indispensable. It established structural types for elements and simple ionic compounds, tables for standard metallic, ionic, covalent and non-bonded atomic radii. With parallel developments in crystal chemistry principles and theoretical chemistry the growth of this area of science has become prolific in recent years.

How do We See Atoms?

The size of atoms and molecules are seen only through a *super microscope*, the logic being that we can see details of an object only if the details are separated by half of the wavelength of the radiation used to probe the object. The distance between atoms in a molecule is of the order of 10^{-8} cm (0.1 nm) and hence visible light microscopes with wavelengths of three orders of magnitude higher are not suitable. X-rays are of the order of 0.1 nm and hence are ideally suited. However X-ray detectors are sensitive only to intensities and not to phases and this is an unsolved problem in crystallography. The job of a lens is done via Fourier synthesis and the interpretation is done by crystallographic methods. The nearest phases are estimated via Patterson synthesis or Direct methods, the latter approach has already resulted in

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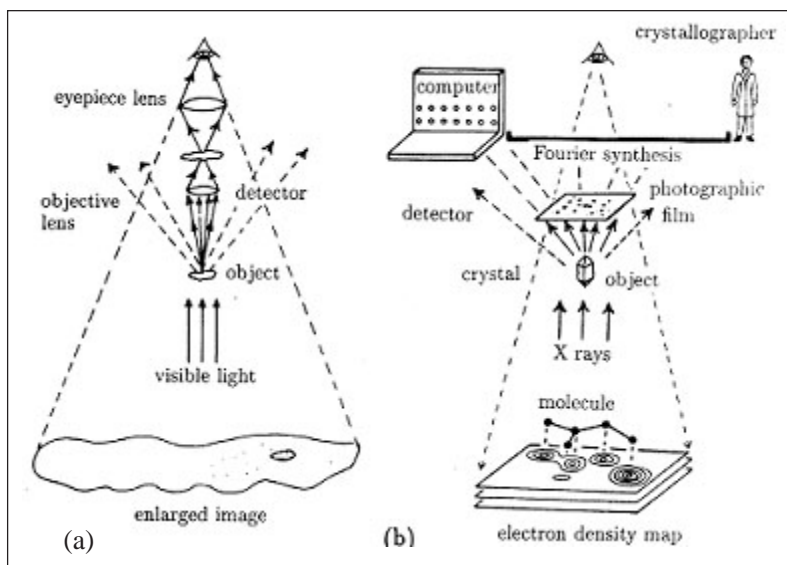


Figure 1. Comparison between optical microscopy and X-ray diffraction.

a Noble Prize for Jerome Karle and Herbert Hauptman. If both intensities and phases are known, then the image reconstruction can be done as given in *Figure 1*.

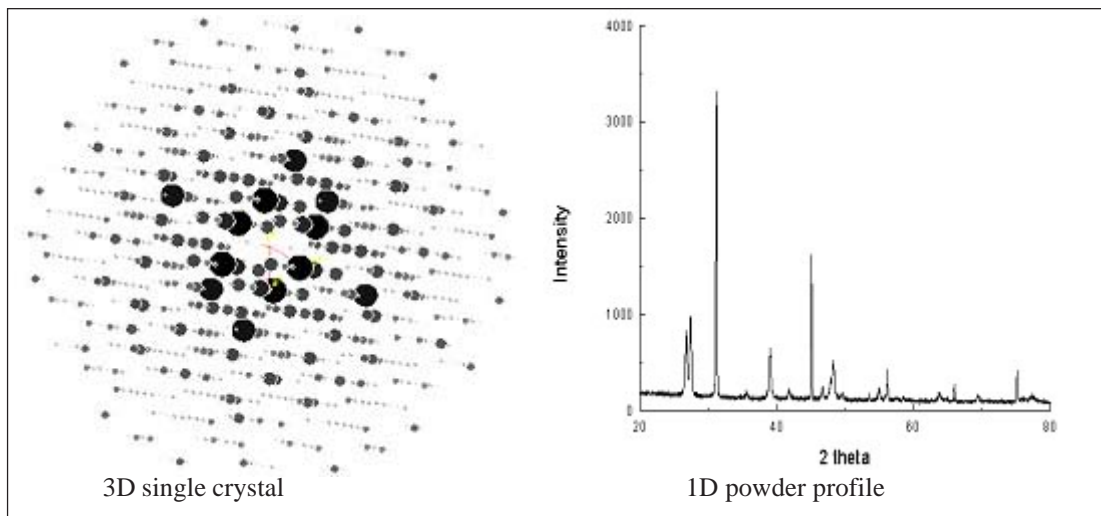
The practitioners of chemical crystallography have tended to concentrate on using single crystal X-ray diffraction to determine the structure of what may be thought of as ‘small molecules’, the upper limit is about 500 atoms. Compounds, which are of both chemical and biological interest, e.g. new synthetic chemicals, catalysts, pharmaceuticals, natural products and supra-molecular assemblies are the current day targets. *Figure 2* shows the difference between the two types of data sets one obtains and even though the entire data is condensed on the 1D profile in powder the extraction of the 3D data required becomes a challenge. More recently, structure determination by powder diffraction has become increasingly important to chemical crystallographers as growing single crystals of good quality in many situations become difficult and sometimes impossible.

The Growth of Chemical Crystallography

Historically, the first crystal structures were of alkali halides, diamond and graphite and hexamethylbenzene. The structure

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of benzene was first determined in 1954 at -3°C . It is indeed very difficult to imagine what chemistry would be like if X-ray methods were never discovered. We would not know even to this day the atomic arrangement in ionic crystals, minerals, metals and alloys and certainly nothing about the conformation of complex organic molecules including biological molecules like proteins, viruses and polynucleotides. The growth of chemical crystallography was pioneered by several individuals but more so by the rapid growth in technology and computation. Several thousands of crystal structures are solved every year of varying complexity with minimum human intervention. The advances made in computational techniques make the methodology available to any chemist who need not have any formal training as a crystallographer. Several exciting structures have been determined, outstanding problems in chemistry have been resolved with this technique. Chemical crystallography has advanced so much since it was conceived in the early twentieth century that a significant percentage of Nobel Prizes have been awarded to the structural characterization of a wide range of materials of chemical and biological significance, prominently for the crystallographic analysis. It has reached a stage of maturity and it is now time for expansion into new vistas.

The current day X-ray diffraction system is extremely user

Figure 2. The difference between single crystal data and powder data: Single crystals give well-resolved 3-dimensional distribution of intensities and each spot can be identified as a lattice point and indexed. The powder patterns of poly crystalline samples give all this data but condensed into a 1D profile of intensity vs. the scattering angle 2θ .



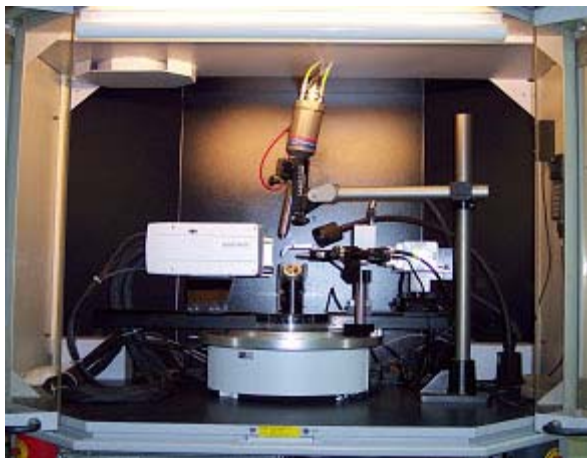
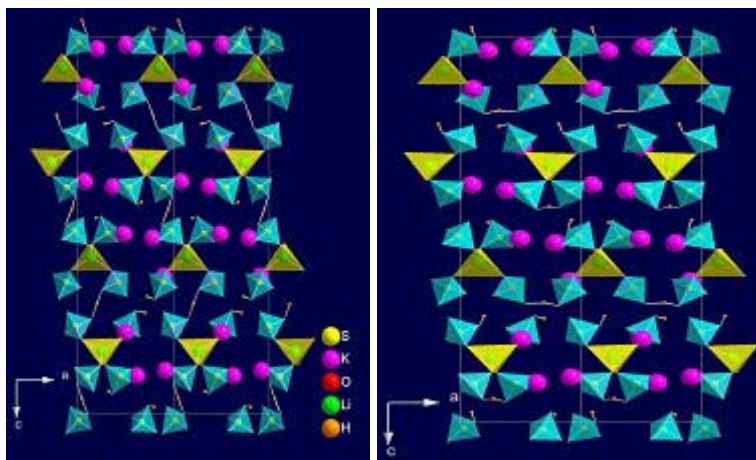


Figure 3. State of the art laboratory X-ray diffraction system.

friendly and is equipped with charged couple device (CCD) area detector (*Figure 3*), which measures the intensities accurately, rapidly and is highly sensitive. A very major contributor to the modern day chemical crystallography is molecular graphics. The packages clearly illustrate the complexity involved in both molecular and crystal structure. Single crystal chemical crystallography has expanded beyond the determination the structure of a molecule – increasingly, the interaction

of molecules with each other in the solid state has become the focus of chemical crystallographic research. The systematic study of the way molecules pack in the solid, the so called crystal engineering, has direct application in the pharmaceutical industry, in the study of polymorphism and further application in materials science for the design of new materials. A couple of examples from the work done in our group are given in *Figure 4* to give a flavor of the type of structures one encounters in chemical crystallography today. *Figure 4(a)* shows the structure of $K_4LiH_3(SO_4)_4$ at two different temperatures, which has paved the way for understanding in terms of hydrogen bonding patterns the anomalies observed in the behavior of EPR spectra of this compound. *Figure 4(b)* illustrates the complex packing in

Figure 4(a). Structure of $K_4LiH_3(SO_4)_4$ at 293K and 100K show different H-bonding patterns.



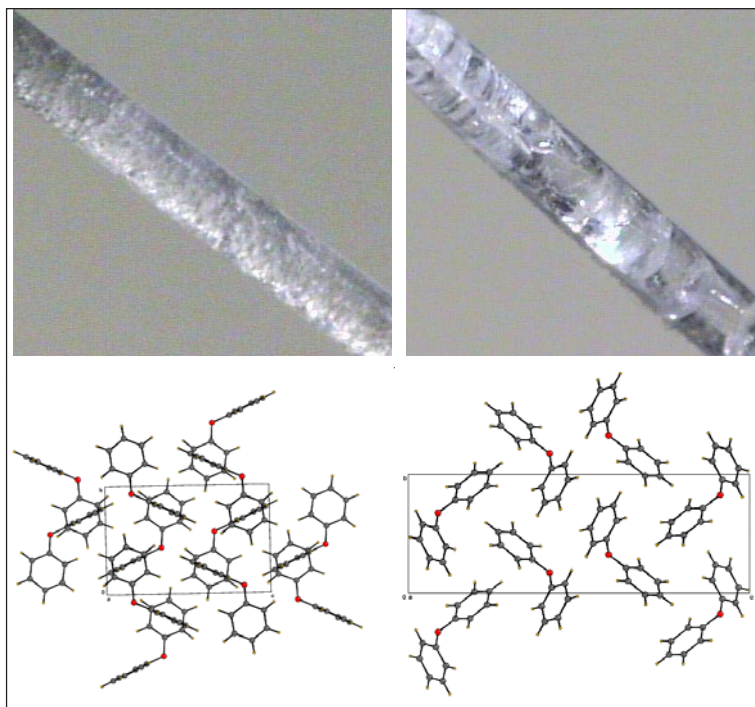


Figure 4(b). Polymorphism in diphenyl ether has been identified during *in situ* crystallization via single crystal X-ray diffraction. Only weak inter and intra molecular C-H... π interactions control the packing of the molecules in both crystal forms; monoclinic centrosymmetric ($P2_1/n$) in form I and orthorhombic non-centrosymmetric ($P2_12_12_1$) in form II.

diphenyl ether, a liquid at room temperature, which displays polymorphism on cryo-crystallization. These illustrations bring the state of the art chemical crystallography methods to explore new regions of unexplored structural chemistry.

With the efforts of the Cambridge Crystallographic data Centre, the single crystal structure data (CSD) of organic and organometallic compounds (the latest version has 322241 structures) are available and it has served as a gold mine for deriving similarities in structures, classifying structures based on chemical nomenclature and as a source for evaluating the nature of bonded and non-bonded contacts. A similar database, ICSD, is available for Inorganic structures. Powder diffraction data on almost all compounds are stored in the ICDD database. In all these cases, interactive online programs help to search, match and analyze any data that is deposited in these databases.

New Horizons in Chemical Crystallography

The availability of synchrotron radiation has in recent years

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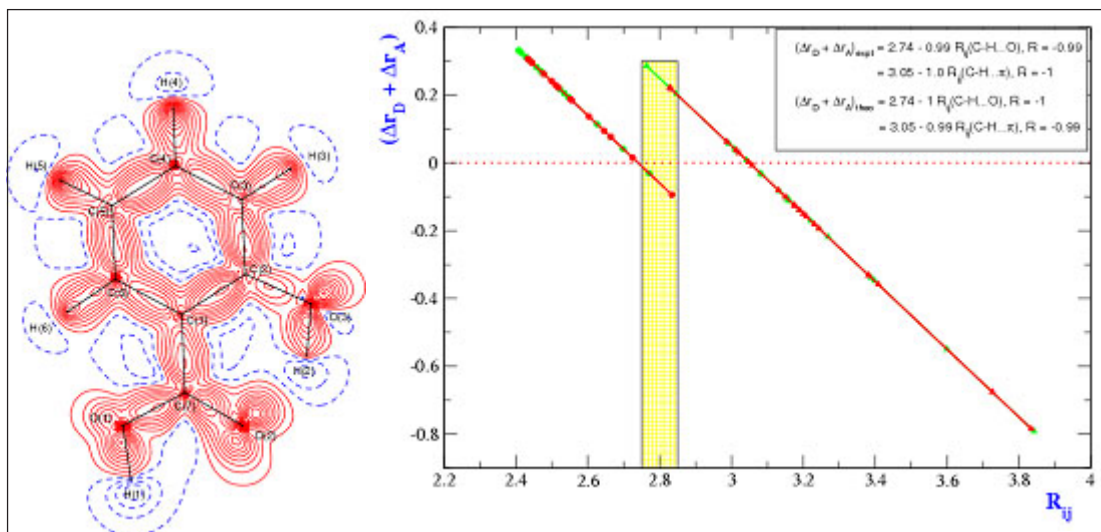


provided the launch pad for new, novel and exciting experiments in chemical crystallography. In areas like microporous solids and supramolecular chemistry, the crystals do not grow to a size required in a routine X-ray diffraction experiment. The limits of conventional X-ray diffraction facilities are thus extended because of the marked improvements in resolution and intensity. As is clear from the example in *Figure 4(b)* use of cryo coolers to reach temperatures down to 100K (liquid Nitrogen) and even lower than 10K (liquid helium) have added a further dimension to the quality and quantity of diffraction data that can be obtained from good quality crystals.

It is possible to ask questions like “*What happens to an atom when it becomes a part of a molecule and further what happens to a molecule when it is packed with several others in a crystal lattice?*”

Figure 5. Deformation density map of salicylic acid, showing the electron lone pair of oxygen atoms (left) and the separation of hydrogen bonds from van der Waal interactions with the donor-acceptor distance, R_{ij} (right).

Chemical crystallography now gives the solution for viewing the electron density distributions (more appropriately charge density distributions) in crystals, since the diffraction is mainly from the electron density in the crystal. However, a very accurate, precise data is a prerequisite and the derived results should agree well with theoretical calculations, which have made significant progress in recent times. A recent work from our laboratory explored the lower limit of a hydrogen bond and *Figure 5*



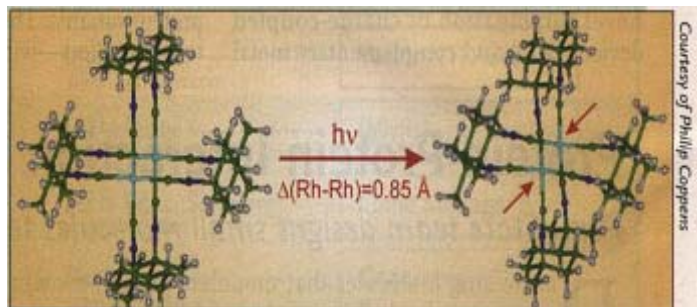


Figure 6. Contraction of Rh-Rh bond measured via time resolved crystallography.

shows a sample deformation density map and the plot of the quantity, which separates H-bond from van der Waal interaction with the donor-acceptor distance, R_{ij} .

The ability to perform time-resolved experiments on very short-lived species at pulsed X-ray sources opens the possibility to follow chemical changes in real time. The first experiments ever were done by Philip Coppens and his group in which the three dimensional structure of an excited state of a Cu (I) metallo-organic complex with 60 μ s lifetime has been determined at atomic resolution. They have also measured laser-induced NO linkage isomerism of transition metal nitrosyl complexes, including Ru and Fe porphyrins. *Figure 6* shows the measurement of contraction in Rh-Rh bond, which occurs in the microsecond regime measured by this group using the time resolved crystallographic technique.

Chemical crystallography has a bright future, as bright as synchrotron source can be! It is expected to make inroads into nano sciences, reaction pathways and above all make significant contributions to biological sciences.

*The road goes ever on and on
Down from the door where it began
Now far ahead the road has gone
And I must follow, if I can
Pursuing it with weary feet
Until it joins some larger way
Where many paths and errands meet.
And whither then? I cannot say*
From: *The Lord of the Rings*, J R R Tolkien

Suggested Reading

- [1] Jenny P Glusker with Mitchell Lewis and Miriam Rossi, *Crystal structure analysis for chemists and biologists*, (Ed.) Alan P March, VCH publishers, USA.
- [2] Jack D Dunitz, *X-ray analysis and the structure of Organic Molecules*, Cornell University Press, USA.

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