

1.2. Historical background

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1.2.1. Introduction

Crystallography ranks with astronomy as one of the oldest sciences. Crystals, in the form of precious stones and common minerals, have attractive properties on account of their symmetry and their refractive and reflective properties, which result in the undefinable quality called beauty. Natural philosophers have long pondered the unusual properties seen in the discontinuous surface morphologies of crystals. Hooke (1665) and Huygens (1690) came close to grasping the way repeating objects create discrete crystal faces with reproducible interfacial angles. The symmetry of mineral crystals was explored systematically in the 18th and 19th centuries by measuring the angles between crystal faces, leading to the classification into symmetry systems from triclinic to cubic and the construction of symmetry tables (Schoenflies, 1891; Hilton, 1903; Astbury *et al.*, 1935) – the predecessors of today's *International Tables*.

1.2.2. 1912 to the 1950s

It was not until the interpretation of the first X-ray diffraction experiments by Max von Laue and Peter Ewald in 1912 that it was possible to ascertain the size of the repeating unit in simple crystals. Lawrence Bragg, encouraged by his father, William Bragg, recast the Laue equations into the physically intuitive form now known as 'Bragg's law' (Bragg & Bragg, 1913). This set the stage for a large number of structure determinations of inorganic salts and metals. The discovery of simple structures (Bragg, 1913), such as that of NaCl, led to a good deal of acrimony, for crystals of such salts were shown to consist of a uniform distribution of positive and negative ions, rather than discrete molecules. These early structure determinations were based on trial and error (sometimes guided by the predictions of Pope and Barlow that were based on packing considerations) until a set of atomic positions could be found that satisfied the observed intensity distribution of the X-ray reflections. This gave rise to rather pessimistic estimates that structures with more than about four independent atomic parameters would not be solvable.

The gradual advance in X-ray crystallography required a systematic understanding and tabulation of space groups. Previously, only various aspects of three-dimensional symmetry operations appropriate for periodic lattices had been listed. Consequently, in 1935, the growing crystallographic community put together the first set of *Internationale Tabellen* (Hermann, 1935), containing diagrams and information on about 230 space groups. After World War II, these tables were enlarged and combined with Kathleen Lonsdale's structure-factor formulae (Lonsdale, 1936) in the form of *International Tables* Volume I (Henry & Lonsdale, 1952). Most recently, they have again been revised and extended in Volume A (Hahn, 1983).

Simple organic compounds started to be examined in the 1920s. Perhaps foremost among these is the structure of hexamethylbenzene by Kathleen Lonsdale (Lonsdale, 1928). She showed that, as had been expected, benzene had a planar hexagonal structure. Another notable achievement of crystallography was made by J. D. Bernal in the early 1930s. He was able to differentiate between a number of possible structures for steroids by studying their packing arrangements in different unit cells (Bernal, 1933). Bernal ('Sage') had an enormous impact on English crystallographers in the 1930s. His character was immortalized by the novelist C. P. Snow in his book *The Search* (Snow, 1934). By the mid-1930s, J. Monteath Robertson and I. Woodward had determined the structure of nickel phthalocyanine (Robertson, 1935) using the heavy-atom method.

This was a major crystallographic success and perhaps the first time that a crystallographer had succeeded in solving a structure when little chemical information was available.

Another event which had a major impact was the determination of the absolute hand of the asymmetric carbon atom of sodium tartrate by Bijvoet (Bijvoet, 1949; Bijvoet *et al.*, 1951). By indexing the X-ray reflections with a right-handed system, he showed that the breakdown of Friedel's law in the presence of an anomalous scatterer was consistent with the asymmetric carbon atom having a hand in agreement with Fischer's convention. With that knowledge, together with the prior results of organic reaction analyses, the absolute hand of other asymmetric carbon atoms could be established. In particular, the absolute structure of naturally occurring amino acids and riboses was now determined.

Until the mid-1950s, most structure determinations were made using only projection data. This not only reduced the tremendous effort required for manual indexing and for making visual estimates of intensity measurements, but also reduced the calculation effort to almost manageable proportions in the absence of computing machines. However, the structure determination of penicillin (Crowfoot, 1948; Crowfoot *et al.*, 1949), carried out during World War II by Dorothy Hodgkin and Charles Bunn, employed some three-dimensional data. A further major achievement was the solution of the three-dimensional structure of vitamin B₁₂ by Dorothy Hodgkin and her colleagues (Hodgkin *et al.*, 1957) in the 1950s. They first used a cobalt atom as a heavy atom on a vitamin B₁₂ fragment and were able to recognize the 'corrin' ring structure. The remainder of the B₁₂ structure was determined by an extraordinary collaboration between Dorothy Hodgkin in Oxford and Kenneth Trueblood at UCLA in Los Angeles. While Dorothy's group did the data collection and interpretation, Ken's group performed the computing on the very early electronic Standard Western Automatic Computer (SWAC). Additional help was made available by the parallel work of J. G. White at Princeton University in New Jersey. This was at a time before the internet, before e-mail, before usable transatlantic telephones and before jet travel. Transatlantic, propeller-driven air connections had started to operate only a few years earlier.

Many technical advances were made in the 1930s that contributed to the rapidly increasing achievements of crystallography. W. H. Bragg had earlier suggested (Bragg, 1915) the use of Fourier methods to analyse the periodic electron-density distribution in crystals, and this was utilized by his son, W. L. Bragg (Bragg, 1929*a,b*). The relationship between a Fourier synthesis and a Fourier analysis demonstrated that the central problem in structural crystallography was in the phase. Computational devices to help plot this distribution were invented by Arnold Beevers and Henry Lipson in the form of their 'Beevers-Lipson strips' (Beevers & Lipson, 1934) and by J. Monteath Robertson with his 'Robertson sorting board' (Robertson, 1936). These devices were later supplemented by the XRAC electronic analogue machine of Ray Pepinsky (Pepinsky, 1947) and mechanical analogue machines (McLachlan & Champayne, 1946; Lipson & Cochran, 1953) until electronic digital computers came into use during the mid-1950s.

A. Lindo Patterson, inspired by his visit to England in the 1930s where he met Lawrence Bragg, Kathleen Lonsdale and J. Monteath Robertson, showed how to use F^2 Fourier syntheses for structure determinations (Patterson, 1934, 1935). When the 'Patterson' synthesis was combined with the heavy-atom method, and (later) with electronic computers, it transformed analytical organic chemistry. No longer was it necessary for teams of chemists to