

3.7. CRYSTALLOGRAPHIC DATABASES

cation of the simple inorganic compounds which are often present in commercial vitamins.

A Hanawalt search using these peaks easily identified iron fumarate (00-062-1294), szmikite [$\text{MnSO}_4(\text{H}_2\text{O})$; 00-033-0906],

L-ascorbic acid (02-063-2295), monetite (CaHPO_4 ; 01-070-0359) and calcite (CaCO_3 ; 00-005-0586). Note that these hits come from four different data sources; searches based on just one source would not have identified all of these compounds.

There were strong high-angle peaks that had not yet been accounted for at d -spacings of 2.4762, 2.1068, 1.4900 and 1.4783 Å. These four peaks were entered into a new Hanawalt search, which identified periclase (MgO ; 01-071-3631) and zincite (ZnO ; 01-075-9742).

Superimposing the peaks for all of these compounds onto the raw data made it clear that there were broad peaks in the pattern at d -spacings of approximately 5.8750, 5.3273, 4.3277 and 3.9217 Å. Since the lowest and highest angles of these four were the best defined, separate searches for compounds having each of these peaks as one of their three strongest lines were combined using a Boolean 'and'. Among the hit list was cellulose I_β (00-060-1502), which is a common constituent of pharmaceuticals. The structure model from PDF entry 00-056-1718 was added to the Rietveld refinement as a ninth phase.

One last peak at 5.9915 Å was unaccounted for. A search for pharmaceutical-related compounds with this peak as one of the three strongest included nicotinamide (02-063-5340; niacin or vitamin B_3). Ten phases were thus identified and these account for all of the peaks in the pattern.

3.7.3. Cambridge Structural Database (CSD)

Some features of the Cambridge Structural Database system (CSD; <https://www.ccdc.cam.ac.uk>; Groom *et al.*, 2016) are described in Chapter 22.5 of *International Tables for Crystallography* Volume F (Allen *et al.*, 2011). The CSD contains X-ray and neutron diffraction analyses of carbon-containing molecules with up to 1000 atoms (including hydrogens), including organic compounds, compounds of the main-group elements, organometallic compounds and metal complexes. The CSD covers peptides of up to 24 residues; higher polymers are covered by the Protein Data Bank. The CSD also covers mononucleotides, dinucleotides and trinucleotides; higher oligomers are covered by the Nucleic Acid Database (<http://ndbserver.rutgers.edu>). There is a small overlap between the CSD and the Inorganic Crystal Structure Database in the area of molecular inorganics.

Capabilities particularly useful for structure validation are covered in Chapter 4.9 of this volume. This discussion will not attempt a comprehensive description of the capabilities of the CSD, but will concentrate on features that are particularly relevant to powder diffraction.

The principal interface to the CSD is the program *ConQuest* (Bruno *et al.*, 2002). Its most distinctive feature is the ability to draw molecular structures and fragments and carry out substructure searches. Such searches eliminate the ambiguities that can arise when searching by compound name or other text-based properties. These chemical-connectivity

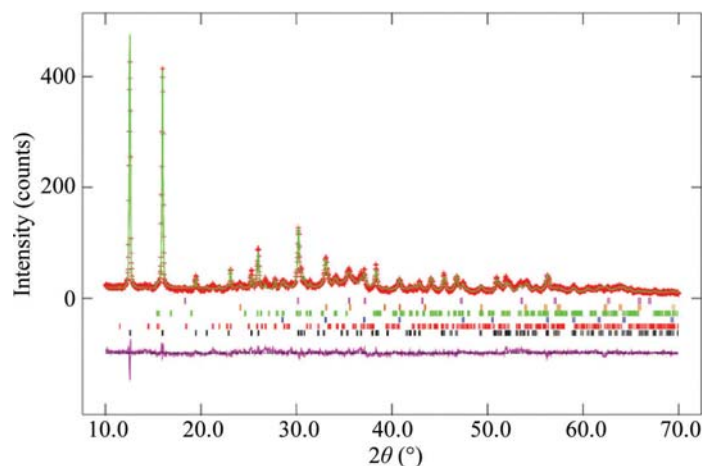


Figure 3.7.10

The final Rietveld plot from refinement of the isocracker deposit.

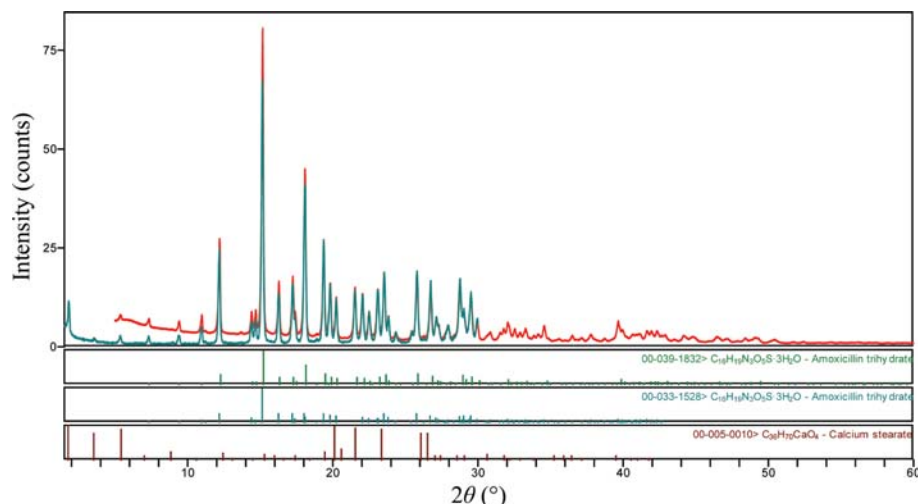


Figure 3.7.11

Phases identified in amoxicillin powder from a commercial capsule.

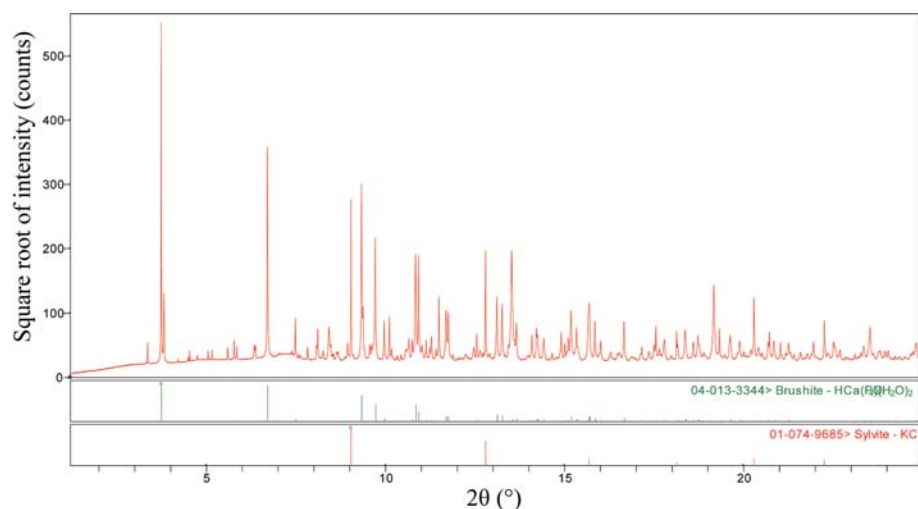


Figure 3.7.12

Phases identified by automated search/match in a Centrum A to Zn multivitamin tablet. Additional phases were identified using the native capabilities of the Powder Diffraction File.

3. METHODOLOGY

searches can include the number of H atoms bonded to a particular atom, the charge, the number of bonded atoms and whether the atom is part of a ring. In addition, three-dimensional quantities can be defined, tabulated and analysed. These quantities can be analysed in *Mercury* (Macrae *et al.*, 2008) and *Mogul* (Bruno *et al.*, 2004). Such analyses are useful for defining geometrical restraints in a Rietveld refinement. A general practice is to use the mean and standard deviations directly output by *Mogul* for the restraints. It is important to understand the CSD conventions for defining bond types to obtain successful results.

In *ConQuest*, searches can be carried out on author and/or journal name, as well as the normal bibliographic characteristics. Compounds can be located by chemical and/or common names, but such searches should be complemented by chemical-connectivity searches. It is possible to limit the search universe by chemical class, including carbohydrates, nucleosides and nucleotides, amino acids, peptides and complexes, porphyrins, corrins and complexes, steroids, terpenes, alkaloids and organic polymers. Searches on elements and formulae are possible, as well as searches on space groups and crystal systems. Particularly useful in searching for structure analogues are reduced-cell searches. Queries on *Z*, *Z'* and density are useful in data mining. A wide variety of searches on experimental parameters are possible; there is an option to exclude powder structures. Searches on both pre-defined terms and general text searches are possible. Particularly convenient for users of the PDF-4/Organics database is the retrieval of individual refcodes; the refcode from the PDF entry can be input directly into *ConQuest*. Starting with the 2013 release of the PDF-4/Organics database this link is live; the display of a PDF entry will result in import of the coordinates from the CSD entry. Boolean operations can be used to combine search queries in many flexible ways.

In recent years, many (if not most) single-crystal structures have been determined at low temperatures, while most powder-diffraction measurements are made under ambient conditions. Thermal expansion (often anisotropic) can result in differences between the observed peak positions and those in a PDF-4/Organics entry calculated from a CSD entry. For successful phase identification, larger than default tolerances must often be used in the search/match process. Transparency effects in pure organic compounds can also lead to significant peak shifts to lower angles, as well as significant asymmetry, so wider search windows may be necessary for phase identification.

3.7.3.1. *Mercury*

The structure-visualization program *Mercury* (Macrae *et al.*, 2008) is available as a free version and as a version with the CSD which has additional capabilities that are useful for powder diffraction. *Mercury* reads and writes a variety of molecular and crystal structure file formats, but is most commonly used with CIFs. Structures can be edited, and among the edit options is Normalize Hydrogens. This is particularly useful to improve the approximate H-atom positions that are often used in the early and intermediate stages of a Rietveld refinement. It is always worth including the H atoms in the structure model (in at least approximate positions) because better residuals and improved molecular geometry are obtained.

The Display Symmetry Elements tool is particularly useful for teaching symmetry. The Display Voids tool is useful in validating structures after solution. For most materials (zeolites and metal-organic frameworks are notable exceptions) we do not expect

empty spaces in the crystal structure, so the presence of voids suggests the presence of an incomplete structure model and/or errors.

Among the options in the Calculate menu is Powder Pattern. The calculation can be customized by the user to match the desired instrumental configuration. The calculated pattern can be saved in several formats for comparison in the user's instrument software. *Mercury* expects the displacement coefficients to be given as *U* values. CIFs can come from many sources and can use different conventions for the displacement coefficients or may be missing them entirely. Manual editing of the input CIF is often required, otherwise strange powder patterns can be calculated.

Among the CSD-Materials/Calculations options is BFDH morphology (Bravais, 1866; Friedel, 1907; Donnay & Harker, 1937). Although a simple calculation, it is often realistic enough to suggest the likelihood of profile anisotropy and preferred orientation, along with expected directions. The calculation can thus save guessing about preferred directions.

The Structure Overlay and Molecule Overlay options are very useful for comparing structures quantitatively. There is also an interface to the semi-empirical code *MOPAC*, which can also be a useful tool for assessing structural reasonableness. The H-Bonds and Short Contacts options are useful in completing a structure solved using powder data, as often the 'interesting' H-atom positions have to be deduced. There is a relatively new Solid Form menu, which contains several tools for analysing crystal structures.

3.7.4. Inorganic Crystal Structure Database (ICSD)

The Inorganic Crystal Structure Database (ICSD; <https://icsd.fiz-karlsruhe.de>; Bergerhoff & Brown, 1987; Belsky *et al.*, 2002; Hellenbrandt, 2004) strives to contain an exhaustive collection of inorganic crystal structures published since 1913, including their atomic coordinates. It is a joint project between FIZ Karlsruhe and NIST. The database is accessed through the online WebICSD or the locally-installed program *FINDIT*. Typical interatomic distances in inorganic compounds derived from the ICSD have been collected in Chapter 9.4 of *International Tables for Crystallography* Volume C (Bergerhoff & Brandenburg, 1999). Applications of the ICSD have been discussed by Kaduk (2002), Behrens & Luksch (2006) and Allmann & Hinek (2007).

The ICSD began as an inorganic crystal structure database of published structures with atomic coordinates. The scope was gradually extended to include intermetallic compounds. Since 2003, FIZ Karlsruhe has started to fill in the gaps, and the aim is for the ICSD to include all published intermetallic compounds. Originally the ICSD did not contain structures with C–H or C–C bonds. After 2003, this rule was modified so that new entries should not contain both C–H and C–C bonds; compounds containing tetramethylammonium and oxalate ions are now included.

The ICSD contains fully determined structures with atomic coordinates. Coordinates of light atoms (such as H atoms) or extra-framework species (such as in zeolites) may be missing. Structures described as isotopic to other structures, but without determination of the atomic coordinates, are included using the coordinates from the corresponding structure-type prototype. Such entries get a special remark/comment: 'Cell and Type only determined by the author(s). Coordinates estimated by the editor in analogy to isotopic compounds.' Currently there are more than