9. BASIC STRUCTURAL FEATURES

(which must be subgroups of the sphere-packing groups) become necessary to ensure space filling with the repetitive patterns of complex molecular shapes. In a similar manner, other objects with infinite elements of symmetry (*e.g.* rods; Lidin, Jacob & Andersson, 1995) can be subjected to a rigorous analysis of close packing.

9.7.7.2. *The hydrogen bond and the definition of the packing units*

The variously shaped molecular packing units of organic crystal structures are not necessarily identical with the individual molecule. The molecule (of a shape defined by chemical bonds on the inside and van der Waals forces on the outside) can be subjected to clustering under formation of intermolecular hydrogen bonds. Although far weaker than the chemical bond, hydrogen bonds are strong enough to alter the shape of the packing units of the crystal structure significantly. This may have far-reaching consequences for the adopted packing and symmetry. An extreme example is represented by the clustering of H_2O molecules, where two hydrogen bonds and two regular O—H bonds create a $\bar{4}3m$ point symmetry at each O atom, and a highly symmetrical structure emerges with an infinite bond network, similar to that in quartz, SiO_2. From the point of view of an individual H_2O molecule, the structure is very open. In contrast, a pseudo-close-packed structure of crystalline water, assuming an effective H_2O radius of $1.38 \text{\AA}$, would have specific density of 1.8 g cm^{-3}.

Analogous principles apply to organic structures with hydrogen bonding. CH_3OH, for example, forms hydrogen-bonded zigzag chains in its crystal structure. Obviously, the shape of the hydrogen-bonded cluster of molecules depends on the number and orientations of the hydrogen bonds relative to the size and shape of the molecule, causing three-dimensional, planar and linear 'polymers', or the formation of dimers and trimers. As in the example of water, this introduces additional symmetry elements and decreases the degree of space filling.

There is a general rule that ensures that this phenomenon is widespread. The principle of maximum hydrogen bonding states that all the H atoms in the active (polar) groups of a molecule are employed in hydrogen-bond formation (Evans, 1964). Therefore, as the O···HO and O···HN hydrogen bonds are both energetic and common, they are also of the greatest importance in this respect. Although most pronounced in smaller molecules, the symmetry-altering influence of hydrogen bonding also applies to relatively large molecules with a lower proportion of hydrogen bonding as, for example, in long-chain carboxylic acids that are linked in pairs. In large molecules with many active groups, however, the hydrogen bonds merely become the new delimiters of the shape of the individual molecule. The perils of the symmetry-statistical treatments of the hydrogen-bonded structures are well recognized and, for some purposes, the strategy adopted is to exclude such systems from the statistical pool (Filippini & Gavezzotti, 1992).

9.7.8. *A priori* predictions of molecular crystal structures

As physical properties of a molecular compound are a function of the spatial arrangement of molecules, an important goal of the structural chemist is to predict the space group and crystal structure from the molecular shape. On the basis of the observation that many structures of organic compounds are formed on the principle of periodic close packing of variously shaped molecules, it seems that such prediction would be a more or less straightforward computational task. However, the task of predicting the crystal structure of a specific molecular solid is complicated owing to the occurrence of hydrogen bonding (Subsection 9.7.7.2) and the widespread phenomenon of polymorphism (Gavezzotti, 1994). With only subtle differences in their Gibbs free energies, the occurrence of the structural modifications can be influenced by various non-equilibrium factors during crystallization.

In spite of the above problems, experience has shown that prediction algorithms can often be used to generate several reasonable structures for any given molecule and that in many cases the correct structure is among them. There are two general strategies that have been adapted for structure prediction. In the first one, developed by Kitajgorodskij (1955, 1973), the molecular shape is physically constructed from models of atoms having van der Waals radii, resulting in the calot model. The physical calot model is then used for an analogue calculation of the space filling using a mechanical instrument that relates the molecules in three-dimensional space so that the projection of one molecule fits into the voids of other molecules. When the unit-cell dimensions are known, the entire crystal structure can be derived in this way. In the second approach, the same yet abstract 'fused sphere model' is analysed for its symmetry by what can be called a 'morphic' (as opposed to metric) transformation by the methods of molecular topology (Mezey, 1993). The abstract topological molecular shapes can in principle be treated more rigorously and are computable into probable crystal structures.

Such *a priori* predictions of molecular structures are still in a relatively early stage of development. Several recent studies are indicative of the current progress in the field. For layered structures, good predictions can be obtained using construction techniques, symmetry probabilities, and potential energy functions (Scaringe, 1991). An algorithm for the generation of crystal structures by the optimization of packing potential energy over several possible space groups has been devised by Gavezzotti (1991, 1994). In a third approach, energy minimization without symmetry constraints is used for determining molecular crystal structures (Gibson & Scheraga, 1995).

In spite of recent progress, the conceptual link between the molecular and crystal structures still relies to a large extent on the chemical intuition of scientists. The space-group statistics have played a critical role, as they provide the researcher with a summary of what happens in nature. It is likely that the prediction process can be enhanced by calculating statistics of the space-group frequencies and symmetry for molecules that are the most closely related to the shape or chemistry of the molecule under study. As such statistical subsets are often significantly different from the overall statistics, they may prove more valuable in the *a priori* prediction of the crystal structure for a specific molecule. The space-group frequencies and symmetry statistics remain one of the important strings in this link.