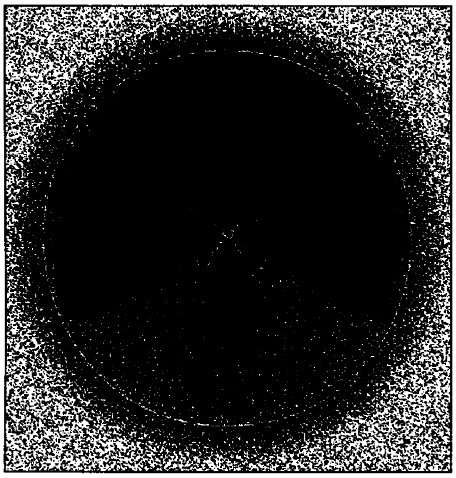

Simulation of the distribution of starlight in the occultation shadow of a satellite with a dynamically distorted atmosphere and nonuniform hazes. The density of points is proportional to the stellar flux at that point in the shadow. The solid curve shows the geometrical limb of the satellite. The central caustics have been exaggerated by a factor of 4 for clarity.

Even without an atmosphere, a spherical occulter can produce a bright spot in the center of its shadow, the so-called Poisson spot, produced by constructive interference of wavelets diffracted around the sphere's edge. No airless planet can be so perfectly spherical, but an imperfectly spherical atmosphere refracts light into central caustics (that is, regions where light rays cross over one another), with the positioning and size of the caustics determined by the varying curvature of the atmosphere along the limb. Such varying curvature must be produced by atmospheric dynamics if the underlying gravity has spherical symmetry. For more distant occultations, with the propagation distance measured in light years rather than astronomical units—the so-called microlensing events used to search for unseen objects in our galaxy—the main source of bending is gravity rather than refraction in neutral gas, and the caustics are formed by asymmetries in the gravity field (*3*).

The only previous observation of a central flash by a satellite was in 1989, when the center line of a stellar occultation by Saturn's satellite Titan passed over western Europe and yielded seven closely spaced observations of Titan's central flash, along with six more-distant observations of the shadow (*4*). The central caustics were unexpectedly large and gave evidence for rapid and complex zonal flows in Titan's high atmosphere, along with an equally complex distribution of high haze particles. The figure shows a numerical simulation of Titan's occultation shadow based on these measurements.

Although several stellar occultations by Triton have been observed to date, the 1995 event observed from Hawaii by Elliot *et al.* is the only one where observers were fortuitously located close enough to the center line to see the central enhancement of the signal; their path did not penetrate within the central caustics but came close enough to reveal their presence. If Triton's atmosphere were in perfect hydrostatic equilibrium rotating with the solid surface, it should be almost perfectly spherical, and the shadow should have circular symmetry. Evidently it does not. Effects from the hazes that Voyager 2 found in Triton's atmosphere have not yet been revealed in any of the stellar occultation data, but the results of Elliot *et al.* suggest that the analog of the illustration for Triton will be equally complex when enough data have been obtained to construct it. The underlying model for Triton's atmosphere is likely to be a dynamical one.

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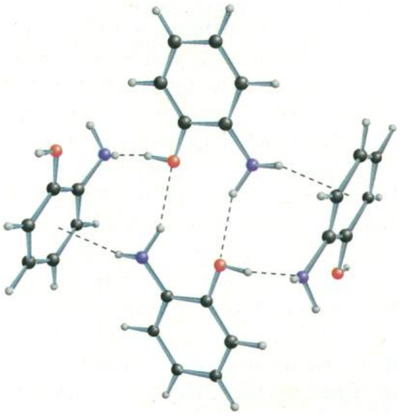
SOLID-STATE CHEMISTRY

Crystal Gazing: Structure Prediction and Polymorphism

Gautam R. Desiraju

Crystal engineering, the design of organic solids with specified architectures and therefore particular physical or chemical properties, continues to elicit intense interest (*1*, *2*). Crystals are built with molecules, and ideally one would like to predict the crystal structure of an organic substance from nothing more than its molecular structure. Indeed, given the molecular basis of organic chemistry, such a goal seems almost intuitive. A particular molecular structure can also yield more than one crystal structure, and this phenomenon of polymorphism (*3*) has been in the forefront, most notably in litigation surrounding the widely used ulcer medication Zantac (*4*).

The major obstacle in routinely predicting crystal structures from molecular structures is that in any kind of molecular recognition, and this includes the recognition between identical molecules during crystallization, it is the dissimilar functionalities that come into closest contact and not the similar surfaces (*5*). Steric and electronic complementarity thus characterize the crystallization event. The functional group approach, so central to molecular chemistry, is of limited applicability because the supramolecular behavior of a particular functional group depends acutely on the nature and even the location of the other functionalities in the molecule. This issue is greatly complicated by the fact that hydrocarbon residues, not normally considered functional groups in molecular chemistry, are quite respectable supramolecular functionalities. All this means that the crystal structures of many "simple" organic compounds need not be simple at all. What is surprising, however, and this is what provides the vital impetus to the subject, is that although the energy differences between the plethora of putative crystal structures for a given molecule can be quite small, many organic compounds are not polymorphic. Molecules seem to know exactly how to crystallize, even as chemists seem unable to accurately foresee such events.



Odd bonds. An unusual N–H···π hydrogen bond is found in the crystal structure of 2-aminophenol. Although conventional O–H···N and N–H···O hydrogen bonds are also seen, saturation of the hydrogen bonding capabilities of the $-NH_2$ and $-OH$ groups with conventional hydrogen bonds, as predicted (*6*, *7*), is not observed.

Sometimes, it is possible to predict the outcome of crystallization. In seminal papers, Ermer (*6*) and Hanessian (*7*) and their col-

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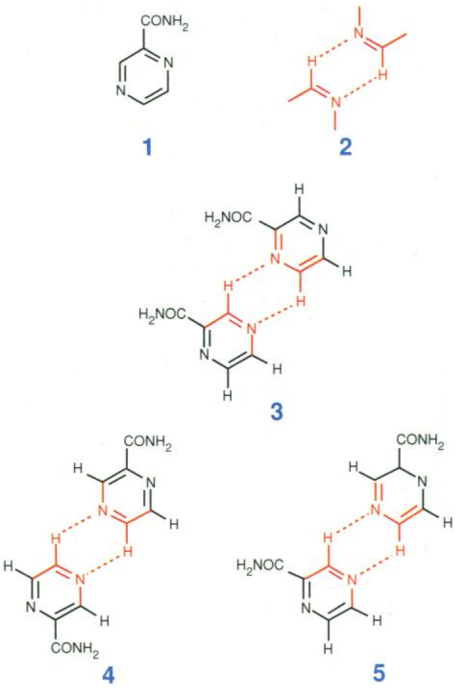
The author is in the School of Chemistry, University of Hyderabad, Hyderabad 500 046, India. E-mail: grdch@uohyd.ernet.in

leagues showed that predictable structures can be obtained in systems containing equal stoichiometries of $-NH_2$ and $-OH$ groups. This predictability arises from the 2:1 and 1:2 hydrogen bond donor:acceptor ratios in these functional groups, leading (i) to tetrahedral configurations at both heteroatoms in the hydrogen bond network and consequently (ii) to variants of the arsenic and wurtzite structures. In particular, 4-aminophenol is identifiable as an archetype of this family. Yet, how predictable are these crystal structures? We determined the structures of the isomeric 2- and 3-aminophenols with single-crystal low-temperature neutron diffraction, and rather than the expected tetrahedral network, an unusual N-H···π hydrogen bond was observed (*8*) (see figure). The reason for this unexpected structure is that the packing in all three aminophenols is dominated by the herringbone packing of aromatic rings rather than by hydrogen bonding. In 4-aminophenol, the aromatic packing is able to coexist with the hydrogen-bonded wurtzite network; in other words, the interference between these two sets of interactions is minimal. In 2- and 3-aminophenols, however, the same packing of aromatic rings is incompatible with the tetrahedral network that is replaced by the unconventional hydrogen-bond arrangement.

If functional groups do not adequately reflect molecule-to-crystal transforms, how then does one attempt to understand crystallization events in chemical terms? The descriptor "supramolecular synthon" signifies larger multimolecular units, within the most robust and useful of which is encoded the optimal information inherent in the mutual recognition of molecules to yield solid-state supermolecules, that is, crystals (*9*). Pyrazine carboxamide (see **1** in scheme 1) is a bizarre compound that exists in no less than five distinct polymorphic forms, and the supramolecular synthon **2** found in all of them is indicative of the importance of C–H···N hydrogen bonding. The multiple yet distinctive occurrences of the heterocyclic N atom and the aromatic =CH group in the molecular skeleton of **1** means that synthon **2** can be generated in several ways, as shown in **3** through **5**, leading more or less directly to polymorphism.

Just as a given molecule may adopt different crystal structures, a given network structure may be accessed by distinct molecules. In this sense, there is some flexibility in crystal engineering strategies that are aimed at networks, if a particular network structure can lead to a property of interest. However, there are some areas wherein a molecule-based approach is still mandated. A good example is the crystallization of pharmaceuticals.

The complex legal issues raised by the Zantac litigation demonstrate how state-of-the-art scientific knowledge can impinge on purely legal issues with tremendous commercial ramifications (*4*). In general, for any given drug molecule, one needs to know if it is likely to be polymorphic or pseudopolymorphic, that is, if it crystallizes with variations in the nature or amount of solvent. Such efforts at crystal structure prediction are usually computational in nature with a greater or lesser reliance on crystallographic and close-packing arguments (*10–13*). These methods have been moderately successful, but there is still much that can be learned. A Monte Carlo simulated-annealing process is the basis for a well-known software package (*14*). Molecular dynamics–based approaches offer new perspectives, and recent studies by Gavezzotti (*15*) show how solvent and kinetic effects can be simulated. Experimental methods are less common, but the recent work of Davey *et al.* (*16*) on the stabilization of a metastable form of L-glutamic acid by conformational mimicry is of considerable relevance because it highlights the importance of kinetic and thermodynamic factors in crystallization.



Scheme 1. The C–H···N hydrogen-bonded supramolecular synthon **2** is optimized in the polymorphs of pyrazine carboxamide (**1**) in alternative arrangements **3** through **5**.

An appreciation of polymorphism is fundamental to an understanding of the crystallization process itself. It is possible that a molecule with more recognition sites can more easily cascade into a stable crystal structure, with alternative crystallization possibilities being more efficiently excluded (*17*). In this respect, a certain resemblance between the crystallization of a small organic molecule and the folding of a protein may be noted. Both processes could proceed through intermediate (and perhaps kinetically stabilized) states, which could be semicompact random globules for proteins (*18*) and structure-determining clusters that contain robust supramolecular synthons for small molecules. These intermediate states could result in a considerable increase in crystallization or folding efficiency, even as the correction of mistakes is facile.

Crystallization and polymorphism are complex phenomena, and a distinct branch of crystal engineering has developed that attempts to sidestep the difficult issues involved in their understanding. In the study of coordination polymers, use is made of relatively strong bonds between ligands and metal ions with unambiguous coordination geometries to generate open networks, some of which are stable to the loss of included solvent (*19*). But microporosity is not the only beneficial property in the world of solids and the design of crystal structures of small organic molecules remains an attractive research area with considerable intellectual challenge and potentialities for further applications as materials (*20*).

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