CRYSTAL ENGINEERING

Putting Molecules Behind Bars

Steven C. Zimmerman

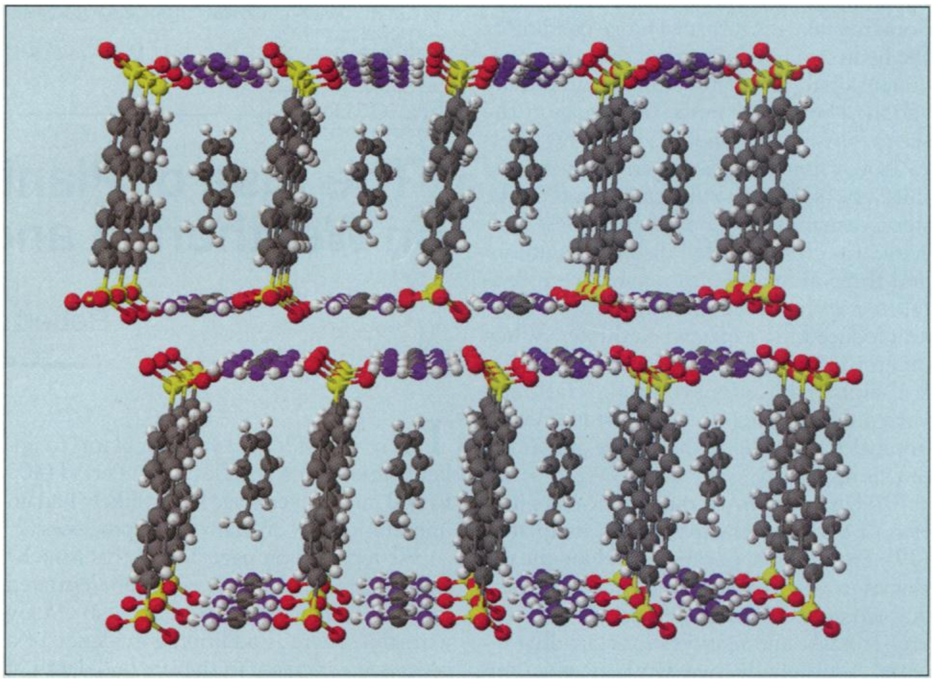
One of the most fundamental unsolved problems in chemistry is predicting, based solely on its molecular structure, how a molecule will pack in the solid state (*1*). The development of a theory of the solid state, called "crystal engineering" by Schmidt (*2*), is considered a prerequisite for the design and control of crystal packing arrangements. Because such a theory is not currently available, chemists have had to be content with looking for recurring packing patterns adopted by certain functional groups or their arrays and relying on the robustness of such motifs to create new solid-state structures. This empirical approach, which often involves "encoding and decoding" preferred local packing arrangements, has been remarkably productive with important advancements reported by the Weizmann school (*3*), Etter (*4*), and others (*5*). On page 575 of this issue, a particularly elaborate and advanced example of crystal engineering is reported by Russell *et al.* (*6*).

The type of crystalline solids synthesized by this group (*6*) are among the most difficult to create because they do not adequately fill space, leaving substantial voids that must be filled by solvent molecules or other guest molecules (*7*). These solid-state host-guest complexes are called clathrates, a term introduced in 1948 by Powell (*8*), derived from the Latin word *clathratus*, meaning "enclosed by the bars of a grating." Literally, clathrates imprison small molecules behind the bars of a crystalline jail. The first clathrate was reported by Davy in 1811 (*9*), but Powell's pioneering x-ray studies in the mid-1940s provided the impetus for modern studies on clathrates and other inclusion phenomena.

Most of the clathrates reported in the intervening years were discovered by serendipity. However, two decades ago MacNicol and co-workers reported the first rationally designed clathrate host (*10*). Their strategy was to replace a cyclic array of six intermolecularly hydrogen-bonded alcohols with an isostructural benzene ring. Thus, six separate molecules that form a cavity in the crystal lattice are replaced by a single hexa-substituted benzene with a similar shape and cavity. Other rational approaches involve the synthesis of awkwardly shaped molecules (dumbbell-shaped, for instance) that are less likely to pack closely (*11*, *12*).

These examples of rationally designed clathrates represent significant advances, but they are not crystal engineering as initially envisioned by Schmidt (*2*) because the precise crystal packing is not controlled. The first true de novo design of an organic clathrate was reported in 1991 (*13*). This work involved the formation of an infinite three-dimensional, diamond-like lattice built from a single Tinker Toy–type subunit containing four tetrahedrally arrayed pyridone groups. Pyridones are known to form hydrogen-bonded dimers with a well-defined geometry, so they act as "connectors" to assemble the subunits together. There are two main reasons why this general approach often fails. First, even when a specific hydrogen-bonding motif is desired and expected, the connectors may instead interact in a nonstandard way if doing so allows a close-packed structure (*14*). In a sense, the porous lattice collapses because the desire for close-packing outweighs the preference for optimum hydrogen-bonding contacts. The second cause of failure is more insidious. It involves the formation of more than one of the desired networks, which then interpenetrate—often in an aesthetically pleasing way—thereby filling the free volume (*15*). For example, trimesic acid (1,3,5-benzene tricarboxylic acid) forms a two-dimensional, chicken wire–like lattice with 14 Å holes, which are created by six trimesic acid molecules in a hydrogen-bonded ring (*16*). An infinite number of such lattices stack, which would lead to a very porous material with large channels. However, a second set of stacked lattices, making a 70° angle to the first, occupy the channels as three stacked trimesic acid "rings" concatenate and fill a second set of three stacked rings.

One way to prevent interpenetration is to build macrocyclic compounds whose covalently closed rings cannot concatenate. This strategy is beautifully illustrated in the work of Moore (*17*). Russell *et al.* take a clever alternative approach that greatly simplifies many aspects of the crystal engineering problem (*6*). Their premise is that dense two-dimensional sheets cannot interpenetrate and must lie in parallel layers (see figure). In previous work it was shown that alkyl sulfonates and guanidinium cations crystallize in stacked two-dimensional sheets, as either bilayers or continuous stacks of interdigitated single layers (*18*). By replacing the sulfonate anions with disulfonate anions, these molecular "floors" become directly linked by "studs." Varying the length and thickness of the stud allows the size of the voids to be controlled, which in turn dictates



Molecular sandwich. An engineered crystal composed of hydrogen-bonded networks of guanidinium ions and sulfonate groups.

The author is in the Department of Chemistry, University of Illinois, Urbana, IL 61801, USA. E-mail: sczimmer@uiuc.edu

the size and number of solvent molecules included in the crystal lattice. Thus, by starting with two-dimensional sheets, the crystal engineering problem is reduced to controlling a single dimension.

As noted above, the caveat in all crystal engineering efforts is that seemingly reliable motifs may fail to form when packing densities are low. Several features of the alkyl sulfonate–guanidinium sheet structure make it particularly robust and less prone to this problem (*6*, *18*). Most importantly, many hydrogen bonds are formed, which are strong and ionic yet pliable enough to allow for small adjustments to accommodate the particular alkyl substituent. These adjustments primarily take the form of a hinge bending by the hydrogen bonds between the quasi–one-dimensional sulfonate anion–guanidinium cation ribbons (the "joists") that make up the sheet. This hinge bending allows the sheets to show varying degrees of corrugation, and thus, the sulfonate stud can adapt to the steric demands of the particular guest molecule. In all, three alkyl disulfonate anions and three aromatic disulfonates were crystallized with the guanidinium cation, and all produced the expected clathrates. When different-sized guests were present with a 4,4′-biphenyldisulfonate stud, clathrates with different floor-to-floor distances were obtained, again pointing to the generality of this approach.

Weber has pointed out that the application of clathrate chemistry is in its infancy (*19*). Promising applications include the purification and resolution of drugs, trapping and storage of toxic materials, off-peak energy storage, and matrices for slow drug release. Additionally, new synthetic reactions with altered chemical selectivities may take place within the confines of the crystal lattice. One of the oldest practical uses of clathration is in petroleum refining, where products ranging from gasoline to light lubricating oil exhibit enhanced performance when linear paraffins are removed in processing. Extractive crystallization with urea is particularly attractive because straight-chain alkanes from C_7 to C_{70} are selectively bound in urea clathrate channels. In fact, there have been processing plants successfully operating on a scale of 320 barrels per day with this technology.

Clathrate lattices generally decompose upon loss of the imprisoned guest. Although clathrates formed from metal ion coordination networks might better allow reversible release and adsorption of guests (*20*), it seems unlikely that these nanoporous solids will ever compete with zeolites. Nonetheless, the ability of clathrate hosts to shape or enantioselectively surround a guest and then release it upon mild dissolution conditions suggests a bright future in the resolution and purification of specialty chemicals such as pharmaceuticals. Whatever may be the future applications of this class of inclusion complexes, it is clear that the study of clathrates has already contributed substantially to our understanding of the crystal engineering problem and will inspire continuing attempts to create nanoporous solids.

References and Notes

1. A. Gavezzotti, *Acc. Chem. Res.* **27**, 309 (1994).
2. G. M. J. Schmidt, *Pure Appl. Chem.* **27**, 647 (1971).
3. I. Weissbuch, R. Popovitz-Biro, M. Lahav, L. Leiserowitz, *Acta Crystallogr. B* **51**, 115 (1995).
4. M. C. Etter, *Acc. Chem. Res.* **23**, 120 (1990).
5. G. R. Desiraju, *Crystal Engineering* (Elsevier, New York, 1989).
6. V. A. Russell, C. C. Evans, W. Li, M. D. Ward, *Science* **276**, 575 (1997).
7. J. S. Moore and S. Lee, *Chem. Ind.*, p. 556 (1994).
8. H. M. Powell, in *Inclusion Compounds*, J. L. Atwood, J. E. D. Davies, D. D. MacNicol, Eds. (Academic, London, 1984), vol. 1, p. 1.
9. H. Davy, *Philos. Trans. R. Soc. London* **101**, 30 (1811).
10. D. D. MacNicol, J. J. McKendrick, D. R. Wilson, *Chem. Soc. Rev.* **7**, 65 (1978).
11. H. Hart, L.-T. W. Lin, D. L. Ward, *J. Am. Chem. Soc.* **106**, 4043 (1984).
12. F. Toda and K. Akagi, *Tetrahedron Lett.* **1968**, 3695 (1968).
13. M. Simard, S. Dan, J. D. Wuest, *J. Am. Chem. Soc.* **113**, 4696 (1991).
14. S. V. Kolotuchin, E. E. Fenlon, S. R. Wilson, C. J. Loweth, S. C. Zimmerman, *Angew. Chem. Int. Ed. Engl.* **34**, 2654 (1995).
15. O. Ermer, *J. Am. Chem. Soc.* **110**, 3747 (1988).
16. D. J. Duchamp and R. E. Marsh, *Acta Crystallogr. B* **25**, 5 (1969).
17. D. Venkataraman, S. Lee, J. Zhang, J. S. Moore *Nature* **371**, 591 (1994).
18. V. A. Russell, M. C. Etter, M. D. Ward, *J. Am. Chem. Soc.* **116**, 1941 (1994).
19. E. Weber, *Top. Curr. Chem.* **140**, 3 (1987).
20. The work of J. S. Moore, R. Robson, O. Yaghi, and M. Zaworotko is particularly relevant. For an overview, see M. Zaworotko, *Chem. Soc. Rev.* **23**, 283 (1994).

PALEOCLIMATE

The Rise of Plants and Their Effect on Weathering and Atmospheric CO_2

Robert A. Berner

The spread of rooted vascular plants to upland areas during the Devonian Period (400 to 360 million years ago) most likely had an important effect on many Earth processes (*1*, *2*). As reported on page 583 of this issue by Retallack (*1*), the first well-differentiated forest soils appeared in the Devonian. Along with this, there is additional evidence of a progressive increase in the size and depth of roots from the Silurian to the late Devonian (*1*, *3*), with relatively deep rooting appearing as early as the late Early Devonian (390 million years ago) (*4*). Chemical differentiation, combined with deep rooting, suggests that the dissolution of bed rocks by weathering at this time was accelerated by the growth of plants. This enhanced chemical weathering would have resulted in enhanced removal of CO_2 from the atmosphere, because the net effect of silicate mineral weathering is to convert soil carbon, derived ultimately from photosynthesis, into dissolved HCO_3^-. A representative reaction is

$$2CO_2 + 3H_2O + CaAl_2Si_2O_8 \rightarrow Ca^{2+} + 2HCO_3^- + Al_2Si_2O_5(OH)_4 \quad (1)$$

After formation by weathering, the dissolved HCO_3^- is carried to the ocean by rivers and, if accompanied by dissolved Ca^{2+} or Mg^{2+}, the carbon is removed from the oceans as Ca-Mg carbonate minerals. In this way, if Ca and Mg silicates are involved in weathering, the overall process results in the removal of CO_2 from the atmosphere.

The activities of vascular plants should result in enhanced weathering and, thus, enhanced removal of atmospheric CO_2. There are several reasons for this enhancement: (i) Rootlets (plus symbiotic microflora) with high surface area secrete organic acids and chelates, which attack minerals in order to gain nutrients; (ii) organic litter decomposes to H_2CO_3 and organic acids, providing additional acid for weathering; (iii) on a regional scale, plants recirculate water by means of transpiration followed by rainfall and thereby increase water-mineral contact time; and (iv) plants anchor clay-rich soil, retarding erosion and allowing the retention of water and

---

The author is in the Department of Geology and Geophysics, Yale University, New Haven, CT 06520–8109, USA.