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# Building molecular frameworks with tailored pore structures

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ABSTRACT: Interest in materials made from molecular components, driven by the promise of new systems with precisely tailored properties, is accelerating at a rapid pace. The last decade has witnessed tremendous advances in the sophistication of molecular materials based on supramolecular building blocks that can be interchanged at will to generate materials with properties and function that can be finely tuned in a systematic manner. This is exemplified here by examples that illustrate the role of hydrogen bonding in generating low-density 'porous' frameworks capable of forming lamellar host–guest inclusion compounds with tunable inclusion cavities and solid-state architectures, topologically related tube-like structures and two-dimensional porous molecular monolayers with structures mimicking layered motifs in molecular crystals. These systems demonstrate that low-density molecular frameworks can be systematically engineered to generate rather predictable and robust structures, particularly if they possess an intrinsic softness that enables the frameworks to self-optimize the non-covalent interactions governing their supramolecular architectures. Copyright © 2000 John Wiley & Sons, Ltd.

KEYWORDS: hydrogen bonding; inclusion compounds; clathrates; crystal engineering; Langmuir films

## INTRODUCTION

At the time of this writing, the end of the 20th century has passed and we are tempted to comtemplate the revolutionary leaps in science and technology that will occur in the next 100 years and the impact they will have on society. Looking back, it is safe to say that most advances, including the explosion in new materials, were unanticipated by 19th century prognositicators. It seems presumptous, therefore, to forecast new materials for the 21st century, particularly at such an early stage. Nevertheless, one can be quite confident that materials in the 21st century will rely increasingly on molecular components assembled in organized structures having desirable function and properties.

Molecular materials are attractive for one obvious reason—the versatility of organic synthesis can be exploited to make designer molecules that will be integrated into novel materials endowed with finely tuned properties. This approach requires 'bottom-up' design strategies rather than the 'top-down' approaches that have characterized most 20th century technologies. Materials made in this manner promise more precise control of function, and also more facile and economical processing and fabrication. These bottom-up strategies require molecules, equipped with selected properties, that are 'programmed' to assemble through non-covalent intermolecular interactions such as hydrogen bonding, metal–ligand binding and shape-conforming dispersive interactions. This, in turn, requires manipulation of these delicate intermolecular forces and elucidation of their role in molecular assembly.

The interest in bottom-up approaches to molecular materials has motivated a substantial amount of effort in 'supramolecular engineering,' which involves the synthesis of extended 'higher order' structures based on non-covalent ensembles of molecules. Our group has been particularly interested in a subset of this discipline commonly referred to as 'crystal engineering,' which is probably best described as the skillful contrivance of *crystal* architectures using principles of molecular assembly. The practitioners of crystal engineering aim to design molecules with specific symmetries and functional groups that undergo assembly into predictable motifs and, ultimately, into solids with properties that ensue from the solid-state structure. Unfortunately, these efforts are routinely frustrated by an inability to maintain control over the delicate intermolecular interactions that direct molecular assembly into the solid state. Even the most minor alterations to the structure of the molecular

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components, introduced to make slight adjustments to the solid-state properties, often produce unanticipated crystal architectures that differ significantly from the intended structure, preventing systematic engineering of solid state structure and properties.

Much of the activity in supramolecular and crystal engineering is driven by a fundamental quest for understanding the rudimentary principles of molecular assembly, which affects chemistry and biology as well as materials science. There also exists, however, a strong interest in the properties, e.g. electrical, magnetic and optical, of such tailored materials and their applications. The explosive growth of liquid crystals and their applications is illustrative in this respect.

During the past decade, interest in host–guest systems based on porous molecular architectures and their associated guests has emerged, driven in part by the developments in the synthesis and applications of inorganic zeolites, layered clays and mesoporous inorganic oxides.[1,2] The interest in molecular analogs of these materials has largely been driven by a recognition that, in principle, pore structure, shape and character of porous host frameworks can be adjusted at the molecular level through synthetic organic chemistry. Furthermore, structurally reliable porous architectures allow the separation of crystal architecture, provided by the host framework, from function, introduced by the included guests. This feature promises considerable versatility in materials design based on host–guest inclusion materials. Porous architectures based on surfactant or polymeric vesicular structures,[1,2] polymeric worm-like micelles,[3] metal–ligand coordination networks[4–7] and hydrogen-bonded host frameworks[8–11] are illustrative of this growing interest. Applications include drug delivery,[12–14] in which bioactive molecules are trapped inside the pores of materials designed to release their contents at targeted sites, highly specific separations of small molecules based on materials having pore sizes and structure with molecular-scale uniformity,[15] and heavy metal encarceration for toxic remediation.[16] Tailor-made porous architectures may also serve as chemical storage media, and as nanoscale reaction compartments that guide or constrain reaction pathways for molecules contained inside the pores, generating novel materials not attainable through conventional methods. It is reasonable to suggest that applications such as these will be of substantial interest in much of the 21st century.

In addition to the practical aspects of molecular porous architectures, there are numerous issues of considerable fundamental appeal—pore stability and its dependence on length scale, the relationship between bond strength and pore stability, the mechanism of pore formation, and synthetic routes that allow the controlled formation of predictable porous architectures. Our laboratory has been examining only a small portion of this growing field, focusing on low-density crystalline host frameworks, assembled by hydrogen bonding, that are capable of encapsulating guest molecules. The topology and dimensions of these frameworks are governed by the symmetry and size, respectively, of their molecular components. Several key principles have emerged from these studies: (i) robust two-dimensional supramolecular building blocks simplify crystal engineering by constraining the design to the last remaining third dimension, (ii) soft, flexible frameworks can be more structurally robust than rigid ones because they can compensate for imprecise packing of host and guest molecules, (iii) guest molecules can guide the formation of the host frameworks and control the architectural isomerism, (iv) compositionally identical two-dimensional supramolecular building blocks can exist as sheets or tubes and (v) two-dimensional porous networks can emulate porous layered motifs existing in three-dimensional crystal structures. We anticipate that these principles can provide guidance for the design and synthesis of a diverse range of crystalline molecular materials.

## HOST–GUEST INCLUSION COMPOUNDS

### Lamellar materials from hydrogen-bonded building blocks

The void shapes and sizes supplied by inorganic porous materials typically are dictated by rather rigid frameworks (e.g. metal oxides) that are not readily amenable to the precise chemical modification that is required for many applications. Consequently, the past several years have witnessed considerable efforts directed toward the design and synthesis of organic or metal–organic analogs of inorganic host frameworks. These efforts have relied largely on modular strategies based on molecular building blocks that assemble into supramolecular motifs by directional non-covalent bonding such as hydrogen bonding or metal coordination. In principle, libraries of molecular building blocks can be rationally designed and synthesized, using the principles of organic synthesis, to create host frameworks with void shapes, sizes and chemical attributes that can be systematically and precisely adjusted for molecular recognition between a host and functional guests. Molecular hosts may have a clear advantage over their inorganic relatives in that they can be reversibly disassembled, under mild conditions by simple dissolution of the non-covalent host framework, so that the guests can be easily liberated, providing a route to separations of fine chemicals (Fig. 1). The reversible nature of their assembly also favors the formation of structures near or at the thermodynamic minimum.

Two-dimensional films of porous molecular networks, which can also be generated by hydrogen bonding or metal–ligand coordination, can be employed as membranes with pore shape and dimensions governed by the symmetry and size of the molecular components. Such

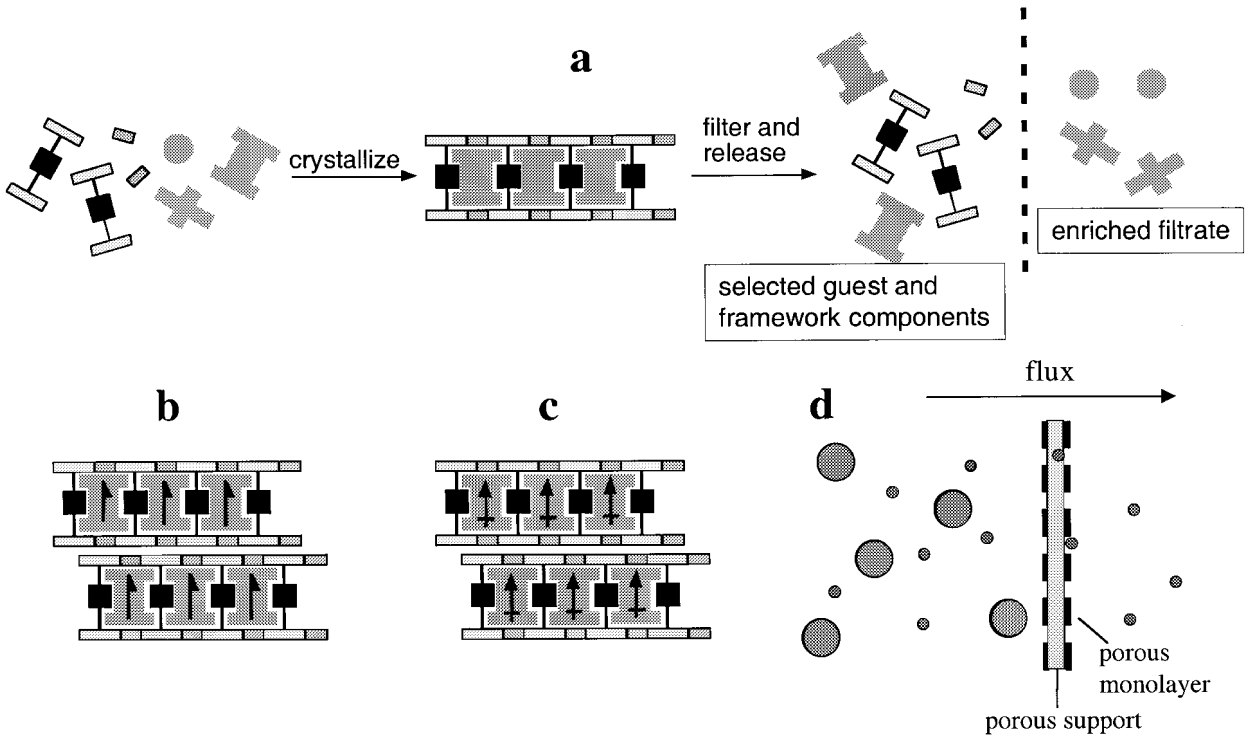



**Figure 1.** (a) Schematic representation of a crystallization-based separations protocol based on reversible assembly and disassembly of a host–guest inclusion compound. (b) Schematic representation of a hypothetical host framework with dipolar guest molecules aligned to generate a polar crystal. (c) Schematic representation of a hypothetical host framework with magnetic guests. Host frameworks may be held together by non-covalent interactions such as hydrogen bonding, with the guests included by the hosts during formation of the inclusion compound. (d) Schematic representation of a two-dimensional porous film on a permeable substrate that is capable of highly selective separations

membranes would, in principle, have a crucial advantage over conventional ones—the uniformity of the pores and the ability to control pore size at the molecular level—that could substantially improve selectivity. It is also possible that such materials, because of their non-covalent and self-assembling character, will have fewer defects than their inorganic covalent counterparts. Furthermore, the solubility of the molecular components can make these materials more amenable to processing.

Historically, organic solid-state host frameworks have been discovered by chance, e.g. the well-known (thio )urea, tri-*o*-thymotide, phenolic, perhydrotriphenylene, choleic acid or cyclotriveratrylene hosts.[17,18] These hosts, however, are considerably limited because their molecular components cannot be modified without destroying the basic crystal architecture required for guest inclusion, thereby preventing significant modification of the inclusion cavities. The challenge, therefore, is to design molecular hosts that are structurally robust toward modification of a generic framework. Numerous attempts have been made to introduce structural robustness by modules that generate *rigid* frameworks. However, inclusion of a specific guest molecule in a rigid framework would require that the shape of the inclusion cavity framework be precisely engineered to match that of the guest. In the absence of such a precise fit, inclusion can involve multiple guest molecules, each much smaller than the inclusion cavity, that as an ensemble conform to the shape of the rigid cavity. This argues that crystal engineering of inclusion compounds is likely to be more successful when design strategies are based on soft frameworks that can adapt to the steric landscape of guest molecules while retaining their general architectural features, particularly their inherent dimensionality and supramolecular connectivity.

Recent crystal engineering studies in our laboratory have demonstrated an unusually persistent supramolecular building block based on topologically complementary guanidinium (**G**, $[C(NH_2)_3]^+$) cations and the sulfonate (**S**) moieties of organomonosulfonate or organodisulfonate anions that assemble via (**G**)N—H···O(**S**) H-bonds (Fig. 2).[19,20] The threefold symmetry of the **G** ions and **S** moieties, and the equivalent numbers of guanidinium hydrogen-bond donors and sulfonate oxygen atom, guide assembly into a quasi-hexagonal hydrogen-bonded sheet or occasionally a closely related 'shifted ribbon' motif). The hydrogen bonding in this supramolecular network is further fortified by its ionicity. These features make the **GS** sheet remarkably robust, as evidenced by its existence in nearly 200 different crystalline phases prepared in our laboratory.

The **GS** network actually can be dissected into one-

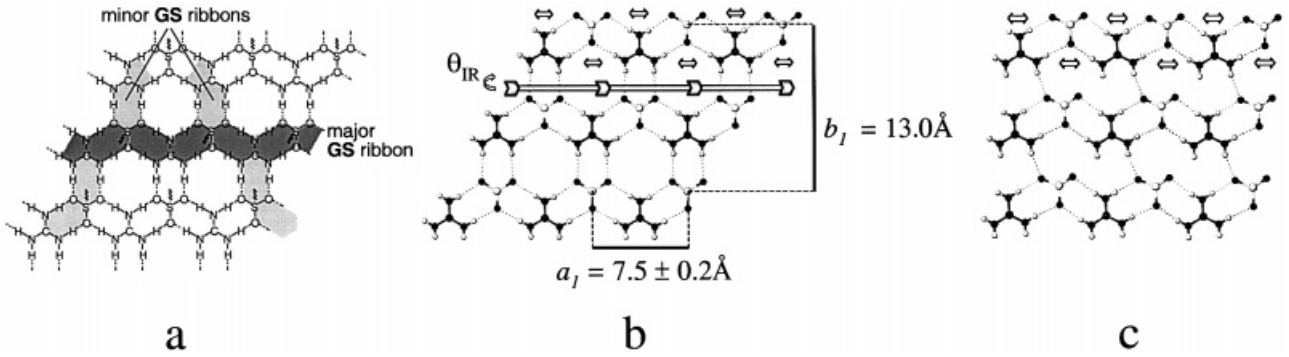
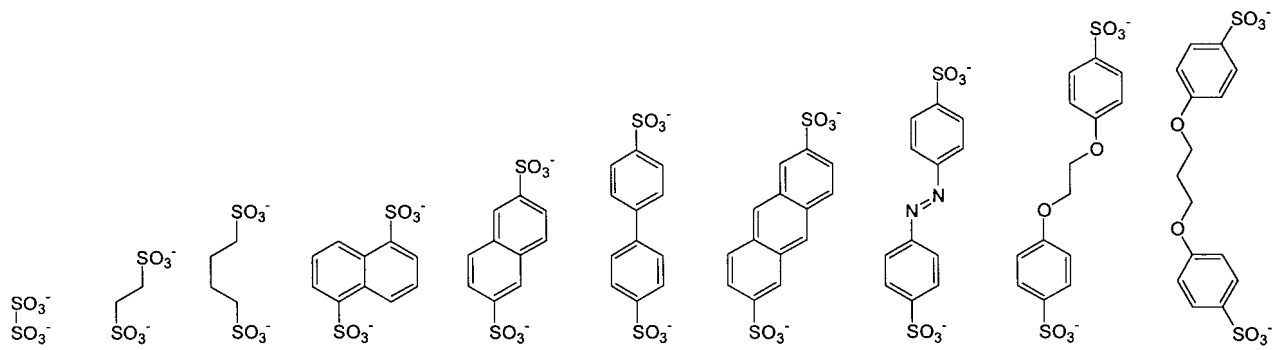



**Figure 2.** (a) Schematic representation of the quasi-hexagonal two-dimensional hydrogen-bonded guanidinium–sulfonate network, which can be regarded as a sheet formed by fusion of **GS** ribbons. One of these ribbons can be assigned as a 'major' ribbon; and the other two as 'minor' ribbons. Accordion-like puckering of the **GS** sheet occurs by bending about flexible hydrogen bonds that connect the major **GS** ribbons. (b) Wireframe model of a perfectly flat quasi-hexagonal **GS** sheet ($\theta_{IR}$), illustrating the critical metrics. (c) Wireframe model of the 'shifted ribbon' GS sheet, which is produced by a shift of $a_1/2$ and has one less hydrogen bond than the quasi-hexagonal motif

dimensional **GS** 'ribbons' connected to each other via lateral (**G**)N—H···O(**S**) H-bonds that serve as flexible hinges. These hinges allow the **GS** sheet to pucker, like an accordion, without an appreciable change in the near-linear geometries, which are considered to be optimal, of the (**G**)N—H···O(**S**) H-bonds. The range of repeat distances within the **GS** ribbons (denoted as $a_1$) is fairly narrow, reflecting stiffness along the ribbon direction. In contrast, repeat distances normal to the ribbon direction, within the plane of the **GS** sheet (denoted $b_1$), vary considerably due to changes in the inter-ribbon puckering angle ($\theta_{IR}$), observed values ranging from as small as $b_1 = 7.3$ Å for highly puckered sheets ($\theta_{IR} = 75°$) to $b_1 = 13.0$ Å for perfectly flat sheets ($\theta_{IR} = 180°$).

The persistence of the **GS** network and its two-dimensional character effectively reduce crystal engineering to the last remaining (third) dimension. This has enabled us to synthesize reliably a family of lamellar host frameworks based on organodisulfonates, in which the organodisulfonate anions serve as 'pillars' that connect opposing **GS** sheets in a manner reminiscent of pillared metal organophosphonates,[21] thereby generating porous galleries between the opposing **GS** sheets. Importantly, the close packing of atoms within the **GS** sheet precludes self-interpenetration of equivalent networks, a problem that plagues the design of many open framework structures.[22] The sizes, heights, shapes and chemical environment of the resulting voids, formed in the gallery regions between opposing sheets can be manipulated by the choice of molecular pillar. The organodisulfonates **I–X** (Scheme 1), with lengths ranging from $l = 2.1$ to 15.6 Å (where $l$ is the S···S separation), are representative of the pillars that have been used to generate **GS** host frameworks in our laboratory.[23,24] The ease with which disulfonates can be synthesized has enabled us to create a substantial library of pillars, affording a diverse set of inclusion compounds in which pore characteristics can be systematically adjusted and crystal engineering principles tested and developed. In most cases, the inclusion compounds are prepared by treatment of the acid form of the pillars with [**G**][$BF_4$] in acetone, which results in the immediate precipitation of **GS** salts, generally as acetone




**Scheme 1**

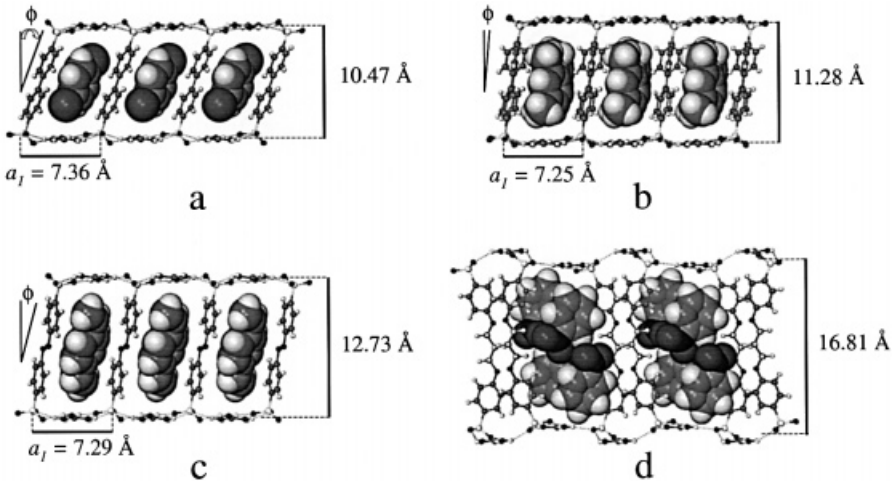



**Figure 3.** Some examples of **GS** bilayer inclusion compounds: (a) Shifted ribbon **$G_2$VI**·1,4-dichlorobenzene; (b) shifted ribbon **$G_2$VI**·*o*-xylene; (c) shifted ribbon **$G_2$VIII**·1,4-divinylbenzene; (d) quasi-hexagonal **$G_2$X**·2(nitrobenzene)

clathrates. These materials readily lose solvent upon standing in air to yield pure apohosts (host material without guests), which can then be used, in dissolved form, for the crystallization of desired inclusion compounds. Single crystals of the inclusion compounds with other suitable guests can then be obtained by standard crystallization techniques.

Illustrative examples of **GS** inclusion compounds with a discrete bilayer architecture are depicted in Fig. 3. The gallery heights, as defined by the shortest distance between the mean planes of the nitrogen and oxygen atoms of the **GS** sheets, and the corresponding available volume for guests increase systematically with increasing pillar length. The bilayer host frameworks, however, are not entirely rigid. A systematic investigation of over 30 bilayer inclusion compounds with the composition **$G_2$VI**·*n*guest revealed that the bilayer host framework can conform to the size and shape of a diverse collection of guests, essentially 'shrink-wrapping' about the guests to achieve optimized host–guest packing. The inclusion cavity volume in this system varies by as much as 34% for guest molecules!

In cases where guests are too small to fill adequately the inclusion cavities of the bilayer framework, the host can adapt by slight puckering of the quasi-hexagonal **GS** sheet and tilting of the pillars, which combine to reduce the gallery heights. In either the quasi-hexagonal or shifted ribbon arrangements, the pillars can rotate freely about their C—S bonds like turnstiles such that one-dimensional channels, flanked by the pillars, are created within the galleries between the **GS** sheets of the bilayer host framework. The pillars in compounds having the quasihexagonal motif typically are rotated with their arene planes nominally *parallel* to the **GS** ribbons. Consequently, the guest-filled channels run parallel to the ribbon direction. The widths of these channels are defined by $b_1/2$ (ca 6.5 Å for these nearly flat **GS** sheets). In contrast, the pillars in compounds that adopt the shifted ribbon motif are rotated with the arene planes, and the guest-occupied channels, nearly *orthogonal* to the **GS** ribbons. The widths of the channels in these compounds are roughly defined by $a_1$ (ca 7.3 Å, but more accurately, $a_1\cos\phi$, where $\phi$ is the tilt angle of the pillars with respect to the normal to the **GS** sheet). For a given host, larger values of $\phi$ are synonymous with shorter gallery heights and, consequently, smaller pore volumes. These bilayer frameworks can also be constructed with flexible pillars such as **IV, IX** and **X**. Torsional twisting about the central C—C bond of the axially rigid biphenyl pillar in bilayer **$G_2$VI** inclusion compounds enables the pillar to conform to the shape of the guests while behaving as synchronous molecular gears that relay instructions for guest ordering from one pore to another.[25]

Although it is tempting to posit that the gallery height and pore volume would scale with the molecular volume of the guests, numerous examples of these compounds demonstrate that simple sterics, based on molecular volume, are not the sole structure directing influence in these inclusion compounds. Attractive ion–dipole interactions between the guanidinium ions, which are exposed at the floor and ceiling of the channels, and the C—X dipoles of polar guest molecules tend to shrink the gallery height.

Interestingly, the **GS** host exhibits architectural isomerism (or equivalently, topological isomerism) in which the structures of compositionally identical framework isomers differ with respect to the up/down arrangement of the organic residues projecting from each **GS** sheet and the resulting connectivity between the **GS** sheets (Fig. 4). A simple 'brick' isomer, in which the **GS** sheets are continuously connected by organodisulfonate pillars, can be generated by stacking **GS** sheets in which the orientation of the pillars on adjacent **GS** ribbons alternates up/down about each sheet (Fig. 5). This

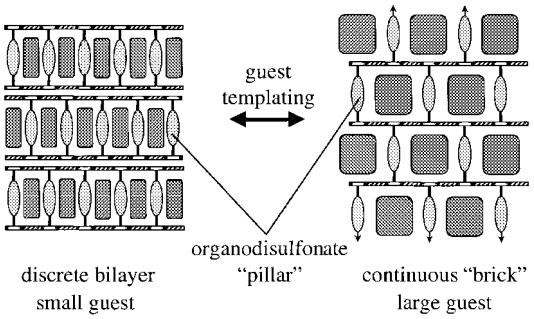



**Figure 4.** Schematic representation of the bilayer–brick isomerism and its dependence upon guest size. The sulfonate groups in the GS sheets are depicted as gray rectangles and the guanidinium ions as cross-hatched rectangles

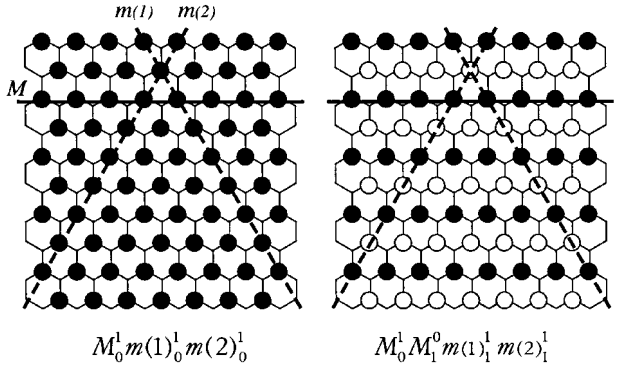



**Figure 5.** Top-view representations of the pillar topology for the bilayer (left) and simple brick (middle) architectures, depicting the up (filled circles) and down (open circles) orientations of the organodisulfonate pillars, projecting from sulfonate nodes in each individual **GS** sheet. The 'up' pillars connect to the adjacent **GS** sheet above the plane of the page and the 'down' pillars connect to the adjacent **GS** sheet below the plane of the page. The guanidinium ions sit on the undecorated nodes of the quasi-hexagonal tiling. The up/down arrangement of the pillars about each **GS** sheet can be described generally by a formalism, $M(n)^{u(M(n))}_{d(M(n))}m(1)^{u(1)}_{d(1)}m(2)^{u(2)}_{d(2)}$, where *M(n)*, *m(1)* and *m(2)* denote the major and two minor ribbons, respectively, and *u* and *d* are indices that describe the up/down sequence of the pillars on the respective ribbons. The major ribbons in the simple brick architecture can be assigned to the 'pleats' if the sheets are puckered. The notations for the bilayer and brick isomers are $M^1_0m(1)^1_0m(2)^1_0$ and $M^1_0M^0_1m(1)^1_1m(2)^1_1$, respectively

produces a framework with roughly twice as much void space as the bilayer form. Consequently, the formation of the simple brick isomer is promoted by guests, or guest aggregates, that are too large to fit into the inclusion cavities of the bilayer frameworks.[26] In this respect, the guests serve as templates that direct the assembly of the molecular framework, reminiscent to the role played by surfactant microstructures or organic 'imprinting' in the templation of open framework zeolites[27,28] and more recently in the formation of oligo(3,5-pyridine) nanotubes.[29] In general, the role played by guest molecules in templating solid-state frameworks is not completely understood, but certainly sterics, combined with host–guest interactions, plays an important role.

We have established the bilayer-to-brick isomerism for **GS** inclusion compounds based on numerous pillars, including those with the 4,4′-biphenyldisulfonate pillar (Fig. 6). It is important to point out that the isomerism can also be achieved by interchanging the pillars for a given guest,[30] demonstrating that the isomerism depends upon the *combined* sterics of the pillars and guests within the galleries. In principle, there exist an infinite number of topological sets for the infinite two-dimensional **GS** sheet, each set describing the up/down arrangement of the pillars projecting from the sulfonate nodes. We have recently observed three additional architectural isomers, promoted by guests of various sizes and shapes (K. T. Holman and M. D. Ward, in preparation), that indicate the intrinsic adaptability of the **GS** host system. That is, the inclusion cavities in the host essentially adopt a size and shape required by the guests, with further fine tuning provided by the puckering of the **GS** sheets and the rotational and conformation freedom of the pillars.

Puckering can occur to a much greater extent in the brick architectures because of steric considerations, providing the brick framework with a substantially greater range of conformational flexibility than the bilayer framework. Consequently, the available volume for included guests (i.e. the volume of the crystal not occupied by the host), in these brick frameworks is extremely variable. In the brick $\mathbf{G_2VI}\cdot n$guest system, this value varies from 346 Å$^3$ per pillar in $\mathbf{G_2VI}\cdot$3-nitrostyrene to 859 Å$^3$ per pillar in $\mathbf{G_2VI}\cdot$3(anthracene), a range of nearly 150%! The volume occupied by the host framework was calculated by subtracting the 'available volume,' after removal of the guest molecules, from the volume of the unit cell. 'Available volumes' were calculated with Molecular Simulations Cerius2 (v. 3.5) software using a probe radius of 0.5 Å and 'fine' grid spacing). Highly puckered sheets can afford brick architectures with void volumes that are only slightly greater than the corresponding bilayer architecture.

Highly puckered brick frameworks by necessity possess highly tilted pillars. The arene planes of aromatic pillars are aligned roughly orthogonal to the **GS** ribbon direction, enforcing gallery regions with one-dimensional channels, perpendicular to the **GS** ribbons, of width $a_1$. The highly puckered framework is observed for guest molecules that are just beyond the upper steric limit for inclusion in the bilayer framework of a given pillar, but much smaller than the void volume existing in an unpuckered brick framework. Consequently, the brick framework puckers severely to collapse about the guest. In compounds where the **GS** sheets are much less puckered, however, the distance between the pillars is increased to the extent that they cannot form continuous walls flanking the one-dimensional channels. This results

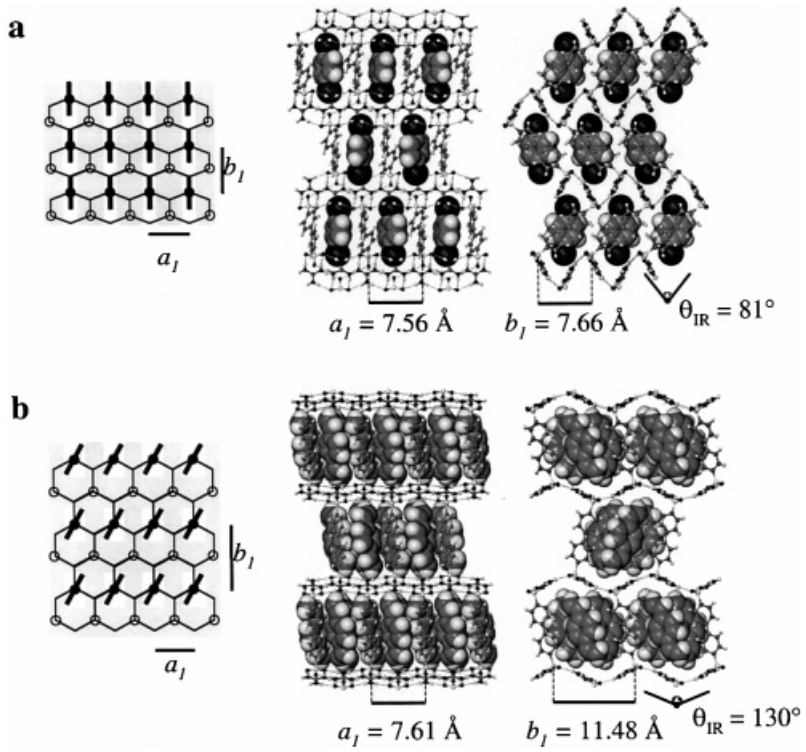



**Figure 6.** Flexibility of the brick host architecture leads to conformers that differ with respect to the pore structure in the galleries. (a) Highly puckered **GS** sheets, with pillars aligned orthogonal to the **GS** ribbon direction, yield gallery regions with one-dimensional channels, flanked by the pillars, of width $a_1$ (depicted here for **$G_2$ VI**·1,4-dibromobenzene). (b) Less puckered sheets in **$G_2$ VI**·3(1,4-divinylbenzene) yield a two-dimensional continuous guest network in which the guests surround the pillars. The illustrations at the left depict the gallery regions within their respective inclusion compounds as viewed normal to a **GS** sheet. The **GS** sheets are represented as hexagons, and the filled and open circles represent pillars that project above and below the **GS** sheet, respectively. The guest-filled channels are shaded. A third conformer (not shown) has been observed in which the pillars align parallel to the ribbon direction, producing gallery regions with one-dimensional channels of width $b_1$, e.g., **$G_2$VI**·4(nitrobenzene)

in galleries with a two-dimensional pore structure and larger void volumes capable of including a significant amount of guest, typically with a 1:3 host:guest stoichiometry. The arene planes of the pillars can also align *parallel* to the **GS** ribbon direction, creating channels with a width $b_1$, which can vary (up to 13.0 Å) with the degree of puckering as defined by $\theta_{IR}$.

The structural adaptability exhibited by the **GS** host frameworks, in either the discrete bilayer or simple brick form, is achieved through a variety of mechanisms (Fig. 7) associated with their intrinsic conformational softness, including (i) formation of the 'shifted-ribbon' **GS** sheet motif in the bilayer form, whereby adjacent ribbons are shifted from the quasihexagonal arrangement, by as much as $a_1/2$, such that the ribbons are connected by one strong (**G**)N—H···O(**S**) H-bond ($d_{O\cdots H} \approx 2.0$ Å) and one very weak one ($d_{O\cdots H} \approx 2.5$ Å), (ii) slight puckering of the **GS** sheet ($\theta_{IR}$), (iii) turnstile rotation of the pillars about the C—S bonds ($\rho$), (iv) tilting of the pillars with respect to a normal to the **GS** sheets ($\phi$) and (v) twisting and flexing of the pillar ($\chi$), if possible.

Recently, we discovered that the simple brick form of $G_2$ (**VI**) promoted the polar alignment of centric guest molecules,[31] producing noncentrosymmetric polar crystals in an orthorhombic space group, $Pna2_1$, that is considered ideal for second harmonic generation. This was surprising because organic crystals tend to be centrosymmetric and the brick framework is not

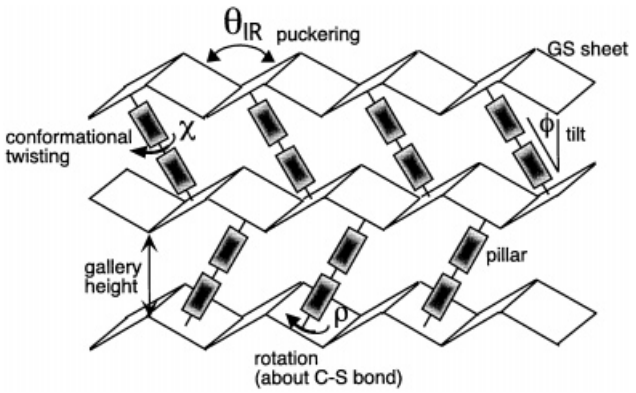



**Figure 7.** Schematic representation of the various contributions to conformational softness in the **GS** bilayer framework. These features are depicted here for the simple brick architecture

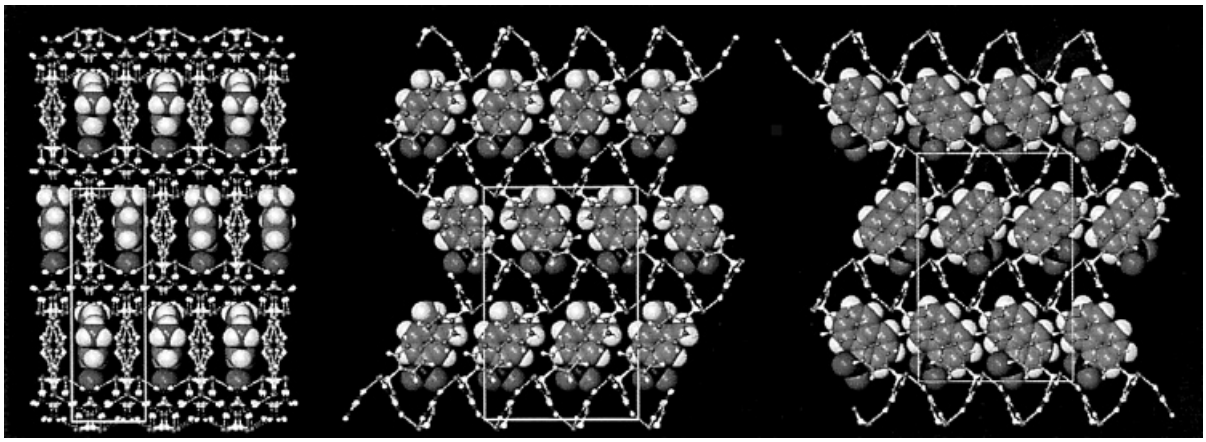


**Figure 8.** The molecular packing in crystals of **$G_2$(VI)**·(4-nitro-*o*-xylene) (left, middle) and **$G_2$(VI)**·(1-nitronaphthalene) (right). The left panel illustrates the guest organization as viewed down the channels of the brick framework. The middle and right panels depict the guest organization in these channels, running left to right across the page. The **GS** ribbons are orthogonal to the page in this view, which illustrates the puckered pockets that contain the guest molecules

intrinsically polar (Fig. 8). Such ordering can only be attributed to specific host–guest interactions, which must be cooperative in nature so that bulk polar order can be achieved. Inspection of the single-crystal x-ray structures of these materials revealed close contacts between the polar C—X substituents of the guest molecules (nitro-*o*-xylene, 1-nitronaphthalene, 1-iodonaphthalene and 1-cyanonaphthalene) and the guanidinium ions of the **GS** sheets, suggesting ion-dipole interactions (similar to those in the shrunken bilayer frameworks, see above).

The architecture of the simple brick host prevents direct guest–guest contact along the polar direction, which is orthogonal to the **GS** sheets, while the large separation between the inclusion cavities suppresses dipolar interactions between the guests. Within each gallery the guests exist as polar arrays, most likely as a consequence of shape-directing ordering along each channel and host–guest cooperative packing involving the turnstile-like biphenyldisulfonate pillars. The crystal structures of the inclusion compounds suggested that polar ordering *normal* to the **GS** sheets is driven by cooperative ion–dipole interactions between the **G** ions and the guest, during assembly of the pillared lamellae. The C—X dipole of each guest is nestled in a host 'pocket' created by the puckering of the **GS** sheet, bringing the guest dipole into ion–dipole contact with two **G** ions in the pocket. This would suppress the ion–dipole interaction with C—X dipoles of guests in the next layer, if they were to align antiparallel. This, in turn, would promote *parallel* alignment in the next layer, thereby prompting the C—X dipoles of the guests in the second layer to interact with 'uncommitted' **G** ions in the next **GS** sheet. In other words, shared ion–dipole interactions between **G** ions and guests approaching from opposite sides of a **GS** sheet, which can only occur if the guests are aligned antiparallel about the **G** ions, are not as favorable as unshared ones. This postulate is supported by the observation of increased polar ordering with increased guest dipole moment. Although this mechanism needs to be examined more thoroughly, these compounds illustrate the concept of using host lattices to control guest organization and the guests to provide function, in this case as potential frequency-doubling chromophores. The ability to change the size of the inclusion cavities in the **GS** frameworks provides an opportunity to include chromophores with larger molecular hyperpolarizabilities, possibly generating efficient second harmonic materials.

Although not yet fully developed, the **GS** host system already has demonstrated the importance of flexibility and constrained dimensionality in the design of molecular materials. A remarkably wide range of guest molecules can be included through a variety of structural mechanisms (architectural isomerism, puckering, pillar rotation/conformational twisting) intrinsic to these soft frameworks. This flexibility compensates for our inability to engineer inclusion cavities with the precision required for a 'hand-in-glove' fit with guest molecules. The two-dimensional character of the **GS** sheets substantially simplifies the design by restricting engineering to the last remaining (third) dimension and allows the use of a variety of different pillars without perturbing the lamellar character of the host architectures. The engineering principles resemble those used in the construction of modular housing, for which floor-to-ceiling heights and walls can be adjusted easily without dramatically changing the generic format of the building.

## Folding sheets into tubes

The **GS** sheets described in the preceding section display a remarkable degree of flexibility, as evidenced by their accordian-like puckering in numerous inclusion com-

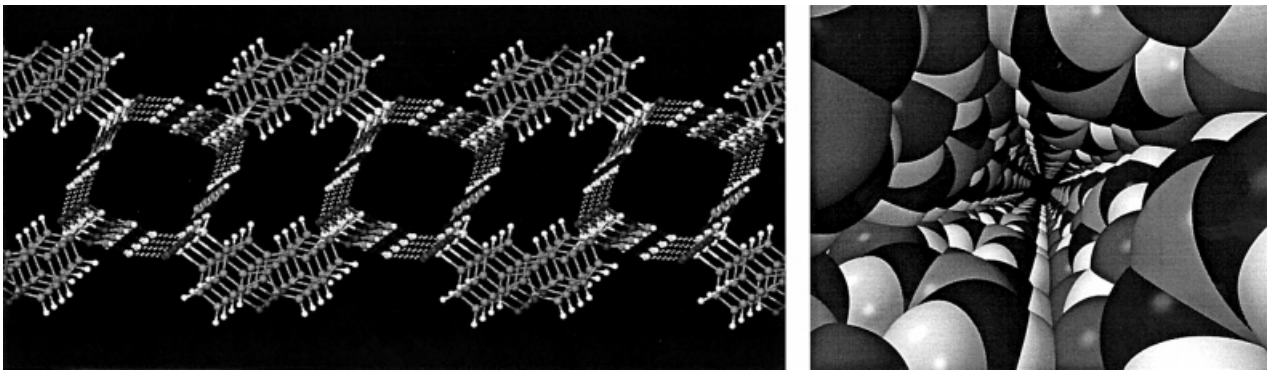


**Figure 9.** The crystal structure of (**G**)$_2$(4,4′-dibenzofurandisulfonate)·1.5(ethyl acetate)·0.5(methanol) reveals polar hydrogen bonded 'tubes,' formed by the lengthwise fusion of four **GS** ribbons into a continuous surface. These tubes are connected by the 4,4′-dibenzofurandisulfonate pillars, which generates a second type of tube in the structure. The panel on the right is a view of the internal structure of the polar tube with the **GS** ribbons depicted with their van der Waals radii to convey space-filling. The compound crystallizes in the $P\bar{1}$ space group with $a$ = 7.1076 Å, $b$ = 11.8099 Å, $c$ = 15.6524 Å, $\alpha$ = 95.431 °, $\beta$ = 101.401 ° and $\gamma$ = 90.108°

pounds. The lamellar structure is preserved, however, because the tilt of each ribbon is compensated by a tilt of an adjacent ribbon in the opposite direction. In principle, the flexibility of the **GS** inter-ribbon hydrogen bonds should allow continuous bending of the **GS** sheet in the same direction, about the same hydrogen-bonded hinges that allow puckering, to generate tubes with a continuous hydrogen-bonded surface (Fig. 9). Such structures would resemble peptide and carbon nanotubes.[32–35]

The lamellar **GS** inclusion compounds described in the preceding section were based on linear organodisulfonate pillars, which have antiparallel C—S (sulfonate) bond vectors on opposite sides of the pillar that naturally promote the formation of lamellar structures. We surmised that 'bent' organodisulfonates, in which the C—S (sulfonate) bond vectors form an obtuse angle of $<$180°, would frustrate the formation of bilayer frameworks and introduce 'curvature' to make tubular structures more likely. Indeed, we have discovered such a tubular framework in single crystals of (**G**)$_2$(4,4′-dibenzofurandisulfonate)·1.5(ethyl acetate)·0.5(methanol) (K. T. Holman and M. D. Ward, unpublished results). The structure of this compound actually reveals two tubes, one consisting of four **GS** ribbons fused into the quasihexagonal motif but forming a continuous closed surface through severe inter-ribbon bending ($\theta_{IR} \approx +90°$) in the same direction. The second tube has sidewalls consisting of **GS** ribbons, but a floor and ceiling consisting of the organic pillars, which connect the **GS** tubes. The two different tubes have much different character, the former having a more polar interior. Both tubes are filled with disordered guest molecules.

Although a tube clearly has a different *overall* topology to a sheet, the topology described by the up/down arrangement of the pillars on the **GS** surfaces (see Fig. 6) in the (**G**)$_2$(4,4′-dibenzofurandisulfonate) tube framework is *identical* with that of the **GS** sheets in the bilayer frameworks with the quasi-hexagonal motif (*i.e.* all pillars projecting from the same side of each **GS** sheet). The observation that the **GS** surface can curl and join itself to form tubes prompts several speculations. Can the diameter of the tubes be controlled by varying the effective curvature introduced by the organodisulfonate pillar? Can worm-like micelle structures, similar to those reported for surfactants and polymers, be generated with appropriate organomonosulfonates that introduce curvature through steric crowding on the **GS** sheet? Can chiral tubes be generated by designing systems with an odd number of **GS** ribbons on the surface of the tube? Are multiwalled tubes possible? Are spheroidal structures possible? How stable are such supramolecular tubes, which are held together only by non-covalent hydrogen bonds? Finally, can such objects be used as vehicles, decorated with appropriate sulfonate organic groups, for site-selective drug delivery? The observation of sheets and tubes with the same **GS** quasihexagonal motif illustrates how softness in supramolecular ensembles can impart structural robustness, enabling formation of diverse structures from common building blocks.

## Porous hydrogen-bonded molecular layers

A rudimentary examination of the known structures of organic crystals ($>$200 000 available in the Cambridge Structural Database at the time of this writing) reveals that many crystalline organic materials can be described as stacks of two-dimensional layers, a feature that has been long recognized.[36] This suggests a paradigm wherein layer motifs in bulk single crystals, which can be easily characterized by single-crystal diffraction techniques, can be used as a starting point for the design and synthesis of related two-dimensional films. We have recently demonstrated this concept, although in only a preliminary manner, for molecular films that assemble on

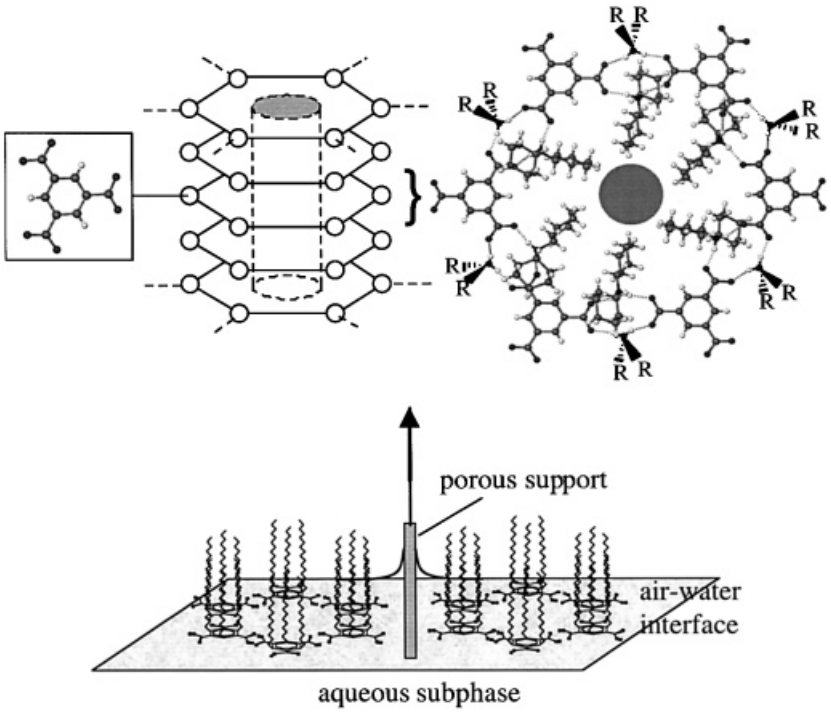



**Figure 10.** Schematic representation of the porous channel structure in $[NH_2(c\text{-}C_6H_{11})_2{}^+]_3[TMA^{3-}]\cdot CH_3(CO)CH_3\cdot 0.5$ MeOH. The hexagons portray one of the hexagonal hydrogen-bonded cyclamers observed in the single-crystal structure. The pore is continuous through the stacked layers and is filled by guest molecules (depicted here as a gray circle) in the single crystals. The layer structure can be generated as a single monolayer on an air–water interface in a Langmuir trough (see text). The bottom panel illustrates the creation of a Langmun–Blodgett monolayer from a porous hydrogen-bonded monolayer, portrayed here as a monolayer of trialklylated trimesic acid amphiphiles that form a cyclic network through intermolecular hydrogen bonds between the carboxylic acid groups (D. J. Plaut, unpublished results)

an air–water interface.[37] These investigations began with the synthesis of single crystals, grown from various solvents, consisting of trimesic acid and either dicyclohexylamine or di-tert-butylamine and having the compositions $[NH_2(c\text{-}C_6H_{11})_2{}^+]_3[TMA^{3-}]\cdot CH_3(CO)CH_3\cdot 0.5$ MeOH, $[NH_2(c\text{-}C_6H_{11})_2{}^+]_3[TMA^{3-}]\cdot 2.5$ (2-propanol) and $[NH_2(t\text{-}Bu)_2{}^+]_3[TMA^{3-}]\cdot CH_3(CO)CH_3$. Single-crystal x-ray diffraction of each of these materials revealed two-dimensional hydrogen-bonded 'honeycomb' networks (Fig. 10), which could be regarded as expanded versions of the 'chicken-wire' motif reported for trimesic acid alone.[38,39] Pairs of ammonium cations acts as 'spacer' molecules between pairs of carboxylate substituents on the $TMA^{3-}$ anions, creating large hexagonal pores. The cyclohexyl substituents project into the hexagonal pores, with six cyclohexyl groups lying in the midplane of the pore, three projecting above the plane, and the remaining three projecting below the plane. Adjacent honeycomb layers stack by interlocking so that the pores, although occupied by the solvent molecules, are continuous through the stacked layers. The structures of the three compounds differ with respect to the degree of chair-like puckering of the hexagonal networks, reflecting the intrinsic flexibility of hydrogen bonding that allows this generic architecture to adjust to different alkyl substituents and solvent occupancy.

These layer motifs were used as models for Langmuir monolayers based on long-chain alkylamines (instead of cyclohexyl or *tert*-butyl) that provided the amphiphilicity required for monolayer organization at the air–water interface, which in this case should mimic the structure of the hydrogen-bonded honeycomb networks in the bulk crystals. Similar strategies were used previously to create monolayers that mimicked layer motifs in amino acids.[40] Amphiphiles such as octadecylamine were spread over an aqueous subphase of $H_3TMA$ in a Langmuir trough. Pressure–area isotherms exhibited lift-off at a molecular area of 59 $Å^2$/amine and extrapolation of the linear compression regime afforded a molecular area of 51 $Å^2$/amine. Similar isotherms were exhibited when methyloctadecylamine and dioctadecylamine were used. Interestingly, the lift-off and extrapolated values bracket the range of the molecular areas occupied by the hydrogen-bonded layers in the three aforementioned crystalline materials (51.5–58.6 $Å^2$/amine). This suggests that the hydrogen-bonded monolayer at the air-water interface has a flexibility that mimicks that of the solid-state networks, in this case puckering under the influence of surface pressure exerted by the trough barrier.

Langmuir monolayers such as these may promote the nucleation and growth[41,42] of metastable crystalline phases with porous frameworks through structural

mimicry at the nucleation interface beneath the monolayers. Additionally, porous monolayers, transferred to permeable solid substrates by the Langmuir–Blodgett method, may also be useful as size exclusion membranes in which the pore sizes can be adjusted by molecular design. Preliminary experiments in our laboratory indicate that these monolayers can be transferred from the Langmuir trough to solid substrates which, if permeable, can produce composite membrane structures. A key advantage here is the uniformity of pore size and the ability to adjust pore size and shape through molecular engineering, features that can lead to membranes with highly specific permeabilities.

## CONCLUSION

Interest in materials made from molecular components, driven by the promise of new systems with precisely tailored properties, is accelerating at a rapid pace. The last decade has witnessed tremendous advances in the sophistication of molecular materials based on supramolecular building blocks. The synthesis of these materials has become increasingly based on modular design in which molecular components can be interchanged at will to generate materials with properties and function that can be finely tuned in a systematic manner. When combined with the power of organic synthetic chemistry, the ability to build hierarchical structures from molecular or supramolecular modules, described elsewhere as a supramolecular *aufbau* approach,[43] introduces a versatility with respect to materials design that is unmatched. The key to advancing this field is the elucidation of molecular assembly principles that will enable precise control of the supramolecular synthesis. The noncovalent bonding involved in these molecular assembly processes already has provoked comparisons with polymers and proteins, materials that also rely on noncovalent self-organization and self-assembly. The hydrogen-bonded materials described above possess lattices that are robust because they are intrinsically 'soft' and self-adapting, characteristics that one frequently associates with the folding of proteins or the development of microstructure in polymers. One easily anticipates that the comparisons between materials, polymers, and proteins will only accelerate, bringing mutual benefits that will significantly advance 'soft materials.' If the last 10 years of the 20th century are any indication, the next 100 hold great promise for new molecular materials.

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## REFERENCES

1. Kennedy MT, Korgel BA, Monbouquette HG, Zasadzinski JA. *Chem. Mater*. 1998; **10**: 2116–2119.
2. Discher BM, Won YY, Ege DS, Lee JCM, Bates FS, Discher DE, Hammer DA. *Science* 1999; **284**: 1143–1146.
3. Won YY, Davis HT, Bates FS. *Science* 1999; **283**: 960–963.
4. Li H, Eddaoudi M, O'Keeffe M, Yaghi OM. *Nature (London)* 1999; **402**: 276–279.
5. Subramanian S, Zaworotko MJ. *Angew. Chem., Int. Ed. Engl.* 1995; **34**: 2127–2129.
6. Hagrman PJ, Hagrman D, Zubieta J. *Angew. Chem., Int. Ed. Engl.* 1999; **38**: 2639–2684.
7. Chui SSY, Lo SMF, Charmant JPH, Orpen AG, Williams ID. *Science* 1999; **283**: 1148–1150.
8. Weber E (ed). *Topics in Current Chemistry*: *Molecular Inclusion and Molecular Recognition. Clathrates I and II*, Vols 140 and 149. Springer: New York, 1987 and 1988.
9. Ermer O, Lindenberg L. *Helv. Chim. Acta* 1991; **74**: 825–877.
10. Brunet P, Simard M, Wuest JD, *J. Am. Chem. Soc.* 1997; **119**: 2737–2738.
11. Endo K, Koike T, Sawaki T, Hayashida O, Masuda H, Aoyama Y. *J. Am. Chem. Soc.* 1997; **119**: 4117–4122.
12. Desai TA, Hansford DJ, Kulinsky L, Nashat AH, Rasi G, Tu J, Wang Y, Zhang M, Ferrari M. *Biomed. Microdevices* 1999; **2**: 11–40.
13. Edlund U, Albertsson AC. *J. Polym. Sci., Part A: Polym. Chem.* 2000; **38**: 786–796.
14. Nam YS, Park TG. *J. Biomed. Mater. Res.* 1999; **47**: 8–17.
15. Hendel RA, Nomura E, Janout V, Regen SL. *J. Am. Chem. Soc.* 1997; **119**: 6909–6918.
16. Arena G, Contino A, Magri A, Sciotto D, Lamb JD. *Supramol. Chem.* 1998; **10**: 5–15.
17. Atwood JL, Davies JED., MacNicol DD, Vögtle F, Suslick KS (eds). *Comprehensive Supramolecular Chemistry, Vol. 6, Solid-State Supramolecular Chemistry: Crystal Engineering*. Pergamon Press: Oxford, 1996.
18. Atwood JL, Davies JED, MacNicol DD (eds). *Inclusion Compounds*, Vol. 2, *Structural Aspects of Inclusion Compounds Formed by Organic Host Lattices*. Academic Press: London, 1984.
19. Russell VA, Etter MC, Ward MD. *J. Am. Chem. Soc.* 1994; **116**: 1941–1952.
20. Russell VA, Etter MC, Ward MD. *Chem. Mater.* 1994; **11**: 1206–1217.
21. Cao C, Hong HG, Mallouk TE. *Acc. Chem. Res.* 1992; **26**: 420–427.
22. Batten S, Robson R. *Angew. Chem., Int. Ed. Engl.* 1998; **37**: 1461–1494.
23. Russell VA, Evans CC, Li W, Ward MD. *Science* 1997; **276**: 575–579.
24. Holman KT, Ward MD. In *Stimulating Concepts in Chemistry*, Vögtle F, Stoddart JF, Shibasaki (eds). Wiley-VCH: Weinheim in press.
25. Swift JA, Reynolds AM, Ward MD. *Chem. Mater*. 1998; **10**: 4159–4168.
26. Swift JA, Pivovar AM, Reynolds AM, Ward MD. *J. Am. Chem. Soc.* 1998; **120**: 5887–5894.
27. Davis ME, Katz A, Ahmad WR. *Chem. Mater*. 1996; **8**: 1820–1839.
28. Huo Q, Margolese DI, Stucky GD. *Chem. Mater*. 1996; **8**: 1147–1160.
29. Aoyagi M, Biradha K, Fujita M. *J. Am. Chem. Soc.* 1999; **121**: 7457.

30. Evans CC, Sukarto L, Ward MD. *J. Am. Chem. Soc.* 1998; **121**: 320–325.
31. Swift JA, Ward MD. *Chem. Mater.* in press.
32. Ghadiri MR, Granja JR, Buehler KK. *Nature (London)* 1994; **369**: 301–304.
33. Iijima S. *Nature (London)* 1991; **354**: 56–58.
34. Xie SS, Chang BH, Li WZ, Pan ZW, Sun LF, Mao JM, Chen XH, Qian LX, Zhou WY. *Adv. Mater.* 1999; **11**: 1135–1138.
35. Ebbesen TW. *Phys. Today* 1996; **49**: 26–32.
36. Scaringe RP. In *Electron Crystallography of Organic Molecules*, Fryer JR, Dorset DL, (eds). Kluwer: Boston, 1991; 85.
37. Plaut DJ, Lund KM, Ward MD. *Chem. Commun.* 2000; 769–770.
38. Herbstein FH. *Top. Curr. Chem.* 1987; **140**: 108–139.
39. Melendez RE, Sharma CVK, Zaworotko MJ, Bauer C, Rogers RD. *Angew. Chem. Int. Ed. Engl.* 1996; **35**: 2213–2215.
40. Jacquemain D, Wolf SG, Leveiller F, Deutsch M, Kjaer K, Als-Nielsen J, Lahav M, Leiserowitz L. *Angew. Chem., Int. Ed. Engl.* 1992; **31**: 130–152.
41. Mann S, Heywood BR, Rajam S, Walker JBA. *J. Phys. D: Appl. Phys.* 1991; **24**: 154–164.
42. Frostman LM, Ward MD. *Langmuir* 1997; **13**: 330–337.
43. Mio MJ, Moore JS. *Mater. Res. Soc. Bull.* 2000; **25**: 36–41.