Crystal engineering with sterically-hindered molecular modules: unique supramolecular synthons and novel molecular self assembly

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Abstract | The influence of steric on the manifestation of supposedly robust supramolecular synthons has been examined in rationally designed molecular modules to afford novel insights as to the molecular self-assembly in the solid state. It is shown that novel molecular modules created by incorporating steric factors can be exploited to engineer porous crystals, which are sustained by hydrogen bonds and metal-ligand coordination bonds.

1. Introduction
It is the molecular ordering in crystals that determines the macroscopic property of a given solid. Therefore, the ability to predict crystal packing based on structures of the constituent molecules is invaluable in designing solid materials that exhibit properties such as nonlinear optical activity, ferromagnetic behavior, electrical conductivity, zeolite-like behavior, pharmaceutical property, solid state reactivity, etc.1 Unfortunately, the control as well as prediction of crystal packing based on the structures of constituent molecular components is a formidable task. The crystal structure prediction is frustrated by a multitude of weaker interactions that lead to a number of free-energy minima very near the global minimum. A consequence is the so-called ‘polymorphism’—the phenomenon of occurrence of two or more crystal modifications for a given compound.2 It is therefore not surprising that the ‘crystal structure prediction of even simplest crystalline solids based on the knowledge of their chemical composition’ has long been perceived almost impossible.3 Despite this cynicism, a remarkable progress has been made over the last few years toward the ultimate goal of preparing solid materials with pre-determined organization. Now, the organic structures are controllable through ‘crystal engineering’, which is defined as the understanding of intermolecular interactions in the context of crystal packing and in the utilization of such understanding in the design of new solids with desired physical and chemical properties.4 Further, it appears that the crystal structures can now be predicted from first principles; in a recent break-through, Neumann et al. have demonstrated crystal structure prediction of test molecules by combining quantum mechanical calculations with classical force-field simulations.5 The success with control of molecular organization, in general, is traceable to recognition and identification of intermolecular interactions and their modes (patterns) of manifestation, viz., supramolecular synthons,6 which play a pivotal role in the overall crystal packing. The target crystal structures can now be approached through dissection analysis in complete analogy to the retrosynthetic analysis of a target molecule in the realm of synthetic organic chemistry. Of course, the approach entails design of both molecular as well as supramolecular structures.
According to Desiraju, three cardinal facets, viz., the study of (i) intermolecular interactions, (ii) molecular packing modes/synthons and their design thereof and (iii) properties of solids and their modulation with judicious variations, represent what, how and why of crystal engineering, which has grown to be an area of immense importance in wider intersections of science and technology. Intermolecular interactions lie at the heart of supramolecular chemistry. A better appreciation of intermolecular interactions is mandatory for any advance in such areas as molecular recognition, molecular self-assembly, crystal structure design and prediction, etc., which exemplify supramolecular chemistry. Understanding of various possible ways in which the intermolecular interactions may manifest is also important from the point of view of crystal design and prediction.

In our research, we have been concerned with all of the above-mentioned facets that constitute crystal engineering. In particular, the emphasis of our investigations is to apply the riches of crystal engineering to control molecular order, thermal and photochemical molecular reactivity, and also prohibit crystallization to develop amorphous molecular materials—a bright advantage of what is otherwise a ‘dark-side of crystal engineering’. Insofar as the exploitation of intermolecular interactions is concerned, it must be noted that it is with the application of such knowledge that the area of crystal engineering emerged through the pioneering work of Schmidt. The control of reaction coordinates of organic transformations via stabilization of transition state geometries by intermolecular interactions is nothing new; the enzyme-mediated catalysis occurs based on the same very principle. However, a deliberate utilization of the wealth of intermolecular interactions toward achieving selectivities in organic reactions (be it in terms of product profiles or regio- or stereochemical sense) is beginning to be more intensely exploited only now; organocatalysis and hydrogen-bonded catalysis have emerged as exciting areas in the domain of organic synthesis. Our interests are also concerned with this goal of putting the knowledge of intermolecular interactions to best use as applied to organic reactions. Herein, I shall summarize some results gleaned from our work that exemplify (i) how sterically-hindered molecules in conjunction with other factors lead to recognition of novel modes of molecular self-assembly based on hydrogen bonding, and (ii) how the sterically-hindered molecular systems based on a rational design may be exploited for creation of porous metal-organic coordination networks.

While the literature is abound with a variety of intermolecular interactions associated with functional groups and their manifestation in terms of supramolecular synthons, how the steric factors influence their identity has not been a subject of systematic investigation. The knowledge of how structural attributes influence supramolecular synthons is important from the point of view of crystal engineering. In addition to exploring the influence of steric on synthons manifestations, we have also exploited sterics for creation of porous materials through a rational design at the molecular level.

2. Molecular self-assembly based on hydrogen bonding

An invaluable approach for crystal engineering is the identification of the ability of certain molecular subunits (functional groups) that self-interact in a noncovalent fashion and conserve specific pattern/motif (supramolecular synthon) persistently. It is the persistence of synthons due to functional groups that lends predictability as to the overall organization. Due to strength and directionality, the hydrogen bonds have been exploited as a noncovalent glue between molecules with astonishing results. The influence of sterics on the synthons of carboxylic acids, amides and alcohols are discussed below.

**Helical assembly of sterically-hindered carboxylic acids**

The organic compounds containing carboxyl and amide functionalities are among the widely investigated functional group compounds to understand the hydrogen bonding in solution and solid states. In general, the carboxylic acids exhibit a remarkable diversity in terms of their self-assembly in the solid state. Leiserowitz and co-workers were the first examine in detail the hydrogen bonding patterns exhibited by carboxylic acids in their crystal structures. In principle, there exist two distinct conformations for carboxyl groups, which are described as syn-palmar and anti-planar, Scheme 1.

The syn conformation is more stable than that of the anti isomer by ca. 2 kcal/mol due to the anomeric effect arising from the sp² hybridized orbital of the oxygen carrying the hydrogen. Thus, it is more preferred. The Cambridge Structural Database (CSD) analyses have revealed that 90% of the acids assemble via the dimer motif with syn-syn conformation. Indeed, the carboxylic acid dimer synthon has been elegantly exploited since the emergence of molecular self-assembly; the formation of hexagonal rosette structure from trimesic acid and 3-dimensional diamondoid structure from adamantane tetracarboxylic acid constitute prototype examples of self-assembly based on carboxyl groups. The remaining 10%...
of the acids are found to take up three different types of motifs; the catemer motif, mediated by either syn-syn, anti-anti and syn-anti, is observed in 4% of the crystal structures, and the dimers expanded by incorporation of solvent molecules are observed in the rest.\textsuperscript{16} While the inexplicable preponderance for the occurrence of dimer motif in the crystal structures of carboxylic acids continues to be an enigma, Desiraju and co-workers showed that the catemeric motif becomes favored in the crystal packing of a family of phenylpropionic acids and cubanecarboxylic acids in which an ancillary C–H···O hydrogen bond augments adoption of catemeric motif.\textsuperscript{16c,19}

In the course our photochemical investigations on substituted mesitaldehydes,\textsuperscript{20} we stumbled on a chance observation that 3,5-dibromomesitoic acid 1 crystallizes with unusual packing motif. It emerged from a careful analysis of the crystal packing that the acids undergo a novel helical assembly. This led us to examine the factors that are responsible for a paradigm shift in the conventional knowledge as to the self-assembly of carboxylic acids. In a systematic study, we designed, synthesized and analyzed the crystal structures of a series of sterically-hindered and halogen-substituted benzoic acids shown in Chart 1.\textsuperscript{21}

The X-ray crystal structure analyses of acids 1 and 2 revealed that they are isostructural (tetragonal, \textit{I}4\textsubscript{1}/\textit{a}). The conformation of the carboxyl group in both cases was found to be syn-planar. Due to steric hindrance, the plane of the carboxyl group lies
almost orthogonal to that of the aromatic ring in both cases (82.1 and 80.4° in 1 and 2, respectively). The crystal structures of both 1 and 2 revealed an unusual helical organization of the molecules along the 41-screw axis (Figure 1), linked together by O–H···O hydrogen bonds. Thus, each coil of the helix was found to contain 4 residues with a distance of ca. 8.60 Å between the coils, which corresponds to the unit cell dimension along the c-axis. Further, a closer inspection of the molecular packing revealed that the crystal lattice is stabilized by X···X and C–H···X interactions in addition to the O–H···O hydrogen bonds (Figure 1). Of the two halogens, only one was found to be involved in nonbonded X···X (d_{Br···Br}(1) = 3.72 and d_{Cl···Cl}(2) = 3.67 Å) and C–H···X interactions (d_{H···X} and θ_{C–H···X} are 2.99 Å and 141.0° for 1 and 2.83 Å and 147.7° for 2). Interestingly, the second halogen atom was found to be a noninteractive “spectator”. By contrast, the sterically-unhindered m-chloro-and m-bromobenzoic acids exhibited the standard dimer motif in their crystal structures. On the other hand, the durene carboxylic acids 6 and 7 were found to be isostructural as those of 1 and 2. These acids were found to exhibit a packing pattern involving the dimer motif and X···X interactions that lead to a tape/ribbon (Figure 1). In contrast to acids 1 and 2, no weaker C–H···X interactions were found in 6 and 7. The isostructurality of 1 and 2, and the involvement of only one of the two halogen atoms in the crystal lattice stabilization led us to examine the 3-bromo-5-chloro (3), 3-chloro-5-methyl (4) and 3,5-dimethy (5) analogs of 1 and 2. The acids 3 and 4 were found to crystallize in the tetragonal crystal system and exhibit absolute isostructurality with those of the acids 1 and 2. In the crystal structure of 4, the methyl group at the meta position simply assumed the role of a “spectator” halogen atom in acids 1 and 2, while the chloro group was found to stabilize the lattice (Figure 1). In a noteworthy contrast, the pentamethylbenzoic acid 5 was found to crystallize in the P21/c space group and exhibit entirely different crystal packing involving the dimer motif. It is well known that for structures in which the methyl and/or chloro groups participate in intermolecular interactions characteristic of their own, the chloro-methyl exchange based on their isosteric relationship cannot be expected.22 This is precisely what is observed when the “interacting” halogen that is involved in the crystal lattice stabilization in 1 and 4 is replaced by an isosteric methyl group as in 5. The crystal packing changes entirely, emphasizing the importance of the secondary interactions mediated by the halogen atom in the crystal packing. In contrast, the exchange of the “spectator” halogen in 1 by a methyl as in 4 does not result in a similar change of the crystal packing, as they are simply involved in close-packing. Thus, we convincingly demonstrated that the unusual helical assembly in 1 and 2 is indeed mediated by a simultaneous operation of weaker X···X and C–H···X interactions on the strong and directional O–H···O hydrogen bonds. These constituted unambiguous demonstration of how the weaker interactions when coupled with
sterics may decisively modify the supposedly robust dimeric association pattern of aromatic carboxylic acids.

**Bimesityl-3,3′-dicarboxylic acid–entrapment of planar cyclic water hexamer**

In continuation of above studies on sterically-hindered benzoic acids, we designed dicarboxylic acids 8-10 based on 3-dimensional core, viz., bimesityl, in pursuit of creating helices in 2-dimensions. The biaryls 9 and 10 essentially incorporate all the structural features of 1 and 2, and we anticipated that the weaker X⋯X and C–H⋯X interaction would bring about the helical self assemblies in 2-dimensions. While these compounds never crystallized at all, the unsubstituted dicarboxylic acid 8 crystallized out with a molecule of water incorporated in the crystal lattice.23 The space group symmetry (R-3) led to the generation of a planar cyclic ring form of water hexamer in which each water molecule is hydrogen bonded to four other molecules (Figure 2).

This observation was deemed very important to chemists working on water cluster problems. The structural knowledge of water clusters is believed to offer crucial insights as to the structure of macroscopic water and associated dynamic intermolecular hydrogen bonding. We claimed that our characterization of a planar cyclic hexamer of water constituted first ever of a structural form that is observable in ice II modification, which is formed only under high pressures.24 In addition to characterization of the water hexamer, we unraveled yet another novel motif for the carboxylic acid association (Figure 2).

**In hunt of the centrosymmetric dimer motif in sterically-hindered aromatic dicarboxylic acids**

It is intriguing that the sterically-hindered aromatic carboxylic acids appear to represent rather sensitive systems from the point of view of molecular self assembly. While the dimer motif has indeed been observed in some hindered benzoic acids, e.g., pentamethylbenzoic acid,21 the location of a weakly interacting halogen group as in 1-4 completely diverted the self-assembly based on strongly interacting carboxyl groups in favor of a helical motif. In a similar manner, the conjoined and sterically-hindered dicarboxylic acid 8 did not adopt the dimer motif, but exhibited unusual crystal packing in which a unique planar hexameric water was found to be entrapped in the crystal lattice via hydrogen bonding. Thus, it was tempting to probe how the diacids 8-1 and 11-1 (Chart 3) separated by a methylene spacer would exhibit crystal packing. Further, we were motivated by the finding of Jacco van de Streek that the molecules that contain strongly interacting functional groups in non-coplanar aromatic rings, e.g., 1,1′-binaphthyl-2,2′-dicarboxylic acid, exhibit more than average tendency to form solvates.25 We were delighted to recognize immediately that our own discovery of the inclusion of a hexameric planar water cluster in the crystal lattice of bimesityl-3,3′-dicarboxylic acid23 mentioned above fell in line with this observation.

The sterically-hindered methylene-tethered dicarboxylic acids 8-1 and 11-1 may explore two extreme low-energy conformational, viz., syn and anti. The molecular topology in conjunction with steric hindrance appear to divert the syn-diacid 8-1 the adoption of the otherwise prevalent dimer motif.26 While the unhindered diacid 11-1 was found not to crystallize at all, the sterically-hindered one, i.e., 8-1, was found to crystallize in the syn conformation with a very rare tetrameric association (Figure 3). Interestingly, the molecular topology and the other attributes mentioned earlier appear to impart guest-binding propensity to the diacid molecules in their anti conformations leading to pseudopolymorphism with DMSO and PhOH–H₂O; only the crystal packing of the pseudopolymorph of Ph–H₂O is shown in Figure 3. Clearly, the conformation-dependent crystal packing and observation of pseudopolymorphism for the diacid 8-1 in its syn and anti conformations suggest that the sterically-hindered acids are highly susceptible to exhibiting variations in association modes. Further, the fact that the simple un-hindered dicarboxylic acid 11-1 did not crystallize in various attempts underscores
Figure 2: The molecular structure of the complex of bimesityl-3,3'-dicarboxylic acid 8 and water (a), the entrapped water with hydrogen-bonded carboxyl groups (b), and the overall crystal packing of the complex (c). In the latter, the hexameric cluster that is hydrogen bonded to the diacids 8 is highlighted.
Figure 3: The crystal packing diagram of the diacid 8-1 with syn conformation (a), and the unusual tetrameric association found in its crystal lattice (b). The molecular packing of the phenol-water pseudopolymorph of 8-1 (c). Notice that the conformation adopted by the diacid in this case is anti.

The crystal packing diagram of the diacid 8-1 with syn conformation (a), and the unusual tetrameric association found in its crystal lattice (b). The molecular packing of the phenol-water pseudopolymorph of 8-1 (c). Notice that the conformation adopted by the diacid in this case is anti.

the influence of structural changes, effected via methylene tethering, on the self-assembly of aromatic carboxylic acids.26

The inexplicable and conspicuous absence of the dimer motif in diacids 8, 8-1 and 11-1 was a further motivation to examine the extent to which the tether connecting two hindered acids modifies the packing motif of carboxylic acids. Thus, a series of diacids shown in Chart 3, i.e., 8-2 to 8-4, 11-2, 11-3, 12-2 and 12-3, were synthesized and the crystal structures of some of them determined.27

The mesitylene and isodurene dicarboxylic acids connected by an ethylene spacer, i.e., 8-2 and 12-2, resisted crystallization in a variety of solvents. The crystals suitable for X-ray studies could be obtained only from MeOH and DMF for 8-2 and from only MeOH for the case of 12-2. In the case of the DMF solvate of 12-2, the solvent simply terminated the possible hydrogen-bond mediated polymeric propagation of the diacid molecules, Figure 4. In contrast, we observed what may be regarded as a ‘solvent-expanded catemeric motif’ in 8-2:2MeOH solvate, Figure 4; while the acid hydrogen was found to be bonded to the methanol oxygen, the methanol hydrogen was seen to be bonded to the carbonyl oxygen of 21-screw-related molecule leading to a novel solvent-expanded polymeric chain, Figure 4. The crystal structure of 12-2:2MeOH was found to be completely isostructural with that of 8-2:2MeOH. It should be noted that the crystals of 11-2 could not be grown. In the same vein, our best efforts to obtain the crystals of propylene-tethered dimesitoic acid 8-3 as well as diisodurene carboxylic acid 12-3 were in vain in a range of solvents that did not contain an organic base such as 2,4,6-collidine. In the case of the former, the crystals were obtained only in the presence of added collidine base. The crystals of diacid 11-3 were obtained from its solution in DMSO over a period of 2–3 weeks. The X-ray structure determination revealed the absence
of any solvent molecule, Figure 4. Gratifyingly, the diacid was found to adopt a coiled/twisted conformation and undergo self-assembly via cyclic dimer motif. The crystals of diacid 8-4 were obtained by evaporation of its saturated solution in DMSO and DMF. The X-ray diffraction analyses of the crystals grown from the two solvents gave rise to identical cell parameters. The crystals were found to be orthorhombic (space group: Pbcn). Remarkably, the carboxyl groups were found to undergo self-assembly via the typical dimer motif of carboxylic acids. The self-assembly in this instance led to a 1-dimensional zigzag chain via strong O–H⋯O hydrogen bonded dimeric motif.27

Clearly, the above investigations established that a C₄-tether appears to suffice for each of the acid moieties to independently exhibit the preponderant centrosymmetric dimer synthon; the situation appears little relaxed for unhindered diacids such that a C₃ tether is sufficient for adoption of centrosymmetric dimer synthon-mediated organization of the molecules in the crystal lattice. The topological changes, i.e., skewed (for odd) and extended (for even), imparted by the tether appear to render the close packing, while simultaneously exploiting the strong O–H⋯O hydrogen bonds, difficult even for diacids with a C₂ tether. Thus, for short chain lengths, the tether typically behaves like a functional group, which perturbs the molecular association based on O–H⋯O hydrogen bonds of an otherwise strongly interacting carboxyl groups.27

**Sterically-hindered benzamides and alcohols**

It is amply evident from the investigations discussed above that sterically-hindered benzoic acids substituted with halogen atoms or connected by a tether elude predicted pattern of assembly, thereby suggesting the sensitivity of such systems to even minor structural modifications. Given that the acids normally exhibit robustness in terms of molecular self-assembly, it was important to unravel conditions under which their occurrence is not tolerated by subtle changes in structural features. We have extended these studies to test the occurrence of similar and most reliable synthons of primary amides under analogous situations. The hydrogen bonds involving amide functionality (–CONHR) play a crucial role in the constitution as well as diverse functions of biological systems. Further, due to well-defined and robust supramolecular synthons that the amides lend themselves to (Scheme 2), they have been reliably exploited in the contemporary supramolecular chemistry.28 Thus, we set out to
investigate the self-assembly of sterically-hindered amides and alcohols (Chart 4), which are analogous to those of the acids 1-7 discussed earlier. The self-assembly of alcohols is quite variable and vastly structure-dependant.\textsuperscript{29} It was, therefore, of interest to explore how steric hindrance and weakly interacting groups such as halogens impact their self-assembly.

In general, the supramolecular synthons that are observed for primary amides in their crystal structures are dimeric and ribbon/tape motifs as shown in Scheme 2.\textsuperscript{30} The preliminary X-ray diffraction studies of the amides 13-NH$_2$–H$_2$–NH$_2$ have led us to a remarkable observation of polymorphism,\textsuperscript{2} which has elicited an upsurge of interest in recent years. We have observed that some of the amides exhibit 2–3 crystal modifications with a notable variation in the number of crystallographically independent molecules (Z') in the asymmetric unit cell;\textsuperscript{31} indeed, this number has been found to vary in the range of 1–16. While the crystals are stable in air, which of the polymorphic forms results from a given crystallization experiment seems difficult to be established. In Figure 5 are shown the crystal packing diagrams observed for the two modifications of 13-NH$_2$ with Z' = 1 and 16. This phenomenon appears to apply equally for mono-bromo and mono-chloro amides as well; comprehensive investigations are still underway.

It is both intriguing and remarkable that such simple systems self-assemble in unique ways into what appear to be clusters. The issue related to the structures with high Z' is of tremendous contemporary interest in view of the fact that...
such structures might offer invaluable insights into the mechanism of crystallization.\textsuperscript{32} As mentioned earlier, the investigations that are still in progress preclude us from drawing definitive conclusions regarding the unusual crystallization modes observed with amides in Chart 4.

We have determined the crystal structures of some sterically-hindered alcohols 13-OH–17-OH.\textsuperscript{33} To our astonishment, we observe that the structures in these cases are absolutely unaffected by weakly interacting halogen groups. Besides, several of them are found to exhibit a rather unusual helical pattern, as shown in Figure 6. We also observe a close analogy with the crystal packing of the acids 1-8 in Chart 1 in that all of these alcohols, i.e., 13-OH–17-OH crystallize uniformly in the same space group (I4\textsubscript{1}/a). The self-assembly of alcohols is not readily predictable as in the case of acids and amides. As mentioned earlier, the alcohols are known to explore a variety of synthons that are crucially dependent on the structures of alcohols.\textsuperscript{29} From the isostructurality observed with several of the sterically-hindered alcohols in Chart 4, it appears that the hydrogen-bonded self-assembly of sterically-hindered alcohols is largely governed by shapes of the molecules, and that it is least perturbed by weakly interacting groups as in the case of acids and amides.

3-Dimensional D\textsubscript{2d}-symmetric scaffolds based on bimesityl core for porous H-bonded networks

As mentioned at the outset, control of crystal packing is pivotal for the development of organic solids with functional properties; the molecular ordering in organic crystals hinges on two aspects, viz., rational design of molecular modules and judicious selection and location of certain functional groups, which lend themselves to reliable, repetitive and robust motifs/synthons. Whereas the literature in supramolecular chemistry is replete with examples of control of molecular organization in 1- and 2-dimensions, that in the 3rd dimension continues to be a challenging proposition. One of the reasons for this is the limited 3-dimensional molecular scaffolds, which may be exploited for self-assembly in 3-dimensions by installing the functional groups responsible for reliable synthons at strategic locations. The literature reveals only a few molecular systems, which have been exploited
Figure 6: The crystal packing of sterically-hindered 13-OH (space group: I41/a). The hydrogen-bonded assembly of the alcohols is shown at the bottom.

for crystal packing in 3-dimensions. These are based on bipyrazolyls,34 biphenyls,35 spirobifluorenyls,36 tetraarylmethanes,37 adamantans,38 and conformationally-flexible pentaerythritols.38 Although bipyrazolyls, spirobifluorenyls and biphenyl-derivatives correspond to the topology of an allene, their limited flexibility for further structural modifications/elaborations coupled with rather difficult synthetic accessibility spurred us to conceive of simple and yet unexplored (in supramolecular chemistry) 3-D molecular scaffolds based on tetraarylallenes. However, the acid lability in the case of electron-rich allenes and tedious general synthetic procedures to access a large set of compounds forced us to look for an alternative molecular system with a similar (D2d-symmetry) topology. Therefore, we considered ‘bimesityl’ as a fantastic core to construct a broad set of 3-dimensional molecules with diverse functional groups based on a general and facile synthetic procedure. Our ultimate goal was to develop organic functional mimics of inorganic zeolites in view of the chirality, which can be readily introduced at the molecular level.39,40 It was surmised that 4-fold p-hydroxyphenyl- and p-carboxyphenyl-functionalized bimesityls (20 and 22, Chart 5) might assemble into porous networks based on their self-assembly involving a linear linkage. The advantage with such a bimesityl core was the feasibility for easy structural expansion as can be seen, for example, with the expanded derivatives 21 and 23 (Chart 5).

It was anticipated that the carboxy- and the hydroxy-biaryls (21,23 and 20,22) would self-assemble into 3-dimensional architectures with empty channels as shown in Figure 7. We were gratified to recognize that the 4-hydroxyphenyl-substituted bimesityl derivatives 20 and 22 do indeed undergo self-assembly via structure-determining O–H···O hydrogen bonds into 3-dimensional porous frameworks, as revealed from 1H NMR analyses of the host-guest complexes, and also from X-ray structure determination of a complex of one of the derivatives, viz., tetrakis(4-hydroxyphenyl)bimesityl 20.41 The crystal packing revealed a unique hydrogen-bonded helical motif, which acts as a ‘spine’ along the b-axis (Figure 8). The molecules that constitute the spine enclose tubular voids, in which the guest molecules reside; notably space
group acentricity introduced chirality into the voids. We believe that the expanded tetraphenol 22 also undergoes self-assembly analogous to that of 20; the tetraacid 22 exhibited inclusion of guest molecules as large as xylene, mesitylene, anisole, etc., as revealed by \textsuperscript{1}H NMR spectroscopy of the complex crystals, which were unsuitable for structural studies.\textsuperscript{41}

The crystallization of tetraacid 21 from solvents such as methanol, ethanol, ethyl acetate, acetone, etc., was unsuccessful despite innumerable crystallization experiments. However, crystallization in DMSO/toluene yielded seemingly excellent crystals, which diffracted only poorly. The reason for the latter was traced subsequently to the severely-disordered solvent molecules. The single crystal X-ray structural of 21 revealed that solvent molecules, viz., DMSO and H\textsubscript{2}O, reside in the channels, Figure 9. While the expected dimer motif was not observed due to competitive hydrogen bonding of DMSO/H\textsubscript{2}O with the carboxylic acid hydrogens, the formation of channels in the crystal lattice amply illustrates the potential of 3-dimensional modules based on biaryls in the development of functional mimics of inorganic zeolites. As simple desymmetrization of the bimesityl core may lead to chiral atropisomers, whose resolution chemistry is well founded, these scaffolds may offer a facile entry into chiral porous materials.

3. Rational approaches to the development of metal-organic frameworks based on sterically-hindered 3-dimensional scaffold

The use of transition metals and coordination chemistry for directing the formation of discrete and infinite supramolecular networks has gained
significant attention in the last two decades.\textsuperscript{42} The coordination bonds formed between transition metal ions and anionic or neutral organic molecules containing functional groups such as \(-\text{CN}, \text{COOH}\) and N-containing heterocycles are of intermediate strength between noncovalent interactions and carbon–carbon bonds of most organic compounds. Thus, the coordination bonds offer structural integrity, and the metal-assisted discrete as well as infinite assemblies find applications in catalysis, luminescent materials, magnetism, nonlinear optics, porous or zeolitic materials and in controlling chirality.\textsuperscript{43}

Wells described the crystal structures in terms of their topology, by reducing them to series of points (vertices/nodes) of certain geometry (tetrahedral, trigonal, octahedral, etc.) that are connected to a fixed number of other points.\textsuperscript{44} The resulting structures, which can be calculated mathematically, can be either discrete (zero-dimensional) polyhedra or infinite (1-, 2-, and 3-dimensional) periodic nets, many of which have concrete counterparts in the form of real chemical structures that provide convenient names to the nets. Robson was primarily responsible for the initial studies that facilitated rapid development of the field of coordination polymers.\textsuperscript{45} He extrapolated Wells work on inorganic network structures to coordination polymers, which are also known as metal-organic frameworks (MOF). The resulting

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Figure 8: The crystal packing of tetraphenol 20 exhibiting the voids for guest inclusion (left). The space-filling CPK model of the crystal packing with the guest molecules removed (right).

Figure 9: The crystal packing of the tetra-acid 21 viewed down a-axis (space-filling model). The guest DMSO and water molecules have been excluded for clarity. Notice the formation of channels.
“node and spacer” approach has been remarkably successful in producing architectures predictably.\(^{42}\)

The targets for crystal engineering of discrete self-assemblies include 2-D rings, squares, Platonic solids (regular polyhedra such as tetrahedron, cube, octahedron, etc.), Archimedean solids\(^{46}\) (regular polygons such as cuboctahedron, snub cube, etc.), spheres, rings, prisms, etc. In the case of coordination polymers, the targets include 1-D helices, 2-D square grids and hexagonal nets. Some simple examples of targets in 3-dimensions are: α-Polonium-(NaCl, 6-connecting octahedral centers), the diamond-, lonsdaleite-, quartz-, and zeolite-related nets (with 4-connecting tetrahedral centers), the NbO net (involving square planar 4-connecting centers with a 90° twist along each connection), the PtS net (with equal number of tetrahedral and square planar centers), various 3-connected (n,3)-nets described by Wells, (3,4)-connected nets such as Pt₃O₄ (square planar and trigonal centers), Ge₃N₄ (tetrahedral and trigonal centers), (3,6)-connected nets such as rutile and pyrite nets, etc.\(^{42}\) Many other uniform nets include (4,6)-connected, (4,8)-connected, and more complex nets with higher connectivity.

Our journey into MOFs was driven by the unique topology of tetraarylimesityls (i.e., 20-23) described earlier.\(^{41}\) We readily recognized that tetrapyridylimesityls (24 and 25, Chart 6) and tetracarboxyphenylimesityls (21 and 23, Chart 5) correspond to unique D\(_{2d}\)-symmetric tetradentate ligands with extended tetrahedral geometry, which may lead to MOFs of unprecedented structures. We have explored metal-assisted coordination polymerization of tetradentate ligand 24 and its tetracarboxyphenyl analog 21. In the following are described the applications of tetrapyridylimesityl 24 to the creation of (i) discrete M₆L₁₂ metal-organic cubes and (ii) 3-dimensional MOFs of unique configurations.

**Discrete metal-organic cubes based on tetrapyridylimesityl 25**

A slow evaporation of the solution of 1:1 molar equiv of Cu(OAc)\(_2\)·H\(_2\)O and the tetrapyridyl ligand 25 in MeOH over a period of 7-10 days yielded dark blue crystals of 26 in 60–65% yield. In a similar manner, pale green crystals of 27 were obtained from a methanolic solution of Ni(NO\(_3\))\(_2\)·6H\(_2\)O and the ligand 25. The single crystal X-ray crystallographic analyses of both of the compounds 26 and 27 showed that they crystallize in the cubic space group, viz., Pn-3n, with only a marginal difference in their cell parameters attesting to their isostructurality. The structure solution in both cases revealed the structures of the compounds to be discrete supramolecular cubes with a perfect O\(_h\) symmetry.\(^{47}\)

As can be seen from Figure 10, 12 ligands and 6 Cu(II) ions assemble to generate a metal organic cube; the six metal cations lie at the centres of six faces of the cube. The coordination geometry of the metal in both of the compounds 26 and 27 is octahedral; while the pyridine rings of four distinct tetratopic ligands 25 were found to be coordinatively bonded to the metal along the equatorial positions, two H\(_2\)O molecules were found to coordinate axially. The formation of cubes might be described as resulting from coordinate covalent bonding between two orthogonally-disposed pyridyl rings of the tetratopic ligand 25 and the metal cations effectively functioning as square-planar centres. Each of the ligands contributes two pyridyl rings towards coordination with the metal ion, while the other two remain uncoordinated. The latter are disposed towards the corners and serve to close up the edges of the cube. Insofar as the dimensions of the cube are concerned, the distance between any two adjacent face-centered metal atoms was found to be ca. 14.75 Å, while that between two opposite face-centered ones was ca. 21.00 Å.
Each cube was found to be surrounded by 8 symmetry-related cubes at the vertices forming a 3D-checker board network (Figure 10). A careful analysis revealed that the lattice is constructed by a vertex-to-vertex alliance of cubes sustained presumably by solvent-mediated interactions, which results in intracube as well as intercube void enclosures. The integrity of the crystal lattice appeared to be sustained by the solvent molecules occupying the void spaces in the crystal lattice. The counter anions, namely CH$_3$COO, could not be identified from difference electron density maps. Supposedly, these anions do not have an ordered structure, and the dynamic nature of their interaction with the atoms of the main skeleton prevents their detection by X-ray diffraction analyses. Otherwise, the construction of 3-dimensional cubic architectures via self-assembly of 12 unique ligands of orthogonal geometry and 6 metal cations with octahedral coordination yet effectively functioning as square-planar centers constituted the first unequivocal X-ray characterization of a metal-organic cube of this particular type. Subsequent to our publication, Yaghi et al. reported an analogous MOF and associated gas adsorption studies.48

Metal-organic frameworks based on tetrapyridylbimesityl 25

We were encouraged by the unique $D_{2d}$-symmetric tetrapyridylbimesityl ligand 25 to explore the construction of 3-dimensional coordination networks by metal-directed self-assembly in particular with $O_h$, $T_d$ and $D_{4h}$ metal centers. The network construction using a combination of $T_d$ ligands and $O_h$ metal centers has been regarded very difficult.49 Best compromise between a 4-connecting ligand and an octahedral metal center turns out to be that of the corundum form of Al$_2$O$_3$ in which both Al$^{3+}$ and O$^{2-}$ ions are distorted from their ideal octahedral and tetrahedral geometries, respectively.50 Thus, by considering the $D_{2d}$-symmetric ligand as a distorted-tetrahedral building block (Figure 11), we envisaged that a metal-organic equivalent of the corundum net could be accessed as shown in Figure 12. Similarly, the combination of $D_{2d}$-symmetric ligand and $T_d$ metal center was surmised to yield an analog of the diamond net, with a difference that each ring in the resultant net is an 8-membered one as opposed to a 6-membered ring in the ideal diamond net (Figure 12). Indeed, Wells pointed out long ago that (10,3)-a and (10,3)-b nets derive from the replacement of tetrahedral nodes of a diamond net by pairs of 3-connecting nodes.44 He showed that (8, 3/4)-b net results from replacement of alternate tetrahedral nodes in a diamond net by pairs of 3-connecting nodes. Further, the combination of a $D_{2d}$-symmetric tetratopic ligand with a square-planar $D_{4h}$ metal center was conceived to afford the PtS network, again with the difference that the resulting network would be constituted by 4- and 12-membered rings instead of 4- and 8-membered rings in the ideal PtS net (Figure 12).

As expected, the reaction of 25 with Zn(ClO$_4$)$_2$.6H$_2$O, Cd(ClO$_4$)$_2$.6H$_2$O, AgNO$_3$ and MnCl$_2$.4H$_2$O led to the corresponding complexes 28-31, respectively.51 While the compounds 28 and 29 (Figure 13) corresponded to the metal-organic equivalents of corundum architecture with no
Figure 11: Representation of tetrapyridylbimesityl 25 as a pair of 3-connecting nodes (similar to allene) and as a polyhedron.

Figure 12: The ideal corundum, diamond and PtS networks are shown on the top. The nets resulting from replacement of tetrahedral nodes by pairs of 3-connecting nodes are shown in the bottom.

interpenetration, those of 30 and 31 led to metal-organic adamantoid and PtS frameworks (Figures 14 and 15), respectively. In both of these cases, the networks were found to be doubly interpenetrated. In spite the interpenetration, the MOFs were found to be highly porous. Clearly, the utility of unique $D_{2d}$-symmetric-tetratopic tetrapyridylbimesityl ligand 25 as a pair of 3-connecting node in coordination polymerization was elegantly demonstrated.

4. Conclusions

As mentioned at the outset, I have described some results of our research that demonstrate exploitation of steric in uncovering some novel synthons and engineering molecular organization toward porous hydrogen-bonded as well as metal-ligand coordination networks; it must be noted that exhaustive citation to the literature has been deliberately avoided. A lot of unpublished work
concerns with sterically-hindered pyrenes, which exhibit remarkable lattice inclusion property with a variety of guest molecules; these systems have been applied to separate closely related regio and stereo isomers, trap one of the two tautomeric forms of 1,3-diketones, freeze out a high-energy conformer
of otherwise flexible cyclic alkanes, etc. We have applied ‘sterics’ to inhibit \( \pi \)-stacking and also prohibit crystallization itself to develop amorphous materials for application in organic light emitting diodes.\(^{52}\) Clearly, exploration of the influence of sterics on the manifestation of intermolecular interactions and utilization in the rational design of molecular modules are exciting prospects; of course, steric- and intermolecular interaction-control of thermal as well as photochemical reactions is one of our research interests.\(^{13}\)

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