JOC *Note*

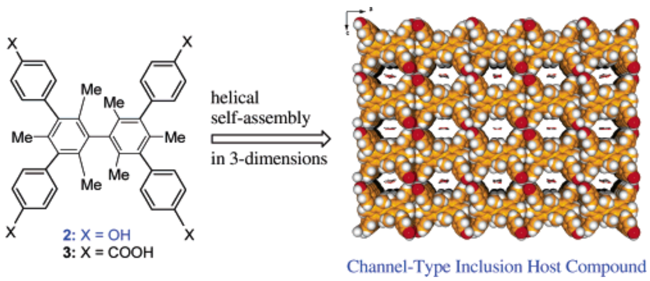
Three-Dimensional Four-Connecting Organic Scaffolds with a Twist: Synthesis and Self-Assembly

Jarugu Narasimha Moorthy,*,†
Ramalingam Natarajan,† and Paloth Venugopalan‡

Department of Chemistry, Indian Institute of Technology, Kanpur - 208 016, India, and Department of Chemistry, Panjab University, Chandigarh - 160 014, India

moorthy@iitk.ac.in

Received June 14, 2005



Channel-Type Inclusion Host Compound

We have synthesized a novel class of *four-connecting three-dimensional* molecular scaffolds **2**−**5** based on biaryls for supramolecular self-assembly. The X-ray crystal structure analysis of **2** with ethanol reveals a novel *O−H···O hydrogen-bonded helical self-assembly in three dimensions* leading to the generation of channels in the crystal lattice. The tetraacid **3** also forms analogous channels in which the solvent molecules, viz., DMSO and H_2O, reside. The structures of **2** and **3** amply illustrate the potential of three-dimensional four-connecting biaryls in developing functional mimics of inorganic zeolites.

Control of molecular organization is pivotal for the development of organic solids with predefined functional properties.[1] Whereas the recent literature in supramolecular chemistry is replete with examples of control of molecular organization in one and two dimensions,[2,3] that in the third dimension continues to be a challenging proposition;[4] one of the reasons for this may be traced to a limited number of three-dimensional molecular scaffolds that could be exploited for self-assembly in three dimensions by installing functional groups responsible for reliable synthons[5] at strategic locations.[6] Control of molecular ordering in three dimensions is particularly relevant to developing porous organic solids. In view of the fact that the chirality can be readily introduced at a molecular level, there is a growing interest in developing molecular networks that functionally mimic the properties of inorganic zeolites.[7] A prudent approach to the development of porous organic materials constitutes molecular tectonics,[6e] an art of building solids based on molecules with predesigned topologies and properties, which hinges on two key aspects, viz., the geometrical features of the building block and location as well as choice of functional groups that lend themselves to reliable, repetitive, and robust association motifs/synthons. We have recently conceived of a unique *four-connecting three-dimensional module* (**1**, Scheme 1) based on bimesityl core for supramolecular self-assembly, and demonstrated its utility in the self-assembly of three-dimensional discrete[8a] as well as polymeric coordination architectures.[8b] We reasoned that installation of functional groups such as hydroxyl and carboxyl at the para positions of 3,3′,5,5′-tetraphenylbimesityl (**2** and **3**, Scheme 1) could yield hydrogen-bonded networks with voids for guest inclusion.[9] Indeed, it was readily surmised that linear linkage, for example, of the tetraacid **3** via the dimeric motif of the carboxyl group, should afford the polymeric (10,3)-b net[10] as shown in Figure 1, in which the channels run in a perpendicular direction. We have thus synthesized the unique three-dimensional modules **2**−**5** based on bimesityl core and explored their self-assembly based on O−H···O hydrogen bonding. A further advantage with bimesityl core unit could be gauged from the feasibility for facile structural expansion as can be seen, for example, with the expanded derivatives **4** and **5** (Scheme 1). Herein, we report the facile synthesis of structurally novel tetrarylbimesityls **2**−**5** based on a 4-fold Suzuki coupling protocol and novel self-assembly

---

[†] Indian Institute of Technology.

[‡] Panjab University.

[1] (a) Desiraju, G. R. *Crystal Engineering. The Design of Organic Solids*; Elsevier: Amsterdam, The Netherlands, 1989. (b) Langley, P. J.; Hulliger, J. *Chem. Soc. Rev.* **1999**, *28*, 279. (b) Hollingsworth, M. D. *Science* **2002**, *295,* 2410.

[2] (a) MacDonald, J. C.; Whitesides, G. M. *Chem. Rev.* **1994**, *94*, 2383. (b) Lawrence, D. S.; Jiang, T.; Levett, M. *Chem. Rev.* **1995**, *95*, 2229.

[3] (a) Melendez, R. E.; Hamilton, A. D. *Top. Curr. Chem.* **1998**, *198*, 97. (b) Tanaka, T.; Tasaki, T.; Aoyama, Y. *J. Am. Chem. Soc.* **2002**, *124*, 12453.

[4] (a) Gong, B.; Zheng, C.; Skrzypczak-Jankun, E.; Yan, Y.; Zhang, J. *J. Am. Chem. Soc.* **1998**, *120*, 11194. (b) Sharma, C. V. K.; Clearfield, A. *J. Am. Chem. Soc.* **2000**, *122*, 4394. (c) Malek, N.; Maris, T.; Perron, M.-E.; Wuest, J. D. *Angew. Chem., Int. Ed.* **2005**, *44*, 4021.

[5] Desiraju, G. R. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2311.

[6] Our thorough literature search has revealed only a limited number of three-dimensional molecular systems, which have been exploited for crystal packing in three dimensions; see: (a) Ermer, O. *J. Am. Chem.* Soc. **1988**, *110*, 3747. (b) Boldog, I.; Rusanov, E. B.; Sieler, J.; Blaurock, S.; Domasevitch, K. V. *Chem. Commun.* **2003**, 740. (c) Holy, P.; Zavada, J.; Cisarova, I.; Podlaha, J. *Angew. Chem., Int. Ed.* **1999**, *38*, 381. (d) Holy, P.; Zavada, J.; Cisarova, I.; Podlaha, J. *Tetrahedron Asymmetry* **2001**, *12*, 3035. (e) Wang, X.; Simard, M.; Wuest, J. D. *J. Am. Chem. Soc.* **1994**, *116*, 12119. (f) Reddy, D. S.; Craig, D. C.; Desiraju, G. R. *J. Am. Chem. Soc.* **1996**, *118*, 4090. (g) Brunet, P.; Simard, M.; Wuest, J. D. *J. Am. Chem. Soc.* **1997**, *119*, 2737. (h) Reddy, D. S.; Dewa, T.; Endo, K.; Aoyama, Y. *Angew. Chem., Int. Ed.* **2000**, *39*, 4266. (i) Thaimattam, R.; Sharma, C. V. K.; Clearfield, A.; Desiraju, G. R. *Cryst. Growth Des.* **2001**, *1*, 103. (j) Fournier, J.-H.; Maris, T.; Wuest, J. D.; Guo, W.; Galoppini, E. *J. Am. Chem. Soc.* **2003**, *125*, 1002. (k) Fournier, J.-H.; Maris, T.; Simard, M.; Wuest, J. D. *Cryst. Growth Des.* **2003**, *3*, 535. (l) Boldog, I.; Rusanov, E. B.; Chernega, A. N.; Sieler, J.; Domasevitch, K. V. *Angew. Chem., Int. Ed.* **2001**, *40*, 3435. (m) Sauriat-Dorizon, H.; Maris, T.; Wuest, J. D. *J. Org. Chem.* **2003**, *68*, 240. (n) Laliberte, D.; Maris, T.; Wuest, J. D. *J. Org. Chem.* **2004**, *69*, 1776.

[7] (a) Janiak, C. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1431. (b) Seo, J. S.; Whang, D.; Lee, H.; Jun, S. I.; Oh, J.; Jeon, Y. J.; Kim, K. *Nature* **2000**, *404*, 982. (c) Wu, C.-D.; Hu, A.; Zhang, L.; Lin, W. *J.* Am. Chem. Soc. **2005**, *127*, 8940. (d) Fang, Q.; Zhu, G.; Xue, M.; Sun, J.; Wei, Y.; Qiu, S.; Xu, R. *Angew. Chem., Int. Ed.* **2005**, *44*, 3845.

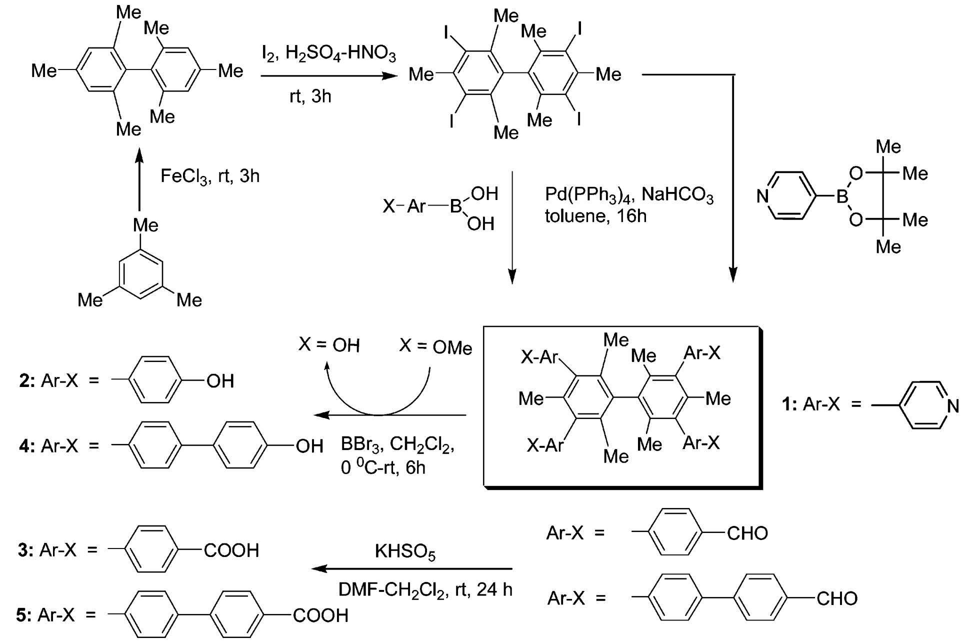
[8] (a) Natarajan, R.; Savitha, G.; Moorthy, J. N. *Cryst. Growth Des.* **2005**, *5*, 69. (b) Natarajan, R.; Savitha, G.; Dominiak, P.; Wozniak, K.; Moorthy, J. N. *Angew. Chem., Int. Ed.* **2005**, *44*, 2115.

[9] For remarkably porous networks based on anthracene-bisresorcinol by Aoyama and co-workers, see: (a) Endo, K.; Ezuhara, T.; Koyanagi, M.; Masuda, H.; Aoyama, Y. *J. Am. Chem. Soc.* **1997**, *119*, 499. (b) Dewa, K.; Endo, K.; Aoyama, Y. *J. Am. Chem. Soc.* **1998**, *120*, 8933.

[10] Wells, A. F. *Three-Dimensionanl Nets and Polyhedra*; Wiley-Interscience: New York, 1977.

10.1021/jo051205z CCC: $30.25

SCHEME 1. Synthesis of Bimesityls 1−5



of tetraphenol **2** and tetraacid **3** into channel-type inclusion host compounds.[11]

The synthesis of tetraaryl derivatives of bimesityl was accomplished by Suzuki coupling[12] between arylboronic acids and 3,3′,5,5′-tetraiodobimesityl; the latter was synthesized by subjecting the readily prepared bimesityl[13] to tetraiodination with I_2 in acetic acid containing a mixture of Conc $H_2SO_4-HNO_3$. Thus, the coupling of tetraiodobimesityl with *p*-methoxyphenylboronic acid and 4′-methoxybiphenyl-4-boronic acid[14] followed by demethylation with BBr_3 yielded tetrakis(4-hydroxyphenyl)bimesityl **2** and tetrakis(4-hydroxybiphenyl)bimesityl **4**, respectively (Scheme 1). The coupling of tetraiodobimesityl with formyl-substituted boronic acids in a similar way led to the isolation of formyl derivatives, which were oxidized with oxone ($KHSO_5$) to the corresponding acids **3** and **5**.[15]

The phenolic OH groups exhibit a varied array of packing motifs of which the helical motif is the most frequently observed one, while the dimeric one is the least encountered.[16] In contrast, the carboxyl groups predominantly adopt the dimeric/catemeric motif,[17] although other modes of association are known with a low statistical probability.[18] Given that the tetrarylbimesityls are rigid architectures, the least encountered linear self-assembly of the hydroxyl and most frequently observed dimeric motif of the carboxyl groups located at para positions of the phenyl rings as in **2** and **3** was, in principle, expected to yield a porous (10,3)-b net as shown in Figure 1. Expectedly, the tetraphenols **2** and **4** were found to exhibit ready guest inclusion as revealed by the ^1H NMR analyses of the crystals grown from different solvents. Whereas **2** was found to incorporate in its lattice the guest molecules such as ethanol, ethyl formate, and ethyl acetate, the expanded analogue **4** was found to include larger molecules such as *p*-xylene (1H:3G), mesitylene (1:1G), and anisole (1H:2G); see the Supporting Information. While good single crystals suitable for X-ray analysis could be grown readily for **2** from ethanol with the stoichiometry **2**•2 EtOH (vide infra), our attempts to obtain the inclusion compounds of **2** with other guest molecules were in vain. Figure 2 shows the crystal-packing diagram of the tetraphenol **2**. The core mesitylene rings are almost orthogonal with the molecule sitting on the 2-fold *c*-axis (orthorhombic, $P2_12_12$). The *p*-hydroxyphenyl rings are also almost orthogonal (83.3 and 94.3°) to each of the mesitylene rings of the bimesityl skeleton. The remarkable crystal packing, which results in the formation of voids for guest incorporation, may be described as follows. Each of the hydroxyl groups is a

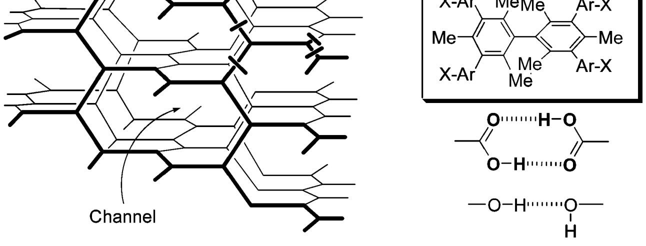


FIGURE 1. Packing type anticipated for three-dimensional modules **2−5**.

---

[11] Bishop, R. *Chem. Soc. Rev.* **1996**, *25*, 311.

[12] Hassan, J.; Sevignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359.

[13] Cahiez, G.; Chaboche, C.; Mahuteau-Betzer, F.; Ahr, M. *Org. Lett.* **2005**, *7*, 1943.

[14] Virgil, P.; Peihwei, C.; Masaya, K. *Macromolecules* **1994**, *27*, 4441.

[15] Travis, B. R.; Sivakumar, M.; Hollist, G. O.; Borhan, B. *Org. Lett.* **2003**, *5*, 1031.

[16] (a) Brock, C. P.; Duncan, L. L.; *Chem. Mater.* **1994**, *6*, 1307. (b) Thallapally, P. K.; Katz, A. K.; Carrel, H. L.; Desiraju, G. R. *Chem. Commun.* **2002**, 344.

[17] (a) Kolotuchin, S. V.; Fenlon, E. E.; Wilson, S. R.; Loweth, C. J.; Zimmerman, S. C. *Angew. Chem., Int. Ed.* **1995**, *34*, 2654. (b) Almarsson, Ö.; Zaworotko, M. J. *Chem. Commun.* **2004**, 1889.

[18] For example, for unique helical self-assembly of aromatic carboxylic acids, see: Moorthy, J. N.; Natarajan, R.; Mal, P.; Venugopalan, P. *J. Am. Chem. Soc.* **2002**, *124*, 6530.

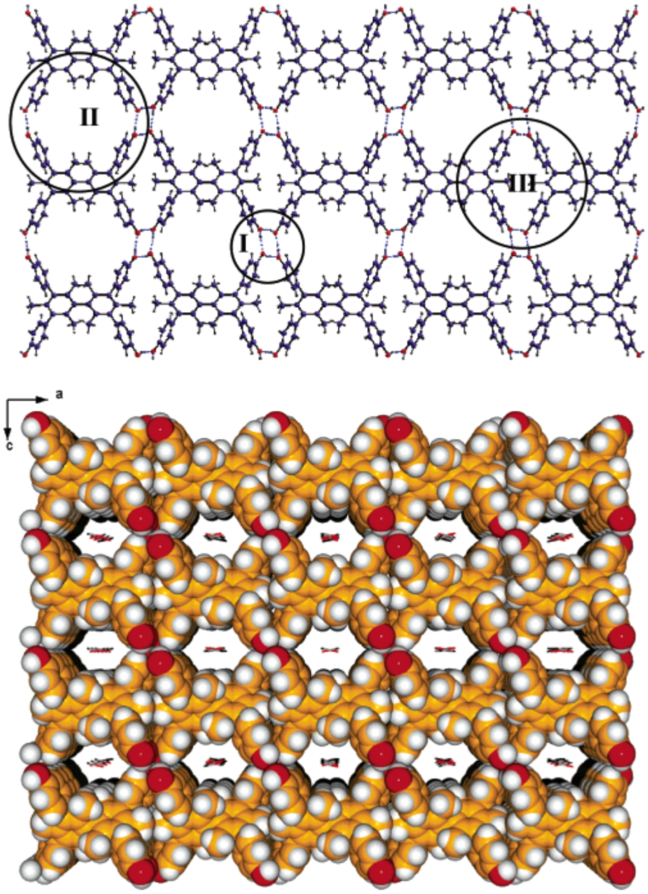


FIGURE 2. Crystal packing of tetraphenol **2**. The bottom space-filling diagram reveals the voids (guest EtOH molecules are shown with a ball-and-stick model) resulting from the self-assembly of **2** via O−H···O hydrogen bonds.

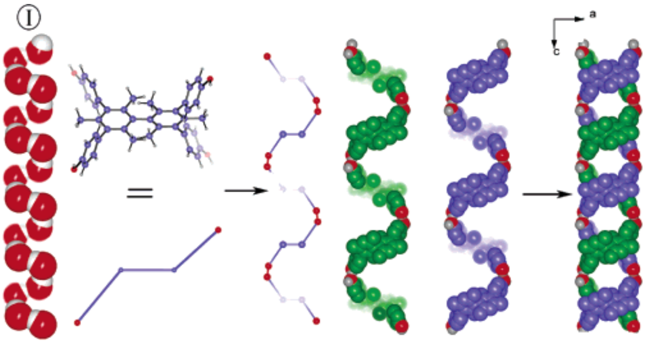


FIGURE 3. Helical self-assembly of the hydroxy groups of four symmetry-related molecules (**I**). Also shown is how the helical propagation of **2** occurs along the *Z*-axis via O−H···O hydrogen bonds between two of the hydroxyphenyl rings of the tetraphenol **2**.

donor as well as an acceptor. The hydroxyl groups of four distinct translation- and 2_1-screw-related molecules self-assemble to produce a hydrogen-bonded "*psuedo helical spine*" along the *b*-axis as shown by the pattern I in Figures 2 and 3; the geometrical parameters for the two O−H···O hydrogen bonds are as follows: $d_{\mathrm{O-H\cdots O}} = 1.863(4)$ Å, $D_{\mathrm{O\cdots O}} = 2.663(5)$ Å, and $\theta_{\mathrm{O-H\cdots O}} = 164.8°$; $d_{\mathrm{O-H\cdots O}} = 1.993(4)$ Å, $D_{\mathrm{O\cdots O}} = 2.788(6)$ Å, and $\theta_{\mathrm{O-H\cdots O}} = 163.3°$. The unique hydrogen-bonding ensures helical self-assembly along both *a*- and *c*-axes as well (see patterns II and III); the propagation along the latter is typically shown in Figure 3. Remarkably, the helical *spine* formation results in the generation of parallel channels down *b*-axis in which the guest molecules reside.[19] Indeed, each channel may be described as arising from two parallel helices constructed via hydrogen bonding between the tetraphenols **2** by utilizing only two of the four *p*-hydroxyphenyl rings (pattern II) as shown in Figures 2 and 4. Thus, the crystal packing of **2** is mediated entirely by O−H···O hydrogen bonded helices in all three dimensions.[20]

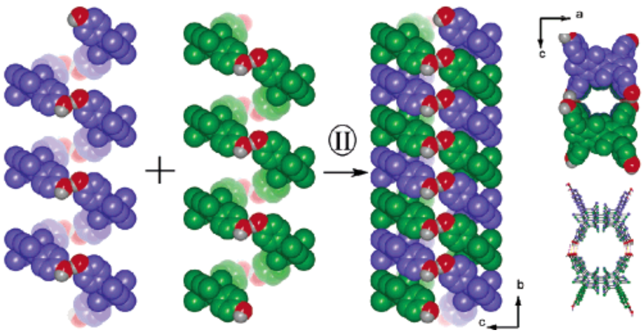


FIGURE 4. Formation of a porous channel from two parallel helices generated each by the self-assembly of **2** via O−H···O hydrogen bonds. Note that only two *p*-hydroxyphenyl groups are involved in the assembly.

As mentioned earlier, the expanded analogue **4** yielded only needles with various aromatic guest molecules, which were unsuitable for X-ray work. We believe that hydrogen bonding between the phenolic OH groups, as observed in the case of **2,** control the crystal packing in the complexes of **4** as well. The crystallization of tetraacid **3** 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, vide infra. The crystals were found to lose crystallinity once they were removed from the mother liquor. The crystal structure analysis shows that the tetraacid **3** crystallizes in the space group *Pbca* with each of the carboxyl hydrogens bonded to DMSO/H_2O via a hydrogen bond (Figure 5). From the difference Fourier analysis, we succeeded in locating five DMSO and two H_2O molecules. The overall crystal packing of **3** is as follows. The glide-related acid molecules **3** along the *a*-axis associate via aryl−aryl edge-to-face[21] (C−H···π) stacking interactions, cf. Supporting Information; it should be noted that one of the hydrogens of the *p*-carboxyphenyl rings points toward the e-rich mesitylene core. This mode of association leads to the formation of strands running along *a*-axis, within which occur the channels in which the solvent molecules reside, cf. the Supporting Informa-

---

(19) For hydrogen-bonded helical (3_1-screw) assembly of aliphatic cyclic diols into inclusion host systems, see: Kim, S.; Bishop, R.; Craig, D. C.; Dance, I. G.; Scudder, M. L. *J. Org. Chem.* **2002**, *67*, 3221 and references therein.

(20) An altogether different mode of packing has been reported for the analogous tetraphenols based on spirobifluorene and tetraphenylmethanes, which presumably is due to various ways in which the phenolic hydroxyl groups self-assemble, see: (a) Fournier, J.-H.; Maris, T.; Wuest, J. D. *J. Org. Chem.* **2004**, *69*, 1762. (b) Fournier, J.-H.; Maris, T.; Simard, M.; Wuest, J. D. *Cryst. Growth Des.* **2003**, *3*, 535.

(21) (a) Jennings, W. B.; Farrell, B. M.; Malone, J. F.; *Acc. Chem. Res.* **2001**, *34*, 885. (b) Meyer, E. A.; Castellano, R. K.; Diedrich, F. *Angew. Chem., Int. Ed.* **2003**, *42*, 1210. (c) Aravinda, S.; Shamala, N.; Das, C.; Sriranjini, A.; Karle, I. L.; Balaram. P. *J. Am. Chem. Soc.* **2003**, *125*, 5308.

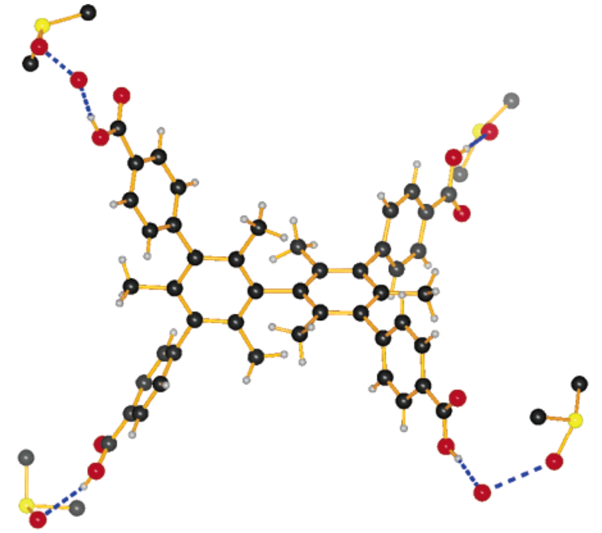


FIGURE 5. Ball-and-stick representation of acid **3**, which is hydrogen bonded directly and via H_2O to four DMSO molecules; for the sake of clarity, only major positions of DMSO are shown.

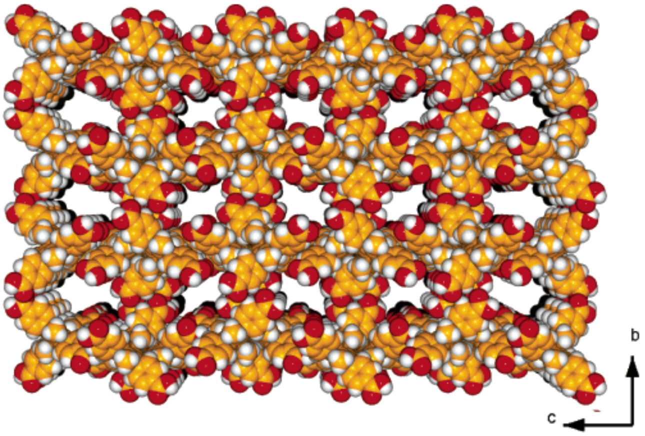


FIGURE 6. Crystal packing of acid **3** viewed down the *a*-axis. Notice the formation of channels.

tion. Presumably, these solvent molecules act as an adhesive to hold the strands together. The formation of channels between the strands is shown in Figure 6.

Due to weak diffraction of the crystals caused by severe disorder of the solvent molecules in the channels, which leads to a structure with poor figures of merit ($R_1 =$ 0.174), we have not attempted to analyze various interactions involved in the overall crystal packing. Otherwise, the ability of the three-dimensional D_{2d}-symmetric tetraacid **3** to exhibit inclusion properties is amply revealed from the X-ray crystal structure analysis, although the expected dimer motif of the carboxyl groups is not observed due to competitive hydrogen bonding by DMSO/H_2O with the acid hydrogens. Our attempts to obtain inclusion crystals of the expanded acid **5** have heretofore been unsuccessful. Given the various possible ways in which both acids as well as phenols may self-assemble, tetraphenol **2** and the tetracid **3** may in principle crystallize out in different polymorphic forms depending on the conditions of crystalllization. We have, however, not been successful in identifying polymorphic growth of **2** and **3** thus far.

In summary, we have accomplished the synthesis (4-fold Suzuki coupling) of a novel class of three-dimensional four-connecting molecular scaffolds based on biaryls and explored their hydrogen-bonded self-assembly. The tetraphenol **2** is found to include in its crystal lattice the guest molecules such as ethyl formate, ethyl acetate, ethanol, etc. The X-ray crystal structure analysis of the inclusion compound with ethanol reveals a novel helical self-assembly based on O−H···O hydrogen bonds in all of the three dimensions, which results in the creation of channels in the lattice. The biphenyl-expanded tetraphenol **4** is found to include *larger* guest molecules such *p*-xylene, anisole, mesitylene, etc., as revealed from ^1H NMR spectroscopic analysis of the solid inclusion crystals. That the tetraacid **3** also forms analogous channels in which the solvent molecules, viz., DMSO and H_2O, are found to reside is revealed by the single-crystal X-ray structural analysis. While the expected dimer motif is not observed due to competitive hydrogen bonding of DMSO/H_2O with the carboxylic acid hydrogens, the formation of channels in the crystal lattice amply illustrates the potential of three-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, particularly with tetrapyridyl derivatives. We are presently exploring the utility of these unique scaffolds in the development of porous and chiral organic and metal-organic frameworks.

Experimental Section

The synthetic procedures and characterization data for the tetraarylbimesityls **2**−**5** are described in the Supporting Information.

X-ray Crystal Structure Determination of 2 and 3. The tetraphenol **2** was crystallized by slow evaporation of the solution of **2** in ethanol over 4−5 days, and the tetraacid **3** was crystallized by slow diffusion of toluene into a solution of **3** in DMSO. The X-ray intensity data were collected for **2** on an Enraf-Nonius CAD4 and for **3** on a Bruker SMART APEX CCD diffractometer. For both **2** and **3**, a graphite-monochromated MoKα (λ = 0.71073 Å) radiation was employed at 293(2) and 100(2) K, respectively. Both of the structures were solved by direct methods using SHLEXS-97 and refined by full-matrix least-squares method based on F^2 using SHLEXL-97.

Crystal data for 2: molecular formula $C_{42}H_{38}O_4\cdot C_2H_6O$; orthorhombic, $P2_12_12$ (No. 18), a = 25.418(5) Å, b = 6.2412(12) Å, c = 12.466(3) Å, V = 1977.6(1) Å^3, Z = 4, 3047 reflections collected of which 893 are unique, GOOF = 0.974, R_1 = 0.0580; wR_2 = 0.0785, for [$I > 2\sigma(I)$].

Crystal data for 3: molecular formula $C_{56}H_{42}O_{15}S_5$; orthorhombic, *Pbca* (No. 61), a = 13.5422 (14) Å, b = 28.132(3) Å, c = 1 31.458(3) Å, V = 11985(2) Å^3, Z = 8, 9369 reflections collected of which 4103 are unique, GOOF = 1.755, R_1 = 0.1746; wR_2 = 0.3086, for [$I > 2\sigma(I)$].

Acknowledgment. We are thankful to the Department of Science and Technology (DST, India) for generous financial support.

Supporting Information Available: The details of synthesis of bimesityls **2**−**5**, ^1H and ^{13}C NMR spectra of **2**−**5**, and packing diagrams of **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO051205Z