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Crystal Engineering: Lattice Inclusion Based on O–H···O Hydrogen-Bonded Self-Assembly and Guest-Induced Structural Mimicry

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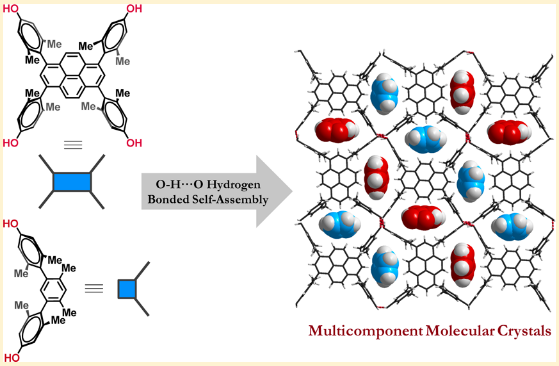
S Supporting Information

ABSTRACT: Pyrene–tetraphenol **TP2** constitutes a molecular system with inherent features for inclusion of two or more guest molecules that are complementary in terms of size and shape. Hydrogen-bonded self-assembly of **TP2** in the solid state is shown to lead to voids within which the guest molecules are incorporated. A large aromatic expanse extant to the pyrene core in **TP2** permits inclusion of two different types of guest species interchangeably. The robust association manifests in packing equivalence in all of the inclusion compounds of **TP2** with the exception of the compound formed with pyridine and *o*-dichlorobenzene guests; in the latter, pyridine terminates the otherwise 3-dimensional hydrogen-bonded organization. The half-component of **TP2**, i.e., 4,6-bis(4-hydroxyphenyl)-*m*-xylene (**BX**), deduced by simple structural reduction, is shown to exhibit guest inclusion, but with considerably less guest accessible volume. The limited yet meaningful set of guests allows mimicry of the two expected patterns of molecular organization based on hydrogen bonding for both **TP2** and **BX** in the solid state.



INTRODUCTION

Strong and directional hydrogen bonds[1] are an invaluable glue in the tool kit of a molecular engineer concerned with constructing functional supramolecular structures.[2] As the properties of macroscopic bulk solids depend on organization of the constituent molecular modules, the functional properties can in principle be fine-tuned via subtle changes at the molecular level.[2] The knowledge of supramolecular synthons[3] has advanced significantly in the past few years to facilitate targeted self-assembly. The molecules can now be programmed to self-assemble in a specific fashion by incorporating certain functional groups that manifest in the form of supramolecular synthons–the aggregation motifs between functional groups that are reproduced reliably in molecular crystals.[3,4] The prime goal of *crystal engineering*[5] is to exploit the wealth of intermolecular interactions to control organization of molecules in pursuit of predetermined functions. One aspect of research that continues to be actively pursued is the development of porous organic solids based on hydrogen bonds,[6] which are being increasingly uncovered for a variety of applications such as gas adsorption in a manner akin to metal–organic open frameworks,[7] separation,[8] stereoselective reactions of the included guest molecules,[9] etc. Further, lattice inclusion of guests permits access to binary or higher order multicomponent molecular crystals,[10] which are of immense importance in pharmaceutical industry.[11]

Development of organic solids with voids for inclusion of guest species is challenging and entails a diligent design at the molecular level.[6,12] We showed recently that 1,3,6,8-tetrakis(4-methoxy-2,6-dimethylphenyl)pyrene **TP1**—a molecular system that is devoid of any strongly interacting functional groups and characterized by a planar base decked up at its four corners with aromatic panes—exhibits three different domains, namely trough, basin, and concave, for inclusion of guest species in the solid state,[10c,d,f,g] Chart 1; the sterics incorporated through the methyl groups at the ortho positions of the aryl rings ensure that the latter lie almost orthogonally. The otherwise moderate conformational flexibility inherent to the aryl rings was shown to impart the molecular system with considerable adaptability to bind diverse guest molecules, despite the fact that the host molecules in the lattice are stabilized by weak interactions.[10c,d,f,g] The abundant inclusion behavior exhibited by the host **TP1** spurred us to examine O–H···O hydrogen-bonded aggregation of such host systems. Of course, the objectives were to (i) control molecular organization in pursuit of creating porous solids with well-defined voids for guest inclusion and (ii) examine the possibility of formation of biporous organic solids that may allow size- and/or shape-selective guest inclusion of two or more guest species leading to multicomponent molecular materials. We specifically chose phenolic functionality as in 1,3,6,8-tetrakis(4-methoxy-2,6-dimethylphenyl)pyrene **TP2** to engineer O–H···O hydrogen-bonded aggregation of molecules in view of the noted propensity of the phenolic hydroxyl groups to exhibit varied set of synthons,[13] which were surmised to manifest in different

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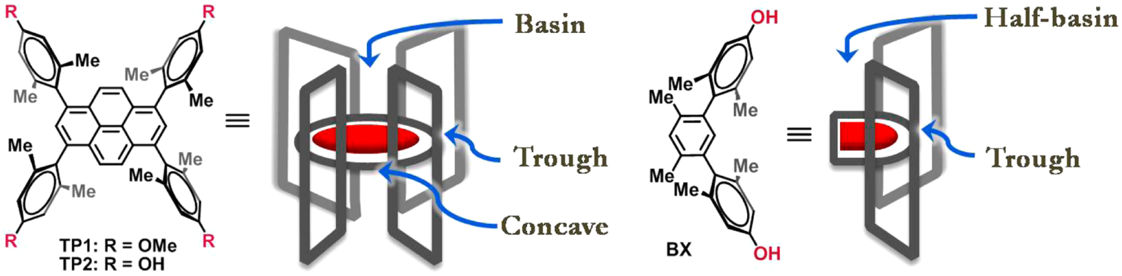
Chart 1



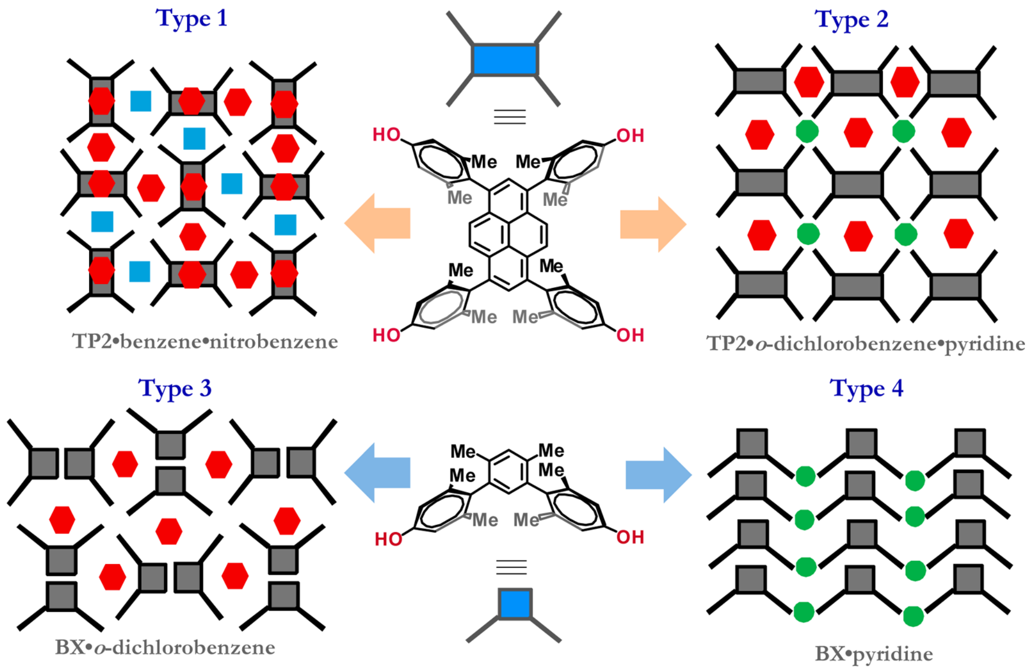


Figure 1. Schematic representation of the two different modes by which the hosts **TP2** and **BX** pack with inclusion of the guests.

modes of the assembly of **TP2**. A simple and naïve analysis of the assembly of host **TP2** based on the most prevalent "chain" synthon suggests two ways, i.e., types 1 and 2, cf. Figure 1, by which the molecules might be glued together. We herein demonstrate that these two modes of organizations can be mimicked with different guests. Further, the topological features of the host system allow simultaneous inclusion of two distinct guests. It is also shown that the half-component **BX** deduced by slicing the host into two halves, i.e., bis(4-hydroxyphenyl)-*m*-xylene, likewise undergoes self-assembly in a manner akin to **TP2** (Figure 1), but that the lack of aromatic expanse alleviates its inclusion behavior.

■ RESULTS AND DISCUSSION

Synthesis and Inclusion Behavior of the Hosts TP2 and BX. The syntheses of hosts **TP2** and **BX** were accomplished via BBr_3-mediated demethylation of the known precursor methoxy derivatives,[10c] Scheme 1. The inclusion behavior of both **TP2** and **BX** was examined by dissolving the compounds in methanol and ethyl acetate, repectively, in the presence of added guest. The crystals that grew with time were analyzed by ^{1}H NMR as well X-ray crystal structure determinations. In Table 1 are consolidated the results of guest inclusion for both **TP2** and **BX** with benzene, benzonitrile, nitrobenzene, *o*-dichlorobenzene, and pyridine.

Table 1. Inclusion Compounds of TP2 and BX, Host:Guest Ratios, Their Codes, Space Groups, and Guest-Accessible Volumes (V)

host	inclusion compound	host/ guest ratio	code	space group	*V* (%)
TP2	**TP2**·benzene	1:4	**TP2**-B	$P2_1$	57
TP2	**TP2**·nitrobenzene	1:2	**TP2**-NB	$P2_1/c$	42
TP2	**TP2**·nitrobenzene·benzene	1:1:2	**TP2**-NB-B	$P2_1$	59
TP2	**TP2**·benzonitrile	1:2	**TP2**-BN	$P2_1/c$	34
TP2	**TP2**·*o*-dichloro benzene·pyridine	1:4:2	**TP2**-C-P	*P*-1	63
BX	**BX**·benzene	1:1	**BX**-B	$P2_1/c$	29
BX	**BX**·nitrobenzene	1:1	**BX**-NB	$P2_1/c$	34
BX	**BX**·benzonitrile	1:1	**BX**-BN	$P2_1/c$	31
BX	**BX**·*o*-dichlorobenzene	1:1	**BX**-C	*P*-1	33
BX	**BX**·pyridine	1:1	**BX**-P	$P2_1/c$	35

As shown in Table 1, crystallization with benzene and nitrobenzene led to ternary crystals with well-defined stoichiometry. The crystallization with pyridine in the presence of various guests was attempted, but the crystals were obtained only with *o*-dichlorobenzene. In a similar vein, crystallization of **BX** led to binary inclusion compounds with each of the guests, but none of the attempts led to ternary crystals suggesting thereby no evidence for their formation. The host-guest ratios

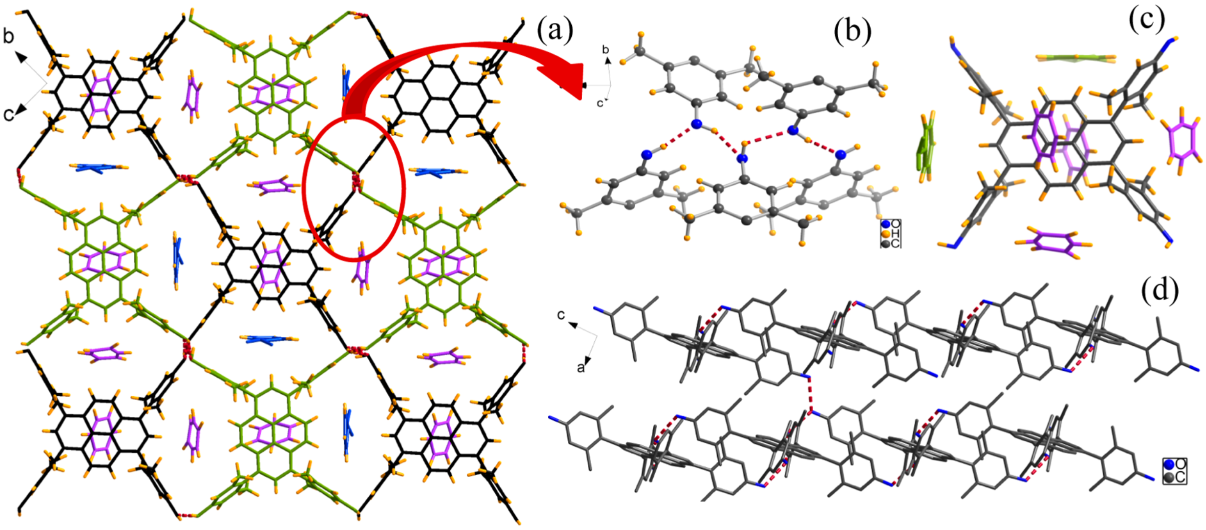
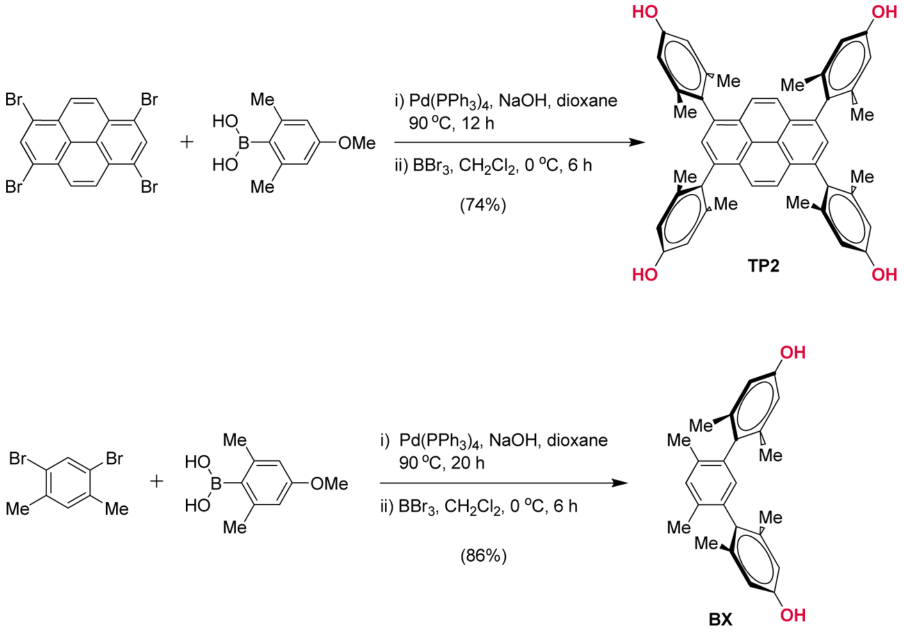


Figure 2. Crystal packing of **TP2**-NB-B, which depicts alternate orientations of the adjacent host molecules. Notice the relative dispositions of benzene (purple) and nitrobenzene (blue) channels (a). A section has been magnified to show the zigzag O−H···O hydrogen bonds down the *a*-axis, which connect the 2-D layers formed along the *bc*-plane down the *a*-axis (b). The various domains of the host molecule occupied by the guest benzene (purple) and nitrobenzene (green) are shown (c). A section of the 2-D layers propagating along the *a*-axis is shown with the hydrogen atoms omitted for clarity (d).

Scheme 1



for all of the inclusion compounds were established by ^{1}H NMR as well as thermogravimetric analyses; the TGA profiles and ^{1}H NMR spectra are included as part of the Supporting Information. In the following sections are discussed the inclusion modes of various guests in **TP2** and **BX**.

The Guest Inclusion by 1,3,6,8-Tetrakis(4-hydroxy-2,6-dimethylphenyl)pyrene, TP2. The crystal structure of **TP2**·nitrobenzene·benzene, i.e., **TP2**-NB-B, is representative of the guest inclusion phenomenon exhibited by **TP2** with benzene (**TP2**-B), benzonitrile (**TP2**-BN), and nitrobenzene (**TP2**-NB), while the crystals of **TP2**-B, **TP2**-BN, and **TP2**-NB-B are isostructural and contain guest molecules in all three domains, i.e., trough, concave, and basin. Those of **TP2**-NB differ marginally in the sense that the basin regions are devoid of guests, vide infra. Thus, the crystal structure of **TP2**-NB-B suffices to illustrate the inclusion phenomenon of **TP2** in **TP2**-B, **TP2**-BN, and **TP2**-NB. The crystals of **TP2**-NB-B were found to belong to the $P2_1$ space group with the asymmetric unit cell containing one molecule each of the host and nitrobenzene and two molecules of benzene. Analysis of the crystal structure shows that the host molecules are stitched up by O−H···O hydrogen bonds leading to molecular self-assembly in all the three dimensions, cf. Figure 2. One observes that the host molecules in the *bc*-plane are organized in a particular readily recognizable manner. As shown in Figure 2, the trough region formed between the two dimethylphenol rings of one **TP2** molecule is closed up by two dimethylphenol rings of a symmetry-related **TP2** molecule that afford concave enclosure. In other words, two host **TP2** molecules that are orthogonally oriented in the *bc*-plane are linked up by O−

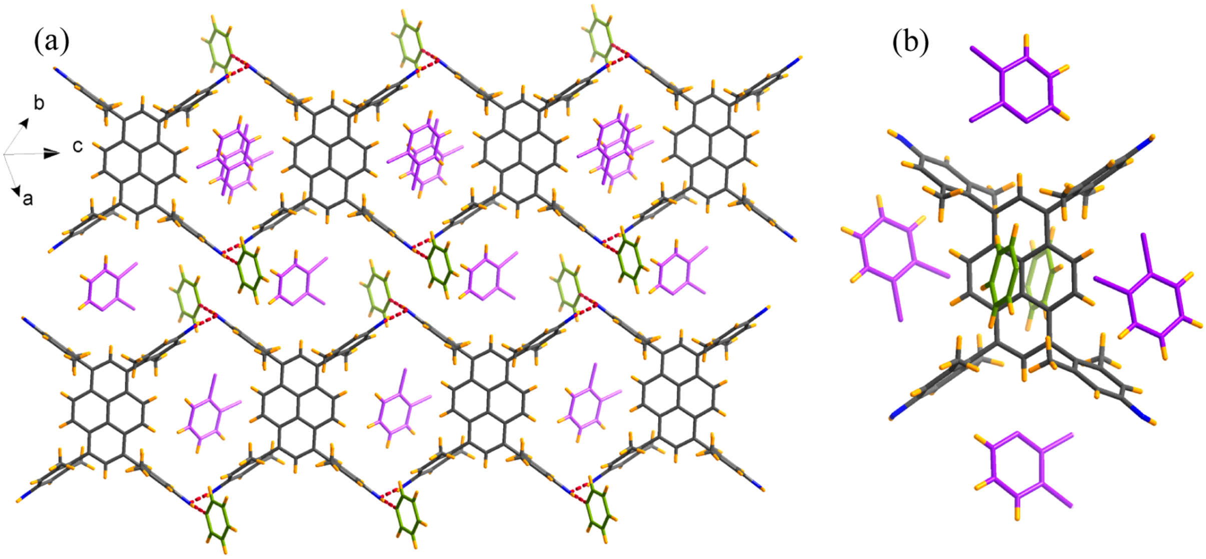


Figure 3. Crystal packing of **TP2**-C-P depicting the large empty spaces, which extend as channels down the *a*-axis. These channels are filled by *o*-dichlorobenzene guest (purple). Each host molecule accommodates *o*-dichlorobenzene guests in trough and concave regions and pyridine (green) in the basin region. Pyridine molecules (green) act as terminators of hydrogen-bonding resulting in the formation of 1-D linear strands that propagate along the *c*-axis (a). In each host molecule, *o*-dichlorobenzenes occupy the trough and concave regions, while the pyridine occupies the basin region (b).

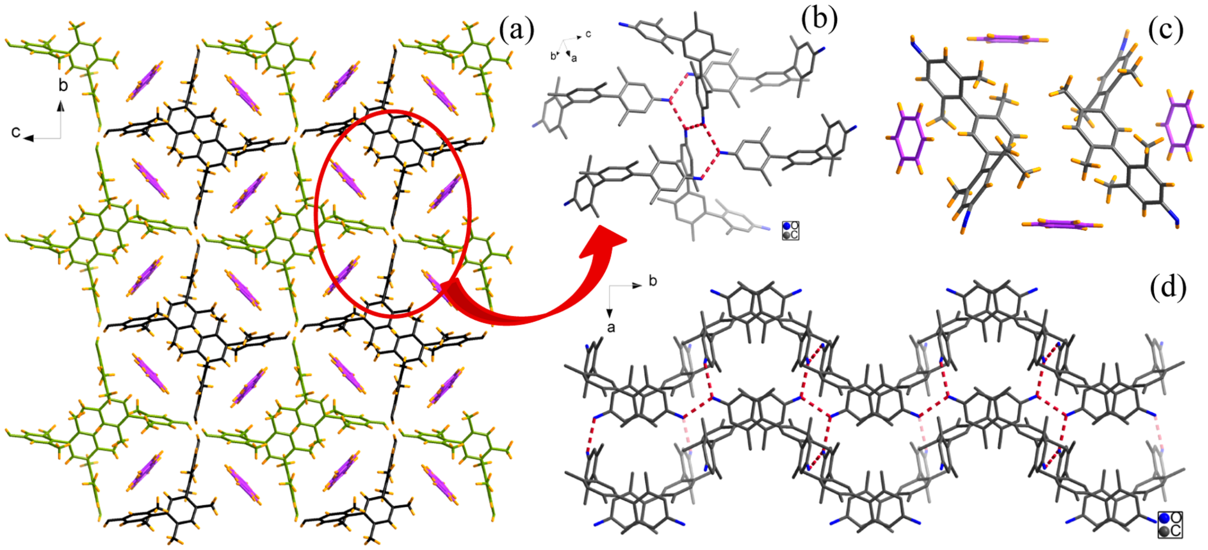


Figure 4. Crystal packing diagram of **BX**-B, which reveals remarkable similarity with that of **TP2**-NB-B in Figure 2 (a). Hydrogen bond mediated propagation (b) and relative disposition of the "paired up" host molecules along with guest benzenes (purple) (c). 2-D undulating layers formed in the *bc*-plane are shown separately (d).

H···O hydrogen bonds such that the union of concave and trough regions of the neighboring host molecules gives rise to pentagonal voids that run down the *a*-axis. Within the pentagonal voids are found guest benzene and nitrobenzene molecules arranged in the *bc*-plane in a checkerboard fashion (type 1, Figure 1). Additional benzene guests are found to be sandwiched between basin regions of the **TP2** host molecules stacked down the *a*-axis. As mentioned previously, the molecular packing of **TP2**-NB is similar to **TP2**-B/**TP2**-NB-B/**TP2**-BN in the *bc*-plane but is devoid of guest molecules in the basin regions of the host **TP2** down *a*-axis, cf. Supporting Information; otherwise, the host is found to include two guest molecules in the concave and trough regions. Presumably, size of the guest is sufficiently large as to be sandwiched between the basin regions of the host **TP2** to give rise to the crystal packing that is similar to others discussed above. The crystal lattice, in the absence of guests in the basin region, is seemingly stabilized by sliding of layers such that the aryl rings of the host molecules in the neighboring layer occupy the basin regions.

Crystallization of **TP2** in the presence of pyridine was carried out in an attempt to explore how the latter may intercept O—H···O hydrogen-bonded self-assembly of the host tetraphenols; it should be noted that the phenols interact strongly with azaaromatics, and this has been exploited tremendously to engineer stereoselective [2 + 2] cycloaddition reactions in the solid state.[5] From several experiments, crystals suitable for X-ray studies were obtained when **TP2** was crystallized with pyridine in the presence of *o*-dichlorobenzene. The crystals

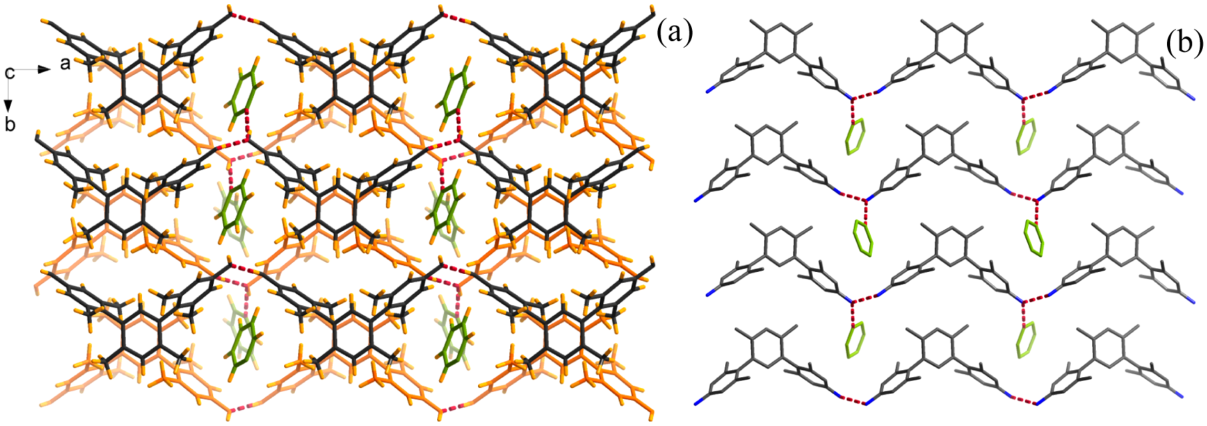


Figure 5. Crystal packing of **BX**-P showing the hydrogen-bonding pattern that leads to closely stacked 1-D strands. The void spaces extending as channels down the *c*-axis are filled with pyridine molecules (green) (a). Notice the relative orientations of host molecules belonging to the two adjacent layers (black and orange). The pyridine guests terminate the O−H···O hydrogen bonding, thereby limiting the propagation of the host **BX** into 1-D strands (b).

were found to belong to the space group $P\bar{1}$ with one host, four *o*-dichlorobenzene and two pyridine molecules in the asymmetric unit cell. The crystal structure analysis shows that *o*-dichlorobenzene molecules occupy trough and concave regions, while pyridine guests are located in basin region of the host **TP2** (Figure 3). In this instance, the host molecules are O−H···O hydrogen bonded in a manner that the concave regions of the adjacent host **TP2** molecules are joined to give rise to 1-dimensional linear strands. The pyridine guests are hooked up to these strands as pendants, thereby restricting the formation of an interconnected 3-D network structure. In other words, pyridine guests dissect the 3-D network into 1-D linear strands (Figure 3) that enclose large void spaces for inclusion of *o*-dichlorobenzene guests (Type 2, Figure 1). Indeed, the voids containing *o*-dichlorobenzene guests extend as channels down *a*-axis. The pyridine molecules that lie as pendants of 1-dimensional strands protrude into the basin regions of the hosts in the adjacent strand leading to a compact lattice.

Guest Inclusion Behavior of 2,4-Bis(4-hydroxy-2,6-dimethylphenyl)-1,5-dimethylbenzene (Bis-(hydroxyaryl)-*m*-xylene, BX). As in the case of **TP2** discussed above, the half component **BX** also exhibits guest inclusion with various guests. Indeed, the inclusion compounds of **BX** with benzene (**BX**-B), benzonitrile (**BX**-BN), nitrobenzene (**BX**-NB) and *o*-dichlorobenzene (**BX**-C) exhibit packing equivalence despite the fact that the crystals of **BX**-C correspond to $P\bar{1}$, while those of all others correspond to $P2_1/c$. The crystal structure of **BX**-B described below serves to illustrate the packing features of all. In contrast, the inclusion compound of **BX** with pyridine, i.e., **BX**-P, corresponds to an altogether different pattern as should be expected.

Figure 4 shows the crystal packing of **BX**-B down *a*-axis, which is strikingly similar to the **TP2**-NB-B structure (Figure 2a). Like tetraphenol **TP2**, its half component bisphenol **BX** also undergoes O−H···O hydrogen-bonded self-assembly as though two of them are joined together to yield a 4-connecting **TP2**-like module that self-assembles. As the half-component **BX** modules contain methyl groups at the 1,3 positions, they cannot remain in plane and are displaced vertically. This expectedly should destroy the aromatic expanse that is inherent to **TP2** to preclude guest inclusion in the basin region. Thus, the self-assembly should correspond to the case of **TP2**-nitrobenzene (**TP2**-NB) that is devoid of guests in the basin region. Indeed, all of its inclusion compounds with benzene, nitrobenzene, and benzonitrile crystallize in $P2_1/c$ as that of **TP2**-NB. Further, the crystal packing of **BX**-C is similar to those of **BX**-B, **BX**-BN, and **BX**-NB except that it crystallizes in the $P\bar{1}$ space group, cf. the Supporting Information. The crystal packing analysis shows that the trough and the seemingly concave regions of neighboring molecules are joined together by O−H···O hydrogen bonds to yield pentagonal voids that are filled by the guest molecules (Type 3, Figure 1). Due to the slight offset of such "paired-up" host molecules, the 2-D layers undulate in the *bc*-plane.

The host molecule in **BX**-P was found to readily yield chunky cubic crystals in ethyl acetate with pyridine and *o*-dichlorobenzene as additives. The inclusion compound so obtained was found to contain only pyridine as the guest. The crystals were found to belong to the space group $P2_1/c$ with one molecule each of the host **BX** and the pyridine guest in the asymmetric unit. The crystal packing analysis reveals that the host molecules are interconnected by O−H···O hydrogen bonds with voids that lead to channels down the *c*-axis (Figure 5a). The pyridine molecules seemingly compel the host molecules to be confined to 1-D linear strands by terminating the propagation of O−H···O hydrogen bonds via O−H···N hydrogen bonding ($d_{\text{O−H}\cdots\text{N}}$ = 1.81 Å, $D_{\text{O}\cdots\text{N}}$ = 2.64 Å, $\theta_{\text{O−H}\cdots\text{N}}$ = 166.9°). Because of the angular geometry of the host **BX**, the adjacent strands fit tightly into the neighboring strands, leaving virtually no space for further guest inclusion (type 4, Figure 1). In other words, the host **BX** undergoes self-inclusion in the trough region of the adjacent host molecule such that the 2-D layers in the *ab*-plane are compactly packed (Figure 5b).

Overall Rationalizations. In comparison to the aggregation of carboxylic acids, phenolic compounds are known to exhibit considerable flexibility in terms of the synthon adoption.[12] The synthons that are exhibited by hydroxyl groups include (a) dimers, (b) chains, and (c) rings (Figure 6).[12] Therefore, the host systems based on phenols may be expected to display guest-dependent adaptability. Indeed, there are diverse host systems known that are based on the self-assembly of hydroxyl groups.[12] By assuming the prevalence of "chain" synthon in the crystals of the hosts **TP2** and **BX**, which is typically observed in rigid 2-/3-dimensional molecular modules, one may envisage two types of assembly for the tetraphenol **TP2** and bis-phenol **BX** as shown schematically at

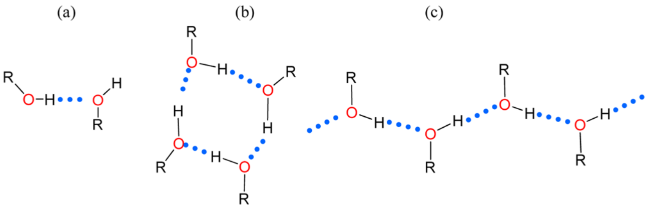


Figure 6. Typical synthons observed for the self-assembly of OH groups: (a) dimer, (b) ring, and (c) chain.[13]

the outset in Figure 1. The first type in which the union of concave and trough regions of the host leads to pentagonal voids is observed in all four inclusion compounds of **TP2**, i.e., **TP2**-B, **TP2**-NB-B, **TP2**-NB, and **TP2**-BN. Based on packing equivalence exhibited by **TP2**-B and **TP2**-NB, we surmised that both benzene and nitrobenzene could be interchangeably incorporated simultaneously in the crystal lattice. The fact that one does indeed obtain ternary inclusion compound with benzene and nitrobenzene is reflected by the crystal structure of **TP2**-NB-B. What is noticeable in these cases is that benzene gets accommodated in the basin region as well, while nitrobenzene and a second molecule of benzene are located in the pentagonal voids formed between the enclosure between concave and trough domains. Our attempts with pyridine that may terminate the hydrogen-bonded aggregation led to crystals containing *o*-dichlorobenzene. As the crystal packing in Figure 3 suggests, it corresponds to the second type 2 in Figure 1. As can be seen in Figure 3, **TP2** host molecules form 1-dimensional strands via linkage of the concave regions, which close up to yield further voids in the trough regions within which *o*-dichlorobenzene guests get accommodated. Clearly, the mimicry of two packing types 1 and 2 that are conceived a priori for **TP2** is demonstrated via variation of the guests.

Based on the molecular packings observed in the crystals for **TP2**-B, **TP2**-NB, **TP2**-BN, and **TP2**-NB-B, we wondered as to how the half-component deduced by slicing **TP2** host into two halves may undergo hydrogen-bonded self-assembly. Of course, the importance of aromatic expanse inherent to pyrene core in **TP2** host molecules was thus expected to be revealed in the lattice inclusion of various guests. As in the case of **TP2**, the methyl groups at 2,6 positions of the phenolic moieties in the half-component **BX** ensure orthogonality. Thus, one may expect only the trough domain to become accessible for guest inclusion such that the region for guest inclusion is substantially attenuated. In line with these expectations, the host **BX** was indeed found to exhibit guest inclusion. A remarkable equivalence is observed in the crystal packings of the crystals **BX**-B with those of **TP2**-B/**TP2**-BN-B. The loss of basin region is reflected in the reduction of volume accessible for guests, which is 29% for **BX**-B as compared to 57% for **TP2**-B. Indeed, **BX** is likewise found to include other guests such as nitrobenzene, benzonitrile, and *o*-dichlorobenzene, which are found to be included in the trough region in the inclusion crystals of **TP2**. The packing in all of these cases (type 3, Figure 1) is synonymous with the type 1 observed for inclusion compounds of **TP2**. The pyridine guests serve to truncating the otherwise hydrogen-bonded propagation. It turns out that in the crystals of **BX**-P, the pyridine guests interdigitate into the adjacent 1-dimensional strands that are formed by the aggregation of phenolic moieties (type 4, Figure 1).

The host-guest stoichiometries as determined from the inclusion compounds were also established by ^{1}H NMR analyses of the solutions of their crystals. TGA analyses of the crystals further corroborate the host-guest ratios, cf. the Supporting Information. More incisive analysis of the thermogravimetric analysis reveals incremental release of the guests in the case of **TP2**-NB-B, cf. the Supporting Information; this is particularly appealing from the point of view of correlating the binding of the guests with their exclusion from the crystals. In this instance, benzene guests are found to be located in basin and trough regions, while nitrobenzene can be said to be found in the concave domain. Accordingly, one observes three steps for release of the guests in the TGA, cf. the Supporting Information. Insofar as the binding of the guest species in all of the inclusion compounds is concerned, the crystal packing analyses show that the guests occupying the voids are held by weak C−H···O and C−H···π hydrogen bonds. It is the size and shape complementarity that appears to drive the inclusion of guests in the solid state of the host systems that seemingly behave like tweezers with some conformational flexibility for the aryl arms. The crystal structure analyses show that there exists a small window within which the aryl rings lie near orthogonally; the angle between the aryl rings and the planar pyrene core is found to vary in the range of 73−90°.

The results clearly demonstrate how the molecular design with more than one location for guest binding in conjunction with the knowledge of supramolecular synthons may be exploited to develop cocrystals with packing types that may be a priori expected. Quite remarkable is how *structural reduction* based on the results of tetraaryl phenol **TP2** has paved the way for the inclusion phenomenon to be demonstrated for diarylbenzene **BX** that incorporates all of the attributes of **TP2**, except the aromatic expanse. It is compellingly evident that the aromatic expanse in **TP2** plays a crucial role for the observed guest inclusion behavior (Table 1).

■ CONCLUSIONS

Tetraarylpyrene host **TP2** decked up with rigid 2,6-dimethyl-4-hydroxyphenyl rings as panes at the four corners is shown to undergo O−H···O hydrogen-bonded self-assembly adopting the "chain" synthon into two expected patterns. The union of the concave and trough regions of the neighboring host permits pentagonal voids within which aromatic guests are readily incorporated. That the assembly is robust is reflected from the isostructurality exhibited by the host **TP2** with different guests. It is shown that benzene and nitrobenzene can be simultaneously included in the lattice of the host **TP2**. Guest-induced switchover allows the realization of alternative packing mode; in the presence of pyridine, which truncates the hydrogen bond-mediated propagation, the host **TP2** crystallizes by including *o*-dichlorobenzene. That the half-component **BX**—obtained by slicing host **TP2**—should expectedly exhibit guest inclusion likewise is demonstrated by X-ray structural characterization of its inclusion compounds with analogous guests. The structural analyses of the inclusion compounds of **TP2** and **BX** reveal remarkable similarities in terms of the crystal packings that are mediated in both cases by O−H···O hydrogen bonds. As in the case of **TP2**, the guest-induced packing permits mimicry of the two possible modes of crystal packings based on the chain synthon of the phenolic hydroxyl groups of **BX**, Figure 1.

EXPERIMENTAL SECTION

The starting materials, viz., 1,5-dibromo-2,4-dimethylbenzene and 2,6-dimethyl-4-methoxyphenylboronic acid, were synthesized according to the previously reported procedures.[10c]

Synthesis of Tetrakis(hydroxyaryl)pyrene (TP2) and Bis(hydroxyaryl)-*m*-xylene (BX). The preparation of the precursor 1,3,6,8-tetrakis(2,6-dimethyl-4-methoxyphenyl)pyrene has previously been reported.[10c] The precursor of **BX**, namely 2,4-bis(4-methoxy-2,6-dimethylphenyl)-1,5-dimethylbenzene, was prepared starting from 1,5-dibromo-2,4-dimethylbenzene; the latter was subjected to Suzuki coupling with 2,6-dimethyl-4-methoxyphenylboronic acid under Pd(0) catalysis. Demethylation of these precursor compounds using BBr_3/CH_2Cl_2 led to **TP2** and **BX**.

Preparation of 2,4-Bis(4-methoxy-2,6-dimethylphenyl)-1,5-dimethylbenzene. In a two-necked round-bottom flask were taken 1,5-dibromo-2,4-dimethylbenzene (0.1 g, 0.38 mmol), 2,6-dimethyl-4-methoxyphenylboronic acid (0.24 g, 1.3 mmol), $Pd(PPh_3)_4$ (0.024 g, 0.021 mmol), and NaOH (0.06 g, 1.50 mmol). To the resultant mixture was added 15 mL of 1,4-dioxane−water mixture (2:1), and the contents were heated at reflux for 12 h. After completion of the reaction as monitored by thin-layer chromatography, the reaction was quenched. The solvent, i.e., dioxane, was removed in vacuo, and the solid residue was extracted with $CHCl_3$. The combined extract was washed with brine and dried over anhyd Na_2SO_4 and solvent removed in vacuo to obtain the crude product. Silica gel column chromatography (25% $CHCl_3$/petroleum ether) yielded the required product as a colorless solid: yield 91% (0.13 g, 0.35 mmol); mp 133−137 °C; ^1H NMR (500 MHz, acetone-d_6) δ 1.96 (s, 12H), 1.97 (s, 6H), 3.78 (s, 6H), 6.57 (s, 1H), 6.70 (s, 4H), 7.25 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.8, 21.7, 55.6, 95.5, 112.4, 121.1, 130.4, 133.6, 138.2, 156.7, 158.1; HRMS *m/z* calcd for $C_{26}H_{31}O_2$ 375.2324, found 375.2328 $[M+H]^+$.

General Procedure for Demethylation of Aryl Methyl Ether. To a solution of aryl methyl ether (2 mmol) in 20 mL of dry CH_2Cl_2 at 0 °C was added dropwise BBr_3 solution (3 mmol) under N_2 atmosphere. The reaction mixture was allowed to stir overnight. Subsequently, it was quenched with 10% HCl and extracted with ethyl acetate. The combined extract was dried over anhyd Na_2SO_4, treated with charcoal, filtered, and concentrated. The pure product was obtained as a colorless solid after filtration over a short pad of silica gel using a mixture of ethyl acetate and petroleum ether (50:50) followed by recrystallization from ethyl acetate and petroleum ether.

1,3,6,8-Tetrakis(2,6-dimethyl-4-hydroxyphenyl)pyrene (TP2): colorless solid; yield 96% (0.97 g, 1.42 mmol); mp >300 °C; IR (KBr) cm^{-1} 3320, 3050, 2925, 1591, 1476, 1429, 1298, 1190; ^1H NMR (500 MHz, DMSO-d_6) δ 1.77 (s, 24H), 6.60 (s, 8H), 7.40 (s, 2H), 7.44 (s, 4H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 21.1, 114.8, 124.9, 125.8, 128.6, 128.8, 130.6, 136.6, 137.7, 157.0; HRMS *m/z* calcd for $C_{48}H_{43}O_4$ 683.3161, found 683.3163 $[M + H]^+$.

2,4-Bis(4-hydroxy-2,6-dimethylphenyl)-1,5-dimethylbenzene (BX): colorless solid; yield 96% (0.11 g, 0.32 mmol); mp 163−167 °C; IR (KBr) cm^{-1} 3270, 3024, 2922, 1606, 1496; ^1H NMR (500 MHz, CD_3OD) δ 1.86 (s, 12H), 1.92 (s, 6H), 6.49 (s, 1H), 6.52 (s, 4H), 7.17 (s, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 19.3, 20.7, 114.9, 131.9, 132.6, 133.8, 135.9, 138.0, 139.6, 156.9; HRMS *m/z* calcd for $C_{24}H_{27}O_2$ 347.2011, found 347.2013 $[M + H]^+$.

Preparation of Inclusion Compounds. The inclusion compounds were prepared by slow evaporation of the solution of host **TP2**/**BX** in a mixed solvent system comprising of one in which the host dissolves and the second that functions as a guest. Both **TP2** and **BX** were found to be readily soluble in polar solvents such as methanol, ethyl acetate, acetone, ethanol, and 2-propanol. From the screening of a range of solvents, methanol and ethyl acetate were reckoned to be the most suitable solvents for obtaining good-quality single crystals of the inclusion compounds of **TP2** and **BX**, respectively. Indeed, change of solvent from methanol to ethyl acetate in the case of **TP2** was found not to influence the formation of the inclusion compound with the added guest/second solvent. However, the host **BX** preferably underwent crystallization in ethyl acetate in the presence of added guest to yield the corresponding inclusion compounds; crystals of the latter were not easily obtained when other solvents were employed, which suggests that the solvent plays an important role in the formation of the inclusion compounds of **BX**.

In a typical experiment, the host **TP2** (50.0 mg, 0.07 mmol) was dissolved in 20 mL of ethyl acetate/methanol, and a few drops of guests was introduced without causing precipitation. The resultant solution was allowed to evaporate over a period of 7−10 days to yield colorless crystals quantitatively. The crystals were characterized by ^1H NMR, TGA, and X-ray crystallography. A similar procedure was used for the synthesis of inclusion compounds of **BX**.

ASSOCIATED CONTENT

Ⓢ Supporting Information

NMR spectral reproductions, crystal data, X -ray crystallographic information files (CIF), and TGA profiles. This information is available free of charge via the Internet at http://pubs.acs.org/.

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Notes

The authors declare no competing financial interest.

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