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Abundant Lattice Inclusion Phenomenon with Sterically Hindered and Inherently Shape-Selective Tetraarylpyrenes

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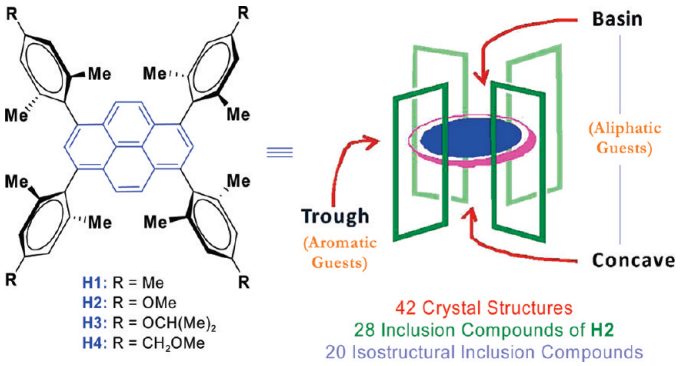

Tetraarylpyrenes **H1**−**H4** that typify molecular systems with orthogonal planes and lack hydrogen bonding functional groups were designed as new host systems with three distinct domains for guest inclusion. In particular, **H2** and **H4** hosts are found to include a variety of guest molecules. We have determined 42 crystal structures overall (i) to establish the importance of skeletal features of the hosts, (ii) to determine their adaptability in binding diverse guest molecules, and (iii) to delineate favored domains for location of guest molecules and preferred modes of association of the host systems. The unique features of **H1**−**H4** are found to permit binding of aliphatic and aromatic guest species differently: the small-sized guest molecules such as $CHCl_3$, $(CH_3)_2S$, etc. are found to be bound in the basin domain, whereas aliphatic and aromatic guests are found to be included in the channel/concave and trough regions, respectively. The crystal structure analyses reveal that as many as 20 out of 28 inclusion compounds of **H2** are isostructural with one or more; we have identified 8 different crystal packing types with which each inclusion compound may be associated. The guest-binding potential of host **H2** has been exploited to demonstrate the utility of these host systems in (i) the separation of regioisomeric methyl-substituted benzenes and mixtures of *cis*−*trans* isomers of decalin, perhydroisoquinoline, and cinnamonitrile, (ii) the stabilization of the keto-enol form of 1,3-diketones, and (iii) the conformational locking of flexible cycloalkanes.

Introduction

Although crystal structure prediction is not yet possible,[1] it is increasingly becoming evident that the molecular packing can indeed be controlled via exploitation of a wealth of intermolecular interactions that manifest in certain readily conceivable synthons.[2−4] The creation of organic[5] and metal-organic[6] porous materials constitutes one of the actively pursued contemporary themes. An emphasis of interest in organic materials that functionally mimic inorganic zeolites[7]

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(3) (a) Desiraju, G. R. *Angew. Chem., Int. Ed.* **1995**, *34*, 2311. (b) Nangia, A.; Desiraju, G. R. *Top. Curr. Chem.* **1998**, *198*, 57.
(4) It appears that the crystal structure can now be predicted from first principles; see: Newmann, M. A.; Leusen, F. J. J.; Kendrick, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 2427.

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is due to their promising applications in gas adsorption,[6,8] separation and purification,[9] catalysis and asymmetric synthesis,[10] optical resolution,[11,12] etc. In a broad sense, the organic compounds that accommodate guest molecules can be classified into two categories, "unimolecular"' and "multimolecular" inclusion compounds.[13] Molecules such as cyclodextrins, calixarenes, cucurbiturils, crown ethers, cryptands, spherands, etc. with inherent potential to bind guest molecules constitute excellent examples of unimolecular inclusion host compounds.[14] The multimolecular inclusion compounds, also termed lattice inclusion host compounds, differ in the sense that two or more host molecules are involved in the construction of cavities for guest inclusion; urea, choleic acids, Dianin's compound, hydroquinone, gossypol, etc. are well-known examples of this category.[13,15] The chemistry of unimolecular host systems is fairly advanced.[16] However, creation of multimolecular inclusion compounds with cavities for guest inclusion is challenging and continues to elicit tremendous interest.[8,17]

In our recent investigations focused on the development of functional organic materials,[18] we surmised that flat pyrenes decked up at the four corners with highly rigid aromatic panels as shown in Scheme 1 should exhibit packing difficulty in the solid state, so that such molecular systems may a priori be anticipated to crystallize with guest inclusion.[19] Indeed, metalated tetraarylporphyrins in which the aryl rings at meso positions orient orthogonally are well-known to form inclusion compounds with a variety of guest molecules.[20] We reasoned that tetraarylpyrenes should be markedly different from metalated tetraarylporphyrins from several points of view: (i) whereas tetraarylporphyrins are of D_{4h} symmetry, tetraarylpyrenes are of reduced D_{2h} symmetry, which increases the number of possible packing modes in the crystal lattice; (ii) tetraarylpyrenes offer three readily conceivable domains for guest inclusion, namely, trough, concave, and basin, cf. Scheme 1, to permit inclusion of two or more guest molecules simultaneously; (iii) the excellent fluorescence property of tetraarylpyrenes may permit guest inclusion in the solid state to be signaled via fluorescence; and (iv) tetraarylpyrenes can be readily adapted as spacers with unique topology for porous metal-organic frameworks (MOFs). Thus, we have explored the guest inclusion behavior of tetraarylpyrenes **H1**−**H4**. Herein, we report the results of our comprehensive investigations on the guest inclusion behavior of **H1**−**H4** with a variety of guest molecules. In particular, the methoxy hosts **H2** and **H4** are shown to (i) include a number of diverse guest molecules in all three distinct domains, viz., trough, channel, and basin, and (ii) exhibit remarkable discrimination in the binding of

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(19) Our extensive search of the Crystal Structure Database (ConQuest Ver-1.11, CCDC-2009) revealed only 6 structures of tetraalkyl/arylpyrenes (ref codes: GANQES, MEBZID, MEBZOJ, WENJUV, COBDAZ, HIZBUO). Only in one case, i.e., 1,3,6,8-tetrakis(4-methoxyphenyl)pyrene (GANQES), was inclusion of THF observed. Notably, no systematic investigations as to the phenomenon of guest inclusion by pyrenes have heretofore been reported to the best of our knowledge.

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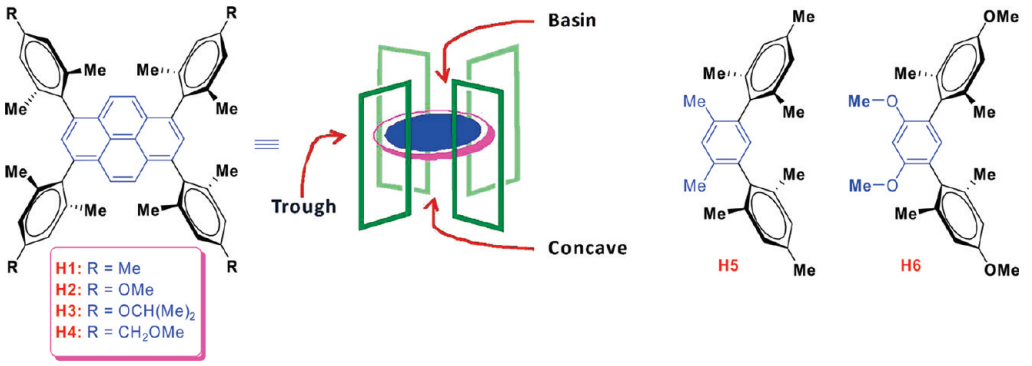
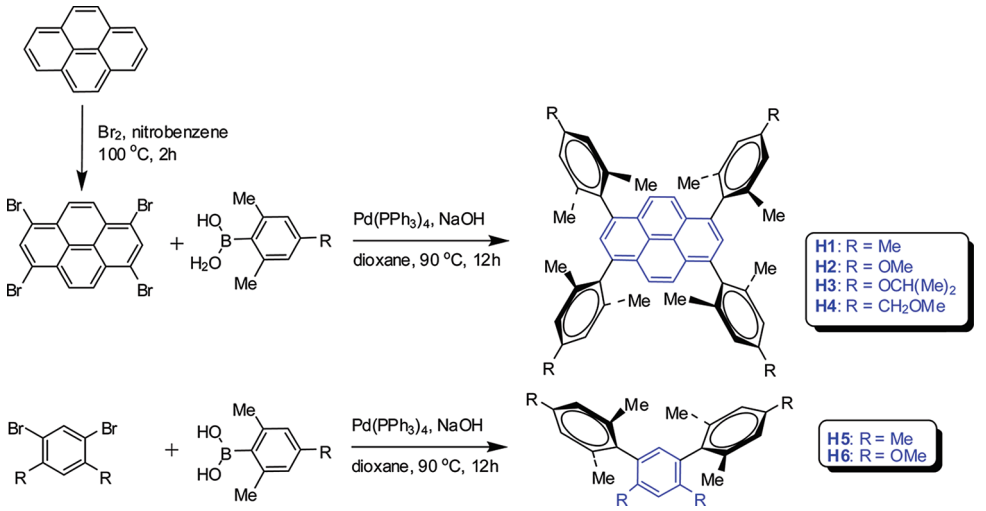
SCHEME 1. Molecular Structures of Hosts H1−H4, Half Components H5 and H6, and Cartoon Drawing That Typifies Hosts H1−H4



SCHEME 2. Synthetic Routes for Inclusion Hosts H1−H4 and the Half Components H5 and H6



stereo- and regioisomeric mixtures. In addition to separation, their utility is demonstrated in freezing conformationally flexible molecules in one/two of their conformation/s and trapping of one of the tautomeric forms from an equilibrium mixture of keto-enol and 1,3-diketone forms.

Results and Discussion

Synthesis of Host Pyrenes H1−H4. The synthesis and characterization of host pyrenes **H1** and **H2** have already been published by us in the context of their application in organic light emitting diodes (OLEDs).[18c] The hosts **H3** and **H4** were similarly prepared via Suzuki coupling protocol by employing 4-isopropoxy-2,6-dimethylphenylboronic acid and 4-methoxymethyl-2,6-dimethylphenylboronic acid, respectively, Scheme 2. A similar protocol was employed for the synthesis of **H5** and **H6** using dibromo-substituted *m*-xylene and 1,3-dimethoxybenzene; see Supporting Information.

Guest Inclusion Behavior of Hosts H1−H4. Initial crystallization experiments with hosts **H1−H4** in the presence of simple aliphatic and aromatic guest molecules revealed that the former exhibit solid-state guest inclusion behavior, as revealed by ^{1}H NMR and X-ray structural analyses of some crystals. More critical analyses were performed for hosts **H1**, **H2**, and **H4** with some common guest molecules.[21] To gauge the relative abilities of these host systems in particular, X-ray determined structures of the inclusion compounds with two aliphatic and two aromatic guest molecules were analyzed for host:guest ratios, and the guest-accessible volumes were calculated by the program "PLATON". These data collated in Table 1 clearly show that **H4** is far superior to **H1** and **H2** and that the latter is comparatively better than **H1**. On the basis of the consideration that the methoxy groups in

TABLE 1. Comparison of H:G Stoichiometries and Guest-Accessible Volumes for Inclusion Compounds of H1, H2, and H4 with Common Aliphatic and Aromatic Guest Molecules[a]

	H1		H2		H4	
guest	H:G	V (%)	H:G	V (%)	H:G	V (%)
decalin	1:2	38	1:1	25	1:4	46
dodecene	1:2	48	1:2	50	1:3	56
benzene	1:1	13	1:2	28	1:2	21
mesitylene	1:0.5	12	1:2	36		

[a] H:G = host/guest ratio; V = guest-accessible volume.

(21) CCDC 726009−726023, 726028−726030, 726970−726973, 726976−726978, 726980−726985 and 726987−726997 contain the supplementary crystallographic data for **H2**, **H4−H6** and all of the inclusion compounds of **H1−H4**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

TABLE 2. Various Guests That are Bound by Hosts H1−H4 and Host:Guest Ratios of the Inclusion Compounds

host	guest molecules (host:guest)
H1	cyclododecene (1:2), decalin (1:2), benzene (1:1), mesitylene (1:0.5)
H2	dimethyl sulfide (1:2), $CHCl_3$ (1:2), CCl_4 (1:2), dichloroethane (1:2), acetylacetone (1:2), THF (1:2), chlorocyclohexane (1:4), bromocyclohexane (1:4), 2-cyclohexen-1-one (1:2), cyclooctane (1:4), cyclodecane (1:1), cyclododecene (1:2.5), dicyclopentadiene (1:3), decalin (1:1), perhydroisoquinoline (1:1), benzene (1:2), toluene (1:1), phenylacetylene (1:2), benzonitrile (1:1), nitrobenzene (1:2), cinnamonitrile (1:2), *o*-xylene (1:2), *p*-xylene (1:2), mesitylene (1:2), biphenyl (1:4), diphenyl ether (1:1), naphthalene (1:2), *p*-terphenyl (1:2)
H3	*p*-xylene (1:3)
H4	cyclododecene (1:3), decalin (1:4), benzene (1:2), benzonitrile (1:1), pyrene (1:1)

TABLE 3. Crystal Data for Representative Inclusion Compounds of H2 with Various Guests

	H2·chloroform	**H2**·decalin	**H2**·cyclooctane	**H2**·benzonitrile
formula	$C_{54}H_{52}Cl_6O_4$	$C_{62}H_{68}O_4$	$C_{84}H_{114}O_4$	$C_{119}H_{109}N_2O_4$
FW	977.89	877.16	1187.75	1696.43
crystal system	orthorhombic	monoclinic	monoclinic	monoclinic
space group	*Pbca*	$P2_1/n$	$C2/c$	$C2/c$
a (Å)	17.706(2)	7.3082(2)	36.839(2)	20.637(3)
b (Å)	11.613(1)	14.4393(2)	10.456(2)	21.858(3)
c (Å)	25.186(1)	23.831(1)	21.481(1)	22.694(3)
α (deg)	90.0	90.0	90.0	90.00
β (deg)	90.0	97.946(2)	122.196(2)	108.444(4)
γ (deg)	90.0	90.0	90.0	90.00
V (Å^3)	5179(4)	2490.6(1)	7002(2)	9711(2)
Z	4	2	4	4
F(000)	2040	944	2600	3808
GOF	1.061	1.034	1.046	1.019
final R_1	0.0895	0.0744	0.0787	0.0794
final wR_2	0.2471	0.1873	0.2022	0.1976
host:guest	1: 2	1:1	1: 4	1: 1
	H2·mesitylene	**H2**·dichloroethane	**H2**·naphthalene	**H2**·cinnamonitrile
formula	$C_{70}H_{74}O_4$	$C_{56}H_{58}Cl_4O_4$	$C_72H_{66}O_4$	$C_{70}H_{64}N_2O_4$
FW	979.29	936.82	995.25	997.23
crystal system	monoclinic	monoclinic	monoclinic	orthorhombic
space group	$P2_1/c$	$P2_1/c$	$P2_1/n$	$Pna2_1$
a (Å)	12.9180(1)	7.8862(2)	14.227(2)	19.600(2)
b (Å)	15.7692(2)	21.289(1)	14.854(3)	9.8101(1)
c (Å)	14.2495(1)	15.369(1)	14.478(3)	28.415(4)
α (deg)	90.0	90.0	90.0	90.0
β (deg)	106.017(1)	95.306(1)	117.304(3)	90.0
γ (deg)	90.0	90.0	90.0	90.0
V (Å^3)	2790.0(1)	2569.3(1)	2718.8(8)	5475.0(1)
Z	2	2	2	4
F(000)	1052	988	1060	2120
GOF	1.030	1.023	1.087	1.035
final R_1	0.0546	0.0615	0.0896	0.0528
final wR_2	0.1282	0.1470	0.2113	0.1217
host:guest	1: 2	1: 2	1: 2	1: 2

H2 may contribute to lattice stabilization via possible C−H···O and C−H···π interactions,[22] we rigorously examined the potential of host **H2** to include a variety of guest molecules and demonstrate the functional utility of such host systems. In Table 2 are consolidated a variety of guest molecules with which the inclusion compounds of **H1**−**H4** were formed. Also, the host:guest ratios for all inclusion compounds are indicated in parentheses.

In the following, we shall first consider the abundant lattice inclusion phenomenon observed for **H2**, various modes in which it includes diverse guest molecules and isostructurality of several of its inclusion compounds.[21] Subsequently, the inclusion phenomena observed for analogous hosts **H1**, **H3**, and **H4** are discussed briefly to exemplify the novelty associated with the structural attributes of all hosts. Also discussed are the crystal structures of **H5** and **H6**, which represent approximately the half components of hosts **H1** and **H2**, respectively.

Lattice Inclusion Compounds of H2. In Table 2 are shown diverse guest molecules with which the host **H2** was crystallized readily as a solid material by slow evaporation of its solution in the neat guest itself (when the guest is a liquid) or its solution in chloroform in the presence of the guest.[23]

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(23) Although host **H2** crystallizes itself by including $CHCl_3$, the inclusion of added guests was preferably observed. The preferential inclusion of an added guest in a solvent that itself acts as a guest is well known; for example, see: Nakano, K.; Mochizuki, E.; Yasui, N.; Morioka, K.; Yamauchi, Y.; Kanehisa, N.; Kai, Y.; Yoswathananont, N.; Tohnai, N.; Sada, K.; Miyata, M. *Eur. J. Org. Chem.* **2003**, 2428.

TABLE 4. Isostructural Inclusion Compounds of H2 with Various Guest Molecules and Their Space Groups

entry	guest compounds	packing type	space group
1	chloroform and carbon tetrachloride	1	*Pbca*
2	cyclodecane, decalin, and perhydroisoquinoline	2	$P2_1/n$
3	chlorocyclohexane, bromocyclohexane, and cyclooctane	3	$C2/c$
4	2-cyclohexen-1-one and benzonitrile	4	$C2/c$
5	acetylacetone, benzene, nitrobenzene, *p*-xylene, mesitylene, and *p*-terphenyl	5	$P2_1/c$
6	1,2-dichloroethane and cyclododecene	6	$P2_1/c$
7	phenylacetylene and naphthalene	7	$P2_1/n$

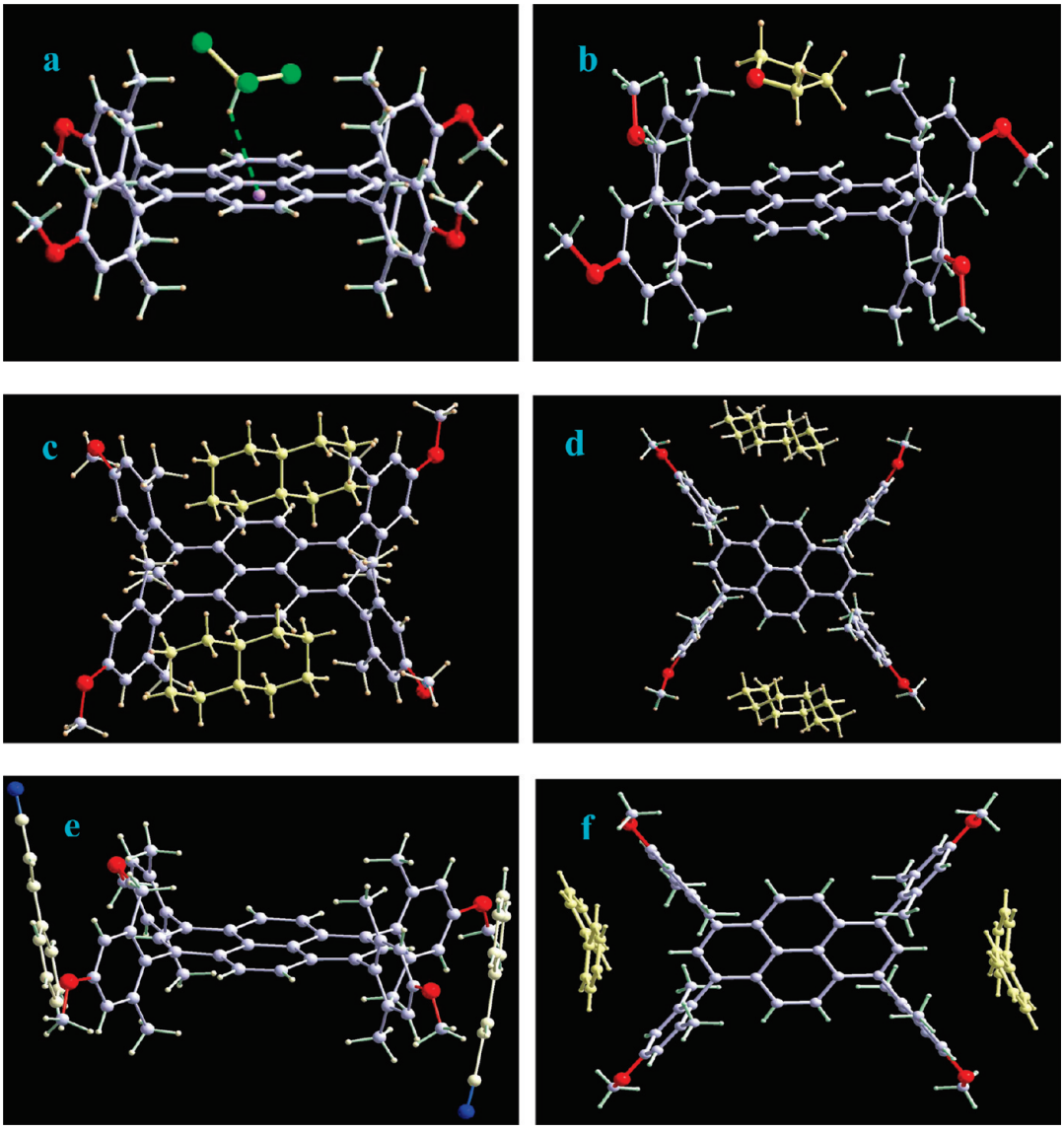


FIGURE 1. Molecular structures of the inclusion compounds of host **H2** with chloroform and THF (a and b), *trans*-decalin and cyclodecane (c and d), and *trans*-cinnamonitrile and biphenyl (e and f). Notice that the guests sit in the basin of the host in the top row and in the concave and trough regions in the middle and bottom rows, respectively.

Crystallization of **H2** alone in ethyl acetate yielded guest-free crystals (vide infra). The crystal structures of the inclusion compounds of **H2** with all of the guest molecules in Table 2 were determined by X-ray crystallography. The details of crystal data and structure determination for representative inclusion compounds are given in Table 3; these details for others are provided in Supporting Information. In most cases, the guest inclusion was independently established by TGA, ^{1}H NMR spectroscopy, and PXRD analyses; see Supporting Information.

As mentioned earlier, the host design features three distinct domains in which the guest molecules may be included in the crystal lattice. The analyses of X-ray determined crystal structures of the inclusion compounds unambiguously establish the inclusion of guest molecules in all three domains of the host as presupposed. In Figure 1 are shown

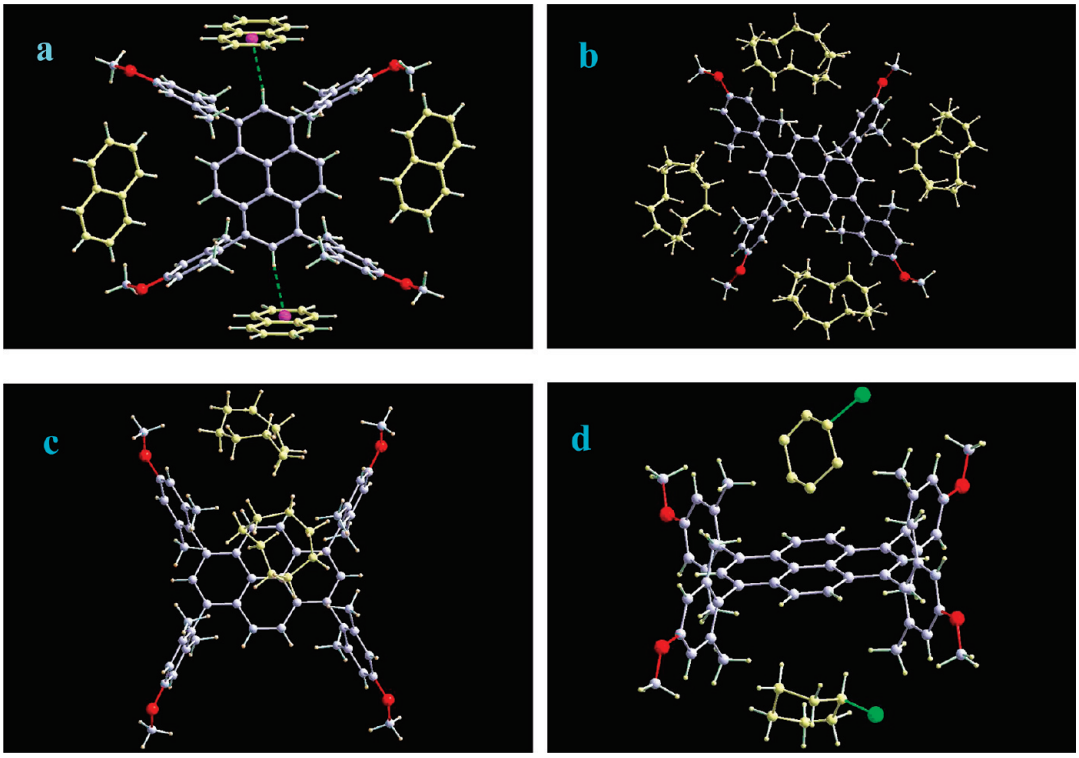


FIGURE 2. Structures of the inclusion compounds of **H2** with naphthalene (a), cyclododecene (b), cyclooctane (c), and chlorocyclohexane (d).

the molecular structures of **H2** with chloroform, THF, *trans*-decalin, cyclodecane, cinnamonitrile, and biphenyl.

Remarkably, the small guest molecules such as dimethyl sulfide, chloroform, CCl_4, and THF were found to be located in the basin region of the host **H2**, while aromatic guests such as cinnamonitrile and biphenyl were found to be located in troughs. Aliphatic guest molecules such as cyclodecane, decalin, and perhydroisoquinoline were found to be included in the concave domain of the host **H2**. Of course, some guest molecules were found to occupy two domains at the same time. For example, cyclooctane and chlorocyclohexane occupy the basin and concave domains, and naphthalene and cyclododecene are found in both trough and concave regions as shown in Figure 2.

As the inclusion of guest molecules with diverse structures must occur via different modes of association of the host **H2**, we have examined the crystal packings of all compounds to identify preferred modes of association of the hosts that augment guest inclusion. The fact that the host **H2** undergoes crystal packing in certain preferred ways is suggested by the isostructurality observed for several of its compounds with different guests. The compounds that exhibit isostructurality are given in Table 4; as many as 20 out of 28 inclusion compounds of **H2** are found to be isostructural with two or more compounds. By reducing the host structure to a cartoon consisting of a rectangle joined at the vertices by solid lines, the crystal structures of 28 inclusion compounds of **H2** were analyzed to discern common modes of packing among themselves. In all, 8 different types were identified in which the host molecules were found to organize by including the guest molecules in the crystal lattices. These 8 types of association of the host **H2** are shown in Figure 3. In essence, almost all inclusion compounds may be associated with one of these types. The locations of guests in these packing modes are shown by an elliptical solid.

Self-Inclusion of Guest-Free Host H2. Host **H2** was found to crystallize readily from its solution in ethyl acetate in its guest-free state. The crystals were found to belong to $P2_1/c$ space group with two distinct molecules (half each in the asymmetric unit) A and B lying on the crystallographic inversion centers. In Figure 4 are shown typical crystal packing diagrams. A careful inspection of the crystal packing reveals that the molecules of type A are connected via C−H···π interactions[22] between the methoxy methyl hydrogens and the central pyrene rings to form squares, within which the molecules of type B are located; see Supporting Information. By positioning the dimethylanisyl rings into the trough regions of molecules A, the molecules B function as guests in a manner that the crystal system may be viewed as a case of self-inclusion as shown in Figure 4. Indeed, a comparison of the crystal packing with those of its inclusion compounds with acetyl acetone, benzene, toluene, nitrobenzene, *o*-xylene, *p*-xylene, mesitylene, and *p*-terphenyl leads to the compelling inference that guest-free modification truly represents a case of self-inclusion. It is only recently that Barbour et al. have documented precedence for such a scenario.[24]

Isostructurality of Inclusion Compounds of H2. Isostructurality refers to identical crystal packings. In the context of host−guest chemistry, the isostructurality refers to similar organization of host molecules. The isostructural lattice inclusion compounds are believed to present a unique

(24) Lloyd, G. O.; Alen, J.; Bredenkamp, M. W.; De Vries, E. J. C.; Esterhuysen, C.; Barbour, L. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 1.

(25) (a) Isostructurality: Caira, M. R. *Encyclopedia of Supramolecular Chemistry*; Marcel Decker: New York, 2004; p 767. (b) Cincic, D.; Friscic, T.; Jones, W. *Chem.—Eur. J.* **2008**, *14*, 747.

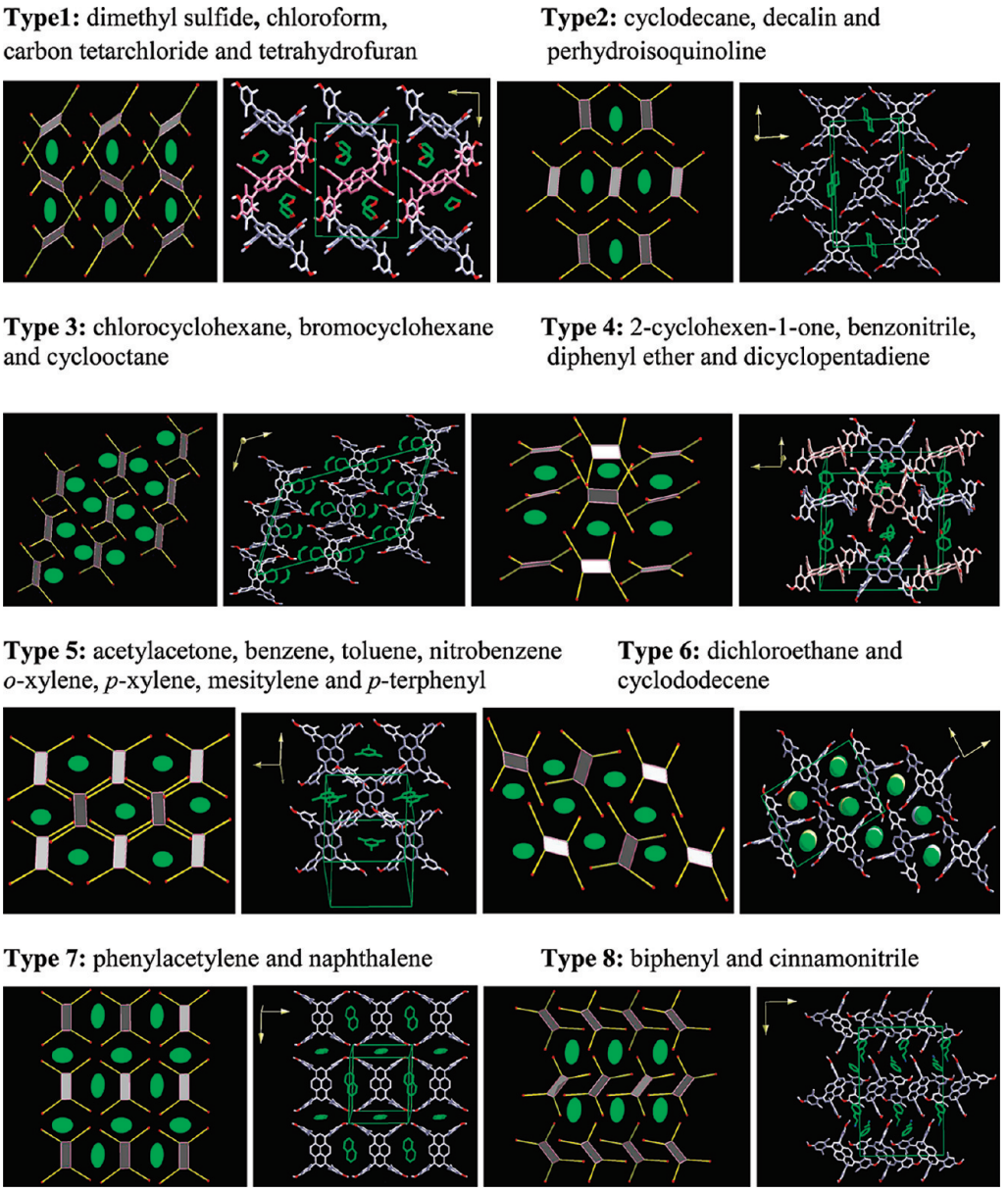


FIGURE 3. Various modes of association of host **H2** and vacant spaces that the guest molecules occupy (shown with solid ellipses). Also indicated are the guests whose inclusion compounds belong to the corresponding type. Type 1: dimethyl sulfide, chloroform, carbon tetarchloride, and tetrahydrofuran. Type 2: cyclodecane, decalin and perhydroisoquinoline. Type 3: chlorocyclohexane, bromocyclohexane and cyclooctane. Type 4: 2-cyclohexen-1-one, benzonitrile, diphenyl ether and dicyclopentadiene. Type 5: acetylacetone, benzene, toluene, nitrobenzene *o*-xylene, *p*-xylene, mesitylene and *p*-terphenyl. Type 6: dichloroethane and cyclododecene. Type 7: phenylacetylene and naphthalene. Type 8: biphenyl and cinnamonitrile.

opportunity to investigate structure property relationships.[25] For example, analysis of the loss of guest molecules thermally in isostructural compounds may benefit us with the knowledge of distinct thermodynamic and kinetic parameters, which may be intimately connected with the host−guest interplay.

As shown in Table 4, 20 structures out of 28 inclusion compounds of **H2** are isostructural. Aside from the adaptability, which seemingly confers the host system with flexibility to explore diverse crystal packings, cf. Table 2, most packing types being common to one or more inclusion compounds reflects appreciable preference of the host system to adopt certain limited packing modes frequently. Thus, the analysis of the crystal packings of a large number of inclusion compounds with varying guests may permit the prediction of the crystal packing of an inclusion compound with a given guest. For example, we were guided in our initial studies by the isostructurality of **H2**·benzene, **H2**·nitrobenzene, and **H2**·mesitylene to determine the structures of **H2**·*p*-xylene and **H2**·*p*-terphenyl. The latter were indeed found to be isostructural to those of **H2**·benzene, **H2**·nitrobenzene, and **H2**·mesitylene (Table 4 and Supporting Information). In a similar manner, **H2**·cyclodecane was initially anticipated to be isostructural to those of **H2**·decalin and **H2**·perhydroisoquinoline, and this was indeed found to be so.

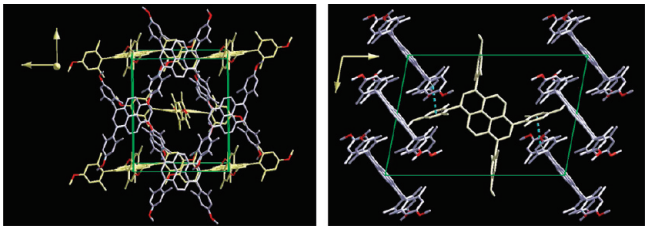


FIGURE 4. Crystal packing of **H2** down the *a*- and *b*-axes. The two different molecules in the asymmetric unit cell are shown in different colors.

Inclusion Compounds of Host H1. The inclusion compounds of **H1** with aliphatic and aromatic guest molecules such as cyclododecene, decalin, benzene, and mesitylene were grown readily from the solutions of **H1** in chloroform containing the added guest. The crystals of inclusion compounds formed with decalin, cyclododecene and benzene were found to correspond to a triclinic system (*P*-1), while those with mesitylene belonged to a monoclinic crystal system ($P2/n$).

The crystal packings of the inclusion compounds of **H1** with cyclododecene and decalin were found to be similar to those of the respective inclusion compounds with host **H2** (see Supporting Information); they correspond to the pattern typified by type 3, Figure 3. Likewise, the organization of aromatic guest molecules such as benzene and mesitylene are found to be similar to those in the inclusion compounds of **H2** corresponding to types 3 and 1, respectively.

Inclusion Compounds of Host H3. Although the host **H3** was found to include aromatic guest molecules readily, the crystals were found to be either too thin or were found to lose the guest molecules instantaneously when removed from the mother liquor. We were successful in determining the crystal structure of the compound with guest *p*-xylene, whose crystal packing is shown in Figure 5. The crystals of **H3**·*p*-xylene were found to belong to triclinic crystal system (space group *P*-1); see Supporting Information. The asymmetric unit cell was found to contain one host and three guest molecules such that **H3**:guest ratio is 1:3. In the crystal lattice, the host molecules lie in the *bc*-plane with an angle of inclination and interact via C−H···O hydrogen bonds with the molecules that are related by inversion symmetry (along the *c*-axis) and translation symmetry (along the *b*-axis). The guest *p*-xylene molecules are found to be located in both trough and concave domains of the host pyrene structure. The PLATON calculation reveals that the guest-accessible volume is approximately 40%.

Inclusion Compounds of Host H4. The objective in synthesizing the host **H4** was to examine if structural expansion by changing the methoxy to methoxy methyl group manifests in increased void spaces for guest inclusion. The consequences of introduction of a methylene group include (i) change of hybridization of the oxygen from sp^2 in **H2** to sp^3 in **H4**, (ii) increased flexibility of the methoxy oxygen to participate in weak intermolecular interactions[22] and (iii) elongation of the aryl ring structurally so that even large molecules could possibly be bound. So, modified behavior toward guest inclusion was expected, while similar mode of inclusion as that of **H2** with some guest species was not deemed surprising.

The host **H4** was found to exhibit inclusion property similar to those of all other analogues. It was found to bind both aliphatic as well as aromatic guest molecules. We have determined the crystal structures of the inclusion compounds

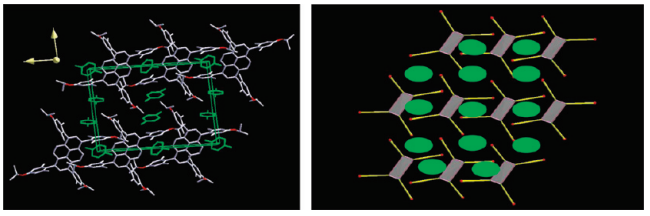


FIGURE 5. Crystal packing diagram of **H3**·*p*-xylene and its cartoon representation (right).

formed with aliphatic guest molecules such as cyclododecene and *trans*-decalin and aromatic guest molecules such as benzene, benzonitrile, and pyrene (Supporting Information). Of course, the host **H4** was found to selectively include the *trans*-isomer of decalin when the crystallization was carried out in the presence of a mixture of *cis* and *trans* isomers. Notably, the **H4** was also found to crystallize in its guest-free form (monoclinic, $P2_1/n$).

The crystal packing of the inclusion compounds of **H4** with cyclododecene and decalin were found to be similar to those of the compounds with host **H2**; they correspond to the patterns typified by type 3 and type 2 (Figure 3). Likewise, the organization of aromatic guest molecules such as benzene, benzonitrile, and pyrene were found to be similar to those of the inclusion compounds of **H2** corresponding to types 2, 1, and 8, respectively.

As mentioned previously, simple comparison of the structures of the inclusion compounds of **H2** and **H4** with common guest molecules, namely, decalin, dodecene, benzene, and mesitylene, points to considerable flexibility of **H4** (Table 1). For decalin as the guest, the host:guest ratio is 1:4 for **H4**, whereas it is 1:1 for **H2**; the guest-accessible volume in the inclusion compound of **H4** is 46% and for **H2** it is ca. 25%. In contrast, for guest molecules such as dodecene, both **H2** and **H4** exhibit comparable host:guest ratios and void volumes. Otherwise, the fact that **H4** can exhibit highly flexible guest-dependent crystal packing is compellingly evident.

Crystal Structure of H5 and H6. To illustrate the fact that the skeletal features intrinsic to hosts **H1**−**H4** are important in determining their inclusion property, we synthesized model compounds **H5** and **H6**. The latter can be considered half components of pyrene hosts **H1** and **H2** and are bereft of the central core skeleton. The methyl and methoxy groups were meant to ensure that the mesityl and dimethyl-*p*-anisyl rings in **H5** and **H6** lie orthogonally to the central benzene ring such that the trough domain in host pyrenes **H1**−**H4** is replicated. Several attempts to obtain inclusion compounds of these systems with a variety of aliphatic as well as aromatic guest molecules were in vain. In all attempts, the crystals that gave unique cell dimensions were obtained. The X-ray structure determinations revealed that the crystals of **H5** and **H6** were devoid of any guest inclusion (Supporting Information). Indeed, it is noteworthy that both **H5** and **H6** were found to be isostructural, despite considerable differences in terms of the substituents present in each.

Flexibility of Hosts H1−**H4.** It is amply evident from a comparison of the behavior of hosts **H1**−**H4** with those of **H5** and **H6** that the unique structural features inherent to hosts **H1**−**H4** are responsible for the remarkable inclusion behavior exhibited by them. The inclusion behavior cannot be said to arise solely from packing difficulties, as the hosts

H2 and **H4** also crystallize in their guest-free forms.[26] The host pyrenes seemingly enjoy considerable packing flexibility to exhibit highly guest-dependent inclusion behavior. From where do the hosts **H1**−**H4** derive their packing flexibility?

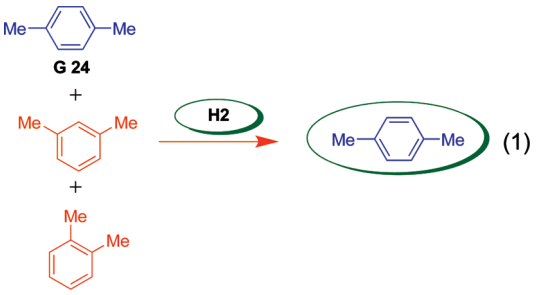
Insofar as the intermolecular interactions are concerned, all inclusion compounds **H1**−**H4** are devoid of any strongly interacting functional groups that may decisively control the crystal packing. A careful analysis of intermolecular interactions suggests that the inclusion compounds are stabilized by weak C−H···O and C−H···π interactions between host−host and host−guest molecules.[22] Although sterics due to the methyl groups are expected to render the aryl rings orthogonal to the flat pyrene ring, we wondered if their orientations are disturbed in pursuit of guest binding. In other words, do the aryl rings exhibit some flexibility in their orientations to adopt structures that are complementary to the guests for binding? We have critically examined the angles between the aryl rings and the central pyrene ring in all 42 compounds for which the structures have been determined in the present investigation. The angles are found to vary by ca. 20°, with the lowest being 68.10° and the highest being 89.90° (Supporting Information). This is evidently a large enough window for the aryl rings to exhibit orientational flexibility, which may confer the host systems with the incentive to adopt structures in accordance to the shapes of the guest molecules. Further, the flexible methoxy and methoxymethyl groups in **H2** and **H4** may contribute to guest binding by positioning themselves in an appropriate manner. Of course, the fact that all compounds crystallize in centrosymmetric space groups suggests that the crystallographic symmetry supposedly imposes certain restrictions on the geometries found.

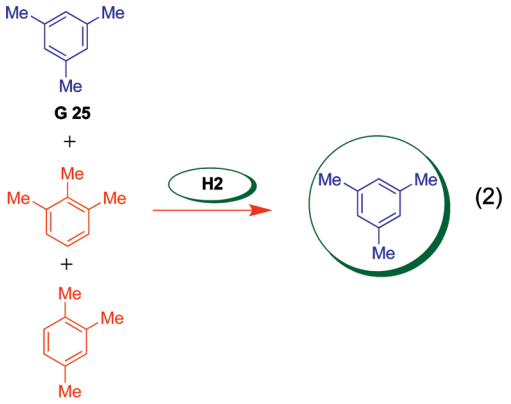
The inclusion phenomenon driven by conformational flexibility and inherent topological features is akin to conformational polymorphism being uncovered in recent times.[27] The presently described structures compellingly demonstrate how the conformational flexibility when combined with molecular attributes may be elegantly exploited for host−guest phenomena.

Applications of Hosts H1−H4. The remarkable inclusion behavior of the hosts **H1**−**H4** prompted us to explore their utility to (i) achieve separation of closely related structural isomers, (ii) trap organic volatile molecules in the crystal lattice, (iii) freeze out one of the equilibrium tautomeric forms of a 1,3-diketone, and (iv) trap conformationally flexible cyclic molecules in one/two of their conformations. In particular, we have employed the methoxy-pyrene **H2** to demonstrate each of the aforementioned objectives.

Trapping of Volatile Organic Molecules. The inclusion phenomenon may modify volatility of the guest molecules.[13] The host **H2** was found to readily form crystals with low boiling solvents such as dimethyl sulfide (bp = 38 °C), $CHCl_3$ (bp = 61 °C), and CCl_4 (bp = 76 °C). The TGA analyses reveal that the guest molecules are released at temperatures 10−20 °C higher than their respective boiling points (Supporting Information). For the case of the inclusion compound of **H2** with dimethyl sulfide, complete exclusion of the guest was found to occur at ca. 75 °C. Clearly, the host−host and host−guest interactions manifest in stronger binding of the guest molecules to reduce their volatility.[22]

Separation of Structural Isomers. One of the pressing problems in chemical industry is the separation of isomers with a very marginal difference in their boiling points.[9,13] Of particular relevance is the separation of regioisomers of dimethylbenzenes, namely, xylenes. We found that the host **H2** independently binds all three isomers when crystallized separately. However, when **H2** was crystallized in the presence of an equimolar mixture of the three isomers, only *p*-xylene was found to be selectively included as revealed by ^{1}H NMR and PXRD analyses of the isolated crystals (eq 1).[23] The host:guest stoichiometry was found to be 1:1. The crystal packing, shown in Figure 3, reveals that the guest molecules are located in the trough domain of the host structure, type 5. In a similar manner, 1,3,5-trimethylbenzene was selectively bound by **H2** when the crystallization was carried out in an equimolar mixture of 1,2,3-, 1,2,4-, and 1,3,5-trimethylbenzenes (eq 2). The selective inclusion of the 1,3,5-isomer was independently established by ^{1}H NMR and PXRD analyses of the isolated crystals as in the case of the **H2**·*p*-xylene compound. Indeed, the crystal packing of **H2**·1,3,5-trimethylbenzene is akin to that of the inclusion compound of **H2**·*p*-xylene (Supporting Information).

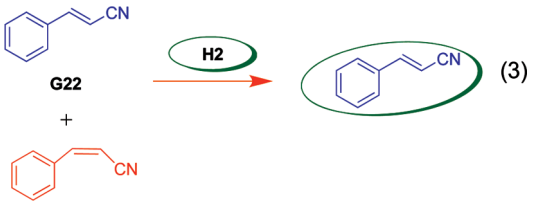




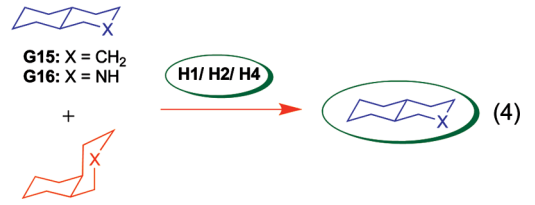
The difference in the boiling points of *cis* and *trans* isomers of cinnamonitrile is very marginal, and the commercially available compound is generally a mixture. Crystallization of **H2** in $CHCl_3$ with an added mixture (40:60) of *cis*- and *trans*-cinnamonitrile led to crystals containing exclusively the *trans* isomer (eq 3). As in the earlier case, this was verified by ^{1}H NMR and PXRD analyses (Supporting Information). Here again, the

(26) We have not deliberately attempted to crystallize **H1** and **H3** in their guest-free states. In the absence of any such effort, there is no reason to believe that they will not crystallize without guest molecules.
(27) Nangia, A. *Acc. Chem. Res.* **2008**, *41*, 595.

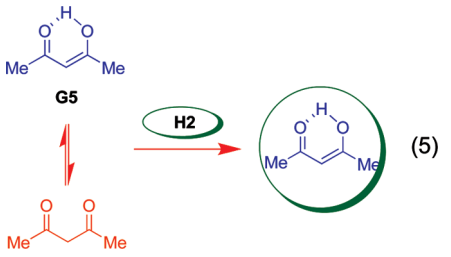
guest is found to occupy the trough domain of the host (Figure 1).



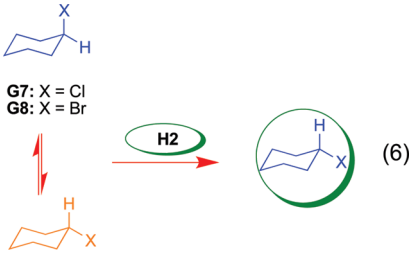
The *cis* and *trans* isomers of decalin and perhydroisoquinoline constitute excellent examples of aliphatic guest molecules with a very low difference in their boiling points. The host **H2** was found to crystallize in each case with the *trans* isomer, when the crystallization was carried out in the presence of a mixture (52:48) of *cis*- and *trans*-decalin/perhydroisoquinoline (eq 4). The structures of **H2**·*trans*-decalin and **H2**·*trans*-perhydroisoquinoline are isostructural, and the host:guest stoichiometry is 1:1. In contrast to aromatic guest molecules discussed above, the *trans*-fused decalin molecules are found in the concave domains of the host. The fact that the crystals grown uniformly contained the *trans*-isomer was established by combining ^{1}H NMR with GC as well as PXRD analyses of the bulk sample. The crystal packing is shown in Figure 3 for the case of **H2**·*trans*-decalin. The crystal structure analyses reveal virtually no interactions between the host and guest molecules. It appears that the structural (shape) complementarity is the riding factor in determining the guest inclusion and hence the crystal formation. We have found that the host molecules **H1** and **H4** also include selectively the *trans* isomer; in the case of **H4**, however, the expanded structure permits inclusion of two guest molecules in the asymmetric unit cell such that the host:guest stoichiometry is 1:4 (Supporting Information).



Trapping of Keto-Enol Form of 1,3-Diketones. In general, 1,3-diketones exist in equilibrium with their keto-enol forms, whose relative concentrations are determined by the solvent characteristics. There have been early attempts to trap either of the two forms exclusively by host:guest chemistry. While the early reports appear to be irreproducible,[9] Toda et al. showed that acetylacetone is included in the crystal lattices of 1,1,-di(*p*-hydroxyphenyl)cyclohexane and (*R*,*R*)-(−)-*trans*-4,5-bis(hydroxydiphenylmethyl)-2,2-dimethyl-1,3-dioxacyclopentane (Taddol)[28] in its keto-enol form. In our experiments, we found that acetylacetone readily gets incorporated in the lattice of **H2**, when the crystallization of the latter is carried out in $CHCl_3$ containing acetylacetone. The X-ray crystal structure reveals that the guest is trapped in its keto-enol form (Supporting Information and eq 5). The guest is found to occupy the trough region of the host with a C−H···O hydrogen bond (between C2H of pyrene and the oxygen atom of the guest enol) primarily playing the binding force; of course, the shape of the guest is also important in filling the vacant space. The crystal packing of **H2**·acetylacetone is similar to those of the inclusion compounds of **H2** with benzene, toluene, nitrobenzene, *o*-xylene, *p*-xylene, mesitylene, and *p*-terphenyl shown in Figure 3. It is noteworthy that the enol form has been trapped in four lattice inclusion hosts so far.[29] It turns out that acetylacetone is hydrogen-bonded to the host molecules via O−H···O hydrogen bond in all of these cases, unlike in the present scenario where it is C−H···O hydrogen bonded to the nonpolar host molecule.



Freezing of Flexible Molecules in Dynamic Conformational Equilibrium. One of the fascinating applications of host−guest inclusion chemistry is the isolation of liquid samples as crystalline materials at room temperature. This protocol has traditionally inspired chemists to gain exciting X-ray structural insights concerning compounds that are otherwise liquids.[12,13] Crystallization of **H2** in 1,2-dichloroethane led to inclusion crystals of the solvent molecules (Table 2). The conformation of 1,2-dichloroethane was found to be *anti* (Supporting Information). It turns out that the *anti* conformation does indeed correspond to the lowest energy, while *gauche* corresponds to the higher energy form.[30] In a similar manner, both chloro- and bromocyclohexanes were found to be included by the host **H2**. The X-ray structural investigations reveal that both compounds exhibit isostructurality with chloro/bromo exchange bringing about no change in the crystal packing. In both structures, the halogen is found to occupy the equatorial position (eq 6).[31]



Various possible conformations with marginally varying energies are theoretically possible for cyclooctane and cyclodecane as shown in Figure 6. The host **H2** was found to freeze

(28) Lipkowska, Z. U.; Yoshizawa, K.; Toyota, S.; Toda, F. *CrystEngComm* **2003**, *5*, 114.

(29) (a) Gallardo, O.; Csoeregh, I.; Weber, E. *J. Chem. Crystallogr.* **1995**, *25*, 769. (b) Camerman, A.; Mastropaoto, D.; Camerman, N. *J. Am. Chem. Soc.* **1983**, *105*, 1584.

(30) Sidhu, P. S.; Enright, G. D.; Ripmeester, J. A. *J. Phys. Chem. B* **2002**, *106*, 8569.

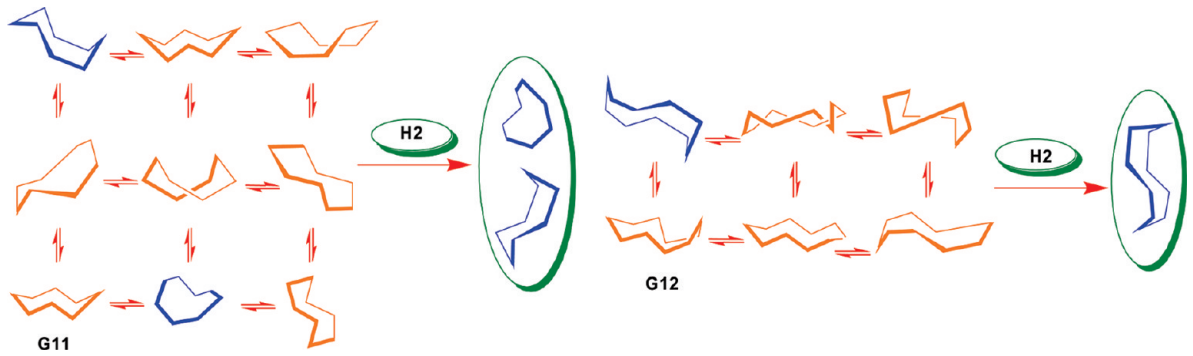


FIGURE 6. Various low-energy conformations of cyclooctane (left) and cyclodecane (right). Also shown are the conformations that are found in their inclusion compounds with **H2**.

cyclooctane in its chair-boat and boat-boat conformations (the asymmetric unit cell contains 2 molecules of cyclooctane). The more flexible cyclodecane was found to be trapped in **H2** in its boat-chair-boat conformation. The most stable conformations for cyclooctane and cyclodecane are boat-chair and boat-chair-boat, respectively. Clearly, the host−guest chemistry with **H2** enables realization of high energy forms at room temperature.[32]

Generalizations about the Properties of Inclusion Hosts H1−H4 and Their Adaptability. The inclusion behavior observed with hosts **H1**−**H4** amply suggests that their skeletal features are robust to minor structural modifications. This is significant given that the crystal packings of organic molecules in general change dramatically with subtle structural modifications. It emerges from a comparative study of the inclusion compounds of **H1**, **H2**, and **H4** with aliphatic as well as aromatic guest molecules in Table 1 that the void volumes can be modulated. Although **H4** is advantageous as revealed by the data on guest-accessible volumes, cf. Table 1, the entropically more labile methoxymethyl groups in **H4** might in some instances reduce the guest-accessible volume. One is tempted to believe that the highly symmetrical molecular systems with orthogonal aromatic planes might lack conformational freedom to pack efficiently in the solid state and that this inefficiency in close packing should be the origin for the observed guest inclusion. This indeed was our initial premise on the basis of which the hosts **H1**−**H4** were designed. However, this is entirely not true; the host systems **H2** and **H4** that are largely explored for guest inclusion also crystallize in their guest-free form. The inclusion behavior of host **H2** with almost any guest clearly points to the fact that **H2** and its analogues, i.e., **H1**, **H3** and **H4**, are highly *adaptable*. The adaptability appears to owe its origin to two important factors, moderate conformational flexibility and lattice energy conservation through weak intermolecular interactions. For guest-induced adaptability of the host systems, it is imperative that the hosts are able to explore moderate conformational flexibility to include guests efficiently. As mentioned earlier, the 2,6-dimethylaryl rings that are orthogonal to the central pyrene rings are indeed associated with *moderate* rotational freedom. The angles between the central pyrene ring and the dimethylaryl rings in the inclusion compounds of all **H1**−**H4** are found to vary in the range of 68.1−89.9°. We believe that this rotational freedom confers the hosts **H1**−**H4** with sufficient flexibility to adopt structures complementary to those of the guests. Further, the crystal packings in all of the inclusion compounds of **H1**−**H4** are governed by weak intermolecular interactions such as C−H···O hydrogen bonds and C−H···π interactions.[22] As a result, change in the crystal packing with a change in the guest structure may not lead to dramatic variation in the crystal lattice stabilization energy. This implies that hydrogen-bonded host systems are most likely to be sensitive to changes in guest structures, unless the structures of the hosts intrinsically contain several functional groups capable of strong intermolecular interactions and contribute to the overall lattice stabilization, e.g., choleic acids[15c] and gossypol.[15] The conformation and lattice energy compensation put forward by Nangia and co-workers in the context of polymorphism observed with 4,4-diphenyl-2,5-cyclohexanedione is noteworthy in this context.[27] The conformational changes to accommodate the guest molecules by hosts **H1**−**H4** appear to be compensated for by crystal lattice stabilization.

The unique feature of the hosts **H1**−**H4** is the binding of aliphatic and aromatic guests differently. In general, the small-sized guest molecules are found to be located in the basin region, while aliphatic and aromatic guests are found in the channels and troughs, respectively. This novel mode of guest binding may pave the way for exploiting inclusion of two or more guest molecules in a single component to access multicomponent molecular crystals in a predictive manner.

Conclusions

On the basis of a rational design, we have developed tetraarylpyrenes **H1**−**H4** as a new class of inclusion host systems that exhibit remarkable guest inclusion. In particular, **H2** is found to include a broad range of guest molecules. We have determined 42 crystal structures in all, of which 28 structures correspond to the inclusion compounds of **H2** alone. The X-ray crystal structure analyses reveal favored locations for the guests in that the small-sized guest molecules such as dimethyl sulfide, chloroform, etc. are found to occupy the basin regions of the host (Scheme 1), whereas aliphatic guests are found to be included in concave/channel regions and the aromatic guests in troughs. In essence, the hosts are found to behave like molecular tweezers in including a variety of guest molecules with a high degree of

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adaptability. The crystal structure analyses also reveal a varied yet limited number of modes in which the host molecules are found to organize. Indeed, as many as 20 inclusion compounds of **H2** out of 28 are found to be isostructural. The comprehensive structural investigations of a number of inclusion compounds demonstrate how conformational flexibility when combined with molecular attributes may be elegantly exploited for remarkable host−guest phenomena. We have exploited the shape-selective inclusion behavior observed with **H2** to demonstrate its utility in (i) the separation of the regio- and stereoisomeric mixtures, (ii) the stabilization of one of the tautomeric forms of 1,3-diketone, and (iii) the locking of conformationally flexible cycloalkanes in one/two of their conformations. In addition to applications in chiral resolution and fluorescence-based guest signaling, these novel inclusion host systems with inherently different domains for guest inclusion are believed to be attractive to predictively access multicomponent organic molecular crystals, which are a challenge. We are continuing our investigations to exploit the unique structural attributes of **H1**−**H4** for development of functional organic materials.

Experimental Section

The general procedure for the synthesis of tetrarylpyrenes **H1**−**H4** involved four-fold Suzuki coupling of 1,3,6,8-tetrabromopyrene with suitably functionalized boronic acids using Pd(PPh_3)$_4$ as a catalyst (Supporting Information); 1,3,6,8-tetrabromopyrene was synthesized by bromination of pyrene in nitrobenzene.[18c] The preparation of hosts **H1** and **H2**, i.e., 1,3,6,8-tetrakis(2,4,6-trimethylphenyl)pyrene and 1,3,6,8-tetrakis(2,6-dimethyl-4-methoxyphenyl)pyrene, have previously been published by us.[18c] 2,6-Dimethyl-4-isopropoxyphenylboronic acid, required for **H3**, was synthesized according to a literature procedure[33] using 2,6-dimethyl-4-isopropoxybromobenzene as a starting material. 4-Methoxymethyl-2,6-dimethylphenylboronic acid required for **H4** was prepared starting from bromomesitylene (Supporting Information). The diarylbenzenes **H5** and **H6** were similarly prepared by Suzuki coupling of 4,6-dibromo-*m*-xylene and 4,6-dibromoresorcinol dimethyl ether with appropriately functionalized boronic acids under Pd(0)-catalyzed conditions (Supporting Information). A representative procedure for the Suzuki coupling is described below for the preparation of **H4**.

A 100-mL two-necked round-bottom flask, removed hot from an oven, was cooled under a N_2 atmosphere and charged with tetrabromopyrene (1.0 g, 1.93 mmol), 2,6-dimethyl-4-methoxymethylphenylboronic acid (2.3 g, 11.6 mmol), Pd(PPh_3)$_4$ (0.25 g, 10 mol %), dioxane (40 mL), and 20% NaOH solution (10 mL). The reaction mixture was heated at 90 °C. The pale-green turbid solution turned clear yellow in 6 h. Subsequently, the heating was continued for additional 6 h, after which time the reaction mixture turned dark brown. At this stage, the reaction mixture was cooled and extracted with $CHCl_3$. The combined extracts were washed with brine, dried over Na_2SO_4 , and concentrated. The pure tetraarylpyrene **H4** was isolated by silica gel column chromatography using petroleum ether as an eluent. Yield 1.02 g (70%): mp 251−253 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.90 (s, 24H), 3.38 (s, 12H), 4.41 (s, 8H), 7.16 (s, 8H), 7.44 (s, 4H), 7.51 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 58.2, 74.8, 124.8, 125.9, 126.8, 128.4, 128.6, 136.2, 137.1, 137.2, 139.4; ESI-MS$^+$ m/z calcd for $C_{56}H_{58}O_4$ 795.442 [M + H], found 795.4413.

Formation of Inclusion Compounds. In a typical experiment, 50 mg of host (**H1**−**H4**) and 15 mg of guest were taken in a 10-mL glass vial and dissolved in ca. 3−4 mL of chloroform. Slow evaporation of the resulting solution over 2−3 days led to crystals in a quantitative yield, which were carefully isolated. For volatile liquid guests, the host (**H1/H2/H3/H4**) was directly dissolved in the neat guest (2 mL). Slow evaporation of the solution led to crystals of the inclusion compound in a quantitative yield.

X-ray Crystal Structure Determinations. A good quality crystal in each case was mounted in a glass capillary and cooled to 100 K, and the intensity data were collected on a Bruker Nonius SMART APEX CCD detector system with Mo-sealed Siemens ceramic diffraction tube (λ = 0.71073) and a highly oriented graphite monochromator operating at 50 kV and 30 mA. The data were collected on a hemisphere mode and processed with SAINTPLUS. Empirical absorption correction was made using SADABS. The structure was solved in each case by Direct Methods using the SHELXTL package and refined by full matrix least-squares method based on F^2 using the SHELX97 program.[34] All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were included in the ideal positions with fixed isotropic U values and were riding with their respective non-hydrogen atoms. The experimental details of crystal data, intensity measurements, structure solution, and refinement are contained in Supporting Information.

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Supporting Information Available: Details of synthesis, spectroscopic characterization data, spectral reproductions, crystal data for all compounds, TGA profiles, experimental and simulated PXRD patterns, ORTEP drawings of the molecular structures of all compounds, crystal packing diagrams, and CIF files. This material is available free of charge via the Internet at http://pubs.acs.org.

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