



Hydrogen Bonds Assist the Organization of Up to 11 Guests Within Self-assembling Cavities of Nanometer Dimensions

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Abstract—The self-assembly of C-methylresorcin[4]arene with 4,4'-bipyridine affords the formation of closed solid state cavities with internal volumes of ca. 1.0 nm³ which encapsulate up to an unprecedented 11 guests involving three different molecules. These cages exhibit functionality directed into the cavities, in the form of hydrogen bond donor and acceptor sites, which assists the organization of their guests. In one case, the guests interact, with each other and the walls of the host, via 15 hydrogen bonds, to produce chiral molecular assemblies within the solid. © 2002 Published by Elsevier Science Ltd.

Introduction

Self-assembling cavities in solution^{1–3} (e.g., hydrogen-bonded capsules) and in the solid state⁴ (e.g., gas-clathrate hydrates) permit the isolation of reactive and/or stable chemical species into chambers larger than those accessible via conventional covalent methods, with potential applications in separations, catalysis, and chemical synthesis. Whereas it is becoming increasingly clear that factors such as size, positioning, and number of components that make up such cages dictate cavity volume,^{2,3,5–7} less is known about those recognition processes which occur within their interiors.^{8,9} Moreover, as these cavities begin to approach nanometer dimensions,^{2,3,6–9} it is expected that they will become large enough to accommodate multiple guests and thus provide an opportunity to study assemblies-within-assemblies. Questions must then be raised concerning guest organization: How many guests fit within the cavity? What spatial arrangements do the guests adopt? How do the guests interact with the host? Are the guests oriented in such a way so as to react?

Results and discussion

We have demonstrated that cocrystallization of C-methylresorcin[4]arene, **1**, with 4,4'-bipyridine, **2**, yields 1D extended arrays owing to the ability of **1** to function as a quadruple hydrogen bond donor.¹⁰ The syntheses of these multi-component frameworks relied on a crystal engineering design strategy¹¹ in which pairs of **2** serve as bifunctional hydrogen bond acceptors, forming four O–H···N hydrogen bonds to the upper rim of **1**.

During studies aimed at determining the robustness of this supramolecular synthon,¹¹ we have discovered the ability of **1**, in a T-shaped conformation,¹² to function as an eight-fold hydrogen bond donor. This conformation is expressed, upon cocrystallization with **2** from hydrogen bond donor/acceptor solvents (i.e., acetone, ethanol), to yield skewed molecular bricks, **1·2·4**(acetone), **3a**, and **1·2(2)·3.5**(ethanol)·H₂O, **3b**, which pack within the crystal so as to enforce closed cavities (C_{2h} symmetry) with internal volumes of ca. 1.0 nm³ and walls lined with hydrogen bond donor/acceptor sites (Scheme 1).¹³ In the case of **3b**, the guests interact with each other and the walls of the host, via 15 hydrogen bonds, to form isolated chiral molecular assemblies within the solid. We now report the synthesis, X-ray crystal structures, and host–guest properties of **3**.

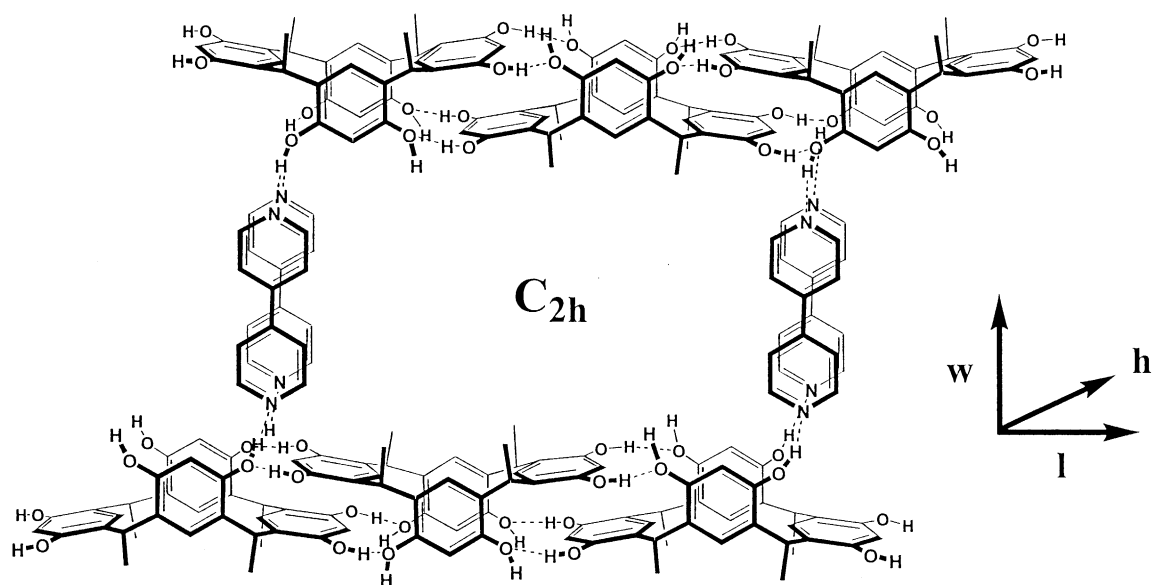
When **1** (0.020 g) was added to a solution of either acetone or ethanol (10 mL) containing an excess of **2**, a light yellow precipitate immediately formed. Colorless crystals of **3a** and **3b** suitable for X-ray analysis were grown by slow evaporation of the redissolved product

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Scheme 1.

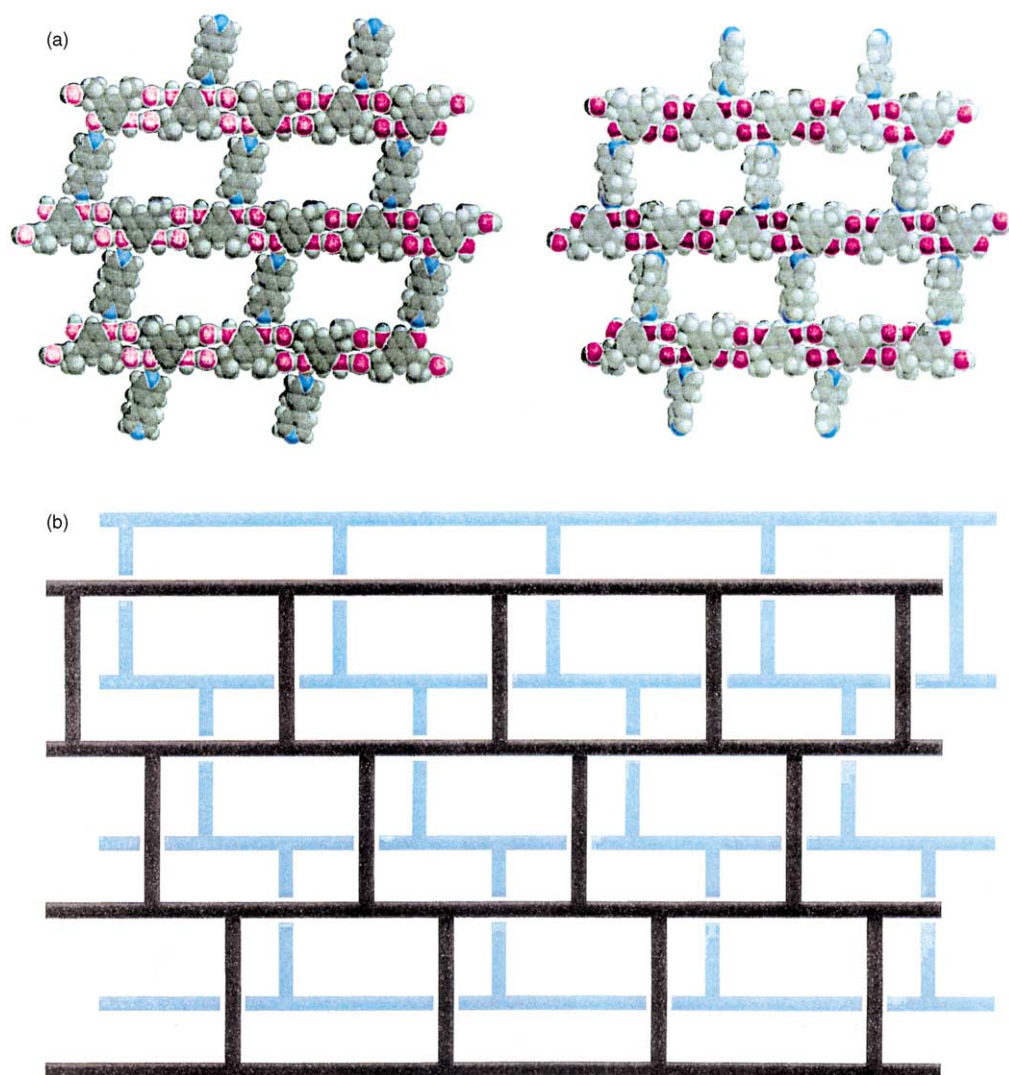


Figure 1. Brick framework adopted by the components of **3**: (a) X-ray crystal structures of **3a** and **3b**, (b) the ...ABA... solid-state packing exhibited by the bricks. Color scheme: C, grey; H, white; O, red; N, blue.

from the appropriate solvent. We note that the composition of the initial precipitate from the reaction involving acetone corresponds to a 1D wave-like polymer.¹⁴ The formulations of **3a** and **3b** were confirmed by single-crystal X-ray diffraction¹⁵ and ¹H NMR spectroscopy.

Views depicting the frameworks of **3** are shown in Figure 1a. **1** has adopted a T-shaped conformation in which a pair of **2** forms two O–H···N hydrogen bonds to the upper rim of **1** while neighboring resorcin[4]arenes interact by way of four O–H···O hydrogen bonds yielding 1D polymeric chains. Owing to the ability of **2** to serve as a bifunctional hydrogen bond acceptor, **2** is observed to link resorcin[4]arenes of adjacent chains giving rise to 2D frameworks which conform to skewed molecular bricks that possess guest-filled box-like cavities (guests: eight acetone molecules, **3a**, two water molecules, two 4,4'-bipyridine molecules and seven ethanol molecules, **3b**). Notably, the **1**·**2** framework exhibits idealized C_{2h} symmetry, a meso form in which the upper and lower halves of the network are mirror images (corner **1**··**1** separations: ca. 2.1, 1.6 nm), with effective cavity dimensions ca. 1.4×1.3×0.7 nm and internal cavity volumes¹⁶ of ca. 1.0 nm³. Indeed, the cavities of **3** are spacious, being two to three times larger than those of most zeolites.¹⁷ Importantly, four hydroxyl groups from two different resorcin[4]arenes line each cavity at opposite corners and form four O–H···O hydrogen bonds to four guest species.

A view depicting the solid-state packing of **3** is shown in Figure 1b. The bricks of **3a** and **3b** have assembled such that they form identical . . .ABA. . . stacking patterns, the corners of the bricks lying above and below the cavities of another. As a result, the guests are completely enclosed such that there are no pores connecting adjacent cavities. The major difference between **3a** and **3b** lies in the nature of the included guests and the levels of organization the guests display within the cavities which we now address.

Views depicting the guests of **3a** and **3b** are shown in Figure 2. As stated, the cavities of **3a** (of 0.94 nm³ volume) contain eight guests of a single type, namely acetone, whereas the cavities of **3b** (of 1.04 nm³ volume) contain 11 guests consisting of three different components, namely two waters, two 4,4'-bipyridines, and seven ethanols. In the case of **3a**, the guests, which lie around a crystallographic center of inversion (Fig. 2a), exist as a racemic pair of *R* and *S* configurations, hereafter referred to as *A_R* and *A_S*, in which each enantiomer forms a hand-in-glove fit with the upper and lower half of the box (Fig. 2b). Notably, four acetones participate in four O–H···O hydrogen bonds to four hydroxyl groups of **1** located at the corners of the box while the remaining guests occupy the center and corners of the cavity. In **3b**, the guests are bisected by a crystallographic two-fold rotation axis such that they interact with each other and with the walls of the host,

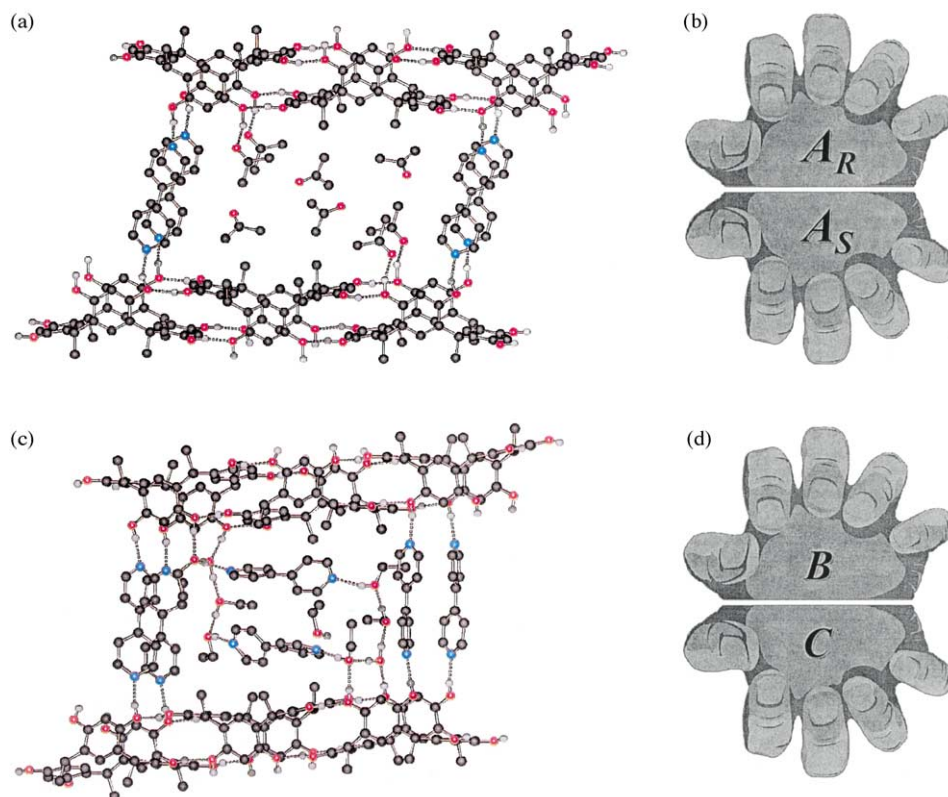


Figure 2. The guests of **3**: (a) X-ray crystal structure of **3a** displaying the achiral organization of the eight guests, (b) hand-in-glove fit of the enantiomeric configurations of **3a**, (c) X-ray crystal structure of **3b** displaying the chiral organization of the 11 guests, (d) hand-in-glove fit of the chemically distinct configurations of **3b**, (e) a close-up view of the guests of **3b** outlining the *B* and *C* designations, (f) organization of the guests of **3b** with respect to neighboring cavities, (g) schematic of **3b** showing the guest configurations on one side of the brick framework (we note that the guests of the opposite side are of the opposite chirality), (h) dipoles realized in **3a** and **3b**.

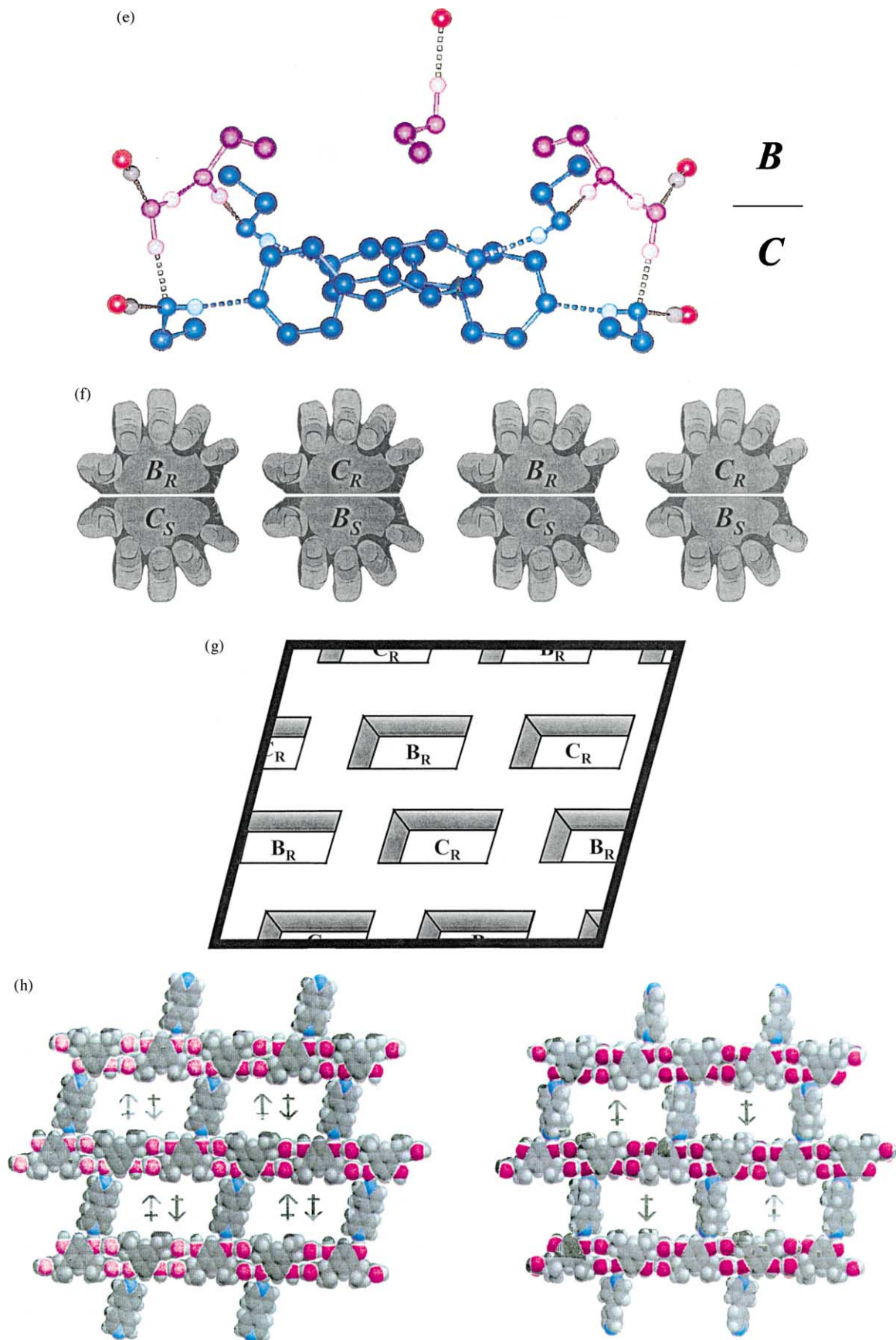


Figure 2 (continued).

via 15 O–H···X (X = O, N) hydrogen bonds (Fig. 2c), to produce an isolated chiral assembly in which the center of inversion of the box has been destroyed. In a similar way to **3a**, two waters and two ethanols participate in four O–H···O hydrogen bonds with four hydroxyl groups of **1**. In both **3a** and **3b**, guests of neighboring boxes are related by a crystallographic center of inversion, meaning that guest assemblies of adjacent boxes of **3a** are identical, whereas those of **3b** are enantiomers.

A closer inspection of the boxes of **3b** reveals that the guests form a double layered array within each cavity such that the top and bottom halves of the box, in a similar way to **3a**, contain chiral guest configurations. Unlike **3a**, however, the configurations, hereafter referred to as *B* and *C* (Fig. 2d), are chemically distinct and are therefore not enantiomers. As shown in Figure 2e, *B* consists of two waters and three ethanols held together by four O–H···O hydrogen bonds, while *C* consists of two 4,4'-bipyridines and four ethanols held together by six O–H···X hydrogen bonds. An ethanol of the former also participates in an O–H···O hydrogen bond to a hydroxyl group of **1** located at the top of the box. *B* and *C* are then linked together, by four O–H···O hydrogen bonds, giving rise to chiral domains $B_R + C_S$ and $B_S + C_R$ which alternate between neighboring cavities of the solid (Fig. 2f). Notably, as a result of this arrangement, adjacent cavities of **3b**, unlike **3a**, are observed to display chemically distinct, rather than identical, guest configurations along each face of the brick framework (Fig. 2g).

In principle, the guests of **3b**, in a similar way to **3a**, may have assembled within each box forming a racemate, *R*, involving all 11 guests, an assembly which possesses a net dipole moment of zero. Indeed, it is well known that organic compounds tend to crystallize such that local dipole moments cancel.¹¹ To account for the observation that the cavities of **3b** include chiral, rather than achiral, guest assemblies, we suggest that, in addition to geometric and electronic constraints imposed by cavities,¹⁸ fit and intermolecular forces between guests must be considered when designing multi-guest host-guest systems. As demonstrated by **3b**, it is possible, using appropriately functionalized achiral guests, to break achiral symmetry in cavities, giving rise to chiral domains, net dipole moments, in regions of space which are not inherently chiral (Fig. 2h). To our knowledge, this observation is unprecedented in host-guest and solid-state chemistry and we attribute our finding to the size and molecular recognition properties, supplied by **1**, of the boxes.

In addition to the organization displayed by the guests within each cavity, that the guests of **3b** are not randomly distributed within the solid is surprising since occupancy of either $B_R + C_S$ or $B_S + C_R$ within each box is, in principle, equally probable. Further inspection of the boxes, however, reveals that the cavities (i.e., the framework) and pyridine units of **2** have undergone a conformational reorganization, compared to **3a**, such that they match the chirality of the guests (Fig. 2g). Since each cavity of **3b** shares **2** with neigh-

boring boxes, adjacent boxes are preorganized to complex guests of opposite chirality. In effect, spontaneous separation of $B_R + C_S$ and $B_S + C_R$ has occurred, in a similar way to that observed in two dimensional Langmuir–Blodgett films and smectic liquid-crystal phases,^{19–21} by way of a cooperative process involving the shapes of the boxes.

We have presented a self-assembling framework, **1-2**, which, by virtue of its multicomponent nature, possesses cavities which are large, flexible, and host an unprecedented number of guests that adopt both achiral and chiral arrangements. Indeed, by using interior-directed functionality (e.g., hydrogen bond donor/acceptor sites), our findings suggest that it should be possible to control spatial arrangements of large numbers of the same and different guests, as well as large conformationally mobile guests, within nanometer sized cavities perhaps yielding 'designer cavities' which constitute assemblies-within-assemblies. Moreover, in addition to the organization displayed by the guests here, it seems that as self-assembling cavities continue to grow, higher degrees of complexity in terms of guest organization should be realized.

Acknowledgements

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