

## Rational Design of *Multicomponent Calix[4]arenes* and Control of Their Alignment in the Solid State

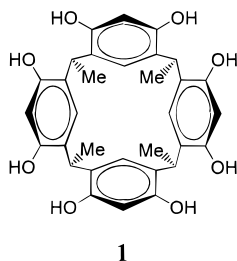
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A major impetus for the design of supramolecular complexes is structural and functional mimicry of those large, *multicomponent*, self-assembling processes found in Nature.<sup>1</sup> In such a context, the area of host–guest chemistry has offered numerous examples of *two*-component molecular recognition processes involving noncovalent interactions (*e.g.*, hydrogen bonds,  $\pi$ – $\pi$  interactions).<sup>2</sup> Such an approach, however, often involves *monomolecular* hosts<sup>3</sup> which are typically designed *via* the elaborate formation and breakage of covalent bonds.<sup>2</sup>

With this in mind, we have embarked upon a program of study aimed at the design of *multicomponent* hosts held together by noncovalent forces. As a starting point, we have chosen the readily available *C*-methylcalix[4]resorcinarene<sup>4</sup> (**1**) as a



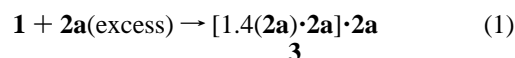
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platform for the assembly process. Indeed, solid state studies have revealed the ability of **1** to adopt a bowl-like conformation in which four of its upper rim hydroxyl hydrogen atoms are pointed upward, above its cavity,<sup>5</sup> which effectively makes **1** a multiple hydrogen bond donor. Using a design strategy recently employed for the crystal engineering<sup>3,6</sup> of one- (1D) and two-dimensional (2D) resorcinol-based lattices,<sup>7</sup> we reasoned that co-crystallization of **1** with hydrogen bond acceptors such as pyridines **2** would result in the formation of four O–H···N hydrogen bonds between the upper rim of **1** and four pyridine units<sup>8</sup> which would, in turn, extend the cavity of **1**<sup>9</sup> and give rise to a *multicomponent* host 1.4(**2**) capable of entrapping large guests 1.4(**2**)·guest.<sup>10</sup>

- (1) Lawrence, D. S.; Jiang, T.; Levett, M. *Chem. Rev.* **1995**, *95*, 2229.  
 (2) (a) Gutsche, C. D. In *Inclusion Compounds*; Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Eds.; Oxford University Press: Oxford, 1991; Vol. 4, pp 27. (b) Gokel, G. In *Crown Ethers & Cryptands*; Stoddart, J. F., Ed.; Black Bear Press: Cambridge, 1991.  
 (3) Desiraju, G. R.; Krishnamohan Sharma, C. V. In *The Crystal as a Supramolecular Entity*; Desiraju, G. R., Ed.; John Wiley & Sons: New York, 1996.  
 (4) Högberg, A. G. S. *J. Am. Chem. Soc.* **1980**, *102*, 6046.  
 (5) The remaining hydroxyl hydrogen atoms of **1** typically form intramolecular O–H···O hydrogen bonds along its upper rim: Murayama, K.; Aoki, K. *Chem. Commun.* **1997**, 119 and references therein.  
 (6) Desiraju, G. R. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2311.  
 (7) Aoyama, Y.; Endo, K.; Anzai, T.; Yamaguchi, Y.; Sawaki, T.; Kobayashi, K.; Kanehisa, N.; Hashimoto, H.; Kai, Y.; Masuda, H. *J. Am. Chem. Soc.* **1996**, *118*, 5562.  
 (8) **1** has been observed to participate in intermolecular hydrogen bonds with either anions, adventitious solvent molecules, or **1** in the solid state (ref 5).  
 (9) Juneja, R. K.; Robinson, K. D.; Johnson, C. P.; Atwood, J. L. *J. Am. Chem. Soc.* **1993**, *115*, 3818.  
 (10) Few examples exist in which hydrogen bonds have been exploited along the upper rim of calixarenes: Shimizu, K. D.; Rebek, J., Jr. *Proc. Natl. Acad. Sci. U.S.A.* **1995**, *92*, 12403 and references therein.

In this contribution we report the syntheses and X-ray structure determinations of the first examples of *multicomponent* calixarenes. We demonstrate the ability of pyridine (**2a**) and its *exo*-bidentate analog 4,4'-bipyridine (**2b**) to elaborate the cavity of **1** by forming walls which enable **1** to form inclusion compounds, [1.4(**2a**)·**2a**]·**2a** (**3**) and 1.2(**2b**)·**5** (**4**, where **5** = MeCN), with guests previously unobserved for this macrocycle. In the case of **2b**, the assembly process has also resulted in the formation of a 1D self-included hydrogen bonded array owing to the ability of **2b** to act as a linear bifunctional hydrogen bond acceptor.<sup>11</sup> Such observations illustrate a novel manner in which the principles of crystal engineering may be exploited for (1) the construction of *multicomponent* host–guest assemblies based on **1** and (2) the control their alignment in the solid state.<sup>7</sup>

Addition of **1** (0.020 g) to a boiling aliquot of **2a** (5 mL) according to (1) yielded yellow crystals of **3** suitable for X-ray analysis upon cooling. The formulation of **3** was confirmed by single-crystal X-ray diffraction,<sup>12</sup> <sup>1</sup>H NMR spectroscopy, and thermogravimetric analysis.

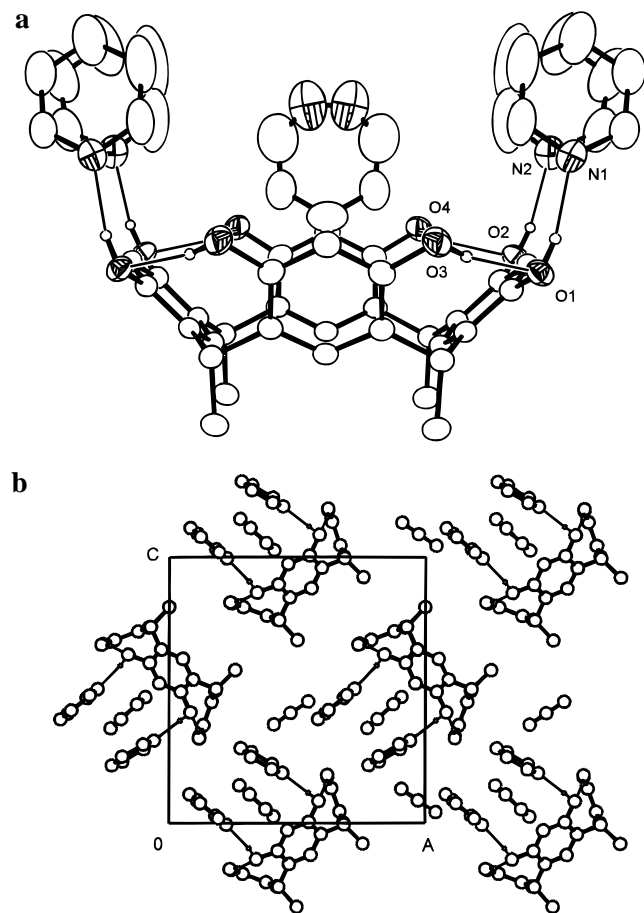


A view of the six-component complex 1.4(**2a**)·**2a** is shown in Figure 1a. The assembly is bisected by a crystallographic mirror plane and consists of **1** and five molecules of **2a**, four of which form O–H···N hydrogen bonds, as two face-to-face stacked dimers, with the resorcinols parallel to the mirror plane such that they adopt an orthogonal orientation with respect to the upper rim of **1** [O(1)···N(1) 2.675(3) Å, O(2)···N(2) 2.687(4) Å].<sup>13</sup> As a consequence of this spatial arrangement, a cavity has formed, inside which a disordered molecule of **2a**, which lies perpendicular to the mirror plane, is located, interacting with **1** *via* C–H··· $\pi$ -arene interactions. As in **1**·(Et<sub>3</sub>HN)<sub>2</sub>SO<sub>4</sub>·4EtOH,<sup>5b</sup> the remaining hydroxyl groups form *intramolecular* O–H···O interactions along the upper rim of **1** [O(3)···O(1) 2.769(3) Å, O(4)···O(2) 2.755(3) Å],<sup>5</sup> which reinforce its bowl-like conformation, resulting in a total of eight structure-determining O–H···X (X = N, O) hydrogen bonds. Indeed, the inclusion of **2a** within 1.4(**2a**) is reminiscent of the ability of covalently modified calix[4]arenes such as *p*-*tert*-butylcalix[4]arene to form molecular complexes with aromatics such as benzene and toluene.<sup>14</sup>

A view along the crystallographic *b* axis depicting the crystal structure of **3** is shown in Figure 1b. **3** self-assembles to form a 2D layered architecture within the *ac* plane such that the cavities of the 1.4(**2a**) moieties lie at approximate right angles to each other. Interestingly, the molecule of **2a** present in the clathrate is not hydrogen bonded, presumably since all of the strong hydrogen bond donors in **3** are satisfied.<sup>15</sup>

The orthogonal geometry and dimeric face-to-face stacking arrangements adopted by the aromatic units in 1.4(**2a**) are virtually identical with the spatial arrangements displayed by

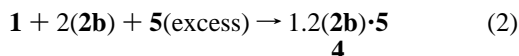
- (11) Krishnamohan Sharma, C. V.; Zaworotko, M. J. *Chem. Commun.* **1996**, 2655.  
 (12) Crystal data for **3**: crystal size 0.35 × 0.35 × 0.37 mm, orthorhombic, space group *Pnma*, *a* = 14.4603(7) Å, *b* = 25.407(1) Å, *c* = 15.0258(8) Å, *U* = 5520.4(5) Å<sup>3</sup>,  $\rho_{\text{calcd}}$  = 1.23 g cm<sup>-3</sup>,  $2\theta_{\text{max}}$  = 45°, Mo K $\alpha$  radiation ( $\lambda$  = 0.71069 Å) for *Z* = 4. Intensity data were collected with use of the Siemens SMART system at 298 K. Least-squares refinement based on 3170 reflections with  $I_{\text{net}} > 2.0\sigma(I_{\text{net}})$  (out of 3710 unique reflections), and 359 parameters on convergence gave a final value of *R* = 0.0612.  
 (13) In the absence of hydrogen bond acceptors such as **2**, **1** self-assembles to form a sphere-like hexamer. The structure of the hexamer has been determined in the space group *I432*, *a* = 24.343(4) Å, *U* = 14425-(4) Å<sup>3</sup>, *Z* = 12; MacGillivray, L. R.; Atwood, J. L. Unpublished work.  
 (14) Andreetti, G. D.; Uguzzoli, F.; Ungaro, R.; Pochini, A. In *Inclusion Compounds*; Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Eds.; Oxford University Press: Oxford, 1991; Vol. 4, pp 64.  
 (15) Etter, M. C. *J. Phys. Chem.* **1991**, *95*, 4601.



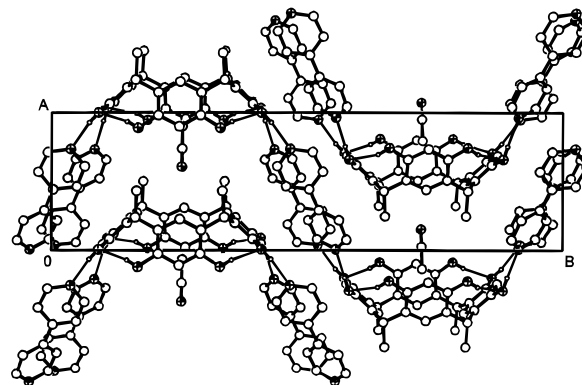
**Figure 1.** X-ray crystal structure of **3**: (a) the six-component complex  $1.4(\mathbf{2a})\cdot\mathbf{2a}$ ; (b) the 2D assembly within the  $ac$  plane. Selected interatomic distances (Å): O(1)···N(1) 2.675(3), O(2)···N(2), 2.687(4), O(3)···O(1) 2.769(3), O(4)···O(2) 2.755(3).

the resorcinol and quinone moieties in the polymeric material anthracene-bis(resorcinol)·2(9,10-anthraquinone) (**6**), which also interact *via* O—H···X hydrogen bonds.<sup>7</sup> This observation confirms that this supramolecular synthon is robust enough to be exchanged from one structure to another<sup>6</sup> and suggests that it should be possible to elaborate the cavity of **1** with further derivatives of **2**. In principle, it should also be possible to link together molecules of **1**, in a similar way to **6**, by utilizing a linear *exo*-bidentate spacer unit such as **2b**.<sup>11</sup>

To test this hypothesis, **1** (0.020 g) was added to a hot solution of **5** (20 mL) containing 2 equiv of **2b** (0.011 g) according to (2), which immediately yielded a yellow precipitate **4**. Crystals of **4** suitable for X-ray analysis were obtained by dissolving a portion of the precipitate in a hot aliquot of **5** (4 mL) and allowing the solution to slowly cool and stand over a period of 1 day. The formulation of **4** was confirmed by single-crystal X-ray diffraction,<sup>16</sup> <sup>1</sup>H NMR spectroscopy, and thermogravimetric analysis.



A view depicting the crystal structure of **4** is shown in Figure 2. As in **3**, the assembly process has resulted in four O—H···O



**Figure 2.** X-ray crystal structure of **4**: the solvent- and self-inclusion exhibited by  $1.4(\mathbf{2b})$ , the 1D hydrogen bonded polymer. Selected interatomic distances (Å): O(1)···N(1) 2.736(2), O(2)···N(2) 2.685(2), O(3)···O(1) 2.828(2), O(4)···O(2) 2.753(2).

hydrogen bonds along the upper rim of **1** [O(3)···O(1) 2.828(2) Å, O(4)···O(2) 2.753(2) Å] and four O—H···N hydrogen bonds between four hydroxyl groups of **1** and two pyridine dimers [O(1)···N(1) 2.736(2) Å, O(2)···N(2) 2.685(2) Å]. In contrast to **3**, the 4,4'-pyridyl substituents of **2b** have extended the cavity of **1** such that the host includes two guests: a molecule of **5**, which interacts with **1** *via* CH··· $\pi$  interactions, and a molecule of **1**, which lies above **5** and interacts with two pyridyl groups *via* edge-to-face C—H··· $\pi$  interactions. Thus, **4** is both a solvent- and self-inclusion compound which exhibits head-to-tail arrangement of **1** owing to the electronic and geometric complementarity of the constituent molecules.<sup>17</sup>

Unlike **3**, **4** self-assembles in the solid state to form a 1D hydrogen bonded wave-like polymer owing to the ability of **2b**, and its stacked dimer, to act as a linear bifunctional hydrogen bond acceptor.<sup>11</sup> As a consequence of these interactions, the cavities of the hosts, in contrast to **3**, are aligned, being propagated along the  $a$  axis in an antiparallel fashion. To our knowledge, this is the first case in which calixarenes have been linked together with a spacer unit such as **2b** in the solid state.

The results reported herein illustrate a novel approach for the construction of a new family of *monomeric* and *polymeric* host-guest assemblies based on **1**. By recognizing **1** as a quadruple hydrogen bond donor and employing a crystal engineering strategy, we have demonstrated the ability of **2a** and **2b** to elaborate the cavity of **1** which, in turn, has given rise to *multicomponent* hosts,  $1.4(\mathbf{2a})$  and  $1.4(\mathbf{2b})$ , which exhibit molecular recognition properties analogous to their *monomolecular* predecessors. Such observations attest to the structural and functional consequences of the self-assembly process, and we anticipate this approach to be viable for the design of similar host-guest complexes based on **1**, other hydrogen bond acceptors, and other guest molecules.

**Acknowledgment.** We are grateful for funding from the National Science Foundation and the Natural Sciences and Engineering Research Council of Canada (NSERC) for a research fellowship (L.R.M.).

**Supporting Information Available:** Crystallographic reports and tables of positional and thermal parameters, bond lengths and angles, NMR data, and TGA traces for **3** and **4** (18 pages). See any current masthead page for ordering and Internet access instructions.

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(16) Crystal data for **4**: crystal size 0.30 × 0.30 × 0.45 mm, monoclinic, space group  $P2_1/m$ ,  $a = 7.893(1)$  Å,  $b = 29.243(3)$  Å,  $c = 10.054(1)$  Å,  $\beta = 99.67(1)^\circ$ ,  $U = 2287.8(5)$  Å<sup>3</sup>,  $\rho_{\text{calcd}} = 1.30$  g cm<sup>-3</sup>,  $2\theta_{\text{max}} = 120^\circ$ , Cu K $\alpha$  radiation ( $\lambda = 1.54060$  Å) for  $Z = 2$ . Intensity data were collected on an Enraf-Nonius CAD-4 diffractometer equipped on a rotating anode generator at 298 K. Least-squares refinement based on 3000 reflections with  $I_{\text{net}} > 2.0\sigma(I_{\text{net}})$  (out of 3466 unique reflections) and 359 parameters on convergence gave a final value of  $R = 0.0362$ .

(17) Head-to-tail alignment of calixarenes maximizes the interactions between the bowl-shaped cores and facilitates addition of their dipoles making such assemblies natural building blocks for the design of ferroelectric and second-order NLO active materials. (a) Xu, B.; Swager, T. M. *J. Am. Chem. Soc.* **1993**, *115*, 1159. (b) Koh, K. N.; Araki, K.; Komori, T.; Shinaki, S. *Tetrahedron Lett.* **1995**, *36*, 5191.