Molecular Capsules

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Hydrogen-Bonded Supramolecular Assemblies as Robust Templates in the Synthesis of Large Metal-Coordinated Capsules**

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The synthesis of large multicomponent spheroid cage structures that offer the possibility of encapsulating numerous molecules is an important theme in supramolecular chemistry.[1] Strategies developed in their construction have mainly relied on self-assembly by means of multiple hydrogen bonds[2] or metal–ligand coordination.[3] Although there are numerous reports[4] of metal coordination to calixarene-based macrocycles, the formation of larger molecular cage structures involving more than two units remains limited.[5]

The bowl-shaped resorcin[4]arene and pyrogallol[4]arene macrocycles lend themselves amenable to the formation of large hexameric cage structures by hydrogen bonding.[6] From a pictorial point of view, substitution of hydrogen atoms for metal ions within these hexameric capsules[6] would result in structural preservation of the hexameric assembly while introducing new variables such as inorganic functionality. Indeed, limited consideration has been given to using pyrogallol[4]arene units as multibranched chelate ligands. Caulder and Raymond have shown the concept of using multibranched chelate ligands in the synthesis of cage structures, however, these structures contain relatively small cavities.[7] Herein we report the formation of a large neutral hexameric coordination cage structure assembled from six pyrogallol[4]arene ligands and twelve Ga^{III} ions.

Treatment of *C*-propyl-pyrogallol[4]arene (Figure 1) with four equivalents of $Ga(NO_3)_3 \cdot H_2O$ in a mixture of acetone and water resulted in the metal-directed self-assembly of $[Ga_{12}(H_2O)_{24}(C_{40}H_{42}O_{12})_6 \subset (acetone)_8(H_2O)_6]$ (**1**; Figure 2). Single-crystal X-ray analysis shows that **1** is assembled from 18 components: 6 pyrogallol[4]arene ligands and 12 Ga^{III} ions.[8] This large "rugby ball" shaped coordination cage is arranged such that the centroids of the six pyrogallol[4]arene ligand components reside on the vertices of a skewed octahedron and encloses approximately 1150 $Å^3$ of space.[9] The cage structure within **1** is held together by four slightly curved six-membered $[Ga_3O_3]$ arrays ($Ga\cdots O_{equatorial}$: 1.886–

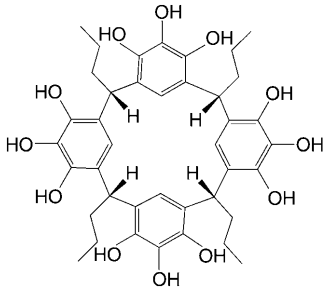

Figure 1. *C*-propyl-pyrogallol[4]arene macrocycle.

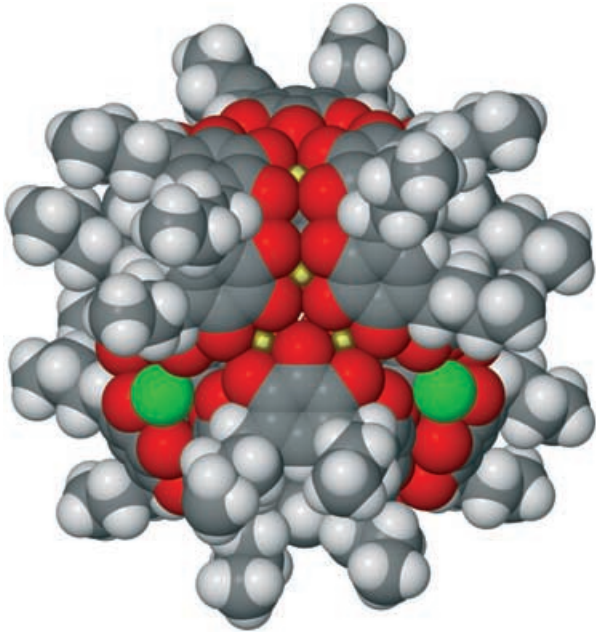

Figure 2. Space-filling representation of **1**. Surface-coordinated water molecules represented in green, gallium in gold; axial-coordinated water molecules and phenol hydrogen atoms removed for clarity.

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2.009 Å, O–Ga–O: 85.18–98.77°, Ga–O–Ga: 137.97–148.07°; Figure 3). All four equatorial positions on each octahedral gallium center are occupied by oxygen atoms from the macrocycle framework, with the axial positions (Ga···O_{axial}

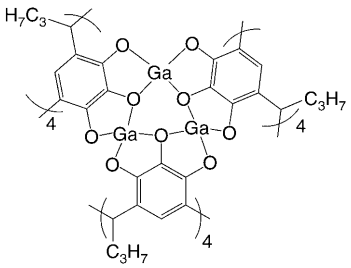

Figure 3. One of the four $[Ga_3O_3]$ six-membered arrays that hold **1** together.

1.924–2.104 Å) occupied by water molecules, twelve of them pointing inwards towards the cavity center. These axial bond distances correspond clearly to Ga···OH_2 coordination rather than Ga···OH bonds.[10] Embedded on the surface of **1** are four water molecules that participate in intermolecular hydrogen bonding with the upper-rim framework of the macrocycle which seals up potential surface voids. Indeed, these surface-coordinated water molecules may be viewed as occupying gates to the interior of the capsule.

The previously reported metal-directed self-assembly of pyrogallol[4]arene macrocycles with four equivalents of Cu^{II} ions resulted in the formation of a large spherical coordination cage $[Cu_{24}(C_{40}H_{40}O_{16})_6]$ (**2**).[11] Each face within the octahedral structure was capped by eight six-membered $[Cu_3O_3]$ planar arrays. In contrast to the Cu^{II} structure **2**, only half of the octahedral faces within **1** are capped with $[Ga_3O_3]$ arrays (Figure 4).

Within the hydrogen-bonded hexameric structure previously determined, there are 24 intramolecular hydrogen bonds, that is, 4 intramolecular hydrogen bonds per macrocycle that seam the capsule together.[6] These intramolecular hydrogen bonds are important for holding and stabilizing each macrocycle into its rigid cone or bowl-shaped conformation. Indeed, within the spherical Cu^{II} coordination capsule **2**, there are 24 intramolecular hydrogen bonds of the type OH···O^- that hold the framework together. However, from a pictorial view, the addition of 12 Ga^{III} metal ions into the hydrogen-bonded hexameric framework results in the substitution of 36 hydrogen atoms. It should be noted that 36 phenol groups, 6 from each macrocycle, remain to participate in hydrogen bonding as determined by ^1H NMR spectral analysis. Therefore, within **1** there are 48 Ga–O coordination bonds, 16 intramolecular hydrogen bonds of the type OH···O^-, 4 intramolecular hydrogen bonds of the type OH···OH, and 16 phenol groups remaining that can participate in intermolecular hydrogen bonding. Thus, the gallium coordination capsule **1** has only a total of 20 intramolecular hydrogen bonds that seam the framework together. A reasonable explanation for the structural difference between **1** and **2** is the loss of four intramolecular hydrogen bonds as a result of Ga^{III} versus Cu^{II}, which has the possibility of

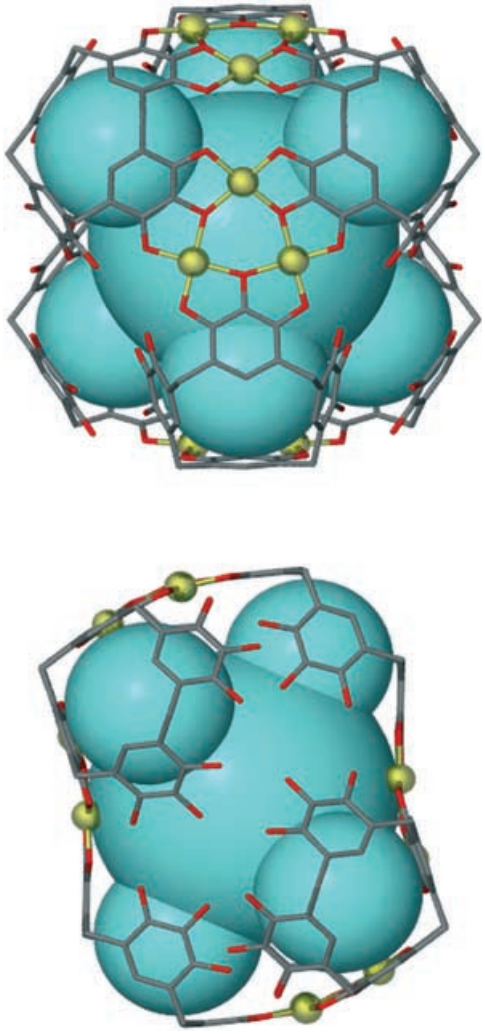

Figure 4. Structure **1** showing half of the octahedral faces capped with $[Ga_3O_3]$ arrays. Axial coordinated water molecules, hydrogen atoms, and alkyl tails removed for clarity.

introducing greater flexibility and decreasing structural rigidity within the cone conformation. This flexibility alters the spherical topology framework found within **2** to a "rugby ball" topology **1**. Since the "rugby ball" topology distorts the remaining phenol framework, further insertion of metal ions is less favored.

The combination of hydrogen bonds and metal–ligand coordination that hold supramolecular cage frameworks together is limited.[12] The advantage of using combinations of noncovalent interactions is a greater degree of freedom and control to build interesting supramolecular assemblies. For example, by alternating the number of intramolecular hydrogen bonds within the metal-coordinated hexameric structure by changing the oxidation state of the metal ion, slightly different structures are formed.

Steric interactions tend to be the main force in organizing guest molecules within large spheroid supramolecular cage assemblies, although there are some exceptions.[13] This implies that many guest molecules within large cavities are highly disordered as determined from X-ray analysis. How-

ever, within structure **1**, the axial metal-coordinated sites from the corresponding Ga^{III} ions are advantageously located orthogonal to the surface framework. These coordination sites have a profound influence on guest arrangements within **1**. Embedded within the large cavity are eight acetone molecules, twelve metal-coordinated water molecules, and six noncoordinated water molecules yielding an effective encapsulation of approximately 66%.[9] The packing coefficient within various molecular recognition systems is calculated to be approximately 55%.[14] The metal-coordinated water molecules within the cavity form hydrogen bonds with each acetone guest molecule. Interestingly, within the asymmetric unit, two axial metal-coordinated water molecules demonstrate evidence of a strong hydrogen bond (O···O 2.501 Å) that connects two neighboring $[Ga_3O_3]$ units together. Furthermore, the metal-coordinated water molecules show hydrogen bonding to each other within each $[Ga_3O_3]$ array (O···O 2.797–2.913 Å). Thus the Ga^{III} geometry is distorted sufficiently away from octahedral symmetry (O_{axial}-Ga-$O_{equatorial}$: 82.85–97.44°).

Found within **1** are two pseudo-linear hydrogen-bonded water $(H_2O)_5$ chains; hydrogen bonds are inferred from short O···O distances. The adjacent O···O distances are 2.711–2.823 Å and the O···O···O angles are 91.01–133.18°. X-ray analysis could not determine the position of hydrogen atoms within the water chain. The free water molecules adjacent to the Ga^{III}-coordinated water molecules also form hydrogen bonds to the phenol groups from the macrocycle framework. The free water molecules within the cavity do not form hydrogen bonds with acetone guest molecules. Within each linear water $(H_2O)_5$ chain, the three non-metal-coordinated water molecules, as a supramolecular entity, in effect act as a bridging ligand by connecting two opposite $[Ga_3O_3]$ arrays within **1** by hydrogen bonding to a metal-coordinated water molecule from each $[Ga_3O_3]$ array (Figure 5). The prevailing

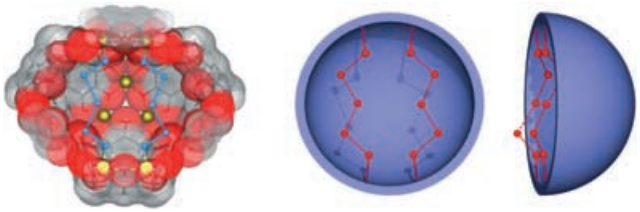

Figure 5. The pseudo-linear hydrogen-bonded water $(H_2O)_5$ chains within **1**. Acetone guest molecules within **1** removed for clarity.

knowledge is that the global minima of hydrogen-bonded water $(H_2O)_n$ clusters with $3 \le n \le 6$ have a general tendency to associate into two-dimensional planar ringlike architectures which is supported by both theoretical and experimental observations.[15] However, it is possible that confined space can offer an alternative environment to enforce different water topologies.

In conclusion, we have demonstrated the synthesis of a large hexameric cage structure stitched together from a combination of metal coordination and hydrogen bonds. Thus, the advantageous structural features from the hydrogen-bonded capsules are preserved while introducing new variables such as inorganic functionality. Indeed, this resulting combination of binding forces has led to architectures that organize the enclosed guest molecules in unique ways.

Experimental Section

Butyraldehyde (11.4 g, 0.16 mol) was added dropwise over a period of 2 h to a solution of pyrogallol (20 g, 0.16 mol) in ethanol (100 mL) and conc. HCl (10 mL) under N_2 gas. The resulting mixture was heated at reflux for 24 h, filtered, washed with water (3×500 mL), and recrystallized from methanol. *C*-propyl-pyrogallol[4]arene (14.2 g, 49%) was collected as a colorless powder. ^{1}H NMR (300 MHz, [D_6]acetone): $\delta = 0.95$ (12H, t, $^3J = 7.4$ Hz), 1.32 (8H, sextet, $^3J = 7.4$ Hz), 2.26 (8H, q, $^3J = 7.5$ Hz), 4.37 (4H, t, $^3J = 7.9$ Hz), 7.14 (4H, s), 7.18 (4OH, s), 8.09 ppm (8OH, brs); ^{13}C NMR ([D_6]acetone): $\delta = 13.3$, 20.8, 33.6, 34.9, 113.5, 124.7, 132.6, 139.1 ppm.

Single colorless crystals of **1** suitable for X-ray crystallographic analysis were grown from a sealed container, with a solution of *C*-propyl-pyrogallol[4]arene (0.20 g) in acetone (5 mL) added to a solution of $Ga(NO_3)_3 \cdot H_2O$ (0.28 g) in water (2 mL).[8] Yield: 48%, based on pyrogallol[4]arene ligand. ^{1}H NMR of **1** (300 MHz, CD_3CN): $\delta = 0.98$ (72H, t, $^3J = 7.5$ Hz), 1.29 (48H, m), 2.22 (48H, m), 4.26 (24H, t), 6.89 (12OH + 24Ar, brs), 7.38 ppm (24OH, brs); ^{1}H NMR of **1** (CD_3CN + D_2O): the peak at $\delta = 6.89$ ppm reduces to 24Ar.

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[1] J. Rebek, Jr., *Angew. Chem.* **2005**, *117*, 2104; *Angew. Chem. Int. Ed.* **2005**, *44*, 2068.
[2] L. J. Prins, D. N. Reinhoudt, P. Timmerman, *Angew. Chem.* **2001**, *113*, 2446; *Angew. Chem. Int. Ed.* **2001**, *40*, 2382.
[3] M. Fujita, M. Tominaga, A. Hori, B. Therrien, *Acc. Chem. Res.* **2005**, *38*, 369.
[4] a) R. Pinalli, V. Cristini, V. Sottili, S. Geremia, M. Campagnolo, A. Caneschi, E. Dalcanale, *J. Am. Chem. Soc.* **2004**, *126*, 6516; b) K. Kobayashi, Y. Yamada, M. Yamanaka, Y. Sei, K. Yamaguchi, *J. Am. Chem. Soc.* **2004**, *126*, 13896; c) F. A. Cotton, P. Lei, C. Lin, C. A. Murillo, X. Wang, S.-Y. Yu, Z.-Z. Zhang, *J. Am. Chem. Soc.* **2004**, *126*, 1518; d) Z. Zhong, A. Ikeda, M. Ayabe, S. Shinkai, S. Sakamoto, K. Yamaguchi, *J. Org. Chem.* **2001**, *66*, 1002; e) S. J. Park, J.-I. Hong, *Chem. Commun.* **2001**, 1554; f) O. D. Fox, J. F.-Y. Leung, J. M. Hunter, N. K. Dally, R. G. Harrison, *Inorg. Chem.* **2000**, *39*, 783; g) O. D. Fox, N. K. Dalley, R. G. Harrison, *J. Am. Chem. Soc.* **1998**, *120*, 7111; h) P. Jacopozzi, E. Dalcanale, *Angew. Chem.* **1997**, *109*, 665; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 613.
[5] a) O. D. Fox, M. G. B. Drew, P. D. Beer, *Angew. Chem.* **2000**, *112*, 139; *Angew. Chem. Int. Ed.* **2000**, *39*, 135; b) O. D. Fox, M. G. B. Drew, E. J. S. Wilkinson, P. D. Beer, *Chem. Commun.* **2000**, 391.
[6] a) G. W. V. Cave, J. Antesberger, L. J. Barbour, R. M. McKinlay, J. L. Atwood, *Angew. Chem.* **2004**, *116*, 5375; *Angew. Chem. Int. Ed.* **2004**, *43*, 5263; b) J. L. Atwood, L. J. Barbour, A. Jerga, *J. Supramol. Chem.* **2001**, *1*, 131; c) T. Gerkensmeier, W. Iwanek, C. Agena, R. Fröhlich, S. Kotila, C. Näther, J. Mattay, *Eur. J. Org. Chem.* **1999**, 2257; d) L. R. MacGillivray, J. L. Atwood, *Nature* **1997**, *389*, 469.
[7] D. L. Caulder, K. N. Raymond, *Acc. Chem. Res.* **1999**, *32*, 975.
[8] Crystal data for $[Ga_{12}(H_2O)_{24}(C_{40}H_{42}O_{12})_6] \cdot 19(CH_3COCH_3) \cdot 16(H_2O)$, $M_r = 6949.4$, monoclinic, $a = 23.579(3)$, $b = 27.299(3)$, $c = 27.025(3)$ Å, $\beta = 93.886(2)°$, $V = 7356(4)$ Å^3, space group $P21/n$,

$Z = 4$, $\rho_{calcd} = 1.308\ g\,cm^{-3}$, $\lambda(Mo_{K\alpha}) = 0.70930$ Å, $F(000) = 7073$, $T = 173(2)$ K, 38365 unique reflections ($2\theta \leq 56°$), of which 18300 were observed [$I_o > 2\sigma(I)$]. Final R factors: $R_1 = 0.0872$, $wR_2 = 0.2380$ for 2230 parameters. Data were collected on a Bruker SMART 1000 CCD diffractometer with $Mo_{K\alpha}$ radiation using the ω-scan mode. Data were corrected for absorption using the SADABS program, and solution and refinement of the structure were performed using the SHELX-97 software package. All non-hydrogen atoms and non-guest molecules were refined anisotropically, whereas the hydrogen atoms were included at geometrically calculated positions and allowed to ride on their parent atoms. The hydrogen atoms from water molecules were not assigned. CCDC 243837 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[9] L. J. Barbour, **2003** MCAVITY, program for calculating the molecular volume of closed capsules, University of Missouri-Columbia, Missouri, USA. http://www.x-seed.net/cavity.html. Maximum free volume within the cavities was calculated with guest molecules removed. It was assumed that the molecular volume of acetone and water is 61.3 and 14.7 Å^3, respectively. The volume of cavity **1** was subject to an error of $\pm 10\,\%$ as the capsule was distorted from perfect spheroid geometry.

[10] O. Jarjayes, A. Du Moulinet D'Hardemare, A. Durif, M.-T. Averbuch-Pouchot, *Acta Crystallogr. Sect. C* **1998**, *54*, 931.

[11] R. M. McKinlay, G. W. V. Cave, J. L. Atwood, *Proc. Natl. Acad. Sci. USA* **2005**, *102*, 5944.

[12] a) R. Garía-Zarracino, H. Höpfl, *Angew. Chem.* **2004**, *116*, 1533; *Angew. Chem. Int. Ed.* **2004**, *43*, 1507; b) M. A. Alam, M. Nethaji, M. Ray, *Angew. Chem.* **2003**, *115*, 1984; *Angew. Chem. Int. Ed.* **2003**, *42*, 1940.

[13] J. L. Atwood, L. J. Barbour, A. Jerga, *Proc. Natl. Acad. Sci. USA* **2002**, *99*, 4837.

[14] A. S. Mecozzi, J. Rebek, Jr., *Chem. Eur. J.* **1998**, *4*, 1016.

[15] K. Liu, J. D. Cruzan, R. J. Saykally, *Science* **1996**, *271*, 929.

