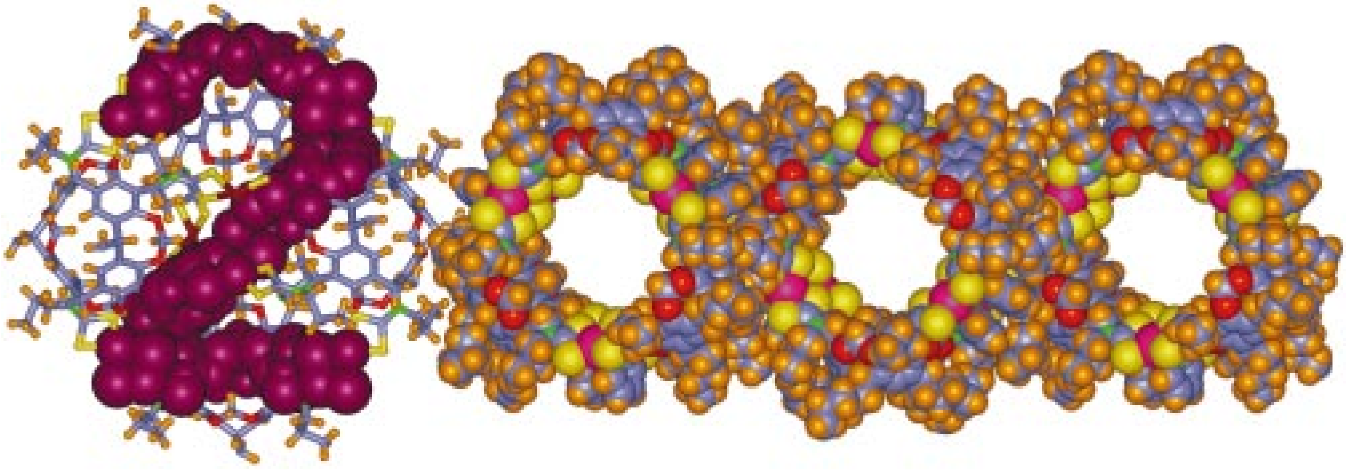
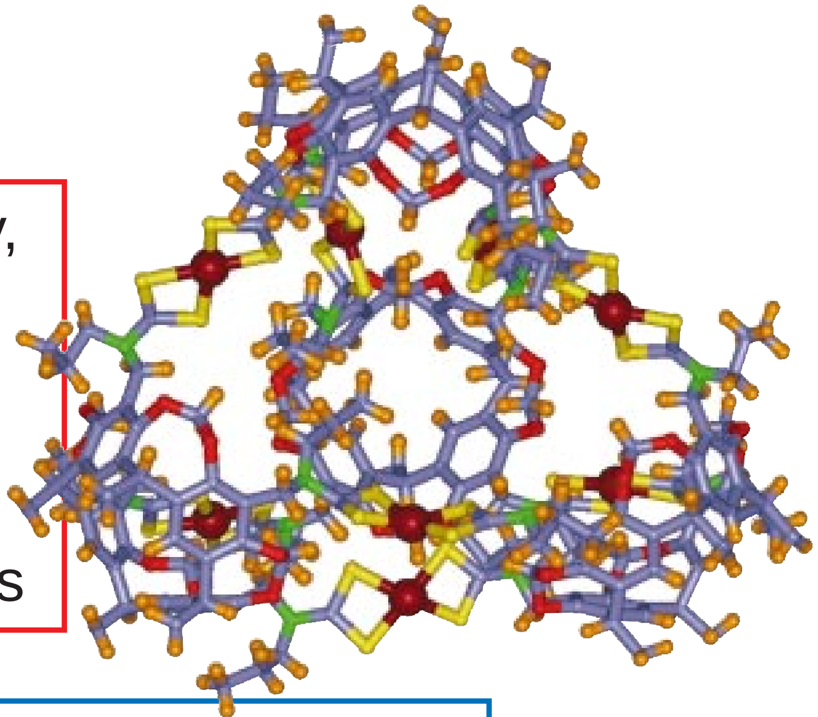
Nanoscale Molecular Hosts and Containers



Zinc(II) ions assemble molecular loops from calixresorcarene ligands



More remarkably, copper(III) ions assemble a molecular tetrahedron of calixresorcarenes

Find out more about this new family of nanosized hosts on the following pages

Resorcarene-Based Nanoarchitectures: Metal-Directed Assembly of a Molecular Loop and Tetrahedron[**]

O. Danny Fox, Michael G. B. Drew, and Paul. D. Beer*

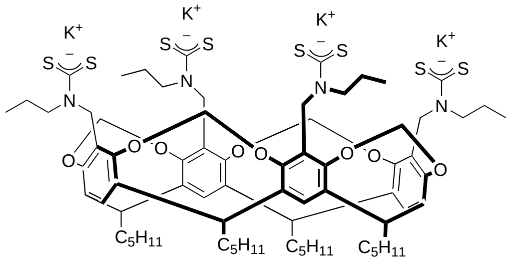
Dedicated to Professor Jean-Marie Lehn
on the occasion of his 60th birthday

Nature employs both covalently bonded and self-assembled protein shells to store, protect, and transport inorganic and organic molecules. Both naturally occurring and synthetic molecular containers offer the possibility of synthesizing and/or stabilizing novel molecules and materials within their frameworks.[1] Metal ions in conjunction with ligands are particularly suited to the assembly of molecular architectures and may confer upon the resulting structures a variety of properties—such as charge, magnetism, color, and chemical and redox activity—that are much more difficult to attain with purely organic molecules.[2] Because assembly of such molecules with labile metal ions is often a thermodynamically driven process,[3] yields of self-assembled containers can often far exceed those of containers created by formation of covalent bonds.[4] Frequently, these assembly-driven processes can be controlled, for example, by templation of the host architecture around guest molecules or ions.

Calixarene-based molecules can be multiply functionalized with a variety of ligating moieties, and their bowl shape lends them amenable to formation of host structures suitable for the binding of guest molecules.[5] Although there are now numerous examples of hydrogen-bonded, self-assembled calixarene-based dimers,[6] the synthesis of larger molecular containers involving assembly of multiple units is still very much in its infancy.[7] Dimeric, calixarene-based molecular capsules formed by metal-induced self-assembly processes have been synthesized,[8] and a recent example has been shown to bind guest molecules as a function of pH value.[9]

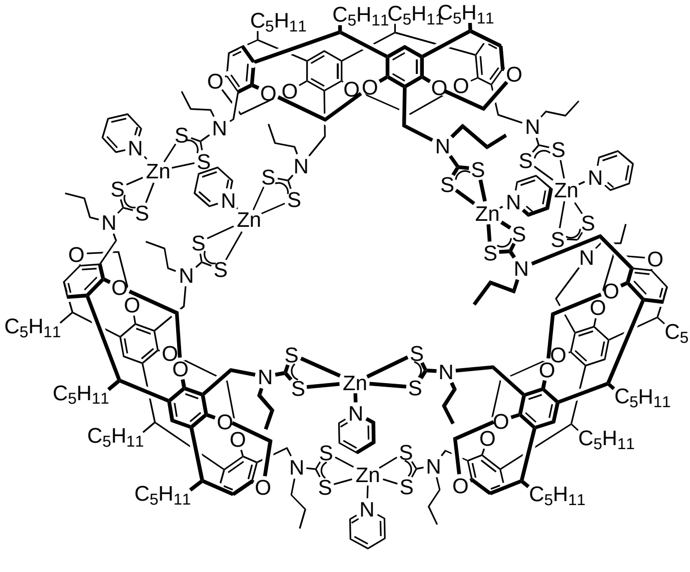
Here we present preliminary findings concerned with the design and synthesis of metal-assembled molecular containers whose structures can be varied by choice of metal ion and its respective oxidation state(s). We detail the synthesis of nanosized molecular structures assembled from dithiocarbamate–resorcarene ligand units and copper or zinc ions. The dithiocarbamate unit is a most versatile ligand with a rich history of coordination chemistry, but remarkably has not yet been exploited in the field of self-assembly.[10] The ability of this ligand to stabilize metal ions in a range of oxidation states and coordination geometries offers plenty of opportunity for the generation of novel self-assembled molecular architectures with unique properties.

Dithiocarbamate (dtc) **1** is prepared by treatment of a solution of the parent resorcarene secondary amine[18] in ethanol/water with carbon disulfide and potassium hydroxide. This bowl-shaped ligand is functionalized with four *N*-propyl(dtc) ligating moieties and possesses a potential C_4 axis. Although the potassium salt of **1** could be isolated by removal of the solvent, in all cases polynuclear metal complexes were prepared directly by treatment of **1** in ethanol/water with metal(II) acetate to afford the crude compounds as powders.



1

Recrystallization of the zinc(II) complex from pyridine(py)/water gives large, yellow, prismatic crystals of molecular loop $[Zn_6(\mathbf{1})_3(py)_6]\cdot 7.5\,EtOH$ ($\mathbf{2}\cdot 7.5\,EtOH$). The structure of this hexanuclear zinc(II) complex is shown in Figure 1. Nanosized complex **2** is, to the best of our knowledge, the first structure of a metal-assembled, trimeric, calixarene-based molecule and the first example of a calixarene-based molecular loop or ring.



$[Zn_6(\mathbf{1})_3(py)_6]$

2

There is one independent zinc atom and the species has crystallographic 32 symmetry. The three resorcarene cups provide the corners for an equilateral molecular triangle with two zinc ions positioned at the midpoints of each side.[11] The zinc(II) ions are five-coordinate, with two bidentate dtc

---

[*] Prof. P. D. Beer Dr. O. D. Fox
Inorganic Chemistry Laboratory
University of Oxford
Oxford OX1 3QR (UK)
Fax: (+44) 1865-272690
E-mail: paul.beer@chem.ox.ac.uk
Prof. M. G. B. Drew
Department of Chemistry
University of Reading
Whiteknights, Reading RG7 4PR (UK)

[**] This work was supported by AWE Aldermaston. We thank Dr. N. Rees for MALDI-TOF mass spectrometry, and the EPSRC and University of Reading for funds for the Image Plate System.

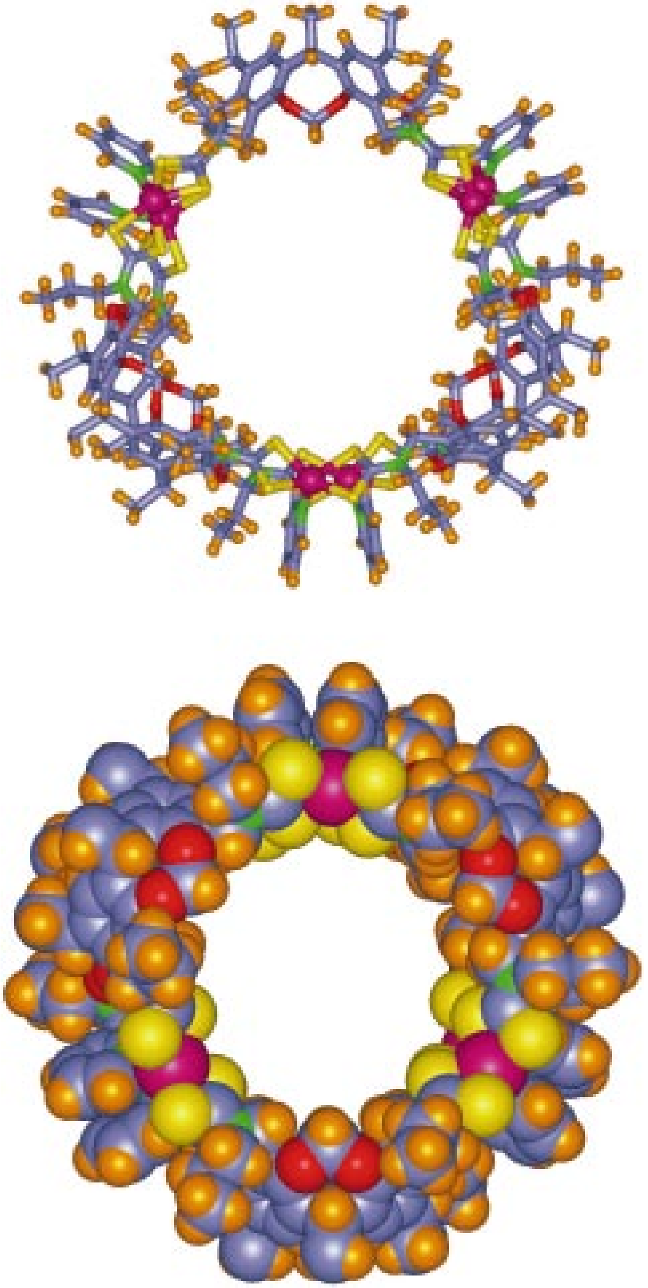


Figure 1. Molecular structure of zinc(II)-assembled molecular loop **2**. Top: Ball-and-stick representation; bottom: CPK representation. In both pictures the *n*-butyl chains from the base of the resorcarene have been omitted for clarity. Zn: pink, S: yellow, O: red, N: green, C: blue, H: orange.

moieties forming the square plane (Zn–S 2.424(2)–2.520(2) Å); the fifth, axial site is occupied by a pyridine molecule (Zn–N 2.086(6) Å), which pulls the metal ion above the square plane by 0.58 Å. Two metal–ligand bridges are formed between adjacent resorcarenes from a pair of non-interacting NCS_2-Zn-S_2CN moieties on opposite sides of the bowl. Adjacent zinc atoms are 6.61 Å apart; across the cavity opposite zinc atoms are 14.69 Å apart. The sides of an equilateral triangle (defined by carbon atoms close to the base of each resorcarene bowl) are 19.1 Å in length (see Figure 4).[12] Although based on a triangle of resorcarene cups, space-filling models reveal the cavity to be circular; the diameter of this circle is approximately 16.4 Å. The cavity contains 7.5 ethanol molecules (not shown), but apart from these guest molecules appears mostly unoccupied. In the solid state each trimeric resorcarene loop is surrounded by six neighbors. Interestingly, the packing of these loops in the crystal lattice generates a "molecular honeycomb" (Figure 2).

Characteristic but unexpectedly broad resonances due to the resorcarene structure are observed in the ^1H NMR spectrum of **2** ([D$_8$]toluene, 23 °C), which sharpen considerably on heating to 80 °C. We attribute this broadening to slow rotation around the C–N bonds of the Zn(dtc)$_2$ units, resulting in the presence of numerous stereoisomers (*syn* or *anti*) within the molecular aggregate.[10, 13] Investigation of **2** by MALDI-TOF mass spectrometry gave only ions corresponding to fragmentation of the trimeric resorcarene structure into monomeric species, for example 1597 $[(\mathbf{1}-H^+)Zn_3]^+$; 1621 $[(\mathbf{1}-2H^+)Zn_3Na]^+$.

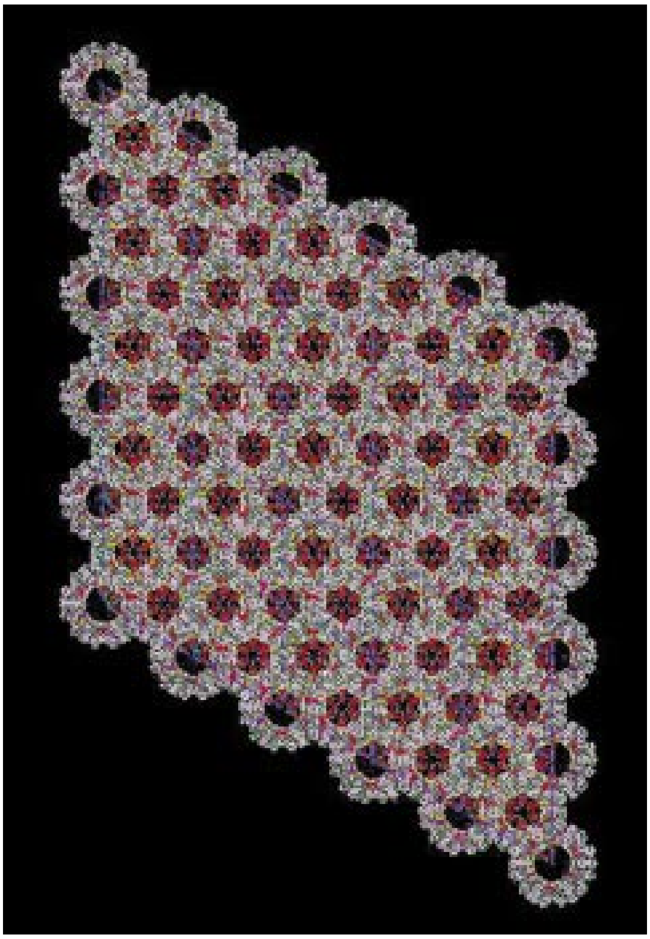
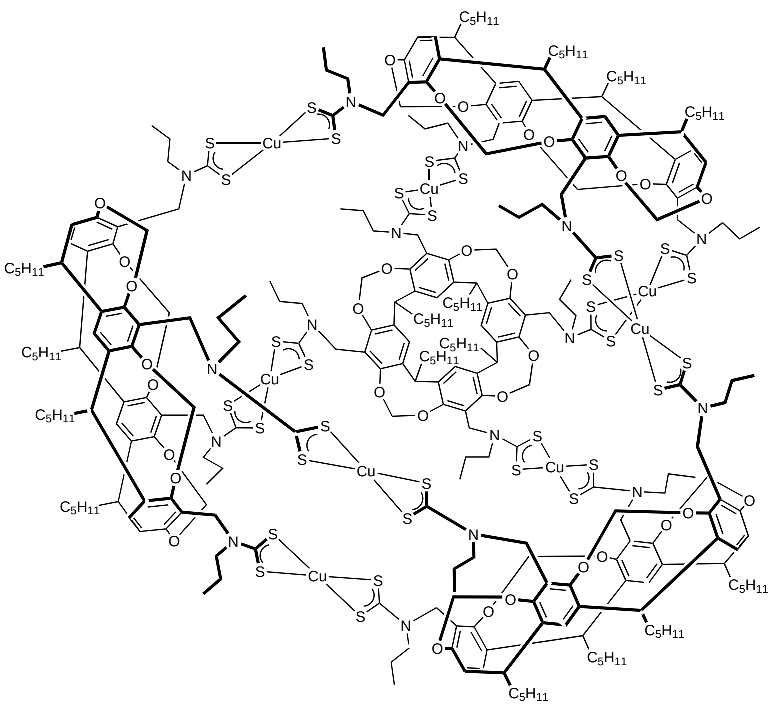


Figure 2. View down the unique *c* axis in the crystal structure of **2**, showing the "molecular honeycomb" formed by the packing of the individual loops. The cavity is sparsely occupied by a few disordered solvent molecules.

Treatment of **1** with copper(II) acetate provided an intermediate copper(II) complex **3**, which was oxidized to the octanuclear copper(III) complex $[Cu_8(\mathbf{1})_4][I_3]_7[I]\cdot 6H_2O$ (**4**) by treatment with iodine; complex **4** was isolated as a mixed triiodide/iodide salt.[14] The structure of octacation $[Cu_8(\mathbf{1})_4]^{8+}$ in **4** (which displays S_4 symmetry) is shown in Figure 3. We believe **4** to contain the first example of a metal-assembled,



$[Cu_8(\mathbf{1})_4]^{8+}$

tetrameric resorcarene structure to be crystallograhically characterized. Four resorcarene ligands lie at the apices of a distorted tetrahedron, and are connected to each other by eight copper(III) ions.[15] To form a tetrahedral array, geometrical requirements dictate that at two sides of the tetrahedron two copper ions are coordinated to the same resorcarene. The gross structural effect of this is to distort the symmetry of the molecule, twisting the cups of the resorcarenes away from the line of the apices and resulting in a flattening of the tetrahedron (Figure 4). The sides of the tetrahedron differ therefore, with two being 25.0 and four being 19.5 Å in length. The assembly of **4** is, to our knowledge, the first example of copper(III) in the role of self-assembly. Indeed the synthesis of an octanuclear copper(III) complex is in itself unusual.

Crystallographically there are two unique copper(III) ions present in **4**. Each copper(III) ion is chelated by two bidentate dtc moieties in an approximately square-planar fashion. The C−S bond distances (2.11(2)–2.47(2) Å) are consistent with those reported previously in mononuclear $[Cu^{III}(n\mathrm{Bu}_2\text{-}dtc)_2][I_3]$ complexes.[16, 17] The variance in Cu−S bond lengths is most probably a consequence of stress forces applied to the metal–ligand bonds due to the imperfect arrangement of the four resorcarene units. Seven triiodide and one iodide anions are associated with the cationic octamer. There are weak apical interactions between the copper centers and the triiodide anions (Cu2−I 3.26, Cu1−I 3.19 Å) . Interestingly for Cu1 a triiodide anion bridges between two adjacent copper centers (both Cu1) of a tetrahedron, generating a Cu-I(I_2)-Cu complex, with a much shorter Cu ⋯ Cu distance (4.98 Å). Notably, both ends of the linear triiodide molecule are coordinated by copper ions, and this links the tetrahedra to each other through the crystal lattice.

Magnetic susceptibility measurements (250–300 K) determined that crystals of **4** are diamagnetic. This is consistent with the pseudo-square-planar nature of the

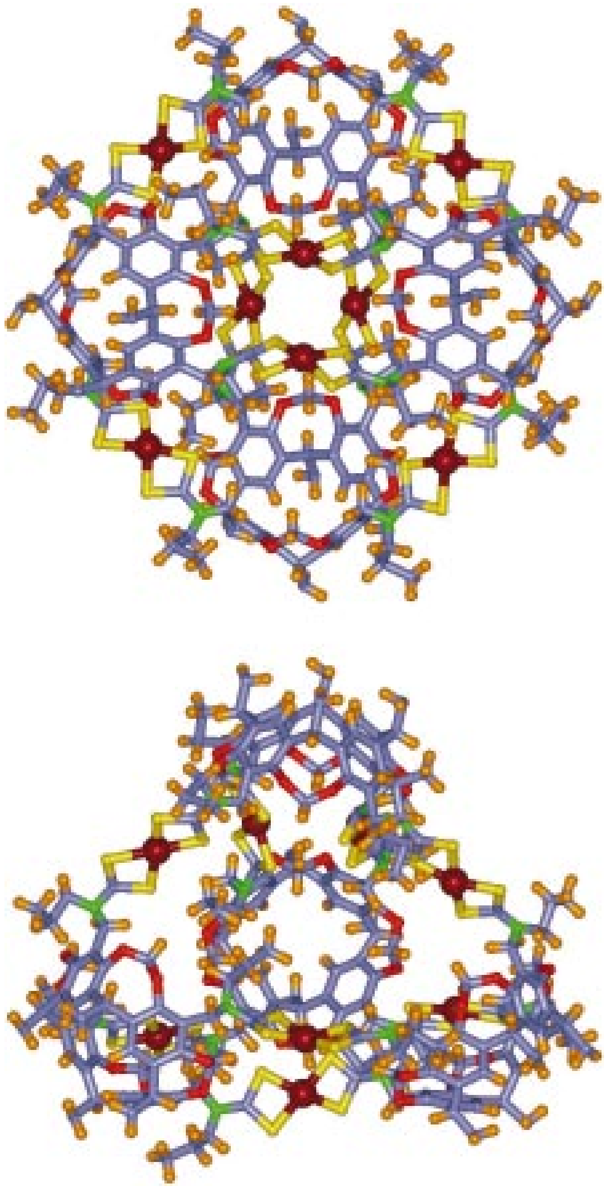


Figure 3. Two views of the molecular structure of the octacation $[Cu_8(\mathbf{1})_4]^{8+}$ in **4** shown as ball-and-stick representations. The *n*-butyl chains from the base of the resorcarene have been omitted for clarity. Cu: dark red, S: yellow, O: red, N: green, C: blue, H: orange.

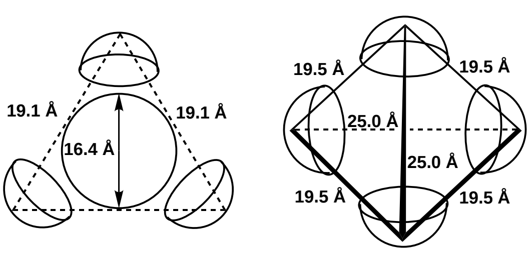


Figure 4. Cartoon representations of the geometrical shapes formed by structures **2** (left) and **4** (right).

d^8 copper(III) centers, and more importantly shows that oxidation of all copper(II) ions occurs. Complex **4** is insoluble in nonpolar solvents, and upon dissolution in polar or protic solvents such as pyridine or methanol **4** is reduced back to a copper(II) complex. Spontaneous reduction of $[Cu^{III}(dtc)_2][I_3]$ complexes in polar solvents has been reported previously.[16] The ^1H NMR spectra of **4** prepared in situ by oxidation of **3** with iodine in $CDCl_3$ or C_6D_6 give resonances that are characteristic of the resorcarene structure but, like those of **2**, are broad and uninformative.

If **4** is observed down one of the four possible C_3 axes, a portal suitable for guest inclusion can clearly be discerned. The size of each portal can be crudely defined as an approximate equilateral triangle with copper atoms occupying the corners. The Cu ··· Cu distances—that is, the sides of this triangle—are approximately 14 Å. This is clearly a large enough gateway through which a large guest molecule could potentially pass. The center of the tetrahedron (at 0, 0, 1/2) is a crystallographic S_4 site and has eight copper neighbors, four at 7.283 Å and the remaining four at 10.19 Å. The Cu ··· Cu distances across the tetrahedron can reach as high as 20.4 Å, clearly demonstrating the large size of the cavity.

In conclusion, we have demonstrated the facile, metal-assembled synthesis of trimeric and tetrameric resorcarene host architectures and characterized their solid-state structures. Clearly, a number of factors are involved in the assembly processes including the choice of metal, its oxidation state, and possibly the nature of the anion. Furthermore, we conjecture that the incorporation of redox-active metal–ligand moieties within these nanohosts confers upon them a range of novel physical properties that may allow them to sense, report, and possibly even facilitate chemical reaction of their guest substrates.

Experimental Section

The parent secondary amine tetrakis[(propylamino)methyl]resorcarene was prepared following the method of Boerrigter et al.[18]

2: To solution of tetrakis[(propylamino)methyl]resorcarene (1.0 g, 0.92 mmol) and potassium hydroxide (0.216 g, 3.96 mmol) in ethanol/water (100 mL/50 mL) was added carbon disulfide (0.294 g, 4.0 mmol), and the solution stirred for 2 h.[22] Zinc(II) acetate hydrate (0.41 g, 2.0 mmol) was added and the mixture allowed to stir overnight. The white precipitate that formed was removed by filtration and recrystallized from dichloromethane/ethanol. Crystals suitable for X-ray structure analysis were grown by slow vapor diffusion of water into a solution of **2** in pyridine (0.95 g, 62 %). Crystals of **2** appear to desolvate on removal from mother liquor. Elemental analysis calcd for $[Zn_6(\mathbf{1})_3(py)_6]$ ($C_{246}H_{318}N_{18}O_{24}S_{24}Zn_6$): C 58.24, H 6.32, N 4.97; found: C 58.29, H 6.62, N 5.23.

Crystallographic data for $[Zn_6(\mathbf{1})_3(py)_6]\cdot 7.5\,EtOH$ ($\mathbf{2}\cdot 7.5\,EtOH$; $C_{261}H_{363}N_{18}O_{31.5}S_{24}Zn_6$): $M_r = 5418.3$, rhombohedral, space group $R\bar{3}c$, $a = 36.98(4)$, $c = 56.52(6)$ Å, $V = 66945$ Å^3, $Z = 6$, $\rho_{calcd} = 0.806\ g\,cm^{-3}$, $F(000) = 17226$, $\mu = 0.470\ mm^{-1}$; of 23468 data measured on a Mar Research Image Plate with $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å; $T = 293$ K, $\theta_{max} = 26.03°$), 11762 were independent ($R(int) = 0.0853$). Data analysis was carried out with the XDS program.[19] The structure was determined by direct methods. Non-hydrogen atoms were included with anisotropic thermal parameters, and hydrogen atoms in calculated positions. A total of 44 distance constraints were included for the alkyl chains. No absorption correction was applied. The structure was refined on F^2 with Shelx97[20] to give $R1 = 0.1033$ and $wR2 = 0.2847$ for 4279 data with $I > 2\sigma(I)$ and $R1 = 0.2012$ and $wR2 = 0.3350$ for all data.[21]

4: To a solution of tetrakis[(propylamino)methyl]resorcarene (1.0 g, 0.92 mmol) and potassium hydroxide (0.216 g, 3.96 mmol) in ethanol/water (100 mL/50 mL) was added carbon disulfide (0.294 g, 4.0 mmol), and the solution stirred for 2 h.[22] Copper(II) acetate (0.41 g, 4.0 mmol) was added, and the mixture allowed to stir overnight. The fine, dark brown powder that formed was removed by filtration and recrystallized from dichloromethane/ethanol to give **3** (0.88 g, Iodine (40 mg, 0.157 mmol) in toluene (20 mL) was added dropwise over 20 min to a stirred solution of **3** (50 mg) in chloroform (20 mL). The resulting red-brown solution was filtered, then allowed to stand and after two weeks gave black prismatic crystals of **4** (42 mg). Elemental analysis calcd for $[Cu_8(\mathbf{1})_4][I_3]_7[I]\cdot 6\,H_2O$ ($C_{288}H_{396}I_{22}N_{16}O_{38}S_{32}Cu_8$): C 38.36, H 4.43, N 2.49; found: C 37.94, H 4.30, N 2.15.

Crystallographic data for $[Cu_8(\mathbf{1})_4][I_3]_7[I]\cdot 6\,H_2O$ (**4**; $C_{288}H_{396}I_{22}N_{16}O_{38}S_{32}Cu_8$): $M_r = 9036.15$, tetragonal, space group $P\bar{4}2_1c$, $a = 32.09(4)$, $c = 23.91(3)$ Å, $V = 24626$ Å^3, $Z = 2$, $\rho_{calcd} = 1.219\ g\,cm^{-3}$, $F(000) = 8908$, $\mu = 1.90\ mm^{-1}$; of 24807 data measured on a Mar Research Image Plate with $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å; $T = 293$ K, $\theta_{max} = 22.58°$), 10192 were unique ($R(int) = 0.0919$). The data analysis was carried out with XDS.[19] The structure was determined by direct methods. Only the iodine atoms were refined anisotropically. The three triiodide anions were refined with occupancies of 1.0, 0.65, and 0.10, respectively. In addition there was an iodide atom with a population parameter of 0.25. A total of 125 distance constraints proved necessary for convergence, primarily over the alkyl chains. The phenyl rings were refined as rigid groups. No absorption correction was applied. The structure was refined on F^2 with Shelxl[20] to give $R1 = 0.1450$ and $wR2 = 0.3522$ for 3229 data with $I > 2\sigma(I)$ and $R1 = 0.2400$ and $wR2 = 0.3942$ for all data.[21]

Received: August 23, 1999 [Z13910]

---

[1] a) T. Douglas, M. Young, *Nature* **1998**, *393*, 152–155; b) D. J. Cram, M. E. Tanner, R. Thomas, *Angew. Chem.* **1991**, *103*, 1048–1051; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1024–1027.

[2] Recent reviews: a) R. W. Saalfrank, B. Demleitner in *Transition Metals in Supramolecular; Perspectives in Supramolecular Chemistry* (Ed.: J. P. Sauvage), Wiley-VCH, Weinheim, **1999**, *5*, 1–51; b) R. W. Saalfrank, I. Bernt, *Curr. Opin. Solid State Mater. Sci.* **1998**, *3*, 407–413; c) M. Fujita, *Chem. Soc. Rev.* **1998**, *27*, 417–425; d) C. J. Jones, *Chem. Soc. Rev.* **1998**, *27*, 289–299; e) B. Linton, A. D. Hamilton, *Chem. Rev.* **1997**, *97*, 1669–1680; f) P. N. W. Baxter in *Comprehensive Supramolecular Chemistry, Vol. 9* (Eds.: J. P. Sauvage, M. W. Hosseini), Pergamon, Oxford, **1996**, 165–211.

[3] M. Fujita, D. Oguro, M. Miyazawa, H. Oka, K. Yamaguchi, K. Ogura, *Nature* **1995**, *378*, 469–471.

[4] D. J. Cram, M. J. Cram in *Container Molecules and Their Guests, Monographs in Supramolecular Chemistry* (Ed.: J. F. Stoddart), The Royal Society of Chemistry, Cambridge, **1994**, and references therein.

[5] D. M. Roundhill, *Prog. Inorg. Chem.* **1995**, *43*, 533–592.

[6] M. M. Conn, J. Rebek, Jr., *Chem. Rev.* **1997**, *97*, 1647–1668, and references therein.

[7] L. R. MacGillivray, J. L. Atwood, *Nature* **1997**, *389*, 469–472.

[8] a) E. Dalcanale, P. Jacopozzi, *Angew. Chem.* **1997**, *109*, 665–667; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 613–615; b) K. Fujimoto, S. Shinkai, *Tetrahedron Lett.* **1994**, *35*, 2915–2918.

[9] O. D. Fox, N. K. Dalley, R. G. Harrison, *J. Am. Chem. Soc.* **1998**, *120*, 7111–7112.

[10] D. Coucouvanis, *Prog. Inorg. Chem.* **1979**, *26*, 301–469.

[11] Recent examples of triangular based complexes: a) J. R. Hall, S. J. Loeb, G. K. H. Shimizu, G. P. A. Yap, *Angew. Chem.* **1998**, *110*, 130–133; *Angew. Chem. Int. Ed.* **1998**, *37*, 121–123; b) R. D. Schenbeck, L. Randacio, E. Zangrando, B. Lippert, *Angew. Chem.* **1998**, *110*, 128–130; *Angew. Chem. Int. Ed.* **1998**, *37*, 119–121; c) D. Whang, K. M. Park, J. Heo, P. Ashton, K. Kim, *J. Am. Chem. Soc.* **1998**, *120*, 4899–4900.

[12] The triangle is defined by three carbon atoms situated at the base of the resorc[4]arene ligand (C28a, C28b, and C28e).

[13] Q. J. McCubbin, F. J. Stoddart, T. Welton, A. J. P. White, D. J. Williams, *Inorg. Chem.* **1998**, *37*, 3753–3758.

[14] To date, we have been unsuccessful in our attempts to obtain crystals of **3** suitable for an X-ray structure determination.

[15] a) D. L. Caulder, K. N. Raymond, *J. Chem. Soc. Dalton Trans.* **1999**, 1185–1200, and references therein; b) C. Bruckner, R. E. Powers, K. N. Raymond, *Angew. Chem.* **1998**, *110*, 1937–1940; *Angew. Chem.*

Int. Ed. **1998**, *37*, 1837 – 1839; c) J. S. Fleming, K. L. V. Mann, C. A. Carraz, E. Psillakis, J. C. Jeffery, J. A. McCleverty, M. D. Ward, *Angew. Chem.* **1998**, *110*, 1315 – 1318; *Angew. Chem. Int. Ed.* **1998**, *37*, 1279 – 1281; d) R. W. Saalfrank, R. Burak, A. Breit, D. Stalke, R. Herbst-Irmer, J. Daub, M. Porsch, E. Bill, M. Muther, A. X. Trautwein, *Angew. Chem.* **1994**, *106*, 1697 – 1699; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1621 – 1623.

[16] a) J. G. Wijnhoven, T. E. M. van den Hark, P. T. Beurskens, *J. Cryst. Mol. Struct.* **1972**, *2*, 189 – 196; b) G. M. Larin, G. A. Zvereva, P. A. Kozmin, T. B. Larina, M. D. Svrazhskaya, *Izv. Akad. Nauk SSSR Neorg. Mater.* **1984**, *20*, 530 – 533; *Inorganic Materials (Engl. Transl.)* **1984**, *20*, 451.

[17] R. M. Golding, C. M. Harris, K. J. Jessop, W. C. Tennant, *Aust. J. Chem.* **1972**, *25*, 2567 – 2576.

[18] H. Boerrigter, W. Verboom, D. N. Reinhoudt, *J. Org. Chem.* **1997**, *62*, 7148 – 7155.

[19] W. Kabsch, *J. Appl. Crystallogr.* **1988**, *21* 916.

[20] SHELXL, Program for Crystal Structure Refinement, G. M. Sheldrick, Universität Göttingen, **1997**.

[21] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-133532 (**2**) and CCDC-133533 (**4**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[22] At this point, removal of the solvent under reduced pressure affords the potassium salt of the dtc ligand [K_4] [**1**]: ^{1}H NMR (300 MHz, [D_6]DMSO): $\delta = 7.47$ (4H, s, ArH), 5.95 (4H, d, OCH_2O outer), 5.18 (8H, s, $ArCH_2$), 4.67 (4H, t, $ArCHC_5H_{11}$), 4.15 (4H, d, OCH_2O inner), 2.2 – 2.4 (8H, br. m, CH_2), 1.05 – 1.25 (40H, br. m, CH_2), 0.81 (12H, t, CH_3), 0.55 (12H, t, CH_3); ES-MS (positive-ion): *m/z* calcd for $[C_{72}H_{96}N_4O_8S_8K_5]^+$: 1595.23; found: 1595.51.

Carbohydrates Exhibit a Distinct Preferential Solvation Pattern in Binary Aqueous Solvent Mixtures**

Aleksey Vishnyakov, Göran Widmalm, and Aatto Laaksonen*

Many substances are readily soluble in solvent mixtures but not in the pure components and vice versa.[1] Some examples of such solvents are binary mixtures of water, alcohols, acetonitrile, and dimethyl sulfoxide (DMSO), including both aqueous and nonaqueous mixtures of them. Selective solvation of ions from salts in mixed solvents is another, early discovered, property. The classic example is the heteroselective solvation of the ions of silver nitrate in a water – acetonitrile mixture, as demonstrated in 1958 by Strehlow and Koepp in a Hittorf experiment.[2] They found that in an equimolar solvent mixture, the nitrate anions were mainly solvated by the water molecules, while the silver cations were approximately four times more solvated by acetonitrile than by water molecules, although acetonitrile is generally known to solvate cations poorly. The unusual solvation properties of some binary liquid mixtures can, to a large extent, be related to a strong deviation from the ideality of Raoult's law. For example, the guide "like dissolves like" is challenged in the mixture of the highly polar molecules water and acetonitrile. This particular mixture exhibits a liquid – liquid separation, with an upper critical point at −1 °C at 38 mol% of acetonitrile. Both IR measurements[3, 4] and computer simulations[5, 6] have confirmed the existence of "micro-heterogeneities" and conglomerate water structures at higher acetonitrile concentrations. The often peculiar properties of liquid mixtures have fascinated many, including Mendeleev, who studied the nonideal behavior of water – alcohol mixtures some 130 years ago.[7] The ions of salts are not the only examples of selectively solvated species in mixed solvents. Many amphiphilic[8] and biomolecular systems[1] are better dissolved in mixtures, as a result of preferential solvation.

We have studied a model disaccharide molecule (α-D-Man*p*-(1 →3)-β-D-Glc*p*-OMe, **1**) in a mixture of DMSO and water. The solvent mixture is not needed for the purpose of increasing solubility, since disaccharides easily dissolve in both water and DMSO. Our emphasis is to study the resulting preferential solvation of the disaccharide and to learn about the behavior of the 1:3 DMSO – water molar mixture used. We would stress that the characteristic properties of the solvent mixture itself are very different from those of either water or DMSO. Based on neutron diffraction[9] and computer simulation studies,[10, 11] it has been suggested that DMSO – water mixtures contain complexes with either two or three water molecules attached to one DMSO molecule, held together by hydrogen bonds, as shown schematically in Figure 1. Near to its astonishingly low freezing point of −62 °C (roughly 80 °C below the freezing point of pure DMSO), the 1:3 mixture of DMSO and water behaves essentially like a one-component system.[12] Our own molecular dynamics (MD) simulations of this 1:3 DMSO – water, both at +15 and −50 °C, confirm that hydrogen-bonded associates (Figure 1) are formed. Besides being a popular cryosolvent, DMSO – water mixtures have been used in applications ranging from antibacterial activity to membrane permeability.[13] Most of these effects are, however, still not well understood. The solvation of carbohydrates in the DMSO – water mixture should be of some broader interest, not least because this group of biomolecules is associated with cell membranes and is involved in processes such as cell – cell recognition.[14]

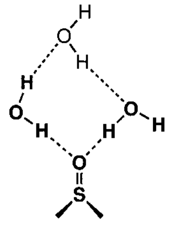


Figure 1. Schematic representation of a 1:3 DMSO – water complex in the binary mixture, observed in MD simulations of the mixture.

---

[*] A. Laaksonen
Division of Physical Chemistry
Arrhenius Laboratory, Stockholm University
10691 Stockholm (Sweden)
Fax: (+46) 8 15 21 87
E-mail: aato@tom.fos.su.se

A. Vishnyakov
Department of Chemistry
St. Petersburg State University
Universitetski pr. 2, 198904
St. Petersburg (Russia)

G. Widmalm
Department of Organic Chemistry
Arrhenius Laboratory, Stockholm University
10691 Stockholm (Sweden)

[**] This work has been supported by the Swedish Natural Science Research Council (NFR), the Nordic Minister Council, and the Swedish Institute.