Cooperative hydrogen bonding and yttrium(III) complexation in the assembly of molecular capsules

Michaele J. Hardie,[a] Julian A. Johnson,[b] Colin L. Raston*[a] and Helen R. Webb[a]

[a] *Department of Chemistry, Monash University, Clayton, Melbourne, Victoria 3800, Australia*
[b] *CSIRO Minerals, PO Box 90, Bentley, WA, 6982, Australia*

Received (in Columbia, MO, USA) 20th December 1999, Accepted 24th March 2000

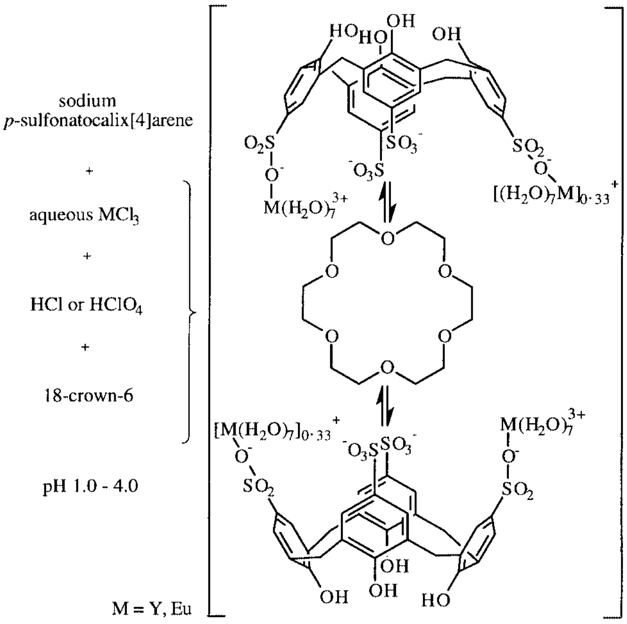
A combination of hydrogen bonding and metal coordination leads to the formation of the new solid state molecular capsule [{18-crown-6}⊂{($Y(H_2O)_7^{3+}$)$_{1.33}$(*p*-sulfonatocalix[4]arene^{4-})}$_2$] at pH between 1.0 and 4.0.

Certain rigid, non-planar molecules with curved or bowl shaped micro-environments have the extraordinary ability to assemble into capsules or cage molecules or ions.[1–12] These species may form nano-structures of relevance to materials and biological science, and their encapsulation of guest molecules has implications for drug delivery and catalysis.[13] The hydrophobic, bowl shaped motif of calixarenes and related resorcinarenes make them inherently versatile building blocks for the construction of ionic or molecular capsules. They afford capsules based on the assembly of two[4] or six[3] sub-units or supramolecular tectons in which the assembly is primarily driven by the interplay of hydrogen bonding between the subunits. This may involve additional hydrogen bonding associations with solvent molecules. Capsules derived from aqueous media usually rely on metal ion complexation to drive the assembly process.[10,11] An exception is the ionic capsule [{Na^+⊂(18-crown-6)(OH_2)$_2$}⊂{*p*-sulfonatocalix[4]arene^{4-})$_2$} + *n*H^+]$^{(7+n)-}$, which incorporates both hydrogen bonding and metal complexation.[12]

Herein, we report the use of a combinatorial approach for the synthesis of a complex based on molecular capsules, [{18-crown-6}⊂{($Y(H_2O)_7^{3+}$)$_{1.33}$(*p*-sulfonatocalix[4]arene^{4-})}$_2$] **1**.† Combinatorial chemistry has thus far been of limited application in supramolecular chemistry.[14] The supramolecular combinatorial library used contains all the interacting synthons including the degree of protonation of the calixarene (achieved by varying pH) and the relative ratios of the synthons, with crystallisation indicative of capsule formation. Its noteworthy that Atwood *et al.* have established a rich supramolecular chemistry of *p*-sulfonatocalix[4]arene and the lanthanides in the absence of crown ethers.[15,16]

Complex **1** crystallises from an aqueous solution of sodium *p*-sulfonatocalix[4]arene, 18-crown-6, yttrium(III) chloride, and hydrochloric acid as the tetrahydrate at a pH between 1.0 and 4.0 (Scheme 1). The highest optimised yield of 68% was for a pH close to 2.0 with the pH varied by 0.25 pH units. Above pH 4.0 and below pH 1.0 no complex precipitated from solution. Interestingly using perchloric acid resulted in oxidation of the calixarene and formation of crystalline $Y_2(SO_4)_3(H_2O)_8$ at pH < 2.0,‡ isostructural with other known $Ln_2(SO_4)_3(H_2O)_8$ complexes.[17] Complex **1** was characterised by electron microprobe analysis, which indicated a Y : S ratio of *ca.* 1 : 3, as well as microanalysis, IR spectroscopy and single crystal X-ray crystallography.§ The IR spectrum displayed a shift in the sulfonate absorptions from 1186 and 1048 cm^{-1} (for the sodium salt) to 1166 and 1041 cm^{-1}, which is indicative of metal coordination through oxygen centres.[18] Similar reactions were tried using other lanthanoid salts, and an isostructural Eu^{3+} complex has also been obtained at an optimal pH 2.5.¶

Complex **1** crystallises in the space group $P2_1/n$ with the capsule residing over a centre of inversion. The unit cell also contains eight solvent water molecules disordered over several positions. Results are shown in Fig. 1. Yttrium cations coordinate to the 1,3-sulfonate groups of the calixarene with two calixarene sub-units encapsulating an 18-crown-6 molecule, and indeed the crown ether may be the primary building component around which the capsule is formed. Surprisingly the 18-crown-6 is devoid of Na^+, and also Y^{3+}, but this ion is not well suited to interact with this crown ether.[19] The absence of Na^+ is in direct contrast to the ionic capsule [{Na^+⊂(18-crown-6)(OH_2)$_2$}⊂{(*p*-sulfonatocalix[4]arene^{4-})$_2$} + *n*H^+]$^{(7+n)-}$ and the related perched ‘Ferris wheel’ structure [{La^{3+}⊂(18-crown-6)(OH_2)$_3$}∩{(*p*-sulfonatocalix[4]arene^{4-} + $2H^+$)}]$^+$.[20]



Scheme 1

There are two types of Y metal, one of which is partially occupied and disordered, and both coordinate to seven water molecules [Y(1)–O 2.324(4)–2.405(4) Å, Y(2)–O 2.31(2)–2.38(2) Å], and one sulfonato group of the calixarene [Y(1)–O 2.308(4) Å, Y(2)–O 2.30(2) Å]. This is unexceptional for Y^{3+}.[21] Both are involved in RSO–Y–HOH···OSR hydrogen bonding leading to the dimerisation of calixarene sub-units in two distinct modes, shown schematically in Fig. 1(a). The first mode, of the ordered Y(1), involves a head-to-head dimerisation of the calixarenes [Fig. 1(a)(i)] to form the capsule, with YO···OS separations of 2.71–2.80 Å. This is undoubtedly facilitated by the encapsulation of the crown ether macrocycle (as discussed later). The second mode forms an S-type motif and involves the partially occupied $Y(2)(H_2O)_7$, [Fig. 1(a)(ii)]. This moiety is disordered over two adjacent sites by symmetry and each site has an occupancy of 1/3, determined by microprobe analysis, analysis of anisotropic displacement parameters and charge balance considerations. The YO···OS separations are 2.70 and 2.76 Å. The combination of the two modes of RSO–Y–HOH···OSR hydrogen bonding leads to a linear chain of

DOI: 10.1039/a910256f

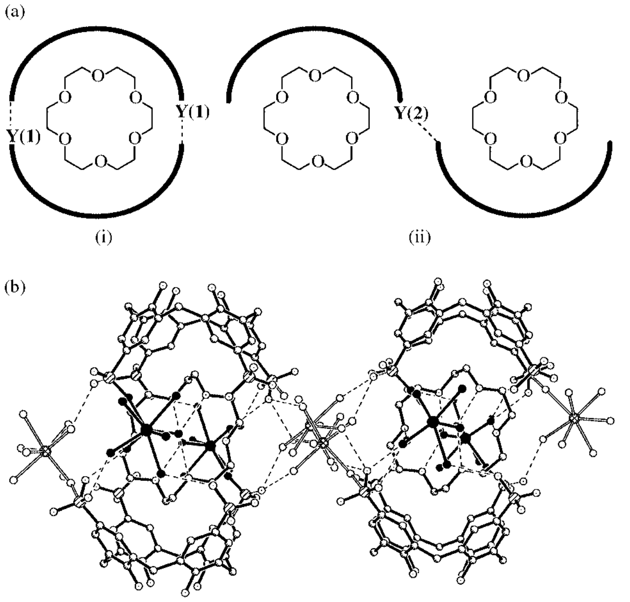


Fig. 1 (a) Schematic diagram of RSO–Y–HOH···OSR hydrogen bonding modes in $[(18\text{-crown-6})_{0.5}(\mathrm{Y(H_2O)_7})_{1.33}(p\text{-sulfonatocalix[4]arene})]\cdot 4\mathrm{H_2O}$ **1**, (i) head-to-head dimerisation of calixarenes around an 18-crown-6 molecule, (ii) S-type motif; (b) section of the crystal structure of **1** showing the linear chian of capsules,¶ $\mathrm{Y(1)(H_2O)_7}$ is shown in black, while $\mathrm{Y(2)(H_2O)_7}$ which is disordered with 1/3 occupancy is white. Hydrogen atoms have been removed for clarity and implied hydrogen-bonding interactions are represented by dashed lines. An isostructural complex can be formed with Eu.

capsules, a section of which is shown in Fig. 1(b). It is noteworthy that the sulfonatophenol group involved in Y(2) coordination has the largest tilt angle from the calixarene phenolic O_4 plane of 126.3° *cf.* 119.3, 115.6 and 124.5° for the other phenols.

The crown ether is at the core of the capsule. Hydrogen bonding occurs through each oxygen centre to water molecules coordinated to Y(1) at O···O separations of 2.77, 2.76 and 2.80 Å [Fig. 1(b)]. Driven primarily by this hydrogen bonding, but also by the complementarity of curvature of the calixarene cavity with the curvature of the crown ether (which optimises van der Waals interactions) the crown ether is held in the hydrophobic interior of the capsule. It is significantly distorted from its usual 'crown' shape due to exo-crown ether cavity hydrogen bonding, and hydrophobic interplay with the calixarenes.

In conclusion, using a combinatorial approach we have gained access to a novel multi-component capsule containing either Y^{3+} or Eu^{3+}. The same conditions for the formation of the capsule for solutions containing La^{3+} affords a perched structure involving one calixarene, one crown ether and a metal centre.[20] Other structural types are likely to be obtained from subtle changes in metal ion size and pH. We note that in the absence of crown ether, Ln^{3+} (Ln = Yb, Eu) can form complexes with *p*-sulfonatocalix[4]arene with the metal centre also bound to one sulfonato group, but ionic capsules do not form.[16] Clearly the presence of the crown ether is important for the formation of the capsule. However, other molecules with complementary size and curvature, which are also capable of hydrogen bonding, may also result in the formation of capsules.

We are grateful to the Australian Research Council for support of this work.

Notes and references

† *Synthesis* of **1**: $\mathrm{YCl_3\cdot 6H_2O}$ (4.4 mg, 14.5 μmol), 18-crown-6 (5 mg, 18.9 μmol) and tetrasodium *p*-sulfonatocalix[4]arene (6 mg, 7.25 μmol) were dissolved in water (700 μL) and the pH adjusted to 2.0 using concentrated HCl. Colourless crystals of **1** grew overnight (6.1 mg, 68%). The crystals were sensitive to solvent loss. Electron microprobe results indicate that sulfur is *ca.* three times more abundant than yttrium (microanalysis: C, 32.0; S, 10.44%).

‡ $\mathrm{Y_2(SO_4)_3(H_2O)_8}$ unit cell parameters: monoclinic, space group *C*2/*c*. a = 13.474(2), b = 6.688(1), c = 18.237(2) Å, β = 102.02(1)°.

§ *X-Ray Crystallography*: a crystal of dimensions 0.25 × 0.13 × 0.10 mm was grown from aqueous perchloric acid. Data were collected at 123(1) K on an Enraf-Nonius KappaCCD diffractometer with Mo-Kα radiation. The structure was solved by a combination of Patterson map and partial structure expansion (SHELXS-97) and refined using full-matrix least squares on F^2(SHELXL-97). All non-hydrogen atoms were refined anisotropically. All C–H and calixarene O–H hydrogens were fixed at geometrically calculated positions. *Crystal data* for $[(18\text{-crown-6})_{0.5}(\mathrm{Y(H_2O)_7})_{1.33}(p\text{-sulfonatocalix[4]arene})]\cdot 4\mathrm{H_2O}$ **1**: $\mathrm{C_{34}H_{58.67}O_{32.33}S_4Y_{1.33}}$: M_r = 1231.59; monoclinic, space group $P2_1/n$; a = 12.0226(2), b = 28.2424(7), c = 15.1695(4) Å, β = 97.512(1)°; Z = 4; U = 5106.6(2) Å^3; μ = 1.776 mm^{-1} (no correction); 67206 data collected, 13671 unique (R_{int} = 0.101); number of parameters = 738, final GOF = 1.062, R_1 = 0.0851 [on 8255 observed data with $I > 2\sigma(I)$], wR_2 = 0.2559, (all data).

CCDC 182/1599. See http://www.rsc.org/suppdata/cc/a9/a910256f/ for crystallographic files in .cif format.

¶ Unit cell parameters for the isostructural complex $[(18\text{-crown-6})_{0.5}(\mathrm{Eu(H_2O)_7})_{1.33}(p\text{-sulfonatocalix[4]arene})]\cdot 4\mathrm{H_2O}$: monoclinic, space group $P2_1/n$, a = 11.9930(4), b = 28.4063(15), c = 15.0737(7) Å, β = 96.890(3)°.

1 J. Kang and J. Rebek, *Nature*, 1997, **385**, 50.
2 T. Heinz, D. M. Rudkevich and J. Rebek, *Nature*, 1998, **394**, 764; J. Kang, J. Santamaria, G. Hilmersson and J. Rebek, *J. Am. Chem. Soc.*, 1998, **120**, 7389; T. Szabo, G. Hilmersson and J. Rebek, *J. Am. Chem. Soc.*, 1998, **120**, 6193; Y. Tokunaga, D. M. Rudkevich, S. Goran and J. Rebek, *Chem. Eur. J.*, 1998, **4**, 1449; K. R. Castellano, D. M. Rudkevich and J. Rebek, *J. Am. Chem. Soc.*, 1996, **118**, 10 002.
3 L. R. MacGillivray and J. L. Atwood, *Nature*, 1997, **389**, 469.
4 K. N. Rose, L. J. Barbour, G. W. Orr and J. L. Atwood, *Chem. Commun.*, 1998, 407.
5 O. Mogek, M. Pons, V. Bohmer and W. Vogt, *J. Am. Chem. Soc.*, 1997, **119**, 5706.
6 R. G. Chapman and J. C. Sherman, *J. Am. Chem. Soc.*, 1995, **117**, 9081.
7 K. Nakamura, C. Sheu, A. E. Keating, K. N. Houk, J. C. Sherman, R. G. Chapman and W. L. Jorgensen, *J. Am. Chem. Soc.*, 1997, **119**, 4321.
8 K. Murayama and K. Aoki, *Chem. Commun.*, 1998, 607.
9 J. de Mendoza, *Chem. Eur. J.*, 1998, **4**, 1373 and references therein.
10 M. Fujita, D. Oguro, M. Miyazawa, H. Oka, K. Yamaguchi and K. Ogura, *Nature*, 1995, **378**, 469; T. Kusukawa and M. Fujita, *Angew. Chem., Int. Ed.*, 1998, **37**, 3142; T. Ibukuro, T. Kusukawa and M. Fujita, *J. Am. Chem. Soc.*, 1998, **129**, 8561; N. Takeda, K. Umemoto, K. Yamaguchi and M. Fujita, *Nature*, 1999, **398**, 794; B. Olenyuk, J. A. Whiteford, A. Fechtenkötter and P. J. Stang, *Nature*, 1999, **398**, 796 and references therein.
11 T. N. Parac, D. L. Caulder and K. N. Raymond, *J. Am. Chem. Soc.*, 1998, **120**, 8003; C. Bruckner, R. E. Powers and K. Raymond, *Angew. Chem., Int. Ed.*, 1998, **37**, 1837; D. L. Caulder, R. E. Powers, T. N. Parac and K. Raymond, *Angew. Chem., Int. Ed.*, 1998, **37**, 1840 and references therein.
12 A. Drljaca, M. J. Hardie, C. L. Raston and L. Spiccia, *Chem. Eur. J.*, 1999, **5**, 1828.
13 T. Douglas and M. Young, *Nature*, 1998, **393**, 152; G. D. Stucky and J. E. MacDouglas, *Science*, 1990, **247**, 669; K. Park, *Controlled Drug Delivery: Challenges and Strategies*, American Chemical Society, Washington DC, 1997 and references therein.
14 M. C. Calama, R. Hulst, R. Fokkens, N. M. M. Nibbering, P. Timmerman and D. N. Reinhoudt, *Chem. Commun.*, 1998, 1021.
15 J. L. Atwood and S. Bott, *Calixarenes: A Versatile Class of Macrocyclic Compounds*, ed. J. Vicens and V. Bohmer, Kluwer Academic Publishers, Boston, MA, 1991.
16 J. L. Atwood, G. W. Orr, N. Means, F. Hamada, H. Zhang, S. Bott and K. Robinson, *Inorg. Chem.*, 1992, **31**, 603; J. L. Atwood, G. W. Orr and K. D. Robinson, *Supramol. Chem.*, 1994, **3**, 89; G. W. Orr, L. J. Barbour and J. L. Atwood, *Science*, 1999, **285**, 1049.
17 E. G. Sherry, *J. Solid State Chem.*, 1976, **19**, 271; L. Hiltunen and L. Niinistö, *Cryst. Struct. Commun.*, 1976, **5**, 561.
18 L. J. Bellamy, *The Infrared Spectra of Complex Molecules: Advances in Infrared Group Frequencies*, Chapman and Hall, London, 1980, vol. 2.
19 R. Rogers and C. Bauer, in *Comprehensive Supramolecular Chemistry*, ed. J. L. Atwood, J. Davies, D. Macninol and F. Vogtle, Pergamon, New York, 1996, vol. 1, p. 315.
20 A. Drljaca, M. J. Hardie, J. A. Johnson, C. L. Raston and H. R. Webb, *Chem. Commun.*, 1999, 1135.
21 See, for example: M. Bukowska-Strzyzewska and A. Tosik, *Acta Crystallogr., Sect. B*, 1982, **38**, 950.