ChemComm
www.rsc.org/chemcomm

Conformation perturbation of *p*-sulfonatocalix[5]arene *via* complexation of 1,4-diazabicyclo[2.2.2]octane

Scott J. Dalgarno,[a] Michaele J. Hardie[a] and Colin L. Raston*[b]
[a] *Department of Chemistry, University of Leeds, Woodhouse Lane, Leeds, UK LS2 9JT*
[b] *School of Biomedical and Chemical Sciences, University of Western Australia, Crawley, Perth WA 6909, Australia. E-mail: clraston@chem.uwa.edu.au; Fax: (+61)8 9380 1005*

Received (in Columbia, MO, USA) 25th June 2004, Accepted 5th August 2004
First published as an Advance Article on the web 1st November 2004

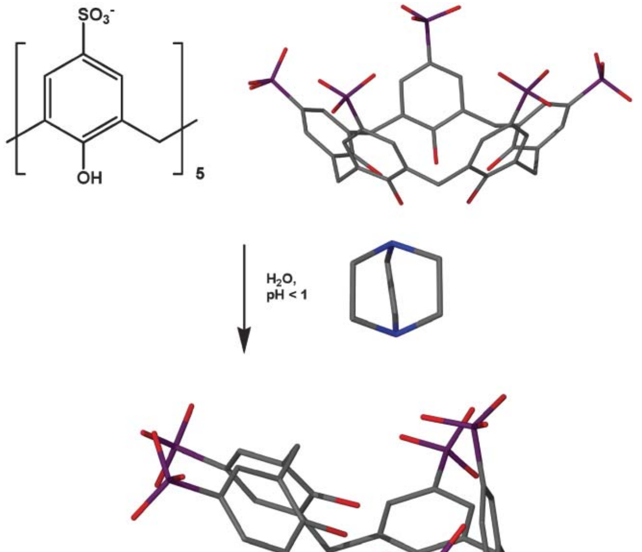
A novel conformation of *p*-sulfonatocalix[5]arene has been established in the solid state with two calixarenes organised in a '*bis*-molecular capsule' shrouding two di-protonated DABCO molecules and two water molecules within.

The solution and solid state supramolecular chemistry of the *p*-sulfonatocalix[*n*]arenes ($n = 4,5,6,8$) display a range of properties with biological relevance and also the ability to act as enzyme mimics.[1] This partly relates to the hydrophobic 'pockets' generated within the macrocycles which can interact with various guests to form complexes in solution or supramolecular architectures of varying complexity in the solid state.[1,2] Inspection of the solid state structures for the smallest of these molecules (where $n = 4$) in the Cambridge Crystallographic Database shows that with one exception, the calixarene regularly adopts the cone conformation. Although the cone conformation is flexible in its ability to accommodate various guests, the molecule packs to form hydrophilic–hydrophobic bi-layers through a series and/or variety of intermolecular interactions which encompass π-stacking, lower to upper rim hydrogen bonding and methylene CH···π interactions. Deviation from such bi-layers for *p*-sulfonatocalix[4]arene are rare but can be achieved through judicious choice of guest and counterion, resulting in the formation of nanometre scale spheres and tubules of varied geometry depending on the guest employed.[3] As mentioned above, formation of the cone conformation of *p*-sulfonatocalix[4]arene in the solid state has been attenuated with the formation of a supramolecular architecture where the calixarene adopts the 1,3-alternate conformation.[4] This arises from non-covalent interactions and the structure is the only example of its kind for that particular molecule. Similar examination of *p*-sulfonatocalix[5]arene ($SO_3[5]$) structures on the Cambridge Crystallographic Database shows no such deviation from the typically observed cone conformation or bi-layer arrangement.[5] Indeed further examination of the basic calix[5]arene fragment shows that significant deviation from the commonly encountered truncated cone shape is achieved either by 'upper'/'lower' rim functionalisation or by 'lower' rim coordination of various transition metal or lanthanide ions.[6]

Our investigation into the inclusion capabilities of $SO_3[5]$ towards (bis)amino functionalised (bi)cyclic guests has afforded a novel '*bis*-molecular capsule' arrangement with the calixarene in a hitherto unknown solid state conformation.

Crystals of **1**, $[\{(\text{DABCO} + 2\ \text{H}^+)(\text{H}_2\text{O})\} \subset (p\text{-sulfonatocalix[5]arene} + \text{H}^+)][\text{DABCO} + 2\ \text{H}^+]\cdot\text{H}_2\text{O}_{9.25}$ grew from an acidified solution containing $Na_5SO_3[5]$ and 1,4-diazabicyclo[2.2.2]octane (DABCO).† The asymmetric unit comprises one $SO_3[5]$ molecule, a total of two and a half di-protonated DABCO molecules (stoichiometry confirmed by NMR) and a total of nine and a quarter water molecules which are disordered over twenty five positions. There are several exceptional features associated with complex **1**, the first of which is the aforementioned '*bis*-molecular capsule' which comprises two $SO_3[5]$ molecules shrouding two di-protonated DABCO molecules and two water molecules. This is indeed the first time that the molecule has shown the ability to multi-host in such a manner. The guests are held snugly within the small hydrophobic cavities generated through the conformation distortion of the calixarenes which adopt a 'pseudo-double cone' arrangement, see Scheme 1 and Fig. 1. Hydrogen bonding contacts are evident from one protonated nitrogen atom of the enclosed DABCO molecule being directed towards the sulfonate group of the calixarene which has folded in on itself (N···O distance 2.750 Å). The other protonated nitrogen atom hydrogen bonds to a disordered water molecule which resides at the periphery of the capsule (N···O distance of 2.779 Å). Additional disordered di-protonated DABCO molecules (one and a half) reside at the periphery of the 'capsule' and provide overall charge balance for the complex. Given the extent of disorder surrounding the peripheral DABCO molecules, hydrogen atoms could not be located on some of the nitrogen atoms but protonation is highly likely given the pK_a values for DABCO (2.97 and 8.82) and the pH of the solution (<1).‡.

The extended structure also reveals that the *p*-sulfonatocalix[5]arenes are not packed in a bi-layer arrangement but are in fact arranged in chains whilst still optimising intermolecular hydrophobic and hydrophilic interactions, Fig. 2. The presence of the di-protonated DABCO has evidently exerted intermolecular forces which are strong enough to overcome the affinity of $SO_3[5]$ to self-assemble into a bi-layer arrangement. Architectures which display unusual calixarene conformational behaviour for the smaller calixarenes are rare but are one of our primary research goals as 'breaking the bi-layer' can have spectacular consequences overall.[3] The $SO_3[5]$ molecules in the aforementioned hydrophobic chains



Scheme 1 Diagram showing the conformational change in *p*-sulfonatocalix[5]arene which is induced by the presence of DABCO (centre). The change is from a traditional truncated cone shape (top right) to a distorted pseudo-double cone conformation (side view of, bottom centre).

DOI: 10.1039/b410242h

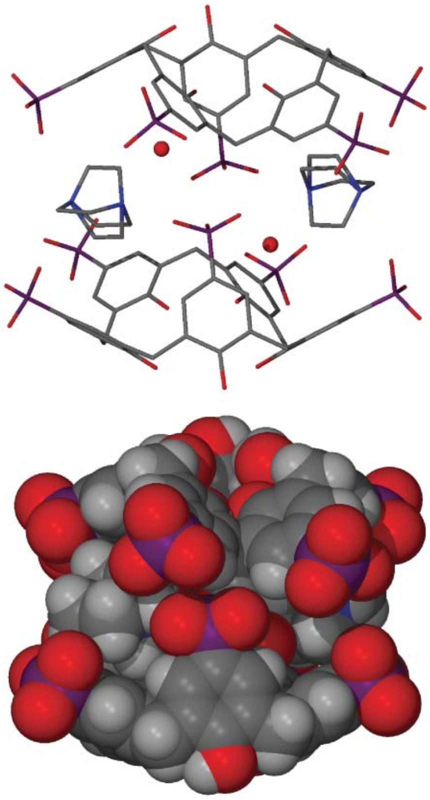


Fig. 1 Stick (partial) and space filling representations of the '*bis*-molecular capsule' showing the distortion of the calixarene, the double inclusion of DABCO and the snug fit of the guests within the small cavities in the arrangement (hydrogen atoms {stick representation above}, exterior DABCO and water molecules have been omitted for clarity).

assemble through one π-stacking interaction (aromatic centroid···centroid distance 4.004 Å), one aromatic hydrogen···π interaction (ArH···π distance 2.934 Å) and a total of three hydrogen bonds from lower rim hydroxyl groups to adjacent sulfonate groups (OH···OS distances range from 2.833 to 2.883 Å). These chains are linked *via* hydrogen bonding from one disordered DABCO molecule (occupancy 0.5 over two positions) with N···OS distances of 2.762 and 2.768 Å. The other remaining DABCO molecule (occupancy 0.5) hydrogen bonds to disordered water molecules (N···O distances of 2.696 and 2.832 Å). The overall structure does, however, retain some layered structure character when both internal and external DABCO molecules are taken into account within the extended structure.

In conclusion a new solid state conformation for *p*-sulfonatocalix[5]arene has been observed and has shown DABCO to be an influential supramolecular building block. The molecule does not reside in the typical cone shaped cavity of the host, as expected, but results in SO_3[5] distortion and '*bis*-molecular capsule' formation. The exceptional influence of DABCO is further demonstrated by disruption to the traditionally observed bi-layer arrangement with resulting formation of hydrophobic chains. Work continues on investigating the hosting capabilities of *p*-sulfonatocalix[5]arene with a view to using the disturbance of the bi-layer as a tool in constructing larger and more complex supramolecular arrays.

We thank the EPSRC for support of this work.

Notes and references

† *Crystal data*: $C_{47}H_{67.5}N_4O_{29.25}S_5$, $M = 1316.85$, triclinic, $a = 12.7511(2)$, $b = 15.9188(3)$, $c = 16.7800(4)$, $\alpha = 85.759(1)$, $\beta = 79.554(1)$, $\gamma = 74.439(1)$, Å, $U = 3225.72(11)$ Å^3, $\mu = 1.356$ mm^{-1}, $T = 150(1)$ K, space group $P\bar{1}$ (no. 2), $Z = 2$, Mo–Kα radiation ($\lambda = 0.71073$ Å), Final GOF = 1.776, $R_1 = 0.1001$, 68418 reflections measured, 14409 unique ($R_{\text{int}} = 0.0941$) which were used in all calculations. The final $wR(F^2)$ was 0.2892 (all data). Two disordered carbon atoms of one DABCO molecule and several disordered water molecules were refined isotropically. Hydrogen atoms of one di-protonated DABCO molecule were refined with constraints and calixarene base hydrogen atoms were geometrically calculated and then fixed in positions suggested by residual peaks. CCDC 244468. See http://www.rsc.org/suppdata/cc/b4/b410242h/ for crystallographic data in .cif or other electronic format.

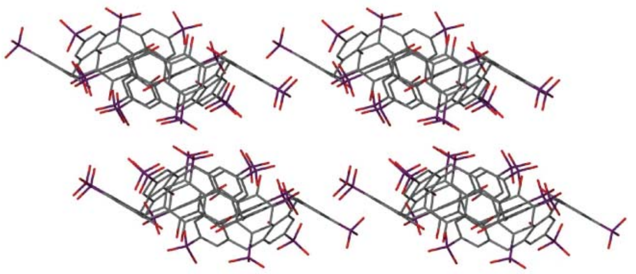


Fig. 2 Packing diagram showing the hydrophobic chains of SO_3[5] in the extended structure (chains running perpendicular to the plane of the page).

‡ Synthesis of [{(DABCO + 2 H^+)(H_2O)} ⊂ (*p*-sulfonato-calix[5]arene + H^+)][DABCO + 2 H^+]·$H_2O_{9.25}$, **1**: a solution containing Na_5SO_3[5] (10 mg, 9.6 μmol) and DABCO (5 mg, 45 μmol) was acidified using 1 M hydrochloric acid until pH < 1. Over two days large prismatic colourless crystals formed which were suitable for X-ray diffraction studies, 8.6 mg, 66%. ^{1}H NMR (D_2O) $\delta = 7.58$ (s, 10 H, Ar*H*), 3.93 (s, 10 H, ArCH_2), 3.48 (s, 30 H, NCH_2).

1 J. L. Atwood, F. Hamada, K. D. Robinson, G. W. Orr and R. L. Vincent, *Nature*, 1991, **349**, 683; J. L. Atwood, G. W. Orr, K. D. Robinson and F. Hamada, *Supramol. Chem.*, 1993, **2**, 309; S. J. Harris, 1995, *PCT Int. Appl.*, WO 9519974; D. Hulmes, A. Coleman and E. Aubert-Foucher, 2000, *PCT Int. Appl.*, WO 2000007585; R. Lamartine, M. Tsukada, D. Wilson and A. Shirata, *C. R. Chim.*, 2002, **5**, 163; J. M. Dormann and H.-U. Wolf, 2003, *PCT Int. Appl.*, WO 2003105904; R. Zadmard, M. Junkers, T. Schrader, T. Grawe and A. Kraft, *J. Org. Chem.*, 2003, **68**, 6511.

2 M. Selkti, A. W. Coleman, I. Nicolis, N. Douteau-Guével, F. Villain, A. Tomas and C. D. Rango, *Chem. Commun.*, 2000, **2**, 161; E. D. Silva and A. W. Coleman, *Tetrahedron*, 2003, **59**, 7357; J. L. Atwood, L. J. Barbour, M. J. Hardie and C. L. Raston, *Coord. Chem. Rev.*, 2001, **222**, 3; S. J. Dalgarno, M. J. Hardie and C. L. Raston, *Cryst. Growth Des.*, 2004, **4**, 227; A. T. Yordanov, O. A. Gansow, M. W. Brechbiel, L. M. Rogers and R. D. Rogers, *Polyhedron*, 1999, **18**, 1055; P. C. Leverd, P. Berthault, M. Lance and M. Nierlich, *Eur. J. Org. Chem.*, 2000, **1**, 133; C. Bonal, Y. Israëli, J.-P. Morel and N. Morel-Desrosiers, *J. Chem. Soc., Perkin Trans. 2*, 2001, **7**, 1075.

3 G. W. Orr, L. J. Barbour and J. L. Atwood, *Science*, 1999, **285**, 1049; J. L. Atwood, L. J. Barbour, S. J. Dalgarno, M. J. Hardie, C. L. Raston and H. R. Webb, *J. Am. Chem. Soc.*, 2004, **126**, 13170.

4 L. J. Barbour and J. L. Atwood, *Chem. Commun.*, 2001, **19**, 2020.

5 J. W. Steed, C. P. Johnson, C. L. Barnes, R. K. Juneja, J. L. Atwood, S. Reilly, R. L. Hollis, P. H. Smith and D. L. Clark, *J. Am. Chem. Soc.*, 1995, **117**, 11426; C. P. Johnson, J. L. Atwood, J. W. Steed, C. B. Bauer and R. D. Rogers, *Inorg. Chem.*, 1996, **35**, 2602; M. J. Hardie, M. Makha and C. L. Raston, *Chem. Commun.*, 1999, **23**, 2409.

6 D. R. Stewart, M. Krawiec, R. P. Kashyap, W. H. Watson and C. D. Gutsche, *J. Am. Chem. Soc.*, 1995, **117**, 586; G. Ferguson, A. Notti, S. Pappalardo, M. F. Parisi and A. L. Spek, *Tetrahedron Lett.*, 1998, **39**, 1965; S. E. J. Bell, J. K. Browne, V. McKee, M. A. McKervey, J. F. Malone, M. O'Leary and A. Walker, *J. Org. Chem.*, 1998, **63**, 489; M. Fan, H. Zhang and M. Lattman, *Chem. Commun.*, 1998, **1**, 99; L. J. Charbonnière, C. Balsiger, K. J. Schenk and J.-C. G. Bunzli, *J. Chem. Soc., Dalton Trans.*, 1998, **3**, 505; F. Arnaud-Neu, Z. Asfari, B. Souley, J. Vicens, P. Thuéry and M. Nierlich, *J. Chem. Soc., Perkin Trans. 2*, 2000, **3**, 495; P. Sood, H. Zhang and M. Lattman, *Organometallics*, 2002, **21**, 4442; M. Makha, P. J. Nichols, M. J. Hardie and C. L. Raston, *J. Chem. Soc., Perkin Trans. 1*, 2002, **3**, 354.