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Manipulating the conformation and interplay of *p*-sulfonated calix[4]arene by lower rim tri-substitution with N'-cyanocarbamimidate groups

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Abstract

p-Sulfonatocalix[4]arene with three of the lower rim hydroxyl groups substituted with N'-cyanocarbamimidate groups crystallizes in the 1,3-alternate conformation rather than the common cone conformation for the unsubstituted calixarene which also results in departure from the common bilayer arrangement of sulfonated calix[4]arenes.

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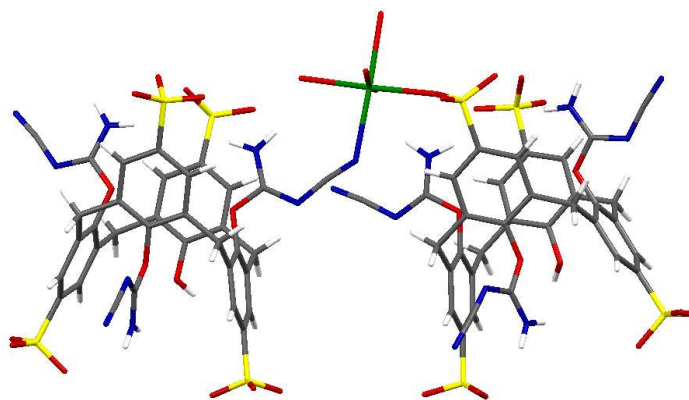
ARTICLE

Manipulating the conformation and interplay of *p*-sulfonated calix[4]arene by lower rim tri-substitution with N'-cyanocarbamimidate groups

Irene Ling[a]*, Brian W. Skelton[b], Alexandre N. Sobolev[b,c], Yatimah Alias[a] and Colin L. Raston[d]

p-Sulfonatocalix[4]arene with three of the lower rim hydroxyl groups substituted with N'-cyanocarbamimidate groups crystallizes in the 1,3-alternate conformation rather than the common cone conformation for the unsubstituted calixarene which also results in departure from the common bilayer arrangement of sulfonated calix[4]arenes. The new calixarene formed via reaction of the phenolic moieties of *p*-sulfonatocalix[4]arene with the dicyanamide anion derived from an ionic liquid with an imidazolium cation.

Introduction

Condensation reaction of formaldehyde and *para*-substituted phenols under basic conditions in the presence of alkali metal hydroxide as the templating catalyst yields macrocyclic compounds known as calixarenes. One of the most interesting features of these calixarenes is their structural flexibility and their ability to assume a variety of shapes *via* conformational interconversion.[1] Cornforth first identified that the smallest of the calixarene oligomers, calix[4]arene can exist in four different conformations, which were later named by Gutsche as the cone, partial cone, 1,2-alternate and 1,3-alternate conformers, with the structures having C_{4v}, C_s, C_{2h} and D_{2d} symmetry respectively.[2,3] Controlling the conformation of this calixarene can be achieved by introducing bulky substituents on either the upper or lower rim.

Calixarenes with upper rim functionalized with sulfonate groups have good solubility in water.[4,5] The ability of sulfonated calixarenes to form various inclusion complexes with different guest species in water has opened new applications which are reflected by their potential uses in analytical chemistry and separation science.[6,7] For an extensive number of solid state studies, the water soluble calix[4]arene derivatives have shown a diversity of selective binding properties. In addition, *p*-sulfonatocalix[4]arene can assemble into a wide range of remarkable structural motifs,[8-11] where in most cases the calixarenes are assembled in an up-down manner with the water-soluble sulfonate groups aligned at the surfaces of the bilayers, separated by a distinct hydrophilic layer containing the guest molecules and water molecules.[12]

We have recently developed the self-assembly of *p*-sulfonatocalix[4]arene incorporating various ionic liquid based components (symmetrical and unsymmetrical) in the presence of lanthanides and phosphonium cations as a strategy for building multi-component nanomaterials.[13] Structurally authenticated solid state structures based on *p*-sulfonatocalix[4]arene and a variety of ionic liquid based cations demonstrate the preferential binding of calixarene cone conformer towards these components rather than towards selected phosphonium cations while consistently retaining the up–down antiparallel bilayer arrangement of the calixarenes with the lower rim hydroxyl groups arranged in a back-to-back fashion at the van der Waals limit involving hydrogen bonding of the phenolic OH groups.

Herein we report the synthesis involving reaction with an imidazolium dicyanamide ionic liquid, and structure elucidation in the solid state of the resulting lower rim functionalised *p*-sulfonatocalix[4]arene bearing three N'-cyanocarbamimidate groups, revealing a complex self-assembled array. This structure represents a new structural motif involving the 1,3-alternate conformation of the water-soluble *p*-sulfonatocalix[4]arene with three of the hydroxyl groups substituted with N'-cyanocarbamimidate groups; an imidazolium cation is positioned away from the calixarene cavity (*exo*) as established in previous systems.[13] Importantly, one comparable example of the *p*-sulfonatocalix[4]arene in a 1,3-alternate conformation, stabilized as its bipyridinium salt was reported by Barbour et al., where the calixarene is surrounded by eight 4,4'-bipyridinium cations.[14] Four of the 4,4'-bipyridinium cations are situated at the 4-fold axis while the remaining four protrude into the small clefts beside the sulfonate upper rim head groups which interact strongly via hydrogen bonds and aromatic π-π interactions.
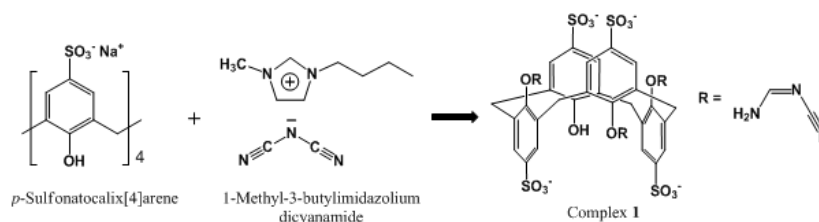
Scheme 1 Synthesis of compound **1**.

Dicyanamide based ionic liquids are low viscosity liquids that can dissolve a broad range of hydroxylated compounds and can function as active base catalysts for O-acetylation reaction.[15] Different studies have been carried out on the O-acetylation of various types of alcohols including naphthol, tertiary butyl alcohol, cyclohexanol and several saccharides using dicyanamide ionic liquids.[15] In the present work, we employed 1-methyl-3-butylimidazolium dicyanamide as one of the components for constructing multi-component nanomaterials with *p*-sulfonatocalix[4]arene, along with lanthanides ions, Scheme 1, as an extension of previous studies.[16] However, in this case, we find that the dicyanamide anion condenses selectively with three of the four phenolic groups of the calixarene, with a change in its conformation, at least in the solid state. The self assembly of the novel compound bearing a high degree of functionality is of interest in gaining access to new materials, for potential technological advances.

Results and Discussion

Compound **1** crystallized in space group *C*2/*m*, *Z*=2, comprising two calixarene molecules in asymmetric unit, along with one imidazolium molecule, 1.75 gadolinium(III) cations distributed between 5 positions and 1.75 sodium ions distributed between 3 positions and disordered water molecules. The structure has the *p*-sulfonatocalix[4]arene molecule in the 1,3-alternate conformation, with three of the lower rim hydroxyl groups deprotonated and substituted with dicyanamide via nucleophilic addition, as N'- cyanocarbamimidate groups with the O–C bond length ranges from 1.33 to 1.34 Å, Fig. 1. Each N'-cyanocarbimimidate group has a planar conjugated arrangement of atoms in the *E*-conformation with respect to the nitrile group and the oxygen atom, with the amino group *cis* to the nitrile moiety. This overall arrangement represents a new structural motif for the interplay of *p*-sulfonatocalix[4]arenes, albeit now covalently modified, in the 1,3-alternate conformation. This is distinctly different to the usual bilayer structures containing unsubstituted *p*-sulfonatocalix[4]arene in cone conformation. We have previously prepared multi-component ionic solids in conjunction with *p*-sulfonatocalix[4]arene and different ionic liquid based cations (namely imidazolium, pyrrolidinium and pyridinium) along with selected large phosphonium cations and aquated lanthanides(III) and established that the ionic liquid based cation is consistently and selectively taken up into the

hydrophobic cavity of *p*-sulfonatocalix[4]arene in the cone conformation. It is also important to note that in structure **1**, the positively charged butylimidazolium ion is positioned outside (*exo*) the calixarene cavity, unlike in the previously reported butylimidazolium complexes of *p*-sulfonatocalix[4]arene[16] and reflects a smaller cavity for the new calixarene.

The overall packing of **1** consists of linear arrays of multiple repeating hydrophobic and hydrophilic layers which are built up by calixarene anions and metal cations (Gd^{3+} and Na$^+$) with the upper rims of the calixarenes aligned, essentially creating hydrophilic regions interposed with disordered metal ions and water molecules, Fig. 2. The composite layers are stabilized in part by the electrostatic interaction and hydrogen bonding of the coordinated sodium ions and hydrated gadolinium ions along with bridging water molecules in the hydrophilic region which balances the negative charge on the sulfonate groups of the calixarene. The thickness of the hydrophobic layer is *ca.* 11.3 Å while the hydrophilic layer is *ca.* 4.4 Å with the closest approach between the adjacent layers of the sulfonate groups
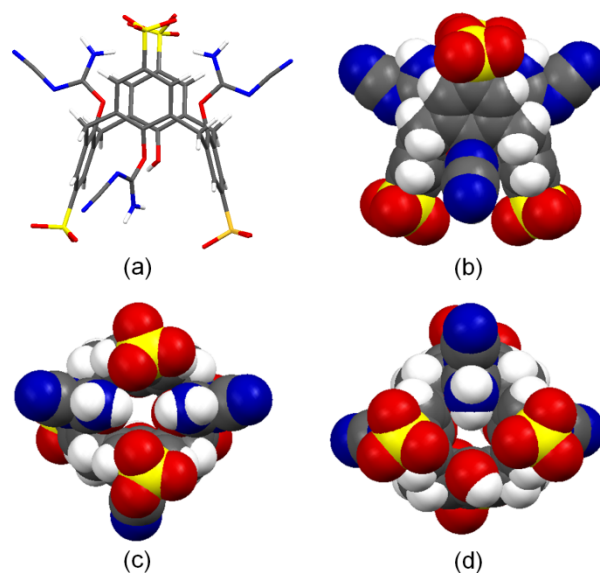

Fig. 1. (a) Stick representation of compound **1** showing the 1,3-alternate conformation of *p*-sulfonatocalix[4]arene with three of the phenolic groups substituted with N'-cyanocarbimimidate group, and (b-d) as equivalent space-filling representation viewed from side, top and bottom respectively.

represented by O···O distances at 3.29 to 3.90 Å. The hydrophilic layer contains large quantities of water molecules in addition to aquated metal ions that are involved in extensive hydrogen bonding. Two Gd^{3+} cations at full occupancy (octa-aqua and nona-aqua), two disordered octa-aqua Gd^{3+} species (half populated across a mirror plane) and one disordered Gd^{3+} centre (0.25 occupancy) were identified with Gd-O distances at 2.323(17) to 2.60(2) Å. The homoleptic Gd^{3+} ions form secondary coordination sphere with the calixarene through hydrogen bonding, as judged by the close proximity of the O-atom of the sulfonate group to the aquated Gd^{3+} cations, closest Gd–O···O–S distances being 2.72 to 2.84 Å.
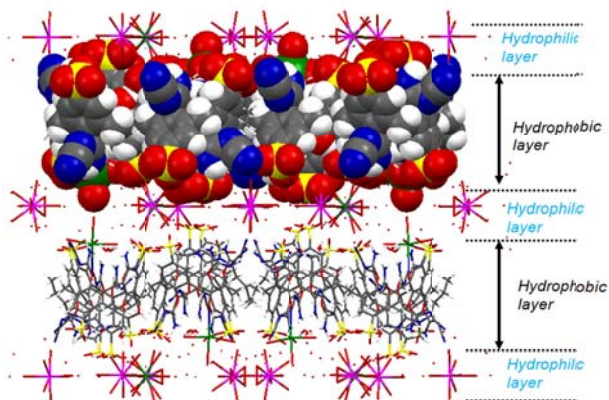

Fig. 2. Composite layers of compound **1** showing the alternating hydrophilic and hydrophobic layers in the extended structure.

The hydrophilic layers also contain Na^+ ions which interact simultaneously with calixarene and water molecules in different coordination environments. One of the three Na^+ centres links two calixarenes (A & B) together by bridging to an oxygen atom of one calixarene sulfonate group and a nitrogen atom from the nitrile moiety of N'-cyanocarbamimidate group with the Na(1)–O(32B) and Na(1)–N(23A) distance at 2.365(11) Å and 2.579(13) Å, respectively, Fig. 3. The remaining coordination sphere for the Na^+ ion is fulfilled by four water molecules (Na(1)–O distances ranging from 2.322(18) Å to 2.58(5) Å). Two other Na^+ ions are aquated with water molecules where one of the independent Na^+ centres is fully ligated with seven water molecules (Na(2)–O distances ranging from 2.35(3) Å to 2.891(17) Å) while the other Na^+ centre is disordered and is coordinated with water molecules with Na(3)–O distances ranging from 2.21(3) Å to 2.95(4) Å. These sodium coordinated pairs of calixarenes (A & B) are linked into the three dimensional network via the π(centroid)···π(centroid) interactions involving the calixarene aromatic moieties devoid of the N'-cyanocarbamimidate group substitution, with the closest distance at 3.56 Å. The same aromatic moieties are also engaged in weak hydrogen bonding where an oxygen atom of a calixarene sulfonate group hydrogen bonds to an adjacent calixarene hydroxyl groups,

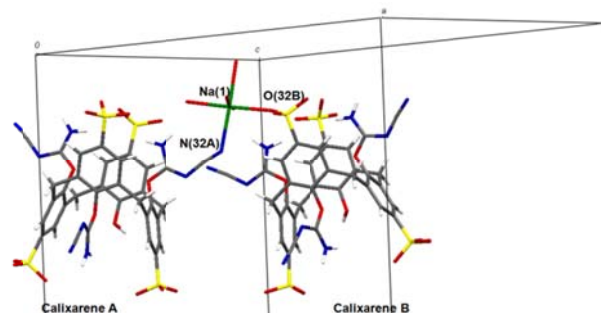forming pseudo-centrosymmetric cluster, with S–O···H–O short contacts at 1.94 and 1.95 Å.

Fig. 3. Coordination environment for Na(1) bridging two calixarene molecules involving hydrogen bonding.

The 1,3-alternate conformer for *p*-sulfonatocalix[4]arene provides less polarity than the other conformers[17-21] and better topological advantages because it affords two cavities; one on each side of the calix[4]arene framework, comprising two phenolic oxygen donor atoms and two aromatic moieties.[21] In this case, the calixarene cavity is smaller than the parent compound with the distances between the aromatic rings confronting each other ranging at 5.7 to 5.8 Å. It is noteworthy that in compound **1**, there are water molecules (O17W, O18W, O19W and O20W) included inside the cavities on both side of the calixarenes (A & B) in close proximity to the sulfonate groups and involved in multiple hydrogen bonding to i) O-atom of sulfonate group, O–H···O–S distances at 2.08 to 2.10 Å; ii) O-atom of the unsubstituted phenolic group, O–H···O distance at 2.10 Å and iii) amino group, H–O···H–N distances at 2.02 to 2.03 Å, Fig. 4. Such interaction of water molecules embedded in the deep cavity of calixarene has been established for the cone conformer of *p*-sulfonatocalix[4]arene, with the hydrogen atoms directed toward the closest aromatic centroids at distances ranging from 3.16 to 4.19 Å. The interactions of the water molecules with its surroundings in both side of the calixarene cavities, have been further investigated using Hirshfeld surface analysis (generate from CrystalExplorer[22]) with the breakdown of the fingerprint plot for pattern identification associated with the hydrogen bonding interaction depicted in Fig. 4. The presence of water molecules in both sides of the calixarene cavities is vital in providing higher stabilization of the conformer. A molecular model of *p*-sulfonatocalix[4]arene with and without included water molecule, optimized without any constraint followed by standard B3LYP method using the 3-21G* basis set were applied to calculate the *ab initio* absolute energies (in atomic unit), Fig. 5. The calculation suggest that the intermolecular H-bonded network of included water molecules with calixarene significantly influences the stability of the conformer, with calculated energy lower than the calixarene 1,3-alternate conformer alone.
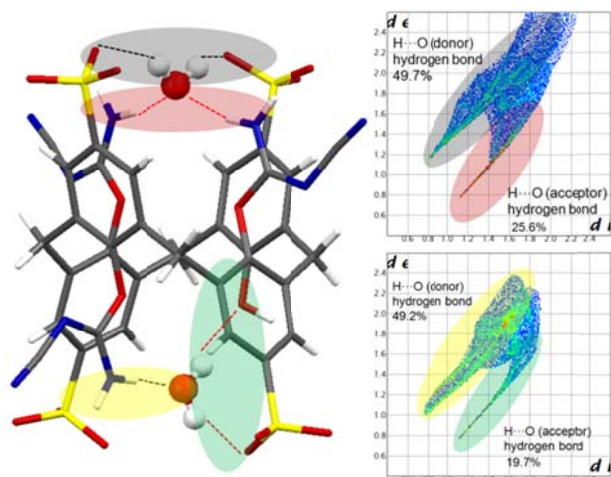
Fig. 4. Stick representation showing close contacts between included water molecule and calixarene (H···O (donor) and H···O (acceptor) are shown as red and black dashed lines. Corresponding fingerprint plot on right.
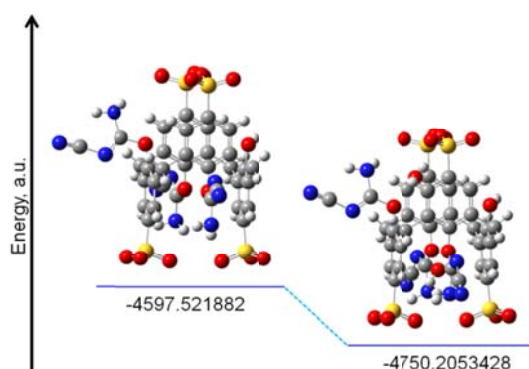

Fig. 5. Molecular structure of **1** without and with included water molecules (left and right), the geometry optimization was performed using DFT B3LYP/6-31G*.

An additional feature of compound **1** is the presence of positively charged *n*-butylimidazolium ions, which are positioned outside the calixarene cavities, Fig. 6, unlike in the previous reported structures with the imidazolium cation consistently drawn into the calixarene cavity. The butylimidazolium molecule is positioned between two calixarene molecules, in the cleft associated with the bridging sodium ion, with the charged head group having a close C–H···π(centroid) contact to one of the calixarene methylene bridges, (C···π(centroid) distance at 3.86 Å); the *n*-butyl terminal is directed towards the coordinated sodium ion beside the nitrile group and is in close contact with the nearest calixarene through C–H···H–C hydrogen bonds, at 2.53 to 2.73 Å, Fig. 6. The unique H-atom of the butylimidazolium interacts with a cyano group with C–H···N contact at 2.41 Å while other H-atoms interacts with surrounding sulfonate groups with H···O–S contact at 2.55 to 2.95 Å. The corresponding fingerprint plots for the close interactions of butylimidazolium with percentage contribution to the Hirshfeld surface are summarized in Fig. 7.
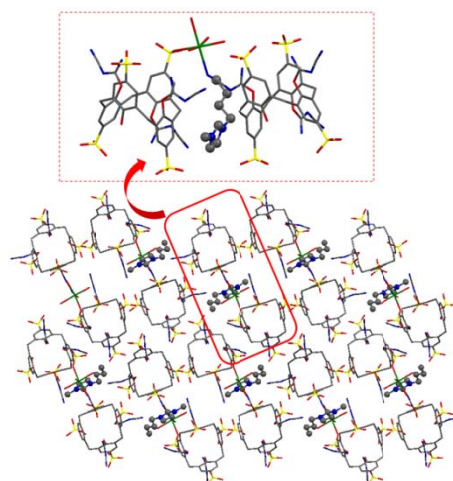

Fig. 6. *n*-Butylimidazolium molecule (represented in ball and stick) positioned *exo*-cavity to the calixarene in the overall structure.
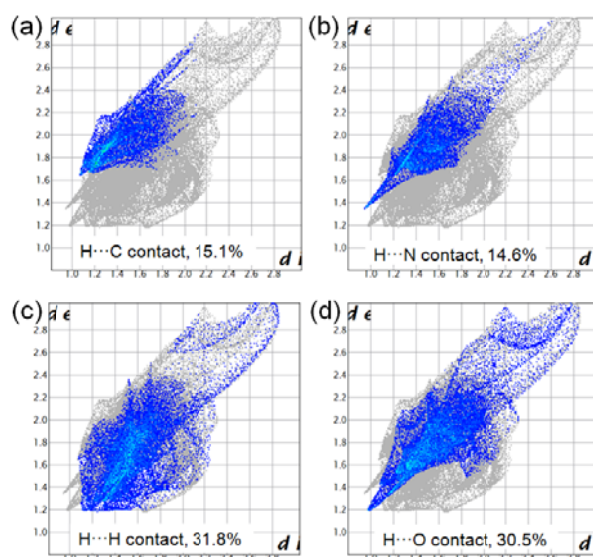

Fig. 7. Fingerprint plots for *n*-butylimidazolium in compound **1** showing (a) C–H···π(centroid); (b) C–H···N; (c) C–H···H–C and; (d) H···O–S interactions.

Conclusions

We have established a new building block for crystal engineering, based on a covalently modified *p*-sulfonatocalix[4]arene, which adopts an 1,3-alternate rather than the ubiquitous cone conformation for the parent compound. The condensation reaction of the parent compound with dicyanamide in affording N'-cyanocarbamimidate groups is without precedence, with the selectivity of condensation to three rather than all of the four phenolic positions presumably arising from steric limitations in generating the bulky moieties. Also noteworthy, is that each of the divergent cavities of the calixarenes contains water molecules rather than charged

imidazolium head group, as would otherwise be expected on electrostatic grounds, and is also presumably a size effect.

Experimental

Synthesis of **1**: The sodium salt of *p*-sulfonatocalix[4]arene was synthesized according to literature procedures.[23] 1-Methyl-3-butylimidazolium dicyanamide and gadolinium(III) chloride were purchased from Sigma Aldrich and were used without purification. Compound **1** was crystallized from a hot solution of *p*-sulfonatocalix[4]arene sodium salt (0.020 M) with excess of 1-methyl-3-butylimidazolium dicyanamide (0.030 M) and gadolinium(III) chloride in de-ionized water (0.060 M), followed by concentration by slow evaporation from water at room temperature. Crystals formed over several days and the homogeneity of the materials was checked from the X-ray diffraction determination of cell dimensions. Hirshfeld surface analysis and corresponding fingerprint plot was generated from the CrystalExplorer.[22] All calculations were performed with GAUSSIAN 09W Version 9.0 software package.

§ *X-Ray Crystallography*:

Data were measured at $T = 100(2)$K from a single crystal using an Oxford Diffraction Xcalibur-S diffractometer equipped with CCD detector using monochromatic MoKα radiation ($\lambda = 0.71073$ Å). The images were interpreted and integrated with the program CrysAlisPRO, Oxford Diffraction Ltd. The structure was solved by direct methods and refined by full-matrix least-squares on F^2 using the SHELXL-97[24] and X-seed[25] interface crystallographic package. Lp and absorption corrections applied.

Compound 1: $8(C_{34}H_{23}N_9O_{16}S_4^{4-})$, $4(C_8H_{15}N_2^+)$, $7(Gd^{3+})$, $7(Na^+)$, $126(H_2O)$, $C_{304}H_{496}N_{80}Na_7O_{254}S_{32}Gd_7$, $M = 11623.41$, colourless needle, 0.18 x 0.09 x 0.08 mm^3, monoclinic, space group $C2/m$ (No. 12), $a = 39.799(2)$, $b = 31.5266(9)$, $c = 22.9740(11)$ Å, $\beta = 117.023(6)$ $V = 25679(2)$ Å^3, $Z = 2$, $D_c = 1.503$ g/cm^3, $m = 1.13$ mm^{-1}. $F_{000} = 11898$, $2q_{max} = 57.2°$, 100592 reflections collected, 31123 unique ($R_{int} = 0.1131$). Final $GooF = 1.177$, $R1 = 0.1418$, $wR2 = 0.2832$, R indices based on 16365 reflections with $I > 2s(I)$ (refinement on F^2), $|Dr_{max}| = 3.4(2)$ e Å^{-3}, 1798 parameters, 692 restraints. CCDC number = 952812.

Most of the calixarene sulfonate groups were modelled as being disordered over two sets of sites at fixed occupancies parameters and their complements, obtained after trial refinement. Geometries of the disordered components were restrained to ideal values. The aquatic metal cations are distributed inside of the hydrophilic dynamic area of the crystal structure. Some of them, but not all, were interpreted as partially occupied and disordered with impossibility to identify their proper coordination environment (see discussion above). The hydrogen ions (presumably as hydronium ions), required for charge balance could not be located. Electron density that could not be reasonably modelled as such was effectively removed by use of the program Squeeze.[26] Water molecule hydrogen atoms were not located. All remaining H-atoms were added at calculated positions and refined by use of a riding model with isotropic displacement parameters based on those of the parent atom. Anisotropic displacement parameters were employed for the non-hydrogen ordered atoms.

Notes and references

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† Footnotes should appear here. These might include comments relevant to but not central to the matter under discussion, limited experimental and spectral data, and crystallographic data.

Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

1 C. D. Gutsche, Calixarenes An Introduction 2nd Edition, United Kingdom: RSC Publishing, 2008.
2 J. W. Cornforth, P. D'Arcy Hart, G. A. Nicholls, R. J. W. Rees and J. A. Stock, *Br. J. Pharmacol.* 1955, **10**, 73-86.
3 C. D., Gutsche, B., Dhawan, J. A., Levine, K. H. No and L.Bauer, *Tetrahedron*, 1983, **39**, 409-426.
4 S., Shinkai, T., Usubaki, T. Sone and O. Manabe, *Tetrahedron Lett.*, 1985, **26**, 3343-3344.
5 C. D. Gutsche, Calixarenes, Monographs in Supramolecular Chemistry, J. Frase Stoddart Series Ed. London: The Royal Society of Chemistry, 1989.
6 D. Diamond and K. Nolan, *Anal. Chem.*, 2001, **73**, 22A-29A.
7 R. Ludwig, *Fresenius' J. Anal. Chem.* 2000, **367**, 103-128.
8 M. J. Hardie and C. L. Raston, *J. Chem. Soc., Dalton Trans.*, 2000, 2483-2492.
9 A. Drljaca, M. J., Hardie, J. Johnson, C. L. Raston and H. R.Webb, *Chem. Commun.*, 1999, **12**, 1135-1136.
10 G. W. Orr, L. J. Barbour and J. L. Atwood, *Science*, 1999, **285**, 1049-1052.
11 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**, 13170-13171.
12 A. W. Coleman, S. G. Bott, S. D. Morley, C. M. Means, K. D. Robinson, H. Zhang and J. L. Atwood, *Angew. Chem. Int. Ed.* 1988, **27**, 1361-1362.
13 I. Ling, Y. Alias and C. L. Raston, *New J. Chem.*, 2010, **34**, 1802–1811.
14 L. J. Barbour and J. L. Atwood, *Chem. Commun.*, 2001, 2020–2021.
15 S.A. Forsyth, D. R. MacFarlane, R. J. Thomson and M. von. Itzstein *Chem. Commun.*, 2002, 714-715.
16 I. Ling, Y. Alias, A. N. Sobolev and C. L. Raston, *CrystEngComm*, 2010, **12**, 1869–1875.
17 B. Pulpoka, V. Ruangpornvisuti, Z. Asfari and J. Vicens, Cyclophane Chemistry for the 21st Century (H. Takemura Ed.), Research Signpost, Trivandrum, 2002.

18 S. Shinkai, K. Iwamoto, K. Araki and T. Matsuda, *Chem. Lett*., 1990, 1263-1266.

19 E. Kelderman, L. Derhaeg, G. J. T. Heesnik, W. Verboom, J. F. J. Engbersenm, N. F. van Hulst, A. Persoons and D.N. Reinhoudt, *Angew. Chem., Int. Ed. Engl.* 1992, **31**, 1075-1077.

20 J. de Mendoza, P. Prados, N. Campillo, P. M. Nieto, C. Sánchez, J.-P. Fayet, M. C. Vertut, C. Jaime and J. Elguero, *Rec. Trav. Chim. Pays-Bas*, 1993, **112**, 367-369.

21 B. Pulpoka and J. Vicens, *J. Nano and Bio Tech*, 2004, **1**, 55-72.

22 S. K. Wolff, D. J. Grimwood, J. J. McKinnon, M. J. Turner, D. Jayatilaka and M. A. Spackman, University of Western Australia, Perth, 2013; http://hirshfeldsurface.net

23 M. Makha and C. L. Raston, *Tet. Lett.,* 2001, **42**, 6215-6217.

24 G. M. Sheldrick, *Acta Cryst*., 2008, **A64**, 112–122.

25 L. J. Barbour, *J. Supramol. Chem*., 2001, **1**, 189.

26 A. L. Spek, *J. Appl. Cryst.,* 2003, **36**, 7-13.