Successive Inclusion of Water, $[H_3NCH_2CH_2NH_3]^{2+}$ and $[H_3NCH_2CH_2NH_2]^+$ in the Aromatic Cavity of (*p*-Sulfonato)calix[4]arene

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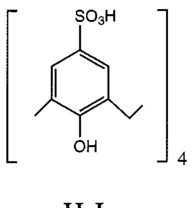
Titration of the sulfonic protons of (*p*-sulfonato)calix[4]arene (H_8L) with two equivalents of ethylenediamine affords $[H_3NCH_2CH_2NH_3]_2[H_4L(H_2O)_3]\cdot H_2O$, a molecular complex in which water is included inside the macrocycle. Deprotonation of one of the phenolic groups expels the water molecules from the aromatic cavity, leading to the formation of $[H_3NCH_2CH_2NH_3]_{1.5}[(H_3L)(H_3NCH_2CH_2NH_3)]\cdot(H_2O)_{5.5}$, which represents an unprecedented example of the inclusion of a dication in a calixarene. Further addition of ethylenediamine affords the mixed salt $[H_3NCH_2CH_2NH_3]_2[(H_3L)(H_3NCH_2CH_2NH_2)]\cdot(H_2O)_{4.5}$ in which the monocation $[H_3NCH_2CH_2NH_2]^+$ is preferentially bound to the cavity through a non-classical hydrogen bond involving an N–H···π facial aromatic contact. Inclusion phenomena are indicated both by NMR and X-ray structure determinations. In the same way as their inorganic–organic counterparts, these clay-like materials are organised into parallel organic–organic layers.

Introduction

The π-electron-rich cavity of the water-soluble (*p*-sulfonato)calix[4]arene (H_8L) represents a model system for the study of the interaction of species such as water or cations with aromatic moieties that are encountered in many recognition processes in both biology and chemistry.[1] Much research work has already been devoted to molecular complexes where an organic cation is present within such a cavity.[2] The pH dependence of this inclusion phenomenon has been interpreted in terms of electrostatic interactions in neutral solution or hydrophobic repulsion in acidic solutions.[3]



H_8L

In the absence of hydrophobic guests, the presence of water inside $[H_4L]^{4-}$ has in one case been revealed by X-ray crystallography.[4] Aromatic π-hydrogen bonding between the guest and the host clearly helps to stabilize this molecular complex. Although to date there has been no other example of such inclusion of water into a calixarene, another kind of non-classical hydrogen bonding has been observed in the form of C−H···π aromatic contacts in the molecular compounds of *o*-$C_2B_{10}H_{12}$ in CTV[5] and calix[5]arene,[6] and of CH_2Cl_2 in $[HNMe_3]_2[(t\text{Bu-calix[4]arene})Al_2]$.[7]

Another interesting feature of H_8L derivatives in the solid state is their very well ordered layer structure, which often earned them the name of organic clays. However, all examples in the literature involve either metals or NH_3^+ as counterions and there has not yet been a report of an organic−organic clay-like structure.[2a,3,4,8]

In an effort to study the possible influence of the bridging of these layers with an organic dication, we set out to study the organic salts produced by the reactions of H_8L with ethylenediamine. We report here the synthesis in the presence of possible organic guests of $[H_3NCH_2CH_2NH_3]_2[H_4L(H_2O)_3]\cdot H_2O$, a molecular compound of $[H_4L]^{4-}$ and water. Water is expelled from the cavity by the deprotonation of one of the phenolic oxygen atoms of the macrocycle and replaced by $[H_3NCH_2CH_2NH_3]^{2+}$ to form $[H_3NCH_2CH_2NH_3]_{1.5}[(H_3L)(H_3NCH_2CH_2NH_3)]\cdot(H_2O)_{5.5}$. Addition of excess ethylenediamine affords the mixed organic salt $[H_3NCH_2CH_2NH_3]_2[(H_3L)(H_3NCH_2CH_2NH_2)]\cdot(H_2O)_{4.5}$, where the monocation $[H_3NCH_2CH_2NH_2]^+$ is included in the calixarene cavity through N−H···π aromatic contacts. NMR studies show that these inclusion phenomena persist in solution. Crystal structures of the molecular complexes have been determined, including the first of a dication and the first of a non-classical N−H···π aromatic hydrogen bond in the cavity of a calixarene. The organic layers observed in the solid state are bridged by hydrogen bonds at both ends of the organic dication, resulting in a new class of organic−organic clays.

Results and Discussion

Treatment of H_8L with two equivalents of ethylenediamine in water led to the precipitation of the organic ethylenediammonium salt in the form of a white solid.

$$H_8L + 2\ H_2NCH_2CH_2NH_2 \xrightarrow{H_2O} [H_3NCH_2CH_2NH_3]_2[(H_4L)(H_2O)_3]$$

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The molecular structure of the crystalline compound revealed the exact formula of this salt to be $[H_3NCH_2CH_2NH_3]_2[H_4L(H_2O)_3]\cdot H_2O$ (**1**) and showed the presence of water molecules inside the calixarene (Figure 1).

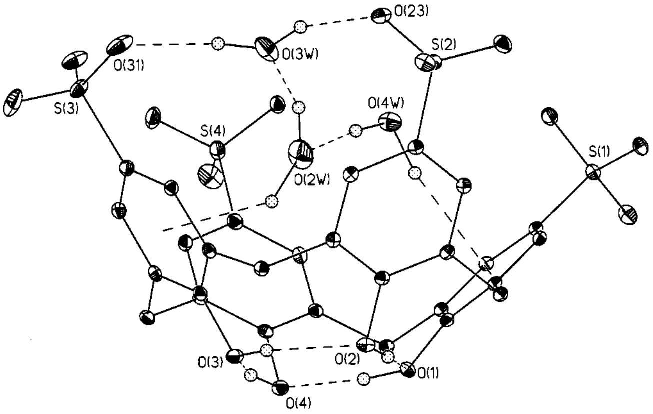

Figure 1. View of compound **1** showing partial atom labelling; molecules of water and of ethylenediammonium present in the lattice, as well as hydrogen atoms not involved in hydrogen bonding, have been omitted for clarity

If the oxygen atoms of the sulfonate groups that point toward the interior of the macrocycle are considered as the lips of the calixarene and the plane they define as the limit of the cavity, all three water molecules can be considered as being included in the calixarene. The O−plane distances amount to 0.207(3), 0.700(3) and 1.796(4) Å for O(3w), O(4w) and O(2w), respectively. O(2w), the oxygen atom of the deepest embedded water molecule, is positioned slightly to the side of the aromatic cavity, close to the phenolic ring bearing S(3) {distances to the centroids of the aromatic faces bearing S(1), S(2), S(3) and S(4) [which will be called X(I), X(II), X(III) and X(IV)] amount to 4.603(5), 3.627(4), 3.298(4) and 3.997(5) Å, respectively}. This water molecule is held in position by hydrogen bonds (Table 1). It accepts an H-bond from the second deepest water molecule of O(4w) and acts as a twofold H-bond donor to the centroid X(III) and to O(3w). The environment about O(2w), formed by three H atoms, is almost perfectly planar (standard deviation ± 0.001 Å). The water molecule of O(4w) also forms an H-bond to the opposite phenolic face. Although weaker than the previous one [the O(4w)−X(I) distance measures 3.524(4) Å], it is undoubtedly present as the H atom points towards the centre of the phenolic face [O(4w)−H−X(I) = 153.5°]. The least deeply embedded water molecule of O(3w) is also connected to the calixarene, but through more classical hydrogen-bond donation to the oxygen atoms of two adjacent sulfonate groups [O(31) and O(23)]. As observed for $Na_4[(H_4L)(H_2O)]\cdot(H_2O)_{12.5}$,[4] the aromatic π-hydrogen bonding in **1** seems to be of paramount importance for the stabilization of the guest inside the host. However, in the case of ref.[4], only one water molecule interacted with the calixarene through the donation of hydrogen bonds to two opposite phenolic faces of the macrocycle. The oxygen-to-centroid distances were 3.16 and 3.19 Å, shorter than the 3.298(4) and 3.524(4) Å found here for O(2w) and O(4w). On the other hand, H-to-centroid distances are of the same order of magnitude at 2.38 and 2.50 Å, compared to 2.390 and 2.496 Å in **1**. The way in which water molecules can organize into clusters in hydrophobic cavities is a matter of importance in biochemistry.[9] In compound **1**, the three water molecules interact with their receptor through the donation of H-bonds.

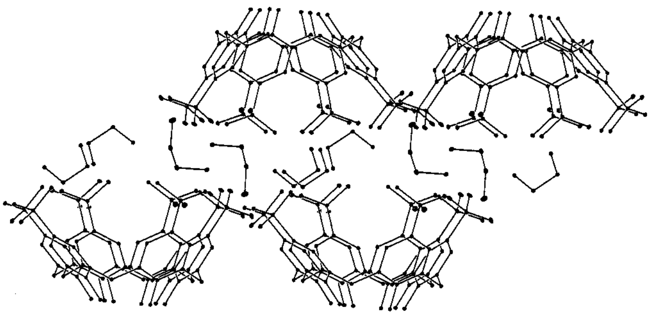

Figure 2. View of the extended structure of **1**; water molecules and hydrogen atoms have been omitted for clarity

Table 1. Selected hydrogen bond lengths [Å] and angles [°] in **1**

Donor	Acceptor	D−H	H···A	D−A	D−H···A
O(2w)	O(3w)	1.101	1.666	2.721(3)	158.7
O(2w)	X(III)	1.104	2.390	3.298(4)	138.5
O(3w)	O(31)	1.015	1.908	2.899(3)	164.8
O(3w)	O(23)	1.042	1.808	2.793(3)	156.1
O(4w)	O(2w)	0.990	1.783	2.724(3)	173.7
O(4w)	X(I)	1.109	2.496	3.524(4)	153.5
O(1)	O(4)	0.897	1.797	2.679(3)	167.5
O(2)	O(1)	0.824	1.866	2.647(3)	157.8
O(3)	O(2)	0.832	1.946	2.687(3)	147.8
O(4)	O(3)	1.084	1.742	2.780(3)	158.6

The extended structure of **1** is composed of layers of calixarene molecules bridged by hydrogen bonds through the dication, which is found to be in the *syn* conformation [N−C−C−N torsion angle equal to 76.5(2) and 72.7(2)°] (Figure 2). Thus, it is the first compound of this class to be composed of parallel organic layers as all the other reported examples contain either metals or NH_4^+ as counterions.[2a,3,4,8] The width of this organic layer is 8.62(1) Å and the repeat distance is 14.31(1) Å, both slightly larger than the values reported previously for their inorganic counterparts.

Remarkably, water is bound inside the aromatic cavity of the calixarene even though ethylenediammonium is also available in solution. Such inclusion in the presence of a potential organic guest has not previously been observed and was considered unlikely. Atwood et al. insisted on the fact that the water inclusion compound $Na_4[(H_4L)(H_2O)]\cdot(H_2O)_{12.5}$[4] was synthesized in the absence of any possible hydrophobic guests. Moreover, Shinkai et al. found that the aromatic nucleus of the trimethylanilinium cation was preferentially inserted into the calixarene at low pH because of hydrophobic effects.

In order to detect possible inclusion phenomena of the organic guests in the liquid phase, we decided to make use of soft 1D NMR experiments with pulsed field gradient encoding. The sequence is based on the GOESY[10] one, but with slight modifications. The experiments were set up in order to observe magnetization transfer from the aromatic protons of the host to potential guests (Figure 3). Noteworthy is the lack of any through-space interaction with the water protons in spectrum 1′. This is easily explained by the fact that very few HDO molecules are present in solution, the majority being D_2O. The quantity of HDO potentially interacting with the cavity is therefore negligible. No dipolar interaction between the aromatic protons and the methylenic protons of the calixarene could be observed because of the broadening of their signals due to coalescence. However, the absence of dipolar interactions between the aromatic protons of the calixarene and the methylenic protons of the ethylenediammonium dication, as observed in spectrum 1′, can only be interpreted in terms of a lack of through-space interaction between the dication and the macrocycle, confirming that it is kept outside of the cavity in the solution.

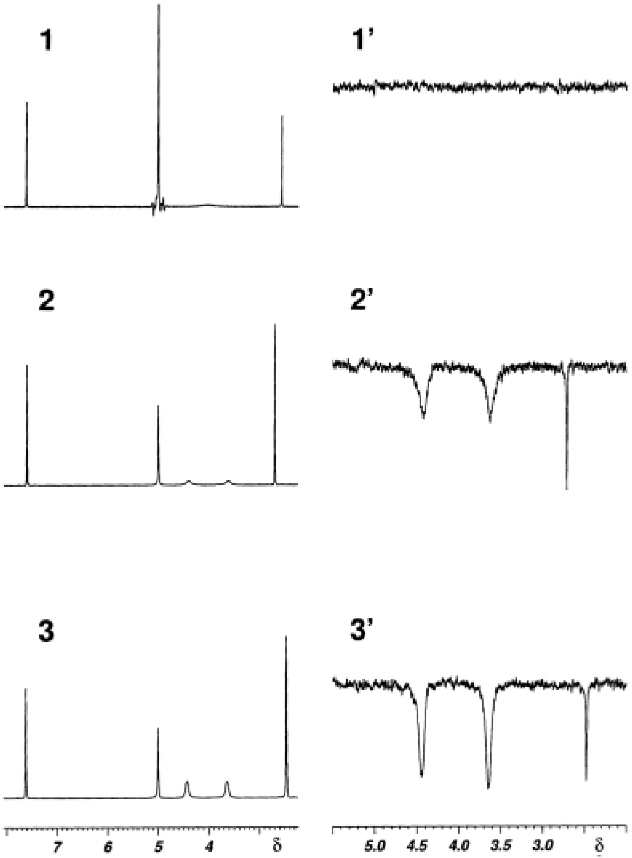

Figure 3. ^{1}H-NMR spectra of **1**, **2** and **3**; 1′, 2′ and 3′ depict enlargements of the δ = 5.5−2.0 region of the soft ROESY subspectra

As a charged species such as $[H_3NCH_2CH_2NH_3]^{2+}$ may not be considered as being very hydrophobic, the synthesis of **1** was repeated in the presence of excess phenol and propan-1-ol. No evidence for the formation of any compound other than **1** could be found, either by NMR or by recrystallization experiments. This points to the fact that the formation of the water inclusion compound is rather favoured, at least among these three guests. Furthermore, elemental analysis of dried **1** confirmed the presence of the three water molecules, indicating that the molecular compound is rather stable. This result is somehow contradictory to the accepted idea that water clusters provide little hindrance to the entry of non-polar ligands into the aromatic cavities of biological systems.[11]

If 2.5 equivalents of ethylenediamine are added to H_8L or a further half-equivalent of ethylenediamine is added to **1**, one phenolic moiety of the calixarene core is deprotonated, leading to the formation of a pale-yellow solution of the organic salt.

$$H_8L + 2.5\ H_2NCH_2CH_2NH_2 \xrightarrow{H_2O} [H_3NCH_2CH_2NH_3]_{1.5}[(H_3L)(H_3NCH_2CH_2NH_3)]$$

$[H_3NCH_2CH_2NH_3]_{1.5}[(H_3L)(H_3NCH_2CH_2NH_3)]\cdot(H_2O)_{5.5}$ (**2**) could be isolated in its monocrystalline form. The molecular structure of crystalline **2** reveals that the included water molecules present in **1** have been expelled from the aromatic cavity, leaving it available for the ethylenediammonium dication (Figure 4), which we believe to be the first dication to be included in a calixarene.

The crystal structure contains two independent molecules that differ from one another in the way that the guest resides in the cavity. In molecule **2a**, the ethylenediammonium cation is positioned to the side of the cavity, forming hydrogen bonds with two oxygen atoms of two adjacent sulfonate groups [O(41) and O(13)] (Figure 4a). Conversely, in molecule **2b**, it is hydrogen-bonded across the cavity to all four sulfonate groups (Figure 4b). Both incorporated ethylenediammonium dications are stabilized in their respective positions by the donation of six hydrogen bonds, either to sulfonate groups or to solvated water molecules (Table 2). They adopt a *syn* conformation [N−C−C−N torsion angles of 64.4(2)° and 72.4(2)° for **2a** and **2b**, respectively], as opposed to the molecules outside the cavity that are in the *anti* conformation [mean N−C−C−N torsion angle equal to 177.1(3)°]. Interestingly, the ethylenediammonium dication included in **2a** forms a hydrogen bond with **2b** through O(73). In fact, **2a** is also bound to **2b** through three water molecules [O(2w), O(3w) and O(4w)] (Figure 4c). This hydrogen-bond network brings the packed calixarene layers towards each other such that the width of the organic layer is just 6.94(1) Å, the shortest ever found for a (*p*-sulfonato)calix[4]arene clay-like material.[2a,3,4,8] Thus, the dication, which could have been seen as a potential spacer between the layers, produces exactly the opposite effect! The repeat distance between the layers is found to be 12.69(1) Å, which is more classical.

The deprotonation of the phenolic oxygen atom in **2** is evidenced by both the stoichiometry (one calixarene for 2.5 ethylenediammonium cations) and the hydrogen bond lengths between the phenolic groups. Two strong hydrogen bonds are classically donated to oxygen atoms of the anionic phenolate group, O(3) in **2a** and O(8) in **2b**, leaving no hydrogen atom left for bonding O(1) to O(4) and O(5) to O(6) [3.034(4) and 3.041(4) Å, respectively]. This negative charge at the lower rim of the calixarene is probably

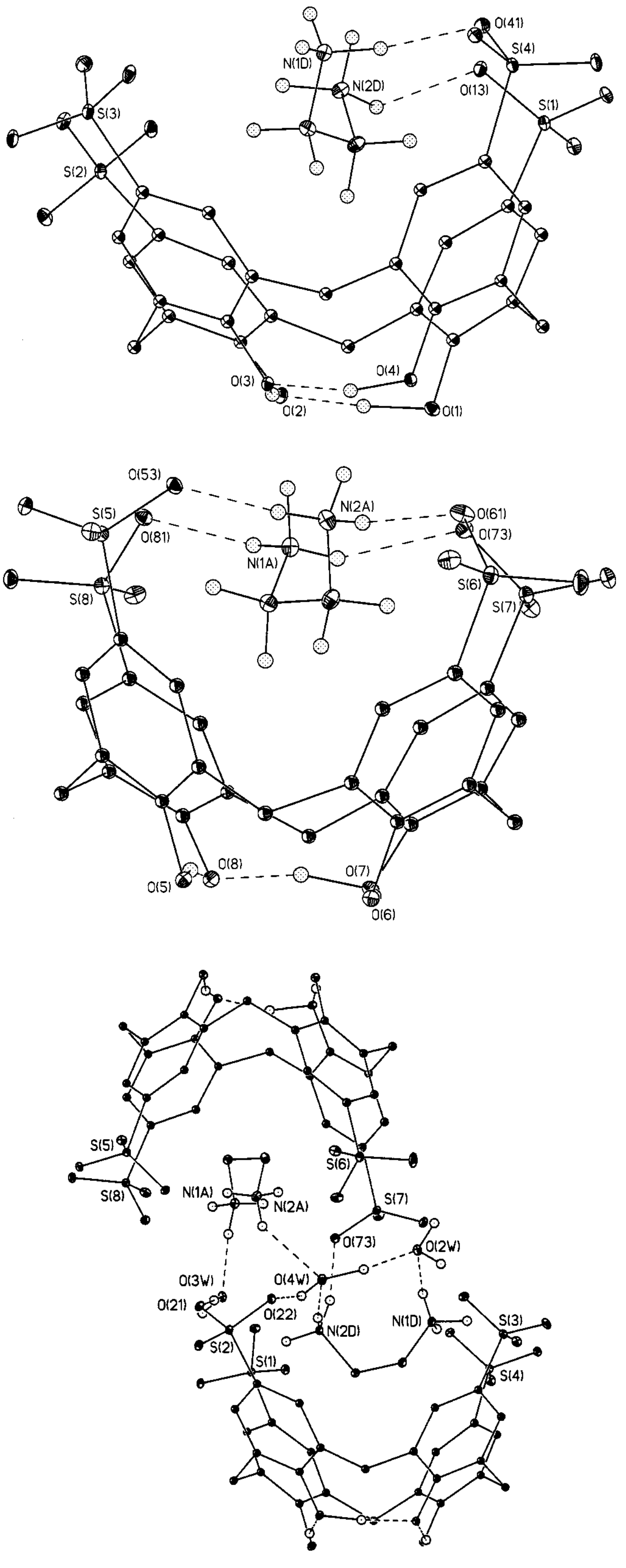

Figure 4. Crystal structure of compound **2** showing partial atom labelling; molecules of water and of ethylenediammonium present in the lattice, as well as hydrogen atoms not involved in hydrogen bonding, have been omitted for clarity; (a) view of the molecule **2a** (top), (b) view of the molecule **2b** (middle), (c) view of the hydrogen-bonded dimer of molecules **2a** and **2b** (bottom)

Table 2. Selected hydrogen bond lengths [Å] and angles [°] in **2**

Molecule **2a**					
Donor	Acceptor	D−H	H···A	D−A	D−H···A
N(1D)	O(41)	1.000	1.855	2.847(4)	171.4
N(1D)	O(1w)	1.017	1.731	2.709(4)	160.3
N(1D)	O(2w)	0.794	2.272	2.809(4)	125.6
N(2D)	O(13)	1.085	2.135	2.823(4)	136.9
N(2D)	O(73)	0.995	1.836	2.773(4)	166.5
N(2D)	O(4w)	1.016	1.793	2.780(4)	162.8
O(1)	O(2)	1.206	1.463	2.650(3)	166.4
O(2)	O(3)	1.136	1.461	2.591(3)	172.3
O(4)	O(3)	1.075	1.481	2.508(3)	157.5
Molecule **2b**					
Donor	Acceptor	D−H	H···A	D−A	D−H···A
N(1A)	O(73)	0.820	2.207	2.971(4)	155.4
N(1A)	O(81)	0.875	2.029	2.859(4)	157.9
N(1A)	O(3w)	0.978	1.754	2.706(4)	163.3
N(2A)	O(53)	0.879	1.941	2.817(4)	174.7
N(2A)	O(61)	0.908	1.925	2.799(4)	161.1
N(2A)	O(4w)	0.822	2.160	2.859(4)	143.0
O(5)	O(8)	1.158	1.354	2.487(3)	163.7
O(6)	O(7)	1.139	1.491	2.628(3)	174.9
O(7)	O(8)	1.198	1.426	2.551(3)	153.0

the cause of a change in polarity of the cavity, attracting the dication inside the host by electrostatic forces. Evidence that the structure of this new kind of molecular compound is retained in solution was provided by NMR studies (Figure 3). Spectrum 2′ unequivocally shows dipolar interactions between the aromatic protons of the calixarene core and the methylenic protons of the ethylenediammonium dication, confirming the presence of the dication in the cavity.

If one equivalent of nitric acid is added to **2**, the organic dication is in turn expelled from the calixarene and **1** is easily regenerated, demonstrating the reversibility of the inclusion phenomenon and providing an even easier synthetic route to **1**.

If 3 equivalents of ethylenediamine are added to H_8L or a further half-equivalent of ethylenediamine is added to **2**, the phenolic protons of the calixarene are not further deprotonated. The addition of excess ethylenediamine leads to a proton exchange reaction between the diamine and the diammonium dication and therefore to the formation of the monocation $[H_3NCH_2CH_2NH_2]^+$ which can compete with the dication for inclusion inside the cavity.

$$H_8L + 3\ H_2NCH_2CH_2NH_2 \xrightarrow{H_2O} [H_3NCH_2CH_2NH_3]_2[(H_3L)(H_3NCH_2CH_2NH_2)]$$

The resulting mixed salt could be obtained in monocrystalline form and characterized by X-ray crystallography. The crystal structure reveals the exact stoichiometry of the compound to be $[H_3NCH_2CH_2NH_3]_2[(H_3L)(H_3NCH_2CH_2NH_2)]\cdot(H_2O)_{4.5}$ (**3**) and shows that it is the monocation $[H_3NCH_2CH_2NH_2]^+$ that is selectively included in the cavity. Four independent calixarene molecules are present in the lattice, in each of which the cation is bound in the same fashion (Figure 5). The $-NH_3^+$ end of the cation points towards the exterior of the calixarene aromatic cavity, forming strong H-bonds with oxygen atoms of either water molecules or sulfonate groups, while the other $-NH_2$ end is embedded in the cavity and interacts with the calixarene core through a π interaction. Each $-NH_2$ group bears one hydrogen atom, which is unequivocally directed towards the centroid of the aromatic ring (Table 3). This interaction can be described as a weak, non-classical N−H···π hydrogen bond. N···centroid distances range from 3.449(4) to 3.603(4) Å and H···centroid contacts from 2.599 to 2.881 Å. Amine interactions with aromatic faces are a matter of importance in the folding and recognition of biological polymers.[12] N−H···π facial hydrogen bonds have been reported in the crystal structure of human haemoglobin[13] (N···C distances 3.6 Å) and in a molecular compound of a macrocyclic tetraamide in chloroform (N···centroid distances 3.58 and 3.85 Å).[14] The $\Delta G°$ value of the latter was determined as -4.5 kJmol^{-1}.[15] After C and O, to the best of our knowledge, N is only the third element that has been proved to be capable of such donation. N···centroid distances in **3** are relatively short in comparison to the O···centroid distances, which have been found to measure 3.238(4) Å in **1** and 3.16 Å in $Na_4[H_4L(H_2O)]\cdot(H_2O)_{12.5}$,[4] but compare well with those in its carbon counterparts, where values of 3.299−3.503, 3.44−3.55, and 3.54 Å have been reported for $[(CTV)_2(o\text{-}C_2B_{10}H_{12})]$,[6] $[(calix[5]arene)(o\text{-}C_2B_{10}H_{12})]$,[5] and $[HNMe_3]_2[(t\text{Bu-calix[4]arene})_2Al_2(CH_2Cl_2)]$,[7] respectively. The H···centroid distances in **3** are somewhat longer than those in $[(t\text{Bu-calix[4]arene})Al_2]^{2-}$ and $[(CTV)_2(o\text{-}C_2B_{10}H_{12})]$, which were measured as 2.46 and 2.184−2.556 Å, respectively. **3** features the first example of an N−H···π contact in a calixarene[16] and represents a unique example of such bonding involving a charged species.

Table 3. Selected hydrogen bond lengths [Å] and angles [°] in **3**

	N−H	H···centroid	N−centroid	N−H···centroid
Molecule 1	0.984	2.599	3.539(4)	174.4
Molecule 2	1.041	2.672	3.603(4)	148.8
Molecule 3	0.959	2.634	3.473(4)	146.4
Molecule 4	0.996	2.881	3.449(4)	116.9

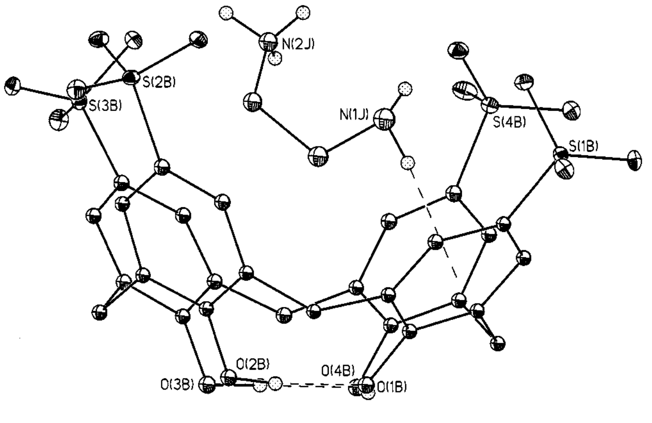

Figure 5. View of the crystal structure of compound **3** showing partial atom labelling; molecules of water and of ethylenediammonium present in the lattice, as well as hydrogen atoms not involved in hydrogen bonding, have been omitted for clarity

The soft ROESY spectrum of **3** (Figure 3) shows an interaction between the calixarene and an ammonium salt, although it is not possible to distinguish between the mono- and the dication. Interestingly, the negative peak for the methylenic protons of the calixarene core at $\delta = 3.63$ is more intense than that at $\delta = 4.43$, indicating that the two corresponding positions are not equivalent in their response to magnetization transfer (Figure 3, spectrum 3′). This behavior is also observed to a small extent for compound **2** (Figure 3, spectrum 2′). It is explained by the fact that the peak furthest downfield is due to the proton closest to the aromatic protons, and hence through-space magnetization yield is made more efficient by this proximity.

$[H_3NCH_2CH_2NH_3]^{2+}$ dications bridge the calixarene layers in the lattice and $[H_3NCH_2CH_2NH_2]^+$ cations form dimers in the same fashion as in **2**. The widths of the organic and repeat layers in **3** amount to 7.35(1) Å and 12.98(1) Å, respectively, and are thus larger than those in **2**. Hence the structure of this organic−organic clay-like material does seem to depend on the number of organic molecules included in the packing.

The successive appearance of **1**, **2** and **3** upon addition of ethylenediamine to H_8L constitutes an exceptional example of the versatility of inclusion phenomena that can take place within the aromatic cavity of water-soluble (*p*-sulfonato)calix[4]arene. This work has added the first dication to the list of molecular guests in calixarenes. The dramatic changes in the binding ability of the macrocycle can be efficiently tuned by simple titration of its acidic protons. Non-classical hydrogen bonding with π-facial aromatic contacts participate in stabilizing the molecular complexes **1** and **3**. Work is currently in progress aimed at using these results in the construction of new organic materials and the assembly of complex structures

Experimental Section

General: All NMR spectra were recorded with a Bruker DRX-500 spectrometer at 282 K and 11.7 T. The experimental conditions were the same for all samples; 10 mg of pure crystals of **1**, **2** and **3** were dissolved in 0.4 mL of D_2O. The pD values of the respective solutions were measured as 3.4, 5.2 and 7.3, respectively. − Elemental analyses were performed at the Service de Microanalyse, CNRS, F-91191 Gif-sur-Yvette, France and at the Analytische Laboratorien, D-51789 Lindlar, Germany. − Copies of the crystallographic data of **1**, **2** and **3** can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Synthesis and Recrystallization Experiments

Synthesis of 1: H_8L (0.300 g, 0.4 mmol) was treated with ethylenediamine (0.048 g, 0.054 mL, 0.8 mmol) in water (20 mL) for 15 min at 323 K. The white precipitate of **1** thus formed was then filtered off, washed with water, and dried in vacuo for 24 h to afford $[H_3NCH_2CH_2NH_3]_2[H_4L]\cdot 3H_2O$ (0.334 g, 0.36 mmol, 91%). − ^1H NMR: $\delta = 2.57$ (8 H, C−CH_2−N), 4.02 [br., Full Width at Half Maximum (FWHM) = 280 Hz, 8 H, Ar−CH_2−Ar], 7.62 (8 H, ArH). − $C_{32}H_{46}N_4O_{19}S_4$ (918): calcd. C 41.83, H 5.01, N 6.10; found C 41.85, H 4.92, N 6.06. − Another convenient route to **1** is the addition of HNO_3 (0.1 mol·L^{-1} solution in water) to a solution of **2**. The white powder obtained is then simply filtered off and washed with water (95% yield).

Synthesis of 2: H_8L (0.300 g, 0.4 mmol) was treated with ethylenediamine (0.060 g, 0.067 mL, 1 mmol) in water (20 mL) for 15 min at 353 K. The yellow suspension of **2** thus formed was filtered and the collected solid was dried in vacuo. The pale-yellow powder obtained was then recrystallized from water (5 mL) by leaving the solution overnight and then dried in vacuo to afford $[H_3NCH_2CH_2NH_3]_5[H_3L]_2 \cdot H_2O$ (0.307 g, 0.17 mmol, 85%). − ^1H NMR: δ = 2.70 (10 H, C−C*H*$_2$−N), 4.61 and 4.40 (br. FWHM = 55 Hz, 2 × 4 H, Ar−C*H*$_2$−Ar), 7.60 (8 H, Ar*H*). − $C_{66}H_{90}N_{10}O_{33}S_8$ (1806): calcd. C 43.85, H 4.98, N 7.75; found C 43.85, H 5.21, N 7.61.

Synthesis of 3: H_8L (0.300 g, 0.4 mmol) was treated with ethylenediamine (0.072 g, 0.080 mL, 1.2 mmol) in water (20 mL) for 15 min at 353 K. The yellow suspension of **3** thus formed was filtered and the collected solid was dried in vacuo. The pale yellow powder obtained was then recrystallized from water (5 mL) by leaving the solution overnight and dried in vacuo to afford $[H_3NCH_2CH_2NH_2][H_3NCH_2CH_2NH_3]_2[H_3L]$ (0.305 g, 0.33 mmol, 82%). − ^1H NMR: δ = 2.47 (12 H, C−C*H*$_2$−N), 3.63 and 4.43 (br., FWHM = 33 Hz, 2 × 4 H, Ar−C*H*$_2$−Ar), 7.62 (8 H, Ar*H*). − $C_{34}H_{48}N_6O_{16}S_4$ (924): calcd. C 44.15, H 5.19, N 9.01; found C 44.46, H 5.76, N 9.47.

Recrystallization: Compounds **1**, **2** and **3** were submitted to recrystallization experiments in the presence of a twofold excess of *n*-propanol or phenol in water. No inclusion complex other than **1** and **2** could be detected either by NMR or by cell measurements of the crystals obtained. The recovered yields of the recrystallizations were quantitative.

NMR Studies: In the 1D soft ROESY experiments, the first 90° hard pulse is replaced by a soft excitation of the source signal and the mixing time incorporates an off-resonance spin-lock r.f. field, ensuring magnetization transfer in the case of through-space interactions and a distinction between exchange cross-peaks and dipolar ones by virtue of their signs. The advantage of this sequence is that the signals of the protons not involved in the interaction do not need to be suppressed by phase cycling, i.e. by obtaining a difference between two sub-spectra. Gradient encoding removes the magnetization that does not follow the adequate coherence transfer pathway in each scan and is a priori artefact-free. The first two pulses selectively excite and invert the aromatic signal (Figure 6). The first one is a Gaussian of 2 ms duration, the second one a Q3 Gaussian[17] cascade of 4 ms. The thin black rectangles represent 90° hard pulses, the larger one a 180° hard pulse. The spin-lock field is trapezium-shaped in order to allow adiabatic rotation of the magnetization at the beginning and at the end of the irradiation.[18] Its strength is 10 kHz and its frequency is shifted by 8 kHz from the centre to give an angle between the effective field axis and the static axis of 54.7°. Spin-lock duration is 100 ms. The values of the gradients are: $G1$ = 10 G·cm^{-1}, $G2$ = 40 G·cm^{-1}, $G3$ = 50 G·cm^{-1}, Gp (purge gradient) = 33 G·cm^{-1}. All FIDs were apodized by a 2 Hz Lorentzian function prior to Fourier transformation.

X-ray Crystallographic Studies: 1, 2 and **3** were obtained in monocrystalline forms by slowly (48 h) allowing the respective saturated solutions (30 mg) in hot water (1 mL, 363 K) to cool to room temperature.

Crystal Data of 1: $[H_3NCH_2CH_2NH_3]_2[H_4L] \cdot 4H_2O$, $C_{32}H_{48}N_4O_{20}S_4$ (936.98), 0.35 × 0.25 × 0.10 mm, monoclinic, $P2_1/c$, $Z = 4$, $a = 11.909(2)$, $b = 11.664(2)$, $c = 28.615(6)$ Å, β = 96.68(3)°, V = 3947(1) Å^3, $\rho_{calcd.}$ = 1.576 g·cm^{-3}, $F(000)$ = 1968, $2\theta_{max}$ = 49.5°, μ_{Mo} = 0.330 cm^{-1}, Nonius Kappa-CCD diffractometer (T = 123 K, crystal-to-detector distance d_x = 30 mm, 90 images were recorded by applying a 180° scan on ϕ in 2° increments; data were 94% complete to a 2θ value of 49.2°). The structure was solved by direct methods[19] and refined on F^2 using SHELXTL.[20] Of the 23921 reflections measured, 6564 were found to be independent (R_{int} = 0.057), 5350 of which were considered as observed [$I > 2\sigma(I)$] and were used in the refinement of the 553 parameters, leading to a final R_1 of 0.0487 and an R_{all} of 0.0652. Individual weights were applied in the refinement according to the scheme $w = [\sigma^2(F_o^2) + (0.0485P)^2 + 6.2143P]^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$. wR_{obs} and wR_2 were equal to 0.1116 and 0.1316, respectively. The goodness-of-fit parameter S was 1.029 and the maximum residual density 0.669 eÅ^{-3}. All non-hydrogen atoms were considered anisotropic. The water molecule that remains outside the cavity was found to be disordered over two positions that could be refined to final occupancies of 0.405(9) and 0.51(1). The hydrogen atoms incapable of hydrogen bonding (N−C*H*$_2$−C, Ar−*H*, Ar−C*H*$_2$−Ar) were introduced in the calculation as riding on calculated positions (U = 1.2 times that of the corresponding atom). All the other hydrogen atoms (*H*$_3$N−C, *H*$_2$O) were introduced in the positions found in the final Fourier map and were not refined. Selected geometrical parameters are given in Table 1. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-116141.

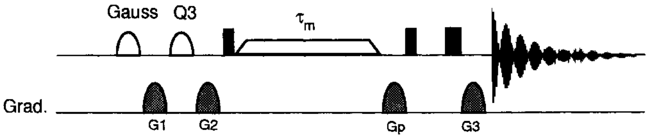

Figure 6. Pulse scheme of the 1D soft ROESY experiment

Crystal Data of 2: $[H_3NCH_2CH_2NH_3]_5[H_3L]_2 \cdot 11H_2O$, $C_{66}H_{110}N_{10}O_{43}S_8$ (1988.12), 0.35 × 0.20 × 0.10 mm, triclinic, $P{-}1$, $Z = 2$, $a = 11.5496(3)$, $b = 16.7398(8)$, $c = 22.367(1)$ Å, α = 93.191(2), β = 92.764(3), γ = 104.120(3)°, V = 4179(1) Å^3, $\rho_{calcd.}$ = 1.580 g·cm^{-3}, $F(000)$ = 2096, $2\theta_{max}$ = 49.4°, μ_{Mo} = 0.320 cm^{-1}, Nonius Kappa-CCD diffractometer (T = 123 K, d_x = 30 mm, 90 images were recorded by applying a 180° scan on ϕ in 2° increments; data were 95% complete to a 2θ value of 49.2°). The structure was solved by direct methods[19] and refined on F^2 using SHELXTL.[20] Of the 25804 reflections measured, 13182 were found to be independent (R_{int} = 0.039), 10669 of which were considered as observed [$I > 2\sigma(I)$] and were used in the refinement of the 865 parameters, leading to a final R_1 of 0.0477 and an R_{all} of 0.0639. Individual weights were applied in the refinement according to the scheme $w = [\sigma^2(F_o^2) + (0.0375P)^2 + 8.8156P]^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$. wR_{obs} and wR_2 were equal to 0.1075 and 0.1217, respectively. The goodness-of-fit parameter S was 1.034 and the maximum residual density 0.504 eÅ^{-3}. All non-hydrogen atoms were considered anisotropic, except for the carbon atoms of the calixarene core, which were considered isotropic in order to maintain a reasonable data/parameters ratio. The hydrogen atoms incapable of hydrogen bonding (N−C*H*$_2$−C, Ar−*H*, Ar−C*H*$_2$−Ar) were introduced in the calculation as riding on calculated positions (U = 1.2 times that of the corresponding atom). All the other hydrogen atoms (*H*$_3$N−C, *H*$_2$O) were introduced in positions found in the final Fourier map and were not refined. Selected geometrical parameters are given in Table 2. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-116142.

Crystal Data of 3: $[H_3NCH_2CH_2NH_3]_8[H_3NCH_2CH_2NH_2]_4$-$[H_3L]_4 \cdot 18H_2O$, $C_{136}H_{228}N_{24}O_{82}S_{16}$ (4024.38), 0.25 × 0.20 × 0.10 mm, monoclinic, $P2_1/c$, $Z = 4$, $a = 38.368(8)$, $b = 25.963(5)$, $c = 17.259(4)$ Å, $\beta = 97.38(3)°$, $V = 17051(6)$ Å^3, $\rho_{calcd.} = 1.568$ g.cm^{-3}, $F(000) = 8496$, $2\theta_{max} = 49.4°$, $\mu_{Mo} = 0.313$ cm^{-1}, Nonius Kappa-CCD diffractometer ($T = 123$ K, $d_x = 30$ mm, 180 images were recorded by applying a 180° scan on ϕ in 1° increments; data were 94% complete to a 2θ value of 49.2°). The structure was solved by direct methods[19] and refined on F^2 using SHELXTL.[20] Of the 84868 reflections measured, 27793 were found to be independent ($R_{int} = 0.08$), 18472 of which were considered as observed [$I > 2\sigma(I)$] and were used in the refinement of the 1495 parameters, leading to a final R_1 of 0.0621 and an R_{all} of 0.1088. Individual weights were applied in the refinement according to the scheme $w = [\sigma^2(F_o^2) + (0.0454P)^2 + 51.3P]^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$. wR_{obs} and wR_2 were equal to 0.130 and 0.1632, respectively. The goodness-of-fit parameter S was 1.046 and the maximum residual density found in the close vicinity of the disordered water molecule was 0.963 eÅ^{-3}. All non-hydrogen atoms were considered isotropic other than those of the sulfonate groups and the nitrogen atom of $[H_3NCH_2CH_2NH_2]^+$, which were considered anisotropic. Such a distinction was dictated by the necessity to keep the number of parameters refined to below 1500, above which our software is unable to operate. The hydrogen atoms incapable of hydrogen bonding ($N-CH_2-C$, $Ar-H$, $Ar-CH_2-Ar$) were introduced in the calculation as riding on calculated positions ($U = 1.2$ times that of the corresponding atom). The only other hydrogen atoms that were introduced and not refined in the calculation were those that could be unequivocally positioned from the final Fourier map (H_3N-C, H_2N-C, H_2O). Selected geometrical parameters are given in Table 3. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-116143.

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