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Supramolecular Chemistry of *p*-Sulfonatocalix[5]arene: A Water-Soluble, Bowl-Shaped Host with a Large Molecular Cavity

Jonathan W. Steed,*,† Carl P. Johnson,‡ Charles L. Barnes,‡ Ravindra K. Juneja,‡ Jerry L. Atwood,*,‡ Sean Reilly,§ Rebecca L. Hollis,§ Paul H. Smith,§ and David L. Clark*,§

Contribution from the Department of Chemistry, King's College London, Strand, London WC2R 2LS, U.K., Department of Chemistry, University of Missouri—Columbia, Columbia, Missouri 65211, and Chemical Science and Technology Division, Los Alamos National Laboratory, Mail Stop G793, Los Alamos, New Mexico 87545

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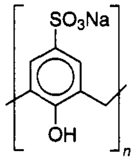
Abstract: The first X-ray crystallographic studies are reported for water-soluble inclusion complexes of the macrocyclic *p*-sulfonatocalix[5]arene[1] (**1b**). The complexes Na_7[*p*-sulfonatocalix[5]arene]·$18H_2O$ (**2**) and Na_5[*p*-sulfonatocalix[5]arene]·py-*N*-O·$8.5H_2O$ (**3**) containing water and pyridine *N*-oxide (py-*N*-O) guest species have been isolated. In **2** the large bowl-shaped cavity of the host molecule is occupied by a total of three water molecules, while for **3** a single molecule of pyridine *N*-oxide is included and interacts with the host *via* a strong hydrogen bond to a protonated sulfonate substituent. The behavior of **1b** as a ligand for a number of lanthanide elements is also reported. Low temperature X-ray structural studies reveal that coordination of the Ln^{3+} metal ions to the calixarene ligand occurs exclusively *via* the sulfonato functionalities and not the phenolic oxygen atoms as suggested by Shinkai *et al.* for the complexation of UO_2^{2+} by **1b**. In complex **2** the calixarene exists as the heptaanion. In contrast, crystallization from acidic solution results in complexes **3**−**8** retaining all their phenolic protons. The protonation constants of **1b** have been measured in aqueous solution: pK_a = 10.96(8), 7.63(5), and 4.31(1) at 25 °C and 0.1 M KNO_3.

Introduction

Water-soluble calix[*n*]arene (n = 4−8) derivatives have received considerable attention in recent years because of their selective metal ion binding properties in aqueous solution,[1] the formation of clay-like bilayer structures in the solid state,[2] and the observation of $H_2O\cdots\pi$-aromatic hydrogen bonding.[3] In particular, Shinkai *et al.* have reported that the *p*-sulfonato derivatives of calix[5]arene (**1b**) and calix[6]arene (**1c**), as well as analogous species possessing carbomethoxy substituents at the base of the macrocycle, exhibit a particular affinity and selectivity for uranyl (UO_2^{2+}) ions (stability constants, $K = 10^{18.4-19.2}$, selectivity over Ni^{2+}, Zn^{2+}, and Cu^{2+}, 10^{12-17})[4] and are of potential application in the extraction of uranium from sea water. Indeed, calixarenes in general show interesting complexation behavior toward a range of lanthanide and actinide elements.[5] It has been suggested that the high affinity exhibited by **1b** and **1c** toward UO_2^{2+} may be attributable to a preorganized[6] pseudoplanar arrangement of the phenolic oxygen atoms of the macrocycle. Recently, however, we have shown that both the sodium salt of the *p*-sulfonatocalix[6]arene octaanion and the parent sulfonic acid exist in a *double partial cone* conformation in the solid state, in which the phenolic donors are distributed in two groups of three rather than exhibiting the



n = 4, **1a**
n = 5, **1b**
n = 6, **1c**

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† King's College London.

‡ University of Missouri—Columbia.

§ Los Alamos National Laboratory.

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proposed coplanar conformation.[7] Furthermore it is a distinct possibility that the binding of oxophilic metal ions by calixarenes **1b** and **1c** occurs *via* the calixarene sulfonato functionalities as opposed to, or in addition to, the phenolic oxygen atoms. In this contribution we extend these structural studies to the water-soluble *p*-sulfonatocalix[5]arene **1b**, in the anticipation of establishing the conformation of the macrocycle and hence degree of preorganization for UO_2^{2+} binding. In addition, as a consequence of the synthetic elusiveness of the odd numbered calix[*n*]arenes (yields of *p-tert*-butylcalix[5]arene based on *p-tert*-butylphenol typically range from 0−10%), the inclusion chemistry of calix[5]arenes has not yet been well explored in spite of the metal ion extraction ability of **1b**. Calix[5]arene derivitaves, however, are of significant interest as a consequence of the large size of the macrocyclic cavity suggesting the possibility of novel host−guest behavior. It is of particular interest to examine the inclusion of water within the large hydrophobic cavity of **1b**. The solid state structure of the related *p*-sulfonatocalix[4]arene **1a** is apparently perfectly preorganized for the inclusion of one molecule of water which is stabilized by OH···π-aromatic hydrogen bonding interactions. The change in cavity size on moving from **1a** to **1b** may well result in a significant change in the OH···π interaction mode, giving additional insights into the more general aspects of the interactions of water with large, hydrophobic molecules, as often encountered in biological systems.

As a model for UO_2^{2+} complexation we have also examined the binding of a range of lanthanide ions by **1b** in the anticipation of establishing the coordination mode of oxophilic metal centers to macrocycles such as **1b** and **1c**. An important question arising from the juxtaposition of a large, water-soluble macrocycle possessing a large number of potential binding modes and a solvated metal ion concerns the relative influences of crystal packing forces and metal−ligand coordination in solid-state self-assembly. In related complexes of **1a** we have found that the claylike bilayer packing mode is extremely prevalent[2] and has a significant influence on the inclusion of guest species and even the stoichiometry of the metal−calixarene coordination complex. Such dominance of crystal packing interactions runs counter to the traditional perception of intermolecular forces as being relatively weak in nature and apparently arises as a consequence of the combination of a large number of supramolecular interactions. In this study we demonstrate the generality of this effect and highlight the importance of supramolecular forces when acting in concert.

Experimental Section

Materials. Na$_5$[*p*-sulfonatocalix[5]arene]•H$_2$O (1b). *p-tert*-Butylcalix[5]arene was synthesized according to the improved method of Gutsche[8] resulting in yields of *ca.* 5−10%. Direct reaction of *p-tert*-butylcalix[5]arene (1.0 g, 1.23 mol) with H_2SO_4 (98%, 10 cm^3) at 80−90 °C for 4 h, with periodic checking of the reaction mixture for solubility in water, resulted in a dark solution in which most of the calixarene had dissolved. The mixture was quenched in ice (10 g) and filtered. Addition of NaCl (0.25 g) to the filtrate resulted in the slow deposition of the product as colorless prisms which were collected by filtration and dried *in vacuo* at 100 °C for 72 h. Yield 1.05 g, 1.01 mol, 82%. Anal. Calcd for $C_{35}H_{25}O_{20}S_5Na_5 \cdot H_2O$: C, 37.15; H, 3.10; Na, 10.15. Found: C, 37.00; H, 3.15; Na, 10.05%. The physical and ^{1}H NMR spectral properties of this material matched those reported previously.[9]

Na$_7$[*p*-sulfonatocalix[5]arene]·8H$_2$O (2). Following a procedure analogous to that given for **1b**, the resulting quenched mother liquor was neutralized with Na_2CO_3 in place of NaCl to give the heptaanionic salt as a white precipitate in yield comparable to that of **1b**. Slow evaporation of an aqueous solution of this gave the inclusion complex **2** as large, colorless prisms which were characterized by X-ray crystallography.

Na$_5$[*p*-sulfonatocalix[5]arene]·py-*N*-O·8.5H$_2$O (3). To a mixture of **1b** (0.150 g, 0.080 mmol) in water (1.5 mL) were added Zn(NO$_3$)$_2$•H$_2$O (0.048 g, 0.16 mmol) and pyridine *N*-oxide (0.059 g, 0.62 mmol), and the mixture was allowed to stand in air for *ca.* 14 d, resulting in the isolation of the inclusion compound as thin, colorless plates in *ca.* 70% yield. Prismatic crystals consisting solely of Zn(NO$_3$)$_2$•H$_2$O (X-ray evidence) were also isolated.

Na$_2$[La(H$_2$O)$_9$][(*p*-sulfonatocalix[5]arene)]·py-*N*-O·10H$_2$O (4), Na$_7$[Gd(H$_2$O)$_6$(*p*-sulfonatocalix[5]arene)$_2$]·2py-*N*-O·34H$_2$O (5), Na[Eu(H$_2$O)$_9$]$_2$[Eu(py-*N*-O)(H$_2$O)$_5$(*p*-sulfonatocalix[5]arene)$_2$]·py-*N*-O·17.5H$_2$O (6), and Na$_8$[Tb$_4$(py-*N*-O)$_4$(H$_2$O)$_{18}$(*p*-sulfonatocalix[5]arene)$_4$]•52H$_2$O (7). To a mixture of Na$_5$[*p*-sulfonatocalix[5]arene] (**1b**) (0.15 g, 0.080 mmol) in water (1.5 mL) were added pyridine *N*-oxide (0.060 g, 0.63 mmol) and Ln(NO$_3$)$_3$•H$_2$O (0.070 g, 0.15 mmol, Ln = La, Gd, Eu, Tb), and the mixture was allowed to stand in air for periods of up to several weeks, resulting in the deposition of the crystalline inclusion compounds as large, colorless prisms as the sole products, in yields ranging from *ca.* 40−60%. In the cases of **4** and **5** analytical data are corrected for the loss of 3 and 6 mol of water, respectively, during transport. Such desolvation is consistent with the observed poor stability of the crystals upon removal from the mother liquor. Anal for **4** calcd for $C_{40}H_{62}O_{37}LaNNa_2S_5$: C, 32.15; H, 4.18; N, 0.94; S, 10.73. Found: C, 32.2; H, 4.5; N, 1.3; S, 10.9%. Anal for **5** calcd for $C_{40}H_{52}O_{35}Gd_{0.5}NNa_{4.5}S_5$: C, 33.15; H, 3.62; N, 0.97; S, 11.06. Found: C, 33.3; H, 4.2; N, 1.0; S, 10.2%. Anal for **6** calcd for $C_{80}H_{131}O_{83.5}Eu_3N_2NaS_{10}$: C, 29.51; H, 4.05; N, 0.86; S, 9.84. Found: C, 29.8; H, 4.3; N, 1.0; S, 10.0%. Anal for **7** calcd for $C_{40}H_{66}O_{40}NNa_2S_5Tb$: C, 30.68; H, 4.25; N, 0.89. Found: C, 30.65; H, 4.05; N, 0.80%.

Na$_2$[Yb(py-*N*-O)(H$_2$O)$_6$(*p*-sulfonatocalix[5]arene)]·13H$_2$O (8). To a mixture of Na$_5$[*p*-sulfonatocalix[5]arene] (**1b**) (0.15 g, 0.080 mmol) in water (1.5 mL) was added pyridine *N*-oxide (0.060 g, 0.63 mmol) and YbCl$_3$•H$_2$O (0.070 g, 0.15 mmol), and the mixture allowed to stand in air for three weeks, resulting in the deposition of the crystalline inclusion compound as large, colorless prisms in *ca.* 40% yield. Analytical data are corrected for the loss of 2 mol of water during transport. Anal. Calcd for $C_{40}H_{65}O_{38}NNa_2S_5Yb$: C, 31.05; H, 4.23; N, 0.91; S, 10.36. Found: C, 31.3; H, 4.0; N, 1.1; S, 11.5%.

X-ray Crystallography. With the exception of complex **7**, all crystallographic measurements were carried out with an Enraf-Nonius CAD4 diffractometer equipped with graphite monochromated Mo Kα radiation using the $\omega-2\theta$ scan mode. Data sets were corrected for Lorentz and polarization effects, absorption (ψ-scans) and crystal decay where appropriate. For compounds **4**−**8** data collection was undertaken at −100 °C in order to minimize decomposition as a result of solvent loss. Details of individual structure determinations are given in Table 1. Severe problems arising from persistent crystal twinning were encountered for **7**. The best data set for **7** was obtained using a Siemens SMART CCD system with 10 s frame intervals. Corrections were made for Lorentz, polarization, and absorption effects using a pseudo ψ-scan method based upon redundant data. Effects of multiple crystal twinning were partially mitigated by the integration software but are apparent in the high *R* factor for this determination. Attempts at twinned refinement were unsuccessful. Structures were solved using the direct methods option of SHELXS-86[10] and developed using conventional alternating cycles of least squares refinement and difference Fourier synthesis (SHELXL-93[11] or SHELXL-76[12] for complex **2**). In all cases, all non-hydrogen atoms were refined anisotropically except disordered lattice water and carbon atoms in the case of **6**, while hydrogen atoms were placed in idealized positions, assigned an isotropic displacement factor based upon that of the atom to which they were attached, and refined using a riding model. All calculations were carried out on an IBM-PC compatible personal computer. Further details consisting of crystal data, details of structure determination, atomic coordinates,

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Table 1. Data Collection and Refinement Parameters for Complexes **2**−**8**

compound	**2**	**3**	**4**	**5**	**6**	**7**[e]	**8**
formula	$C_{35}H_{58}O_{38}$-Na_7S_5	$C_{40}H_{47}O_{29.5}$-NNa_5S_5	$C_{40}H_{68}O_{40}$-$LaNNa_2S_5$	$C_{40}H_{63}O_{39}$-$Gd_{0.5}S_5NNa_{5.5}$	$C_{80}H_{131}O_{83.5}$-$Eu_3N_2NaS_{10}$	$C_{80}H_{106}N_2Na_4O_{63}$-$S_{10}Tb_2$	$C_{40}H_{69}O_{40}$-NNa_2S_5Yb
M (g mol^{-1})	1349.69	1289.04	1573.01	1566.92	3256.34	2858.26	1583.28
space group	$P\bar{1}$	$C2/c$	$Pbcn$	$C2/c$	$P\bar{1}$	$P\bar{1}$	$P2_1/c$
a (Å)	11.305(2)	30.601(8)	19.231(2)	31.079(9)	11.044(6)	18.0032(1)	14.173(4)
b (Å)	12.987(3)	19.184(5)	21.897(2)	19.050(2)	19.854(5)	20.0235(2)	19.157(3)
c (Å)	20.037(5)	21.938(4)	29.524(13)	21.836(7)	29.614(6)	21.9277(2)	21.887(5)
α (deg)	94.17(2)	90	90	90	107.18(2)	114.996(1)	90
β (deg)	92.79(2)	114.37(2)	90	90.48(2)	91.52(3)	101.540(1)	92.466(12)
γ (deg)	104.42(3)	90	90	90	91.01(3)	105.180(1)	90
U (Å^3)	2835(2)	11731(5)	12433(6)	12928(6)	6199(4)	6463.03(9)	5937(2)
$2\theta_{max}$ (deg)	46	44	46	46	46	46.6	48
Z	2	8	8	8	2	2	4
$F(000)$	1360	5320	6352	6396	3306	2924	3232
D_c (g cm^{-3})	1.59	1.46	1.65	1.60	1.74	1.47	1.77
μ (cm^{-1})	2.49	3.21	9.7	8.11	17.9	13.5	18.7
temp (K)	293	293	173	173	173	173	173
decay	<2%	<2%	<2%	15% corr.	<2%	<2%	<2%
refl measured	7825	7552	8858	9398	15605	24223	9647
no. unique	7825	5837	8626	8937	15605	16935	9243
no. $I > 2\sigma(I)$	4220 (3σ)	4088	5159	5890	12939	15716	7969
no. params	750	804	792	855	1268[c]	1524	848
R^a	0.084	0.118	0.083	0.073	0.105	0.181	0.037
$R_w{}^a$	0.091	–	–	–	–	–	–
w$R_2{}^b$	–	0.326	0.252	0.229	0.335	0.588	0.122
gof	3.47	1.06	1.04	1.02	1.24	3.87	1.36
largest peak (e Å^{-3})	0.58	0.89	1.12	1.31	4.84[d]	5.00[d]	0.90

[a] Based on F and including all data with $I > 2\sigma(I)$. [b] Based on F^2 and including all data. [c] Carbon atoms were treated isotropically because of the difficulty in refining meaningful anisotropic displacement factors. [d] Close to one of the metal ions. [e] Data was collected using the Siemens SMART system. Severe crystal twinning and solvent disorder were encountered.

thermal parameters, and bond lengths and angles for **2**−**8** are available as supporting information.

Potentiometry. Potassium hydroxide (carbonate free) and nitric acid titrants were prepared from concentrates (Baker) and ultrapure water to give 0.1 M solutions. The potassium hydroxide titrant was standardized with potassium hydrogen phthalate (99.95%), and the amount of carbonate in the base was determined to be <0.1% by Gran's method.[13] The nitric acid titrant was then standardized against the potassium hydroxide. The 0.10 M supporting electrolyte solution of potassium nitrate was prepared from reagent grade chemical and ultrapure water. All potentiometric equilibrium measurements were conducted in a water-jacketed vessel at 25.0 ± 0.1 °C under ultrapure argon. The ligand concentration in 0.1 M supporting electrolyte was approximately 0.002 M. A Radiometer ABU93 Triburette was used to dispense titrants and perform potentiometric measurements. The ABU93 was interfaced to a personal computer to permit automated data collection using software developed at Los Alamos (PHS). A pK_w of 13.78 (0.10 M ionic strength, 25 °C) was used in all calculations.[14] An Orion ROSS combination pH electrode was calibrated before each titration. In a typical calibration, 0.50 mL of standardized 0.1 M HNO_3 was added to 10 mL of supporting 0.1 M KNO_3 electrolyte. Standardized 0.1 M KOH was then titrated into the solution in 20 0.05 mL aliquots. The electrode potential was recorded before the titration and after the addition of each aliquot of base. Twenty-one data points were thereby collected over a pH range of 2.3−11.4. Linear least squares analysis of the electrode potential (in mV) as a function of the known acid concentration (below pH 3.0 and above pH 10.5) provided the electrode slope and intercept. This slope and intercept enabled the pH electrode to measure−log[H^+] (designated p[H]) directly during subsequent titrations of calixarene **1b**.

Calixarene **1b** was dissolved in 10 mL of KNO_3 electrolyte to give a p[H] 3.6−3.7 solution. This solution was acidified with 0.1 mL of HNO_3 and then titrated with KOH while measuring p[H]. Three separate titrations were performed, and a minimum of 220 data points were collected between a p[H] range of 3.2−11.0 for each data set. Calixarene **1b** is a hygroscopic solid, and its hydration state varied between titrations. The millimoles of **1b** for each titration was determined by calculating the derivative, d(titrant volume)/d(p[H]), and assuming that the difference between the two maxima corresponds to 1 equiv of added base. The derivative peaks were also utilized to establish the degree of protonation of **1b** for each titration using the assumption that the first derivative peak corresponds to α = 1. Overall calixarene protonation constants (log β) were determined separately for each data set by nonlinear least squares analysis of the data using the computer program BETA.[15] A weighted average value of each stepwise protonation constant (log K^H) was calculated using the equation below, where values of σ were obtained from BETA and the sum is over n repetitions. The error in log K is reported as the standard deviation of the (log K)$_i$ values and thus represents the reproducibility of titration results.

$$\text{Log } K = \frac{\sum_{i=1}^{n}[(\log K)_i/\sigma_i^2]}{\sum_{i=1}^{n}(1/\sigma_i^2)}$$

Results and Discussion

Structure and Properties of Na_7[*p*-sulfonatocalix[5]-arene]·$18H_2O$. A number of single crystal X-ray structure determinations[2,16] as well as pK_a measurements[17] have demonstrated that at neutral pH, *p*-sulfonatocalix[4]arene **1a** exists as the pentaanion with all four sulfonate groups as well as one phenolic oxygen atom in the deprotonated form. In contrast, higher calix[*n*]arenesulfonates (n = 6, 8)[7,17] exhibit relatively

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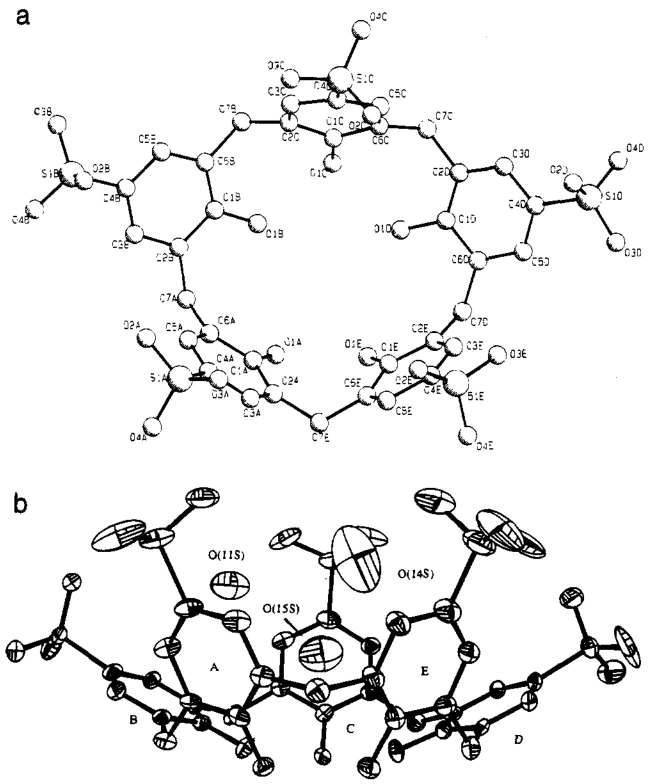

Figure 1. (a) Crystallographically determined structure of the *p*-sulfonatocalix[5]arene ion in Na_7[*p*-sulfonatocalix[5]arene]$\cdot 18H_2O$ (**2**) showing the atom numbering scheme used in the tables. (b) Inclusion of three water molecules within the cavity of Na_7[*p*-sulfonatocalix[5]arene]$\cdot 18H_2O$ (**2**).

high acidity for two of the phenolic protons (*e.g. p*-sulfonatocalix[6]arene, pK_a 4.76(3) [log β_{11} 4.76(3)] and 3.44(4) [log β_{12} 8.20(4)][7]), but the remaining hydroxyl functionalities are extremely difficult to deprotonate. In light of these observations it was unclear whether a 6-, 7-, or 8- species would be expected at pH 7 for *p*-sulfonatocalix[5]arene. Neutralization of **1b** (pH 7) with Na_2CO_3 followed by slow evaporation of an aqueous solution resulted in the formation of the hydrate Na_7[*p*-sulfonatocalix[5]arene]$\cdot 18H_2O$ (**2**) which was characterized by X-ray crystallography. The molecular structure of the *p*-sulfonatocalix[5]arene unit, along with the atom labeling scheme used throughout this work is shown in Figure 1. Unlike both the sodium salt and parent acid of *p*-sulfonatocalix[6]arene, the calixarene unit in **2** adopts the conventional *calix* bowl geometry with all the oxygen atoms in a nearly coplanar arrangement (maximum deviation from best least squares plane 0.18 Å). The aromatic residues which constitute the walls of the *calix* do not lie in a plane, however; two rings (B and D) are flattened forming an angle of only 27.8(3)° (av) with the plane containing O(1A)−O(1E). Conversely, rings A, C, and E are markedly more upright, forming angles of 70.1(3)°, 67.3(3)°, and 71.9(3)°. The flattened conformation of rings B and D is in part due to the inclusion of three molecules of water O(11S), O(14S), and O(15S) within the cavity of the macrocycle (Figure 1b). One of these guest molecules, O(15S), penetrates deeply into the calix cavity in analogy with the structure of Na_4[*p*-sulfonatocalix[4]arene]$\cdot 13.5H_2O$[3] (**9**). Unlike **9**, however, where $H_2O\cdots\pi$-aromatic hydrogen bonding is observed, O(15S) forms weak interactions with the phenolic oxygen atoms O(1B) and O(1D) as well as acting as a hydrogen bond receptor for O(11S) and O(14S); distances O(15S)···(1B) 3.27, O(1D) 3.32, O(11S) 2.95, O(14S) 2.89 Å. The included water molecules are bound to the aqueous portion of the claylike bilayer structure[2] *via* hydrogen bonds from O(11S) to Na(4) and O(7S), and from O(14S) to Na(4) and O(16S). The closest O(15S)···C distances fall in the range 3.46−3.55 Å (for C(1A) and C(1E)) while the O(15S)···ring centroid distances fall between 3.63−4.86 Å, with centroids A and E markedly nearer to the water molecule than the remaining rings. This is in contrast to the structure of **9**, where O···centroid separations of less than 3.2 Å were observed. Long water-centroid distances are also observed for a range of salts of the *p*-sulfonatocalix[4]arene pentaanion M_5[*p*-sulfonatocalix[4]arene]$\cdot xH_2O$ (M = Na, **10a**; K, **10b**; Rb, **10c**; Cs, **10d**; x = 12, 8, 5, 4), but this results from the inclusion of two water molecules near the rim of the cavity rather than one, more deeply embedded. Thus the structure of **2** more closely resembles that of **9** than complexes of type **10**, with the absence of significant $H_2O\cdots\pi$-aromatic interactions resulting from the larger size of the calix[5]arene cavity and the enhanced flexibility of the calix[5]arene bowl.

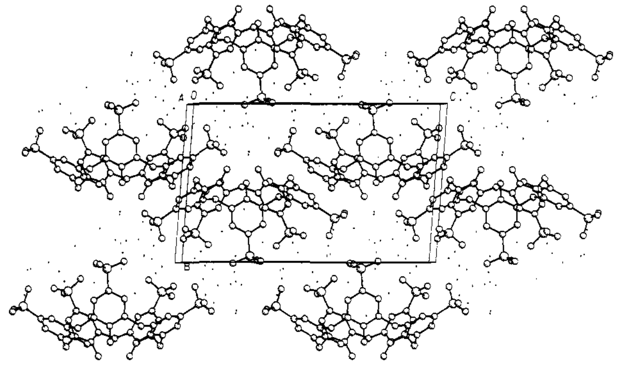

Figure 2. Bilayer structure of Na_7[*p*-sulfonatocalix[5]arene]$\cdot 18H_2O$ (**2**) viewed along the crystallographic *a* axis.

The crystal packing observed in **2** is of the bilayer type, with alternating hydrophilic and hydrophobic layers (Figure 2). The curved shape of the calix[5]arene molecule makes the delineation of the boundaries between the layers difficult, but the hydrophobic and hydrophilic layers are in the region of 8.6 and 4.4 Å wide, respectively, resulting in a repeat distance of 13.0 Å (the crystallographic *b* axis) similar to that of 13.7 Å observed for *p*-sulfonatocalix[4]arene.[3]

The location of a total of seven sodium ions in the crystalline lattice infers a 7-charge associated with the *p*-sulfonatocalix[5]arene anion in **2**. It is also clear from the hydrogen bonding network at the lower rim of the *calix* that two of the five phenolic protons are absent giving rise to three short hydrogen bonded O···O contacts (2.49−2.64 Å) and two longer, nonbonded distances (3.54 and 3.58 Å). As a final confirmation, we have performed pK_a measurements on compound **1b** *via* potentiometric titration.[13] Three measured pK_a values of 10.96(8), 7.63(5), and 4.31(1) were determined and are consistent with the observed formation of the Na_7 heptaanionic species crystallized from a neutral or slightly basic solution. Calixarene **1b** is similar to **1c** in that it has two readily ionizable protons, and the remaining OH groups are stabilized by hydrogen-bonding interactions of the calix moitey.

Reactions with Metal Salts. Attempts were made to use **1b** as a ligand for a number of transition metal and lanthanide elements with a view toward structural investigation of the metal binding properties of the sulfonated calixarene. In each case an approximately two-fold excess of hydrated metal salt (usually nitrate) was dissolved in water with **1b** and an excess of a coligand (either pyridine or pyridine *N*-oxide). Measurement of the pH of the resulting solutions showed them to be somewhat acidic (pH 2−3) presumably as a consequence of the presence of residual sulfuric acid in the macrocycle. Metal-containing inclusion compounds were obtained for Ni(II), Cr(III), Co(II), La(III), Eu(III), Gd(III), Tb(III), and Yb(III) of which the lanthanide-containing species have been characterized by low temperature (−100 °C) X-ray crystallography. The transition metal complexes precipitated either as colored powders or only weakly diffracting crystals and will be reported elsewhere. Attempts to characterize samples containing Tb(III) by X-ray crystallography were hampered by persistent crystal twinning, although a data set was finally obtained using a SMART system (see Experimental Section). Attempts to crystalize metal-containing derivatives at pH 7−9 were unsuccessful.

No metal-containing species were observed for Zn(II) which gave separate crystals of $Zn(NO_3)_2 \cdot H_2O$ and a calixarene−coligand 1:1 inclusion compound. This contrasts to the case of *p*-sulfonatocalix[4]arene in which an octahedral $[Zn(H_2O)_4(py\text{-}N\text{-}O)_2]^{2+}$ ion is included within the cavity of the calixarene.[18] For comparison with the structure of **2** the 1:1 *p*-sulfonatocalix[5]arene−pyridine *N*-oxide host−guest complex Na_5[*p*-sulfonatocalix[5]arene]·py-*N*-O·8.5H_2O (**3**) was also characterized crystallographically.

$Na_2[La(H_2O)_9]$[(calix[5]arene-*p*-sulfonato)]·py-*N*-O·10H_2O. Reaction of $La(NO_3)_3 \cdot H_2O$ with **1b** in the presence of py-*N*-O results in the isolation of $Na_2[La(H_2O)_9]$[(*p*-sulfonatocalix[5]arene)]·py-*N*-O·10H_2O (**4**). The La(III) center is not coordinated to the macrocycle and exists simply as a $La(H_2O)_9{}^{3+}$ counterion.[22a] The relatively long La−OH_2 distance of 2.56(1) Å (av), reflects the high coordination number and larger ionic radius of La(III) relative to later lanthanide elements[19,22a] and is typical of lanthanum aqua species.[19] The calixarene acts as a second sphere ligand to the $[La(H_2O)_9]^{3+}$ ion with a large number of hydrogen bonding interactions (O···O contacts in the range 2.6−2.9 Å) from the lanthanum aqua ligands to the calixarene sulfonato oxygen atoms. The cavity of the calixarene is occupied by a crystallographically disordered py-*N*-O molecule which interacts with sodium ions and lattice water, but not the La^{3+} center, *via* hydrogen bonding and electrostatic interactions.

In the solid state, the *p*-sulfonatocalix[5]arene units adopt a bilayer structure related to that observed for **2** and numerous other *p*-sulfonatocalix[4]arenes,[2] with the La(III) ions along with sodium and water residing in an aqueous layer *ca.* 9.1 Å thick (*cf.* 8.4 Å for **2**). The hydrophobic layer is also thicker than for **2** (5.6 Å compared to 4.4 Å) because of the intercalation of the metal ion coordination sphere.

$Na_7[Gd(H_2O)_6$(*p*-sulfonatocalix[5]arene)$_2$]·2py-*N*-O·34H_2O. Under identical conditions to those employed in the synthesis of **4**, slow evaporation of an aqueous solution of $Gd(NO_3)_3 \cdot H_2O$, pyridine *N*-oxide and **1b** resulted in the deposition of large, colorless crystals of $Na_7[Gd(H_2O)_6$(*p*-sulfonatocalix[5]arene)$_2$]·2py-*N*-O·34H_2O (**5**), which exhibits very similar crystallographic unit cell parameters to **4** (the only noteworthy difference is an approximately 1.5 Å change in length in the longest axes; *a* in the case of **5**, *c* in **4**) suggesting a close similarity between the two structures. Surprisingly, however, the metal ion:calixarene ratio is 1:2 rather than 1:1 in the case of **4**. The crystal structure of **5** is shown in Figure 4. The Gd center adopts an eight coordinate, approximately dodecahedral geometry, comprising six water molecules (Gd−O 2.417(9) Å av) and, in contrast to **4**, the sulfonate oxygen atom O(2A) from two symmetry related calixarene ligands (Gd−O_{sulf} 2.353(8) Å), and hence the "$Gd(H_2O)_6$" moiety bridges the two calixarene units. The relatively short Gd−O bond lengths[19] reflect the relatively small ionic radius of the Gd^{3+} ion. As expected, however, they are markedly longer than in the Yb(III) species $Na[Yb(H_2O)_7$(*p*-sulfonatocalix[4]arene)]·9H_2O (2.335(8) Å av).[1h] It is unsurprising that oxophilic lanthanide ions should bind to the accessible sulfonato oxygen atoms of the calixarene ligand, but it is noteworthy that this binding mode is very different to that suggested by Shinkai[4] for the binding of $UO_2{}^{2+}$ by **1b** and **1c**, albeit at more basic pH.

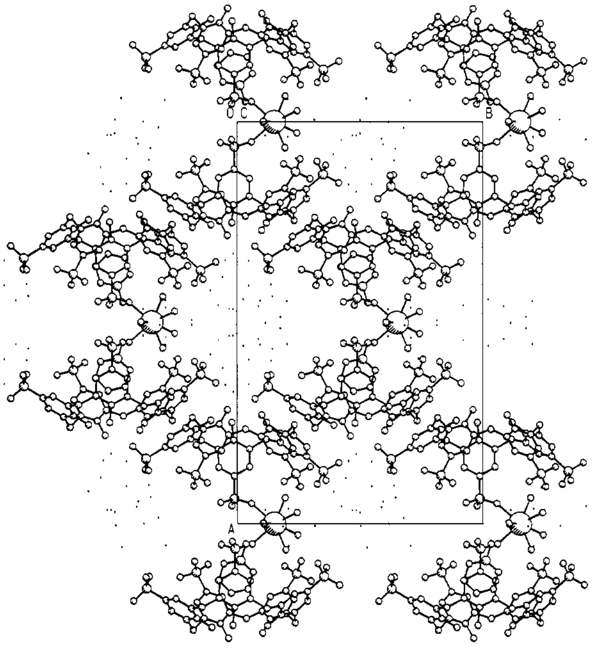

Figure 3. Bilayer packing in **5** viewed along the crystallographic *c* axis.

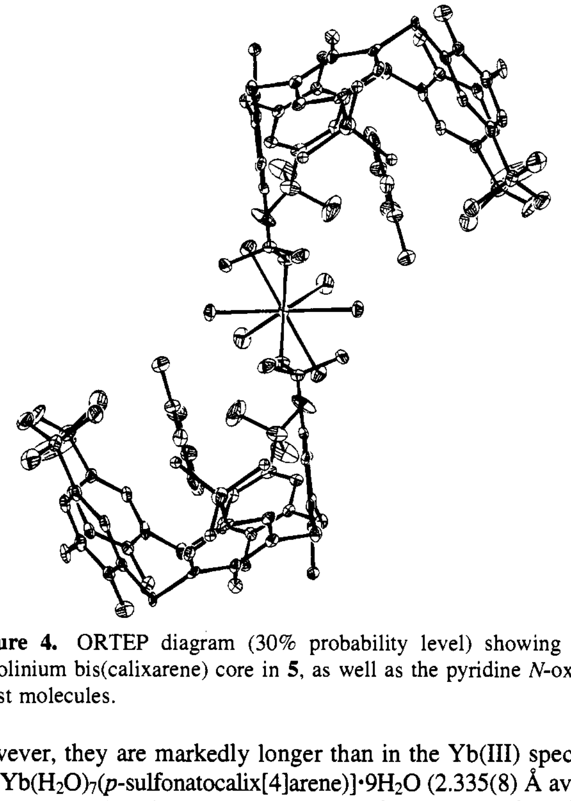

Figure 4. ORTEP diagram (30% probability level) showing the gadolinium bis(calixarene) core in **5**, as well as the pyridine *N*-oxide guest molecules.

The cavity of the bowl-shaped calixarene in **5** is occupied by a py-*N*-O molecule, seated edge on with the hydrophobic pyridyl ring most deeply embedded within the cavity. This edge-on mode of host−guest interaction is reminiscent of that found for the inclusion of tetralin by *p-tert*-butylcalix[5]arene.[20a]

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[18] Atwood, J. L.; Orr, G. W.; Robinson, K. D.; Hamada, F. *Supramol. Chem.* **1993**, *2*, 309.

[19] Orpen, A. G.; Brammer, L.; Allen, F. H.; Kennard, O.; Watson D. G.; Taylor, R. *J. Chem. Soc., Dalton Trans.* **1989**, S1.

[20] (a) Juneja, R. K.; Robinson, K. D.; Orr, G. W.; DuBois, R. H.; Belmore, K. A.; Atwood, J. L., *J. Incl. Phenom.* **1992**, *13*, 93. (b) Perrin, M.; Lecocq, S. *J. Incl. Phenom.* **1991**, *11*, 171. (c) Steed, J. W.; Johnson, C. P.; Juneja, R. K.; Atwood, J. L. Unpublished results.

Related compounds of both toluene and benzene,[20b,c] however, contain aromatic guest molecules situated parallel to the plane of the phenolic oxygen atoms. In this case the orientation of the guest maximizes interaction of the oxygen atom with the aqueous layer of the structure in which the py-*N*-O guest functions chiefly as a bridging ligand between two sodium ions, O(1P)−Na(1) 2.53 Å, −Na(5) 2.50 Å, and is not further associated with either the gadolinium ion or calixarene. The sodium ion Na(1) is particularly well defined and exists in an octahedral environment consisting of three water molecules and two calixarene sulfonato groups (from different molecules) as well as the py-*N*-O ligand. The sulfonato groups in turn are bound to a symmetry equivalent of Na(1) to generate an eight-membered $Na_2O_4S_2$ ring. This situation contrasts sharply with the role of the py-*N*-O ligands in the structure of $Na[Eu_3(p\text{-sulfonatocalix[4]arene})_2(H_2O)_{18}(py\text{-}N\text{-}O)_3]\cdot 14H_2O$ (**11**)[21] in which the three crystallographically independent py-*N*-O ligands act variously as first- and second-sphere ligands for the Eu^{3+} ions as well as being situated both within and without the calixarene cavities.

Examination of the solid state structure of **5** reveals the same packing mode as in **4** with the sole modification being an expansion of the aqueous layer along the longest axis from 9.1 to 9.9 Å, Figure 3. The fact that the lanthanide ion is not coordinated to the calixarene units forces them somewhat apart to allow the incorporation of the metal ion coordination sphere. The sole relevant differences between the chemistry of La^{3+} and Gd^{3+} are the larger size and coordination number of lanthanum. It seems likely therefore that coordination of lanthanum to the calixarene in the same way as gadolinium would lead to an excessively large interlayer separation and as a result the structure collapses to a more stable form in which the metal ion is not coordinated. This hypothesis implies the interesting possibility that crystal packing forces actually override the electrostatic attraction between the sulfonate groups and the La^{3+} ion. This suggestion is further supported by the structure of $(H_3O)[La(py\text{-}N\text{-}O)_2(H_2O)_6(p\text{-sulfonatocalix[4]arene})]\cdot 6.5H_2O$ (**12**) in which the nine coordinate La(III) ion is bound both to two py-*N*-O ligands and one of the calixarene sulfonate functionalities as well as six water molecules[18] suggesting that $La-O_3S$ binding is possible, and even favorable, within a different crystal environment.

$Na[Eu(H_2O)_9]_2[Eu(py\text{-}N\text{-}O)(H_2O)_5(calix[5]arene\text{-}p\text{-sulfonato})_2]\cdot py\text{-}N\text{-}O\cdot 17.5H_2O$. The similarity of the ionic radii of europium and gadolinium suggests that reaction of **2** with $Eu(NO_3)_3\cdot H_2O$ as for **4** and **5** might lead to a product isostructural with **5**, and indeed the species $Na[Eu(H_2O)_9]_2[Eu(py\text{-}N\text{-}O)(H_2O)_5(p\text{-sulfonatocalix[5]arene})_2]\cdot py\text{-}N\text{-}O\cdot 17.5H_2O$ (**6**) obtained as the sole product from three independent crystallizations does incorporate an eight coordinate Eu^{3+} center bridging two independent *p*-sulfonatocalix[5]arene anions (Figure 5), Eu(1)−H_2O 2.420(9) Å (av), Eu(1)−$O_{sulfonate}$ 2.351(9) Å (av). In this case, however, one of the two crystallographically independent py-*N*-O molecules which occupy the calixarene cavities also forms part of the primary coordination sphere of the bridging Eu(III) ion, Eu(1)−O(1P) 2.33(1) Å. The second py-*N*-O molecule coordinates to one of the sodium ions, O(11P)···Na(5) 2.50(1) Å. In addition, two further $[Eu(H_2O)_9]^{3+}$ counterions occupy the hydrophilic layer of the structure in a similar way to the lanthanum aqua ion in **4** [Eu−OH_2 2.42(1) Å (av), typical of Eu−OH_2 distances[19]]. The structure is related to that observed for the *p*-sulfonatocalix[4]arene complex $Na[Eu_3(p\text{-sulfonatocalix[4]arene})_2(H_2O)_{18}(py\text{-}N\text{-}O)_3]\cdot 14H_2O$ (**11**).[21] In the case of **11**, however, simultaneous first-, second-, and third-sphere coordination occur because of hydrogen bonding of the uncoordinated py-*N*-O ligand to the primary coordination sphere of one of the nine coordinate metal centers. Also in **11**, all three crystallographically independent Eu^{3+} ions are coordinated to the calixarenes, one of them *via* one phenolic oxygen atom at the lower rim of the macrocycle as well as the upper rim sulfonate groups on adjacent molecules.

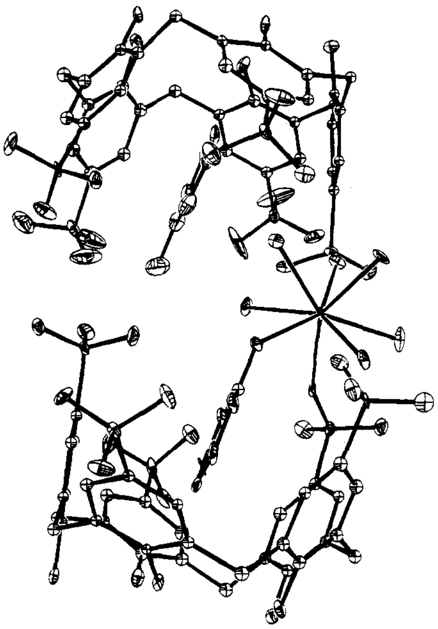

Figure 5. ORTEP diagram of the europium-bridged bis(calixarene) core unit in **6** in various orientations, along with the py-*N*-O guest molecules.

In the solid state, the crystal packing in **6** is remarkably similar to that observed for **4** and **5** and is reflected in the similarity of the unit cell parameters of the three complexes (doubling the length of the *a* axis in **6** results in virtually identical unit cell lengths to **4** in spite of the lower symmetry in the latter case), highlighting the generality of the bilayer structure. In the case of **6** the $[Eu(H_2O)_9]^{3+}$ ions are threaded throughout the 9.3 Å thick hydrophilic layer and simply replace sodium ions and water found in equivalent positions in **4** and **5**. The principal difference between **5** and **6**, coordination of one of the py-*N*-O ligands to the bridging lanthanide ion, probably results from the dominance of crystal packing forces rather than a steric crowding effect, since the slightly smaller[22a] Tb(III) ion in **7** is able to coordinate two py-*N*-O ligands (*vide infra*), as are the Eu(III) ions in **11**.[21]

$Na_8[Tb_4(py\text{-}N\text{-}O)_4(H_2O)_{18}(p\text{-sulfonatocalix[5]arene})_4]\cdot 52H_2O$. Reaction of $Tb(NO_3)_3\cdot H_2O$ with **1b** and py-*N*-O as for **4**−**6** resulted in the isolation of colorless crystals of the fascinating "supercomplex" $Na_8[Tb_4(py\text{-}N\text{-}O)_4(H_2O)_{18}(p\text{-sulfonatocalix[5]arene})_4]\cdot 2H_2O$ (**7**). Extreme crystallographic difficulties were encountered in obtaining meaningful data for this compound. While multiple samples were found to be strongly diffracting, none of the crystals examined were single. Furthermore, the crystals exhibited extreme sensitivity with respect to loss of solvent while refinement revealed a great deal of disordered enclathrated water. All these factors contribute to an rather high *R* factor for this determination (Table 1). However, the structure of **7** is perhaps one of the most interesting encountered in this work and, while the quantitative parameters are not determined to a high degree of precision, the gross

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(21) Atwood, J. L.; Orr, G. W.; Robinson, K. D. *Supramol. Chem.* **1994**, *3*, 89.

(22) (a) Cotton, S. *Lanthanides and Actinides*, Oxford University Press: New York, 1991. (b) Atwood, J. L.; Orr, G. W.; Juneja, R. K.; Bott, S. G.; Hamada, F. *Pure. Appl. Chem.* **1993**, *65*, 1471.

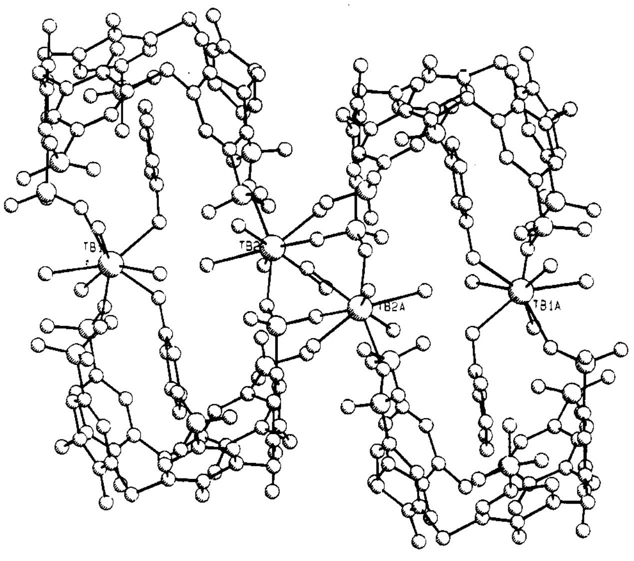

Figure 6. X-ray crystal structure of the supercomplex Na$_8$[Tb$_4$(py-*N*-O)$_4$(H$_2$O)$_{18}$(*p*-sulfonatocalix[5]arene)$_4$]•2H$_2$O showing the two types of bridging Tb(III) ion.

structural details are clear and warrant discussion. As with all the compounds reported, the formulation of **7** is supported by analytical data. Fascinatingly, each host molecule in complex **7** consists of four *p*-sulfonatocalix[5]arene ligands along with four bridging Tb(III) ions which link the structure together, all related in pairs by a crystallographic inversion center, Figure 6. Of the two crystallographically independent, eight-coordinate Tb(III) ions, one of them, Tb(1), situated on the outside of the "supercomplex", bridges between two independent *p*-sulfonatocalix[5]arene 5- anions in a similar way to that observed for both **5** and **6** but is ligated by two py-*N*-O moieties, each of which occupies one of the molecular cavities of the calixarenes, resulting in simultaneous first- and second-sphere coordination of Tb(1) by both calixarene ligands. The other pair of Tb(III) ions, Tb(2) and its symmetry equivalent, are situated at the center of the tetrameric array and engage in a unique triply bridging coordination mode with each metal ion simultaneously binding *via* the sulfonate oxygen atoms to three calixarene ligands. Interestingly, Tb(2) is not coordinated to any py-*N*-O ligands, once again highlighting the dominance of crystal packing forces in the determination of molecular stoichiometry. In general, the bilayer packing arrangement is similar to that observed for complexes **4**−**6**, with an interlayer separation of 15.2 Å and hydrophobic and hydrophilic regions of 6.7 and 8.5 Å, respectively. The relatively narrow hydrophilic layer presumably results from the presence of two bridging metal ions per calixarene pair. A similar effect has been noted for the Mn(II) bridged *p*-sulfonatocalix[4]arene dimer Na$_4$[{Mn(H$_2$O)$_4$-(*p*-sulfonatocalix[4]arene)}$_2$]•.5H$_2$O.[23]

Na$_2$[Yb(py-*N*-O)(H$_2$O)$_6$(calix[5]arene-*p*-sulfonato)]·13H$_2$O. In contrast to the structures of **5**−**7** the product resulting from the interaction of YbCl$_3$·H$_2$O with **1b** in the presence of py-*N*-O, Na$_2$[Yb(py-*N*-O)(H$_2$O)$_6$(calix[5]arene-p-sulfonato)]·13H$_2$O (**8**), involves the first-sphere coordination of the eight coordinate Yb(III) ion to a single calixarene ligand, again *via* one of the sulfonato oxygen atoms, Figure 7. The calixarene is thus capped by a "Yb(H$_2$O)$_6$(py-*N*-O)" moiety instead of a bridging coordination mode of the metal ion between two calixarene units as in **5** and **6**, (Yb−OH$_2$ 2.341(3) Å av, Yb−ONC$_5$H$_5$ 2.275(4) Å, Yb−O$_{\text{calix}}$ 2.313(3) Å). Bond distances to the Yb(III) ion are shorter than the Ln−O distances observed for **5** and **6** consistent with the smaller ionic radius of Yb(III).[22] It is likely that the smaller ionic radius of Yb(III) relative to that of Eu(III) and Gd(III) means that it is not sufficiently large to span the hydrophilic layer of the structure. If this is the case it indicates the high degree of stability possessed by the claylike layered structures adopted by complexes of calix[5]arene sulfonate in the solid state, suggesting that this is the dominant factor in the crystal packing and indeed the determination of the composition of the metal ion coordination spheres. This implies that complexes **4**−**8** are labile in solution, with their stoichiometry and composition becoming fixed upon crystallization. The fact that the packing arrangements are so similar across the series La−Yb is a tribute to the principles of self-assembly in that, even presented with a wide range of metal ions, the same basic crystal packing arrangement is sufficiently robust to accommodate these varying requirements.

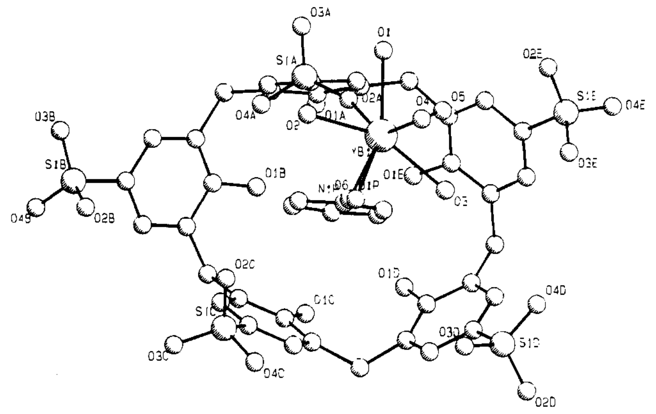

Figure 7. X-ray crystal structure of the [Yb(H$_2$O)$_6$(py-*N*-O)(*p*-sulfonatocalix[5]arene)]$^{2-}$ ion in **8** showing the second sphere coodination of the pyridine *N*-oxide ring by the calixarene.

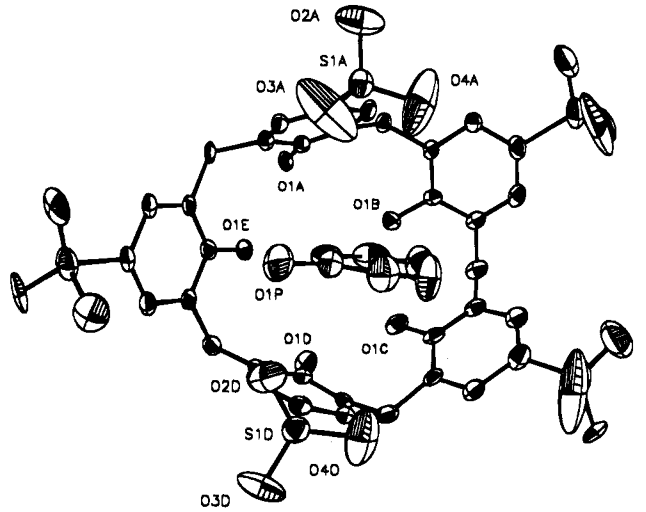

Figure 8. Structure of the 1:1 inclusion complex Na$_5$[calix[5]-arenesulfonato]·py-*N*-O·8.5H$_2$O **3**.

Na$_5$[*p*-sulfonatocalix[5]arene]·py-N-O·8.5H$_2$O. In contrast to the formation of Na$_2$[Zn(H$_2$O)$_4$(py-*N*-O)$_2$][calix[4]arene-*p*-sulfonato]·8.5H$_2$O, reaction of **2** with Zn(NO$_3$)$_2$ and py-*N*-O,[18] results in the separate deposition of crystals of zinc nitrate and the py-*N*-O/*p*-sulfonatocalix[5]arene 1:1 inclusion complex Na$_5$-[calix[5]arenesulfonato]·py-*N*-O·8.5H$_2$O (**3**), Figure 8. While the conformation of the calixarene and geometry of the host−guest interaction is similar to that found for the other py-*N*-O inclusion complexes **4**−**8**, there is a particularly short contact between the py-*N*-O guest oxygen atom and one of the sulfonate groups, O(1P)−O(2D), of only 2.56(1) Å, suggesting a strong

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(23) Iki, H.; Tsuzuki, H.; Kijima, H.; Hamachi, I; Shinkai, S. *Supramol. Chem.* **1994**, *4*, 223.

hydrogen bonding interaction and implying the presence of at least one sulfonic acid proton. The crystal packing in **3** is of the conventional bilayer type seen for **2** and **4**−**8** with the sulfonate groups of single sheets of calixarene units facing one another across a relatively thin hydrophilic layer (7.6 Å, *cf.* 8.6−9.9 Å wide for **2** and **4**−**8**). In the present stage of refinement the aqueous layer is in portions only sparsely filled with sodium ions and water, and it seems likely that there are a number of water molecules and possibly sodium or hydroxonium ions that are unaccounted for, as a consequence of extreme disorder, resulting in the relatively high crystallographic *R* factor for this determination.

Calixarene Conformation. The conformation of the calix[5]arene unit itself in complexes **3**−**8** is considerably different from that observed for **2**. Most notably the near coplanarity of rings B and D in **2** with the O(1A)−O(1E) plane (interplane angle 27.8(3)° av) is much less marked in the remaining structures with two rings forming angles of 30.6−39.1° with the plane containing the phenolic oxygen atoms, while the other three phenolic residues form angles of 55.4−85.2°, suggesting a deeper cup-shaped conformation than for **2**. This difference probably results from the absence of $O(15S)\cdots O_{phenolic}$ hydrogen bonds observed in **2** and the greater bulk of the py-*N*-O guest.

One important consequence of this conformational change is that the cyclic hydrogen bonding network between the phenolic oxygen atoms at the lower rim of the calixarene is significantly disrupted. The $O\cdots O$ contacts at the base of the calix[5]arene unit for complexes **3**−**8** are, without exception, markedly longer than for **2** with hydrogen bonded pairs of oxygen atoms separated by distances of 2.8−3.0 Å (disorder of the py-*N*-O guest in the case of **4** results in two contacts of 3.2 Å rather than one in the vicinity of 3.0 Å), while short contacts are observed to the sulfonate oxygen atoms on neighboring calixarenes and to water molecules (*e.g.* $O(1A)\cdots O(4B)$ 2.713(5), $O(1C)\cdots O(7S)$ 2.666(5) Å for **8**) resulting in a longer $O_{phenolic}\cdots O_{phenolic}$ distance (compared to *ca.* 2.5 Å in **2**) in spite of the fact that all the phenolic oxygen atoms are still protonated.

These observations highlight the importance of host−guest interactions upon gross structural properties of calixarene hosts and may be compared with the conformational modifications undergone by the *p*-sulfonatocalix[4]arene cavity in order to maximize $H_2O\cdots\pi$-hydrogen bonding in **9**[3] and related compounds.[24]

Conclusions

This study has demonstrated that, like related complexes of *p*-sulfonatocalix[4]arene, *p*-sulfonatocalix[5]arene adopts a clay-like bilayer structure in the solid state into which lanthanide ions may be included, generally involving first-sphere coordination of the metal ion to the calixarene sulfonate functionalities. In the solid state the extensive hydrogen bonding networks which serve to knit host, guest, and counterions together play an overriding role and affect not only crystal packing but crystal and molecular stoichiometry. The importance of extremely large-scale self-assembly in such systems cannot be over emphasized. It is quite remarkable that a range of very different structures, based upon the same overriding crystal packing motif, may be obtained *repeatedly* under identical conditions, simply by variation of the identity, and hence ionic radius, of the lanthanide ion. The dominance of crystal packing forces in such systems highlights the problems so often encountered in comparison of solution and solid state data for labile complexes.

Inclusion of py-*N*-O within the large calix[5]arene cavity occurs with the plane of the pyridyl moiety perpendicular to that containing the phenolic oxygen atoms as a consequence of hydrogen bonding or ion−dipole interactions with the py-*N*-O oxygen atom, despite the fact that toluene and benzene are included in a parallel fashion by *p*-alkylcalix[5]arenes.[20b,c] The large calix[5]arene cavity also is too big to accommodate $OH\cdots\pi$ hydrogen bonds to included water molecules and, instead, the calixarene undergoes a conformational change in order to enable the interaction of the included water molecule with the phenolic oxygen atoms.

p-Sulfonatocalix[5]arene possess two readily ionizable phenolic protons, and at neutral pH exists as the $[p\text{-sulfonatocalix[5]arene}]^{7-}$ anion although the acidity of some of the sulfonato and phenolic functionalities may be subject to modification by host−guest interactions. In spite of the relative acidity of at least two phenolic protons, in no case was evidence obtained for a multidentate mode of lanthanide complexation by the calixarene involving the phenolic oxygen atoms as suggested by Shinkai *et al.*,[4] and it seems clear that the sulfonato groups are the preferred binding sites at least under somewhat acidic, aqueous conditions. The X-ray crystal structure determination of complex **2** does, however, demonstrate that, unlike *p*-sulfonatocalix[6]arene,[7] *p*-sulfonatocalix[5]arene is, to some extent, preorganized to chelate a metal center.

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Supporting Information Available: Crystallographic summary for **2**−**8**, including tables of crystal data and structure refinement, atomic coordinates and equivalent isotropic displacement parameters, bond lengths and angles, anisotropic displacement parameters and hydrogen atom coordinates, and isotropic displacement parameters (88 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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