

# NMR and Crystallographic Studies of a *p*-Sulfonatocalix[4]arene-Guest Complex

Seiji Shinkai,<sup>\*1</sup> Koji Araki,<sup>1</sup> Tsutomu Matsuda,<sup>1</sup> Nobuaki Nishiyama,<sup>2</sup> Hiroataka Ikeda,<sup>3</sup> Isao Takasu,<sup>4</sup> and Masakazu Iwamoto<sup>4</sup>

Contribution from the Department of Organic Synthesis, Faculty of Engineering, Kyushu University, Fukuoka 812, Japan, Center of Advanced Instrumental Analysis, Kyushu University, Kasuga, Fukuoka 816, Japan, Department of Physics, Faculty of Sciences, Kyushu University, Fukuoka 812, Japan, and Department of Industrial Chemistry, Faculty of Engineering, Miyazaki University, Miyazaki 889-21, Japan. Received June 7, 1990

**Abstract:** The <sup>1</sup>H and <sup>13</sup>C NMR spectra of a complex formed from tetrasodium *p*-sulfonatocalix[4]arene (**1**<sub>4</sub>) and trimethylanilinium chloride (**2**) in D<sub>2</sub>O showed that **2** is bound to the cavity of cone-shaped **1**<sub>4</sub>: in the acidic pH region (pD 0.4) the phenyl moiety resides in the cavity, whereas in the neutral pH region (pD 7.3) both the trimethylammonium and the phenyl moiety are included nonspecifically in the cavity. The difference was accounted for by the change in the electron density in the benzene π-systems induced by the dissociation of OH groups. The complex was crystallized from acidic aqueous solution. The solid-state <sup>13</sup>C NMR (CP-MAS) supports the inclusion of the phenyl moiety in the cavity. The X-ray crystallographic studies established that (i) **1**<sub>4</sub> adopts a cone conformation, (ii) **1**<sub>4</sub> and **2** form a host-guest-type complex with the phenyl moiety inserted into the cavity, (iii) not only the hydrophobic force but also the electrostatic force operates for guest inclusion, and (iv) the overall structure is similar to that of clays, **1**<sub>4</sub> molecules being arranged into bilayers. These findings serve as a useful cross-link between solution complexes and solid-state complexes.

Calixarenes are cyclic oligomers made from phenol and formaldehyde which belong to the class of [1<sub>n</sub>]metacyclophanes. Since they have a characteristic cavity-shaped architecture, they have been expected to be useful as a basic skeleton in the design of new functionalized host molecules.<sup>5-8</sup> Solid-state complexes of calixarenes have been known for many years, the first unequivocal demonstration of their structure having been provided by the X-ray crystallographic work of Andreotti and co-workers.<sup>9</sup> Evidence for complexation in solution, however, has been obtained more slowly. The earliest examples appeared only in the mid 1980s and involved both aqueous systems with water soluble sulfonatocalixarenes<sup>10,11</sup> and nonaqueous systems with calix[4]arenes and amines.<sup>12</sup> Several additional examples have appeared more recently.<sup>13-15</sup> Interest in this laboratory has centered mainly on water-soluble calixarenes, resulting from our synthesis in 1984 of calixarenes carrying sulfonate groups<sup>10</sup> simultaneously with the synthesis of Ungaro and co-workers<sup>13a</sup> of calixarenes carrying carboxyl groups. Aqueous systems are particularly interesting for complexation studies because one can expect hydrophobic forces to play an important role.

**Table I.** <sup>1</sup>H NMR Chemical Shifts of **2** in D<sub>2</sub>O<sup>a</sup>

sample	pD	δ (ppm) of <b>2</b>			
		<i>o</i> -H	<i>m</i> -H	<i>p</i> -H	N <sup>+</sup> CH <sub>3</sub>
<b>2</b>	0.4	7.86	7.67	7.62	3.67
<b>2</b>	7.3	7.82	7.65	7.61	3.64
<b>2</b> + <b>1</b> <sub>4</sub>	0.4	7.04	6.05	5.20	3.42
<b>2</b> + <b>1</b> <sub>4</sub>	7.3	6.95	6.79	6.46	2.54
Δδ (ppm) of <b>2</b> induced by <b>1</b> <sub>4</sub> <sup>b</sup>					
pD	<i>o</i> -H	<i>m</i> -H	<i>p</i> -H	N <sup>+</sup> CH <sub>3</sub>	
0.4	-0.82	-1.62	-2.42	-0.25	
7.3	-0.87	-0.86	-1.15	-1.10	

<sup>a</sup> 30 °C, [**2**] = [**1**<sub>4</sub>] (when added) = 1.0 mM, 1 M DCl/D<sub>2</sub>O for pD 0.4, 0.1 M phosphate buffer for pD 7.3. Judging from the association constants,<sup>14</sup> more than 98% of **2** is included in the cavity of **2** under the measurement conditions. <sup>b</sup> The negative value denotes the shift to the higher magnetic field.

We have recently estimated the association constants (*K*) for aqueous complexes with *p*-sulfonatocalix[*n*]arenes (**1**<sub>*n*</sub>; *n* = 4, 6, and 8) by the NMR method.<sup>14,15</sup> The purpose of this investigation was to determine if the calixarene cavity is capable of molecular recognition in solution, and it has been found that **1**<sub>4</sub> and **1**<sub>6</sub> form 1:1 complexes with guest molecules such as trimethylanilinium chloride (**2**) and 1-adamantyltrimethylammonium chloride, whereas **1**<sub>8</sub> forms 1:2 **1**<sub>8</sub>-guest complexes. The association con-

- (1) Faculty of Engineering, Kyushu University.
- (2) Center of Advanced Instrumental Analysis, Kyushu University.
- (3) Faculty of Sciences, Kyushu University.
- (4) Miyazaki University.
- (5) Gutsche, C. D. *Acc. Chem. Res.* **1983**, *16*, 161.
- (6) (a) Gutsche, C. D. In *Synthesis of Macrocycles: The Design of Selective Complexing Agents*; Izatt, R. M., Christensen, J. J., Eds.; John Wiley & Sons Inc.: New York, 1987; p 93. (b) Gutsche, C. D. In *Calixarenes*; Royal Society of Chemistry: Cambridge, 1989.
- (7) Shinkai, S. *Pure Appl. Chem.* **1986**, *58*, 1523.
- (8) Shinkai, S.; Manabe, O. *Nippon Kagaku Kaishi* **1988**, 1917.
- (9) (a) Ungaro, R.; Pochini, A.; Andreotti, G. D.; Domiano, P. *J. Chem. Soc., Perkin Trans. 2* **1985**, 197. (b) Andreotti, G. D.; Ungaro, R.; Pochini, A. *J. Chem. Soc., Chem. Commun.* **1979**, 1005. (c) Coruzzi, M.; Andreotti, G. D.; Bocchi, V.; Pochini, A.; Ungaro, R. *J. Chem. Soc., Perkin Trans. 2* **1982**, 1133. (d) In *p*-(1,1,3,3-tetramethylbutyl)calix[4]arene the guest molecule (toluene) is not trapped in the calixarene cavity but in the crystal lattice: Andreotti, G. D.; Pochini, A.; Ungaro, R. *J. Chem. Soc., Perkin Trans. 2* **1983**, 1773.
- (10) Shinkai, S.; Mori, S.; Tsubaki, T.; Sone, T.; Manabe, O. *Tetrahedron Lett.* **1984**, *25*, 5315.
- (11) Shinkai, S.; Mori, S.; Koricshi, H.; Tsubaki, T.; Manabe, O. *J. Am. Chem. Soc.* **1984**, *108*, 2409.
- (12) Bauer and Gutsche reported inclusion of *tert*-butylamine in calix[4]arenes, but the driving force for inclusion is supposed to a combination of proton transfer plus electrostatic attraction: Bauer, L. J.; Gutsche, C. D. *J. Am. Chem. Soc.* **1985**, *107*, 6063.

- (13) Water-soluble calixarenes and its analogues bearing hydrophilic groups such as SO<sub>3</sub><sup>-</sup>, COO<sup>-</sup>, PO<sub>3</sub><sup>-</sup>, SO<sub>2</sub>N(CH<sub>2</sub>CH<sub>2</sub>OH)<sub>2</sub>, etc. were subsequently synthesized. (a) Arduini, A.; Reverberi, S.; Ungaro, R. *J. Chem. Soc., Chem. Commun.* **1984**, 981. (b) Gutsche, C. D.; Alam, I. *Tetrahedron* **1988**, *44*, 4689. (c) Poh, B.-L.; Lim, C. S.; Khoo, K. S. *Tetrahedron Lett.* **1988**, *44*, 4689. (d) Almi, M.; Arduini, A.; Casnati, A.; Pochini, A.; Ungaro, R. *Tetrahedron* **1989**, *45*, 2177. (e) Arimura, T.; Nagasaki, T.; Shinkai, S.; Matsuda, T. *J. Org. Chem.* **1989**, *54*, 3766. (f) Shinkai, S.; Kawabata, H.; Matsuda, T.; Kawaguchi, H.; Manabe, O. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 1272. Water-soluble calixarenes with cationic charges were also synthesized. (g) Shinkai, S.; Arimura, T.; Araki, K.; Kawabata, H.; Satoh, H.; Tsubaki, T.; Manabe, O.; Sunamoto, J. *J. Chem. Soc., Perkin Trans. 1* **1989**, 2039. (h) Shinkai, S.; Shirahama, Y.; Tsubaki, T.; Manabe, O. *J. Am. Chem. Soc.* **1989**, *111*, 5477.
- (14) Shinkai, S.; Araki, K.; Manabe, O. *J. Am. Chem. Soc.* **1988**, *110*, 7214.
- (15) Shinkai, S.; Araki, K.; Matsuda, T.; Manabe, O. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 3856.

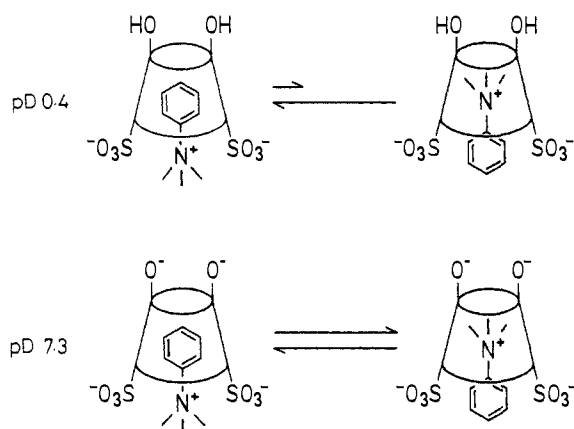


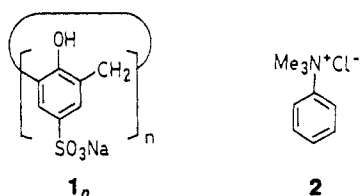
Figure 1. Complexation of **1<sub>4</sub>** with **2** in acidic and neutral pH solutions.

Table II. <sup>13</sup>C NMR Chemical Shifts of **2**

		δ (ppm) of <b>2</b>				
sample	state	C <sub>1</sub>	C <sub>2</sub>	C <sub>3</sub>	C <sub>4</sub>	C <sub>5</sub>
<b>2</b>	D <sub>2</sub> O (pD 0.4) <sup>a</sup>	67.32	156.85	129.84	140.77	140.77
<b>2 + 1<sub>4</sub></b>	D <sub>2</sub> O (pD 0.4) <sup>a</sup>	66.65	155.39	128.31	138.89	138.40
<b>2 + 1<sub>4</sub></b>	solid	56.90	146.39	<i>b</i>	128.28	128.38
		Δ δ (ppm) of <b>2</b> induced by <b>1<sub>4</sub></b> <sup>c</sup>				
		C <sub>1</sub>	C <sub>2</sub>	C <sub>3</sub>	C <sub>4</sub>	C <sub>5</sub>
D <sub>2</sub> O (pD 0.4)		-0.67	-1.46	-1.53	-1.88	-2.37
solid <sup>d</sup>		-10.42	-10.46	<i>b</i>	-12.39	-12.39

<sup>a</sup> 30 °C. [**2**] = [**1<sub>4</sub>**] (when added) = 166 mM, 1 M DCl/D<sub>2</sub>O. <sup>b</sup> The peak could not be found probably because of a vigorous thermal motion. In fact, the general temperature factor for this carbon is much greater than those for other carbons. <sup>c</sup> The negative value denotes the shift to the higher magnetic field. <sup>d</sup> The values are compared with δ for **2** in D<sub>2</sub>O.

stants were  $(5.5\text{--}56.0) \times 10^2 \text{ M}^{-1}$ . These findings support the view that calixarenes (**1<sub>n</sub>**'s) are capable of molecular recognition on



the basis of the ring size. To obtain further insights into calixarene-guest interactions we have carried out X-ray crystallographic studies of a **1<sub>4</sub>**-**2** complex, hoping to establish a cross-link between the solution complex we previously examined and the solid-state complex.

## Experimental Section

The synthesis of **1<sub>4</sub>** was reported previously.<sup>16</sup> The crystals for X-ray analysis and solid-state <sup>13</sup>C NMR were grown from acidic aqueous solution (10 M HCl) containing **1<sub>4</sub>** and **2** in a 1:1 molar ratio. Large, colorless crystals were thus obtained, the crystal system being triclinic: mp > 300 °C. Anal. Calcd for (C<sub>7</sub>H<sub>5</sub>O<sub>4</sub>SNa)<sub>4</sub>·C<sub>4</sub>H<sub>14</sub>NCl·12H<sub>2</sub>O: C, 36.40; H, 4.79; N, 1.15. Found: C, 36.50; H, 4.60; N, 1.16.

The <sup>1</sup>H and <sup>13</sup>C NMR spectra in D<sub>2</sub>O solution were measured with a JEOL GX-400 NMR apparatus. The solid-state <sup>13</sup>C NMR spectra

Table III. Crystal Data

chemical formula	C <sub>28</sub> H <sub>24</sub> O <sub>16</sub> S <sub>4</sub> Na <sub>4</sub> ·C <sub>10</sub> H <sub>17</sub> NCl
f-w	1023.39
crystal system	triclinic
space group	P $\bar{1}$
cell dimensions	
<i>a</i> , Å	12.559 (4)
<i>b</i> , Å	15.127 (3)
<i>c</i> , Å	11.863 (4)
α, deg	97.72 (2)
β, deg	92.27 (3)
γ, deg	93.82 (2)
<i>Z</i>	2
<i>D<sub>c</sub></i> , g cm <sup>-3</sup>	1.794
<i>R</i> , %	15.6

Table IV. Bond Lengths (Å) with Estimated Standard Deviations in Parentheses

C2-C3	1.35 (2)	C22-C21	1.32 (2)	S2-O23	1.433 (15)
C2-C1	1.44 (2)	C6-C5	1.38 (2)	S4-O42	1.39 (2)
C20-C19	1.38 (2)	C6-C1	1.35 (2)	S4-O41	1.47 (2)
C20-C21	1.41 (2)	C5-C01	1.53 (2)	S4-O43	1.40 (2)
C24-C23	1.39 (2)	C17-C18	1.42 (2)	S1-O11	1.36 (2)
C24-C19	1.42 (2)	C17-S4	1.762 (15)	S1-O13	1.31 (2)
C24-O2	1.37 (2)	C14-C13	1.34 (2)	S1-O12	1.46 (2)
C3-C4	1.41 (2)	C14-O4	1.42 (2)	S3-O31	1.42 (2)
C3-C04	1.50 (2)	C23-C02	1.52 (2)	S3-O33	1.40 (2)
C4-C5	1.44 (2)	C10-C11	1.39 (2)	S3-O32	1.36 (2)
C4-O1	1.327 (15)	C10-C9	1.32 (2)	N1-C38	1.49 (2)
C8-C7	1.38 (2)	C13-C18	1.38 (2)	N1-C30	1.53 (2)
C8-C9	1.41 (2)	C13-C03	1.54 (2)	N1-C36	1.49 (2)
C15-C16	1.37 (2)	C19-C01	1.54 (2)	N1-C37	1.55 (2)
C15-C14	1.40 (2)	C11-C03	1.53 (2)	C30-C31	1.28 (3)
C15-C02	1.53 (2)	C7-C04	1.54 (2)	C30-C35	1.42 (3)
C16-C17	1.42 (2)	C9-S3	1.797 (14)	C31-C32	1.30 (3)
C12-C11	1.39 (2)	C1-S1	1.774 (14)	C32-C33	1.21 (4)
C12-C7	1.46 (2)	C21-S2	1.784 (15)	C33-C34	1.54 (4)
C12-O3	1.315 (15)	S2-O21	1.429 (14)	C35-C34	1.47 (4)
C22-C23	1.41 (2)	S2-O22	1.417 (14)	C1-Na1	2.38 (3)

were measured with a Bruker PC-250. The <sup>13</sup>C cross-polarization/magic angle spinning NMR spectra were recorded at 30 °C with a CP-MAS method: the crystalline powder sample was contained in a bullet-type rotor and spun at 3.5 kHz. Contact time was 3 ms, and repetition time was 5 s. The <sup>13</sup>C chemical shifts were calibrated indirectly through external TMS.

The crystals in aqueous solution were initially quite clear and transparent, but they became cloudy in the air. Therefore, we put the solution containing these crystals into a glass capillary (diameter 1 mm) and sealed it with an adhesive agent. Integral intensities were collected by using graphite-monochromatized Cu Kα radiation by the  $\theta$ - $2\theta$  scan technique up to  $2\theta = 120^\circ$ . Of the 6964 reflections measured, the number of reflections observed was 3814 ( $I > 3\sigma(I)$ , where  $\sigma$  is the standard deviation observed from the counting statistics). The structure was solved by the direct method (MULTAN 78). Then, the structure was refined by the full-matrix least-squares procedure with anisotropic thermal parameters. All calculations were performed on a PDP 11/23 PLUS computer with the Enraf-Nonius SDP-PLUS program package. The final *R* value (0.156) was not particularly precise because of the background arising from the aqueous solution and the glass tube, but the ORTEP view has sufficient precision for the discussion of molecular recognition occurring in a water-soluble calix[4]arene.

For a computer graphics, MODRAST-E (developed by Professor Hidehiko Nakano (Himeji Institute of Technology)) was used.

## Results and Discussion

**<sup>1</sup>H and <sup>13</sup>C NMR Spectra of a **1<sub>4</sub>**-**2** Complex.** We previously found that in aqueous solution **1<sub>4</sub>** adopts a "cone" conformation irrespective of the pH of the medium.<sup>15</sup> To clarify how compound **2** is bound to the cone-shaped cavity, we first examined the NMR spectra. The data are summarized in Table I. In the absence of **1<sub>4</sub>** the chemical shifts of **2** are scarcely affected by the pH of the medium. In the presence of **1<sub>4</sub>**, in contrast, the chemical shifts become surprisingly pH-dependent: all resonance peaks move to a higher magnetic field, indicating that **2** is included in the cavity of **1<sub>4</sub>** and affected by the ring current of the aromatic components.

(16) Shinkai, S.; Araki, K.; Tsubaki, T.; Arimura, T.; Manabe, O. *J. Chem. Soc., Perkin Trans. 1* 1987, 2297.

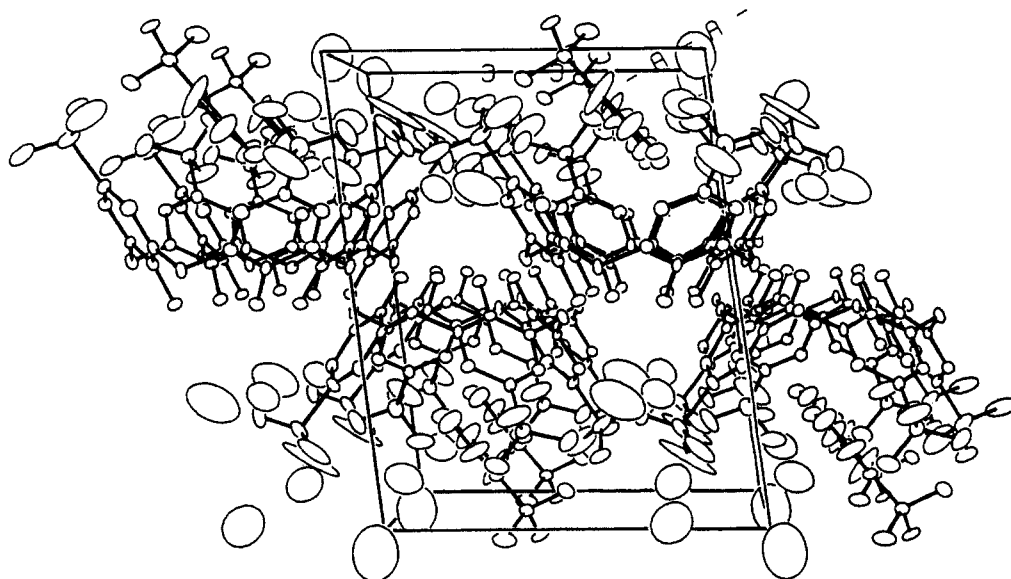


Figure 2. ORTEP view from the A-axis.

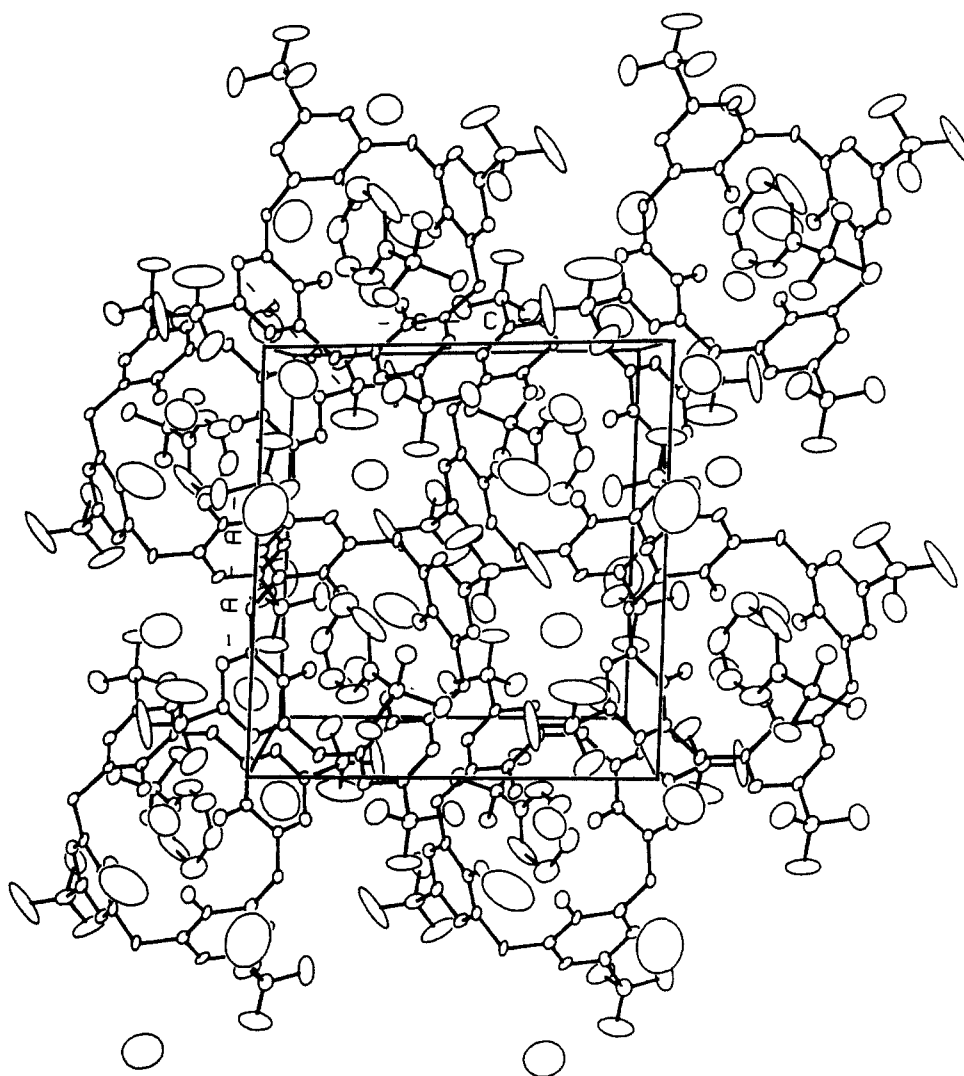


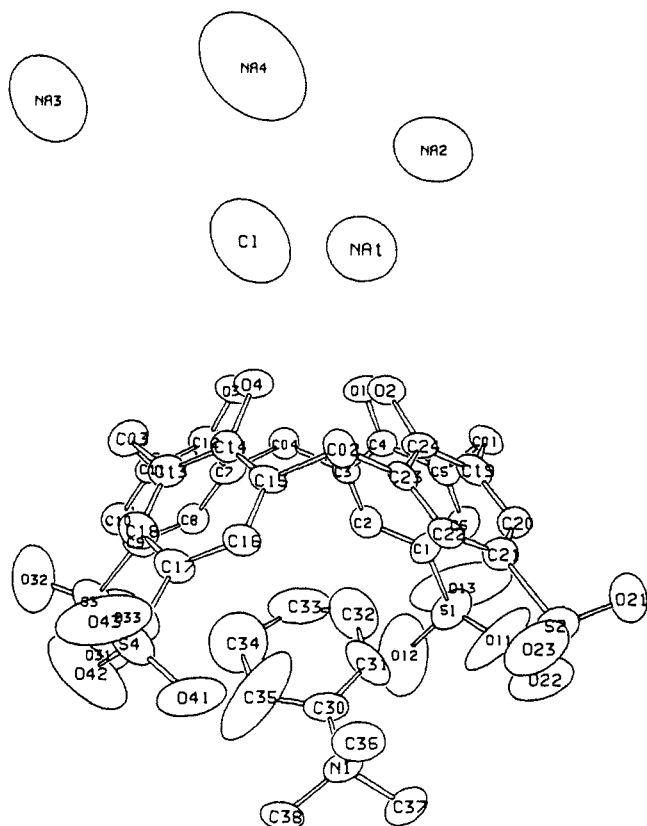
Figure 3. ORTEP view from the B-axis.

Careful examination of each chemical shift reveals that *in acidic aqueous solution* the peaks assignable to aromatic protons specifically shift to the higher magnetic field ( $p\text{-H} > m\text{-H} > o\text{-H} > \text{N}^+\text{-CH}_3$ ), whereas *in neutral aqueous solution* both ammoniomethyl and aromatic protons shift nonspecifically to the higher

magnetic field. The results substantiate that in acidic aqueous solution the phenyl moiety is selectively bound to the calixarene cavity, whereas in neutral aqueous solution both the ammoniomethyl and the phenyl moiety are nonselectively bound to the calixarene cavity (Figure 1).

Table V. Bond Angles (deg) with Estimated Standard Deviations in Parentheses

C3-C2-C1	119.0 (1)	C4-C5-C01	119.0 (1)	C8-C7-C12	117.0 (1)
118.0 (1)	118.0 (1)	C6-C5-C01	121.0 (1)	C8-C7-C04	122.0 (1)
C23-C24-C19	122.0 (1)	C16-C17-C18	122.0 (1)	C12-C7-C04	120.0 (1)
C23-C24-O2	122.0 (1)	C16-C17-C4	120.0 (1)	C8-C8-C10	123.0 (1)
C19-C24-O2	116.0 (1)	C18-C17-S4	119.0 (1)	C8-C9-S3	118.0 (1)
C2-C3-C4	120.0 (1)	C15-C14-C13	124.0 (1)	C10-C9-S3	119.0 (1)
C2-C3-C04	120.0 (1)	C15-C14-O4	118.0 (1)	C2-C1-C6	112.0 (1)
C4-C3-C04	120.0 (1)	C13-C14-O4	119.0 (1)	C2-C1-S1	118.0 (1)
C3-C4-C5	120.0 (1)	C24-C23-C22	116.0 (1)	C6-C1-S1	120.0 (1)
C3-C4-O1	119.0 (1)	C24-C23-C02	122.0 (1)	C20-C21-C22	122.0 (1)
C5-C4-O1	121.0 (1)	C22-C23-C02	122.0 (1)	C20-C21-S2	117.0 (1)
C7-C8-C9	120.0 (1)	C11-C10-C9	120.0 (1)	C22-C21-S2	121.0 (1)
C16-C15-C14	120.0 (1)	C14-C13-C18	119.0 (1)	C21-S2-O21	105.2 (8)
C16-C15-C02	119.0 (1)	C14-C13-C03	124.0 (1)	C21-S2-O22	106.6 (8)
C14-C15-C02	121.0 (1)	C18-C13-C03	117.0 (1)	C21-S2-O23	106.5 (8)
C15-C16-C17	117.0 (1)	C20-C19-C24	119.0 (1)	O21-S2-O22	115.0 (1)
C11-C12-C7	119.0 (1)	C20-C19-C01	120.0 (1)	O21-S2-O23	115.0 (1)
C11-C12-O3	120.0 (1)	C24-C19-C01	121.0 (1)	O22-S2-O23	107.8 (9)
C7-C12-O3	121.0 (1)	C17-C19-C13	119.0 (1)	C17-S4-O42	109.0 (1)
C23-C22-C21	123.0 (1)	C12-C11-C10	120.0 (1)	C17-S4-O41	106.2 (8)
C5-C6-C1	120.0 (1)	C12-C11-C03	120.0 (1)	C17-S4-O43	104.8 (8)
C4-C5-C6	119.0 (1)	C10-C11-C03	120.0 (1)	O42-S4-O41	103.0 (1)
O42-S4-O43	121.0 (1)	C31-S3-O33	105.0 (1)	C30-N1-C37	110.0 (1)
O41-S4-O43	112.0 (1)	O31-S3-O32	113.0 (1)	C36-N1-C37	111.0 (1)
C1-S1-O11	107.9 (9)	O33-S3-O32	120.0 (1)	N1-C30-C31	127.0 (2)
C1-S1-O31	107.0 (1)	O13-S03-O11	110.0 (1)	N1-C30-C35	116.0 (2)
C1-S1-O12	105.0 (1)	C15-C02-O23	113.0 (1)	C31-C30-C35	116.0 (2)
O11-S14-O13	121.0 (2)	C3-C04-C7	113.0 (1)	C30-C31-C32	128.0 (2)
O11-S1-O12	100.0 (1)	C5-C01-C19	114.0 (1)	C31-C32-C33	123.0 (2)
C13-S1-O12	115.0 (2)	C38-N1-C30	112.0 (1)	C32-C33-C34	119.0 (2)
C9-S3-O31	103.0 (8)	C38-N1-C36	107.0 (1)	C30-C35-C34	119.0 (2)
C9-S3-O33	107.9 (9)	C38-N1-C37	108.0 (1)	C33-C34-C35	112.0 (2)
C9-S3-O32	107.0 (1)	C30-N1-C36	109.0 (1)		

Figure 4. ORTEP view of the  $1_4 \cdot 2$  complex.

Why is such a change in a binding manner induced by changes in the pD of the medium? According to the titration data,<sup>17</sup> none or one of the four OH groups is dissociated at pD 0.4, whereas three of them are dissociated at pD 7.3. Hence, the hydrophobic force acts as the sole driving force for complexation in acidic aqueous solution. In neutral aqueous solution, on the other hand, the benzene  $\pi$ -systems become considerably electron-rich because

of the dissociated oxyanions. According to Dougherty and co-workers,<sup>18-20</sup> ammonium cations are bound to the cavity composed of electron-rich benzene  $\pi$ -systems owing to electrostatic interactions. Thus, the ammonium group in **2** can also be included at pD 7.3. This situation results in nonspecific inclusion of **2**: both the phenyl and the ammonium moiety can be bound to the cavity of **1**<sub>4</sub>, the driving forces being both the hydrophobic interactions and the electrostatic attractions.

<sup>13</sup>C NMR spectral data are summarized in Table II. The assignment of each peak was made on the basis of a two-dimensional NMR spectrum between <sup>1</sup>H and <sup>13</sup>C. The magnitude of the up field shift induced by **1**<sub>4</sub> in acidic aqueous solution is on the order of C<sub>5</sub> > C<sub>4</sub> > C<sub>3</sub> > C<sub>2</sub> > C<sub>1</sub> (for the numbering system, see Table II). This order shows good agreement with the <sup>1</sup>H NMR data, supporting the view that the phenyl moiety is selectively included in the cavity.

The crystals used for X-ray analysis, which were grown up in acidic aqueous solution, were also used for the solid-state <sup>13</sup>C NMR measurements. As summarized in Table II, the spectrum is similar to that in acidic aqueous solution although all peaks shift to the higher magnetic field. In particular, the up field shift observed for C<sub>4</sub> and C<sub>5</sub> is greater than that observed for C<sub>1</sub> and C<sub>2</sub>. The result is also compatible with inclusion of the phenyl moiety.

**Crystal Structure of a  $1_4 \cdot 2$  Complex.** The X-ray crystallographic studies that have been reported have shown that in the solid state *p*-*tert*-butylcalix[*n*]arenes and their analogues are capable of inclusion of small molecules such as chloroform, acetone, toluene, anisole, etc.<sup>5,6,9,21,22</sup> In solution, on the other

(17) Shinkai, S.; Araki, K.; Koreishi, H.; Tsubaki, T.; Manabe, O. *Chem. Lett.* **1986**, 1351.

(18) Stauffer, D. A.; Dougherty, D. A. *Tetrahedron Lett.* **1988**, 29, 6063.

(19) Petti, M. A.; Sheppard, T. J.; Barrans, R. E., Jr.; Dougherty, D. A. *J. Am. Chem. Soc.* **1988**, 110, 6825.

(20) Sheppard, T. J.; Petti, M. A.; Dougherty, D. A. *J. Am. Chem. Soc.* **1986**, 108, 6085.

(21) McKervy, M. A.; Seward, E.; Ferguson, G.; Ruhl, B. L. *J. Org. Chem.* **1986**, 51, 3581.

(22) (a) Bott, S. G.; Coleman, A. W.; Atwood, J. L. *J. Am. Chem. Soc.* **1986**, 108, 1709. (b) Coleman, A. W.; Bott, S. G.; Atwood, J. L. *J. Inclusion Phenom.* **1986**, 4, 247.

**Table VI.** Distances from N1 in **2** to Sulfonate Oxygens

sulfonate oxygen	distance, Å	sulfonate oxygen	distance, Å
O11	7.162	O31	7.190
O12	6.984	O32	9.286
O13	8.939	O33	8.639
O21	6.288	O41	3.695
O22	4.117	O42	5.202
O23	4.680	O43	6.028

**Table VII.** Distances from Na<sup>+</sup> to Cl<sup>-</sup> and Sulfonate Oxygens

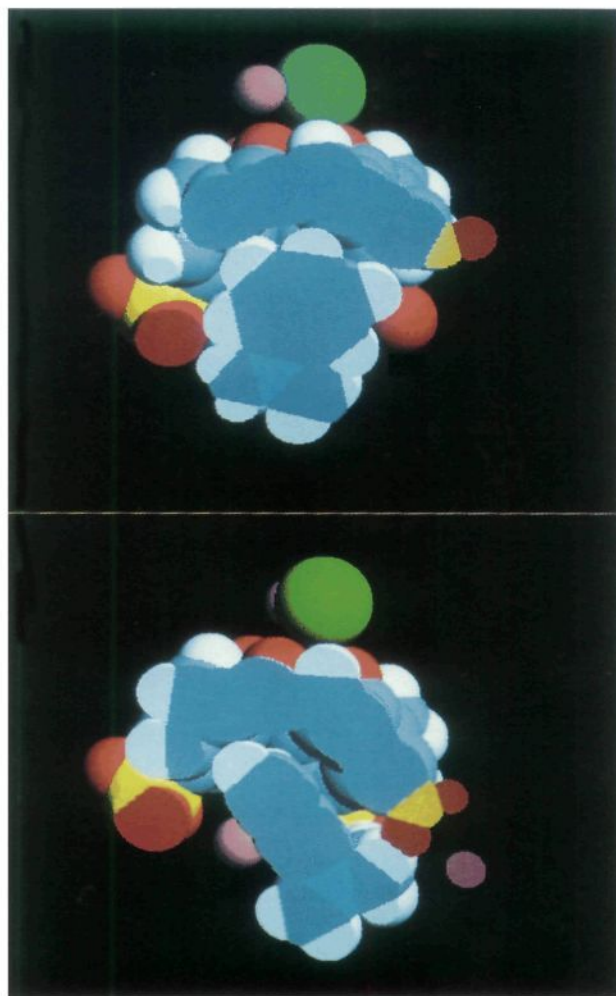
atoms	distance, Å	atoms	distance, Å
Na1-C1	2.378	Na3-O12	2.126
Na2-O11	3.125	Na3-O41	2.570
Na2-O22	2.874	Na4-O31	2.362

hand, there are no published data in support of inclusion of these guest molecules in *p*-*tert*-butylcalix[*n*]arenes. Conceivably, inclusion in *p*-*tert*-butylcalix[*n*]arenes must compete with solvation, and, in most cases, solvation energy is greater than stabilization energy brought forth by inclusion in the calixarene cavities. The sole exception is the inclusion of *tert*-butylamine reported by Bauer and Gutsche.<sup>12</sup> In contrast, compounds **1**<sub>*n*</sub> form host-guest-type complexes in water owing to the hydrophobic force broadly operating on organic molecules,<sup>7,8,10,11,14,15</sup> but such complexes have never been crystallized. Therefore, there are no useful data which can provide a cross-link between the solid-state inclusion complex and the solution complex. It thus occurred to us that if the **1**<sub>4</sub>·**2** complex could be crystallized, its crystal structure would provide important information for understanding how the complex is formed in aqueous solution.

The crystal structure of **1**<sub>4</sub> has been reported by Atwood et al.<sup>23</sup> According to their structure determination, **1**<sub>4</sub> adopts a cone conformation.<sup>23</sup> Interestingly, the crystal system forms a bilayer with a 15-Å repeat unit, which closely mimics the structural behavior of clays: the calix[4]arene rings form two hydrophobic layers, and the sulfonate groups form a hydrophilic layer.<sup>23</sup> The crystal data obtained from the **1**<sub>4</sub>·**2** complex are summarized in Table III. The crystal system is triclinic (space group *P*1) and different from the monoclinic *C*2/*c* or *P*2<sub>1</sub>/*n* obtained for **1**<sub>4</sub>.<sup>23</sup> Bond lengths and bond angles are reported in Tables IV and V, respectively (for the numbering system see Figure 4). The ORTEP views from the A- and B-axis are shown in Figures 2 and 3, respectively, and a **1**<sub>4</sub>·**2** complex is drawn in Figure 4.

A number of interesting points can be raised about the X-ray structure. Firstly, it is seen from Figure 4 that **1**<sub>4</sub> adopts a cone conformation. In aqueous solution, it is known that **1**<sub>4</sub> favorably adopts the cone conformation because of stabilization by intramolecular hydrogen-bonding interactions among OH groups.<sup>14,15</sup> The cone structure is further stabilized by inclusion of guest molecules.<sup>15</sup> Figure 4 shows that this is also the case in the crystal state. The four bond angles for the Ar-CH<sub>2</sub>-Ar linkage (Table V) are 114° for C5-C01-C19, 113° for C15-C02-C23, 110° for C13-C03-C11, and 113° for C3-C04-C7. This indicates that the cylinder is slightly distorted from C<sub>4v</sub> symmetry. The phenyl moiety in **2** is placed exactly in the cone-shaped cavity, and C32 (facing C5-C01-C19) is inserted into the cavity more deeply than C34 (facing C11-C03-C13). The bond angle for C5-C01-C19 is greater than that for C11-C03-C13. This implies that the C5-C01-C19 bond angle is expanded so that the cavity can allow deep insertion of the guest molecule.

Secondly important is the fact that **2** is included in the cavity. As described above, calix[*n*]arenes can be crystallized with small organic molecules, but they are included not only in the cavity (*endo*-calix complexes) but also in the void of the crystal lattice



**Figure 5.** Computer-graphic illustration of the **1**<sub>4</sub>·**2** complex with van der Waals radii cut in the plane of and at right angles to the phenyl moiety of **2** (upper and lower, respectively): N (blue), O (red), S (yellow), Na (purple), and Cl (green).

formed outside calix[*n*]arenes (*exo*-calix complexes).<sup>9,21,22</sup> At present, it is difficult to predict which complex will be formed in the crystal state, the "*endo*-calix" complex or the "*exo*-calix" complex. In a **1**<sub>4</sub>·**2** complex, on the other hand, we have established that it forms a host-guest-type complex in aqueous media.<sup>14,15</sup> The sample used for X-ray analysis was prepared from acidic aqueous solution, so that it could reflect the association mode occurring in acidic aqueous solution. As expected, **2** is bound to **1**<sub>4</sub> with the phenyl moiety inserting into the cavity. This suggests that the hydrophobic force is a primary driving force for complexation. The C-H bond length in benzene is 1.20 Å.<sup>24</sup> The half thickness of the benzene π-system is 1.70 Å.<sup>24</sup> When the aromatic protons in **2** are brought into contact with the benzene π-systems in **1**<sub>4</sub>, the distance between the aromatic carbons in **2** and those in **1**<sub>4</sub> should be about 2.9 Å. This is the case in the **1**<sub>4</sub>·**2** complex: the calculation from the table of positional parameters gives 2.832 Å for C6-C32, 2.867 Å for C5-C32, 2.900 Å for C7-C33, and 2.908 Å for C10-C34. These results support the view that at least three aromatic hydrogens (C32, C33, and C34) are in contact with the benzene π-systems in **1**<sub>4</sub>. To obtain further insights into the hydrophobic interaction we used a computer-graphic technique adding the van der Waals radii to a ball-and-stick model in Figure 4. Two pictures in Figure 5 show cross sections of the **1**<sub>4</sub>·**2** complex cut in the plane of and at right angles

(23) (a) Bott, S. G.; Coleman, A. W.; Atwood, J. L. *J. Am. Chem. Soc.* **1988**, *110*, 610. (b) Coleman, A.; Bott, S. G.; Morley, S. D.; Means, C. M.; Robinson, K. D.; Zhang, H.; Atwood, J. L. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1361. In these papers **1**<sub>4</sub> was crystallized with MeOSO<sub>3</sub><sup>-</sup> or acetone present in crystallization solvents. However, the host-guest-type inclusion properties of these small molecules were not investigated in aqueous solution.

(24) In *Kagaku Binran (Chemistry Data Tables)*; Chemical Society of Japan, Ed.; Maruzen: Tokyo, 1966.

to the phenyl moiety. It is seen from Figure 5 that *m*-H's on C32 and C34 and *p*-H on C33 are in contact with  $\pi$ -systems in calixarene phenyl rings. This supports the view that the hydrophobic force is indispensable to the complex formation.

The third point is related to the question of whether the electrostatic force also operates. We calculated distances from cationic N1 in **2** to anionic sulfonate oxygens. The results (Table VI) indicate that the distance to O41 in S(4)O<sub>3</sub><sup>-</sup> is shortest and those to O22 and O23 in S(2)O<sub>3</sub><sup>-</sup> are the next. This suggests that the ammonium cation is bound to an electrostatic pocket formed by S(4)O<sub>3</sub><sup>-</sup> and S(2)O<sub>3</sub><sup>-</sup>. Thus, one can safely conclude that the electrostatic force also operates on the complex formation. We calculated distances from sodium cations to sulfonate oxygens. The results (Table VII) show that Na1 forms an ion pair with C1<sup>-</sup>, Na2 with S(1)O<sub>3</sub><sup>-</sup> and/or S(2)<sub>3</sub><sup>-</sup>, Na3 with S(1)O<sub>3</sub><sup>-</sup> and/or S(4)O<sub>3</sub><sup>-</sup>, and Na4 with S(3)O<sub>3</sub><sup>-</sup>. This implies that when **2** is bound to **1<sub>4</sub>**, an ion exchange takes place between N<sup>+</sup>Cl<sup>-</sup> in **2** and Na<sup>+</sup>SO<sub>3</sub><sup>-</sup> in **1<sub>4</sub>**. As seen from Figure 4, the benzene ring in **2** is significantly inclined in the cavity. Conceivably, this conformation is favored to attain the maximal multipoint interaction with **1<sub>4</sub>** through both hydrophobic and electrostatic forces.

The fourth point of interest concerns the "assembly structure" of the **1<sub>4</sub>****2** complex. As pointed out by Atwood et al. for the crystal structure of **1<sub>4</sub>** itself,<sup>23</sup> the complex also features the clay-like bilayer structure with a 15.13-Å repeating unit (Figure 2): that is, the calixarene rings form two hydrophobic layers, and the sulfonate groups cover the surface of the bilayer. The ammonium

cation of **2** is placed on the surface. It appears that **2** is bound from the hydrophobic layer into the hydrophobic layer with a phenyl moiety as a head and an ammonium moiety as a tail. This view is compatible with the previous conclusion that not only the hydrophobic force but also the electrostatic force contributes to guest inclusion.

The last point concerns the comparison of the solution state and solid state. The <sup>1</sup>H and <sup>13</sup>C NMR spectral data suggested that in acidic aqueous solution the phenyl moiety in **2** is included deeply in the cavity. As expected, the crystal data established that the phenyl moiety in **2** resides in the cavity. This implies that the **1<sub>4</sub>****2** complex detected in acidic aqueous solution by an NMR method is exactly grown up as crystals.

In conclusion, this is the first example of a calixarene-guest complex that has been well characterized both in the solution and in the solid state. We believe that the findings can serve as a useful cross-link between solution-state and solid-state host-guest chemistry.

**Acknowledgment.** This research was supported by the Grant-in-Aid from the Ministry of Education of Japan. We thank Ms. Mika Shinozaki and Mr. Eiji Ichihara for technical assistance.

**Supplementary Material Available:** Table VIII containing final atomic parameters (2 pages). Ordering information is given on any current masthead page.