

Chlorosulfonylated Calix[4]arenes: Precursors for Neutral Anion Receptors with a Selectivity for Hydrogen Sulfate

Yury Morzherin, Dmitry M. Rudkevich, Willem Verboom, and David N. Reinhoudt*

Laboratory of Organic Chemistry, University of Twente, P.O. Box 217, 7500 AE Enschede, The Netherlands

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Introduction

In nature phosphate and sulfate binding proteins are very important receptors for the active transport systems in the cell.^{1,2} A very high selectivity in binding has been observed in prokaryotic, periplasmic phosphate and sulfate binding proteins, which demonstrate $>10^6$ selectivity for binding phosphate over sulfate and sulfate over phosphate, respectively.³ In both proteins the specific binding exclusively takes place through hydrogen bonding.

Synthetic receptors that bind anions contain either positively charged guanidinium or ammonium groups⁴ or Lewis acid metal centers⁵ to accomplish anion binding. Recently we reported functionalized uranyl-containing salenes⁶ and sulfonamides⁷ derived from tris(aminoethyl)amine (TREN) that form complexes with hard anions in CH_3CN with a selectivity for H_2PO_4^- . In the present paper we report anion receptors based on chlorosulfonylated calix[4]arenes.⁸

Calix[4]arenes are important building blocks in supramolecular chemistry.^{10,11} They can be (selectively) functionalized both at the phenolic OH groups (lower rim) and at the para positions of the phenol rings (upper rim).¹²

Results and Discussion

The starting calixarene tetraamides **1g** and **1h** were obtained by reaction of **1a** with the appropriate *N,N*-

dialkyl-2-chloroacetamide in the presence of potassium iodide and K_2CO_3 as a base in refluxing acetonitrile for 18 h in 78 and 58% yield, respectively. Reaction of calix[4]arenes **1a,c,e,f** (all cone conformation) with 40 equiv of chlorosulfonic acid in CHCl_3 at room temperature for 2–3 h (method A) afforded the tetrakis(chlorosulfonyl)calix[4]arenes **2a,c,e,f** in 52–69% yield upon recrystallization of the crude reaction mixture. The ^1H NMR spectra of **2a,c,e,f** indicate the presence of four identical rings. Under these conditions the tetrapropoxycalix[4]arene **1b** did not give the expected tetrakis(chlorosulfonyl)calix[4]arene **2b** but the tetrahydroxytetrakis(chlorosulfonyl)calix[4]arene **2a** in 35% yield. Apparently under the acidic conditions, the propyl ether groups are not stable.¹³ Only a few examples of calixarenes having reactive chlorosulfonyl (SO_2Cl) groups at the upper rim are known.^{15,16} They were prepared in two steps viz. sulfonylation followed by treatment with thionyl chloride,^{15,16} although it is known that the SO_2Cl moiety can in principle be introduced in a one step¹⁷ like in the synthesis of chlorosulfonyl benzocrown ethers.¹⁸

Under the same conditions, the 1,3-alternate conformer of **1c**, calix[4]arene **1d**, gave a complex reaction mixture. However, heating of **1d** at 50 °C for 20 min (method B) gave the tetrakis(chlorosulfonyl)calix[4]arene **2d** in 54% yield. The ^1H NMR spectrum of **2d** shows a singlet at δ 3.79 for the methylene bridge protons whereas in the ^{13}C NMR spectrum the corresponding carbon absorptions are present at δ 34.5 which are both characteristic for a calix[4]arene in the 1,3-alternate conformation.^{19,20}

Surprisingly, treatment of calix[4]arene amides **1g** and **1h** (cone conformation) with chlorosulfonic acid at room temperature for 2–3 h gave the bis(chlorosulfonyl)calix[4]arenes **3a** and **3b** in 42 and 27% yield, respectively. Probably under the strongly acidic conditions, the amide groups of **1g** and **1h** are protonated²¹ which results in a lower reactivity of the para positions of the corresponding aromatic rings. The two SO_2Cl groups are introduced at diametrical aromatic rings as was concluded from the symmetry of the ^1H NMR spectra. The ^1H NMR spectrum of **3a** exhibits a singlet at δ 7.79 for the hydrogens of the chlorosulfonylated rings and a triplet and a doublet at δ 6.40 and 6.18, respectively, for the hydrogens of the unreacted rings. Because of the symmetry there is only one AB system (δ 5.34 and 3.36) for the methylene bridge protons. Compounds **3a** and **3b** represent the first examples of calix[4]arenes having two SO_2Cl groups. These compounds are not accessible via the two-step procedure because to the best of our knowledge selective sulfonylation

(1) (a) Luecke, H.; Quioco, F. A. *Nature* 1990, 347, 402. (b) He, J.; Quioco, F. A. *Science* 1991, 251, 1479.

(2) Kanyo, Z. F.; Christianson, D. W. *J. Biol. Chem.* 1991, 266, 4264.

(3) Thatcher, G. R. J.; Cameron, D. R.; Nagelkerke, R.; Schmitke, J. *J. Chem. Soc., Chem. Commun.* 1992, 386 and refs cited therein.

(4) (a) Dietrich, B.; Guilhem, J.; Lehn, J.-M.; Pascard, C.; Sonveaux, E. *Helv. Chim. Acta* 1984, 67, 91. (b) Schmidtchen, F. P. *J. Org. Chem.* 1986, 51, 5161. (c) Hosseini, M. W.; Blacker, A. J.; Lehn, J.-M. *J. Am. Chem. Soc.* 1990, 112, 3896. (d) Deslongchamps, G.; Galán, A.; de Mendoza, J.; Rebeck, Jr., J. *Angew. Chem. Int. Ed. Engl.* 1992, 31, 61. (e) Sessler, J. L.; Cyr, M.; Furuta, H.; Kral, V.; Mody, T.; Morishima, T.; Shionoya, M.; Weghorn, S. *Pure Appl. Chem.* 1993, 65, 393.

(5) (a) Blanda, M. T.; Horner, J. N.; Newcomb, M. J. *Org. Chem.* 1989, 54, 4626. (b) Reetz, M. T.; Niemeyer, C. M.; Harms, K. *Angew. Chem. Int. Ed. Engl.* 1991, 30, 1472. (c) Yang, X.; Knobler, C. B.; Hawthorne, M. F. *Ibid.* 1991, 30, 1507. (d) Beer, P. D.; Hazlewood, C.; Heseck, D.; Hodacova, J.; Stokes, S. E.; *J. Chem. Soc., Dalton Trans.* 1993, 1327.

(6) Rudkevich, D. M.; Stauthamer, W. P. R. V.; Verboom, W.; Engbersen, J. F. J.; Harkema, S.; Reinhoudt, D. N. *J. Am. Chem. Soc.* 1992, 114, 9671.

(7) Valiyaveetil, S.; Engbersen, J. F. J.; Verboom, W.; Reinhoudt, D. N. *Angew. Chem.* 1993, 105, 942.

(8) After completion of this work Beer et al.⁹ reported a lower rim functionalized calix[4]arene anion receptor.

(9) Beer, P. D.; Dickson, C. A. P.; Fletcher, N.; Goulden, A. J.; Grieve, A.; Hodacova, J.; Wear, T. *J. Chem. Soc., Chem. Commun.* 1993, 828.

(10) Gutsche, C. D. *Calixarenes*; Monographs in supramolecular chemistry; Stoddart, J. F., Ed.; The Royal Society of Chemistry: Cambridge, 1989; Vol 1.

(11) Vicens, J.; Bohmer, V., Eds. *Calixarenes: a versatile class of macrocyclic compounds*; Topics in inclusion science; Kluwer Academic Press: Dordrecht, 1991.

(12) Van Loon, J.-D.; Verboom, W.; Reinhoudt, D. N. *Org. Prep. Proc. Int.* 1992, 24, 437.

(13) Very recently Katritzky et al.¹⁴ reported the partial demethylation of *o*-nitroanisole upon reaction with chlorosulfonic acid.

(14) Katritzky, A. R.; Wu, J.; Rachwal, S.; Macomber, D.; Smith, T. P. *Synth. Commun.* 1993, 23, 405.

(15) Shinkai, S.; Kawaguchi, H.; Manabe, O. *J. Polym. Sci., Polym. Lett.* 1988, 26, 391.

(16) Shinkai, S.; Kawabata, H.; Matsuda, T.; Kawaguchi, H.; Manabe, O. *Bull. Chem. Soc. Jpn.* 1990, 63, 1272.

(17) Huntress, E. H.; Carten, F. H. *J. Am. Chem. Soc.* 1940, 62, 511.

(18) Markovsky, L. N.; Rudkevich, D. M.; Kalchenko, V. I. *Zh. Org. Khim.* 1989, 25, 1995. *Chem. Abstr.* 1990, 112, 216892w.

(19) Jaime, C.; de Mendoza, J.; Prados, P.; Nieto, P. M.; Sánchez, C. *J. Org. Chem.* 1991, 56, 3372.

(20) Verboom, W.; Datta, S.; Asfari, Z.; Harkema, S.; Reinhoudt, D. N. *J. Org. Chem.* 1992, 57, 5394.

(21) Homer, R. B.; Johnson, C. D. In *The chemistry of functional groups. The chemistry of amides*; Zabicky, J., Ed.; Interscience publishers: London, 1970; pp 188–197.

Scheme I

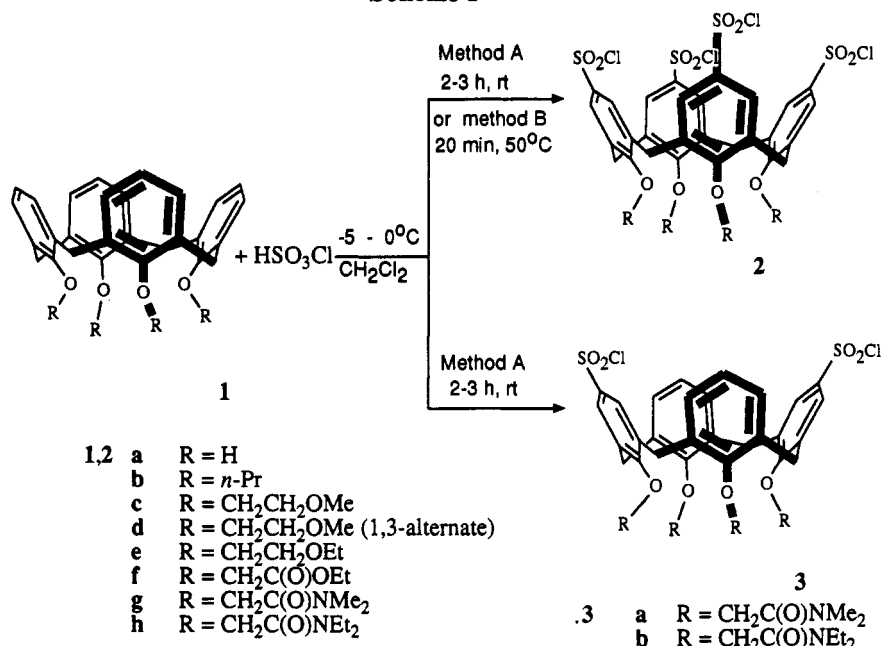
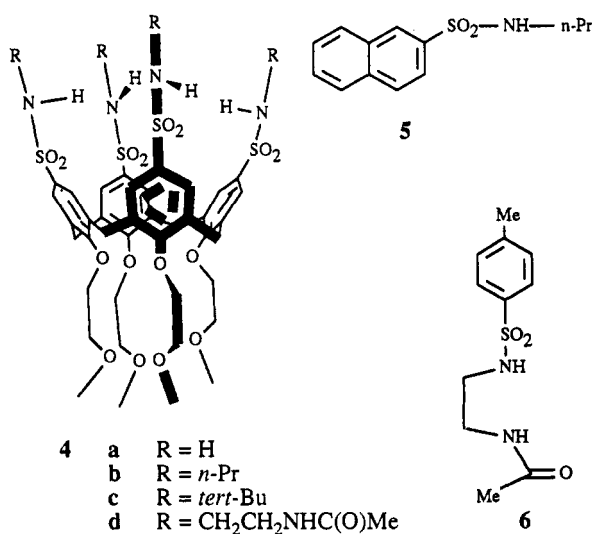


Chart I

Table I. Association Constants (K , M⁻¹, CDCl₃) of Complexation of 4b-d, 5, and 6 with Different Anions^a

compd	anions ^b				
	H ₂ PO ₄ ⁻	HSO ₄ ⁻	Cl ⁻	NO ₃ ⁻	ClO ₄ ⁻
4b	350	970	360	240	<1
4c	<10	134	72	43	<1
4d	c	103400	1250	513	<1
5	14	10	15	<10	16
6	262	350	330	99	84

^a The error is <5%. ^b The counterion is Bu₄N⁺. ^c Compound 4d shows a complicated (mixed) complexation with H₂PO₄⁻ (compare refs 7 and 32); no K value for 1:1 complexation could be determined.

d²² (and of reference compounds 5 and 6) with the tetrabutylammonium salts of H₂PO₄⁻, HSO₄⁻, Cl⁻, NO₃⁻, and ClO₄⁻ in CDCl₃ have been determined with ¹H NMR titration experiments and are summarized in Table I. Surprisingly in all cases a selectivity for HSO₄⁻ was observed. The influence of the presence of four more or less preorganized binding sites is very clear comparing the K values of 4b,c and 4d with those of the corresponding reference compounds 5 and 6, respectively. For all anions 4d shows the highest K values which may be due to the presence of four amide functions in addition to four sulfonamide moieties. However, more important is that 4d exhibits for HSO₄⁻ a selectivity of about 10² over Cl⁻ and NO₃⁻. Obviously the three-dimensional cavity of 4d complexes the tetrahedral HSO₄⁻ better than the spherical Cl⁻ and the planar NO₃⁻. To the best of our knowledge 4b-d represent the first anion receptors with a selectivity for HSO₄⁻.²³

Experimental Section

General. Melting points are uncorrected. ¹H and ¹³C NMR spectra were recorded in CDCl₃ with Me₄Si as internal standard unless stated otherwise. Fast atom bombardment (FAB) mass spectra were obtained with *m*-nitrobenzyl alcohol as a matrix.

(22) Due to the presence of broad signals in the ¹H NMR spectrum of 4a in CDCl₃ the anion complexation behavior has not been studied.

(23) Examples of nonselective (hydrogen) sulfate complexation have been reported in refs 4a, 6, 7, and Smith, P. J.; Reddington, M. V.; Wilcox, C. S. *Tetrahedron Lett.* 1992, 33, 6085.

of calix[4]arenes is unknown. Method B gave the tetrakis(chlorosulfonyl)calix[4]arenes 2g and 2h both in 61% yield.

Because TREN-derived sulfonamides form complexes with anions (vide supra),⁷ these tetrakis(chlorosulfonyl)calix[4]arenes 2 might be suitable precursors for the synthesis of *hydrophobic, neutral anion receptors*. Reaction of 2c with ammonia, *n*-propylamine, *tert*-butylamine, or *N*-acetylenediamine in CH₂Cl₂ for 4 h gave the corresponding calix[4]arene sulfonamides 4a-d in yields of 64, 87, 88, and 59%, respectively. We also isolated the solid complex of 4d with Bu₄NHSO₄, the formation of which was confirmed by a satisfactory elemental analysis. In the ¹H NMR spectrum the NH absorption has been shifted from δ 6.90 (free ligand) to δ 7.75 (complex). In the negative FAB mass spectrum of the solid complex, in addition to a peak of the free ligand, also signals of [L + HSO₄]⁻ and [L + Bu₄NHSO₄]⁻ are present. The association constants K of the 1:1 complexes of 4b-

Table II. Yields, Melting Points, and Characteristic Spectral Data of Compounds 2a,c-h^a

compd	yield (%)	mp (°C)	¹ H NMR (CDCl ₃) (δ)			¹³ C NMR (CDCl ₃) (δ)		FAB-MS <i>m/z</i> (M ⁺) calcd
			ArH (s, 8 H)	OCH ₂	ArCH ₂ Ar	ArC-SO ₂ (s)	ArCH ₂ Ar (t)	
2a ^b	52 ^c	>230 dec	7.37		3.94 (s, 8 H)	138.0	30.4	817.0 (817.5)
2c	69	172-174	7.50	4.32 (t, 4 H, <i>J</i> = 4.4 Hz), 3.80 (t, 4 H, <i>J</i> = 4.4 Hz)	4.74 (d, 4 H, <i>J</i> = 13.5 Hz), 3.43 (d, 4 H, <i>J</i> = 13.5 Hz)	138.5	30.5	1015.3 ^d (1015.3)
2d	54	>290 dec	7.94	4.01 (t, 4 H, <i>J</i> = 1.8 Hz), 3.77 (t, 4 H, <i>J</i> = 1.8 Hz)	3.79 (s, 8 H)	138.1	34.5	1051.0 ^e (1050.9)
2e	53	212-213	7.49	4.35 (t, 4 H, <i>J</i> = 4.4 Hz), 3.80 (t, 4 H, <i>J</i> = 4.4 Hz)	4.77 (d, 4 H, <i>J</i> = 13.7 Hz), 3.42 (d, 4 H, <i>J</i> = 13.7 Hz)	138.8	31.0	1070.9 ^d (1071.1)
2f	65	108-109	7.53	4.88 (s, 8 H)	5.14 (d, 4 H, <i>J</i> = 14.0 Hz), 3.55 (d, 4 H, <i>J</i> = 14.0 Hz)	139.9	31.2	1162.9 (1162.9)
2g ^b	61	208-209	7.21	5.02 (s, 8 H)	4.96 (d, 4 H, <i>J</i> = 13.0 Hz), 3.48 (d, 4 H, <i>J</i> = 13.0 Hz)	140.0	31.9	1159.0 (1158.9)
2h	61	226-228	7.50	5.15 (s, 8 H)	5.66 (d, 4 H, <i>J</i> = 13.7 Hz), 3.48 (d, 4 H, <i>J</i> = 13.7 Hz)	139.1	32.6	1234.9 ^d (1235.6)

^a All compounds gave satisfactory elemental analyses. ^b In DMSO-*d*₆. ^c Starting from 1b the yield is 35%. ^d (M - Cl)⁺. ^e (M - H)⁺.

CH₂Cl₂ was distilled from CaH₂ and stored over molecular sieves. Calix[4]arenes 1a,²⁴ 1b,²⁵ 1c,²⁶ 1d,²⁰ 1e,²⁷ and 1f,²⁸ and reference compounds 5²⁹ and 6³⁰ were prepared according to literature procedures. All reactions were carried out under an argon atmosphere.

In the workup procedures the (combined) organic layers were washed with water (2×) and dried with MgSO₄, whereupon the solvent was removed under reduced pressure. The presence of solvent in the analytical samples was confirmed by ¹H NMR spectroscopy.

General Procedure for the Preparation of 1g,h. A mixture of calix[4]arene 1a (4.24 g, 0.01 mol), *N,N*-dialkyl-2-chloroacetamide (0.1 mol), sodium iodide (15 g, 0.1 mol), and K₂CO₃ (13.8 g, 0.1 mol) in acetonitrile (100 mL) was refluxed for 18 h. After filtration the solvent was removed. The residue was taken up in CH₂Cl₂ (150 mL) and washed with water (3 × 400 mL). Pure compounds were obtained upon recrystallization of the crude reaction products from MeOH.

25,26,27,28-Tetrakis(dimethylcarbamoyl)methoxycalix[4]arene (1g): yield 78%; mp 256-258 °C; ¹H NMR δ 6.7-6.5 (m, 12 H), 5.11 (d, 4 H, *J* = 13.6 Hz), 4.84 (s, 8 H), 3.25 (d, 4 H, *J* = 13.6 Hz), 3.00 and 2.91 (s, 2 × 12 H); ¹³C NMR δ 169.5 (s), 156.4 (s), 134.8 (s), 128.5 (d), 122.4 (d), 71.7 (t), 36.2 (q), 35.4 (q), 31.7 (t); MS-FAB *m/z* 765.4 (M⁺, calcd 764.9). Anal. Calcd for C₄₄H₅₂N₄O₈: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.28; H, 7.05; N, 7.11.

25,26,27,28-Tetrakis(diethylcarbamoyl)methoxycalix[4]arene (1h): yield 58%; mp 212-213 °C; ¹H NMR δ 6.65-6.5 (m, 12 H), 5.23 (d, 4 H, *J* = 13.6 Hz), 4.90 (s, 8 H), 3.4-3.25 (m, 16 H), 3.23 (d, 4 H, *J* = 13.6 Hz), 1.25-1.00 (m, 24 H); ¹³C NMR δ 168.6 (s), 156.6 (s), 134.9 (s), 128.4 (d), 122.2 (d), 71.5 (t), 40.9 (t), 39.9 (t), 31.9 (t), 14.3 (q), 13.1 (q); MS-FAB *m/z* 877.4 (M⁺, calcd 877.1). Anal. Calcd for C₆₂H₈₈N₄O₈: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.54; H, 8.02; N, 6.12.

General Procedure for the Preparation of Bis- and Tetrakis(chlorosulfonyl)calix[4]arenes 2 and 3. To a cooled solution of calix[4]arene 1 (2 mmol) in CHCl₃ (25 mL) was added chlorosulfonic acid (5.6 mL, 80 mmol) at a rate to keep the temperature between 0 and 10 °C. The reaction mixture was stirred at room temperature for 2-3 h (method A) or heated at 50 °C for 20 min (method B). The reaction mixture was poured onto ice (100 g) and extracted with CH₂Cl₂ (4 × 50 mL). The crude products were recrystallized from toluene to afford pure

compounds 2,3. The yields, melting points and selected spectral data of compounds 2 are summarized in Table II.

5,17-Bis(chlorosulfonyl)-25,26,27,28-tetrakis(dimethylcarbamoyl)methoxycalix[4]arene (3a): yield 42%; mp 218-219 °C; ¹H NMR δ 7.79 (s, 4 H), 6.45-6.35 (m, 2 H), 6.2-6.15 (m, 4 H), 5.34 (s, 4 H), 4.59 (s, 4 H), 5.24 and 3.36 (d, 2 × 4 H, *J* = 13.8 Hz), 3.04 (s, 6 H), 2.96 (s, 12 H), 2.91 (s, 6 H); ¹³C NMR δ 169.2 (s), 168.0 (s), 163.7 (s), 155.3 (s), 137.9 (s), 137.1 (s), 132.0 (s), 128.3 (d), 127.9 (d), 123.7 (d), 72.2 (t), 71.9 (t), 36.0 (q), 35.7 (q), 35.5 (q), 35.4 (q), 31.7 (t); MS-FAB *m/z* 961.3 (M⁺, calcd 961.9). Anal. Calcd for C₄₄H₅₆Cl₂N₄O₁₂S₂·1.2CH₂Cl₂: C, 51.03; H, 4.96; N, 5.27. Found: C, 50.98; H, 5.15; N, 5.11.

5,17-Bis(chlorosulfonyl)-25,26,27,28-tetrakis(diethylcarbamoyl)methoxycalix[4]arene (3b): yield 37%; mp 163-165 °C; ¹H NMR δ 7.79 (s, 4 H), 6.5-6.3 (m, 2 H), 6.3-6.2 (m, 2 H), 5.35 (s, 4 H), 4.68 (s, 4 H), 5.38 and 3.25 (d, 2 × 4 H, *J* = 13.0 Hz), 3.5-3.0 (m, 16 H), 1.3-1.0 (m, 24 H); MS-FAB *m/z* 1073.4 [(M + H)⁺, calcd 1073.1]. Anal. Calcd for C₆₂H₈₈Cl₂N₄O₁₂S₂·1.7H₂O: C, 56.43; H, 6.33; N, 5.07. Found: C, 56.10; H, 6.13; N, 4.83. Karl Fisher titration calcd for 2H₂O: 2.75. Found: 2.66.

General Procedure for the Preparation of 4a-d. To a solution of 2c (1.05 g, 1 mmol) in CH₂Cl₂ (40 mL) was added the appropriate alkylamine (10 mmol). In the case of 4a ammonia was bubbled through the solution for 10 min. The reaction mixture was stirred at rt for 4 h and subsequently washed with 1 N HCl (2 × 50 mL) and water (3 × 50 mL). The crude reaction products were recrystallized from MeOH to give pure 4a-d.

25,26,27,28-Tetrakis(methoxyethoxy)-5,11,17,23-tetrakis(sulfamoyl)calix[4]arene (4a): yield 64%; mp 171-173 °C; ¹H NMR (DMSO-*d*₆) δ 7.31 (s, 8 H), 6.96 (s, 8 H), 4.16 and 3.79 (t, 2 × 8 H, *J* = 5.0 Hz), 4.53 and 3.43 (d, 2 × 8 H, *J* = 13.3 Hz), 3.34 (s, 12 H); ¹³C NMR (DMSO-*d*₆) δ 158.6 (s), 138.0 (s), 134.6 (s), 125.9 (d), 73.6 (t), 71.2 (t), 58.0 (q), 30.1 (t); MS-FAB *m/z* 973.2 (M⁺, calcd 973.1). Anal. Calcd for C₄₀H₅₂N₄O₁₆S₄·1.5H₂O: C, 48.04; H, 5.54; N, 5.60; S, 12.82. Found: C, 47.88; H, 5.80; N, 5.42; S, 13.01. Karl Fisher titration calcd for 1.5H₂O: 2.70. Found: 2.66.

25,26,27,28-Tetrakis(methoxyethoxy)-5,11,17,23-tetrakis(propylsulfamoyl)calix[4]arene (4b): yield 87%; mp 191-192 °C; ¹H NMR δ 7.26 (s, 8 H), 4.62 and 3.30 (d, 2 × 4 H, *J* = 13.4 Hz), 4.84 (t, 4 H, *J* = 6.2 Hz), 4.21 and 3.79 (t, 2 × 8 H, *J* = 5.1 Hz), 3.38 (s, 12 H), 2.86 (q, 8 H, *J* = 6.2 Hz), 1.51 (sextet, 8 H, *J* = 6.2 Hz), 0.89 (t, 12 H, *J* = 6.2 Hz); ¹³C NMR δ 159.1 (s), 135.2 (s), 135.1 (s), 127.2 (d), 73.8 (t), 71.6 (t), 58.6 (q), 45.1 (t), 30.7 (t), 23.3 (t) 11.1 (q); MS-FAB *m/z* 1141.4 (M⁺, calcd 1141.5). Anal. Calcd for C₅₂H₇₆N₄O₁₆S₄·0.7H₂O: C, 54.12; H, 6.76; N, 4.85. Found: C, 53.99; H, 6.75; N, 4.83. Karl Fisher titration calcd for 0.7H₂O: 1.09. Found: 1.05.

5,11,17,23-Tetrakis(1,1-dimethylethyl)sulfamoyl)-25,26,27,28-tetrakis(methoxyethoxy)calix[4]arene (4c): yield 88%; mp 129-130 °C; ¹H NMR δ 7.31 (s, 8 H), 4.73 (s, 4 H), 4.59 and 3.29 (d, 2 × 4 H, *J* = 13.6 Hz), 4.19 and 3.76 (t, 2 × 8 H, *J* = 4.6 Hz), 3.35 (s, 12 H), 1.19 (s, 36 H); ¹³C NMR δ 159.0 (s), 138.0 (s), 134.9 (s), 127.4 (d), 73.6 (t), 71.5 (t), 58.6 (q), 54.9 (s), 30.2 (q); MS-FAB *m/z* 1194.5 [(M - H)⁻, calcd 1195.2]. Anal. Calcd for

(24) Gutsche, C. D.; Lin, L.-G. *Tetrahedron* 1986, 42, 1633.

(25) Iwamoto, K.; Araki, K.; Shinkai, S. *J. Org. Chem.* 1991, 56, 4955.

(26) Arduini, A.; Casnati, A.; Fabbri, M.; Minari, P.; Pochini, A.; Sicuri, A. R.; Ungaro, R. *J. Supramol. Chem.* 1993, 1, 235.

(27) Arduini, A.; Manfredi, G.; Pochini, A.; Sicuri, A.; Ungaro, R. *J. Chem. Soc., Chem. Commun.* 1991, 936.

(28) Arnaud-Neu, F.; Collins, E. M.; Deasy, M.; Ferguson, G.; Harris, S. J.; Kaitner, B.; Lough, A. J.; McKervey, M. A.; Marques, E.; Ruhl, B. L.; Schwing-Weill, M. J.; Seward, E. M. *J. Am. Chem. Soc.* 1989, 111, 8681.

(29) Campbell, K. N.; Campbell, B. K.; Salm, E. M. *Proc. Indiana Acad. Sci.* 1948, 57, 97.

(30) Mikiciuk-Olasik, E. *Pol. J. Chem.* 1989, 63, 279.

$C_{56}H_{84}N_4O_{16}S_4 \cdot 0.7H_2O$: C, 55.58; H, 7.11; N, 4.63; S, 10.60. Found: C, 55.41; H, 7.28; N, 4.60; S, 10.53. Karl Fisher titration calcd for $0.7H_2O$: 1.04. Found: 1.02.

5,11,17,23-Tetrakis[(2-acetylamino)ethyl]sulfamoyl]-25,26,27,28-tetrakis(methoxyethoxy)calix[4]arene (4d): yield 59%; mp 89–90 °C; 1H NMR δ 7.25 (s, 8 H), 6.90 (s, 4 H), 6.30 (s, 4 H), 4.61 and 3.32 (d, 2×4 H, $J = 13.3$ Hz), 4.25–4.15 (m, 8 H), 3.8–3.75 (m, 8 H), 3.38 (s, 12 H), 3.35–3.25 (m, 8 H), 3.0–2.9 (m, 8 H), 1.99 (s, 12 H); ^{13}C NMR δ 159.4 (s), 158.9 (s), 134.8 (s), 134.6 (s), 127.0 (d), 73.7 (t), 71.5 (t), 58.5 (q), 45.1 (t), 41.9 (t), 29.9 (t), 22.9 (q); MS-FAB m/z 1313.7 (M^- , calcd 1313.6). Anal. Calcd for $C_{56}H_{80}N_4O_{20}S_4 \cdot 0.5H_2O$: C, 50.86; H, 6.17; N, 8.47; S, 9.70. Found: C, 51.07; H, 5.98; N, 8.52; S, 9.89. Karl Fisher titration calcd for $0.5H_2O$: 0.71. Found: 0.71.

Solid Complex of 4d and Bu_4NHSO_4 . A mixture of 4d (132 mg, 0.1 mmol) and Bu_4NHSO_4 (34 mg, 0.1 mmol) in $CHCl_3$ (20 mL) was stirred at rt for 18 h. The solvent was removed and the resulting solid dried: mp 45 °C; 1H NMR δ 7.75 (s, 4 H), 7.37 (s, 8 H), 4.56 and 3.38 (d, 2×4 H, $J = 13.1$ Hz), 4.18 (t, 8 H, $J = 5.1$ Hz), 3.79 (t, 8 H, $J = 5.1$ Hz), 3.38 (s, 12 H), 3.4–2.9 (m, 24

H), 1.95 (s, 12 H), 1.9–1.3 (m, 16 H), 1.00 (t, 12 H, $J = 7.3$ Hz); MS-FAB m/z 1311.3 [$(L-2H)^-$, calcd 1311.6], 1408.9 [$(L + HSO_4^- - 2H)^-$, calcd 1408.7], 1650.2 [$(L + BuNHSO_4 - 3H)^-$, calcd 1650.2]. Anal. Calcd for $C_{72}H_{117}N_9O_{24}S_5 \cdot 0.75CHCl_3$: C, 50.14; H, 6.76; N, 7.24. Found: C, 49.88; H, 7.07; N, 7.35.

Determination of Association Constants. The measurements were performed by 1H NMR titration experiments in $CDCl_3$ at 298 K using a constant host concentration of 4 mM and a varying guest concentration of 0.3–30 mM. For each K value determination 5–10 different guest concentrations were taken. As a probe the chemical shift of the SO_2NH signal was used. The K values were calculated by nonlinear regression as described in ref 31.

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(31) De Boer, J. A. A.; Reinhoudt, D. N.; Harkema, S.; van Hummel, G. J.; de Jong, F. *J. Am. Chem. Soc.* **1982**, *104*, 4073.

(32) Flatt, L. S.; Lynch, V.; Anslyn, E. V. *Tetrahedron Lett.* **1992**, *33*, 2785.