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A Novel C_{3v}-Symmetrical Calix[6](aza)cryptand with a Remarkably High and Selective Affinity for Small Ammoniums

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The three-step synthesis of a calix[6]arene capped with a TAC unit is presented. The novel C_{3v}-symmetrical calix[6](aza)cryptand displayed an exceptionally high affinity for small ammoniums. NMR and X-ray diffraction analyses demonstrated the formation of *endo*-complexes. These complexes are stabilized thanks to (i) hydrogen bonding to both the aza cap and one phenolic unit of the calixarene and to (ii) cationic and CH−π interactions between the ammonium and the aromatic walls of the host. Combined extraction and competitive binding experiments yielded the free energies of bindings $\Delta G°$ in chloroform. The values are the highest ever obtained with a calixarene-type host. Calix[6]TAC displayed the best affinity for $EtNH_3^+$. Comparison with other small ammoniums emphasizes the high selectivity of the recognition process.

Introduction

With the aim of building biomimetic receptors, the host−guest chemistry of calixarenes has been widely explored in the past decade.[1−3] All studies showed that, whereas calix[4]arenes suffer from the smallness of their cavity, the larger calix[6]arenes are too flexible to provide a good receptor. As a result, the former has been used only as a platform for the preorganization of a binding site, whereas the cavity of the latter could not be exploited, unless their flexibility was restricted. Coordination bonds between a metallic cation and three nitrogenous arms grafted on the phenol units were shown to provide an efficient way for their rigidification, giving rise to a cationic host with a structure constrained in a cone conformation.[4] Alternatively, the challenging introduction of covalent linkages between the phenolic units leads to neutral receptors.[5,6] Some examples with arches that provide oxygen donors as binding sites have been described. They have been reported to be good hosts for

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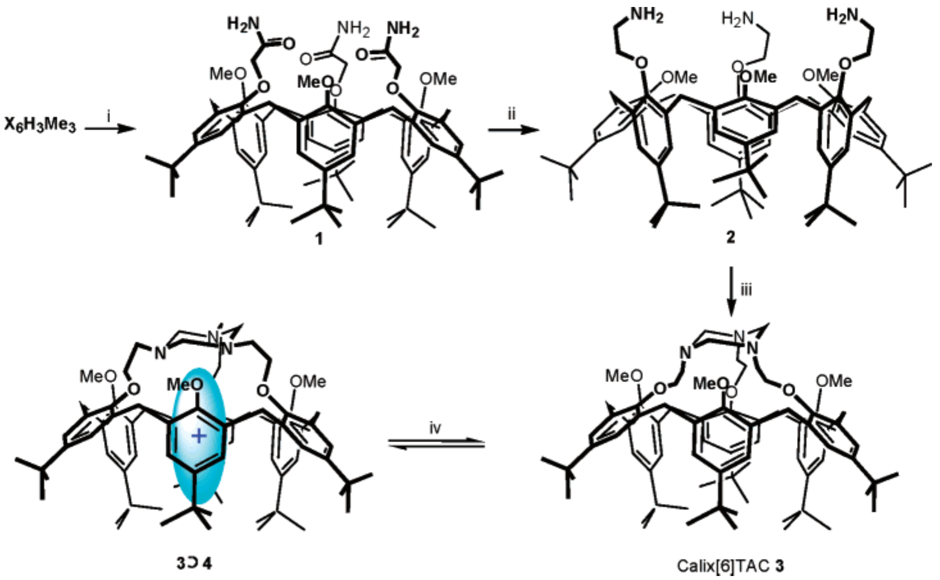
SCHEME 1[a]



[a] Key: (i) $BrCH_2CONH_2$, NaH, THF, reflux, 91%; (ii) BH_3/THF, reflux then EtOH Reflux, 85%; (iii) aq HCHO (30%), $CHCl_3$, 0 °C then rt, 89%; (iv) ammonium salt **4**, $CDCl_3/CD_3OD$.

cations. One of our goals is to design new receptors based on a calix[6]arene core presenting a nitrogenous cage structure thanks to its covalent linkage to a tripodal polyaza cap. Recently, we have described the first synthesis of such a C_{3v}-symmetrical calix[6](aza)cryptand consisting in a calix[6]arene bridged by a tren unit.[7] It was observed that the tripodal aza-cryptand cap prevents ring inversion, constraining the calixarene cavity in a straight cone conformation ideal for host–guest chemistry. In the present paper, we report the straightforward synthesis of a novel C_{3v}-symmetrical (aza)cryptand, namely calix[6]TAC **3** (TAC: 1,3,5-triazacyclohexane). This novel calix-cryptand displays exceptional properties for the selective binding of small alkylammoniums.

Results

Synthesis and Characterization of the C_{3v}-Symmetrical Calix[6](aza)cryptand 3. The novel calix[6](aza)cryptand was synthesized according to an efficient three-step sequence starting from the symmetrically 1,3,5-tris-methylated calixarene $X_6H_3Me_3$[8] (Scheme 1). Alkylation of $X_6H_3Me_3$ with an excess of bromoacetamide and 3.5 equiv of NaH provided the corresponding calixtriamide **1** which was then reduced by BH_3/THF to the desired calixtriamine **2**.[9] Subsequent reaction with aqueous formaldehyde in chloroform gave the TAC-capped calixarene, X_6Me_3TAC **3**, in high yield. This last reaction required a careful ^{1}H NMR monitoring; otherwise, unidentified calixarene-type byproducts were produced after prolonged time reaction. Starting from $X_6H_3Me_3$, the overall yield of the synthesis of calix-cryptand **3** is 69%.

The ^{1}H NMR spectra of new compounds **1**–**3**, recorded in $CDCl_3$, are characteristic of a major flattened cone conformation with C_{3v} symmetry. The methoxy groups of **2** are projected toward the inside of the cavity as indicated by their high-field resonances (δ_{OMe} = 2.66 ppm), whereas their amino arms are rejected outside. This stands in contrast to **1** and **3**, which adopt the opposite alternate conformation with the methoxy groups away from the cavity (δ_{OMe} = 3.60 and 3.75 ppm for **1** and **3**, respectively). This differing behavior between **1** and **2** may be due to the establishment of a hydrogen-bonding network between the amidic arms, as was observed for other related calixarenes bearing protic arms.[7] Moreover, the axial and equatorial ArCH_2Ar and

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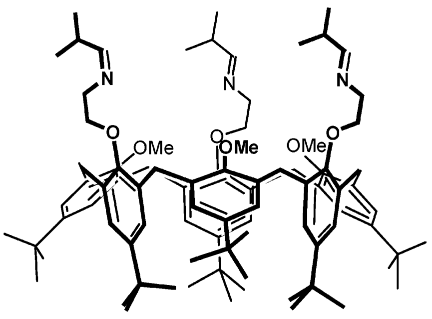
(9) Triamine **2** revealed to be highly acid- and air-sensitive. Therefore, to fully characterize **2** (i.e., elemental analyses), we prepared the less sensitive derivative calixtrisimine **5** by reaction with isobutyraldehyde in dichloromethane (see the Experimental Section).



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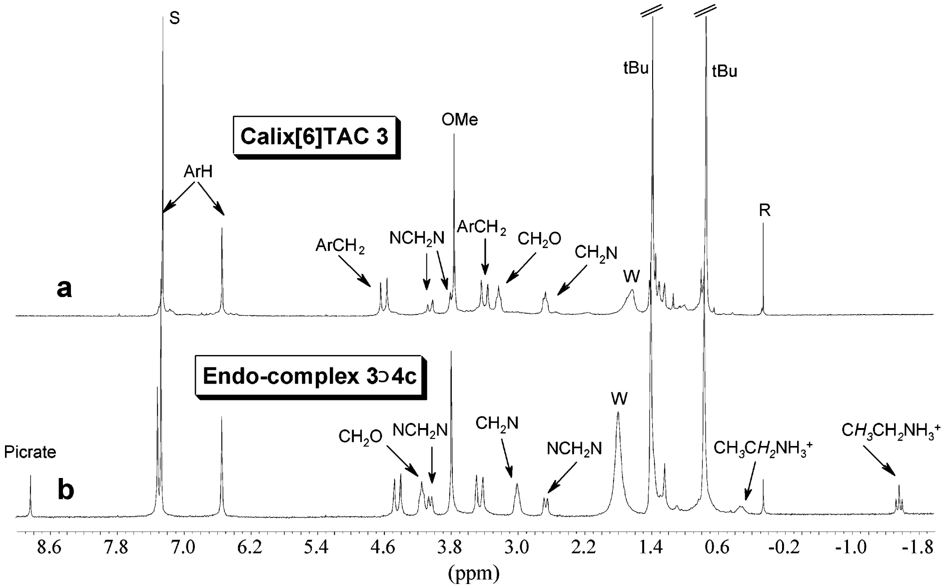

FIGURE 1. (a) ^1H NMR spectrum of calix[6]TAC **3** in $CDCl_3$ at 298 K. (b) ^1H NMR spectrum of the complex **3**⊃**4c** in $CDCl_3$/CD_3OD (98.5:1.5) at 298 K. Solvent, water, and reference are labeled S, W, and R, respectively.

TABLE 1. Percentage Extraction (% E) of Picrate Salts Obtained with Receptor 3, Calculated Association Constant (K_a), and Free Energy of Binding ($\Delta G°$). NMR Chemically Induced Upfield Shifts (CIS) Observed through *endo*-Complexation

					CIS[b] (ppm)			
entry	ammonium picrates **4a**−**g**	% *E*[a]	$K_a \times 10^{-4}$ (M^{-1})	$\Delta G°$ (kJ·mol^{-1})	α	*β*	*γ*	*δ*
1	$NH_4^+Pic^-$ (**4a**)	68	21 100[c]	−47.5				
2	$MeNH_3^+Pic^-$ (**4b**)	74	11 600[c]	−46.0	−2.85			
3	$EtNH_3^+Pic^-$ (**4c**)	81	32 800[d]	−48.6	−2.71	−2.86		
4	$PrNH_3^+Pic^-$ (**4d**)	73	5120[d]	−44.0	−2.43	−2.96	−2.33	
5	$BuNH_3^+Pic^-$ (**4e**)		124[d]	−34.8	−2.51	−2.69	−2.30	−1.64
6	$Me_2NH_2^+Pic^-$ (**4f**)		276[d]	−36.7	−2.78			
7	$Me_3NH^+Pic^-$ (**4g**)		5.2[d]	−26.9	−2.53			
8	$Me_4N^+Pic^-$ (**4h**)				−2.42			

[a] % *E* of picrate salts from water into $CHCl_3$ at 298 K. Arithmetic mean of two experiments. Errors estimated ±5%. [b] Chemically induced shifts defined as $\Delta\delta = \delta$(complexed ammonium) − δ(free ammonium). α, *β*, *γ*, and *δ* refer to the relative position of the protons from the charged nitrogen atom of the ammonium. [c] Calculated from the % *E* measurements and reported K_d values. Errors estimated ±5%. [d] Calculated from the percent competitive binding NMR measurements ($CDCl_3$/CD_3OD 92:8). Errors estimated ±10%.

NCH_2N protons of calix[6]TAC **3** give differentiated and well-defined signals (doublets at $\delta = 3.38$, 4.59 ppm and doublets at $\delta = 3.78$, 4.04 ppm, respectively) indicating that the covalent capping restricts both the TAC and the calix core mobility, leading to a rigidified calix-cryptand (Figure 1a).

Characterization of Host−Guest Complexes with Ammoniums, 3⊃4. ^1H NMR complexation studies were carried out at room temperature by introducing a CD_3OD solution of ammonium picrate salts **4b**−**h** (see Table 1) into a solution of calix[6]TAC **3** in $CDCl_3$. In all cases, formation of an *endo*-complex was evidenced by a novel ^1H NMR profile exhibiting resonances in the high field region for the guest. Figure 1b displays a representative example of *endo*-complex obtained by addition of only 1 equiv of ethylammonium picrate ($CDCl_3$/CD_3OD 98.5:1.5). The presence of a sharp triplet at −1.58 ppm together with a quadruplet at 0.32 ppm attests to the strong binding of the ammonium in the heart of the calixarene cavity. The CH_2N and CH_2O resonances belonging to the arms are strongly downfield shifted whereas one of the two signals corresponding to the NCH_2N protons is shifted upfield.[10] This indicates a deep change in the conformation of the cap upon complexation, the two methylene groups of the arms being projected toward the outside of the cavity. In contrast, the resonances corresponding to the calixarene core are barely affected by the complexation or by the guest nature, due to its rigidified capped structure. The chemically induced shifts (CIS) measured for the proton resonances of the included ammoniums are indicative of their spatial position in the aromatic cavity. Thus, the protons in *β*-positions of the charged nitrogen atom display higher shift values suggesting that they sit in the center of the *π*-basic cavity (see Table 1). With guests **4b**−**d**,**f**, stoechiometric complexation was observed upon addition of 1 equiv of ammonium. Under the same experimental conditions, the larger guests **4e**,**g**,**h** led to only partial complexation as the NMR signatures of free host **3** and free guest **4** were observed next to that of the *endo*-complex. Hence, the *in* and *out* exchange process was slower than the NMR time

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(10) The presence of a small amount of CD_3OD in the NMR spectra of complexes **3**⊃**4b**−**h** is not responsible for these NMR shifts since they were also observed when the spectra of the complexes **3**⊃**4b**−**h** were recorded in pure $CDCl_3$.

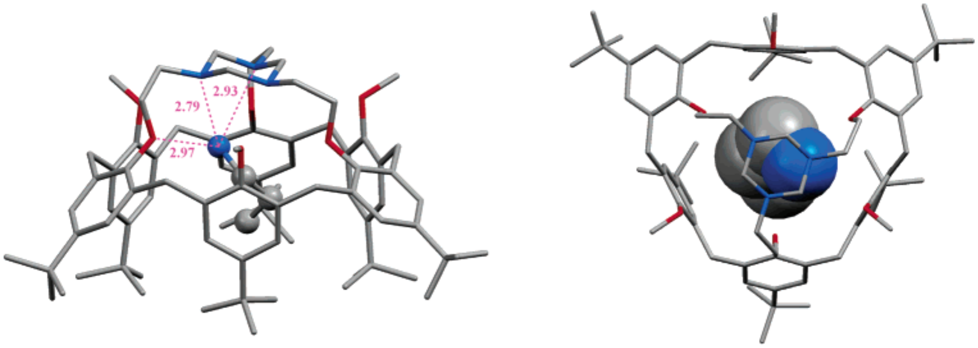

FIGURE 2. X-ray structure of complex **3**⊃**4d**: left, side view; right, top view. Hydrogen atoms, picrate counterion, and solvent of crystallization have been omitted for clarity. Indicated distance measurements are rounded off; see text for precise values.

scale, even at room temperature. This emphasizes the remarkable affinity of receptor **3** for cationic ammonium species. It is noteworthy that complexation still occurs with a quaternary ammonium salt (entry 8, Table 1). This suggests a good fit between the tetramethylated cation and the π-basic C_{3v} cavity. Finally, complexation experiments conducted under similar experimental conditions with calixtriamine **2** or its precursor calixtriamide **1** as potential hosts have not permitted the detection of any *endo*-complexation with ammonium picrates **4b**−**h** even at low temperature. It clearly demonstrates that rigidification of the calixarene cavity achieved by the cap is crucial for molecular recognition applications.

These NMR data were confirmed by an X-ray structure of complex **3**⊃**4d** crystallized out of an acetonitrile solution (Figure 2).[11] The calixarene host stands in a flattened alternate cone conformation. The three *tert*-butyl groups belonging to the anisole units are in the *in* position and close the entrance of the cavity. The TAC ring displays a chair conformation with the nitrogen lone pairs directed toward the inside of the cavity. The methoxy and the methylene groups of the arms are in the *out* position, thereby optimizing the space left for cation complexation. Indeed, the ammonium group of the guest is strongly hydrogen bonded to two nitrogen atoms of the cap [$d(\text{N}\cdots\text{N}) = 2.786(4)$ and 2.933(5) Å] and to one oxygen atom belonging to the calixarene unit [$d(\text{N}\cdots\text{O}) = 2.970(4)$ Å]. A perpendicular $\text{N}^+\cdots\text{Ar}$ distance of ca. 3.3 Å may also be indicative of cation−π interaction. Finally, the guest propyl chain sits in the center of the hydrophobic cavity, establishing CH−π interactions with the aromatic wall [$d(\text{C}\cdots\text{C}{=}\text{C}) = 3.47$ and 3.50 Å] that further stabilize the supramolecular edifice. To our knowledge, this X-ray structure provides the first example of a calix[6]arene with a simple ammonium guest deeply included in a well-defined cavity.[12]

Comparative Study of the Host Property of Receptor 3 toward Ammoniums 4. Extraction Experiments. The ability of calix[6]TAC **3** to extract solid ammoniums into a liquid phase was first studied by ^{1}H NMR. Extraction experiments were carried out at 298 K by introducing an excess of insoluble solid $\text{RNH}_3^+\text{Cl}^-$ (with R = Me, Et, or Pr) into a CDCl_3 solution of receptor **3**. Under these conditions, exactly 1 equiv of the ammonium chloride was solubilized leading to the formation of the corresponding C_{3v}-symmetrical *endo*-complex **3**⊃$\mathbf{RNH_3^+}$.[13] This result shows the efficiency of receptor **3** to perform solid−liquid extraction.

In a second set of experiments, the extraction ability of calix[6]TAC **3** toward ammoniums from water into CHCl_3 was evaluated using the standard solvent extraction technique of picrate salts described by Cram.[14] Thus, the experiments were conducted at 298 K by stirring an aqueous solution of picrate salts [i.e., **4a**−**d**] and an equimolar solution of host **3** in CHCl_3. The percentage extraction (% E) was deduced from the absorbance at 355 nm in the UV spectra of the aqueous layer (see the Supporting Information), and the results are summarized in Table 1.

To our knowledge, the percentage extraction values given in Table 1 are the highest ones ever reported with calixarene type hosts.[15] This remarkable result reveals the crucial contribution of the aza-cryptand cap in the preorganization of the receptor and in the stabilization of cationic species. The observed extraction efficiency sequence is **4c** > **4b** > **4d**. A similar sequence in % E has been found with calix[6]arene-based ester ligands.[15a] It is noteworthy that a high extraction percentage was also obtained for NH_4^+ despite the absence of an alkyl chain.

Determination of the Association Constant (K_a) and Free Energy of Binding ($\Delta G°$) by Competitive Binding NMR Experiments. On one hand, we calculated the association constant (K_a) and the free energy of binding ($\Delta G°$) between ammoniums **4a**,**b** and host **3**

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[11] Two different conformations were experimentally determined for the ammonium guest. One (50%) corresponds to that depicted in Figure 2. In the other one (50%), the propylammonium guest appears to be less strongly hydrogen bonded [$d(\text{N}\cdots\text{N}) = 2.766(7)$, 3.037(6) Å and $d(\text{N}\cdots\text{O}) = 3.107(6)$ Å] but undergoes a trans arrangement for its alkyl chain (see the Supporting Information).

[12] The X-ray of a pseudorotaxane obtained with a calix[6]arene presenting a ditopic binding site for a di-pyridinium salt was reported. See: Arduini, A.; Ferdani, R.; Pochini, A.; Secchi, A.; Ugozzoli, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 3453−3456.

[13] For example in the case of $\text{MeNH}_3^+\text{Cl}^-$, a sharp quadruplet corresponding to the methyl group of the ammonium included in the heart of the cavity was detected at −0.25 ppm while the NH_3^+ resonance was observed at ca. 4.9 ppm.

[14] Moore, S. S.; Tarnowski, T. L.; Newcomb, M.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 6398−6405. Helgeson, R. C.; Weisman, G. R.; Toner, J. L.; Tarnowski, T. L.; Chao, Y.; Mayer, J. M.; Cram, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 4928−4941. Kaplan, L. J.; Weisman, G. R.; Cram, D. J. *J. Org. Chem.* **1979**, *44*, 2226−2233. Cram, D. J.; Dicker, I. B. *J. Chem. Soc., Chem. Commun.* **1982**, 1219−1221.

[15] For percentage extraction values of ammonium picrates reported for calixarene type hosts under similar experimental conditions, see: (a) Han, S.-Y.; Kang, M.-H.; Jung, Y.; Chang, S.-K. *J. Chem. Soc., Perkin Trans. 2* **1994**, 835−839. (b) Reference 6e,f,h,i.

using the distribution constants (K_d) that have been reported by Cram[16] (Table 1, see the Supporting Information). On the other hand, we determined the affinity of ammoniums **4c**−**g** relative to **4b** for host **3** through ^{1}H NMR competitive binding experiments (see the Supporting Information for detailed procedures and salt ratios used for competitive experiments). For each experiment, two different ammonium picrates in CD_3OD solution were added to a solution of calix[6]TAC **3** in $CDCl_3$ at 298 K. The ratios at equilibrium of the corresponding *endo*-complexes and of the free ammoniums of each species were deducted from the integration of the NMR signals and allowed us to calculate the K_a and the $\Delta G°$ values for ammoniums **4c**−**g** toward host **3** (Table 1, see the Supporting Information).

The data reported in Table 1 emphasize the remarkable complexation ability and selectivity displayed by the calixarene cryptand. Indeed, the K_a values are much higher than those ever reported with calix[6]cryptands[6c] (with **4a**, $K_a = (0.7-2.9) \times 10^5$ M^{-1}) or 1,3-bridged-calix[5]arene[6j] (with **4e**, $K_a = (0.83-2.98) \times 10^2$ M^{-1}) bearing macrocyclic polyether subunits. Actually, these values lie among the best ones reported for Cram's receptors.[17] Host **3** and $EtNH_3^+$ **4c** have the best complementarity, and ammoniums possessing an alkyl chain just one carbon shorter ($MeNH_3^+$ **4b**) or longer ($PrNH_3^+$ **4d**) display much lower K_a and free energy of binding values. The affinity also decreases from primary to tertiary ammonium salts. All in all, the selectivity based upon the size and shape of the guest spreads over a range of more than 3 orders of magnitude (see Table 1). Under the same experimental conditions, precise NMR measurement of the K_a for larger ammonium **4h** was not possible, and complexation of the bulkier pyridinium and benzylammonium cations was not detected.

Conclusion

The synthesis of calix[6](aza)cryptand **3** possessing a TAC cap has been achieved via a very efficient three-step synthetic route from the symmetrical tris-methylated tBu-calixarene (69% overall yield). This novel compound presents a rigidified cone structure ideal for the inclusion of organic guests. An ^{1}H NMR study showed that calix[6]TAC **3** can perform *endo*-complexation of cationic ammoniums, the molecular recognition taking place through hydrogen bonding, cation− and CH−π interactions as revealed by the X-ray structure of complex **3**$\supset PrNH_3^+$. The affinity of host **3** toward ammoniums is remarkably high and selective with an optimal complementarity for $EtNH_3^+$. Last, a $CHCl_3$ solution of calixcryptand **3** efficiently extracts ammoniums from water, which may open new perspectives for phase transfer catalysis applications. We are now focusing our effort toward the synthesis of a chiral derivative of calix[6]TAC **3** that would act as an enantioselective receptor for chiral ammoniums.

Experimental Section

General Procedures. THF was distilled over sodium/benzophenone under argon. CH_2Cl_2 was distilled over CaH_2 under argon. Ethanol was distilled over sodium/diethylphthalate under argon. All reactions were performed under an inert atmosphere. Silica gel (230−400 mesh) was used for flash chromatography separations. ^{1}H and ^{13}C NMR spectra were recorded, respectively, at 200 and 50 MHz. Chemical shifts are expressed in ppm. Elemental analyses were performed at the Service de Microanalyze (ICSN, Gif sur Yvette, France) and at the Laboratoire de Microanalyze Organique (IRCOF, France).

5,11,17,23,29,35-Hexa-*tert*-butyl-37,39,41-trimethoxy-38,40,42-tris(carbamoylmethoxy)calix[6]arene 1. A solution of $X_6H_3Me_3$ (2.435 g, 2.40 mmol) in 20 mL of anhydrous THF was added to a solution of NaH (60% in oil, 0.335 g, 8.37 mmol) in 80 mL of anhydrous THF. The reaction mixture was stirred for 20 min at room temperature, and a solution of bromoacetamide (2.005 g, 14.5 mmol) in 10 mL of anhydrous THF was introduced. After 24 h of refluxing, the solvent was removed under reduced pressure and the resulting residue was dissolved in dichloromethane and washed with 25 mL of water. After dichloromethane extraction and solvent evaporation, the resulting crude compound was purified by flash chromatography (acetone/dichloromethane 3:7) giving pure calixtriamide **1** (2.59 g, 91%) as a white solid: mp 201 °C dec; IR ($CHCl_3$) ν 1673 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.94 (s, 27 H, tBu), 1.30 (s, 27H, tBu), 3.60 (s_l, 9H, OCH_3), 3.86 (s_l, 18H, ArCH_2Ar, OCH_2), 5.09 (s_l, 6H, NH_2), 6.55 (s, 6H, Ar*H*), 7.17 (s, 6H, Ar*H*); ^{13}C NMR ($CDCl_3$) δ 31.2, 31.5, 34.0, 34.3, 59.7, 71.5, 124.4, 127.6, 132.9, 146.0, 147.2, 152.1, 153.2, 171.0. Anal. Calcd for $C_{75}H_{99}N_3O_9 \cdot 2\,H_2O$: C, 73.68; H, 8.49; N, 3.44. Found: C, 73.71; H, 8.17; N, 3.52.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,39,41-trimethoxy-38,40,42-tris(2-aminoethoxy)calix[6]arene 2. A solution of BH_3/THF (50.0 mL, 1 M) was slowly added to calixtriamide **1** (1.78 g, 1.50 mmol), and the reaction mixture was refluxed for 24 h. Ethanol was slowly added at 0 °C until the gas liberation ceased. After removal of the solvent under reduced pressure, 50 mL of ethanol was added to the resulting residue and the reaction mixture was refluxed for 48 h. Ethanol was evaporated under reduced pressure, and the resulting viscous compound was pumped overnight under vacuum (0.1 mmHg) at 50 °C yielding calixtriamine **2** as a white solid, which was dissolved in dichloromethane and washed with 50 mL of an aqueous NaOH (1 M) solution. After removal under reduced pressure of the solvent, calixtriamine **2** (1.46 g, 85%) was obtained pure according to its ^{1}H NMR spectrum recorded immediately after isolation (however, irreproducible elemental analyses were obtained). Triamine **2** needs to be stored under argon atmosphere in a freezer: mp 180 °C dec; IR (KBr) ν 3400 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.00 (s, 27 H, tBu), 1.22 (s, 27H, tBu), 2.66 (s_l, 9H, OCH_3), 2.90 (s_l, 6H, CH_2N), 3.66 (s_l, 6H, CH_2O), 3.94 (s_l, 12H, ArCH_2Ar), 6.84 (s, 6H, Ar*H*), 7.09 (s, 6H, Ar*H*); ^{13}C NMR ($CDCl_3$) δ 30.2, 31.3, 31.5, 34.0, 34.1, 42.4, 60.1, 74.9, 125.0, 126.6, 133.1, 133.4, 145.7 (2C), 152.1, 153.9.

Calix[6]TAC 3. An aqueous solution (30%) of formaldehyde (0.100 mL, 1.0 mmol) was added at 0 °C to a solution of calixtriamine **2** (0.120 g, 0.105 mmol) in 2 mL of $CHCl_3$. The reaction temperature was slowly raised to room temperature, and the reaction was carefully monitored by ^{1}H NMR spectroscopy. After 50 min, 3 mL of water was added, the organic layer was separated, and the aqueous phase was extracted with $CHCl_3$. After removal of the solvent under reduced pressure, the resulting residue was recrystallized in $CHCl_3$/CH_3CN affording pure calix[6]TAC **3** (0.110 g, 89%) as a white solid: mp 241 °C; IR ($CHCl_3$) ν 3018 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.73 (s, 27 H, tBu), 1.37 (s, 27H, tBu), 2.66 (sl, CH_2N), 3.22 (sl, 6H, CH_2O), 3.38 (d, J = 16 Hz, 6H, ArC*Heq*), 3.75 (s, 9H, OCH_3), 3.78 (d, $J \sim 10$ Hz, 3H, NCH_2N), 4.04 (d, J = 12 Hz, 3H, NCH_2N), 4.59 (d, J = 16 Hz, 6H, ArC*Hax*), 6.53 (s, 6H, Ar*H*), 7.26 (s, 6H, Ar*H*); ^{13}C NMR ($CDCl_3$) δ 29.7, 31.2, 31.6, 33.9, 34.2, 52.9, 60.2, 69.6, 70.3, 122.9, 127.9, 132.7, 132.8, 145.0, 145.2, 152.5, 155.1. Anal. Calcd for $C_{78}H_{105}N_3O_6 \cdot 2H_2O$: C, 77.00; H, 9.03; N, 3.45. Found: C, 77.19; H, 8.87; N, 3.38.

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5,11,17,23,29,35-Hexa-*tert*-butyl-37,39,41-trimethoxy-38,40,42-tris[2-(2-isobutylideneaminoethoxy)]calix[6]arene 5. A solution of calixtriamine **2** (50 mg, 0.044 mmol) and isobutyraldehyde (0.012 mL, 0.13 mmol) in 3 mL of dry dichloromethane was stirred at room temperature in the presence of molecular sieves (4 Å). After filtration over Celite of the reaction mixture, the solvent was removed under reduced pressure giving pure calixtrisimine **5** (47 mg, 82%) as a white solid: mp 145 °C; IR ($CHCl_3$) ν 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.75 (s, 27 H, tBu), 1.08 (d, $J = 7.0$ Hz, 18H, $(CH_3)_2$CH), 1.37 (s, 27H, tBu), 2.12 (s, 9H, OCH_3), 2.43 (m, 3H, $(CH_3)_2CH$), 3.36 (d, $J = 15.7$ Hz, 6H, ArC*Heq*), 3.84 (t, $J = 5.5$ Hz, 6H, CH_2N), 4.07 (t, $J = 5.5$ Hz, 6H, CH_2O), 4.53 (d, $J = 14.9$ Hz, 6H, ArC*Hax*), 6.60 (s, 6H, Ar*H*), 7.25 (s, 6H, Ar*H*), 7.73 (d, $J = 4.7$ Hz, 3H, C*H*=N); ^{13}C NMR ($CDCl_3$) δ 15.8, 19.6, 30.0, 31.5, 32.0, 34.2, 34.4, 34.6, 60.3, 61.4, 72.1, 123.7, 128.3, 133.5, 133.9, 145.8, 145.9, 151.9, 154.8, 172.6. Anal. Calcd for $C_{87}H_{123}N_3O_6 \cdot 5\,H_2O$: C, 74.80; H, 9.60; N, 3.01. Found: C, 74.92; H, 9.43; N, 3.11.

X-ray Structure Determination of Complex 3⊃4d. Crystal data: $M_w = 1646.09$, triclinic, pale yellow crystal (0.6 × 0.4 × 0.15 mm^3), $a = 16.0412(3)$ Å, $b = 16.4620(6)$ Å, $c = 19.5672(7)$ Å, $\alpha = 92.048(2)°$, $\beta = 96.881(2)°$, $\gamma = 112.039(2)°$, $V = 4736.6(3)$ Å^3, space group *P*-1, $Z = 2$, $\rho = 1.154$ g cm^{-3}, μ(Mo Kα) = 0.77 cm^{-1}, 18 795 reflections measured at 223 K (Brucker-Nonius KappaCCD diffractometer[18]) in the 1.05–26.53° θ range, 18 720 unique, 1064 parametrs refined on F^2 using 18 720 reflections [SHELXL][19] to final indices $R[F^2 > 4\sigma F^2] = 0.077$, wR = 0.20 [$w = 1/[\sigma^2(F_o^2) + (0.1099P)^2 + 4.0995P]$ where $P = (F_o^2 + 2F_c^2)/3$]. Refinement details: complex **3⊃4d** cocrystallized with one molecule of picrate and four molecules of CH_3CN which was the solvent of crystallization. The ammonium complexed in the calixarene cage was found to be disordered and has been refined on two distinct sites of multiplicities equal to 0.5. All hydrogen atoms except those of the *tert*-butyl groups and the solvent molecules were located by a series of Fourier difference, included in the calculations but not refined. The last residual Fourier positive and negative peaks were equal to 0.81 and −0.53, respectively.

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Supporting Information Available: The ^1H and ^{13}C NMR spectra of compounds **1**, **2**, and **5**; the ^{13}C NMR spectrum of compound **3**; the HMQC spectra of compounds **1**–**3** and DEPT 135 spectrum of **1**; the X-ray structure corresponding to the second conformation of guest **4d** in complex **3⊃4d**; the general experimental methods (solid–liquid extraction of ammonium chloride salts by host **3**, percentage extraction measurements by the ultraviolet method, and determination of association constant and free energy of binding). This material is available free of charge via the Internet at http://pubs.acs.org.

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