New mono-ionizable, Li^+-selective calix[4]arenes

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A series of new mono-ionizable cone calix[4]arenes, with either a pendent carboxylic acid or a *N*-(X-sulfonyl)-carboxamide group, is synthesized and their alkali metal cation extraction behavior determined and compared with that for conformationally mobile analogues. These new proton-ionizable, cone calixarenes exhibit good (for the sulfonyl-carboxamides) to excellent (for the carboxylic acid) Li^+-selectivity. Surprisingly, the Li^+-selectivity decreases on going from the conformationally flexible to the cone ionophores due to enhanced Na^+ binding by the latter. During the ligand synthesis, unusual behavior of cone tributoxy-*N*-(trifluoromethylsulfonyl)carbamoylmethoxy-*p*-*tert*-butylcalix[4]-arene suggests a strong tendency for molecular association.

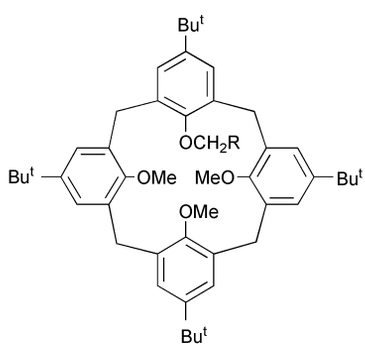
Introduction

Calix[4]arene-based ligands bearing functional groups on the lower rim are utilized widely in metal ion separations.[1] In particular, a number of calix[4]arene derivatives with high selectivities for Na^+, K^+, and Cs^+ have been reported.[2] On the other hand, only a few calix[4]arene dervatives have been found to exhibit selective recognition of Li^+ in the presence of other alkali metal cations (AMC).[3–9]

Lithium, in addition to its technological uses, is a bio-metal with a broad spectrum of physiological activities, which include applications in the treatment of various psychiatric disorders, viral diseases, cancer, and AIDS.[10] The important biochemical and clinical properties of Li^+ require control of its concentrations in biological systems and in the environment. An obstacle to accurate Li^+ determination is interference by other metal cations, particularly by Na^+ and K^+, that are present at much higher levels in biological tissues and natural waters. Development of new methods and reagents for selective separation of Li^+ from Na^+ and K^+ in aqueous solutions is an important and challenging objective.

Most of the reported calix[4]arenes that favor Li^+ binding are restricted to the cone conformation or adopt this conformation upon Li^+ coordination.‡ In general, the highest Li^+/Na^+ and Li^+/K^+ selectivities have been observed with calix[4]arenes that possess an acidic functional group. Most of these calixarene-based, Li^+-selective ionophores utilize a phenolic proton-ionizable group. Due to the low acidity of phenolic groups, metal ion binding by such ionophores requires a highly basic medium. An expanded variety of proton-ionizable groups may give rise to new Li^+-selective calix[4]arenes with enhanced ion-binding efficiency over a broad pH range.

Recently,[13] we reported the synthesis of the conformationally mobile mono-ionizable calix[4]arenes **1** and **2** that contain lower-rim carboxylic acid and *N*-(trifluoromethylsulfonyl)-carboxamide groups, respectively. Initial competitive solvent extraction experiments revealed selectivity of **1** and **2** for Li^+ over Na^+ and K^+. By NMR spectroscopy, it was established that both ligands adopt a dominant cone conformation in $CDCl_3$ in the presence of Li^+.[13] This results suggests that the synthesis of analogous mono-ionizable calix[4]arenes restricted to the cone conformation could provide ligands "preorganized"§ for Li^+ complexation with efficient and selective Li^+ complexation behavior. Herein we report the synthesis of five new mono-ionizable cone calix[4]arenes with a pendent carboxylic acid or *N*-(X-sulfonyl)carboxamide group and their extraction propensities toward alkali metal cations in comparison to the conformationally mobile analogues **1** and **2**.



R
1 CO_2H
2 $C(O)NHSO_2CF_3$

Results and discussion

Synthesis of mono-ionizable cone calix[4]arenes 5–9

Calix[4]arene ligands rigidified in the cone conformation with one proton-ionizable groups were prepared as shown in Scheme 1. The tributoxycalix[4]arene **3**[14] was reacted with ethyl bromoacetate and NaH to give cone ester **4** that was hydrolyzed to the cone calix[4]arene carboxylic acid **5**. Subsequently, **5** was

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‡ As shown in the literature (*e.g.*, references 11–15, Li^+ complexes with functionalized calix[4]arenes adopt the cone conformation predominantly.

§ The term "preorganization" of macrocyclic ligands for metal ion binding was first introduced by D. J. Cram, *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 1039.

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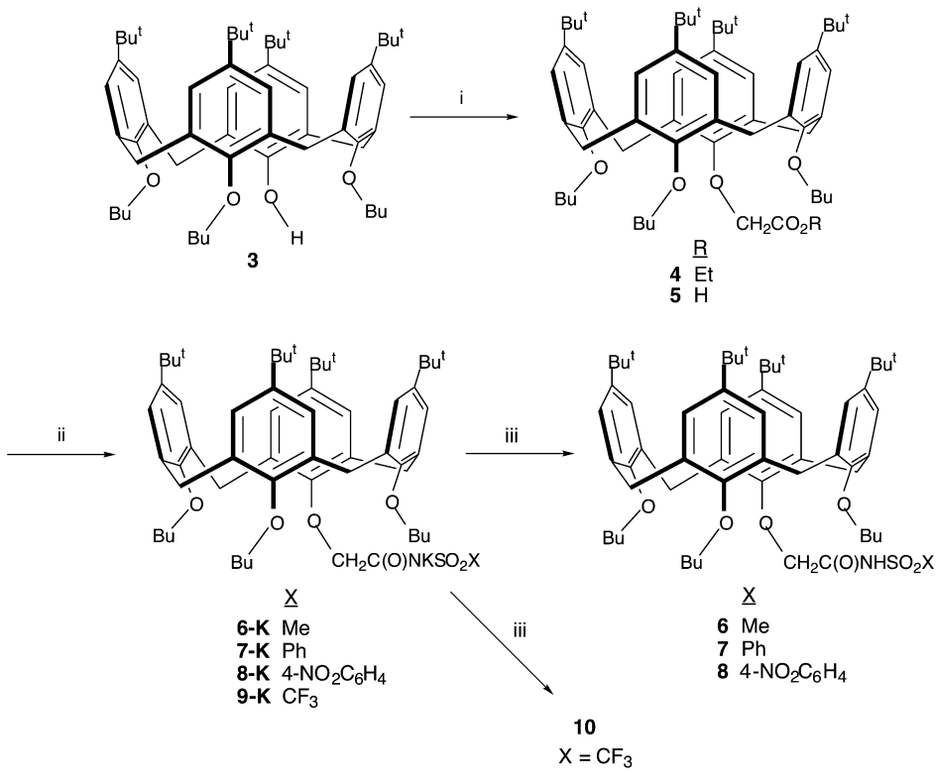

Scheme 1 *Reagents and conditions:* i) 1. $BrCH_2CO_2Et$, NaH, DMF; 2. NMe_4OH, THF–H_2O; ii) 1. $(COCl)_2$, C_6H_6; 2. XSO_2NH_2, KH, THF; iii) 10% HCl.

transformed *via* the corresponding acid chloride into potassium salts of cone calix[4]arene-*N*-(X-sulfonyl)carboxamides **6-K**–**9-K** by adaptation of an established procedure.[15] Salts **6-K**–**8-K** were converted smoothly into neutral calixarenes **6**–**8** upon treatment with 10% aqueous HCl.

Unusual behavior of the calix[4]arene-*N*-(trifluoromethylsulfonyl)carboxamide 9

Surprisingly, application of the same acid treatment to compound **9-K** (X = CF_3) did not provide the desired metal-free ligand **9**. Complete metal ion removal could not be affected even upon treatment of **9-K** with concentrated (36%) HCl. Instead, an unknown product **10** was obtained whose spectral characteristics were different from those anticipated for the neutral ligand **9**. Extended treatment of **9-K** or **10** with aqueous HCl resulted in hydrolysis back to carboxylic acid **5**.

The ^{1}H NMR spectrum of **10** in $CDCl_3$ (see Experimental) showed two sets of signals for each group of protons present. Also, two singlets were observed in the ^{19}F NMR spectrum of this compound in $CDCl_3$. However, both the ^{1}H and ^{19}F NMR spectra of **10** in DMSO-d_6 exhibited only one set of signals. This feature could be explained in terms of two interconverting species in **10**, with slow interconversion on the NMR time scale in $CDCl_3$ and rapid interconversion in DMSO-d_6.

The transformation of **9-K** into **10** by aqueous HCl was reversible. Thus treating **10** with aqueous K_2CO_3 gave **9-K** that was readily identified by its ^{1}H NMR spectrum.

When NaH was used as the base in the reaction of the acid chloride derived from **5** with trifluoromethanesulfonamide, **9-Na** was obtained. Treatment of **9-Na** with 10% aqueous HCl also did not give rise to neutral **9**. Now substance **10*** was obtained. According to the ^{1}H and ^{19}F NMR spectra of **10*** in $CDCl_3$, it was a mixture of **10** and **9-Na**. In DMSO-d_6, **10*** exhibited one set of signals in both the ^{1}H and ^{19}F NMR spectra, implying fast exchange between **9-Na** and **10**. Extended treatment of **10*** with aqueous HCl gave hydrolysis with formation of carboxylic acid **5**. It was found that **10*** or **10** itself could be converted into **9-Na** by treatment with aqueous Na_2CO_3. Also, **9-K** was transformed into **9-Na** by a similar treatment.

All of these results suggest that **10** is composed of two distinct species. Both are derivatives of **9**, contain a CF_3SO_2-fragment (^{19}F NMR signals), and easily interconvert in a polar solvent. These species cannot be attributed to conformational isomers of the calix[4]arene unit in **9** or its derivatives since the $-OC_4H_9$ groups are large enough to prevent rotation of arene units. A hypothetical structure for **10** as an associated dimer (or trimer) of neutral and ionized units of **9** is depicted in Fig. 1.

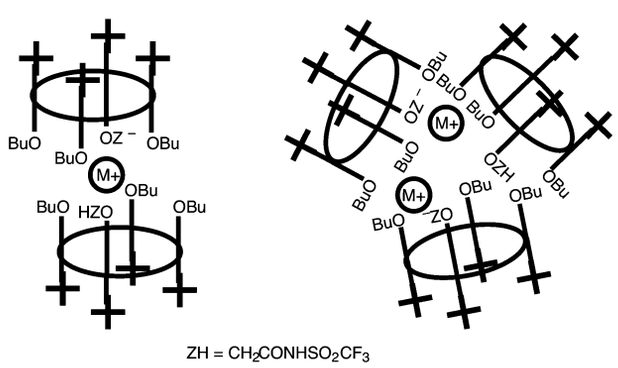

Fig. 1 Proposed structure of **10**.

To evaluate this potential structure for **10**, electrospray ionization (ESI) mass-spectrometry was employed. The positive-ion ESI mass spectrum of **10*** shown in Fig. 2 demonstrates clearly that molecular association does take place in this system. Along with the ions attributed to the "monomeric" species containing one ligand **9** entity (*m*/*z* about 1000), "dimeric" (*m*/*z* about 2000) and "trimeric" (*m*/*z* about 3000) species with two and three entities of **9**, respectively, are observed in the mass spectrum. Representative peaks (the most intense in each series) and their assignments are listed in Table 1. As expected, the relative abundance of the species diminishes as the level of association increases.

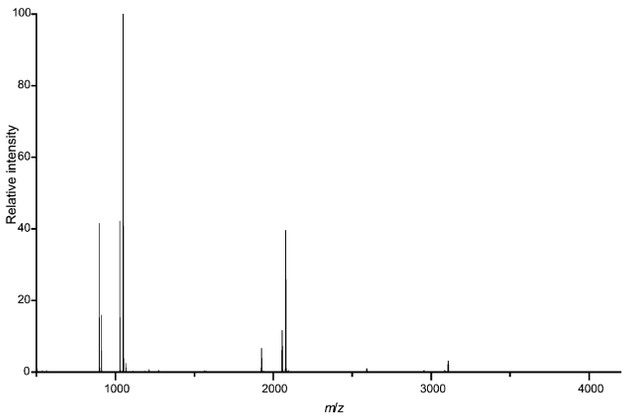

Fig. 2 Positive-ion ESI mass spectrum of **10***.

Table 1 Representative peaks in the positive-ion ESI mass spectrum of **10***

Ion	*m*/*z*	Relative intensity
$[\mathbf{9} + Na + H - SO_2CF_3]^+$	897.50	41.5
$[\mathbf{9} + Na]^+$	1029.50	42.2
$[\mathbf{9} + 2Na - H]^+$	1051.43	100
$[\mathbf{9}_2 + 2Na - SO_2CF_3]^+$	1925.96	6.24
$[\mathbf{9}_2 + 2Na - H]^+$	2057.80	11.6
$[\mathbf{9}_2 + 3Na - 2H]^+$	2079.68	25.8
$[\mathbf{9}_3 + 4Na - 3H]^+$	3108.07	3.05

When the heavier species ("trimer" ions) were subjected to "tandem" MS/MS, fragmentation they produced lighter particles – "dimeric" and "monomeric" ions. Thus assembling of the "monomeric" units into the larger supramolecular structures through weak intermolecular interactions is confirmed. There is only one proton (N*H*) capable of participation in hydrogen bonding of the "monomeric" units present in **9**. Therefore, it appears that binding of a metal ion to multiple donor atoms of two calix[4]arene units plays an important role in this association, together with the hydrogen bonding. The structures presented in Fig. 1 are believed to be present in solutions of **10** in nonpolar solvents.

Increased stability of the associated structures of **10** upon treatment with aqueous HCl compared to those of **6-K**–**8-K** can be rationalized by shielding of its anionic centers from protons by an array of hydrophobic butyl groups and the higher acidity of the proton-ionizable group in **9** compared to those in **6**–**8**.

Solvent extraction of alkali metal cations by the mono-ionizable calix[4]arenes

To probe AMC binding by mono-ionizable calix[4]arenes **1**, **2** and **5**–**9**, competitive solvent extraction of Li^+, Na^+, K^+, Rb^+, and Cs^+ from aqueous solutions (10.0 mM in each alkali metal chloride, pH 11.9) by 1.00 mM ligand in chloroform was conducted. Since ligand **9** could not be obtained in the neutral form, it was utilized in the extraction experiments as its potassium salt **9-K** with the initial KCl concentration in the aqueous phase reduced accordingly.

All seven of the calixarenes exhibited efficient alkali metal cation extraction (total metal loading of the ligand approximately 100%) with significant Li^+ selectivity over the other AMC. The major competing ion was Na^+, with K^+ loadings below 0.1% and undetectable extraction of Rb^+ and Cs^+. Values of the distribution ratios, *D*, determined for Li^+ and Na^+ extraction are presented in Table 2. The Li^+/Na^+ selectivity for these mono-ionizable calixarenes was calculated as the ratio D_{Li}/D_{Na}.

As is evident from the data presented in Table 2, calix[4]arene carboxylic acids **1** and **5** are much more selective Li^+ extractants than are the calix[4]arene-*N*-(X-sulfonyl)carboxamides. This may be explained by a greater affinity of the "hard" electron acceptor Li^+ for binding with a "harder" carboxylate donor group than with the "softer" ionized *N*-(X-sulfonyl)-carboxamide moieties. Within the series of calix[4]arene-*N*-(X-sulfonyl)carboxamides, the Li^+-selectivity decreases somewhat as X is varied in the order: CF_3 > Ph > 4-$NO_2C_4H_6$ > Me.

An interesting and somewhat unexpected observation relates to the difference in Li^+/Na^+-selectivity of the conformationally mobile mono-ionizable calix[4]arenes and their analogs that are restricted to the cone conformation. Although with both the calix[4]arene carboxylic acids and *N*-(X-sulfonyl)carboxamides, the D_{Li} values do not change much on going from the confomationally mobile ligands to the cone compounds, the latter allow larger distributions of Na^+¶ into the organic phase. As a result, mobile ligands **1** and **2** provide more selective extraction of Li^+ than do their rigid cone analogs, **5** and **9**. This observation is in apparent contradiction with an anticipated improvement in Li^+-selectivity due to "preorganization" of the calixarenes in the conformation favored by this metal cation.

To determine the dependence of AMC binding by the mono-ionizable calixarenes on the acidity of the aqueous phase, competitive extraction of Li^+, Na^+, K^+, Rb^+ and Cs^+ from 10.0 mM (in each AMC) aqueous chloride–hydroxide solutions of varying pH into chloroform by 1.00 mM ligands **1**, **2** and **5**–**8** was examined. Calixarene **9**, available only in the form of its potassium salt **9-K**, was omitted from this study. The pH-profiles for extractions by the carboxylic acids **1** and **5** and the *N*-(X-sulfonyl)carboxamides **2** and **6**–**8** are shown in Figs. 3 and 4, respectively.

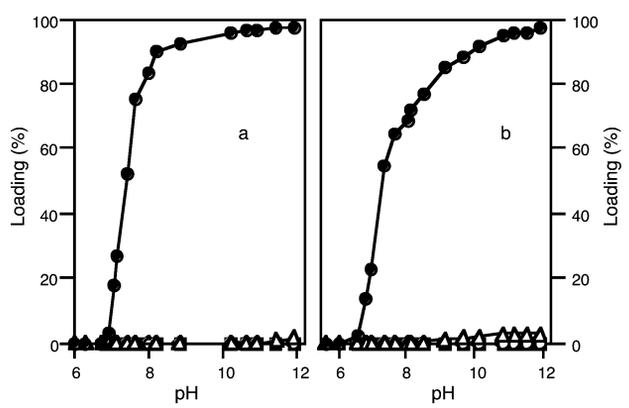

Fig. 3 pH-Profiles for competitive extraction of Li^+ (●), Na^+(△), K^+(○), Rb^+(■) and Cs^+(◇) from 10.0 mM (in each metal ion) aqueous chloride–hydroxide solutions into chloroform by 1.00 mM calix[4]arene carboxylic acids (a) **1** (mobile) and (b) **5** (cone).

As is readily apparent, all of the calixarenes exhibit a preference for Li^+ over the other AMC for a wide pH range. Loadings of the ligands with K^+ were below 0.1%. None of the calixarenes showed detectable extraction of Rb^+ or Cs^+. The efficiency of Li^+ extraction increases dramatically with enhanced aqueous phase basicity. The carboxylic acids (Fig. 3) require higher pH to achieve quantitative metal loading than do their *N*-(X-sulfonyl)carboxamide analogs (Fig. 4). Thus for mobile and cone carboxylic acids (**1** and **5**, respectively), the pH of half-extraction, $pH_{1/2}$, is about 7.3. Within the series of *N*-(X-sulfonyl)carboxamides, the $pH_{1/2}$ values vary from 7.0 for **6** (X = Me, cone) to 6.7 for **7** (X = Ph, cone) to 5.7 for **8** (X = C_6H_4-4-NO_2, cone) to 3.3 for **2** (X = CF_3, mobile). These observations are consistent with the previously discussed[16] different proton-dissociation abilities of calixarene-based ligands containing -CO_2H and -C(O)$NHSO_2X$ groups.

¶ Na^+ does not show preference for any particular conformation of functionalized calix[4]arenes and gives complexes that are mixtures of conformers, mostly cone and partial cone.[13]

Table 2 Competitive extraction of AMC[a] from 10.0 mM aqueous chloride–hydroxide solutions (pH 11.9) into chloroform by 1.00 mM mono-ionizable calix[4]arenes

Ligand	Proton-ionizable group (conformation)	D_{Li}	D_{Na}	D_{Li}/D_{Na}
1	CO_2H (mobile)	0.107	0.00191	57
5	CO_2H (cone)	0.107	0.00332	32
2	$C(O)NHSO_2CF_3$ (mobile)	0.0829	0.0101	8.3
6	$C(O)NHSO_2Me$ (cone)	0.0630	0.0431	1.5
7	$C(O)NHSO_2Ph$ (cone)	0.0791	0.0274	2.9
8	$C(O)NHSO_2C_6H_4$-4-NO_2 (cone)	0.0734	0.0330	2.2
9[b]	$C(O)NHSO_2CF_3$ (cone)	0.0840	0.0225	3.7

[a] Extraction levels of K^+ were too low for accurate D_K determination. Extraction of Rb^+ and Cs^+ was undetectable. [b] Used as the potassium salt **9-K**.

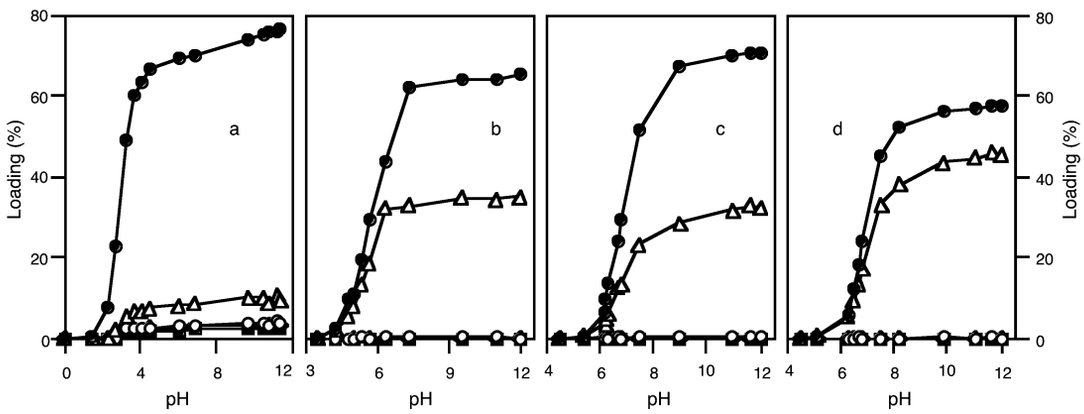

Fig. 4 pH-Profiles for competitive extraction of Li^+ (●), Na^+(△), K^+(○), Rb^+(■) and Cs^+(◇) from 10.0 mM (in each metal ion) aqueous chloride–hydroxide solutions into chloroform by 1.00 mM calix[4]arene-*N*-(X-sulfonyl)carboxamides: (a) mobile **2** (X = CF_3), and cone ligands (b) **6** (X = Me), (c) **7** (X = Ph), and (d) **8** (X = C_6H_4-4-NO_2).

Direct comparison of Li^+-separation efficiency and selectivity of the ionophores described herein with those reported for Li-selective calixarenes is not possible since those were chromogenic/fluorogenic reagents[3–7] studied under different experimental conditions. However, the D_{Li}/D_{Na} selectivity ratios found for ligands **1** and **5** are among the best Li^+/Na^+ selectivities reported. All of the ionophores examined in this work show dramatically improved separation of Li^+ from other AMC compared with their closest reported structural analog,[8] a barely Li^+-selective mono-ionizable calix[4]arene containing a –P(O)(OR)OH group on the lower rim. In contrast with related calixarene-based reagents, new ligands **1**, **2** and **5**–**9** allowed specific extraction of Li^+ from aqueous solutions over a wide pH range.

Concluding remarks

Introduction of one proton-ionizable group on the lower rim of the calix[4]arenes is promising for the design of highly selective extractants for the separation of Li^+ from other AMC, particularly Na^+ and K^+. However, "preorganization" of the ligand for Li^+ binding by restriction to the cone conformation may lead to a decrease of Li^+/Na^+ selectivity compared with conformationally mobile analogues, as was observed herein for the calix[4]arene-*N*-(X-sulfonyl)carboxamides and carboxylic acids.

Experimental

General

NMR spectra were measured with a Varian Unity INOVA spectrometer (499.7 MHz for ^1H, 125.7 MHz for ^{13}C, 470.2 MHz for ^{19}F). Chemical shifts (δ) are expressed in ppm downfield from TMS (^1H and ^{13}C) and CCl_3F (^{19}F), with coupling constant (J) values given in Hz. Electrospray ionization (ESI) mass spectra were measured with an API QSTAR™ Pulsar Hybrid LC/MS/MS System (Applied Biosystems). The pH was determined with a Fisher Scientific Accumet® 50 pH–ion–conductivity meter. Concentrations of alkali metal cations in aqueous solutions were determined with a Dionex DX-120 ion chromatograph. Samples for solvent extraction were shaken with a Glas-Col® Multi-Pulse Vortexer.

Anhydrous alkali metal chlorides (99%, Alfa Aesar®) and LiOH (purified, Fisher Scientific) were used as received. Compounds **1**, **2**,[13] and **3**[14] were prepared by reported procedures.

Synthesis of calixarenes 5–9 restricted to the cone conformation 26,27,28-Tributoxy-25-carboxymethoxy-5,11,17,23-tetrakis-(1,1-dimethylethyl)calix[4]arene 5

To a solution of **3** (17.20 g, 21.0 mmol) in DMF (300 mL) under nitrogen, NaH (0.77 g, 32.0 mmol) was added. After stirring the mixture for 15 min at room temperature, ethyl bromoacetate (7.01 g, 42.0 mmol) was added dropwise and the mixture was stirred under nitrogen for 24 h at 80 °C. Second portions of NaH (0.15 g, 6.3 mmol) and ethyl bromoacetate (1.40 g, 8.4 mmol) were added to the mixture at room temperature and stirring was continued for another 24 h at 80 °C. The mixture was diluted with CH_2Cl_2 (700 mL), washed with 1M aqueous HCl and then water, dried ($MgSO_4$), and evaporated *in vacuo*. The residue was chromatographed on silica gel with CH_2Cl_2–hexanes (1 : 5) and then EtOAc–CH_2Cl_2 (1 : 9) as the eluents, followed by crystallization from CH_2Cl_2–MeOH to give ester **4** as a white solid. Yield 17.70 g (93%); mp 157–158 °C; IR (deposit from CH_2Cl_2 solution on a NaCl plate, cm^{-1}) ν/cm^{-1}1767 (C=O); δ_H: 0.96–1.12 (m, 27 H), 1.19 (s, 18 H), 1.28 (t, J = 7.1, 3 H), 1.33–1.52 (m, 6 H), 1.86–1.97 (m, 4 H), 2.07–2.15 (m, 2 H), 3.09–3.20 (d + d, 4 H), 3.74–3.89 (m, 6 H), 4.19 (q, J = 7.1, 2 H), 4.40 (d, J = 12.4, 2 H), 4.67 (d, J = 12.5, 2 H), 4.88 (s, 2 H), 6.61–6.64 (d + d, 4 H), 6.92 (s, 2 H), 6.93 (s, 2 H). Anal. calcd for $C_{60}H_{86}O_6$: C 79.78, H 9.60. Found: C 79.97, H 9.53%.

A solution of ester **4** (16.71 g, 18.5 mmol) in THF and 10% aqueous Me_4OH (200 mL of each) was refluxed for 16 h. The THF was evaporated *in vacuo* and CH_2Cl_2 and 6 M aqueous HCl were added. The organic layer was washed with water, dried ($MgSO_4$), and evaporated *in vacuo* to give **5** as a white solid. Yield 15.55 g (96%); mp 105–107 °C; IR (deposit from CH_2Cl_2 solution on a NaCl plate, cm^{-1}) ν/cm^{-1} 1765 (C=O); δ_H: 0.83 (s, 18 H), 0.94–1.02 (m, 9 H), 1.28–1.38 (m, 20 H), 1.40–1.49 (m, 4 H), 1.79–1.93 (m, 6 H), 3.16 (d, J = 12.4, 2 H), 3.23 (d, J = 12.8, 2 H), 3.70–3.83 (m, 4 H), 4.05–4.11 (m, 2 H), 4.23 (d, J = 12.8, 2 H), 4.45 (d, J = 12.4, 2 H), 4.67 (s, 2 H), 6.48 (d, J = 2.3, 2 H), 6.58 (d, J = 2.3, 2 H), 7.14 (s, 2 H), 7.15 (s, 2 H), 11.29 (s, 1 H); δ_C: 14.0, 14.2, 18.9, 19.3, 30.9, 31.1, 31.2, 31.61, 31.65, 31.8, 32.0, 33.7, 34.1, 34.2, 70.9, 75.9, 76.4, 124.5, 125.1, 125.4, 126.0, 131.5, 132.6, 135.0, 135.5, 144.9, 145.0, 147.0, 151.2, 152.1, 154.3, 170.7. Anal. calcd for $C_{58}H_{82}O_6$: C 79.59, H 9.44. Found: C 79.69, H 9.31%.

General procedure for preparation of 26,27,28-tributoxy-25-(*N*-potassio-*N*-X-sulfonyl)carbamoylmethoxy-5,11,17,23-tetrakis-(1,1-dimethylethyl)calix[4]arenes 6-K–9-K

A solution of **5** (2.63 g, 3.0 mmol) and oxalyl chloride (0.76 g, 6.0 mmol) in C_6H_6 (30 mL) was stirred under nitrogen at 70 °C for 4 h and the solvent was evaporated *in vacuo*. A solution of the residue in THF was added to a mixture of the appropriate sulfonamide (3.75 mmol) and KH (0.60 g, 15.0 mmol) in THF. The mixture was stirred at room temperature for 12 h (45 minutes for **8-K**). Then 5 mL of H_2O was added and the THF was evaporated *in vacuo*. EtOAc was added to the residue. The organic layer was washed with aqueous K_2CO_3, dried (K_2CO_3), and evaporated *in vacuo*. Salts **6-K**, **7-K**, and **9-K** were crystallized from $CHCl_3$–MeOH (1 : 9). Salt **8-K** was purified by chromatography on alumina with CH_2Cl_2 then CH_2Cl_2–MeOH (99 : 1) as eluents.

26,27,28-Tributoxy-25-*N*-(X-sulfonyl)carbamoylmethoxy-5,11,17,23-tetrakis(1,1-dimethylethyl)calix[4]arenes 6–8 and substance 10

Potassium salts **6-K**–**9-K** were dissolved in CH_2Cl_2. The solution was washed with 10% aqueous HCl and then water, dried ($MgSO_4$), and evaporated *in vacuo*.

6 (X = Me): colorless solid, yield 92%; mp 93–94 °C; IR (deposit from CH_2Cl_2 solution on a NaCl plate, cm^{-1}) ν/cm^{-1} 1712 (C=O); δ_H: 0.85 (s, 18 H), 0.94 (t, J = 7.4, 6 H), 0.98 (t, J = 7.3, 3 H), 1.31 (s, 9 H), 1.32 (s, 9 H), 1.22–1.43 (m, 6 H), 1.66–1.84 (m, 4 H), 1.86–2.01 (m, 2 H), 3.15 (d, J = 12.5, 2 H), 3.28 (d, J = 13.2, 2 H), 3.43 (s, 3 H), 3.73–3.84 (m, 2 H), 3.89–4.04 (m, 4 H), 4.33 (d, J = 13.2, 2 H), 4.38 (d, J = 12.5, 2 H), 5.00 (s, 2 H), 6.45 (d, J = 2.4, 2 H), 6.52 (d, J = 2.4, 2 H), 7.09 (s, 4 H), 10.94 (s, 1 H); δ_C: 14.0, 19.0, 19.1, 31.1, 31.3, 31.6, 31.7, 31.9, 33.6, 34.0, 42.0, 74.1, 74.4, 76.1, 124.2, 125.2, 125.4, 126.5, 131.2, 132.4, 133.7, 135.5, 144.6, 144.9, 145.9, 151.8, 153.7, 153.8, 171.2. Anal. calcd for $C_{59}H_{85}NO_7S$: C 74.41, H 9.00, N 1.47. Found: C 74.53, H 9.08, N 1.35%.

7 (X = Ph): colorless solid, yield 91%; mp 98–99 °C; IR (deposit from CH_2Cl_2 solution on a NaCl plate, cm^{-1}) ν/cm^{-1} 1716 (C=O); δ_H: 0.87 (s, 18 H), 0.91 (t, J = 7.3, 3 H), 0.94 (t, J = 7.4, 6 H), 1.28 (s, 9 H), 1.31 (s, 9 H), 1.23–1.43 (m, 6 H), 1.67–1.88 (m, 4 H), 1.88–2.02 (m, 2 H), 3.16 (d, J = 12.6, 2 H), 3.27 (d, J = 13.3, 2 H), 3.75–3.89 (m, 2 H), 3.91–4.06 (m, 4 H), 4.34 (d, J = 13.3, 2 H), 4.39 (d, J = 12.6, 2 H), 4.92 (s, 2 H), 6.45 (d, J = 2.4, 2 H), 6.53 (d, J = 2.4, 2 H), 7.04 (s, 2 H), 7.08 (s, 2 H), 7.52–7.60 (m, 2 H), 7.61–7.68 (m, 1 H), 8.15–8.22 (m, 2 H), 10.94 (s, 1 H); δ_C: 14.0, 18.9, 19.1, 31.2, 31.5, 31.7, 32.0, 33.7, 74.7, 76.1, 124.2, 125.3, 125.4, 126.5, 128.6, 128.8, 131.3, 132.4, 133.4, 133.7, 135.3, 144.5, 144.9, 151.9, 153.8, 169.8. Anal. calcd for $C_{64}H_{87}NO_7S$: C 75.77, H 8.64, N 1.38. Found: C 75.78, H 8.97, N 1.33%.

8 (X = C_6H_4-4-NO_2: light yellow solid, yield 75%; mp 101–103 °C; IR (deposit from CH_2Cl_2 solution on a NaCl plate, cm^{-1}) ν/cm^{-1} 1718 (C=O); δ_H: 0.84 (s, 18 H), 0.91 (t, J = 7.4, 3 H), 0.95 (t, J = 7.3, 6 H), 1.30 (s, 9 H), 1.33 (s, 9 H), 1.22–1.43 (m, 6 H), 1.66–1.88 (m, 4 H), 1.88–2.01 (m, 2 H), 3.18 (d, J = 12.6, 2 H), 3.29 (d, J = 13.2, 2 H), 3.74–3.87 (m, 2 H), 3.92–4.06 (m, 4 H), 4.30 (d, J = 13.2, 2 H), 4.38 (d, J = 12.6, 2 H), 4.98 (s, 2 H), 6.42 (d, J = 2.4, 2 H), 6.51 (d, J = 2.4, 2 H), 7.08 (s, 2 H), 7.11 (s, 2 H), 8.35–8.43 (m, 4 H), 11.29 (s, 1 H); δ_C: 14.0, 18.9, 19.1, 31.1, 31.3, 31.5, 31.7, 31.9, 32.2, 33.7, 34.0, 73.9, 74.6, 76.2, 124.0, 124.1, 125.3, 125.5, 126.6, 130.1, 130.9, 132.2, 133.4, 135.4, 144.7, 144.8, 145.1, 145.9, 150.6, 151.6, 153.8, 153.9, 171.3. Anal. calcd for $C_{64}H_{86}N_2O_9S$: C 72.56, H 8.18, N 2.64. Found: C 72.66, H 8.40, N 2.56%.

10: colorless solid; δ_H ($CDCl_3$): 0.826 (s) + 0.833 (s) (17 H), 0.90–1.01 (m, 9 H), 1.332 (s) + 1.337(s) + 1.342 (s) (21 H), 1.38–1.48 (m, 3 H), 1.62–1.77 (m, 2 H), 1.81–1.98 (m, 4 H), 3.16 (d, J = 12.3) + 3.18 (d, J = 12.5) (2 H), 3.25 (d, J = 13.0) + 3.31 (d, J = 13.1) (2 H), 3.70–3.82 (m, 2 H), 3.84–3.98 (m, 2 H), 3.99–4.05 (m, 1 H), 4.07–4.15 (m) + 4.15 (d, J = 13.0) (2 H), 4.29 (d, J = 13.1, 0.7 H), 4.39 (d, J = 12.3) + 4.45 (d, J = 12.5) (2 H), 4.88 (s, 1 H), 5.14 (s, 0.7 H), 6.41 (d, J = 2.4, 0.7 H), 6.47 (d, J = 2.4) + 6.50 (d, J = 2.4) (1.9 H), 6.62 (d, J = 2.4, 1.1 H), 7.117 (s) + 7.124 (s) + 7.14 (s) + 7.16 (s) (4 H); δ_F ($CDCl_3$): −74.7 (0.7 F), −80.3 (1 F); δ_H (DMSO-d_6): 0.916 (s) + 0.927 (s) +0.96 (t, J = 7.5) + 0.97 (t, J = 7.5) (27 H), 1.11 (s, 18 H), 1.32–1.42 (m, 4 H), 1.44–1.53 (m, 2 H), 1.88–2.05 (m, 6 H), 3.06 (d + d, J = 12.5, 4 H), 3.59–3.66 (m, 2 H), 3.73–3.80 (m, 2 H), 3.91–3.99 (m, 2 H), 4.29 (d, J = 12.4) + 4.31 (s) (4 H), 4.60 (d, J = 12.5, 2 H), 6.60 (s) + 6.61 (s) (4 H), 6.85 (d, J =2.2, 2 H), 6.89 (d, J =2.2, 2 H); δ_F (DMSO-d_6): −77.3.

Alkali metal salts of calixarene 9

9-K: colorless solid; δ_H ($CDCl_3$): 0.97 (s) + 0.99 (s) + 0.99 (t) (24 H), 1.07 (t, J = 7.4, 3 H), 1.24 (s, 18 H), 1.33–1.47 (m, 4 H), 1.48–1.58 (m, 2 H), 1.73–1.95 (m, 6 H), 3.30 (d, J = 12.6, 4 H), 3.72–3.86 (m, 4 H), 4.09–4.17 (m, 2 H), 4.27 (d) + 4.29 (s) (4 H), 4.32 (d, J = 12.6, 2 H), 6.90 (s, 2 H), 6.92 (s, 2 H), 7.13 (d, J = 2.0, 2 H), 7.17 (d, J = 2.0, 2 H); δ_F ($CDCl_3$): −77.3. Anal. calcd for $C_{59}H_{81}F_3KNO_7S$: C 67.85, H 7.82, N 1.34. Found: C 68.11, H 8.12, N 1.39%.

9-Na: colorless solid; δ_H ($CDCl_3$): 1.03 (s) + 0.96–1.10 (m) (27 H), 1.20 (s) + 1.21 (s) (18 H), 1.31–1.43 (m, 4 H), 1.45–1.53 (m, 2 H), 1.81–1.98 (m, 4 H), 2.03–2.13 (m, 2 H), 3.29–3.39 (m, 4 H), 3.92–4.15 (m, 6 H), 4.23 (d, J = 12.6, 2 H), 4.37 (d, J = 12.5, 2 H), 4.49 (s, 2 H), 6.92–7.00 (m, 4 H), 7.11–7.17 (m, 4 H); δ_F ($CDCl_3$): −77.1.

Competitive solvent extraction of AMC

Aqueous solutions (10.0 mM in each of Li^+, Na^+, K^+, Rb^+ and Cs^+ chlorides with the pH adjusted with dilute HNO_3 or LiOH) were extracted with an equal volume of 1.00 mM calixarene in $CHCl_3$. After extraction, the pH of the aqueous phase was measured, the organic phase was stripped with aqueous 0.10 M HCl, and the AMC concentrations in the stripped solution were determined by ion chromatography.

As found experimentally for extractions with calixarenes **1**, **2** and **5**–**8**, equilibrium was reached within 10 min of vigorous phase contact by vortexing. However, phase equilibration in the extraction with **9-K** took more than 10 h.

Sample preparation for ESI mass-spectrum measurement

A solution of 1.0 mg of **10*** in 1.00 mL of MeOH was vortexed for 2 min to ensure the complete dissolution. This solution was used for the MS measurements.

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