Di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-5 and -crown-6 compounds in the cone conformation: synthesis and alkaline earth metal cation extraction

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Di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-5 and -crown-6 ethers in the cone conformation were prepared and their conformations and regioselectivities were verified by NMR spectroscopy. The metal ion-complexing properties of these ligands were evaluated by competitive solvent extractions of alkaline earth metal cations from water into chloroform. The ligands were found to be efficient extractants with selectivity for Ba^{2+}. The maximal loadings were 95–100% as calculated for formation of 1 : 1 ionized ligand–metal ion complexes. With the variation of proton-ionizable groups, which were oxyacetic acid moieties and *N*-(X)sulfonyl oxyacetamide units with X = methyl, phenyl, 4-nitrophenyl, and trifluoromethyl, "tunable" acidity was obtained.

Introduction

Calixarenes, which are cyclic oligomers derived from condensation reactions of phenols and formaldehyde under basic or acidic conditions, were first synthesized by Zinke in the 1940s. However, calixarene chemistry did not flourish until Gutsche and coworkers developed methods for synthesizing calixarenes in good and reproducible yields and drew attention to the potential use of these oligomers as molecular receptors in the 1970s.[1]

In the absence of structural modification, the calixarene scaffold itself exhibits only weak metal ion affinity and poor selectivity.[2] Structural modification of calixarenes is usually performed on the phenolic hydroxyl groups (lower rim) and the *p*-positions (upper rim). For selective cation complexation, structural variation on the lower rim is more common.

Among various calix[4]arene derivatives, calix[4]crown compounds are receiving considerable attention because introduction of a crown ether loop on the lower rim not only increases the cation binding ability of the parent calix[4]arene, but allows control of the selectivity through modulation of the crown ether size.[1] Two types of crown ether chain bridging on the lower rim of a calix[4]arene molecule are possible: 1,3-bridging of distal phenolic units and 1,2-bridging of proximal phenolic units. Studies of calix[4]crown compounds have focused heavily on the 1,3-bridged isomers. This type of ligand was found to exhibit high binding affinity and selectivity in alkali and alkaline earth metal cation extractions.[3] Compared with 1,3-bridged calix[4]crowns, research on 1,2-bridged calix[4]crowns is limited. In general, the reported 1,2-bridged calix[4]crown compounds exhibit poor binding ability and selectivity toward metal cations.[4]

The first examples of calix[4]arene-1,2-crown compounds, *p-tert*-butylcalix[4]arene-1,2-crown-5 and -1,2,3,4-biscrown-5 were reported by Ungaro and coworkers in 1990.[4a] Three years later Ungaro and coworkers evaluated the complexation of alkali metal cations by *p-tert*-butylcalix[4]arene-1,2,3,4-biscrown-5 and found that the ligand showed very little selectivity.[4b] Arnard-Neu and coworkers synthesized *p-tert*-butylcalix[4]arene-1,2-crown-4, -crown-5, and -crown-6 ethers in the cone conformation bearing one lower-rim α-picolyl pendant group. They tested the complexation abilities of these ligands by metal picrate extraction from water into dichloromethane. The results showed low extraction levels for alkali, alkaline earth, and heavy metal picrates, while up to 25% extraction was found for Ag^+.[4d] The influence of conformation on the complexing ability of *p-tert*-butylcalix[4]arene-1,2-crown-5 was also reported by Arnard-Neu and coworkers. They synthesized *p-tert*-butylcalix[4]arene-1,2-crown-5 ethers in cone, partial cone, and 1,2-alternate conformations with two lower-rim α-picolyl pendant groups. Compared with corresponding *p-tert*-butylcalix[4]arene-1,3-crown ethers, these ligands were much less efficient and selective toward alkali metal cations. Their selectivities varied from K^+ for the cone conformer to both K^+ and Rb^+ for the partial cone isomer and to Cs^+ for the 1,2-alternate conformer.[4e]

Earlier work indicates that incorporating a pendant proton-ionizable group into calix[4]arenes can dramatically enhance their extraction ability toward metal cations compared with their non-ionizable analogues.[5] Recently we found that di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-4 ethers in the cone conformation are efficient extractants of alkaline earth metal cations with high selectivity for Ba^{2+}.[6] Herein we probe the influence of crown ether ring size on the efficiency and selectivity of calix[4]arene-1,2-crown ethers in metal ion separations. Di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-5 and -crown-6 compounds in the cone conformation are prepared and evaluated in competitive solvent extraction of alkaline earth metal cations from aqueous solutions into chloroform.

Results and discussion

Synthetic routes

p-tert-Butylcalix[4]arene, **1**, pentaethylene glycol ditosylate and tetraethylene glycol ditosylate were prepared according to reported methods.[7,8] The *p-tert*-butylcalix[4]arene obtained by the

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literature method usually contains 0.5–1 toluene molecule per host molecule. For the current investigation, the toluene was removed by dissolving the solid in dichloromethane and then evaporating the solvent from the solution *in vacuo*.

When attaching a polyether ring to the lower rim of calix[4]arene, the regioselectivity is governed by the basicity and the metal cation of the base employed. Strong bases and polar solvents lead to 1,2-bridged calix[4]crowns.[9] Compound **2** was synthesized by modification of a reported procedure.[4b] The reaction conditions were changed to 24 hours at 70 °C from the reported reaction conditions of 48 hours at room temperature (Scheme 1). This modification increased the yield by 21%. Compound **3** was obtained in 42% yield by stirring *p-tert*-butylcalix[4]arene, NaH and pentaethylene glycol di(*p*-toluenesulfonate) in DMF at 70 °C for 24 hours. With KH as the base, the yield of **3** increased to 56%. This may be due to a "template effect" in attaching the polyether chain to the calix[4]arene scaffold.[10]

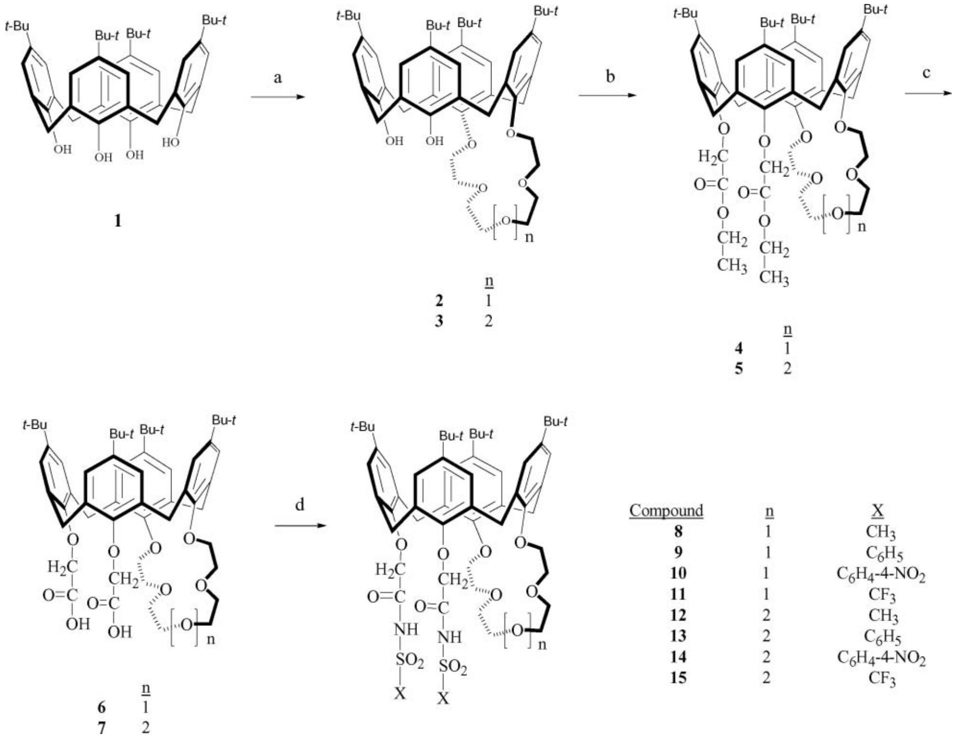
p-tert-Butylcalix[4]arene-1,2-crown-5 ether **2** or -crown-6 ether **3** was reacted with ethyl bromoacetate and NaH in THF at room temperature for 24 hours to give diester **4** (84% yield) or **5** (92% yield), respectively. Subsequent hydrolysis with tetramethylammonium hydroxide in H_2O–THF (1 : 1) gave diacid **6** or **7** in nearly quantitative yield. Diacids **6** and **7** were converted into the corresponding di(acid chloride)s by reaction with oxalyl chloride in benzene at 50–55 °C for 12 hours. Formation of the acid chloride was verified by IR spectroscopy with the appearance of the strong carbonyl group absorption at 1810 cm^{-1} and the disappearance of the carbonyl group absorption for the di(carboxylic acid) at about 1740 cm^{-1}. The di(acid chloride)s were reacted with the appropriate sulfonamide anions to afford compounds **8–15** in 46–72% yields.

Conformation and regioselectivity

Calix[4]arenes have four limiting conformational isomers of cone, partial cone, 1,2-alternate, and 1,3-alternate.[1] Conformational information for the calix[4]arene molecule can be obtained from NMR spectra. For example, there are no peaks between 36–40 ppm in the ^{13}C NMR spectrum of compound **8**, revealing that all four benzene rings have *syn*-arrangements (cone conformation).[11] In the ^1H NMR spectrum, the bridged methylene protons are split into three pairs of doublets with relative integrations of 1, 2, and 1, marked as 2, 3, 4 (axial) and 2′, 3′, 4′ (equatorial) in Fig. 1. They are correlated with each other and demonstrate that the polyether ring is attached to the calix[4]arene scaffold *via* the proximate phenolic positions. The correlated peaks are separated by more than 1 ppm, which provides further evidence that the calix[4]arene molecule is in the cone conformation.[4f,11] The two methylene protons in the ionizable side arms ($-OCH_2C(O)-$), marked as 1 and 1′, are diastereotopic and are correlated with each other.

Competitive solvent extraction of alkaline earth metal cations by di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-5 ligands 6, 8–11 and -crown-6 ligands 7, 12–15

Earlier studies of solvent extraction by proton-ionizable lariat ethers demonstrated that the selectivity in competitive metal ion extraction may be quite different from that obtained by extrapolating the results of single species extractions.[12] In this



Compound	n	X
8	1	CH_3
9	1	C_6H_5
10	1	C_6H_4-4-NO_2
11	1	CF_3
12	2	CH_3
13	2	C_6H_5
14	2	C_6H_4-4-NO_2
15	2	CF_3

Scheme 1 Synthesis of di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-5 and -crown-6 compounds **6–15**. Reagents and conditions: a) i) $n = 1$: $Ts(OCH_2CH_2)_4OTs$, NaH, DMF, 70 °C, 24 h; ii) $n = 2$: $Ts(OCH_2CH_2)_5OTs$, KH, DMF, 70 °C, 24 h; b) $BrCH_2CO_2C_2H_5$, NaH, THF, rt, 24 h; c) i) 10% $Me_4N^+OH^-$(aq), THF, reflux, 24 h; ii) 6 N HCl (aq); d) i) $(COCl)_2$, benzene, 50–55 °C, 12 h; ii) NaH, NH_2SO_2X, THF, rt, 24 h.

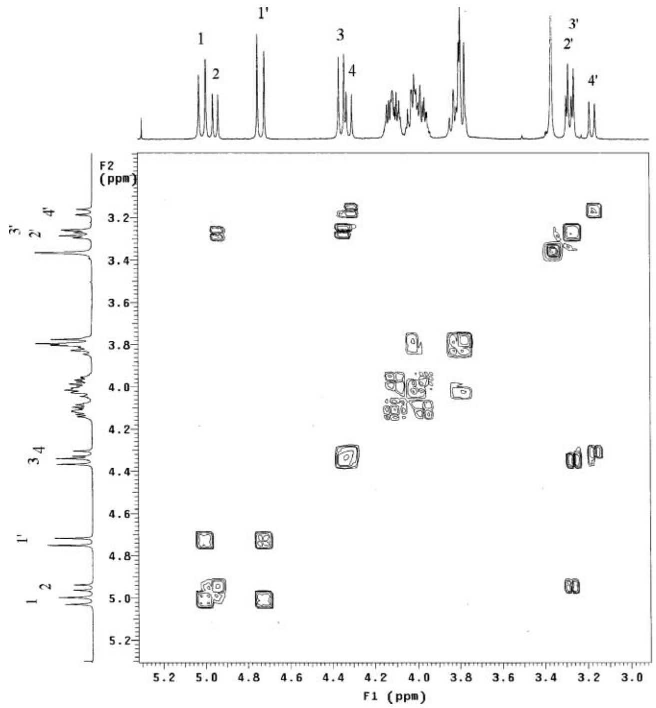


Fig. 1 ^{1}H–^{1}H COSY NMR spectrum of compound **8**.

investigation, competitive solvent extractions of alkaline earth metal cations (Mg^{2+}, Ca^{2+}, Sr^{2+}, and Ba^{2+}) are utilized.

For competitive solvent extractions of aqueous alkaline earth metal cation (2.0 mM in each) solutions by 1.0 mM solutions of di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-5 and -crown-6 di(carboxylic acid)s **6** and **7** in chloroform, plots of metal ion loading of the organic phase *vs.* the equilibrium pH of the aqueous phase are presented in Fig. 2. The observed pH profiles are consistent with the extraction equilibrium shown in eqn (1).

$$\mathrm{LH}_{2\,(\mathrm{Org})} + \mathrm{M}^{2+}_{(\mathrm{aq})} = \mathrm{LM}_{(\mathrm{Org})} + 2\mathrm{H}^{+}_{(\mathrm{aq})} \tag{1}$$

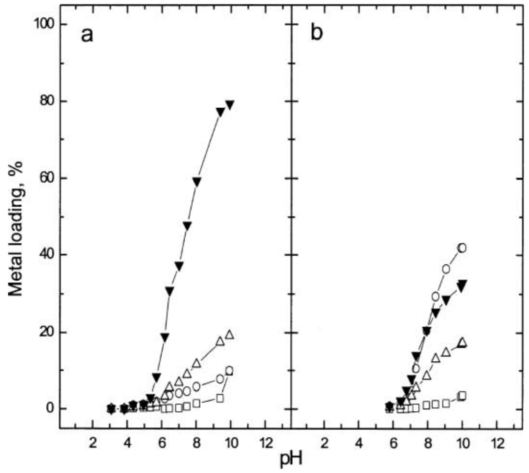


Fig. 2 Percent metals loading *vs.* equilibrium pH of the aqueous phase for competitive solvent extraction of alkaline earth metal ions into chloroform by di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-5 and -crown-6 di(carboxylic acid)s; a) **6**, and b) **7** (□ = Mg^{2+}; ○ = Ca^{2+}; △ = Sr^{2+}; ▼ = Ba^{2+}).

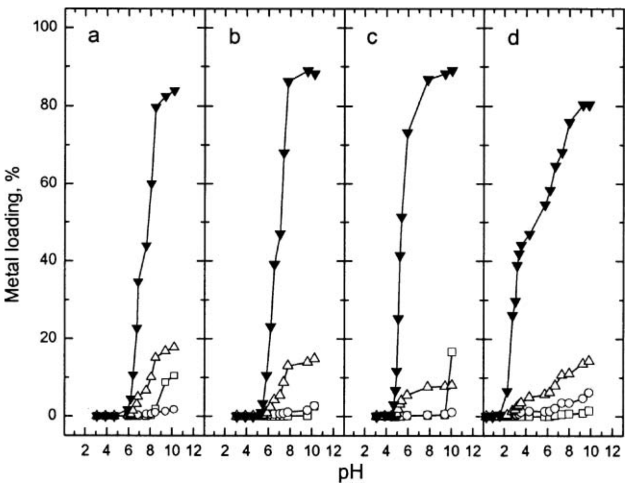


Fig. 3 Percent metals loading *vs.* equilibrium pH of the aqueous phase for competitive solvent extraction of alkaline earth metal ions into chloroform by di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-5 di[*N*-(X)sulfonyl carboxamides]; a) **8**, b) **9**, c) **10**, and d) **11** (□ = Mg^{2+}; ○ = Ca^{2+}; △ = Sr^{2+}; ▼ = Ba^{2+}).

Compound **6** exhibits extraction selectivity for Ba^{2+} over the other three alkaline earth metal ion species and 100% maximum metal loadings (for formation of 1 : 1 metal ion–ligand complexes) (Fig. 2a). The observed total loading somewhat exceeds 100%. This is attributed to extraction of colloidal $Mg(OH)_2$ at higher pHs. Compared with compound **6**, compound **7** (Fig. 2b) is a weaker and much less selective extractant for alkaline earth metal cations.

To probe the effect of changing to a different class of ionizable group in which the acidity can be systematically varied, solvent extractions of alkaline earth metal cations were performed with the calix[4]arene-1,2-crown-5 and -crown-6 di[*N*-(X)sulfonyl carboxamide] ligands **8–15**. The results show that ligands **8–11** exhibit selectivity for Ba^{2+} over the other three alkaline earth metal ion species and 100% maximum metals loading (Fig. 3). All four alkaline earth metal cations are detectably extracted into the chloroform phase and the selectivity order is $Ba^{2+} \gg Sr^{2+} > Ca^{2+} > Mg^{2+}$, the same order as the decreasing metal cation sizes. The Ba^{2+}/Sr^{2+} selectivity is 4.4–11.3 under conditions of high loading. With variation of the X group in the order of CH_3, C_6H_5, C_6H_4-4-NO_2 and CF_3, the ligand acidity is expected to increase as the electron-withdrawing power of the X group is enhanced. The pH for half loading, $pH_{0.5}$, is a qualitative measure of ligand acidity in the biphasic extraction system. For compounds **8–11**, the $pH_{0.5}$ values for Ba^{2+}extraction are 7.6, 6.9, 5.3, and 3.8, respectively, which is in accordance with the electron-withdrawing power of X.

Although di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-6 di(*N*-(X)sulfonyl carboxamides) **12–15** exhibit selectivity for Ba^{2+} over the other three alkaline earth metal ion species, they show somewhat lower extraction efficiencies and selectivities than the corresponding crown-5 analogues. The maximum metal loadings are 95–100% and the selectivity orders differ from each other for ligands **12–15** (Fig. 4). The Ba^{2+}/Sr^{2+} or Ba^{2+}/Ca^{2+} selectivity is 4.2–7.0. For compounds **12–15**, the $pH_{0.5}$ values for Ba^{2+} extraction are 8.3, 8.0, 7.2, and 4.4, respectively. These values reveal considerably lower acidities than the corresponding crown-5 analogues.

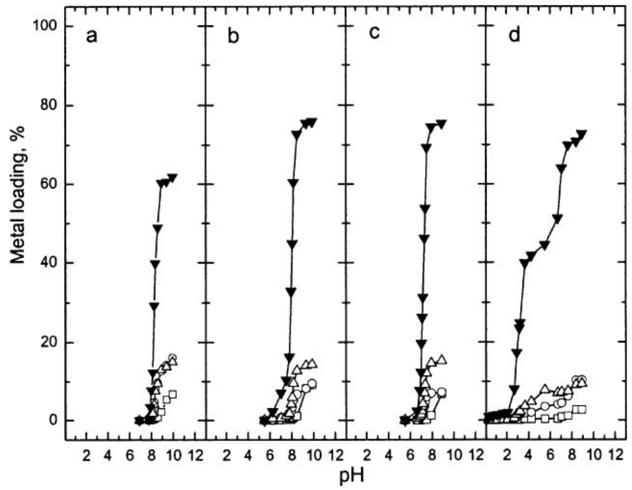
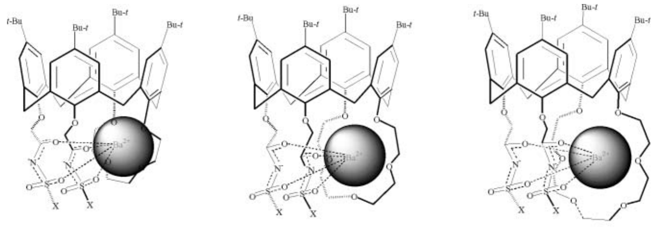


Fig. 4 Percent metals loading *vs.* equilibrium pH of the aqueous phase for competitive solvent extraction of alkaline earth metal ions into chloroform by di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-6 di[*N*-(X)sulfonyl carboxamides]; a) **12**, b) **13**, c) **14**, and d) **15** (□ = Mg^{2+}; ○ = Ca^{2+}; △ = Sr^{2+}; ▼ = Ba^{2+}).

Upon ionization of the new ligands **6–15**, the fixed cone conformation for the calix[4]arene units controls the spatial relationship for a crown-complexed divalent metal ion with respect to the two anionic centers required for electroneutrality in the extraction complex. Upon ionization, the di-ionizable calix[4]arene-1,2-crown-5 or -crown-6 compounds form alkaline earth metal ion complexes with two anionic centers on the same side of the crown unit (Fig. 5).



16 **17** **18**

Fig. 5 Depiction of spatial relationship between a crown-complexed divalent metal ion and the anionic centers formed by ionization of ligands **6**, **8–11** (**17**), **7**, **12–15** (**18**) and the crown-4 analogues **16**.

Both di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-5 and -crown-6 ligands are found to have lower Ba^{2+} extraction selectivities than the corresponding crown-4 analogues.[6] The $pH_{0.5}$ values for Ba^{2+} extraction by the crown-4 analogues were 6.3 (CH_3), 6.2 (C_6H_5), 5.1 (C_6H_4-4-NO_2), 3.8 (CF_3).[6] With a single exception, for a given X, the $pH_{0.5}$ values increase as the polyether ring size is expanded crown-4 < crown-5 < crown-6. (For X = CF_3, the $pH_{0.5}$ values for the crown-4 and crown-5 ligands are the same.) This reveals that the strength of alkali metal cation complexation for a given X decreases as the polyether ring size is expanded crown-4 > crown-5 > crown-6.

For *p-tert*-butylcalix[4]-arene-1,2-crown-4 ligands, the crown ether ring is too small to accommodate Ba^{2+}. The metal ion is tightly clamped between the two anions and the polyether "wall" to form a sandwich complex **16**. When the ring size is expanded to crown-5, Ba^{2+} is still larger than the crown-5 cavity, so the metal ion would again perch on the polyether oxygens, as shown in complex **17**. Then when the ring size is expanded to crown-6, Ba^{2+} can fit within the polyether cavity, as represented in complex **18**. In crown ether chemistry, the strongest binding is usually observed for metal cations that fit the polyether cavity.[13] Therefore, the influence of crown ether ring size on alkaline earth metal cation extraction observed in this study is quite unexpected. Further investigations designed to probe this unexpected behavior of *p-tert*-butylcalix[4]arenecrown ligands are in progress.

Experimental

General

Reagents were obtained from commercial suppliers and used directly, unless otherwise noted. THF was dried over sodium wire with benzophenone ketyl as an indicator. DMF was stored over 4 Å molecular sieves.

Infrared spectral analyses were performed with a Perkin-Elmer 1600 FT-IR spectrophotometer as deposits from CH_2Cl_2 solution onto a NaCl plate. The absorptions are expressed in wavenumbers (cm^{-1}). NMR spectra were measured with a Varian Unity Inova FT-500 spectrometer (499.7 MHz for ^1H, 125.7 MHz for ^{13}C) at 296 K in $CDCl_3$ with TMS as an internal standard. Chemical shifts (δ) are expressed in ppm downfield from TMS and coupling constants (J) values are given in Hz. Melting points were determined with a Mel-Temp melting point apparatus. Elemental analysis was performed by Desert Analytics Laboratory of Tucson, Arizona.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-dihydroxycalix[4]-arene-crown-6 in the cone conformation (3). KH (10.00 eq, 0.62 g, 15.4 mmol) and DMF (30 mL) were added to a 250 mL, three-necked flask under nitrogen. A solution of **1** (1.00 eq, 1.00 g, 1.54 mmol) in DMF (70 mL) was added to the flask dropwise. The mixture was stirred for 30 min. A solution of pentaethylene glycol di-*p*-toluenesulfonate (1.00 eq, 0.84 g, 1.54 mmol) in DMF (30 mL) was added over a 2 h period. The mixture was stirred at 70 °C for 24 h. The reaction was quenched by addition of 2 N HCl (30 mL) at 0 °C. The DMF was evaporated *in vacuo.* CH_2Cl_2 (150 mL) and H_2O (150 mL) were added to the residue. The organic layer was separated and washed with H_2O (2 × 100 mL). The organic layer was separated, dried over $MgSO_4$ and evaporated *in vacuo.* The residue was chromatographed on silica gel with hexanes–EtOAc (1 : 1) as eluent to give 0.66 g (56%) of white solid with mp 202–205 °C. ν_{max} (film)/cm^{-1} 3490 (OH), 1248, 1097, 1018 (C–O). δ_H 8.54 (s, 2H, OH), 6.97–6.87 (m, 8H, ArH), 4.48 (d, J 12.7, 1H, ArCH_2Ar, ax), 4.40 (d, J 12.9, 2H, ArCH_2Ar, ax), 4.36–4.32 (m, 2H, OCH_2), 4.28 (d, J 13.6, 1H, ArCH_2Ar, ax), 4.18–4.14 (m, 2H, OCH_2), 4.07–3.99 (m, 4H, OCH_2), 3.91–3.78 (m, 10H, OCH_2), 3.71–3.67 (m, 2H, OCH_2), 3.30 (d, J 13.8, 2H, ArCH_2Ar, eq), 3.28 (d, J 13.1, 2H, ArCH_2Ar, eq), 1.18 (s, 18H, CH_3), 1.07 (s, 18H, CH_3). δ_C 151.76, 148.91, 146.09, 141.96, 133.61, 133.54, 128.57, 127.71, 125.80, 125.75, 125.07, 125.03 (Ar), 74.76, 71.40, 70.93, 70.87, 70.66 (OCH_2), 33.94, 33.79 ($C(CH_3)_3$), 32.48, 31.72 (ArCH_2Ar), 31.51, 31.24 ($C(CH_3)_3$), 31.14 (ArCH_2Ar). Found: C, 76.54; H, 8.90%. $C_{54}H_{74}O_8$ requires C, 76.20; H, 8.76%.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-bis[(ethoxycarbonyl)methoxy]calix[4]arene-crown-5 in the cone conformation (4). NaH (8.00 eq, 2.18 g, 90.72 mmol), **2** (1.00 eq, 9.15 g, 11.34 mmol), ethyl bromoacetate (6.00 eq, 7.54 mL, 68.04 mmol) and THF (150 mL) were added to a flask under nitrogen. The mixture was stirred magnetically for 24 h. The reaction was quenched by addition of 10% HCl (30 mL) at 0 °C. The solvent was evaporated *in vacuo* and CH_2Cl_2 (200 mL) was added to the residue. The separated organic layer was washed with H_2O (2 × 150 mL), dried over $MgSO_4$ and evaporated *in vacuo.* The residue was chromatographed on silica gel with hexanes–EtOAc (3 : 2) as eluent to give 9.32 g (84%) of white solid with mp 212–215 °C. ν_{max} (film)/cm^{-1} 1762 (C=O), 1248, 1126, 1067 (C–O). δ_H 6.81 (d, *J* 2.2, 2H, ArH), 6.80 (s, 6H, ArH), 4.99 (d, *J* 12.7, 1H, Ar*CH*$_2$Ar, ax), 4.88 (d, *J* 16.4, 2H, O*CH*$_2$C(O)), 4.81 (d, *J* 16.4, 2H, O*CH*$_2$C(O)), 4.59 (d, *J* 12.7, 2H, Ar*CH*$_2$Ar, ax), 4.44 (d, *J* 12.6, 1H, Ar*CH*$_2$Ar, ax), 4.21 (q, *J* 7.2, 4H, O*CH*$_2$CH$_3$), 4.18–4.06 (m, 6H, OCH$_2$), 4.01–3.92 (m, 2H, OCH$_2$), 3.83–3.68 (m, 8H, OCH$_2$), 3.18 (d, *J* 12.7, 1H, Ar*CH*$_2$Ar, eq), 3.17 (d, *J* 12.8, 2H, Ar*CH*$_2$Ar, eq), 3.11 (d, *J* 12.6, 1H, Ar*CH*$_2$Ar, eq), 1.28 (t, *J* 7.1, 6H, OCH$_2$*CH*$_3$), 1.08 (s, 18H, C(*CH*$_3$)$_3$), 1.07 (s, 18H, C(*CH*$_3$)$_3$). δ_C 170.74 (C=O), 153.31, 153.20, 144.85, 144.76, 133.98, 133.67, 133.51, 133.35, 125.27, 125.23, 125.05 (Ar), 73.49 (OCH$_2$), 71.62 (O*CH*$_2$C(O)), 70.96, 70.46, 70.39 (OCH$_2$), 60.28 (O*CH*$_2$CH$_3$), 33.82, 33.80 (*C*(CH$_3$)$_3$), 31.52 (Ar*CH*$_2$Ar), 31.41, 31.38 (C(*CH*$_3$)$_3$), 31.29, 30.66 (Ar*CH*$_2$Ar), 14.22 (OCH$_2$*CH*$_3$). Found: C, 73.99; H, 8.23%. $C_{60}H_{82}O_{11}$ requires C, 73.59; H, 8.44%.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-bis[(ethoxycarbonyl)methoxy]calix[4]arene-crown-6 in the cone conformation (5). The same procedure was employed as that used to synthesize compound **4**. The product was a white solid (92% yield) with mp 92–94 °C. ν_{max} (film)/cm^{-1} 1750 (C=O), 1160, 1022 (C–O). δ_H 6.80–6.79 (m, 8H, ArH), 4.82 (d, *J* 12.3, 1H, Ar*CH*$_2$Ar, ax), 4.81 (d, *J* 16.2, 2H, O*CH*$_2$C(O)), 4.72 (d, *J* 16.2, 2H, O*CH*$_2$C(O)), 4.62 (d, *J* 12.7, 2H, Ar*CH*$_2$Ar, ax), 4.50 (d, *J* 12.4, 1H, Ar*CH*$_2$Ar, ax), 4.23 (q, *J* 7.2, 4H, O*CH*$_2$CH$_3$), 4.14–3.98 (m, 8H, OCH$_2$), 3.79–3.66 (m, 12H, OCH$_2$), 3.20 (d, *J* 12.9, 1H, Ar*CH*$_2$Ar, eq), 3.16 (d, *J* 12.8, 2H, Ar*CH*$_2$Ar, eq), 3.12 (d, *J* 12.7, 1H, Ar*CH*$_2$Ar, eq), 1.30 (t, *J* 7.1, 6H, OCH$_2$*CH*$_3$), 1.08 (s, 18H, C(*CH*$_3$)$_3$), 1.07 (s, 18H, C(*CH*$_3$)$_3$). δ_C 170.43 (C=O), 153.16, 152.94, 145.05, 144.76, 134.03, 133.68, 133.46, 133.19, 125.32, 125.27, 124.96 (Ar), 72.98 (OCH$_2$), 71.57 (O*CH*$_2$C(O)), 70.75, 70.69, 70.54, 70.04 (OCH$_2$), 60.43 (O*CH*$_2$CH$_3$), 33.78, 33.76 (*C*(CH$_3$)$_3$), 31.36, 31.31 (C(*CH*$_3$)$_3$), 31.16, 30.87 (Ar*CH*$_2$Ar), 14.20 (OCH$_2$*CH*$_3$). Found: C, 72.54; H, 8.71%. $C_{62}H_{86}O_{12}$ requires C, 72.77; H, 8.47%.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-bis(carboxymethoxy)calix[4]arene-crown-5 in the cone conformation (6). A solution of **4** (9.23 g, 9.42 mmol) in THF (150 mL) was mixed with 10% aq tetramethylammonium hydroxide (150 mL) and refluxed for 24 h. After cooling to room temperature, 6 N HCl (60 mL) was added and the mixture was stirred for 1 h. The THF was evaporated *in vacuo.* The white precipitate in the resulting aqueous mixture was filtered and dissolved in CH_2Cl_2 (150 mL). The aqueous filtrate was extracted with CH_2Cl_2 (100 mL). The combined CH_2Cl_2 solutions were dried over $MgSO_4$ and evaporated *in vacuo* to give 8.26 g (95%) of white solid with mp 263–265 °C. ν_{max} (film)/cm^{-1} 3363 (br, CO$_2$H), 1738 (C=O), 1263, 1091, 1060 (C–O). δ_H 8.03 (br s, 2H, CO$_2$H), 6.90 (d, *J* 2.2, 2H, ArH), 6.88 (d, *J* 2.1, 2H, ArH), 6.85 (d, *J* 2.2, 2H, ArH), 6.83 (d, *J* 2.2, 2H, ArH), 4.60 (d, *J* 12.6, 1H, Ar*CH*$_2$Ar, ax), 4.57 (s, 4H, O*CH*$_2$C(O)), 4.39 (d, *J* 12.8, 1H, Ar*CH*$_2$Ar, ax), 4.24 (d, *J* 12.6, 2H, Ar*CH*$_2$Ar, ax), 4.19–4.12 (m, 4H, OCH$_2$), 3.93–3.89 (m, 6H, OCH$_2$), 3.84–3.81 (m, 2H, OCH$_2$), 3.72–3.68 (m, 4H, OCH$_2$), 3.25 (d, *J* 12.9, 1H, Ar*CH*$_2$Ar, eq), 3.24 (d, *J* 12.7, 2H, Ar*CH*$_2$Ar, eq), 3.16 (d, *J* 12.6, 1H, Ar*CH*$_2$Ar, eq), 1.08 (s, 36H, CH$_3$). δ_C 171.25 (C=O), 152.19, 150.93, 146.64, 145.41, 134.39, 133.57, 133.31, 133.06, 125.73, 125.60, 125.40, 125.14 (Ar), 74.94 (OCH$_2$), 71.56 (O*CH*$_2$C(O)), 70.86, 70.63, 69.86 (OCH$_2$), 33.96, 33.87 (*C*(CH$_3$)$_3$), 31.35, 31.26 (C(*CH*$_3$)$_3$), 30.92, 30.85, 30.48 (Ar*CH*$_2$Ar). Found: C, 73.20; H, 7.80%. $C_{56}H_{74}O_{11}$ requires C, 72.86; H, 8.08%.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-bis(carboxymethoxy)calix[4]arene-crown-6 in the cone conformation (7). The same procedure was followed as that employed to synthesize compound **6**. The product was a white solid (98% yield) with mp 239–242 °C. ν_{max} (film)/cm^{-1} 3376 (br, CO$_2$H), 1751 (C=O), 1264, 1127, 1058 (C–O). δ_H 9.86 (br s, 2H, CO$_2$H), 6.90–6.82 (m, 8H, ArH), 4.63 (d, *J* 15.7, 2H, O*CH*$_2$C(O)), 4.60 (d, *J* 12.9, 1H, Ar*CH*$_2$Ar, ax), 4.56 (d, *J* 15.7, 2H, O*CH*$_2$C(O)), 4.47 (d, *J* 12.9, 1H, Ar*CH*$_2$Ar, ax), 4.29 (d, *J* 12.7, 2H, Ar*CH*$_2$Ar, ax), 4.27–4.22 (m, 2H, OCH$_2$), 4.15–4.10 (m, 2H, OCH$_2$), 3.95–3.85 (m, 4H, OCH$_2$), 3.83–3.64 (m, 12H, OCH$_2$), 3.25 (d, *J* 13.5, 1H, Ar*CH*$_2$Ar, eq), 3.22 (d, *J* 12.9, 2H, Ar*CH*$_2$Ar, eq), 3.16 (d, *J* 12.7, 1H, Ar*CH*$_2$Ar, eq), 1.08 (s, 36H, CH$_3$). δ_C 171.38 (C=O), 152.30, 151.10, 146.52, 145.35, 134.23, 133.52, 133.30, 133.21, 125.69, 125.57, 125.44, 124.98 (Ar), 74.52 (OCH$_2$), 71.55 (O*CH*$_2$C(O)), 70.92, 70.76, 70.56, 69.58 (OCH$_2$), 33.93, 33.85 (*C*(CH$_3$)$_3$), 31.34, 31.25 (C(*CH*$_3$)$_3$), 31.09, 30.77, 30.71 (Ar*CH*$_2$Ar). Found: C, 72.13; H, 8.37%. $C_{58}H_{78}O_{12}$ requires C, 72.02; H, 8.13%.

General procedure for the synthesis of 5,11,17,23-tetrakis-(1,1-dimethylethyl)-25,26-di[*N*-(X)sulfonyl carbamoylmethoxy]calix[4]arene-crown-5 and -crown-6 ethers in the cone conformation (8–15)

A solution of benzene (40 mL), **6** or **7** (1.00 eq, 2.00 g) and oxalyl chloride (16.00 eq) was stirred at 50–55 °C for 12 h. The benzene was evaporated *in vacuo* to give the corresponding di(acid chloride) which was used directly in the next step. The sulfonamide salt was prepared under nitrogen by adding NaH (10.00 eq) and THF (30 mL) to a three-necked flask. The appropriate sulfonamide (2.2 eq) in THF (30 mL) was added to the flask over a 10 min period. The mixture was stirred for 1.5 h followed by addition of a solution of the di(acid chloride) in THF (10 mL) dropwise. The reaction mixture was stirred for 24 h after which 10 mL of H_2O was added. The solvent was evaporated *in vacuo.* CH_2Cl_2 was added to the residue and the resulting solution was dried over $MgSO_4$. After purification by chromatography on silica gel, the product was dissolved in CH_2Cl_2. The solution was shaken with 6 N HCl. The organic layer was separated and dried over $MgSO_4$. Evaporation of the solvent *in vacuo* gave the product as a solid.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-bis(*N*-methanesulfonyl carbamoylmethoxy)calix[4]arene-crown-5 in the cone conformation (8). Chromatography on silica gel with CH_2Cl_2–MeOH (19 : 1) as eluent gave 1.68 g (72%) of white solid with mp 168–169 °C. ν_{max} (film)/cm^{-1} 3218 (N–H), 1718 (C=O), 1344, 1154 (SO$_2$), 1265, 1123, 1058 (C–O). δ_H 10.36 (s, 2H, NH), 6.82

(d, *J* 2.4, 2H, ArH), 6.80–6.74 (m, 6H, ArH), 5.01 (d, *J* 16.4, 2H, OCH_2C(O)), 4.95 (d, *J* 12.7, 1H, ArCH_2Ar, ax), 4.73 (d, *J* 16.4, 2H, OCH_2C(O)), 4.35 (d, *J* 13.1, 2H, ArCH_2Ar, ax), 4.32 (d, *J* 12.4, 1H, ArCH_2Ar, ax), 4.19–4.07 (m, 4H, OCH$_2$), 4.06–3.91 (m, 6H, OCH$_2$), 3.86–3.69 (m, 6H, OCH$_2$), 3.36 (s, 6H, SO$_2$CH$_3$), 3.28 (d, *J* 12.8, 1H, ArCH_2Ar, eq), 3.27 (d, *J* 13.1, 2H, ArCH_2Ar, eq), 3.17 (d, *J* 12.4, 1H, ArCH_2Ar, eq), 1.08 (s, 18H, C(CH_3)$_3$), 1.07 (s, 18H, C(CH_3)$_3$). δ_C 171.06 (C=O), 153.42, 152.95, 145.48, 145.42, 133.56, 133.41, 133.07, 131.68, 126.02, 125.54, 125.38, 125.26 (Ar), 74.19 (OCH$_2$), 73.79 (OCH_2C(O)), 69.76, 69.66, 69.16 (OCH$_2$), 41.56 (SO$_2$CH$_3$), 33.87, 33.83 (*C*(CH$_3$)$_3$), 32.50 (ArCH_2Ar), 31.35 (ArCH_2Ar & *C*(CH$_3$)$_3$), 31.30 (C(CH_3)$_3$), 30.95 (ArCH_2Ar). Found: C, 64.45; H, 7.32; N, 2.73%. $C_{58}H_{80}O_{13}S_2N_2$ requires C, 64.66; H, 7.48; N, 2.60%.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-bis(*N*-phenylsulfonyl carbamoylmethoxy)calix[4]arene-crown-5 in the cone conformation (9). Chromatography on silica gel with CH$_2$Cl$_2$–MeOH (19 : 1) as eluent gave 1.62 g (62%) of a white solid with mp of 168–171 °C. ν_{max} (film)/cm^{-1} 3364 (N–H), 1717 (C=O), 1350, 1166 (SO$_2$), 1264, 1120, 1060 (C–O). δ_H 10.59 (s, 2H, NH), 8.13 (dd, *J* 8.5, 1.0, 4H, ArH), 7.62–7.59 (m, 2H, ArH), 7.50 (t, *J* 8.2, 4H, ArH), 6.79 (d, *J* 2.0, 2H, ArH), 6.71 (d, *J* 2.0, 4H, ArH), 6.68 (d, *J* 2.2, 2H, ArH), 4.60 (d, *J* 16.4, 2H, OCH_2C(O)), 4.52 (d, *J* 12.9, 1H, ArCH_2Ar, ax), 4.44 (d, *J* 16.1, 2H, OCH_2C(O)), 4.28 (d, *J* 13.1, 3H, ArCH_2Ar, ax), 4.23–4.21 (m, 2H, OCH$_2$), 4.11–4.06 (m, 4H, OCH$_2$), 4.02–4.00 (m, 2H, OCH$_2$), 3.96–3.85 (m, 8H, OCH$_2$), 3.17 (d, *J* 12.4, 1H, ArCH_2Ar, eq), 3.06 (d, *J* 13.7, 1H, ArCH_2Ar, eq), 3.03 (d, *J* 12.9, 2H, ArCH_2Ar, eq), 1.06 (s, 18H, C(CH_3)$_3$), 1.04 (s, 18H, C(CH_3)$_3$). δ_C 169.48 (C=O), 153.14, 153.04, 145.31, 145.12, 138.98, 133.92, 133.31, 133.18, 131.50, 128.88, 128.47, 125.50, 125.30, 125.22 (Ar), 74.44 (OCH$_2$), 73.10 (OCH_2C(O)), 69.30, 69.24, 68.96 (OCH$_2$), 33.84, 33.76 (*C*(CH$_3$)$_3$), 33.04 (ArCH_2Ar), 31.34, 31.29 (C(CH_3)$_3$), 31.18, 31.08 (ArCH_2Ar). Found: C, 67.77; H, 6.82; N, 2.36%. $C_{68}H_{84}O_{13}S_2N_2$ requires C, 67.98; H, 7.05; N, 2.33%.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-bis(*N*-*p*-nitrobenzenesulfonyl carbamoylmethoxy)calix[4]arene-crown-5 in the cone conformation (10). Chromatography on silica gel with CH$_2$Cl$_2$–MeOH (97 : 3) as eluent gave 1.32 g (47%) of yellow solid with mp 175–177 °C. ν_{max} (film)/cm^{-1} 3300–2400 (br N–H), 1723 (C=O), 1532, 1328 (NO$_2$), 1350, 1161 (SO$_2$), 1265, 1122, 1056 (C–O). δ_H 10.73 (s, 2H, NH), 8.37 (dt, *J* 9.0, 2.1, 4H, ArH), 8.32 (dt, *J* 9.2, 2.0, 4H, ArH), 6.81 (d, *J* 2.1, 2H, ArH), 6.73 (d, *J* 2.3, 2H, ArH), 6.72 (s, 4H, ArH), 4.77 (d, *J* 16.6, 2H, OCH_2C(O)), 4.70 (d, *J* 12.7, 1H, ArCH_2Ar, ax), 4.63 (d, *J* 16.5, 2H, OCH_2C(O)), 4.29 (d, *J* 12.3, 1H, ArCH_2Ar, ax), 4.28 (d, *J* 12.8, 2H, ArCH_2Ar, ax), 4.19–4.16 (m, 2H, OCH$_2$), 4.13–4.04 (m, 4H, OCH$_2$), 4.01–3.85 (m, 10H, OCH$_2$), 3.18 (d, *J* 12.7, 1H, ArCH_2Ar, eq), 3.14 (d, *J* 12.9, 2H, ArCH_2Ar, eq), 3.11 (d, *J* 10.7, 1H, ArCH_2Ar, eq), 1.06 (s, 18H, C(CH_3)$_3$), 1.04 (s, 18H, C(CH_3)$_3$). δ_C 169.81 (C=O), 153.06, 152.94, 150.72, 145.54, 145.51, 144.14, 133.67, 133.30, 132.87, 131.38, 129.99, 125.82, 125.56, 125.46, 125.23, 124.16 (Ar), 74.37 (OCH$_2$), 73.09 (OCH_2C(O)), 69.47, 69.40, 69.03 (OCH$_2$), 33.86, 33.80 (*C*(CH$_3$)$_3$), 33.02 (ArCH_2Ar), 31.33, 31.26 (C(CH_3)$_3$), 31.11 (ArCH_2Ar). Found: C, 63.34; H, 6.62; N, 4.33%. $C_{68}H_{82}O_{17}S_2N_4$ requires C, 63.24; H, 6.40; N, 4.34%.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-bis(*N*-trifluoromethanesulfonyl carbamoylmethoxy)calix[4]arene-crown-5 in the cone conformation (11). Chromatography on silica gel with hexanes–EtOAc (3 : 2) as eluent gave 1.47 g (57%) of white solid with mp 203–205 °C. ν_{max} (film)/cm^{-1} 3204 (N–H), 1755 (C=O), 1393, 1204 (SO$_2$), 1264, 1134, 1057 (C–O). δ_H 11.06 (br s, 2H, NH), 6.93–6.62 (m, 8H, ArH), 5.06 (d, *J* 17.3, 2H, OCH_2C(O)), 4.86 (br s, 2H, OCH_2C(O)), 4.62 (d, *J* 12.7, 1H, ArCH_2Ar, ax), 4.42 (d, *J* 13.1, 2H, ArCH_2Ar, ax), 4.27 (d, *J* 12.4, 1H, ArCH_2Ar, ax), 4.27 (d, *J* 12.4, 2H, OCH$_2$), 4.10 (t, *J* 9.6, 2H, OCH$_2$), 4.07–3.88 (m, 8H, OCH$_2$), 3.80 (d, *J* 8.8, 4H, OCH$_2$), 3.27 (d, *J* 13.1, 2H, ArCH_2Ar, eq), 3.25 (d, *J* 12.7, 1H, ArCH_2Ar, eq), 3.20 (d, *J* 12.6, 1H, ArCH_2Ar, eq), 1.08 (s, 18H, C(CH_3)$_3$), 1.07 (s, 18H, C(CH_3)$_3$). ^{13}C NMR: δ_C 169.14 (C=O), 152.89, 145.67, 145.63, 134.01, 133.15, 131.41, 125.80, 125.64, 125.50, 125.32 (Ar), 120.56, 118.00 (CF$_3$), 74.55 (OCH$_2$), 72.72 (OCH_2C(O)), 69.02, 68.67, 68.42 (OCH$_2$), 33.87, 33.85 (*C*(CH$_3$)$_3$), 33.59 (ArCH_2Ar), 31.34, 31.28 (C(CH_3)$_3$), 31.06 (ArCH_2Ar). Found: C, 59.04; H, 6.01; N, 2.35%. $C_{58}H_{74}O_{13}S_2F_6N_2$ requires C, 58.77; H, 6.29; N, 2.36%.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-bis(*N*-methanesulfonyl carbamoylmethoxy)calix[4]arene-crown-6 in the cone conformation (12). Chromatography on silica gel with CH$_2$Cl$_2$–MeOH (97 : 3) as eluent gave 1.09 g (46%) of white solid with mp 155–158 °C. ν_{max} (film)/cm^{-1} 3232 (N–H), 1715 (C=O), 1346, 1152 (SO$_2$), 1250, 1122, 1059 (C–O). δ_H 10.28 (s, 2H, NH), 6.81–6.78 (m, 8H, ArH), 5.11 (d, *J* 16.1, 2H, OCH_2C(O)), 4.95 (d, *J* 12.8, 1H, ArCH_2Ar, ax), 4.52 (d, *J* 16.1, 2H, OCH_2C(O)), 4.37 (d, *J* 13.9, 1H, ArCH_2Ar, ax), 4.34 (d, *J* 13.2, 2H, ArCH_2Ar, ax), 4.28–4.22 (m, 2H, OCH$_2$), 4.04–3.96 (m, 6H, OCH$_2$), 3.82–3.68 (m, 12H, OCH$_2$), 3.38 (s, 6H, SO$_2$CH$_3$), 3.31 (d, *J* 12.9, 1H, ArCH_2Ar, eq), 3.26 (d, *J* 13.1, 2H, ArCH_2Ar, eq), 3.17 (d, *J* 12.8, 1H, ArCH_2Ar, eq), 1.09 (s, 18H, C(CH_3)$_3$), 1.06 (s, 18H, C(CH_3)$_3$). δ_C 170.29 (C=O), 153.21, 152.78, 145.57, 145.17, 133.43, 133.06, 132.81, 131.99, 126.09, 125.36, 124.93 (Ar), 74.25 (OCH_2C(O)), 73.41, 70.42, 69.99, 69.96, 69.90 (OCH$_2$), 41.32 (SO$_2$CH$_3$), 33.75, 33.71 (*C*(CH$_3$)$_3$), 31.56 (ArCH_2Ar), 31.25, 31.18 (C(CH_3)$_3$ & ArCH_2Ar). Found: C, 64.51; H, 7.57; N, 2.52%. $C_{60}H_{84}O_{14}S_2N_2$ requires C, 64.26; H, 7.55; N, 2.50%.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-bis(*N*-phenylsulfonyl carbamoylmethoxy)calix[4]arene-crown-6 in the cone conformation (13). Chromatography on silica gel with CH$_2$Cl$_2$–MeOH (97 : 3) as eluent gave 1.31 g (52%) of white solid with mp 136–138 °C. ν_{max} (film)/cm^{-1} 3439 (N–H), 1721 (C=O), 1360, 1161 (SO$_2$), 1250, 1123, 1057 (C–O). δ_H 10.48 (br s, 2H, NH), 8.15–8.14 (m, 4H, ArH), 7.56–7.47 (m, 6H, ArH), 6.78–6.70 (m, 8H, ArH), 4.83 (d, *J* 15.1, 2H, OCH_2C(O)), 4.76 (d, *J* 12.2, 1H, ArCH_2Ar, ax), 4.37 (d, *J* 15.6, 2H, OCH_2C(O)), 4.31–4.27 (m, 5H, ArCH_2Ar, ax (3H) and OCH$_2$ (2H)), 4.02–3.94 (m, 6H, OCH$_2$), 3.80–3.70 (m, 12H, OCH$_2$), 3.15 (d, *J* 12.3, 1H, ArCH_2Ar, eq), 3.06 (d, *J* 12.2, 3H, ArCH_2Ar, eq), 1.07 (s, 18H, C(CH_3)$_3$), 1.04 (s, 18H, C(CH_3)$_3$). δ_C 168.88 (C=O), 153.12, 152.80, 145.16, 144.99, 138.80, 133.60, 133.36, 133.13, 133.02, 131.89, 131.88, 128.66, 128.41, 125.63, 125.30, 125.15, 124.89 (Ar), 74.09 (OCH_2C(O)), 73.53, 70.50, 70.09, 69.82, 69.47 (OCH$_2$), 33.69, 33.62 (*C*(CH$_3$)$_3$), 31.36 (ArCH_2Ar), 31.22, 31.15 (C(CH_3)$_3$ & ArCH_2Ar). Found: C, 67.26; H, 7.14; N, 2.31%. $C_{70}H_{88}O_{14}S_2N_2$ requires C, 67.50; H, 7.12; N, 2.25%.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-bis(*N*-*p*-nitrobenzenesulfonyl carbamoylmethoxy)calix[4]arene-crown-6 in the cone conformation (14). Chromatography on silica gel with CH_2Cl_2–MeOH (97 : 3) as eluent gave 1.47 g (55%) of yellow solid with mp 146–148 °C. ν_{max} (film)/cm^{-1} 3361 (N–H), 1726 (C=O), 1534, 1307 (NO_2), 1355, 1197 (SO_2), 1272, 1121, 1060 (C–O). δ_H 10.75 (br s, 2H, NH), 8.37–8.32 (m, 8H, ArH), 6.80–6.71 (m, 8H, ArH), 4.98 (d, *J* 15.5, 2H, OCH_2C(O)), 4.82 (d, *J* 12.5, 1H, ArCH_2Ar, ax), 4.47 (d, *J* 15.5, 2H, OCH_2C(O)), 4.33 (d, *J* 12.7, 1H, ArCH_2Ar, ax), 4.29 (d, *J* 11.1, 2H, OCH_2), 4.28 (d, *J* 13.1, 2H, ArCH_2Ar, ax), 3.97–3.95 (m, 6H, OCH_2), 3.81–3.68 (m, 12H, OCH_2), 3.18 (d, *J* 12.8, 1H, ArCH_2Ar, eq), 3.14 (d, *J* 13.1, 2H, ArCH_2Ar, eq), 3.09 (d, *J* 12.9, 1H, ArCH_2Ar, eq), 1.07 (s, 18H, C$(CH_3)_3$), 1.04 (s, 18H, C$(CH_3)_3$). δ_C 169.42 (C=O), 153.14, 152.91, 150.59, 145.64, 145.38, 144.19, 133.36, 132.98, 131.80, 130.06, 126.04, 125.41, 125.03, 125.02 (Ar), 74.01 (OCH_2), 73.60 (OCH_2C(O)), 70.48, 70.23, 69.79 (OCH_2), 33.82, 33.76 ($C(CH_3)_3$), 31.68, 31.41 (ArCH_2Ar), 31.28 (C$(CH_3)_3$), 31.20 (C$(CH_3)_3$ and ArCH_2Ar). Found: C, 62.99; H, 6.32; N, 4.01%. $C_{70}H_{86}O_{18}S_2N_4$ requires C, 62.95; H, 6.49; N, 4.19%.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-bis(*N*-trifluoromethanesulfonyl carbamoylmethoxy)calix[4]arene-crown-6 in the cone conformation (15). Chromatography on silica gel with CH_2Cl_2–MeOH (97 : 3) as eluent gave 1.25 g (49%) of white solid with mp 141–143 °C. ν_{max} (film)/cm^{-1} 3328 (N–H), 1720 (C=O), 1340, 1204 (SO_2), 1266, 1160, 1054 (C–O). δ_H 11.04 (s, 2H, NH), 6.80 (t, *J* 15.4, 8H, ArH), 5.10 (br s, 1H, ArCH_2Ar, ax), 4.98 (d, *J* 15.6, 2H, OCH_2C(O)), 4.75 (d, *J* 16.5, 2H, OCH_2C(O)), 4.40 (d, *J* 12.9, 2H, ArCH_2Ar, ax), 4.38–4.33 (m, 2H, OCH_2), 4.22 (d, *J* 12.6, 1H, ArCH_2Ar, ax), 4.09 (s, 4H, OCH_2), 3.74–3.90 (m, 14H, OCH_2), 3.30 (d, *J* 12.8, 1H, ArCH_2Ar, eq), 3.23 (d, *J* 13.1, 2H, ArCH_2Ar, eq), 3.18 (d, *J* 12.8, 1H, ArCH_2Ar, eq), 1.07 (s, 36H, C$(CH_3)_3$). δ_C 168.87 (C=O), 153.23, 152.59, 145.79, 145.56, 133.53, 133.41, 132.07, 125.77, 125.44, 125.12 (Ar), 120.52, 117.96 (CF_3), 74.30 (OCH_2), 73.85 (OCH_2C(O)), 70.81, 70.58, 69.32, 68.98 (OCH_2), 33.88, 33.84 ($C(CH_3)_3$), 31.65 (ArCH_2Ar), 31.33, 31.26 (C$(CH_3)_3$), 31.06 (ArCH_2Ar). Found: C, 59.02; H, 6.64; N, 2.05%. $C_{60}H_{78}O_{14}S_2F_6N_2$ requires C, 58.62; H, 6.39; N, 2.28%.

Extraction procedure

An aqueous solution of the alkaline earth metal chlorides with hydroxides for pH adjustment (for **11** and **15**, 0.10 M HCl was utilized for pH adjustment) (2.0 mL, 2.0 mM in each alkaline earth metal cation species) and 2.0 mL of 1.0 mM ligand in chloroform in a metal-free, capped, polypropylene, 15 mL centrifuge tube was vortexed with a Glas-Col Multi-Pulse Vortexer for 10 min at room temperature. The tube was centrifuged for 10 min for phase separation with a Becton-Dickinson Clay Adams Brand® Centrifuge. A 1.5 mL portion of the organic phase was removed and added to 3.0 mL of 0.10 M HCl in a new, 15 mL, polypropylene centrifuge tube. The tube was vortexed for 10 min and centrifuged for 10 min. The alkaline earth metal cation concentrations in the aqueous phase from stripping were determined with a Dionex DX-120 Ion Chromatograph with a CS12A column. The pH of the aqueous phase from the initial extraction step was determined with a Fisher Accumet AR25 pH meter with a Corning 476157 combination pH electrode. Comparison of the UV absorptions for the chloroform solutions of a ligand before and after stripping verified that the ligands were sufficiently lipophilic to avoid loss to the contacting aqueous phases.

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