Effect of *para*-substituents on alkaline earth metal ion extraction by proton di-ionizable calix[4]arene-crown-6 ligands in cone, partial-cone and 1,3-alternate conformations

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Two carboxylic acid or *N*-(X)sulfonyl carboxamide groups were incorporated into calix[4]arene-crown-6 compounds to afford di-ionizable ligands for use in divalent metal ion separations. Acidities of the *N*-(X)sulfonyl carboxamide groups were tuned by variation of the electron-withdrawing properties of X. Cone, partial-cone and 1,3-alternate conformations were obtained by different synthetic strategies and their structures verified by NMR spectroscopy. Competitive solvent extractions of alkaline earth metal cations from aqueous solutions into chloroform were performed and the results compared with those reported previously for di-ionizable *p-tert*-butylcalix[4]arene-crown-6 analogues to probe the influence of the *para*-substituent on the calix[4]arene scaffold on extraction selectivity and efficiency.

Introduction

Spherical metal ion recognition is a central theme of supramolecular chemistry. Various types of ligands have been developed and evaluated in separations of such metal ion species. Among them, calixarenes, especially calixarene-crown ethers, are an important type of ligand for spherical metal ion complexation.[1] It has been shown that the efficiency and selectivity of metal ion extraction by calix[4]arene-crown ethers is controlled by the polyether ring size, as well as the conformation of the calixarene scaffold.[2]

It has also been reported that the efficiency and selectivity of alkali metal picrate extraction may be influenced by variation of *para*-substituents on the calix[4]arene scaffold. For example, partial-cone *p-tert*-butylcalix[4]arene-crown-5 conformer **1** (Fig. 1) exhibits higher K^+ association constants in chloroform than the cone or 1,3-alternate analogues. On the other hand, for calix[4]arene-crown-5 ligands with *p*-H substituents, the 1,3-alternate conformer **2** is a better K^+ complexing agent than the cone or partial-cone conformer.[2] These differing conformational preferences were attributed to a steric effect of the *p-tert*-butyl groups. For the 1,3-alternate conformer of *p-tert*-butylcalix[4]arene-crown-5, approach of the metal ion to the cyclic polyether binding site would be hindered by two flanking *p-tert*-butyl groups. This also accounts for the poorer alkali metal cation complexing ability of *p-tert*-butylcalix[4]arene-biscrown-5 (**3**) compared with that of calix[4]arene-biscrown-5 (**4**).[3] Therefore in *p-tert*-butylcalix[4]arene-crown-5 ligand **1**, one aryl group is rotated upward to produce the partial-cone conformation.

Previously, we reported the synthesis of di-ionizable *p-tert*-butylcalix[4]arene-crown-6 ligands conformationally locked in the cone (**5**), partial-cone (**6**) and 1,3-alternate (**7**) conformations (Fig. 2) as alkaline earth metal ion extractants.[4] Upon ionization the two acidic functions provided the requisite anions to form electroneutral extraction complexes. This avoided the need to transfer aqueous phase anions into the organic phase in the solvent extraction process and thereby markedly enhanced the efficiency of metal extraction from aqueous solutions of metal chlorides, nitrates or sulfates.

For competitive solvent extraction of alkaline earth metal ions from aqueous solutions into chloroform, the cone conformers **5** exhibited high extraction efficiency and selectivity for Ba^{2+} over Mg^{2+}, Ca^{2+} and Sr^{2+}. The 1,3-alternate conformers **7** were found to be weaker extractants, but retained high Ba^{2+} extraction selectivity. On the other hand, the partial-cone conformers **6** displayed very poor extraction capability.[4]

To probe the influence of the *p-tert*-butyl group on the calix[4]arene scaffolds upon the metal ion extraction behavior of ligands **5**–**7**, we have now prepared a series of di-ionizable

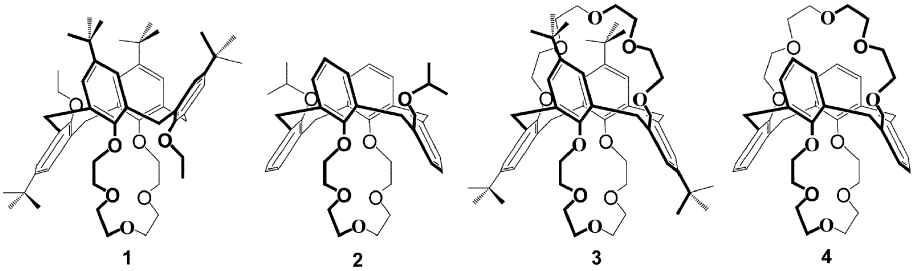
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Fig. 1 Calix[4]arene-crown-5 and -biscrown-5 ligands with different *para*-substituents.

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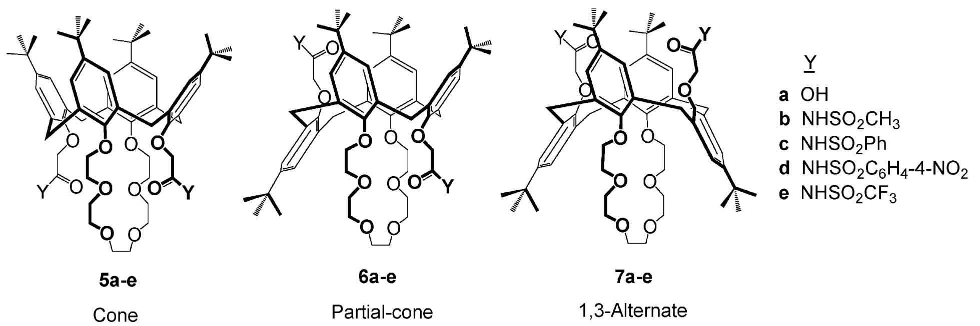


Fig. 2 Proton di-ionizable *p-tert*-butylcalix[4]arene-crown-6 compounds in the cone, partial-cone and 1,3-alternate conformations.

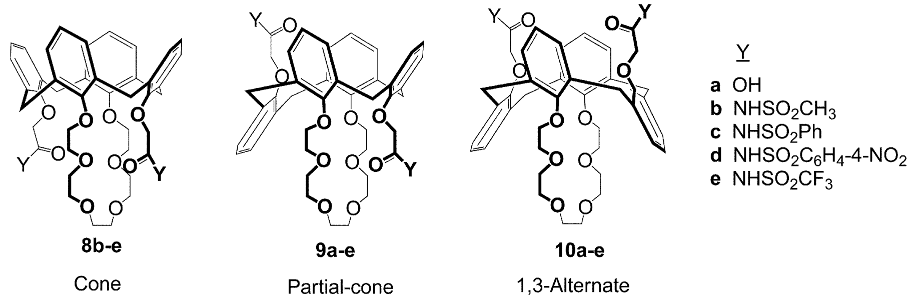


Fig. 3 New proton di-ionizable calix[4]arene-crown-6 ligands in the cone, partial-cone and 1,3-alternate conformations.

p-H-calix[4]arene-crown-6 analogues in cone (**8**), partial-cone (**9**) and 1,3-alternate (**10**) conformations (Fig. 3) and conducted competitive solvent extractions of alkaline earth metal cations. Results from these investigations are described herein.

Results and discussion

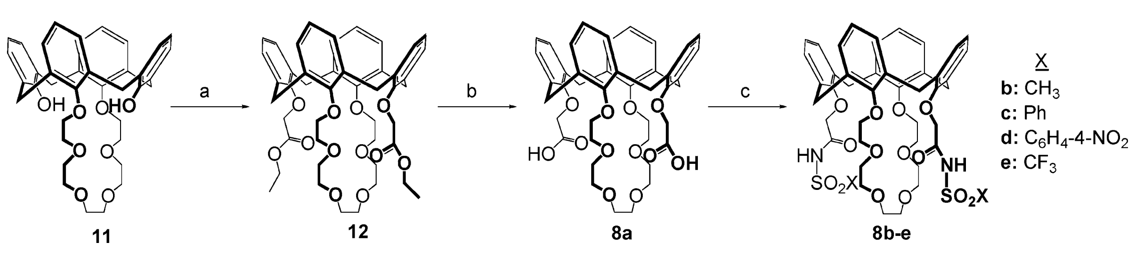
Synthesis of cone di-ionizable calix[4]arene-crown-6 ligands

The synthetic procedure for the cone conformers is shown in Scheme 1. Although it was reported that 1,3-dihydroxycalix[4]-arene-crown-6 (**11**) can be synthesized in 75% yield by direct ring formation from calix[4]arene and pentaethylene glycol ditosylate,[5] this result could not be repeated. Therefore, another reported route was utilized, which included a protection–deprotection sequence.[6] Alkylation of **11** with ethyl bromoacetate and NaH in THF at room temperature gave cone diester **12** in 71% yield. Hydrolysis of diester **12** with tetramethylammonium hydroxide (TMAOH) in aqueous THF gave cone di(carboxylic acid) **8a** in 97% yield. Refluxing di(carboxylic acid) **8a** with oxalyl chloride in benzene gave the corresponding di(acid chloride), which was reacted with the sodium salt forms of appropriate commercially available sulfonamides to provide ligands **8b–e** in 63–86% yields.

The cone conformation for compounds **8a–e** was verified by ^{1}H- and ^{13}C-NMR spectroscopy. As shown in Table 1, the methylene bridge (ArCH$_2$Ar) protons of the cone conformers **8a–e** exhibited a typical AX pattern, that is two widely separated doublets at δ *ca.* 4.5 and *ca.* 3.2 ppm for the *exo-* and *endo*-geminal protons, respectively. Both types of protons correlated with a single type of bridge carbon atom at 31–32 ppm, which is characteristic for bridge carbons in a *syn*-orientation. The two ionizable protons gave a single peak near 10.5 ppm and the protons of the two OCH$_2$C(O) groups appeared as one singlet at about 5.0 ppm.

Synthesis of partial-cone di-ionizable calix[4]arene-crown-6 ligands

Preparation of partial-cone conformers **9a–e** is outlined in Scheme 2. Reaction of **11** with excess ethyl bromoacetate and KH gave partial-cone diester **13** in 75% yield. Diester **13** was hydrolyzed with NMe$_4$OH and gave, after recrystallization, di(carboxylic acid) **9a** in 85% yield. The di(carboxylic acid) **9a** was refluxed with oxalyl chloride in benzene to give the corresponding di(acid chloride), which was reacted with the sodium salts of

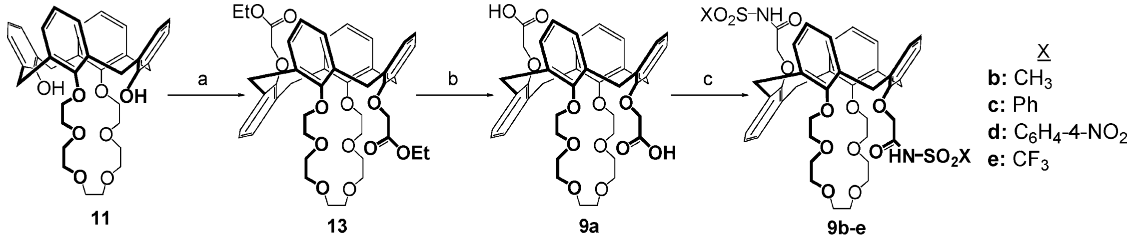


Scheme 1 Synthesis of cone conformers **8a–e**. *Reagents and conditions*: a) BrCH$_2$CO$_2$Et, NaH, THF–DMF, rt; b) 10% aq. NMe$_4$OH, THF, reflux; c) i) (COCl)$_2$, C$_6$H$_6$, reflux; ii) XSO$_2$NH$_2$, NaH, THF, rt.

Table 1 Selected proton and carbon chemical shifts (ppm) for cone, partial-cone, and 1,3-alternate di-ionizable ligands

Ligand	$\mathrm{N}H/\mathrm{O}H$	$\mathrm{OC}H_2\mathrm{C(O)}$	$\mathrm{ArC}H_2\mathrm{Ar}$	$\mathrm{Ar}C\mathrm{H_2Ar}$
8a	10.94	5.03	4.54, 3.26	31.22
8b	10.45	5.13	4.61, 3.26	31.60
8c	10.55	4.98	4.44, 3.11	31.52
8d	10.78	5.01	4.41, 3.13	31.51
8e	10.98	5.18	4.53, 3.23	31.52
9a	8.30	4.54, 4.24 (0.30)[a]	4.46, 3.17; 3.92, 3.66	37.16, 30.51
9b	9.90, 8.20	4.42, 4.34 (0.08)[a]	4.35, 3.18; 3.84, 3.53	36.58, 31.69
9c	10.11, 8.30	4.33, 4.06 (0.27)[a]	4.15, 3.01; 3.75, 3.45	36.50, 31.51
9d	10.31, 8.34	4.36, 4.11 (0.25)[a]	4.15, 3.02; 3.78, 3.46	36.53, 31.51
9e	10.53, 8.20	4.55, 4.08 (0.47)[a]	4.34, 3.18; 3.86, 3.55	36.75, 31.56
10a	—	4.12	3.94, 3.81	37.60
10b	8.46	3.67	3.85, 3.75	37.65
10c	8.82	3.44	3.78, 3.65	37.48
10d	9.19	3.14	—[b]	37.47
10e	8.94	3.39	3.88, —[b]	37.71

[a] Chemical shift differences, Δδ (ppm), for *syn*- and *anti*-$\mathrm{OCH_2C(O)}$ groups shown in parentheses. [b] Signals buried in those for the crown ether ring protons.



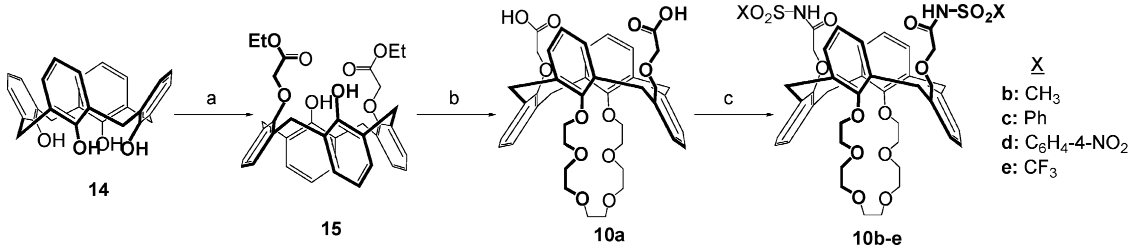
Scheme 2 Synthesis of partial-cone conformers **9a–e**. *Reagents and conditions*: a) $\mathrm{BrCH_2CO_2Et}$, KH, THF, rt; b) 10% aq. $\mathrm{NMe_4OH}$, THF, reflux; c) i) $\mathrm{(COCl)_2}$, $\mathrm{C_6H_6}$, reflux; ii) $\mathrm{XSO_2NH_2}$, NaH, THF, rt.

appropriate sulfonamides to provide the final products **9b–e** in 50–86% yields.

Because of decreased symmetry compared to the cone conformer analogues, partial-cone compounds **9a–e** exhibited more complex signals in their ^{1}H-NMR spectra (Table 1). The ionizable groups showed two singlets at δ *ca.* 10.0 and *ca.* 8.3 ppm. The two $\mathrm{OCH_2C(O)}$ groups appeared as two singlets and the four methylene bridges ($\mathrm{ArCH_2Ar}$) showed two sets of doublets. Unlike their *p*-*tert*-butylcalix[4]arene analogues,[4] the upfield shift of the *anti*-$\mathrm{OCH_2C(O)}$ group protons was quite small, usually less than 0.5 ppm. This indicates that the *anti*-$\mathrm{OCH_2C(O)}$ groups are quite flexible due to the small hydrogen atoms at the *para*-position of the calix[4]arene scaffold. When those hydrogen atoms are replaced with *tert*-butyl groups, the *anti*-$\mathrm{OCH_2C(O)}$ groups are "locked" deeply in the cavities formed by the three surrounding benzene rings. The methylene bridges ($\mathrm{ArCH_2Ar}$) showed two sets of doublets. The *syn*-orientated $\mathrm{ArCH_2Ar}$ protons appeared as two widely separated doublets (AX pattern, $\Delta\delta > 1.0$ ppm), which were correlated with the *syn*-orientated bridge carbons at *ca.* 31.5 ppm. The *anti*-orientated $\mathrm{ArCH_2Ar}$ protons were observed as two closely separated doublets (AB pattern, $\Delta\delta \approx 0.3$ ppm), which were correlated with the *anti*-orientated bridge carbons at *ca.* 36.5 ppm.

Synthesis of 1,3-alternate di-ionizable calix[4]arene-crown-6 ligands

The preparative route to 1,3-alternate conformers **10a–e** (Scheme 3) was adapted from the procedure reported for the synthesis of corresponding *p*-*tert*-butylcalix[4]arene analogues.[4] Alkylation of calix[4]arene (**14**) with ethyl bromoacetate and $\mathrm{K_2CO_3}$ in MeCN gave diester **15** in 81% yield.[7] The diester **15** was hydrolyzed to produce 1,3-alternate calix[4]arene-crown-6 di(carboxylic acid) **10a** following a reported procedure.[8] Di(carboxylic acid) **10a** was converted into **10b–e** in 48–55% yields using the same reaction



Scheme 3 Synthesis of 1,3-alternate conformers **10a–e**. *Reagents and conditions*: a) $\mathrm{BrCH_2CO_2Et}$, $\mathrm{K_2CO_3}$, MeCN, reflux; b) $\mathrm{TsO(CH_2CH_2O)_5Ts}$, $\mathrm{Cs_2CO_3}$, MeCN, reflux; c) i) $\mathrm{(COCl)_2}$, $\mathrm{C_6H_6}$, reflux; ii) $\mathrm{XSO_2NH_2}$, NaH, THF, rt.

conditions as those employed for the cone and partial-cone conformers.

With the same symmetry as that of the cone conformers, the 1,3-alternate conformers **10a–e** exhibited similar patterns in their ^{1}H-NMR spectra (Table 1). The two ionizable protons appeared as a singlet at $\sim$9.0 ppm. The two $OCH_2C(O)$ group protons were observed as a singlet at δ 3.14–4.12. It should be noted that these $OCH_2C(O)$ protons showed a higher upfield shift than the *anti*-$OCH_2C(O)$ protons of the partial-cone conformers, even though the upfield shielding is created by three aromatic rings for the partial-cone conformers instead of two for the 1,3-alternate conformers. This means that the calix[4]arene skeleton is so flexible in the partial-cone conformation that the *anti*-$OCH_2C(O)$ groups can remain outside the hydrophobic "well" created by the three surrounding aromatic rings. The methylene bridge ($ArCH_2Ar$) protons appeared as two closely spaced doublets (AB pattern), which correlated with *anti*-orientated bridge carbons ($\delta \approx 37.5$ ppm).

Competitive solvent extraction of alkaline earth metal cations by di-ionizable calix[4]arene-crown-6 ligands 8a–e, 9a–e and 10a–e

In our earlier paper,[4] competitive solvent extractions of alkaline earth metal cations (Mg^{2+}, Ca^{2+}, Sr^{2+} and Ba^{2+}) by *p-tert*-butylcalix[4]arene-crown-6 ligands **5–7** were performed to probe the effect of spatial relationship between the ionizable groups and the crown ether ring on the efficiency and selectivity of divalent metal ion complexation. This spatial relationship was found to have a very important influence on the extraction efficiency and selectivity. The cone conformation, in which the two ionized groups were located on both sides of the polyether ring-bound divalent metal ion, was the most energetically favorable for divalent metal ion extraction.

Since *para*-substituents on the calix[4]arene scaffold may also affect extraction efficiency and selectivity, competitive solvent extractions of alkaline earth metal cations (2.0 mM in each) by 1.0 mM solutions of ligands **8a–e**, **9a–e** and **10a–e** in chloroform were performed. Fig. 4 presents plots of the metal cation loading of the organic phase *vs.* the equilibrium pH of the aqueous phase for extractions with calix[4]arene-crown-6 di(carboxylic acid)s **8a**, **9a** and **10a** in the cone, partial-cone and 1,3-alternate conformations, respectively. The cone ligand **8a** exhibits pronounced extraction selectivity for Ba^{2+} over Sr^{2+} and Ca^{2+} (Fig. 4a). Significant amounts of Mg^{2+} were also extracted from alkaline aqueous solutions, particularly at higher pH. For comparison, previously reported results[4] for corresponding *p-tert*-butylcalix[4]arene-crown-6 di(carboxylic acid)s **5a**, **6a** and **7a** are shown in Fig. 5. Compared with **5a** (Fig. 5a), cone ligand **8a** shows poorer extraction efficiency and selectivity. This is attributed to greater flexibility of ligand **8a** in which the bulky *p-tert*-butyl groups have been removed from the calix[4]arene scaffold. The partial-cone ligand **9a**, like its *p-tert*-butylcalix[4]arene analogue **6a**, exhibited very poor extraction ability (compare Fig. 4b and 5b). Comparison of the results obtained for 1,3-alternate di(carboxylic acid)s **10a** (Fig. 4c) and **7c** (Fig. 5c) reveals a change from Mg^{2+} as the best extracted alkaline earth metal cation from the most basic aqueous solutions for the former to Ba^{2+} for the latter. This is puzzling, since Mg^{2+} is too small to fit well in the crown-6 cavity.

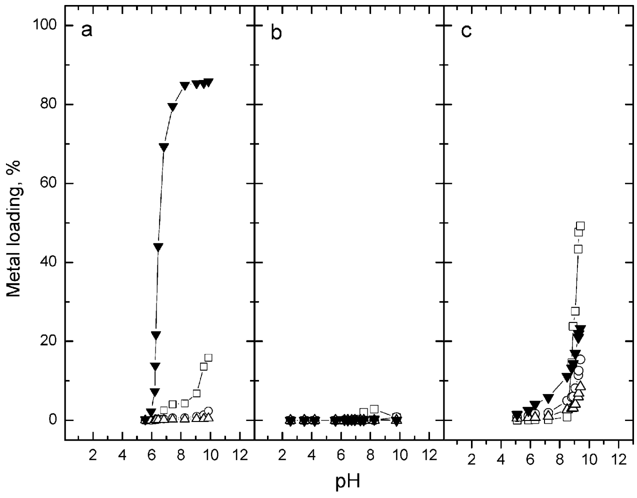


Fig. 4 Percent metals loading *vs.* equilibrium pH of the aqueous phase for competitive solvent extraction of alkaline earth metal ions into chloroform by calix[4]arene-crown-6 di(carboxylic acid)s. a) **8a**, b) **9a**, and c) **10a**. (□ = Mg^{2+}, ○ = Ca^{2+}, △ = Sr^{2+}, ▼ = Ba^{2+}.)

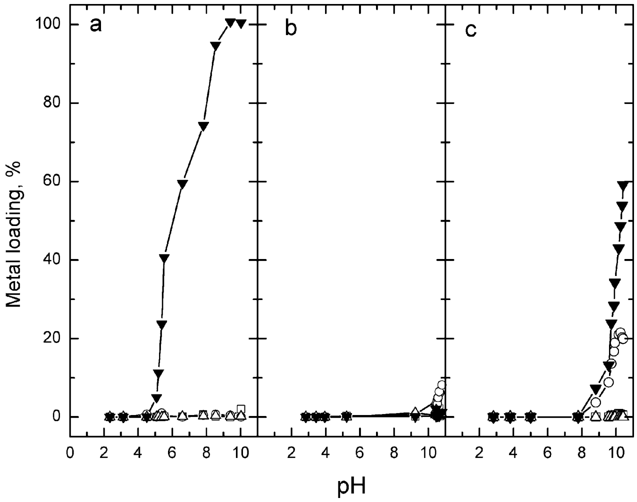


Fig. 5 Percent metals loading *vs.* equilibrium pH of the aqueous phase for competitive solvent extraction of alkaline earth metal ions into chloroform by *p-tert*-butylcalix[4]arene-crown-6 di(carboxylic acid)s. a) **5a**, b) **6a**, and c) **7a**. (□ = Mg^{2+}, ○ = Ca^{2+}, △ = Sr^{2+}, ▼ = Ba^{2+}.)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

By replacing the carboxylic acid groups with *N*-(X)sulfonyl carboxamide functions, the ligand acidity can be systematically varied by changing the X group.[4] A more electron-withdrawing X group will provide a ligand with higher acidity, which enables metal ion extraction from aqueous media of lower pH. Competitive solvent extractions of alkaline earth metal cations from aqueous solutions into chloroform were performed with calix[4]arene-crown-6 di[*N*-(X)sulfonyl carboxamide] ligands **8b–e**, **9b–e** and **10b–e** in the cone, partial-cone and 1,3-alternate conformations, respectively.

Fig. 6 shows the competitive solvent extraction results for cone ligands **8b–e** in which the X group was varied as CH_3, C_6H_5, C_6H_4-4-NO_2 and CF_3, respectively. Contrary to the analogous di(carboxylic acid) **8a** (Fig. 4a), ligands **8b–d** all exhibited very high Ba^{2+} extraction selectivity and efficiency with 100% metals loadings (for formation of 1 : 1 extraction complexes). The pH

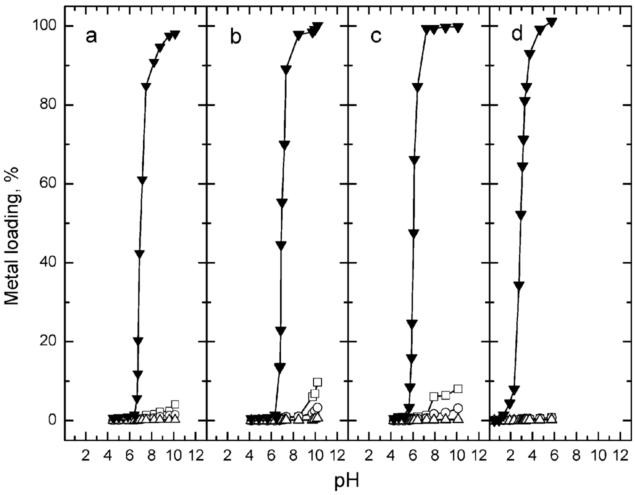


Fig. 6 Percent metals loading *vs.* equilibrium pH of the aqueous phase for competitive solvent extraction of alkaline earth metal ions into chloroform by cone calix[4]arene-crown-6 di[*N*-(X)sulfonyl carboxamides]. a) **8b**, b) **8c**, c) **8d** and d) **8e**. (□ = Mg^{2+}, ○ = Ca^{2+}, △ = Sr^{2+}, ▼ = Ba^{2+}.)

for half loading ($pH_{0.5}$), which is a qualitative measure of ligand acidity in the two-phase extraction system,[4] decreased for the cone *N*-(X)sulfonyl carboxamide calix[4]arene-crown-6 ligands as X was varied in the order: Me (7.0) > C_6H_5 (6.9) > C_6H_4-4-NO_2 (6.1) > CF_3(2.9). This is consistent with enhancement of the electron-withdrawing ability of X which increases the ligand acidity. Compared with the published extraction results for *p-tert*-butylcalix[4]arene analogues **5b–e** (Fig. 7),[4] the selectivity for Ba^{2+} over Mg^{2+}, Ca^{2+} and Sr^{2+} for extractants **8b–d** was slightly poorer, revealing greater selectivity when *p-tert*-butyl groups were present in the di-ionizable calix[4]arene-crown-6 ligands. For the most acidic extractants **8e** and **5e**, the extraction profiles presented in Fig. 6d and 7d, respectively, were virtually identical.

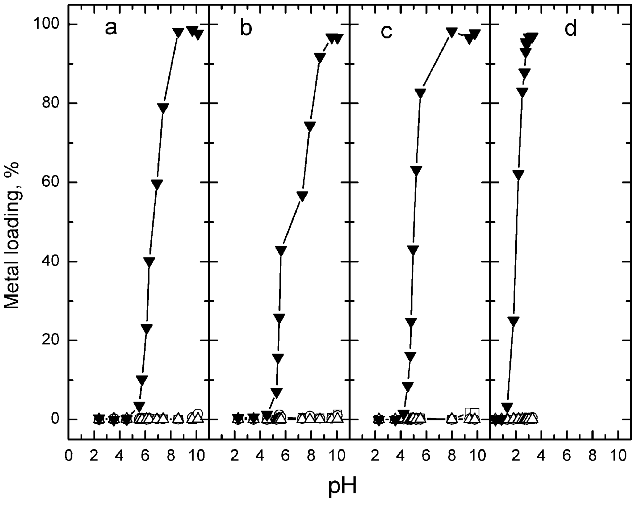


Fig. 7 Percent metals loading *vs.* equilibrium pH of the aqueous phase for competitive solvent extraction of alkaline earth metal ions into chloroform by cone *p-tert*-butylcalix[4]arene-crown-6 di[*N*-(X)sulfonyl carboxamides]. a) **5b**, b) **5c**, c) **5d** and d) **5e**. (□ = Mg^{2+}, ○ = Ca^{2+}, △ = Sr^{2+}, ▼ = Ba^{2+}.) (Data taken from ref. 4.)

In Fig. 8 are presented the results for competitive alkaline earth metal ion extraction by the partial-cone calix[4]arene-crown-6 di[*N*-(X)sulfonyl carboxamide] ligands **9b–e**. Like the analogous di(carboxylic acid) **9a**, these ligands show very poor extraction efficiency and selectivity.

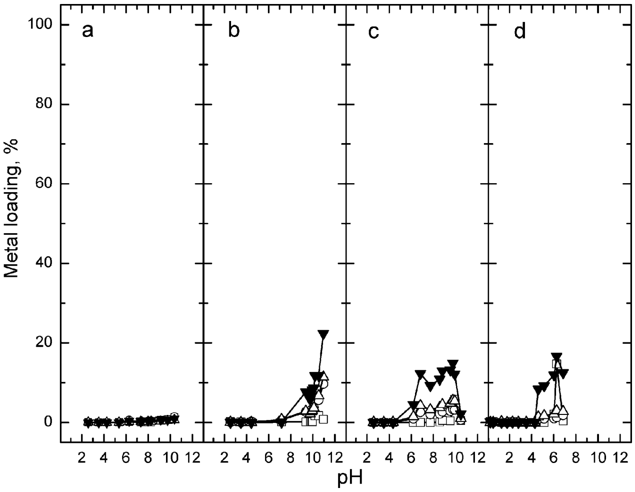


Fig. 8 Percent metals loading *vs.* equilibrium pH of the aqueous phase for competitive solvent extraction of alkaline earth metal ions into chloroform by partial-cone calix[4]arene-crown-6 di[*N*-(X)sulfonyl carboxamides]. a) **9b**, b) **9c**, c) **9d** and d) **9e**. (□ = Mg^{2+}, ○ = Ca^{2+}, △ = Sr^{2+}, ▼ = Ba^{2+}.)

Results for competitive solvent extraction of alkaline earth metal ions from aqueous solutions into chloroform by 1,3-alternate calix[4]arene-crown-6 di[*N*-(X)sulfonyl carboxamide] ligands **10b–e** are portrayed in Fig. 9. Ligand **10b** with X = Me gave the best extraction of Mg^{2+} (Fig. 9a), similar to di(carboxylic acid) **10a** (Fig. 4c). Extractants **10c** and **10d** show somewhat lower Ba^{2+} selectivity (Fig. 9b and 9c) than the corresponding *p-tert*-butylcalix[4]arene analogues **7c** and **7d** (Figs. 10b and 10c,

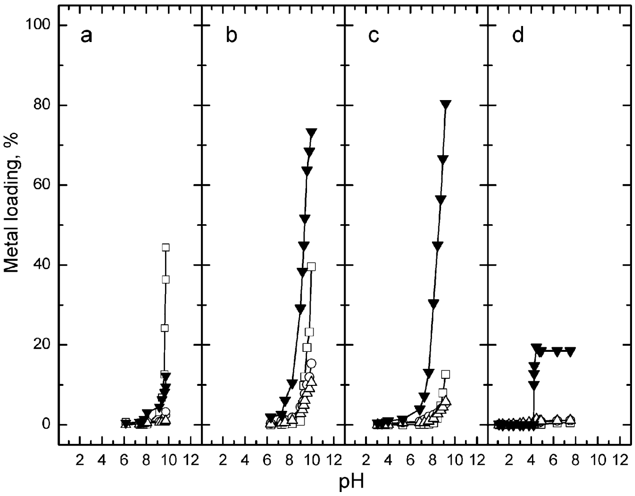


Fig. 9 Percent metals loading *vs.* equilibrium pH of the aqueous phase for competitive solvent extraction of alkaline earth metal ions into chloroform by 1,3-alternate calix[4]arene-crown-6 di[*N*-(X)sulfonyl carboxamides]. a) **10b**, b) **10c**, c) **10d** and d) **10e**. (□ = Mg^{2+}, ○ = Ca^{2+}, △ = Sr^{2+}, ▼ = Ba^{2+}.)

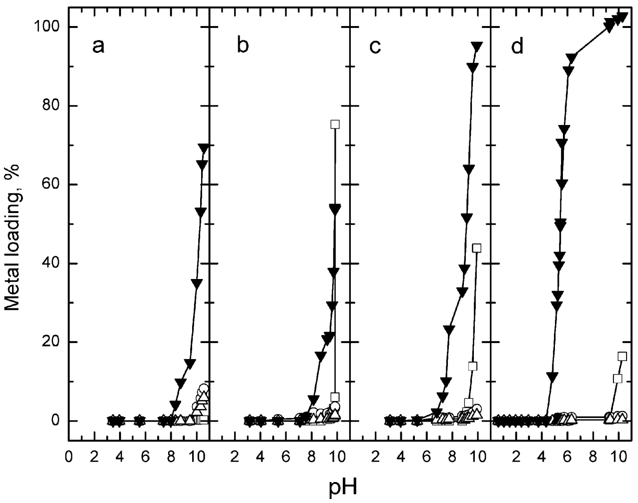


Fig. 10 Percent metals loading *vs.* equilibrium pH of the aqueous phase for competitive solvent extraction of alkaline earth metal ions into chloroform by 1,3-alternate *p-tert*-butylcalix[4]arene-crown-6 di[*N*-(X)sulfonyl carboxamides]. a) **7b**, b) **7c**, c) **7d** and d) **7e**. (□ = Mg^{2+}, ○ = Ca^{2+}, △ = Sr^{2+}, ▼ = Ba^{2+}). (Data taken from ref. 4.)

respectively). The extraction behavior for **10e** with X = CF_3 was unusual. Only 20% metal loading was observed when the organic phase was stripped with the customary 0.1 N HCl. Upon stripping with 1.0 N HCl, the metal loading increased to 55%. This indicated much stronger alkaline earth metal cation binding by **10e** than for the other extractants. The reason for this stronger metal ion binding by **10e** is not apparent at this time. For extractant **10e**, the extraction profile shown in Fig. 9d was observed. In comparison, the corresponding *p-tert*-butylcalix[4]arene analogue gave much higher Ba^{2+} extraction selectivity and efficiency (Fig. 10d).

In summary, like their *p-tert*-butylcalix[4]arene analogues, calix[4]arene-crown-6 di(carboxylic acid) and di[*N*-(X)sulfonyl carboxamide] ligands **8a–e**, **9a–e** and **10a–e** showed alkaline earth metal ion extraction efficiency and selectivity in the order of cone >1,3-alternate ≫ partial-cone. The ^1H NMR spectra of the di-ionizable *p-H*-calix[4]arene compounds indicated greater flexibility than in analogues with *p-tert*-butyl substituents. The generally lower alkaline earth metal ion extraction selectivity and efficiency observed for the *p-H*-compounds is attributed to this greater ligand flexibility.

Experimental

General

Melting points were determined with a Mel-Temp melting point apparatus. Infrared (IR) spectra were recorded with a Perkin-Elmer Model 1600 FT-IR spectrometer as deposits from CH_2Cl_2 solution on NaCl plates. The ^1H and ^{13}C NMR spectra were recorded with a Varian Unity INOVA 500 MHz FT-NMR (^1H 500 MHz and ^{13}C 126 MHz) spectrometer in $CDCl_3$ with TMS as internal standard. Elemental analysis was performed by Desert Analytics Laboratory of Tucson, Arizona.

Acetonitrile (MeCN) was dried over CaH_2 and distilled immediately before use. Tetrahydrofuran (THF) was dried over sodium with benzophenone as an indicator and distilled just before use. Cs_2CO_3 was activated by heating at 150 °C overnight under high vacuum and then stored in a desiccator. Pentaethylene glycol ditosylate[5] and calix[4]arene (**14**)[9] were prepared by literature procedures.

Cone 25,27-bis(ethoxycarbonylmethoxy)calix[4]arene-crown-6 (12). A mixture of **11** (2.81 g, 4.48 mmol), THF–DMF (9 : 1, 60 mL), and NaH (1.08 g, 44.8 mmol) was stirred under nitrogen at room temperature for 30 min. Ethyl bromoacetate (5.99 g, 35.9 mmol) in THF (20 mL) was added slowly. The mixture was stirred at room temperature for 12 h and quenched with 1 N HCl (10 mL). The THF was evaporated *in vacuo* and CH_2Cl_2 (100 mL) and 10% HCl (50 mL) were added to the residue. The organic layer was washed with water (2 × 50 mL), dried over $MgSO_4$ and evaporated *in vacuo.* The residue was purified by chromatography on silica gel with EtOAc–hexanes (2 : 1) as the eluent to give **12** (2.54 g, 71%) as a white solid (mp 201–202 °C). Found: C, 69.41; H, 6.93%. $C_{46}H_{54}O_{12}$ requires C, 69.16; H, 6.81%. ν_{max}(film)/cm^{-1} 1758, 1734 (C=O). δ_H 6.94–7.09 (4 H, m, ArH), 6.80–6.94 (2 H, m, ArH), 6.28–6.38 (2 H, m, ArH), 6.16–6.28 (4 H, m, ArH), 4.46–4.58 (8 H, m, OCH_2CO, $ArCH_2Ar$), 4.18–4.35 (8 H, m, $OCH_2(CH_3)$, OCH_2CH_2O), 3.98–4.08 (4 H, m, OCH_2CH_2O), 3.64–3.82 (12 H, m, OCH_2CH_2O), 3.20 (4 H, d, *J* 13.5, $ArCH_2Ar$), 1.29 (6 H, t, *J* 7.5, OCH_2CH_3). δ_C 169.33, 157.67, 154.46, 136.08, 133.32, 133.18, 128.88, 127.73, 122.76, 122.18, 72.97, 71.54, 70.77, 70.73, 70.56, 69.72, 61.34, 60.76, 60.72, 31.02, 14.18.

Cone 25,27-bis(carboxymethoxy)calix[4]arene-crown-6 (8a). A mixture of **12** (5.80 g, 7.26 mmol), THF (100 mL) and 10% Me_4NOH (100 mL) was refluxed for 24 h. The THF was evaporated *in vacuo* and the resulting aqueous mixture was cooled in an ice-bath and acidified with 6 N HCl. The mixture was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were washed with water (2 × 50 mL) and dried over $MgSO_4$. After evaporation of the CH_2Cl_2 *in vacuo*, **8a** (5.39 g, 97%) was obtained as a white solid (mp 306–309 °C). Found: C, 67.82; H, 6.38%. $C_{42}H_{46}O_{12}$ requires C, 67.91; H, 6.24%. ν_{max}(film)/cm^{-1} 2900–3200 (CO_2H), 1734 (C=O). δ_H 7.14 (4 H, d, *J* 7.5, ArH), 6.97 (2 H, t, *J* 7.5, ArH), 6.26–6.40 (6 H, m, ArH), 5.04 (4 H, s, OCH_2CO), 4.54 (4 H, d, *J* 13.4, $ArCH_2Ar$), 3.93–4.02 (4 H, m, OCH_2CH_2O), 3.86–3.93 (4 H, m, OCH_2CH_2O), 3.76–3.84 (8 H, m, OCH_2CH_2O), 3.70–3.76 (4 H, m, OCH_2CH_2O), 3.26 (4H, d, *J* 13.4, $ArCH_2Ar$). δ_C 171.13, 156.68, 153.58, 135.88, 132.80, 129.19, 128.16, 123.38, 123.27, 74.64, 71.80, 70.60, 70.39, 70.27, 69.43, 31.22.

General procedure for preparation of cone 25,27-bis[*N*-(X)sulfonyl carbamoylmethoxy]calix[4]arene-crown-6 compounds 8b–e. A solution of **8a** (2.00 g, 2.69 mmol) and oxalyl chloride (1.88 mL, 21.5 mmol) in benzene (40 mL) was refluxed for 5 h. The solution was evaporated *in vacuo* and dried under high vacuum for 30 min. The residue was dissolved in THF (20 mL) and added to a mixture of the appropriate sulfonamide (5.90 mmol) and NaH (0.66 g, 26.9 mmol) in THF (40 mL) under nitrogen at room temperature. The reaction mixture was stirred for 12 h (except for *p*-nitrobenzenesulfonamide, 3 h). The reaction was quenched with a small amount of water and the THF was evaporated *in vacuo.* The residue was dissolved in CH_2Cl_2 (100 mL) and washed with 10% aqueous K_2CO_3 solution (2 × 50 mL), 10% HCl (50 mL) and water (2 × 50 mL). The organic layer was dried over $MgSO_4$ (except for trifluoromethyl derivatives). Evaporation of CH_2Cl_2 *in vacuo* gave the crude product, which was purified by chromatography.

Cone 25,27-bis(*N*-methanesulfonyl carbamoylmethoxy)calix[4]arene-crown-6 (8b). Chromatography on silica gel with CH_2Cl_2–MeOH (97 : 3) as eluent, yield 72%, white solid, mp 255–258 °C. Found: C, 58.60; H, 5.87; N, 3.09%. $C_{44}H_{52}O_{14}N_2S_2$ requires C, 58.91; H, 5.84; N, 3.12%. ν_{max}(film)/cm^{-1} 3300–2800 (NH), 1734 (C=O). δ_H 10.45 (2 H, s, NH), 7.13 (4 H, d, *J* 7.5, ArH), 6.97 (2 H, t, *J* 6.5, ArH), 6.20–6.37 (6 H, m, ArH), 5.13 (4 H, s, OCH_2CO), 4.61 (4 H, d, *J* 13.5, $ArCH_2Ar$), 3.89–4.02 (8 H, m, OCH_2CH_2O), 3.76–3.89 (12 H, m, OCH_2CH_2O), 3.26 (4 H, d, *J* 13.5, $ArCH_2Ar$), 3.16 (6 H, s, CH_3SO_2). δ_C 170.07, 155.00, 154.52, 136.52, 132.71, 129.00, 127.84, 123.17, 122.84, 77.25, 77.00, 76.74, 73.40, 70.43, 70.33, 69.94, 69.84, 69.12, 41.42, 31.60.

Cone 25,27-bis(*N*-benzenesulfonyl carbamoylmethoxy)calix[4]arene-crown-6 (8c). Chromatography on silica gel with CH_2Cl_2–MeOH (97 : 3) as eluent, yield 86%, white solid, mp 132–136 °C. Found: C, 63.34; H, 5.35; N, 2.79%. $C_{54}H_{56}O_{14}N_2S_2$ requires C, 63.51; H, 5.53; N, 2.74%. ν_{max}(film)/cm^{-1} 3441 (NH), 1737, 1719 (C=O). δ_H 10.55 (2 H, s, NH), 7.97–8.09 (4 H, m, ArH), 7.54–7.64 (2 H, m, ArH), 7.40–7.53 (4 H, m, ArH), 6.98 (4 H, d, *J* 7.5, ArH), 6.85 (2 H, t, *J* 7.5, ArH), 6.22–6.30 (2 H, m, ArH), 6.19 (2 H, d, *J* 7.5, ArH), 4.98 (4 H, s, OCH_2CO), 4.44 (4 H, d, *J* 13.5, $ArCH_2Ar$), 3.87–3.96 (4 H, m, OCH_2CH_2O), 3.79–3.87 (4 H, m, OCH_2CH_2O), 3.70–3.79 (8 H, m, OCH_2CH_2O), 3.60–3.70 (4 H, m, OCH_2CH_2O), 3.11 (4 H, d, *J* 13.5, $ArCH_2Ar$). δ_C 168.26, 154.72, 154.58, 139.28, 136.17, 133.48, 132.69, 128.91, 128.68, 128.29, 127.74, 122.94, 122.72, 73.43, 70.26, 69.94, 69.77, 69.31, 31.52.

Cone 25,27-bis(*N*-*p*-nitrobenzenesulfonyl carbamoylmethoxy)calix[4]arene-crown-6 (8d). Chromatography on silica gel with CH_2Cl_2–MeOH (97 : 3) as eluent, yield 63%, white solid, mp 226–229 °C. Found: C, 58.29; H, 4.77; N, 4.76%. $C_{54}H_{54}O_{18}N_4S_2$ requires C, 58.37; H, 4.90; N, 5.04%. ν_{max}(film)/cm^{-1} 3417 (NH), 1718 (C=O). δ_H 10.78 (2 H, s, NH), 8.12–8.22 (4 H, m, ArH), 8.23–8.32 (4 H, m, ArH), 6.95 (4 H, d, *J* 7.5, ArH), 6.82 (2 H, t, *J* 7.5, ArH), 6.21–6.30 (2 H, m, ArH), 6.17 (4 H, d, *J* 7.5, ArH), 5.01 (4 H, s, OCH_2CO), 4.41 (4 H, d, *J* 13.4, $ArCH_2Ar$), 3.87–3.99 (8 H, m, OCH_2CH_2O), 3.74–3.87 (12 H, m, OCH_2CH_2O), 3.13 (4 H, d, *J* 13.5, $ArCH_2Ar$). δ_C 168.47, 154.59, 154.49, 150.52, 144.36, 136.16, 132.38, 129.74, 128.96, 127.81, 123.87, 123.07, 122.93, 73.22, 70.59, 70.27, 70.01, 69.73, 69.31, 31.51.

Cone 25,27-bis(*N*-trifluoromethanesulfonyl carbamoylmethoxy)calix[4]-arene-crown-6 (8e). Chromatography on silica gel with CH_2Cl_2–MeOH (97 : 3) as eluent, yield 79%, white solid, mp 216–218 °C. Found: C, 51.79; H, 4.49; N, 2.34%. $C_{44}H_{46}O_{14}N_2S_2F_6\cdot0.3\ CH_2Cl_2$ requires C, 51.64; H, 4.56; N, 2.72%. ν_{max}(film)/cm^{-1} 3416 (NH); 1772 (C=O). δ_H 10.98 (2 H, s, NH), 7.13 (4 H, d, *J* 7.4, ArH), 6.98 (2 H, t, *J* 7.5, ArH), 6.22–6.36 (6 H, m, ArH), 5.18 (4 H, s, OCH_2CO), 4.53 (4 H, d, *J* 13.5, $ArCH_2Ar$), 3.95–4.02 (4 H, m, OCH_2CH_2O), 3.89–3.95 (4 H, m, OCH_2CH_2O), 3.85 (8 H, s, OCH_2CH_2O), 3.79 (4 H, s, OCH_2CH_2O), 3.23 (4 H, d, *J* 13.5, $ArCH_2Ar$). δ_C 167.54, 154.60, 154.24, 136.24, 132.57, 129.13, 127.87, 123.50, 123.01, 120.43, 117.86, 72.74, 70.29, 70.14, 69.92, 69.79, 68.66, 31.52.

Partial-cone 25,27-bis(ethoxycarbonylmethoxy)calix[4]arene-crown-6 (13). A mixture of **11** (10.48 g, 16.7 mmol), KH (4.78 g, 35% dispersion in mineral oil, 41.75 mmol) and THF (400 mL) was stirred under nitrogen at room temperature for 1 h. Ethyl bromoacetate (7.41 mL, 66.8 mmol) was added dropwise to the solution. The reaction mixture was stirred at room temperature for another 3 h and quenched with a small amount of water. The THF was evaporated *in vacuo*, and to the residue was added CH_2Cl_2 (200 mL) and 10% HCl (100 mL). The organic layer was separated and washed with water (2 × 100 mL), dried over $MgSO_4$, and evaporated *in vacuo.* The crude product was purified by recrystallization from CH_2Cl_2–MeOH to give **13** (9.96 g, 75%) as a white solid with mp 163–166 °C. Found: C, 68.78; H, 6.81%. $C_{46}H_{54}O_{12}$ requires C, 69.16; H, 6.81%. ν_{max}(film)/cm^{-1} 1755, 1733 (C=O). δ_H 7.52 (2 H, d, *J* 7.6, ArH), 7.11 (1 H, t, *J* 7.6, ArH), 6.97–7.06 (4 H, m, ArH), 6.85 (1 H, t, *J* 7.5, ArH), 6.53 (2 H, t, *J* 7.5, ArH), 6.42–6.49 (2 H, m, ArH), 4.47 (2 H, s, $OCH_2C(O)$), 4.42 (2 H, d, *J* 13.4, $ArCH_2Ar$), 4.10–4.25 (4 H, m, OCH_2CH_2O, $OCH_2C(O)$), 3.92–3.99 (4 H, m, OCH_2CH_2, $OCH_2C(O)$), 3.67–3.92 (22 H, m, OCH_2CH_2O, $ArCH_2Ar$), 3.15 (2 H, d, *J* 12.5, $ArCH_2Ar$), 1.28 (3 H, t, *J* 7.2, CH_3), 1.08 (3 H, t, *J* 7.2, CH_3). δ_C 170.20, 169.66, 155.99, 155.93, 154.22, 136.44, 133.49, 132.93, 132.72, 131.65, 129.10, 128.82, 128.76, 122.62, 122.60, 122.43, 72.85, 71.30, 70.97, 70.87, 70.47, 69.83, 68.29, 60.59, 59.94, 35.89, 31.54, 14.14, 13.96.

Partial-cone 25,27-bis(carboxymethoxy)calix[4]arene-crown-6 (9a). A mixture of the diester **13** (9.96 g, 12.5 mmol), NMe_4OH (250 mL, 25%), H_2O (150 mL) and THF (400 mL) was heated at reflux for 24 h. The THF was evaporated *in vacuo* and the resulting aqueous solution was cooled in an ice-bath and acidified with 6 N HCl. The solution was extracted with CH_2Cl_2 (2 × 100 mL). The organic phase was washed with water (2 × 100 mL) and dried over $MgSO_4$. After evaporation of CH_2Cl_2 *in vacuo*, the crude product was purified by recrystallization from CH_2Cl_2–MeOH to give **9a** (7.86 g, 85%) as a white solid with mp 251–254 °C. Found: C, 67.15; H, 6.41%. $C_{42}H_{46}O_{12}\cdot0.1\ CH_2Cl_2$ requires C, 67.30; H, 6.20%. ν_{max}(film)/cm^{-1} 3405 (CO_2H), 1754 (C=O). δ_H 8.30 (2 H, br s, CO_2H), 7.37 (2 H, d, *J* 7.6, ArH), 7.24–7.32 (1 H, m, ArH), 7.15 (2 H, d, *J* 7.4, ArH), 6.99 (1 H, t, *J* 7.5, ArH), 6.79–6.87 (2 H, m, ArH), 6.72–6.76 (2 H, m, ArH), 6.69 (2 H, t, *J* 7.4, ArH), 4.54 (2 H, s, $OCH_2C(O)$), 4.46 (2 H, d, *J* 13.2, $ArCH_2Ar$), 4.24 (2 H, s, $OCH_2C(O)$), 4.08–4.19 (2 H, m, OCH_2CH_2O), 3.92 (2 H, d, *J* 14.9, $ArCH_2Ar$), 3.50–3.88 (20 H, m, OCH_2CH_2O, $ArCH_2Ar$), 3.16 (2 H, d, *J* 13.2, $ArCH_2Ar$). δ_C 170.11, 168.18, 154.63, 154.38, 152.18, 135.96, 134.60, 133.40, 132.81, 129.93, 129.33, 128.25, 126.18, 124.21, 123.58, 74.12, 70.77, 70.67, 70.61, 70.52, 69.82, 66.33, 37.16, 30.51.

General procedure for synthesis of partial-cone 25,27-bis[*N*-(X)-sulfonyl carbamoylmethoxy]calix[4]arene-crown-6 compounds 9b–e

The procedure was essentially the same as that employed for the cone conformers. The crude product was purified by either recrystallization or chromatography.

Partial-cone 25,27-bis(*N*-methanesulfonyl carbamoylmethoxy)calix[4]arene-crown-6 (9b). Chromatography on silica gel with CH_2Cl_2–MeOH (20 : 1) as eluent, yield 52%, white solid, mp 292–294 °C (d). Found: C, 59.01; H, 5.89; N, 3.05%. $C_{44}H_{52}O_{14}N_2S_2$

requires C, 58.91; H, 5.84; N, 3.12%. ν_{max}(film)/cm^{-1} 3331 (NH), 1727 (C=O). δ_H 9.90 (1 H, s, NH), 8.20 (1 H, s, NH), 7.45 (2 H, d, *J* 7.6, ArH), 7.14 (1 H, t, *J* 7.6, ArH), 7.07 (2 H, d, *J* 7.4, ArH), 6.90 (1 H, t, *J* 7.5, ArH), 6.76–6.84 (2 H, m, ArH), 6.68 (2 H, t, *J* 7.5, ArH), 6.54–6.62 (2 H, m, ArH), 4.42 (2 H, s, OCH$_2$C(O)), 4.30–4.39 (4 H, m, ArCH$_2$Ar, OCH$_2$C(O)), 3.68–4.08 (22 H, m, OCH$_2$CH$_2$O, ArCH$_2$Ar), 3.54 (2 H, d, *J* 14.0, ArCH$_2$Ar), 3.41 (3 H, s, CH$_3$), 3.18 (2 H, d, *J* 13.5, ArCH$_2$Ar), 3.00 (3 H, s, CH$_3$). δ_C 169.38, 167.66, 155.87, 153.79, 152.95, 136.23, 134.31, 133.15, 132.04, 131.81, 129.92, 129.06, 128.04, 123.57, 123.15, 122.56, 72.76, 70.67, 70.41, 70.16, 70.00, 68.92, 68.49, 41.86, 41.13, 36.58, 31.69.

Partial-cone 25,27-bis(*N*-benzenesulfonyl carbamoylmethoxy)-calix[4]arene-crown-6 (9c). Recrystallization from CH$_2$Cl$_2$–MeOH, yield 85%, white solid, mp 292–295 °C (d). Found: C, 63.42; H, 5.66; N, 2.61%. C$_{54}$H$_{56}$O$_{14}$N$_2$S$_2$ requires C, 63.51; H, 5.53; N, 2.74%. ν_{max}(film)/cm^{-1} 3323 (NH), 1731 (C=O). δ_H 10.11 (1 H, s, NH), 8.30 (1 H, s, NH), 8.13–8.22 (2 H, m, ArH), 7.90–8.02 (2 H, m, ArH), 7.65–7.74 (1 H, m, ArH), 7.52–7.64 (3 H, m, ArH), 7.34–7.46 (4 H, m, ArH), 7.08 (1 H, t, *J* 7.6, ArH), 6.90 (2 H, d, *J* 7.4, ArH), 6.80 (1 H, t, *J* 7.5, ArH), 6.67–6.73 (2 H, m, ArH), 6.64 (2 H, t, *J* 7.5, ArH), 6.49–6.57 (2 H, m, ArH), 4.33 (2 H, s, OCH$_2$C(O)), 4.15 (2 H, d, *J* 13.4, ArCH$_2$Ar), 4.06 (2 H, s, OCH$_2$C(O)), 3.86–4.02 (4 H, m, OCH$_2$CH$_2$O), 3.62–3.86 (18 H, m, OCH$_2$CH$_2$O, ArCH$_2$Ar), 3.45 (2 H, d, *J* 13.8, ArCH$_2$Ar), 3.00 (2 H, d, *J* 13.5, ArCH$_2$Ar). δ_C 167.48, 166.29, 155.85, 153.48, 153.10, 139.46, 138.66, 135.99, 134.34, 134.22, 133.14, 133.10, 131.91, 131.85, 129.78, 129.01, 128.88, 128.44, 128.42, 128.34, 128.01, 123.46, 122.97, 122.60, 72.73, 70.60, 70.52, 70.35, 70.05, 69.17, 68.83, 36.50, 31.51.

Partial-cone 25,27-bis(*N*-*p*-nitrobenzenesulfonyl carbamoyl-methoxy)calix[4]-arene-crown-6 (9d). Recrystallization from CH$_2$Cl$_2$–MeOH, yield 85%, green-yellow solid, mp 292–294 °C (d). Found: C, 58.30; H, 4.70; N, 4.89%. C$_{54}$H$_{54}$O$_{18}$N$_4$S$_2$ requires C, 58.37; H, 4.90; N, 5.04%. ν_{max}(film)/cm^{-1} 3318 (NH), 1733 (C=O). δ_H 10.31 (1 H, s, NH), 8.41–8.46 (2 H, m, ArH), 8.35–8.39 (2 H, m, ArH), 8.34 (1 H, s, NH), 8.17–8.23 (2 H, m, ArH), 8.06–8.13 (2 H, m, ArH), 7.38 (2 H, d, *J* 7.6, ArH), 7.08 (1 H, t, *J* 7.6, ArH), 6.86 (2 H, d, *J* 7.4, ArH), 6.76 (1 H, t, *J* 7.4, ArH), 6.64–6.70 (2 H, m, ArH), 6.62 (2 H, t, *J* 7.4, ArH), 6.49–6.55 (2 H, m, ArH), 4.36 (2 H, s, OCH$_2$C(O)), 4.14 (2 H, d, *J* 13.3, ArCH$_2$Ar), 4.11 (2 H, s, OCH$_2$C(O)), 3.91–4.04 (4 H, m, OCH$_2$CH$_2$O), 3.80–3.90 (4 H, m, OCH$_2$CH$_2$O), 3.66–3.80 (12 H, m, OCH$_2$CH$_2$O, ArCH$_2$Ar), 3.46 (2 H, d, *J* 13.9, ArCH$_2$Ar), 3.02 (2 H, d, *J* 13.5, ArCH$_2$Ar). δ_C 167.55, 166.40, 155.87, 153.33, 153.01, 150.99, 150.28, 144.65, 143.93, 136.02, 134.30, 133.14, 131.89, 131.82, 130.02, 129.83, 129.81, 128.83, 127.87, 124.23, 123.52, 123.49, 123.03, 122.50, 72.72, 70.63, 70.47, 70.34, 69.93, 68.97, 68.81, 36.53, 31.51.

Partial-cone 25,27-bis(*N*-trifluoromethanesulfonyl carbamoyl-methoxy)calix[4]-arene-crown-6 (9e). Recrystallization from CH$_2$Cl$_2$–MeOH, yield 86%, white solid, mp > 224 °C (d). Found: C, 51.48; H, 4.56; N, 2.81%. C$_{44}$H$_{46}$O$_{14}$N$_2$S$_2$F$_6$·0.3 CH$_2$Cl$_2$ requires C, 51.64; H, 4.56; N, 2.72%. ν_{max}(film)/cm^{-1} 3289 (NH), 1762 (C=O). δ_H 10.53 (1 H, s, NH), 8.20 (1 H, s, NH), 7.45 (2 H, d, *J* 7.7, ArH), 7.12 (1 H, t, *J* 7.6, ArH), 7.07 (2 H, d, *J* 7.4, ArH), 6.92 (1 H, t, *J* 7.4, ArH), 6.74–6.81 (2 H, m, ArH), 6.65 (2 H, t, *J* 7.4, ArH), 6.57–6.63 (2 H, m, ArH), 4.56 (2 H, s, OCH$_2$C(O)), 4.33 (2 H, d, *J* 13.4, ArCH$_2$Ar), 4.00–4.18 (4 H, m, OCH$_2$C(O), OCH$_2$CH$_2$O), 3.68–3.96 (20 H, m, OCH$_2$CH$_2$O, ArCH$_2$Ar), 3.55 (2 H, d, *J* 14.2, ArCH$_2$Ar), 3.18 (2 H, d, *J* 13.5, ArCH$_2$Ar). δ_C 167.47, 165.31, 155.94, 153.30, 152.79, 135.91, 134.65, 133.21, 132.10, 132.07, 130.04, 129.17, 127.71, 123.68, 123.52, 122.85, 72.60, 70.56, 70.15, 70.01, 69.89, 69.02, 68.33, 36.75, 31.56.

General procedure for preparation of 1,3-alternate 25,27-bis-[*N*-(X)-sulfonyl carbamoylmethoxy]calix[4]arene-crown-6 compounds 10b–e

The procedure was essentially the same as that employed for the cone conformers. The crude product was purified by chromatography.

1,3-Alternate 25,27-bis(*N*-methanesulfonyl carbamoylmethoxy)-calix[4]arene-crown-6 (10b). Chromatography on silica gel with CH$_2$Cl$_2$–MeOH (97 : 3) as eluent, yield 48%, white solid, mp 218–219 °C. Found: C, 59.11; H, 5.78; N, 3.10%. C$_{44}$H$_{52}$O$_{14}$N$_2$S$_2$ requires C, 58.91; H, 5.84; N, 3.12%. ν_{max}(film)/cm^{-1} 3339 (NH), 1716 (C=O). δ_H 8.46 (2 H, s, NH), 7.19 (4 H, d, *J* 7.5, ArH), 7.13 (4 H, d, *J* 7.5, ArH), 6.91–6.99 (4 H, m, ArH), 3.85 (4 H, d, *J* 15.7, ArCH$_2$Ar), 3.64–3.79 (20 H, m, OCH$_2$CO, ArCH$_2$Ar, OCH$_2$CH$_2$O), 3.49–3.56 (8 H, m, OCH$_2$CH$_2$O), 3.37 (6 H, s, CH$_3$SO$_2$). δ_C 168.54, 156.89, 154.42, 134.41, 133.34, 131.17, 129.98, 124.19, 123.95, 71.31, 71.19, 70.63, 70.23, 69.81, 41.46, 37.65.

1,3-Alternate 25,27-bis(*N*-benzenesulfonyl carbamoylmethoxy)-calix[4]arene-crown-6 (10c). Chromatography on silica gel with CH$_2$Cl$_2$–MeOH (97 : 3) as eluent, yield 55%, white solid, mp 236–242 °C. Found: C, 63.43; H, 5.25; N, 2.57%. C$_{54}$H$_{56}$O$_{14}$N$_2$S$_2$ requires C, 63.51; H, 5.53; N, 2.74%. ν_{max}(film)/cm^{-1} 3334 (NH), 1718 (C=O). δ_H 8.82 (2 H, s, NH), 8.30 (4 H, d, *J* 7.6, ArH), 7.56–7.78 (6 H, m, ArH), 7.16 (4 H, d, *J* 7.6, ArH), 6.82–7.02 (6 H, m, ArH), 6.70 (2 H, t, *J* 7.4, ArH), 3.78 (4 H, d, *J* 15.4, ArCH$_2$Ar), 3.60–3.75 (16 H, m, ArCH$_2$Ar, OCH$_2$CH$_2$O), 3.50–3.60 (8 H, m, OCH$_2$CH$_2$O), 3.44 (4 H, s, OCH$_2$CO). δ_C 167.33, 156.93, 154.20, 138.68, 134.34, 134.10, 133.24, 131.27, 129.97, 129.00, 128.74, 124.15, 123.76, 71.27, 71.23, 71.10, 70.83, 70.46, 69.95, 37.48.

1,3-Alternate 25,27-bis(*N*-*p*-nitrobenzenesulfonyl carbamoyl-methoxy)-calix[4]arene-crown-6 (10d). Chromatography on silica gel with CH$_2$Cl$_2$–MeOH (97 : 3) as eluent, yield 53%, white solid, mp 160–165 °C. Found: C, 58.68; H, 4.74; N, 5.10%. C$_{54}$H$_{54}$O$_{18}$N$_4$S$_2$ requires C, 58.37; H, 4.90; N, 5.04%. ν_{max}(film)/cm^{-1} 3332 (NH), 1745 (C=O). δ_H 9.19 (2 H, s, NH), 8.48–8.56 (4 H, m, ArH), 8.40–8.48 (4 H, m, ArH), 7.20 (4 H, d, *J* 7.6, ArH), 6.88–7.00 (6 H, m, ArH), 6.65 (2 H, t, *J* 7.4, ArH), 3.52–3.88 (28 H, m, ArCH$_2$Ar, OCH$_2$CH$_2$O), 3.14 (4 H, bs, OCH$_2$CO). δ_C 167.96, 157.42, 153.65, 150.93, 144.15, 134.80, 133.18, 131.81, 130.10, 130.05, 124.22, 124.14, 124.00, 71.34, 71.25, 71.20, 71.13, 70.29, 70.01, 37.47.

1,3-Alternate 25,27-bis(*N*-trifluoromethanesulfonyl carbamoyl-methoxy)-calix[4]-arene-crown-6 (10e). Chromatography on silica gel with CH$_2$Cl$_2$–EtOAc (97 : 3) as eluent, yield 51%, white solid, mp 199–202 °C. Found: C, 52.72; H, 4.82; N, 2.95%. C$_{44}$H$_{46}$O$_{14}$N$_2$S$_2$F$_6$ requires C, 52.59; H, 4.61; N, 2.79%. ν_{max}(film)/cm^{-1} 3334 (NH), 1718 (C=O). δ_H 8.94 (2 H, s, NH), 7.22 (4 H, d, *J* 7.6, ArH), 7.09 (4 H, d, *J* 7.6, ArH), 6.97 (2 H, t, *J*

7.5, ArH), 6.93 (2 H, t, *J* 7.5, ArH), 3.88 (4 H, d, *J* 15.6, $ArCH_2Ar$), 3.66–3.82 (16 H, m, OCH_2CH_2O, $ArCH_2Ar$), 3.52–3.62 (8 H, m, OCH_2CH_2O), 3.39 (4 H, bs, OCH_2CO). δ_C 166.87, 157.27, 153.84, 134.70, 133.23, 131.69, 130.07, 124.67, 124.25, 71.29, 71.25, 71.21, 71.03, 70.37, 69.92, 37.71.

Procedure for competitive extraction of alkaline earth metal cations

An aqueous solution of the alkaline earth metal chlorides with hydroxides for pH adjustment (for **8e**, **9e**, and **10e**, 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 HCl solution in a new, 15 mL, polypropylene centrifuge tube (the concentration of the HCl solution is 0.10 M unless stated otherwise). 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.

The metal loading (ML) was calculated by use of the following equation

$$\mathrm{ML}(\%) = 100n_{\mathrm{M,org}}/n^{\mathrm{i}}_{\mathrm{Ligand,org}}$$

where $n_{\mathrm{M,org}}$ was the final metal amount (in moles) that was stripped from the organic phase and $n^{\mathrm{i}}_{\mathrm{Ligand,org}}$ was the initial ligand amount (in moles) in the organic phase.

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